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Clinical Presentation, Care Pathways, and Delays in Access to Specialized Care in Patients With Systemic Lupus Erythematosus: A Study From Lupus Midwest Network (LUMEN)

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Abstract

Objective: To characterize presentation and care pathways of patients with systemic lupus erythematosus (SLE), and delays in access to SLE-specialized care.

Methods: We included patients with incident SLE from the Lupus Midwest Network registry. Time from the first medical encounter for SLE clinical manifestation to access to SLE-specialized care, physician diagnosis, and treatment was estimated. Delays were defined as ≥ 6 months to access specialized care. We compared SLE manifestations, disease activity (SLEDAI-2k), and SLICC/ACR damage indexes (SDI) between patients with and without delays. Logistic regression models assessed associations with delays.

Results: The study included 373 patients with SLE. The median time to access SLE-specialized care was 1.1 months (95% confidence interval [CI] 0.9–1.5); time to diagnosis 30.6 months (95% CI 18.9–48.1), and time to treatment initiation 4.7 months (95% CI 3.9–8.4). Approximately 25% (93/373) of patients experienced delays accessing specialized care, which were associated with fewer SLE manifestations at first SLE-related encounter (< 2 SLE domains; 92% vs 72%, $P < 0.001$). Patients with mucocutaneous or musculoskeletal manifestations were less likely to experience delays, while hematologic (odds ratio [OR] 1.71, 95% CI 1.03–2.84) or antiphospholipid antibodies domains (OR 6.05, 95% CI 2.46–14.88) were associated with delays. Delays were associated with damage at first access to SLE-specialized care (SDI ≥ 1 ; 30% vs 7%, $P < 0.001$).

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Conflict Of Interest Statement
None

Conclusions: Patients follow a heterogeneous pathway to receive care. One-fourth of patients experienced delays accessing SLE-specialized care, which was associated with damage. Fewer manifestations, hematologic, or antiphospholipid antibodies were associated with delays.

Keywords

Systemic lupus erythematosus; healthcare access; diagnostic delays; specialized care

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect any organ system (1). Due to its clinical heterogeneity, making a diagnosis, particularly during the initial stages, can be difficult (2,3). Patients with more recognizable manifestations are likely to be referred earlier to SLE specialists (4), but insidious and nonspecific features frequently precede a clinical diagnosis, leading to delayed referrals to specialty care. Among patients with SLE, a delayed diagnosis may translate into an increased risk of irreversible damage and poor outcomes (2,5). Therefore, minimizing delays in access to specialists could lead to better outcomes. However, little is known about how initial SLE presentations may influence the pathways patients experience to receive care and be diagnosed in the US health care system.

A study conducted in Greece, using a combined approach of medical chart reviews and interviews, revealed that it took patients a median of 24 months to receive a diagnosis after symptom onset (3). An analysis of US administrative insurance data reported that young patients with SLE who had diagnostic codes of thrombocytopenia and venous thromboembolism had the longest delay in receiving an SLE diagnosis (6). However, the generalizability of these findings across different health care systems or countries remains uncertain. Furthermore, studies relying on interviews may be prone to recall bias, and reports from administrative databases could contain misclassified SLE cases.

With these considerations, using a population-based registry, we performed a cohort study of patients with incident SLE, with detailed clinical data predating SLE diagnosis. We explored the pathways of patients with SLE, tracking their journey from the first SLE-related manifestation until first encounter with specialized SLE care. We aimed to study risk factors associated with delays in accessing care, and the associations between delays, disease activity, and damage accrual.

Materials and Methods

Study population.

The Lupus Midwest Network (LUMEN ) is a population-based registry of a 27-county region in southeast Minnesota and southwest Wisconsin, nested in the Rochester Epidemiology Project (REP), a medical records-linkage system (7–9). The REP allows ready access to the medical records from health care providers for the local population, including the Mayo Clinic, Olmsted Medical Center, their affiliated health systems and hospitals, local nursing homes, etc. The demographics, distribution of morbidity, and

mortality rates in the REP region are similar to those in the upper Midwest (10). The characteristics and strengths of the REP, as well as its generalizability, have been described elsewhere (11–13). This study was approved by the institutional review boards of Mayo Clinic (20-006485) and Olmsted Medical Center (036-OMC-20).

