Update on lupus epidemiology: advancing health disparities research through the study of minority populations

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Purpose of review
The current review focuses on recent population-based studies that have examined the burden of lupus, disease outcomes, and gaps in quality of care, with an emphasis in research addressing health disparities.

Recent findings
The Centers for Disease Control and Prevention National Lupus Registries underscored higher susceptibility of both systemic lupus erythematosus (SLE) and primary cutaneous lupus among people of color, compared with whites. Not only does SLE disproportionately strike people from racial and ethnic minorities, those individuals are also at increased risk of developing severe manifestations following SLE diagnosis. Mortality is higher and death occurs at a younger age among blacks, compared with whites. Furthermore, ongoing Centers for Disease Control and Prevention-supported population-based lupus cohorts, along with research by other groups, have provided new insight into the role of social determinants on outcomes and opportunities to improve care in diverse lupus populations.

Summary
While descriptive epidemiological efforts have been critical to providing more accurate estimates of the burden and mortality of lupus across diverse demographic groups, emerging research suggests a significant influence of psychosocial and healthcare system factors on disease outcomes. These current efforts represent important steps toward the development of clinical and public health interventions aimed at eliminating health disparities in lupus populations.

Keywords
epidemiology, lupus, minorities, racial disparities, systemic lupus erythematosus

INTRODUCTION
In the past years, the Centers for Disease Control and Prevention (CDC) have supported a variety of national lupus activities (https://www.cdc.gov/lupus/funded/index.html), including five registries designed to study US-based populations diagnosed with systemic lupus erythematosus (SLE) or cutaneous lupus. Providing more accurate estimates of the burden of lupus, the CDC lupus registries continued to underscore substantial racial disparities across US populations. As SLE severity is worse and mortality remains high among minority groups, new epidemiological efforts, including three longitudinal population-based cohorts formed from the CDC-funded registries, are providing novel insights into the natural history of both SLE and cutaneous lupus across racially and ethnically diverse populations. This review focuses on studies that have examined the burden, mortality, outcomes, and quality of care in US populations with lupus, with emphasis on those that provide insights into health disparities.

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ADVANCING LUPUS HEALTH DISPARITIES RESEARCH IN THE UNITED STATES THROUGH THE CENTERS FOR DISEASE CONTROL AND PREVENTION NATIONAL LUPUS REGISTRIES

The CDC National Lupus Registries were created from an unprecedented national lupus surveillance project aimed at addressing the limitations of previous epidemiologic data, particularly in racial/ethnic minority populations in the United States. Established in selected counties of Georgia, Michigan, California, New York, and at selected Indian Health Service regions, the five sites used similar methods while taking advantage of novel federal, state, and local partnerships with academic institutions (Table 1). The public health surveillance exemption to the Health Insurance Portability and Accountability Act Privacy Rule (https://www.hhs.gov/hipaa/for-professionals/privacy/index.html) allowed investigators to obtain protected health information without written patient consent, which enabled investigators to maximize case ascertainment, determine if potential cases met case definition criteria, and provide enough information to prevent duplicate counting of patients examined in multiple facilities. Primary sources of cases included queries of administrative databases from hospitals, physician offices, as well as laboratories and population databases. The primary aims of the registries were to obtain updated and more accurate incidence and prevalence rates of SLE, which have been published in the past 5 years [1–5,6,7,8].

