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High Health Care Utilization Preceding Diagnosis of Systemic Lupus Erythematosus in Youth

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Abstract

Objective—Childhood-onset systemic lupus erythematosus (SLE) is associated with high risk for organ damage, which may be mitigated by early diagnosis and treatment. We characterized health care utilization for youth in the year preceding SLE diagnosis compared to controls.

Methods—Using ClinformaticsTM DataMart (OptumInsight, Eden Prairie, MN) de-identified administrative data from 2000 to 2013, we identified 682 youth ages 10–24 years with new-onset SLE (3 International Classification of Diseases, Ninth Revision (ICD-9) codes for SLE 710.0, each >30 days apart), and 1,364 age and sex-matched healthy controls. We compared the incidence of ambulatory, emergency, and inpatient visits 12 months before SLE diagnosis, and frequency of primary diagnoses. We examined subject characteristics associated with utilization preceding SLE diagnosis.

Results—Youth with SLE had significantly more visits in the year preceding diagnosis than controls across ambulatory (incidence rate ratio (IRR) 2.48, $p < 0.001$), emergency (IRR 3.42, $p < 0.001$) and inpatient settings (IRR 3.02, $p < 0.001$). The most frequent acute care diagnoses and median days to SLE diagnosis were: venous thromboembolism (313, interquartile range (IQR) 18–356), thrombocytopenia (278, IQR 39–354), chest pain (73, IQR 29.5–168), fever (52, IQR 17–166), and acute kidney failure (14, IQR 5–168). Having a psychiatric diagnosis prior to SLE diagnosis was strongly associated with increased utilization across all settings.

Conclusion—Youth with SLE have high health care utilization throughout the year preceding SLE diagnosis. Examining variable diagnostic trajectories of youth presenting for acute care preceding SLE diagnosis, and increased attention to psychiatric morbidity may help improve care for youth with new-onset SLE.

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Systemic lupus erythematosus (SLE) is a chronic autoimmune condition with a heterogeneous presentation that is often difficult to diagnose. While advances in therapeutic options have led to improved survival, diagnostic delay remains one of the most important risk factors for poor outcomes.¹ Children and adolescents account for 20% of all patients with SLE² and have worse outcomes than their adult counterparts, including higher rates of renal and neuropsychiatric complications^{3–6} and greater mortality.⁷ Therefore, early diagnosis and treatment in this age group are especially critical for preventing irreversible organ damage.⁸

Autoantibodies and clinical symptoms can precede SLE diagnosis by years,^{9,10} but there may be too few clinical features to make a definitive diagnosis early in the disease course. Exploring patterns of health care utilization prior to diagnosis of SLE is a first step in characterizing the trajectory from symptom onset to diagnosis, and may provide insight into strategies to expedite SLE diagnosis and treatment. It has been shown that adults with SLE have more primary care visits for clinical features attributable to SLE than controls in the years leading up to diagnosis.¹¹ Another study of adults with SLE found increased pre-diagnosis ambulatory care utilization associated with respiratory, gastrointestinal, musculoskeletal and cutaneous complaints.¹² To date, there are no studies of health care utilization preceding SLE diagnosis in children and adolescents, or older, transition-age youth.

The present population-based cohort study compares youth with SLE and healthy controls. Our objectives were to: 1) examine health care utilization across ambulatory and acute care settings in the year preceding diagnosis; 2) determine the most common reasons for pre-diagnosis health care visits; and 3) identify patient characteristics associated with increased or decreased pre-diagnosis utilization. We hypothesized that youth with SLE have increased ambulatory and acute care utilization in the year preceding SLE diagnosis compared with their peers, and that these early presentations to care would be associated with diagnosis codes suggestive of initial manifestations of SLE.

Patients and Methods

Study Design

We conducted a retrospective, population-based cohort study comparing youth with SLE to age- and sex-matched healthy controls. Exemption for the study was obtained from the Institutional Review Board at The Children's Hospital of Philadelphia.