Case definition and ascertainment.

Patient identification and ascertainment of the LUMEN registry have been previously published (7,8,14). Briefly, ascertainment of a potential SLE case was identified via two strategies: 1) through International Classification of Diseases 9 (ICD-9) and ICD-10 codes for SLE, cutaneous lupus erythematosus, and other associated diseases, and 2) through laboratory measures associated with SLE—anti-nuclear antibodies (>1:80), low complement, anti-double stranded DNA, anti-Sm, lupus anticoagulant, anticardiolipin (IgG, IgM, and IgA), and anti-beta 2 glycoprotein 1 (IgG, IgM, and IgA) antibodies. We identified all the potential SLE cases in the REP 27-county region, from 1976 to 2018 for Olmsted County, and from 2010 to 2018 in the other 26 counties. We included as cases those patients with SLE who fulfilled the 2019 European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) classification criteria (15). We used the 2019 EULAR/ACR criteria since they perform better than other classification criteria at identifying patients in population-based studies (16). To be considered incident, patients needed to be residents of the 27-county region on the date of criteria fulfillment.

Data collection.

We electronically retrieved demographic variables and self-reported race and ethnicity (Hispanic; non-Hispanic White, Asian, and Black). Educational level and disease manifestations based on the definitions of the 2019 EULAR/ACR classification criteria were manually abstracted from medical records. To understand how patients seek medical care, we identified the medical encounters that were related to SLE and abstracted the dates they occurred. We defined an SLE-related encounter as inpatient or outpatient medical visits during which care for SLE manifestations was provided. Encounters wherein clinical findings could be better explained by conditions other than SLE were not counted (e.g., joint swelling related to trauma, a dermatology visit for a mole check). We considered that a patient received care for SLE if disease manifestations were documented in the medical history, physical examination, or clinical interventions. Inpatient encounters were defined as those requiring at least 1 overnight stay, and each hospitalization was considered a single encounter.

We abstracted the medical specialties of the clinicians involved in SLE-related encounters and grouped them as “SLE-specialized” (Rheumatology, Dermatology, and Nephrology), Internal Medicine and subspecialties (excluding SLE-specialized), Family Medicine, Emergency Medicine, surgical specialties, and other specialties.

We abstracted the dates of the medical encounters wherein a physician diagnosis of SLE and SLE treatment were given for the first time. SLE treatment was based on prescriptions for antimalarials (chloroquine or hydroxychloroquine), or conventional (azathioprine, cyclophosphamide, methotrexate, mycophenolate, or tacrolimus) or biologic

immunosuppressants (rituximab or belimumab). Patients prescribed glucocorticoids, nonsteroidal anti-inflammatory drugs, or topical medications as monotherapy were not considered to have received SLE treatment. We determined the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2k) (17) and the Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index (SDI) (18) at the time patients had an encounter with SLE specialties. If patients did not access SLE specialties, SLEDAI-2k and SDI were obtained when the patient fulfilled the classification criteria.

Three physician abstractors (ASR, JAMA, JXY) underwent an initial calibration phase with a sample of 10% of patients. During several rounds of calibration, a >95% of agreement was considered reliable throughout the abstraction process. Variables subjected to judgment calibration were the dates of the first medical encounter, the number of medical encounters, characteristics of specialties seen, and the total number of encounters. The abstraction was completed using the Research Electronic Data Capture (REDCap) online platform (19,20).

Characterization of SLE care pathways.

To outline the pathways in SLE patients' journeys, we tracked key events, specifically the first: SLE-related encounter, SLE-specialized encounter, SLE diagnosis encounter, and SLE therapy encounter. Patients were followed from the first SLE-related encounter until we identified these three key events: migration out of the 27-county region, death, or until February 11, 2020. We measured the time in months and summarized all encounters between the first SLE-related encounter and the other key events in care.

Outcomes.

We defined a delay in access to SLE-specialized care as a period of 6 months or more between the first SLE-related encounter and the first SLE-specialized encounter. Delays were dichotomized at six months based on prior evidence showing that patients diagnosed within six months from symptom onset have improved prognosis.(5)

Statistical analysis.