Racial and ethnic differences were recently analyzed in lupus manifestations and in the timing and risk of developing severe manifestations in the California Lupus Surveillance Project (CLSP) [9]. This was the first epidemiologic study of lupus comparing manifestations among the four-major racial/ethnic groups in the United States: blacks, whites, Asian/Pacific Islanders (APIs), and Hispanics. Among 724 patients with SLE; the authors found substantial differences in the prevalence of several clinical manifestations between groups. Data indicated that blacks, APIs, and Hispanics are at increased risk of developing severe manifestations following SLE diagnosis. Blacks and APIs had a higher prevalence of lupus nephritis (20 and 52%, respectively), compared with 13–14% among the other groups, and thrombocytopenia (24 and 39%, respectively), compared with 17–19% among the other groups. Neuropsychiatric lupus was less

**Table 1. The National Lupus Registries supported by the Centers for Disease Control and Prevention in the United States**

| Registry (partner) | Public health authority | Surveillance area or health system | Population at risk | Type of lupus | Main racial/Ethnic group | Surveillance period |
|-------------------|-------------------------|-----------------------------------|-------------------|-------------|------------------------|---------------------|
| GLR (Emory University) [1,6] | GA Department of Public Health | Fulton and DeKalb Counties, GA | 1552 970 | SLE, CCLE | White and Black | 2002–2004 |
| MILES (UM) [2,7] | MI Department of Community Health | Wayne and Washtenaw Counties, MI | ~2400 000 | SLE | White and Black, Arab and Chaldean Americans | 2002–2004 |
| MLSP (NYU) [4] | NY City Department of Health | New York County, NY (Borough of Manhattan) | 1585 873 | SLE | White, Asian/Pacific Islander, Hispanic, Black | 2007–2009 |
| CLSP (UCSF) [5] | CA Department of Public Health | San Francisco County, CA | 790 582 | SLE | White, Asian/Pacific Islander, Hispanic, Black | 2007–2009 |
| IHS Lupus Registry (ANTHC) [3,8] | Indian Health Service | IHS Data Warehouse of Alaska, Phoenix & Oklahoma City Areas | 211,916 | SLE, MCTD | American Indian/Alaska Native | 2007–2009 |

ANTHC, Alaska Native Tribal Health Consortium; CA, California; CCLE, chronic cutaneous lupus erythematosus; CLSP, California Lupus Surveillance Project; GA, Georgia; GLR, Georgia Lupus Registry; IHS, Indian Health Service; MCTD, mixed connective tissue disease; MI, Michigan; MILES, Michigan Lupus Epidemiology & Surveillance Program; MLSP, Manhattan Lupus Surveillance Project; NY, New York; NYU, New York University; SLE, systemic lupus erythematosus; UCSF, University of California, San Francisco; UM, University of Michigan.
common among Hispanics, and antiphospholipid syndrome was more common among APIs. Blacks, APIs, and Hispanics were at increased risk of developing lupus nephritis, thrombocytopenia, and antiphospholipid syndrome earlier than whites following SLE diagnosis.

Given the methodology of the CDC registries, other forms of lupus and associated conditions have been evaluated, including mixed connective tissue disease in the American Indian/Alaska Native population [8]. More recently, minimum estimates of the incidence of primary chronic cutaneous lupus erythematosus (CCLE) from the Georgia Lupus Registry (GLR) have been published [6*]. Findings uncovered striking racial disparities in the susceptibility of CCLE, with blacks having a three-fold to five-fold increased risk, compared with white people, depending on the case definition. Black/white disparities in the incidence of CCLE were analogs to those described thorough the GLR for SLE in the same geographic area [1]. Moreover, data suggest that black/white disparities may also concern the age at CCLE diagnosis, with blacks tending to develop CCLE at earlier ages compared with whites, as noted with SLE in the same population [1].

MORTALITY IN LUPUS

The power of the CDC registries can be extended beyond the initial surveillance periods through matching with other population-based databases and leveraging identification of nearly all validated SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment. Incident and prevalent SLE cases in an area without reliance on administrative data for case ascertainment.