Data sources and sample

Administrative health care claims were extracted from the ClinformaticsTM DataMart (OptumInsight, Eden Prairie, MN) de-identified database for a fixed period from 2000 to 2013. OptumInsight data are derived from a large, nationwide database of commercial health insurance and Medicare Advantage (C and D) claims, and include approximately 15% of U.S. residents. The database is updated annually and contains de-identified patient-level demographics, medical diagnoses, prescription drug use, and health care use.

We included all individuals ages 10 through 24 years with an incident diagnosis of SLE. The diagnosis of SLE was defined using previously validated methods as having at least 3 hospital discharge or physician visit claims with an International Classification of Diseases, Ninth Revision (ICD-9) primary diagnosis code for SLE of 710.0, each recorded at least 30 days apart.^{13–15} To select incident cases, we included only those who had at least one year of continuous claims data with no SLE codes in any position preceding the index primary diagnosis of SLE. This method has been published for identifying incident SLE cases in medical records databases^{16,17} and incident rheumatoid arthritis cases using claims data.^{18,19} Date of diagnosis, defined as the date of the first physician visit with an SLE claim or the admission date for the first hospitalization with an SLE claim, was used as the index date. Age was determined at the index date. The upper age limit of the sample was selected to include young adults in the process of transitioning from pediatric to adult health care systems, a population at risk for suboptimal healthcare utilization and poor outcomes.^{20,21} The lower age limit was set to exclude monogenic causes of very early onset SLE. Controls were randomly selected at a ratio of 2:1 from age and sex-matched enrollees during the same eligibility period, without ICD-9 codes specifying a chronic complex condition, per the algorithm developed by Feudtner et al.²² All subjects were continuously enrolled for at least 12 months.

Outcome Measures

The primary outcome measure was the number of health care visits in the 12 months preceding the index date. Health care visits were categorized as ambulatory visits, emergency visits (including urgent care), and hospitalizations. Ambulatory visits were further divided into primary care and subspecialty care by OptumInsight provider codes. Subspecialty care included visits to rheumatology, nephrology, hematology-oncology, cardiology, and neurology, which were determined a priori to be likely ambulatory specialties to which patients with SLE may present. The primary ICD-9 diagnosis code for each visit was used as a proxy for our secondary outcome, visit reason.

Covariates

We included the following demographic and disease-related covariates: geographic region, household education level, race/ethnicity, age group, presence of lupus nephritis at or after diagnosis, presence of neuropsychiatric disorders (seizure, stroke or psychiatric disorder) at or after diagnosis, and the presence of any psychiatric disorder before diagnosis. We categorized geographic region based on subject state of residence using the US Census Bureau Division groupings of US states into the following categories: Northeast, Midwest, South and West.²³ Optum derives household education level using US Census data, while race and ethnicity are derived from a combination of sources including public records, self-report and proprietary ethnic code tables. Age was grouped into two categories, 10–17 and 18–24 years, to examine potential differences in healthcare utilization between adolescents and young adults transitioning to adult care. The presence of SLE nephritis was identified using an algorithm for ICD-9 diagnosis and procedure codes previously validated for identifying SLE nephritis in administrative claims data.^{14,15} The presence of seizure or stroke disorder was identified by at least one ICD-9 code for seizures or cerebrovascular disease, which has been validated for administrative claims data in the pediatric population.

^{24–26} Psychiatric disorders were identified by a primary or secondary ICD-9 diagnosis code pertaining to the categories of depression, anxiety, adjustment/acute stress, and other psychiatric disorders, as previously described.²⁷ Since psychiatric disorders may influence health care use in children^{28,29} and adults,³⁰ and can precede the diagnosis of SLE,³¹ we also examined the presence of psychiatric disorders preceding the index date.

Statistical Analysis

Pearson chi-square tests were used to estimate differences in demographic characteristics between youth with SLE and controls. The mean number of ambulatory visits, emergency visits, and hospitalizations in the year prior to the index date were calculated. Descriptive statistics were used to estimate the proportions of ambulatory visits for primary and subspecialty care.