Descriptive statistics were used to summarize demographic and clinical variables. SLE manifestations seen up to the first SLE-specialized care encounter were presented overall and according to the type of specialized care received. Among patients who never received specialized care, SLE manifestations through the most recent encounter were reported. Using chi-square and rank sum tests, we compared characteristics identified during the initial encounter and assessed differences in the SLEDAI-2k and SDI between patients with and without delays in accessing specialized care. Fisher's exact tests were used to compare categorical variables with expected cell counts less than five. We used Kaplan-Meier methods to estimate median time from first SLE-related encounter to reaching each additional key event, to appropriately account for patients who had not yet reached a key event at last follow-up. Log-rank tests were used to compare median times. Logistic regression models were used to estimate associations between characteristics and delays in access to specialized care—adjusted for age, sex, and calendar year of SLE incidence, with results summarized as odds ratios (OR) and 95% confidence intervals (CIs). Cox models were not used because dichotomizing delays at 6 months was considered to be clinically

relevant and all patients had at least 6 months of follow-up, so there was no censoring. Complete-case analysis was used in all cases. *P* values less than 0.05 were considered statistically significant for all analyses. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

The study included 373 patients with incident SLE. At the time of their first SLE-related encounter, the mean ($\pm$ standard deviation [SD]) age was 42.8 (18.5) years, with 80% being female, 82% identifying as non-Hispanic White, and 61% having at least some college education. The first SLE-related encounter occurred in the outpatient setting for 83% of patients, while 17% were hospitalized.

During the first SLE-related encounter, the most frequent clinical domains from the EULAR/ACR criteria were hematologic (31%), musculoskeletal (25%), and mucocutaneous (18%) (**Table 1**). At first access to SLE specialty care, the median (25th–75th percentile) SLEDAI-2k was 4 (2–8), with 13% having an SDI of ≥ 1 .

The specialties involved in this initial encounter included 34% of patients seen by Internal Medicine (or its branches) and 32% by Family Medicine. Additionally, 12% (44/373) of patients were seen by SLE-specialized physicians during the first encounter, primarily by Dermatology. Patients presenting at first SLE-related encounter with musculoskeletal domain manifestations were predominantly seen in Primary Care, including both Internal Medicine (34%, 31/92) and Family Medicine (43%, 40/92). Meanwhile, those with mucocutaneous symptoms were more frequently seen by SLE-specific specialties, mainly Dermatology (35%, 23/66). Patients exhibiting symptoms in the serositis domain were more likely to be seen in Emergency Medicine (Supplementary Table 1).

Time to access to SLE-specialized care, SLE diagnosis, and SLE treatment.

Among the 373 patients included in this study, 2% (8/373) had no access to SLE-specialized care during follow-up (median 55, range 8–114 months). Of the remaining 365 patients, 274 (75%) had their first SLE-specialized care with Rheumatology, 59 (16%) Dermatology, and 32 (9%) Nephrology. However, as previously mentioned, 44 (12%) accessed SLE-specialized care during their first SLE-related encounter, while the remaining 329 (88%) required multiple consultations before first accessing SLE-specialized care. The median time to access SLE-specialized care was 1.1 months (95% CI 0.9–1.5), with patients typically requiring a median of 3 encounters (interquartile range [IQR] 2–4) to achieve this access (Supplementary Table 2).

SLE manifestations (by EULAR/ACR domains) seen up to the first SLE-specialized care encounter are outlined in Table 2. Patients first visiting Rheumatology exhibited musculoskeletal manifestations (46%), patients visiting Dermatology more frequently had mucocutaneous manifestations (59%), and patients who first visited Nephrology had more renal manifestations (34%). The rest of the clinical domains were more evenly distributed across the three SLE-specialized care services.

A total of 284 patients received an SLE diagnosis by a physician during follow-up, while the rest received other diagnoses including undifferentiated connective tissue disease or inflammatory arthritis (23%), yet all fulfilled the EULAR/ACR criteria for SLE. The median time from the first SLE-related encounter to receiving an SLE diagnosis was 30.6 (95% CI 18.9–48.1) months; those diagnosed with SLE had a median of 6 (IQR 3–12) encounters between these two times. Moreover, 338 patients received SLE treatment during follow-up. The median duration from the first SLE-related encounter to the initiation of SLE treatment was 4.7 months (95% CI 3.9–8.4), involving 5 (IQR 3–9) encounters (Supplementary Table 2).

