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Race, ethnicity, and disparities in risk of end-organ lupus manifestations following SLE diagnosis in a multiethnic cohort

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Abstract

Objective: Data on onset of lupus manifestations across multiple organ domains and in diverse populations is limited. We analyzed racial and ethnic differences in risk of end-organ lupus manifestations following systemic lupus erythematosus (SLE) diagnosis in a multiethnic cohort.

Methods: The California Lupus Epidemiology Study (CLUES) is a longitudinal study of SLE. Data on major end-organ lupus manifestations were collected and categorized by organ system: renal, hematologic, neurologic, cardiovascular, and pulmonary. Multiorgan disease was defined as manifestations in ≥2 of these distinct organ systems. Kaplan-Meier curves assessed end-organ disease-free survival, and Cox proportional hazard regression estimated the rate of end-organ disease following SLE diagnosis adjusting for age at diagnosis, sex, and self-reported race and ethnicity (White, Hispanic, Black, and Asian).

Results: Of 326 participants, 89% were female and had a mean age and age at diagnosis of 45 and 29 years, respectively. Self-reported race and ethnicity was 30% White, 23% Hispanic, 11% Black, and 36% Asian. Multiorgan disease occurred in 29%. Compared to White participants, Hispanic and Asian participants had higher rates of renal (HR 2.9 [95% CI 1.8–4.7], HR 2.9 [95% CI 1.9–4.6]), hematologic (HR 2.7 [95% CI 1.3–5.7], HR 2.1 [95% CI 1.0–4.2]), and multiorgan disease (HR 3.3 [95% CI 1.8–5.9], HR 2.5 [95% CI 1.4–4.4]) following SLE diagnosis.

Conclusion: We found heightened risks of developing renal, hematologic, and multiorgan disease following SLE diagnosis among Hispanic and Asian patients with SLE, as well as a high burden of multiorgan disease among CLUES participants.

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None.

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INTRODUCTION

Many racial and ethnic minority groups experience a disproportionate burden of systemic lupus erythematosus (SLE), including a greater incidence and prevalence of SLE (1,2), higher disease activity (3–5), worse organ damage (6–8), and heightened mortality as compared to White patients (9). Individuals in these groups also tend to develop lupus manifestations (including organ-threatening disease) earlier than White comparators (10). However, data on the onset of lupus manifestations after SLE diagnosis across multiple organ domains is limited, in particular among diverse racial and ethnic groups in the US.

Understanding how SLE disease trajectories differ by race and ethnicity addresses an important knowledge gap in lupus research. Prior studies have shown that racial and ethnic minority groups with SLE have a shorter time to accrual of ACR criteria (10,11), suggesting a more abrupt onset of SLE manifestations. Following a diagnosis of SLE, studies have also shown higher rates of end-organ lupus manifestations among racial and ethnic minority groups (10,12,13). These studies were limited in their capture of SLE-related outcomes as well as in the methods used to detect and confirm manifestations. In addition, details on the timing of onset of end-organ manifestations is lacking in Hispanic and Asian patients in the US, two relatively understudied groups with SLE.

In the present study, we examine disease trajectories among patients enrolled in a multiethnic cohort of SLE patients in the San Francisco Bay Area that collects data on a wide range of physician-confirmed health outcomes in multiple organ domains, and investigate racial and ethnic differences in the risk of renal, hematologic, neurologic, pulmonary, cardiovascular, and multiorgan disease following SLE diagnosis.

PATIENTS AND METHODS

Participants:

The California Lupus Epidemiology Study (CLUES) is a longitudinal study of individuals with physician-confirmed SLE in the San Francisco Bay Area. Initial recruitment was from the population-based California Lupus Surveillance Program (CLSP), a lupus registry funded by the Centers for Disease Control and Prevention that aimed to estimate the incidence and prevalence of SLE in San Francisco County (14). The CLSP identified individuals with SLE living in San Francisco during 2007–2009 from community and academic health centers as described previously (14). SLE was defined as either meeting ≥4 of the 11 American College of Rheumatology (ACR) revised criteria for the classification of SLE (15,16); 3/11 ACR criteria plus a rheumatologist's diagnosis of SLE; biopsy-proven lupus nephritis or medical record documentation of SLE along with dialysis or renal transplantation (14). Patients identified through this surveillance effort were invited to participate in the longitudinal CLUES cohort, which started enrollment in 2014. Additional participants were recruited from 2015–2018 through community and academic rheumatology clinics and local research networks outside of San Francisco County. At in-person study visits that included a history and physical examination performed by a lupus specialist, data on lupus manifestations and end-organ disease were collected, as well as laboratory analyses and biospecimen collection. A subset of the participants also

participated in a second in-person study visit conducted in the third year of CLUES enrollment, which updated lupus manifestation data. The CLUES study was approved by the University of California, San Francisco Institutional Review Board, and all participants provided written informed consent.