To compare the number of visits between SLE patients and healthy controls, unadjusted and adjusted incidence rate ratios (IRR) were estimated using fixed-effects negative binomial regression models, accounting for the matched subject design. Adjusted models included covariates for race/ethnicity and region. Three secondary analyses of health care visit outcomes were performed. First, two separate subgroup analyses were performed to estimate visit IRRs at 12 months for youth with SLE nephritis and for those with seizure/stroke, as these major organ manifestations may influence use of acute versus ambulatory care. Second, to further characterize utilization patterns over time, mean visits were subdivided into 3-month intervals preceding diagnosis, and separate negative binomial regression models were used to compare IRRs at each interval. Third, 12-month IRRs were stratified by psychiatric and non-psychiatric visits; psychiatric visits were defined as those with a primary ICD-9 code for a psychiatric disorder.

To determine the most common pre-SLE visit diagnoses, we ranked all primary diagnosis codes received during the 12-month observation period by frequency and stratified by health care setting (ambulatory, emergency, inpatient). For each of the most common pre-SLE visit diagnosis codes, we calculated the median number of days from first occurrence of the code (in either a primary or secondary diagnosis field) to SLE diagnosis. To determine factors associated with increased pre-diagnosis health care utilization among youth with SLE, we used separate multivariable negative binomial regression models for ambulatory, emergency and inpatient visits.

We performed three sensitivity analyses. To investigate the impact of more stringent incident case definitions, we limited the sample by: 1) including only youth who had at least 24 months of continuous enrollment with no SLE codes preceding the index date, and 2) excluding youth who had any anti-malarial prescription claims preceding the index date. For each of these case definitions we performed our three primary analyses (visit IRRs at 12 months, primary diagnoses, and factors associated with utilization), and the secondary analysis estimating IRRs at 3-month intervals. A third analysis addressed potential ascertainment bias by limiting the sample to matched sets in which the case and both controls each had at least one health care visit of any type during the observation period; unadjusted and adjusted IRRs for visits at 12 months and 3-month intervals were estimated (visit diagnoses and factors associated with utilization were not analyzed for this subset, as

matched sets with zero visits did not contribute to these analyses). Data preparation and analyses were performed using Stata 14.2 statistical software.

Results

Demographics and Health Characteristics

We identified 682 incident cases of SLE and 1,364 controls. More youth with SLE than controls were black or from the South region (Table 1). There were no significant differences by education level. A significantly higher proportion of youth with SLE than controls (17% vs 7%, $p<0.001$) had at least one psychiatric diagnosis preceding SLE diagnosis, of which depression, anxiety, and adjustment/acute stress disorders comprised 46%, 29% and 22%, respectively. Among those with a preceding psychiatric diagnosis, 46%, 27%, 10% and 20% received at least one prescription for antidepressants, anxiolytics, antipsychotics, and stimulants, respectively. Among youth with SLE, subsequent diagnoses of nephritis (24%), seizure or stroke (10%), and psychiatric disorders (25%) were common.

Health care visits

Among the 682 youth with SLE, there were 6,504 ambulatory visits, 2,323 emergency visits, and 899 hospitalizations during the observation period. Ambulatory care visits occurred mostly with primary care providers (39%), followed by rheumatologists (10%), hematology-oncologists (3%), neurologists (2%), cardiologists (1%), and nephrologists (1%).

Youth with SLE had significantly more health care visits in the year before diagnosis than did controls. The mean number of ambulatory visits was 9.5 (standard deviation 10.0) for youth with SLE versus 3.6 (5.2) for controls (adjusted IRR 2.48, $p<0.001$). Similarly, youth with SLE had more emergency care visits, mean 3.4 (5.4) versus 0.9 (2.6) (adjusted IRR 3.42, $p<0.001$), and more inpatient hospitalizations, mean 1.3 (4.1) versus 0.2 (1.8) (adjusted IRR 3.02, $p<0.001$) (Figure 1). Unadjusted and adjusted IRRs for health care visits are shown in Table 2. In the subgroup analysis, youth with SLE nephritis ($n=166$) had an even greater likelihood of pre-diagnosis hospitalization (adjusted IRR 10.39, $p<0.001$) than the full SLE cohort (Table 2) when compared to controls. The subgroup with seizure or stroke ($n=71$) had the highest likelihood of both pre-diagnosis hospitalization (adjusted IRR 18.06, $p<0.001$), and emergency visits (adjusted IRR 5.02, $p<0.001$).