Care pathways compared between initial inpatient and outpatient care.

When comparing the first SLE-related encounters between inpatient and outpatient settings, patients initially assessed in inpatient care more frequently presented with the following domains: constitutional (11% vs 1%, $P < 0.001$), hematologic (42% vs 28%, $P = 0.035$), serosal (22% vs 3%, $P < 0.001$), and renal (8% vs 1%, $P = 0.005$) (Supplementary Table 3). Patients initially assessed in outpatient care more frequently presented with musculoskeletal domain manifestations (28% vs 11%, $P = 0.004$). Additionally, half of the patients (52%) in inpatient care for their first SLE-related encounter were seen by a specialist in Emergency Medicine. Patients hospitalized at first SLE-related encounter also showed higher disease activity at first access to SLE-specialized care compared to those who had their first SLE-related encounter in an outpatient setting (median SLEDAI-2k of 8 [IQR 5–14] vs 4 [IQR 2–7], $P < 0.001$) and were more likely to present with damage at first access to SLE-specialized care (SDI ≥ 1 in 20% vs 11%, $P = 0.048$). Although the time needed to access SLE-specialized care did not differ statistically, the median time for receiving an SLE diagnosis (40.8 [95% CI 28.9–60.2] vs 3.4 [95% CI 1.2–11.1] months, $P < 0.001$) and starting SLE treatment (6.9 [95% CI 4.1–10.2] vs 2.3 [95% CI 1.0–4.8] months, $P = 0.021$) was significantly shorter for those who were initially hospitalized (Supplementary Table 2).

Access to SLE-specialized care and delays.

A total of 75% (280/373) of the patients with SLE gained access to SLE-specialized care within 6 months, while 25% (93/373) experienced a delay in access or never achieved access during follow-up. As detailed in Table 3, there were no differences in demographics or education levels among those with or without delay in access to SLE-specialized care. More patients with delay had manifestations in the hematologic and antiphospholipid antibody domains and were affected in only one SLE domain at the first SLE-related encounter, compared with patients without delay (92% vs 72%, $P < 0.001$). More patients without delay had manifestations in the mucocutaneous, musculoskeletal, specific autoantibodies, and complement domains. The delay in access to SLE-specialized care was associated with a 5-fold increased likelihood of presenting with at least one point on the SDI score at first access to SLE-specialized care (30% vs 7%, adjusted OR 5.30, 95% CI 2.71–10.37, data not tabulated). However, delay in access to SLE-specialized care was not associated with increased disease activity at the time the patient first accessed SLE-specialized care.

After adjusting for age, sex, and calendar year, an initial presentation with hematologic domain was associated with a nearly 2-fold increase in odds of experiencing a delay in

SLE specialty care (OR 1.71, 95% CI 1.03–2.84), and antiphospholipid antibodies domain was associated with a 6-fold increase in odds for delay (OR 6.05, 95% CI 2.46–14.88). Conversely, those who initially presented with mucocutaneous (OR 0.17, 95% CI 0.06–0.44), musculoskeletal (OR 0.47, 95% CI 0.25–0.88), specific autoantibodies (OR 0.44, 95% CI 0.23–0.82), or ≥ 2 SLE domains (OR 0.23, 95% CI 0.10–0.52) were associated with a decreased likelihood of delay. We observed a decreased likelihood of delays over time; specifically, each 10-year increase at the initial SLE-related encounter was associated with a lower risk of delays (OR 0.73, 95% CI 0.60–0.88), and the median time to gain access, which was 2.7 months (95% CI 0.7–8.6) during 1989–1998, decreased to 1 month (95% CI 0.8–1.5) during 2009–2018 (Supplementary Table 2). Age, sex, race and ethnicity, educational level, initial care received in an inpatient or outpatient setting for the first SLE-related encounter, or type of medical specialties at the first SLE-related encounter were not associated with delays (Table 4).