Race and ethnicity:

Participant race (White, Black or African-American, Asian, Native Hawaiian or Pacific Islander, American Indian or Alaska Native, or other) and ethnicity (Hispanic or non-Hispanic) were provided by self-report. For the purposes of this analysis, race and ethnicity was grouped into the following mutually exclusive categories: non-Hispanic White (hereafter, White); Hispanic of any race (Hispanic); non-Hispanic Black or African-American (Black); and non-Hispanic Asian, Native Hawaiian, or Pacific Islander (Asian). Six participants identifying as other or American Indian or Alaska Native were excluded from the analysis due to limited numbers.

Outcomes:

Manifestations including dates of onset were collected and confirmed by study rheumatologists, who are physicians specializing in the care of lupus, through in-person history and physical examinations and careful reviews of the medical record, including documentation in local electronic health record systems and outside hospital records. Musculoskeletal (inflammatory arthritis) and mucocutaneous disease (malar rash, oronasal ulcers, discoid lupus, subacute cutaneous lupus, bullous lupus, panniculitis) was recorded based on documentation of the above manifestations in the chart by a rheumatologist or dermatologist. Serositis was defined as symptomatic pleural or pericardial effusion confirmed by clinical evaluation, radiographs, or echocardiogram. Manifestations of end-organ disease were categorized into five organ domains based on the clinical definitions in Supplementary Table 1: renal (lupus nephritis), hematologic (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura), neurologic (seizure, stroke, peripheral/cranial neuropathy, mononeuritis multiplex, myelitis), cardiovascular (heart failure, myocardial ischemia/infarction, cardiac arrythmia, Libman-Sacks endocarditis), and pulmonary disease (interstitial lung disease, pulmonary hypertension). These manifestations were chosen to reflect internal organ involvement with significant implications for patients with respect to management and/or prognosis, encompassing both reversible and irreversible disease features. Multiorgan disease was defined as manifestations in ≥2 of the following distinct end-organ domains: renal, hematologic, neurologic, cardiovascular, and pulmonary disease. Participants with missing manifestation dates of onset for a particular organ system outcome were excluded from analysis of that respective organ system. Two study subjects died after baseline CLUES study visit; these individuals had multiorgan disease and were included in the analysis of end-organ disease outcomes.

Covariates:

Additional covariates of interest included sex and age at SLE diagnosis calculated from the year during which the participant met the SLE criteria as defined above. Additional socioeconomic variables at baseline CLUES visit included low income (<125% vs. ≥125%

federal poverty level adjusted for household size and income); marital status (never married; married or living with partner; divorced, separated or widowed); insurance (Medicaid, Medicare or San Francisco county-funded health plans vs. other insurance coverage); and education (high school education or less; associate degree or some college; college graduate or higher degree).

Statistical analysis:

Baseline characteristics of each racial and ethnic group were compared with one-way analysis of variance for continuous variables and chi-squared tests for categorical variables. Follow-up periods in years were defined for each participant beginning with SLE diagnosis (index date) and ending with the date of first end-organ manifestation for each organ system listed above. Subjects who did not develop the end-organ outcome of interest were right-censored at their last CLUES study visit. Participants may have developed end-organ disease prior to SLE diagnosis or in the first year of SLE diagnosis; these subjects with end-organ disease by the first year of SLE diagnosis were assumed to have developed the outcome on day 1 after the index date. For subjects with multiorgan disease, the follow-up period was defined from SLE diagnosis to the date of second end-organ system involved. Kaplan-Meier graphs and the log-rank test evaluated freedom from end-organ disease following SLE diagnosis by race and ethnicity. Multivariable Cox proportional hazard regression models assessed the rate of end-organ disease with age at diagnosis, sex, and race and ethnicity as covariates. Of note, Kaplan-Meier graphs and Cox regression were not conducted for the pulmonary disease outcome due to limited numbers. We confirmed the assumption of proportional hazards through analysis of Schoenfeld residuals.

The above analyses may have been biased by delays in SLE diagnosis. For this reason, and to assess factors associated with incident end-organ disease following SLE diagnosis, we conducted sensitivity analyses for the renal and multiorgan disease outcomes, which had the largest number of events, excluding participants who were diagnosed with end-organ disease before the first year of SLE diagnosis. In addition, to address the potential effect of survivor bias and differences between participants with short vs. long disease duration, we also performed Cox regression with age at diagnosis, sex, and race and ethnicity as covariates, stratifying by duration of SLE (<10 years vs ≥10 years). Lastly, we performed Cox regression for the renal and multiorgan outcomes adjusting for additional socioeconomic variables, such as low income, marital status, insurance, and education, as well as age at diagnosis, sex, and race and ethnicity. Statistical analyses were performed using STATA, version 16.1 (StataCorp, College Station, TX).

RESULTS

Patient characteristics:

A total of 332 participants enrolled in CLUES, and after excluding the 6 subjects who reported other or American Indian or Alaska Native race, 326 participants remained. The mean age at baseline was 45±14 years, and 289 (89%) were female (Table 1). The mean age at SLE diagnosis was 29 ±12 years, corresponding to a mean disease duration of 16 ±11 years with a total of 5433 person-years of follow-up. The distribution of self-reported race

and ethnicity was as follows: 97 (30%) White, 76 (23%) Hispanic, 35 (11%) Black, and 118 (36%) Asian. The three most common self-reported racial categories in the Hispanic group were other (54%), White (28%), and Asian (7%). Greater detail on country of origin was available for Asian patients; the three most common groups were Chinese (59%), Filipino (22%), and Korean (4%).