There were other significant studies of mortality in SLE. In 2017, a nationwide population-based study of the United States from the 1968 through 2013 used death certificate data from the CDC’s WONDER (Wide-ranging Online Data for Epidemiologic Research) database and found age-standardized mortality rates over time decreased in SLE, but remained high relative to non-SLE mortality, with higher mortality rates in females, blacks, and residents of the South and West [11]. The same authors utilized the death certificate data from the CDC’s WONDER database and the leading causes of death data from the Web-based Injury Statistics Query and Reporting System database from 2000 to 2015 to rank organic causes of deaths of females of reproductive age by race/ethnicity and age [12]. After excluding the external injury causes of death, namely, unintentional injury, homicide, and suicide from the analysis, the study showed that SLE is among the leading causes of death in young females. For females of all races/ethnicities, SLE ranked seventh as the leading cause of death among females ages 15–24 years and eleventh among both those ages 25–34 years and those ages 35–44 years. Among black and Hispanic females, the rankings for SLE were higher: fifth, sixth, and eighth or ninth among females’ ages 15–24, 25–34, and 35–44 years, respectively.

Using the 2014 National Center for Health Statistics multiple causes of death database, a population-based electronic medical recording of all death certificates issued in the United States and its territories, sex-stratified demographic characteristics and the most commonly listed comorbidities in decedents with and without SLE were compared [13]. Out of 2036 decedents with SLE, 86.2% were females, who were 22 years younger than non-SLE female decedents. The difference was 12 years among male decedents. These data continue to underscore the disproportionate impact of female sex on premature mortality in SLE. There were differences in the most frequently listed causes of deaths between female and male SLE decedents. Septicemia (4.32%) and hypertension (3.04%) were the most common in males. Heart disease (3.70%) and diabetes mellitus with complications (3.61%) were the most common in females. Though these are the same leading comorbid conditions observed in the general population, the sex differential in SLE may help focus efforts to minimize premature SLE mortality.

A prior study observed concurrent poverty and persistent poverty were associated with damage accrual, while exiting poverty was associated with lower levels of accumulated damage [14*]. Building on the same data source, the Lupus Outcomes Study, the authors evaluated 807 completed interviews...
from 2009 for the effect of poverty on mortality from 2009 to 2015 [15]. Cox proportional hazards regression was used to estimate the impact of poverty on other variables on risk of all-cause mortality. The association of mortality risk with poverty adjusted for age was significant (hazard ratio 2.14; 95% confidence interval 1.18–3.88) but lost significance when level of damage was introduced. This suggested that poverty resulted in higher mortality in SLE by increasing damage accumulation. In addition to improving medical care, the authors suggested that potential strategies to reduce damage must include reducing stress associated with poverty, improving access to affordable food and house, improving coping abilities, and aiding transition to better neighborhoods.

THE CENTERS FOR DISEASE CONTROL AND PREVENTION POPULATION-BASED LUPUS COHORTS

The CDC National Lupus Registries established a strong foundation to advance our understanding of lupus outcomes in racially/ethnically diverse populations. Those efforts have been lately galvanized by the creation of three CDC-supported longitudinal cohorts of adults with diagnosed SLE and cutaneous lupus, which are primarily derived from the five national registries:

The Michigan Lupus Epidemiology & Surveillance (MILES) Program Cohort and Biobank has been developed from the CDC-supported population-based lupus registry, which has been established in Detroit and Ann Arbor, encompassing a large white and black population of individuals with SLE. The overarching goal of the cohort is to prospectively collect data and biospecimens to conduct investigations related to risk factors for lupus onset, progression, and comorbidities. Major thematic areas of the MILES Cohort & Biobank include epigenetics, environmental epidemiology, and renal lupus.

The Georgians Organized Against Lupus (GOAL) Cohort was born out of the efforts of the GLR to create a population-based prospective cohort of validated SLE and cutaneous lupus patients, reflecting ‘real world’ lupus in and around metropolitan Atlanta, Georgia, where half of the population is African-American or black. The ongoing GOAL Cohort encompasses over 1000 individuals with validated diagnosis of SLE and nearly 130 with a dermatologist-documented diagnosis of chronic cutaneous lupus confined to the skin. Through the longitudinal collection of a broad battery of patient-reported outcomes and biospecimens and matching of participants with other population databases (e.g., US Renal Data System; US National Death Index; Georgia Comprehensive Cancer Registry; Georgia Hospital Discharge Database; Georgia Birth Records), GOAL is exploring how social determinants of health interact with biologic factors to influence natural history, treatment, and healthcare access through the overarching lens of racial disparities.