Discussion

In this study, we characterized the clinical presentation of patients with SLE at key time points early in their disease course, carefully delineated the care pathways of patients with SLE, and assessed the impact of delayed access on disease activity and damage. In agreement with prior findings (3,21,22), patients with SLE primarily sought care for musculoskeletal and mucocutaneous symptoms. Rheumatology emerged as the predominant first contact within SLE-specialized care, although some patients were seen first by Nephrology or Dermatology. We observed that the time to initiate SLE treatment was shorter than the time to receive an SLE diagnosis. The trajectory towards specialized care, diagnosis, and treatment was notably influenced by disease severity and presentation. A minority of patients initially required inpatient management—characterized by higher SLEDAI-2k and more severe manifestations, leading to more prompt diagnosis and treatment compared to outpatient counterparts. Many patients experienced delays accessing SLE-specialized care, leading to significantly greater damage accrual, despite similar levels of disease activity as those without delays.

The median lag time to be seen by an SLE-specialized physician in our cohort was approximately 1 month. Keeping in mind that universal access to healthcare and the particularities of the country's system play a significant role in access to care, this finding could be compared with a study from Greece, which reported an average time of 3 months from the first physician visit to Rheumatology assessment (3). Our shorter time could be partially due to patients presenting with skin manifestations being promptly seen at first encounter by Dermatology—considered as SLE-specialized for the purposes of this study. In addition, these results have to be understood in the proper context; our study included newly diagnosed patients until 2018, before the COVID-19 pandemic and during the peak of the US Rheumatology workforce (23,24). Future studies will need to assess the impact of the rheumatology US workforce shortages on access to care for patients with incident SLE.

Our findings underscore that the care pathways for patients with SLE are significantly influenced by the disease's clinical presentations. Specifically, the initial severity or sudden onset of systemic manifestations often dictates the health care providers involved and the

settings in which patients receive care. Those requiring inpatient care typically presented with higher SLEDAI-2k scores, frequently had conditions characterized by serositis and renal manifestations, and received a diagnosis and treatment more swiftly than their outpatient counterparts. This observation is closely aligned with the study from Greece, which found that approximately 20% of patients were hospitalized due to their initial SLE manifestations (25). Although our study's approach to abstracting and classifying SLE manifestations differed (for instance, we did not abstract cerebrovascular or thrombotic events as they do not fall under the EULAR/ACR SLE criteria), both studies concur that hematologic, renal, or serosal manifestations were prevalent among patients hospitalized early in their diagnostic journey.

While the median time to access SLE-specialized care was short, the journey to receive a physician diagnosis and SLE treatment initiation was notably longer. Interestingly, while all the patients fulfilled the EULAR/ACR SLE criteria, some patients never received a definitive physician diagnosis of SLE. This discrepancy can be attributed to the application of the novel EULAR/ACR criteria to historical medical records. These criteria have been recognized for classifying a greater number of patients as having SLE compared to previous criteria (16,26). In our study, it became apparent that many patients received a diagnosis of nonspecific conditions, such as inflammatory arthritis or undifferentiated connective tissue disease, before a definitive SLE diagnosis. A diagnosis of lupus is complex, and as the condition evolves, the diagnoses may change over time.. Interestingly, the time needed for diagnosis changed after 2009 to 2018. During this period, the time taken for diagnosis notably decreased, arguably due to advances in SLE care and increased awareness. Reassuringly, the absence of a definitive SLE diagnosis by a physician did not preclude treatment; clinicians frequently initiated treatment based on the patient's clinical presentation.

In our study, many patients experienced a delay of 6 months or longer in accessing a specialist. Currently, there is no universally accepted definition of what constitutes a delay in access to specialized care for patients with SLE. We adopted a 6-month benchmark based on its demonstrated clinical relevance in prior research (3,5). Using this benchmark, we found that the patients who presented with antiphospholipid antibodies or hematologic manifestations were more likely to have delayed access to care. Patients with antiphospholipid antibodies often had a history of unexplained thrombosis or, less frequently, a false positive syphilis test. Conversely, patients with more conventional symptoms such as musculoskeletal and mucocutaneous manifestations, or patients with multiple domains involved, were at a lower risk of experiencing delays. Our findings contrast to the study done in Greece, where those with mucocutaneous manifestations were associated with delays (3). A likely difference between these studies was that we looked at patients in the population as a whole and patients seen by Dermatology and Nephrology in addition to Rheumatology, versus patients seen in a Rheumatology referral center as per the study in Greece. A study by Chang et al, which used administrative diagnostic codes to investigate health care utilization among SLE patients in the year before their diagnosis, found the longest delays among those with diagnostic codes for "Primary thrombocytopenia, unspecified" and for "Other venous embolism and thrombosis" (6). These findings align with the pattern of delay we observed in our study. Clinicians