The most common physician-confirmed SLE manifestations were musculoskeletal (81%) and mucocutaneous (76%). In terms of end-organ disease, the most common manifestations were renal (51%), followed by hematologic (20%), neurologic (20%), cardiovascular (13%), and pulmonary (6%). Multiorgan disease was confirmed in 96 (29%) CLUES participants, of whom 71 (74%) had 2 involved organ systems, 23 (24%) had 3 involved organ systems, and 2 (2%) had 4 involved organ systems. Most participants with multiorgan disease had renal/hematologic disease (29%) and renal/neurologic disease (21%), followed by renal/cardiovascular disease (7%), and renal/hematologic/neurologic disease (7%). Renal disease was present in 83% of participants with multiorgan disease. As shown in Table 1, renal and multiorgan disease were more frequent in Hispanic and Asian participants as compared to White subjects ($p<0.001$ and $p=0.037$, respectively).

Time to onset of lupus end-organ and multiorgan disease:

The median (IQR) time to onset of renal, hematologic, neurologic, cardiovascular, pulmonary, and multiorgan disease in years following SLE diagnosis was 1 (7), 0 (8), 5 (14), 16 (20), 6 (18) and 6 (16) years, respectively. The proportion of participants who developed end-organ disease by the first year of SLE diagnosis varied by end-organ outcome: 45% for renal, 54% for hematologic, 39% for neurologic, 18% for cardiovascular, 32% for pulmonary, and 25% for multiorgan disease (Figure 1). Missing date of onset data for end-organ disease outcomes ranged from 0 participants for the multiorgan disease outcome to 6 participants for the renal disease outcome; these participants were excluded from analysis of that respective organ system.

Kaplan-Meier curves for each end-organ disease outcome were constructed to investigate racial and ethnic differences in time to major SLE manifestations (Figures 2 and 3). As assessed by the log-rank test, there were statistically significant differences in end-organ disease-free survival by race and ethnicity for renal ($p<0.001$), hematologic ($p=0.02$), and multiorgan disease ($p<0.001$), but not neurologic ($p=0.59$) or cardiovascular disease ($p=0.50$).

Cox regression models assessed the relationship between race and ethnicity and risk of end-organ and multiorgan disease after adjusting for age at diagnosis and sex (Table 2). Compared to White study subjects, Hispanic participants had higher rates of renal disease (HR 2.93 [95% CI 1.82–4.71]), hematologic disease (HR 2.72 [95% CI 1.29–5.71]), and multiorgan disease (HR 3.28 [95% CI 1.83–5.89]) after SLE diagnosis. Asian participants also had higher rates of renal (HR 2.92 [95% CI 1.87–4.55]), hematologic (HR 2.07 [95% CI 1.01–4.23]), and multiorgan disease (HR 2.51 [95% CI 1.43–4.39]) compared to White patients. There were no statistically significant associations between race and ethnicity and the neurologic or cardiovascular disease outcomes. Female sex was associated with lower rates of renal disease compared to male sex (HR 0.43 [95% CI 0.28 – 0.66]). Age at

diagnosis (per 1-year increase) was associated with lower rates of renal and hematologic disease, but higher rates of neurologic and cardiovascular disease.

In sensitivity analyses, we excluded participants who developed renal or multiorgan disease by the first year of SLE diagnosis; this did not significantly change the associations between race and ethnicity and risk of end-organ disease for either outcome (data not shown). In addition, we performed Cox regression stratified by SLE disease duration (<10 years vs ≥10 years) for the renal and multiorgan disease outcomes; however, this did not significantly alter our findings (data not shown). The inclusion of additional socioeconomic variables, such as low income, marital status, insurance, and education in Cox regression models for the renal and multiorgan disease outcomes attenuated but did not abrogate the associations between race and ethnicity and risk of end-organ disease (data not shown).

DISCUSSION

To our knowledge this is the most comprehensive study on the relationship between race and ethnicity and time to onset of end-organ manifestations of SLE. Renal and hematologic disease were closely associated with early SLE, while neurologic and cardiovascular disease occurred later in the disease course. Following SLE diagnosis, Hispanic and Asian patients experienced a two-to-threefold higher rate of renal and hematologic disease compared to White participants; in addition, Hispanic and Asian patients developed these manifestations sooner after SLE diagnosis. We also observed multiorgan disease in nearly one-third of patients, with a higher burden of multiple organ involvement among Hispanic and Asian individuals.