Among youth with SLE, the number of visits across every health care setting increased as the index date approached (Figure 2). No such increase over time was evident for controls. Even at the earliest time interval (9–12 months prior to diagnosis), utilization remained nearly two-fold greater for youth with SLE than for controls (Supplemental Table 1). In the secondary analysis stratifying psychiatric and non-psychiatric visits, youth with SLE had significantly more non-psychiatric visits across all health care settings than did controls ($p<0.001$), but there was no significant difference observed for psychiatric visits (Supplemental Table 2).

In sensitivity analyses restricted to either youth with SLE who had at least 24 months of preceding claims data ($n=398$) or those without pre-diagnosis antimalarial prescriptions ($n=542$), the results did not differ (Supplemental Table 3). In the final sensitivity analysis

limited to youth with at least one visit during the observation period, including 656 (96%) youth with SLE and 1,012 (74%) controls, youth with SLE still had significantly more health care visits of all types in the year before diagnosis than did controls ($p<0.001$) (Supplemental Table 3).

Visit diagnoses

The most common primary diagnoses for ambulatory, emergency and inpatient visits are shown in Table 3. “Primary thrombocytopenia, unspecified” and “Chest pain, unspecified” were among the three most common primary diagnosis codes for both emergency visits and hospitalizations among youth with SLE; these were absent from the most common visit diagnoses for controls. “Acute kidney failure, unspecified” was the fourth most common primary diagnosis for hospitalizations in the SLE group. The sensitivity analysis limited to cases with at least 24 months of claims data preceding diagnosis yielded similar results. By excluding youth with SLE who had preceding antimalarial prescription claims, “Unspecified diffuse connective tissue disease” and “Other unspecified nonspecific immunological findings” were no longer among the most frequent primary diagnoses, however the other diagnoses remained unchanged.

For each of the most common pre-SLE primary diagnoses, time to SLE diagnosis varied between specific primary diagnosis codes and between individuals with the same diagnosis code. “Primary thrombocytopenia, unspecified” and “Other venous embolism and thrombosis” were associated with the longest duration to SLE diagnosis, with a median of 278 days (IQR 39–354) and 313 days (IQR 18–356), respectively. In contrast, “Acute kidney failure, unspecified”, “Fever, unspecified” and “Chest pain, unspecified” were associated with a shorter duration to SLE diagnosis (median 14 days (IQR 5–168), 52 days (IQR 17–166) and 73 days (IQR 29.5–168), respectively).

Factors associated with pre-diagnosis utilization

Among youth with SLE, having any preceding psychiatric diagnosis was the most strongly associated with increased utilization across all health care settings (Table 4). Female sex, black and Asian race/ethnicity, higher education level, and seizure/stroke at or after SLE diagnosis were associated with more ambulatory visits, while SLE nephritis was associated with fewer ambulatory visits. All of the above associations remained robust in the sensitivity analyses limited to youth with at least 24 months of enrollment prior to SLE diagnosis and those without antimalarial prescriptions.

Discussion

In this population-based cohort of youth with SLE, we found several important health care utilization patterns in the year preceding diagnosis. First, youth with SLE consistently used more health care in the year prior to diagnosis than their healthy peers, across all health care settings. Second, the most common diagnoses received during that year include many potential signs and symptoms of SLE, with variation among individuals in time from these diagnoses to eventual SLE diagnosis. Third, many youth with SLE carry psychiatric diagnoses prior to being diagnosed with SLE, which we found to be strongly associated with

higher pre-diagnosis health care use. Our findings provide new insight into pre-diagnosis health care interactions for youth with SLE, to guide further study of potential targets to expedite SLE diagnosis and treatment.