should be aware of the association between hematologic and APS manifestations and a potential delay in SLE care. These might include assessing for SLE biomarkers such as anti-DNA, anti-Sm, or low complement in people with APS, cytopenias, or both. Our study has several key strengths. Utilizing a population-based cohort alongside a record linkage infrastructure enabled comprehensive tracking of all SLE manifestations from the earliest recorded classification criterion across various providers and care settings. This approach not only minimized referral bias but also ensured inclusion of patients across the entire severity spectrum, thereby reducing the risk of misclassification. Unlike studies based on surveys, our method was not susceptible to recall bias.

However, it is important to acknowledge certain limitations. First, our findings may not be generalizable to clinical settings outside the American Midwest. Individuals from more diverse backgrounds or from other geographic regions may experience different disease trajectories. Second, the rarity of some disease manifestations within our study's time frame may have resulted in insufficient statistical power for certain comparisons. Third, due to our study's retrospective design, we were constrained by the completeness of clinical documentation. Although not all manifestations of SLE were abstracted—limiting our focus to those listed in the EULAR/ACR SLE criteria—we believe this approach is justified by identifying the manifestations (and using the standardized definitions) that classify a patient as having SLE. These criteria involved a process to identify manifestations most representative of SLE, thereby supporting the robustness of our methodology and assuring generalizability. Fourth, our study spanned four decades, and assessing dynamic changes in social determinants of health longitudinally was not feasible. While we incorporated educational and demographic characteristics into the analysis, not all the social determinants of health were available.

In conclusion, our study provides valuable insights into the initial SLE manifestations and the care pathways of patients with new onset SLE. We uncovered significant heterogeneity in patients' care pathways, revealing that one-fourth of patients first sought SLE-specialized care outside of Rheumatology, and about one-fifth required initial hospitalization. Nearly one-quarter of patients experienced delays in access to SLE-specialized care, delays associated with damage accrual. These findings underscore the need for future research aimed at optimizing patient pathways and coordinated care strategies. Specifically, early identification of patients with the risk factors outlined in our study could lead to interventions designed to prevent irreversible damage.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement:

The data are available after reasonable request and ethical approval.

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Significance and Innovations

- The care pathways for patients with SLE, and related delays, were strongly influenced by the disease's clinical presentations. Specifically, the initial severity or sudden onset of clinical manifestations determined the health care providers involved and the settings in which patients received care.
- Rheumatology emerged as the main specialty by the time patients first accessed SLE-specialized care. However, as many as one-fourth were initially seen by Nephrology or Dermatology.
- One out of four patients experienced delays in access to SLE-specialized care, and these delays were associated with damage.
- Presentations characterized by hematologic or antiphospholipid antibodies domains, as well as fewer SLE manifestations at first SLE-related encounter, were associated with delays accessing SLE-specialized care.

Table 1.

Demographics and clinical characteristics of patients with systemic lupus erythematosus (SLE) at first SLE-related encounter.*