This study sheds light on interesting temporal trends in SLE disease trajectories. Renal and hematologic disease tend to occur early in the disease course, with half of participants developing lupus nephritis or hematologic manifestations within the first year after diagnosis. The early onset of these organ manifestations has been observed in older studies of SLE (17), and interestingly, similar trends continue to be observed in the contemporary era (3). In CLUES, two-thirds of patients were diagnosed with SLE in 1997 or later, potentially highlighting the abrupt onset of renal and hematologic disease in a subset of lupus patients and/or continued unmet needs in early diagnosis of this complex illness. On the other hand, neurologic disease developed throughout the disease course in CLUES participants. This may reflect various factors, including distinct pathophysiologic and immunologic mechanisms or the inclusion of vascular manifestations such as stroke which may be more associated with age, cardiovascular comorbidities, and long-standing inflammation. Likewise, cardiovascular disease tended to occur later in the disease course, with a median time to onset of 16 years, likely reflecting the preponderance of disorders such as myocardial infarction and heart failure. Not surprisingly, renal and hematologic disease tended to present in younger patients, with neurologic and cardiovascular disease both associated with increasing age at diagnosis.

The onset of manifestations such as renal and hematologic disease early in the disease course has been observed with greater frequency in racial and ethnic minority groups. Prior research on SLE cohorts has shown that Hispanic ethnicity is associated with younger age

at onset and shorter time to accrual of SLE classification criteria (10,11), as well as elevated disease activity (3,5) and heightened risk of organ-threatening lupus (6,10,18,19). In our study on the CLUES cohort, lupus nephritis was documented in 66% of Hispanic individuals vs. 29% of White patients. Hispanic participants had an almost threefold increased hazard of developing lupus nephritis (HR 2.9), as well as hematologic manifestations (HR 2.7) compared to White individuals with SLE, suggesting that these patients develop serious renal and hematologic manifestations faster than White comparators. This is an important observation, as both lupus nephritis and hematologic disease are indicators of worse prognosis in SLE (20,21). Of note, the Hispanic population comprises individuals with diverse racial and ethnic backgrounds, and as prior research on Hispanic patients with SLE has shown, self-reported ancestry within this group is also associated with lupus phenotype and severity (22,23).

A heightened risk of end-organ manifestations after lupus diagnosis was also observed among Asian participants in CLUES. Asian individuals with SLE tend to develop disease at a younger age (24,25) and have a higher prevalence of renal involvement (25–27) and renal damage (24,25). However, data on outcomes in Asian patients is mixed. Earlier investigations in the US during the 1960–1970s found marked disparities in SLE-related mortality among Asian or Pacific Islander SLE patients (28,29). More recent studies have found that overall Systemic Lupus International Collaborating Clinics Damage Index (SDI) scores and mortality are comparable to White patients with SLE (24,25,27,30). Nevertheless, studies on hospitalizations in California in the 1990s and the National Inpatient Sample database between 2006–2016 revealed elevated in-hospital mortality among Asian individuals with SLE as compared to White comparators (31,32). Asian patients may have more severe disease trajectories than White patients. One study which primarily recruited patients from a tertiary care hospital in the Bay Area of California from 1997–2000 observed a higher proportion and more rapid onset of lupus nephritis in Asian patients (12). Subsequently, our group reported results of an analysis of registry data from the California Lupus Surveillance Project collected from 2007–2009, which found that Asian patients (as well as Hispanic and Black patients) had greater risks of developing lupus nephritis, thrombocytopenia, and antiphospholipid antibody syndrome (13). Our study reinforces the growing evidence of severe disease among Asian patients, who experienced greater hazards of lupus nephritis and hematologic manifestations following SLE diagnosis. This may not be generalizable to all Asian individuals, as the majority of our cohort self-identified as Chinese or Filipino. Further studies are needed to investigate longitudinal health outcomes in Asian or Pacific Islander patients in the US, with detailed data on disease trajectories, disease activity, organ damage, and mortality.

The findings presented thus far on the burden of severe SLE among Asian and Hispanic populations serve a major goal of lupus research: to identify patients who are at risk for severe disease trajectories. In the same vein, a striking observation in this study was the racial and ethnic disparity in multiorgan disease, defined as involvement of two or more distinct end-organ system domains during the disease course. The motivation for this categorization was to identify a subset of patients with severe SLE, and we included manifestations that are either indicators of poor prognosis and/or require immunosuppression for management. Nearly one-third of patients had multiorgan disease

defined in this manner, although in Hispanic and Asian participants, multiorgan involvement occurred in 39% and 32%, respectively. Multiorgan disease could occur throughout a patient's disease course, as assessed by inspection of the Kaplan-Meier curve (Figure 3), with a median onset of 6 years following SLE diagnosis. This likely reflects the combined effect of inflammatory manifestations in early SLE (e.g., renal and hematologic disease) and the sequelae of long-term comorbidities and inflammation (e.g., cardiovascular disease). Hispanic and Asian patients developed multiorgan involvement earlier than White patients (HR 3.3 and HR 2.5, respectively). The most common form of multiorgan disease was renal/hematologic, followed by renal/neurologic, disease manifestation clusters that have been observed previously (33–35) and which may be enriched with individuals of non-European ancestry as our study suggests.