High pre-SLE-diagnosis health care utilization among youth in our study spanned the entire year of observation, demonstrating that this population becomes a high utilizer of both ambulatory and acute care long before SLE diagnosis. Even in the 12-to-9 month period before diagnosis, youth with SLE had more visits than controls. Our findings are consistent with studies of other autoimmune conditions such as pediatric-onset inflammatory bowel disease, where physician visits for abdominal pain increase several years prior to diagnosis.³² In addition, the increased pre-diagnosis visits in our study extended from physician visits to emergency care and hospitalizations, and involved providers of various specialties. This pattern of multiple health system interactions across ambulatory and acute care settings was similar for both adolescents and transition-age young adults.

There are several potential explanations for the high pre-SLE-diagnosis health care utilization and multiple points of access, including natural evolution of multi-organ disease, or the need for sequential diagnostic evaluation, and avoidable diagnostic delay. In the natural evolution of SLE, an insufficient number of clinical manifestations may contribute to an extended time interval between initial symptoms and definitive SLE diagnosis. Upon clinical suspicion for SLE, sequential diagnostic evaluation would be reasonably expected to occur within a few months. Diagnostic delay, however, would imply missed opportunities for identification of SLE at early presentations to care. Sequential diagnostic evaluation may explain our results showing multiple visits in the 3 months preceding SLE diagnosis, but likely does not fully explain increased visits in the preceding time intervals. Although some youth in our study may have been under close observation for the development of SLE, exclusion of youth with antimalarial prescriptions resulted in eliminating the majority with diagnoses of “Unspecified diffuse connective tissue disease” and did not explain the observed differences in health care utilization or diagnoses assigned. Our results highlight the need to explore whether early health care interactions represent avoidable diagnostic delay or natural progression of early disease manifestations.

Diagnostic delay may arise from several factors, including poor recognition of disease manifestations, ascribing symptoms to functional complaints, insufficient clinical features, lapses in insurance coverage, or wait times for subspecialists. In our study, only 10% of ambulatory pre-diagnosis visits were with a rheumatologist. The growing shortage of both pediatric and adult rheumatologists will only compound delays in access to care.³³ Increasing awareness and education among clinicians, ensuring adequate access to care, and maintaining an adequate rheumatology work force, may all improve earlier identification of youth with SLE.

The patterns of pre-diagnosis health care utilization in different subgroups of youth in our study can inform future studies to identify potential diagnostic delay. Compared with the full SLE cohort, youth with CNS involvement presented the most acutely with a greater incidence of pre-SLE-diagnosis emergency visits and hospitalizations. Studies to better characterize the pre-diagnosis period in this subgroup may need to focus on acute care

settings. Similarly, those with nephritis had a higher incidence of pre-diagnosis hospitalization. Developing inpatient clinical care pathways to expedite work-up for possible or suspected SLE may be one strategy to improve renal outcomes. Further study of pre-diagnosis presentations in these subgroups can inform setting-specific interventions that may expedite disease identification and prevent organ damage.

Our analysis of pre-SLE visit diagnoses also points towards acute care settings for potential opportunities to expedite SLE diagnosis in youth. Among the most common acute care diagnoses were thrombocytopenia, venous thromboembolism, and acute kidney failure. These findings in youth should raise suspicion for SLE, as they represent potential manifestations of SLE. For thrombocytopenia and venous thromboembolism, the median time between the first codes and the first SLE claim suggests a long interval between symptom onset and diagnosis of SLE. While the natural evolution of disease can contribute to this latency period, the wide range of time to SLE diagnosis across individuals with the same visit diagnoses suggests that diagnostic delay could be a contributing factor.