Characteristic	Value* (N=373)
Age, years, mean (SD)	42.8 (18.5)
Sex	
Female	300 (80)
Male	73 (20)
Race and ethnicity	
Non-Hispanic White	305 (82)
Asian	27 (7)
Hispanic	17 (5)
Non-Hispanic Black/African American	14 (4)
Other/Unknown	10 (2)
Educational level	
High school or less	140/363 (39)
Some college or greater degree	223/363 (61)
First SLE domains**	
Constitutional	11 (3)
Hematologic	114 (31)
Neuropsychiatric	1 (<1)
Mucocutaneous	66 (18)
Serosal	22 (6)
Musculoskeletal	92 (25)
Renal	8 (2)
Antiphospholipid antibodies	24 (6)
Complement proteins	31 (8)
Specific autoantibodies	100 (27)
Number of SLE domains	
1 domain	288 (77)
≥ 2 domains	85 (23)
Healthcare setting	
Outpatient care	308 (83)
Inpatient care	65 (17)
Specialty during first SLE-related encounter	
Internal Medicine and Subspecialties [†]	126 (34)
Family Medicine	121 (32)
Emergency Medicine	49 (13)
Surgical Specialties [‡]	19 (5)
SLE-specialized [¶]	44 (12)
Other [#]	14 (4)

Characteristic	Value [*] (N=373)
SLEDAI-2k, median (25 th – 75 th percentile) [*]	4 (2–8)
SDI, median (25 th – 75 th percentile) [*]	0 (0–0)
SDI ≥1 [*]	47 (13)

Abbreviations: SD, standard deviation; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index, measured at the time of access to SLE-specialized care; SLEDAI-2k, Systemic Lupus Erythematosus Disease Activity Index.

^{*} All characteristics measured at first SLE-related encounter except SLEDAI-2k and SDI which were measured at first access to SLE-specialized care. Values are n (%) or n/n tested (%) unless otherwise stated.

^{**} As per the 2019 EULAR/ACR classification criteria for SLE.

[†] Including: Hematology-Oncology, Infectious Diseases, Pulmonary Medicine, Cardiovascular Diseases, Community Internal Medicine, Internal Medicine Hospitalists, Occupational Medicine, and Women's Health.

[‡] Including: General Surgery, Orthopedic Surgery, Transplant Medicine, Vascular Medicine, Gynecology and Obstetrics, Ophthalmology, and Urology.

[¶] Including: Dermatology, Nephrology, and Rheumatology.

[#] Including: Psychiatry, Neurology, and Pediatrics.

Table 2. Systemic lupus erythematosus (SLE) manifestations up to the first access in SLE-specialized care.

Domain*, n (%)	Total who reached specialized care (N=365)	Rheumatology (N=274)	Dermatology (N=59)	Nephrology (N=32)	Never reached specialized care (N=8)	p-value**
Constitutional	15 (4)	14 (5)	1 (2)	0	0	0.371
Hematologic	124 (34)	95 (35)	15 (25)	14 (44)	3	0.188
Neuropsychiatric	3 (1)	3 (1)	0	0	0	1.000
Mucocutaneous	93 (25)	56 (20)	35 (59)	2 (6)	0	<0.001
Serosal	32 (9)	25 (9)	2 (3)	5 (16)	2	0.117
Musculoskeletal	130 (36)	126 (46)	2 (3)	2 (6)	3	<0.001
Renal	19 (5)	8 (3)	0	11 (34)	1	<0.001
Antiphospholipid antibodies	42 (12)	35 (13)	1 (2)	6 (19)	3	0.008
Complement proteins	79 (22)	59 (22)	8 (14)	12 (38)	2	0.030
Specific autoantibodies	161 (44)	134 (49)	12 (20)	15 (47)	6	<0.001

* As per the 2019 EULAR/ACR classification criteria for SLE.

** P-values are from Chi-square tests (or Fisher's Exact tests when counts less than 5 are present) comparing rheumatology versus dermatology versus nephrology.

Table 3.

Demographics, clinical manifestations, disease activity, and specialties according to delay in access to SLE-specialized care in a population-based cohort from a 27-county region of the American upper midwest.*