Multiple organ involvement in SLE is relatively understudied, but prior research has approached this topic from various perspectives. For instance, organ damage assessment captures chronic sequelae of SLE or its treatment over time. The standard measure of organ damage, the SDI, tends to include only a limited set of disorders present for at least six months since SLE diagnosis and may not be sensitive for certain populations with a particular set of disease manifestations, as shown in a recent study on disease activity and organ damage in Asian CLUES participants (36). Prior research has observed increased organ damage among Black individuals versus White comparators (6), although data on Hispanic and Asian populations has been mixed (6,7,36). Other studies have focused on co-existing medical and psychiatric diseases in SLE, and an increasing number of comorbidities has been associated with reduced quality of life (37), greater hospitalizations (38), and mortality (39). More research is needed to better characterize the epidemiology, determinants, and consequences of multiorgan disease in SLE.

The causes of these disparities in SLE disease presentation are multifactorial and complex, and additional studies will be needed to investigate the contributions of social and biologic factors leading to disparate disease outcomes. Possible sociodemographic factors include access to care (40), treatment adherence (41), poverty (42), and racial discrimination (43). These factors are dynamic, and thus may have a complex relationship with SLE onset and disease severity. There is also indisputable evidence for a genetic predisposition to develop SLE, although the role of specific risk variants or epigenetic signatures in the susceptibility to specific end-organ manifestations is poorly understood (44).

One of the strengths of this study was that we were able to collect detailed data on a wide variety of internal organ manifestations across multiple organ domains. We included common but also uncommon syndromes such as thrombotic thrombocytopenic purpura and transverse myelitis. These manifestations were also collected and confirmed by detailed review of medical records by study rheumatologists who specialize in lupus. Our study benefits from inclusion of manifestations with significant management and prognostic implications for individuals with SLE, even though some disease processes (e.g., myocardial ischemia) have a complex relationship to SLE and are likely influenced by multiple mechanisms.

There were several important limitations in this study. First, results from the CLUES cohort may not be generalizable to other populations with SLE. CLUES recruitment was based on an epidemiologic surveillance effort to identify SLE cases in the San Francisco Bay Area, but was supplemented by enrollment of patients actively linked to medical care in local health centers, which may have biased the sample. The small number of Black participants in CLUES also limits conclusions drawn about this population, and may explain the lack of association between Black race and end-organ disease. In addition, patient survival from SLE diagnosis to CLUES enrollment may have differed by race and ethnicity; although stratifying Cox regression by SLE disease duration did not significantly alter our main findings, survivor bias may still have skewed our observations. Second, our analysis of the role of socioeconomic factors in end-organ disease is limited, as this data was collected at time of CLUES visit, so may reflect the sequelae of living with severe SLE. Race, ethnicity, and sex may have complex relationships to delays in SLE diagnosis, which could have impacted temporal assessments of end-organ disease onset (45). While diagnostic delays were not measured specifically, a sensitivity analysis excluding patients with end-organ lupus manifestations prior to or at SLE diagnosis did not significantly alter results for the renal and multiorgan disease outcomes. Third, the targeted medical chart review and patient interview conducted by study rheumatologists to document end-organ disease may have missed or misclassified certain manifestations.

In summary, our study demonstrates that temporal trends in the onset of SLE end-organ manifestations following SLE diagnosis vary by race and ethnicity, with striking disparities in Hispanic and Asian patients, who are at higher risk of developing renal, hematologic, and multiorgan disease as compared to White patients. Our study in particular highlights the burden of multiorgan involvement in Hispanic and Asian participants, which warrants further study to delineate the health impacts of severe, multiorgan SLE in these populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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SIGNIFICANCE AND INNOVATIONS

- In this study conducted on a multiethnic lupus cohort, we examined the relationship between race and ethnicity and onset of end-organ manifestations of SLE.
- Compared to White study subjects, Hispanic and Asian participants experienced a two-to-threefold higher rate of renal and hematologic disease following SLE diagnosis.
- Renal and hematologic disease tended to occur in early SLE, with faster time to onset among Hispanic and Asian patients, while neurologic and cardiovascular disease occurred later in the disease course.
- Multiorgan involvement in SLE was common, affecting up to one-third of participants, with a higher burden and faster time to onset observed among Hispanic and Asian individuals.