We also found that a higher proportion of youth with SLE were diagnosed with a psychiatric disorder prior to SLE diagnosis than their peers without chronic disease. It is unclear whether psychiatric disorders in this cohort represent true neuropsychiatric manifestations of SLE, primary psychiatric disorders, or attribution of symptoms to functional complaints. Regardless, having a psychiatric diagnosis was associated with a two to three-fold increase in pre-SLE-diagnosis health care visits, suggesting that psychiatric disorders are an important determinant of health service use across all settings. Previous studies have shown that adolescents with mental health conditions use more health care and incur significantly higher health care costs.^{34,35} In adults with known SLE, symptoms of depression are also associated with increased overall utilization, especially emergency care.³⁶ Interestingly, in our study only non-psychiatric visits were significantly greater among youth with SLE compared with controls. As a result, the increased pre-diagnosis utilization among youth with SLE cannot be explained by mental health care or psychiatric medication titration. Our results are consistent with previous reports of greater increases in hospitalization rates for non-psychiatric medical conditions among children with comorbid psychiatric disorders than those without.²⁸ This implies that patients with comorbid psychiatric disorders seek health care of all types more frequently than those without psychiatric disorders. Clinicians should at least consider SLE in the differential diagnosis of youth presenting with medical complaints and new onset psychiatric symptoms. In addition, given that comorbid psychiatric disorders are so prevalent and associated with high health care use in our study, mental health resources and psychosocial support should be made more readily available to youth newly diagnosed with SLE.

There are several strengths of our study. By leveraging a large, national, administrative health care database, we have identified one of the largest cohorts of youth with newly-diagnosed SLE in the age range representative of patients cared for by pediatric rheumatologists. The results from this study remain similarly applicable to adult rheumatologists, who are often responsible for older adolescents and transition-age young adults. In some areas, adult providers also care for children with rheumatic diseases due to the shortage of pediatric rheumatologists. In addition, we were able to assess pre-diagnosis

health care utilization by health care setting and provider type. We have identified several potential targets for further study and intervention, including earlier identification of SLE among youth presenting with thrombocytopenia, venous thromboembolism, or psychiatric symptoms in the context of other suggestive symptoms.

There are also several limitations. Although the coding algorithm used to identify SLE cases has been validated for claims data,^{13–15} our definition for incident cases has not been formally validated. We addressed the risk of capturing prevalent SLE cases by performing several sensitivity analyses using more stringent published algorithms,^{14,37} none of which changed our conclusions. Furthermore, recommendations for monitoring people with asymptomatic SLE require at least quarterly screening,^{38,39} so the likelihood of capturing prevalent cases with our methodology is relatively low. A second limitation is that we were unable to determine symptoms using claims data; however, we did assess potential reasons for which subjects presented to care by examining primary diagnosis codes associated with pre-SLE-diagnosis visits, some of which were codes for symptoms. Lastly, as all of the patients within the database are commercially insured, we were unable to assess differences in utilization associated with either type or lapses in insurance.

In conclusion, the youth in our study saw multiple providers of different specialties across both ambulatory and acute care settings, in the year prior to receiving a diagnosis of SLE, which has important implications for improving care of youth with SLE. Future studies to identify potential points of diagnostic delay may need to involve all health care professionals, including primary care, subspecialty, and acute care providers. We have also identified several specific diagnoses associated with acute care settings in which targeted investigation is needed to determine whether there is avoidable diagnostic delay and a potential role for intervention. Efforts directed toward guiding work-up of patients presenting with early features might shorten the interval from symptom onset to SLE diagnosis. Lastly, comorbid psychiatric disorders frequently precede recognition of SLE, highlighting the importance of adequate psychosocial support at the time of SLE diagnosis. A multi-faceted approach will be needed to identify potential diagnostic delay and design targeted interventions to improve outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- In the first population-based study of pre-diagnosis health care utilization among youth with SLE, we demonstrate that youth with systemic lupus erythematosus (SLE) consistently use more health care than age and sex-matched controls.
- Common primary diagnoses for youth presenting to acute care in the pre-SLE-diagnosis period included venous thromboembolism, thrombocytopenia, chest pain, fever and acute kidney failure. High variability in the time between these diagnoses and subsequent SLE diagnosis suggests potential to optimize early diagnosis and treatment.
- Psychiatric disorders commonly precede SLE diagnosis in youth, and are strongly associated with high health care use in the pre-SLE-diagnosis period, supporting a role for psychiatric assessment and resources for newly diagnosed youth with SLE.

Figure 1.