Characteristic	Delayed access to specialized care [†] (n=93)*	Without delays (n=280)*	p-value** *
Age, years, mean (SD)	42.7 (18.1)	42.9 (18.7)	0.965
Sex			0.252
Female	71 (76)	229 (82)	
Male	22 (24)	51 (18)	
Race and ethnicity			0.245
Non-Hispanic White	79 (86)	226 (81)	
Non-Hispanic Black/African American	2 (2)	12 (4)	
Asian	9 (10)	18 (6)	
Hispanic	1 (1)	16 (6)	
Other/Unknown	2 (2)	8 (3)	
Educational level			0.284
High school or less	39/90 (43)	101/273 (37)	
Some college or greater degree	51/90 (57)	172/273 (63)	
First SLE domain***			
Constitutional	3 (3)	8 (3)	1.000
Hematologic	36 (39)	78 (28)	0.049
Neuropsychiatric	0 (0)	1 (<1)	1.000
Mucocutaneous	5 (5)	61 (22)	<0.001
Serosal	8 (9)	14 (5)	0.201
Musculoskeletal	14 (15)	78 (28)	0.013
Renal	0 (0)	8 (3)	0.209
Antiphospholipid antibodies	15 (16)	9 (3)	<0.001
Complement proteins	3 (3)	28 (10)	0.049
Specific autoantibodies	14 (15)	86 (31)	0.003
Number of SLE domains			<0.001
1 domain	86 (92)	202 (72)	
≥ 2 domains	7 (8)	78 (28)	
SLEDAI-2k, median (25 th – 75 th percentile)	5 (4-8)	4 (2-8)	0.204
SDI, median (25 th – 75 th percentile)	0 (0-1)	0 (0-0)	<0.001
SDI ≥1	28 (30)	19 (7)	<0.001
Specialties seen before SLE-specialized care, median (25 th – 75 th percentile)	2 (1-3)	1 (1-2)	<0.001

Abbreviations: SD, standard deviation; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index, measured by the time of access to SLE-specialized care; SLEDAI-2k, Systemic Lupus Erythematosus Disease Activity Index.

* All characteristics measured at first SLE-related encounter except SLEDAI-2k, SDI, and Specialties seen before SLE-specialized care which were measured at first access to SLE-specialized care. Values are n (%) or n/n tested (%) unless otherwise stated.

*** As per the 2019 EULAR/ACR classification criteria for SLE.

*** Categorical variables are compared using Chi-square or Fisher's exact tests. Continuous variables are compared using rank-sum tests.

[†] Delays were defined as 6 months or more to reach access with specialized care.

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Table 4.

Factors at the first systemic lupus erythematosus (SLE)-related encounter associated with delay in access to SLE-specialized care (≥ 6 months) in patients with new onset SLE from the Lupus Midwest Network registry.

Characteristic	Odds Ratio ** (95% CI)
Calendar year (per 10 years increase)	0.73 (0.60, 0.88)
Demographics	
Age (per 10 years increase)	1.03 (0.90, 1.18)
Male sex	1.53 (0.84, 2.78)
Non-white race (n = 371)	0.86 (0.43, 1.72)
College or greater degree (n = 363)	0.79 (0.48, 1.29)
First SLE domains *	
Constitutional	1.00 (0.25, 3.96)
Hematologic	1.71 (1.03, 2.84)
Neuropsychiatric	-
Mucocutaneous	0.17 (0.06, 0.44)
Serosal	2.10 (0.82, 5.38)
Musculoskeletal	0.47 (0.25, 0.88)
Renal	-
Antiphospholipid antibodies	6.05 (2.46, 14.88)
Complement proteins	0.35 (0.10, 1.21)
Specific autoantibodies	0.44 (0.23, 0.82)
Number of SLE domains	
≥ 2 domains	0.23 (0.10, 0.52)
Healthcare settings	
Inpatient care (vs. outpatient)	0.87 (0.45, 1.68)
Specialty seen	
Family Medicine	(Reference)
Emergency Medicine	1.20 (0.55, 2.62)
Internal Medicine †	0.98 (0.53, 1.81)
Surgical specialties ‡	1.99 (0.71, 5.59)

* As per the 2019 EULAR/ACR classification criteria for SLE.

** Estimates and p-values are from adjusted univariable logistic regression assessing the association between the given variable of interest and delay after adjusting for age, sex and calendar year of SLE incidence.

† Internal medicine and subspecialties including Hematology-Oncology, Infectious Diseases, Pulmonary Medicine, Cardiovascular Diseases, Community Internal Medicine, Internal Medicine Hospitalists, Occupational medicine, Women's Health.

‡ Surgical specialties including General Surgery, Orthopedic Surgery, Transplant Medicine, Vascular Medicine, Gynecology and Obstetrics, Ophthalmology, Urology.