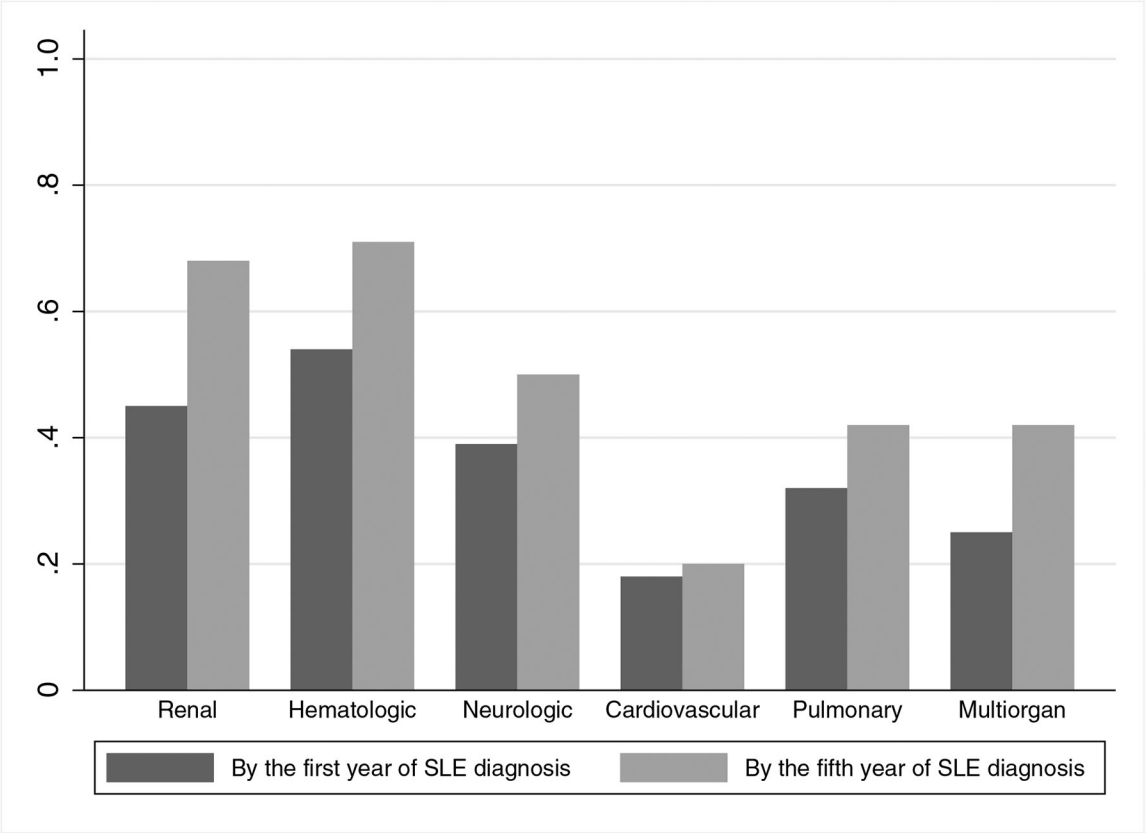

Figure 1: Proportion of participants diagnosed with end-organ disease by the first year and by the fifth year of SLE diagnosis, by organ system domain.

Graph depicts the proportion of participants diagnosed with renal, hematologic, neurologic, cardiovascular, pulmonary, and multiorgan disease by the first year and by the fifth year of SLE diagnosis, including participants diagnosed with end-organ disease prior to SLE diagnosis. Categories of end-organ disease were defined by specific manifestations as follows: renal disease (lupus nephritis), hematologic disease (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura), neurologic disease (seizure, stroke, peripheral/cranial neuropathy, mononeuritis multiplex, myelitis), cardiovascular disease (heart failure, myocardial ischemia/infarction, cardiac arrythmia, Libman-Sacks endocarditis), pulmonary disease (interstitial lung disease, pulmonary hypertension), and multiorgan disease (manifestations in ≥2 of the following distinct end-organ domains: renal, hematologic, neurologic, cardiovascular, and pulmonary disease).