Mean health care visits one year prior to diagnosis in youth with SLE compared to controls. P-values shown refer to comparisons calculated using negative binomial regression models adjusted for race and geographic region.

Figure 2.

Mean visits at 3-month intervals leading up to the index date in youth with SLE compared to controls, stratified by a) ambulatory visits, b) emergency care visits, c) inpatient hospitalizations, and d) all visit types combined. Arrows indicate date of SLE diagnosis.

Table 1

Demographics and Disease Characteristics

		SLE (n = 682)	Controls (n = 1364)	p-value
Age, n (%)	10–17 years old	334 (49)	668(49)	-
	18–24 years old	348 (51)	696 (51)	
Sex	Female, n (%)	599 (88)	1198 (88)	-
Race/Ethnicity	White	383 (56)	806 (59)	<0.001
	Black	115 (17)	121 (9)	
	Hispanic	95 (14)	152 (11)	
	Asian	43 (6)	31 (2)	
	Unknown	46 (7)	254 (19)	
Region	Midwest	178 (26)	437 (32)	0.004
	Northeast	76 (11)	125 (9)	
	South	332 (49)	574 (42)	
	West	96 (14)	227 (17)	
Highest education	Less than 12th grade	9 (1)	10 (1)	0.077
	High School Diploma	174 (26)	374 (27)	
	Less than Bachelor Degree	345 (51)	586 (43)	
	Bachelor Degree or More	124 (18)	196 (14)	
	Unknown	30 (4)	198 (15)	
Preceding psychiatric diagnosis *	119 (17)	99 (7)	<0.001	
Characteristics of SLE subjects (at or after diagnosis)				
SLE nephritis		166 (24)	-	-
Seizure/Stroke disorder	71 (10)	-	-	
Psychiatric disorder	173 (25)	-	-	

* Refers to psychiatric diagnosis prior to the index date for youth with SLE or diagnosis during the observation period for controls

Table 2Visits one year prior to SLE diagnosis among youth with SLE compared to controls, by subgroup[§]

	SLE (n=682)	Controls (n=1364)	Unadjusted	Adjusted [^]
	Mean (SD)	Mean (SD)	IRR [95% CI]	
Ambulatory				
Total SLE	9.5 (±10.2)	3.6 (±5.2)	2.5 [2.3,2.7] *	2.5 [2.3,2.7] *
Nephritis	7.4 (±8.6)	3.2 (±4.2)	2.0 [1.7,2.3] *	2.0 [1.6,2.4] *
Seizure/Stroke	10.8 (±9.4)	4.2 (±5.5)	2.4 [1.9,3.1] *	2.3 [1.8,3.1] *
Emergency				
Total SLE	3.4 (±5.4)	0.9 (±2.6)	3.5 [3.1,4.0] *	3.4 [3.0,4.0] *
Nephritis	3.6 (±6.9)	0.8 (±2.3)	3.8 [3.0,5.0] *	3.6 [2.6,4.9] *
Seizure/Stroke	4.8 (±6.5)	0.9 (±2.7)	4.6 [3.1,6.8] *	5.0 [3.2,7.9] *
Inpatient				
Total SLE	1.3 (±4.2)	0.2 (±1.8)	3.6 [2.7,4.8] *	3.0 [2.2,4.2] *
Nephritis	2.3 (±5.8)	0.1 (±0.6)	10.8 [5.4,21.4] *	10.4 [4.2,25.6] *
Seizure/Stroke	3.0 (±4.5)	0.4 (±3.4)	10.0 [4.5,21.9] *	18.1 [5.3,61.1] *
All Visits				
Total SLE	14.3 (±14.9)	4.7 (±7.4)	2.7 [2.5,3.0] *	2.7 [2.5,3.0] *
Nephritis	13.4 (±15.8)	4.1 (±5.5)	2.5 [2.1,3.0] *	2.5 [2.1,3.1] *
Seizure/Stroke	18.6 (±17.0)	5.6 (±9.4)	3.0 [2.3,3.8] *	3.0 [2.3,3.9] *

Results from negative binomial regression models comparing health care visits between youth with SLE and controls