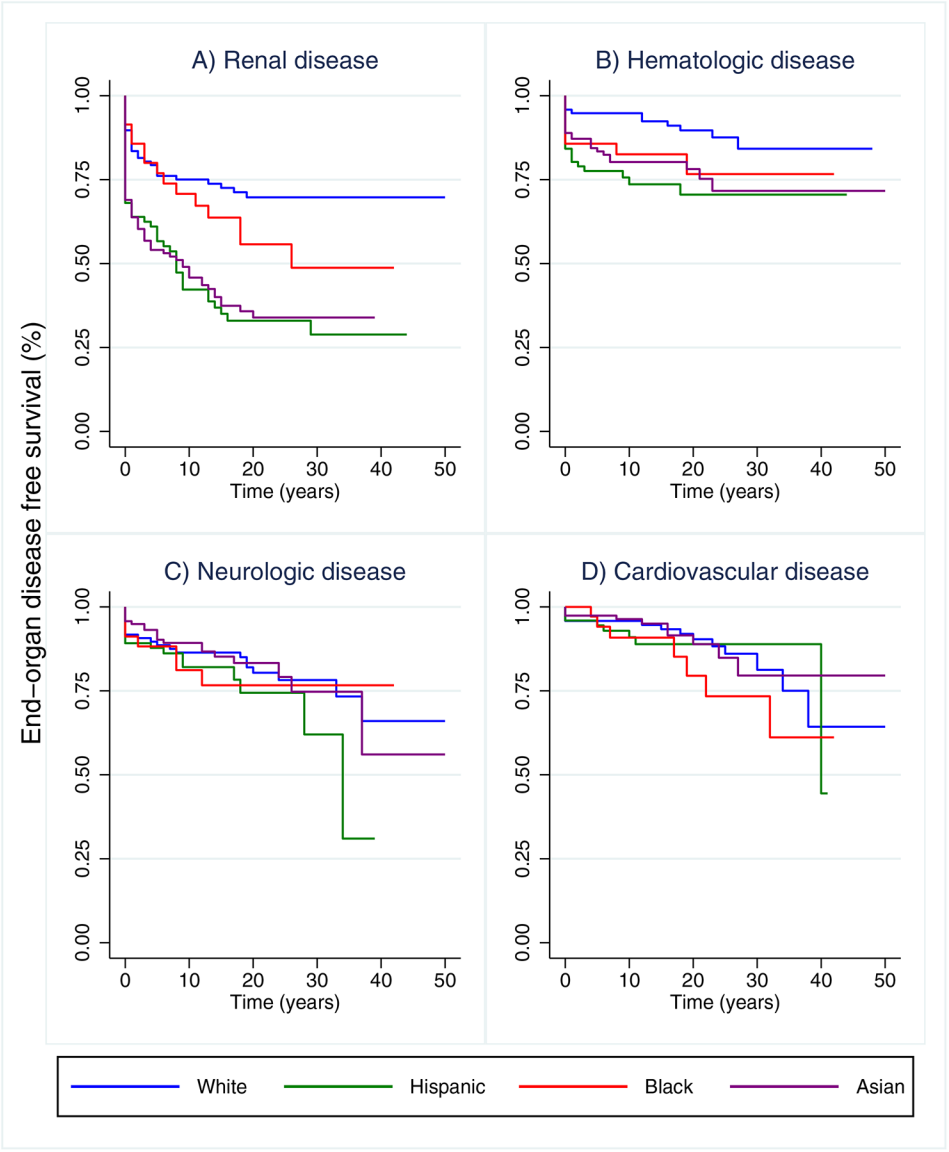

Figure 2: Time to onset of end-organ disease following SLE diagnosis in the CLUES cohort by race and ethnicity.

Kaplan-Meier curves depict time to onset of end-organ disease following SLE diagnosis, stratified by race and ethnicity. 2A) renal disease (lupus nephritis); 2B) hematologic disease (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura); 2C) neurologic disease (seizure, stroke, peripheral/cranial neuropathy, mononeuritis multiplex, myelitis); 2D) and cardiovascular disease (heart failure, myocardial ischemia/infarction, cardiac arrythmia, Libman-Sacks endocarditis).

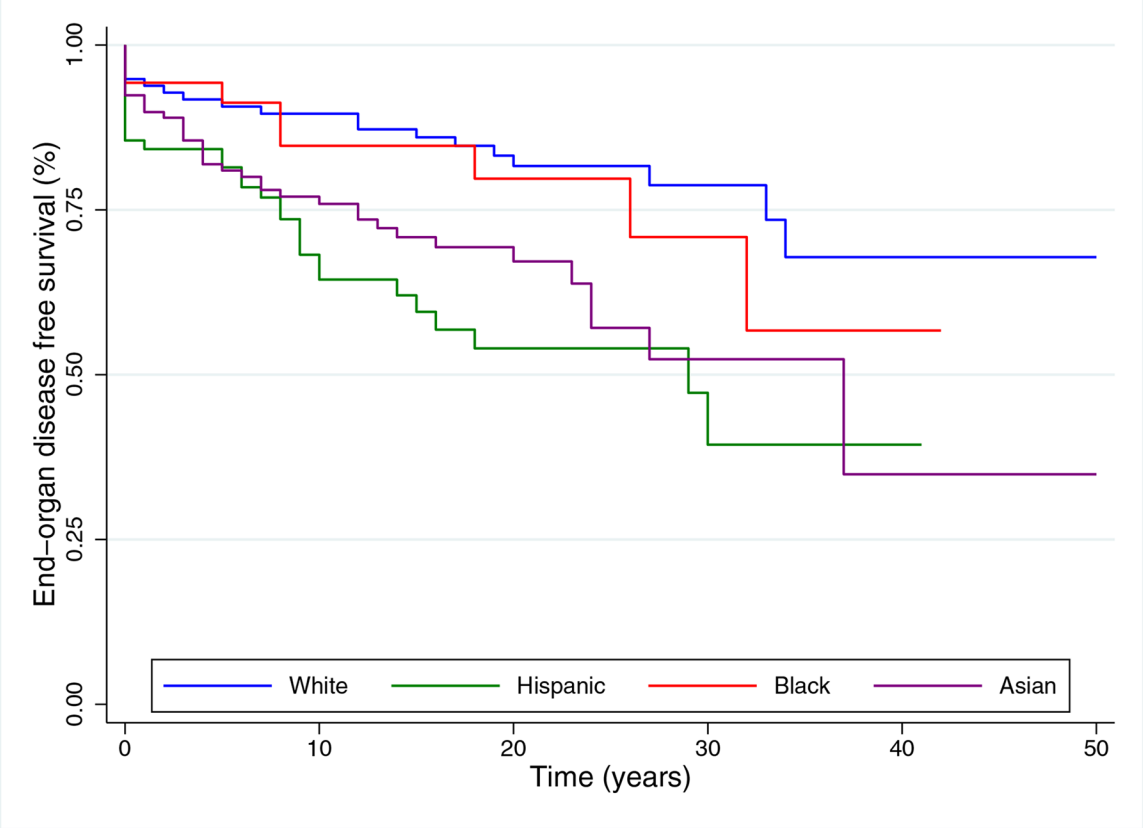

Figure 3: Time to onset of multiorgan disease following SLE diagnosis in the CLUES cohort by race and ethnicity.

The Kaplan-Meier curve depicts time to onset of multiorgan disease following SLE diagnosis, stratified by race and ethnicity. Multiorgan disease was defined as manifestations in ≥2 of the following distinct end-organ domains: renal, hematologic, neurologic, cardiovascular, and pulmonary disease.

Table 1:

Demographic and clinical characteristics of the CLUES cohort, by race and ethnicity

Characteristic*	Total N=326	White** N=97	Hispanic N=76	Black N=35	Asian N=118	p-value
Age, mean years (SD)	44.9 (13.9)	50.2 (12.0)	41.0 (13.2)	49.7 (13.5)	41.7 (14.3)	<0.001
Sex, female	289 (89)	85 (88)	65 (86)	35 (100)	104 (88)	0.15
Age at diagnosis, mean years (SD)	28.8 (12.2)	29.2 (11.0)	27.3 (11.1)	33.3 (11.6)	28.0 (13.7)	0.082
Manifestations by organ system†						
Mucocutaneous	249 (76)	77 (79)	53 (70)	26 (74)	93 (79)	0.42
Musculoskeletal	263 (81)	81 (84)	64 (84)	31 (89)	87 (74)	0.10
Serositis	94 (29)	27 (28)	27 (36)	14 (40)	26 (22)	0.090
Renal	165 (51)	28 (29)	50 (66)	15 (43)	72 (61)	<0.001
Hematologic	65 (20)	12 (12)	20 (26)	7 (20)	26 (22)	0.12
Neurologic	65 (20)	20 (21)	18 (24)	8 (23)	19 (16)	0.58
Cardiovascular	44 (13)	15 (15)	10 (13)	7 (20)	12 (10)	0.44
Pulmonary	21 (6)	3 (3)	6 (8)	0	12 (10)	0.066
Multiorgan disease‡	96 (29)	20 (21)	30 (39)	8 (23)	38 (32)	0.037

*Results are n (%) unless otherwise specified.

**Race and ethnicity was categorized as non-Hispanic White (White), Hispanic of any race (Hispanic), non-Hispanic Black or African-American (Black); and non-Hispanic Asian, Native Hawaiian, or Pacific Islander (Asian).

†Manifestations were categorized into the following organ system domains: mucocutaneous (malar rash, mucosal ulcers, discoid lupus, subacute cutaneous lupus, bullous lupus, panniculitis), musculoskeletal (inflammatory arthritis), serositis (pericarditis or pleuritis), renal (lupus nephritis), hematologic (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura), neurologic (seizure, stroke, peripheral/cranial neuropathy, mononeuritis multiplex, myelitis), cardiovascular (heart failure, myocardial ischemia/infarction, cardiac arrythmia, Libman-Sacks endocarditis), and pulmonary (interstitial lung disease, pulmonary hypertension).

‡Multiorgan disease was defined as manifestations in ≥2 of the following distinct end-organ domains: renal, hematologic, neurologic, cardiovascular, and pulmonary disease.

Table 2:

Factors associated with risk of renal, hematologic, neurologic, cardiovascular, and multiorgan disease following SLE diagnosis, adjusting for age at diagnosis, sex, and race and ethnicity

Characteristic*	Renal†	Hematologic	Neurologic	Cardiovascular	Multiorgan‡
Age at diagnosis	0.99 (0.97–1.00)	0.96 (0.93–0.98)	1.02 (1.00–1.04)	1.03 (1.00–1.06)	1.01 (0.99–1.02)
Sex, female	0.43 (0.28–0.66)	0.94 (0.43–2.08)	0.92 (0.42–2.04)	0.78 (0.27–2.25)	0.62 (0.34 – 1.13)
Race and ethnicity					
White	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Hispanic	2.93 (1.82–4.71)	2.72 (1.29–5.71)	1.57 (0.80–3.08)	1.33 (0.55 – 3.25)	3.28 (1.83 – 5.89)
Black	1.89 (1.00–3.57)	2.36 (0.91–6.15)	1.15 (0.48–2.77)	1.77 (0.69 – 4.54)	1.44 (0.63 – 3.34)
Asian	2.92 (1.87–4.55)	2.07 (1.01–4.23)	1.05 (0.55–1.98)	1.08 (0.47 – 2.48)	2.51 (1.43 – 4.39)

*Hazard ratio (95% confidence interval), estimated using multivariable Cox regression including age at diagnosis (per 1 year increase), sex, and race and ethnicity as covariates. Ref., reference category.

†Categories of end-organ disease were defined by specific manifestations as follows: renal (lupus nephritis), hematologic (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura), neurologic (seizure, stroke, peripheral/cranial neuropathy, mononeuritis multiplex, myelitis), cardiovascular (heart failure, myocardial ischemia/infarction, cardiac arrythmia, Libman-Sacks endocarditis), and pulmonary (interstitial lung disease, pulmonary hypertension).

‡Multiorgan disease was defined as manifestations in ≥2 of the following distinct end-organ domains: renal, hematologic, neurologic, cardiovascular, and pulmonary disease.