[§]Disease manifestation at or after SLE diagnosis (nephritis subgroup n = 166, seizure/stroke subgroup n = 71)[^]IRR adjusted for race and geographic region;

* p < 0.001

Table 3

Most frequent primary diagnoses in the year preceding SLE diagnosis

SLE			Controls	
Visit Type	Primary ICD-9 code	n (%) [*]	Primary ICD-9 code	n (%) [*]
Ambulatory				
	Other acne	136 (3)	Acute pharyngitis	122 (3)
	Routine child health examination	98 (2)	Other acne	120 (3)
	Unspecified diffuse connective tissue disease	91 (2)	Routine child health examination	117 (3)
	Acute pharyngitis	84 (2)	Acute upper respiratory infection	85 (2)
	Allergic rhinitis	84 (2)	Allergic rhinitis	85 (2)
Emergency				
	Other venous embolism and thrombosis	50 (3)	Supervision of other normal pregnancy	36 (4)
	Primary thrombocytopenia, unspecified	47 (3)	Non-allopathic lesions, cervical	30 (3)
	Chest pain, unspecified	46 (3)	Passenger in pick-up truck/van injured in collision	24 (2)
	Other unspecified nonspecific immunologic findings	31 (2)	Lumbago	22 (2)
	Abdominal pain, unspecified	30 (2)	Abdominal pain, unspecified	21 (2)
Inpatient				
	Fever, unspecified	33 (4)	Normal delivery	12 (5)
	Primary thrombocytopenia, unspecified	32 (4)	First-degree perineal laceration, delivered	10 (4)
	Chest pain, unspecified	24 (3)	Abnormality of gait	10 (4)
	Acute kidney failure, unspecified	20 (3)	Syncope and collapse	9 (4)
	Vomiting alone	19 (2)	Major depressive affective disorder	7 (3)

* Indicates percent of visits of the same visit type

Table 4

Factors Associated with Pre-diagnosis Health Care Utilization in Youth with SLE

Factors	Ambulatory	Emergency	Inpatient
Incidence Rate Ratio (95% CI)			
Race/Ethnicity			
White	-	-	-
Black	0.8 (0.7–0.95) *	1.1 (0.8–1.5)	1.6 (0.7–3.5)
Hispanic	1.1 (0.9–1.3)	1.2 (0.9–1.6)	1.5 (0.6–3.6)
Asian	0.7 (0.5–0.95) *	0.5 (0.3–0.8) **	0.7 (0.2–2.4)
Age, years			
10–17	-	-	-
18–24	1.1 (1.0–1.3)	1.1 (0.9–1.3)	1.2 (0.7–2.2)
Female	1.4 (1.2–1.8) ***	1.0 (0.8–1.4)	1.1 (0.4–2.7)
Region			
Midwest	-	-	-
Northeast	1.1 (0.9–1.4)	0.9 (0.6–1.3)	0.7 (0.2–2.0)
South	1.0 (0.9–1.2)	0.8 (0.6–1.0)	1.1 (0.5–2.2)
West	1.0 (0.8–1.2)	1.1 (0.8–1.5)	0.4 (0.2–1.2)
Highest household education			
High school or less	-	-	-
Beyond high school	1.2 (1.01–1.4) *	1.0 (0.8–1.2)	1.1 (0.5–2.2)
SLE nephritis [§]	0.8 (0.7–0.9) **	1.1 (0.8–1.4)	2.1 (1.02–4.3) *
Seizures or Stroke [§]	1.4 (1.1–1.7) **	1.4 (1.0–1.9)	2.6 (1.0–7.0)
Preceding psychiatric diagnosis	1.9 (1.6–2.2) ***	2.1 (1.6–2.7) ***	3.1 (1.4–7.1) **

Results from multivariable negative binomial regression models examining associations between demographic or disease factors and health care utilization. Separate models (n = 631) were used for ambulatory, emergency, and inpatient visits.

* = p < 0.05;

** = p < 0.01;

*** = p < 0.001;

[§] Indicates disease manifestation at or after SLE diagnosis