The California Lupus Epidemiology Study (CLUES) is a racially and ethnically diverse longitudinal cohort of over 400 patients with physician-confirmed SLE derived from the population-based CLSP. A unique contribution of CLUES is the ability to study the natural history and outcomes of SLE among Asian and Hispanic individuals, as these groups currently comprise 34 and 22% of the cohort, respectively. As with the other CDC-funded lupus cohorts, comprehensive longitudinal data are collected, ranging from clinical and patient-reported outcomes to genetic, epigenetic and environmental exposures.

The most recent contributions of the ongoing CDC-supported cohorts are summarized below.

Depression in systemic lupus erythematosus and primary chronic cutaneous lupus erythematosus

Depressive symptoms have been recognized in 10–75% of individuals with SLE or cutaneous lupus [16,17]. Compared with whites, African-Americans with SLE have worse mental health, which in turn can lead to adverse health-related behaviors, such as poor medication adherence [18]. However, African-American patients with SLE have been underrepresented in studies of depression. Moreover, recent data suggest that African-Americans with SLE are less likely to be diagnosed with depression than their white counterparts [19]. Findings from the GOAL cohort underscored that among 635 African-American individuals with SLE, 35% reported moderate to severe depressive symptoms and 54% reported low medication adherence [20]. Moreover, the severity of depressive symptoms had an increasingly negative impact on treatment adherence. Moderately severe-to-severe depressive symptoms versus minimal depressive symptoms rendered the highest odds ratios (ORs) for low medication adherence (OR 4.2, \( P < 0.0001 \)), followed by moderate (OR 3.3, \( P < 0.0001 \)), and mild depressive symptoms (OR 2.7, \( P < 0.0001 \)). Depression was also found to shape an individual’s perceptions of physician–patient interaction in the African-American GOAL population with SLE [21]. Specifically, African-Americans patients with greater disease activity and those with more severe depressive symptoms reported poorer communication and less personable involvement.
by their doctors. Moreover, African-American women with depressive symptoms were more likely to accumulate more organ damage and report lower emotional support, compared with those without depression [22].

In another study, depression was also found to be highly prevalent in GOAL participants with lupus confined to the skin [23]. Among 106 participants with primary CCLE, over one-quarter reported moderate to severe depression, a rate three to five times higher than those previously described in the general population from the same metropolitan Atlanta area. In this predominantly African-American cohort of patients with primary CCLE, depression was directly associated with a patient’s perceptions of staff disrespect and inversely associated with emotional support.

GOAL data suggest that routine mental health screening should be considered in lupus patients, particularly in those from minority groups who do not adhere to their medications. In addition, provider-based interventions on communication and interpersonal style, as well as public health programs that foster social networks and promote resilience may help to reduce the burden of depression in high-risk lupus populations.

Psychosocial stressors and lupus outcomes
Genetic and socioeconomic factors do not fully explain racial disparities in SLE outcomes. Compared with whites, African-Americans are more likely to experience psychosocial stressors, which can potentially aggravate or exacerbate SLE. Three recent publications have addressed the impact of psychosocial stressors on outcomes among SLE participants of the GOAL and CLUE cohorts.

Racial discrimination and vicarious racism
The interpersonal experience of racial discrimination is a source of stress that can activate inflammatory pathways and lead to poor SLE outcomes. A study conducted among 427 African-American women with SLE recruited from the GOAL cohort revealed that 80% of participants reported experiencing racial discrimination in at least one of nine domains (e.g., at school; getting a job; at work; getting housing; medical care; service at a store/restaurant; obtaining a credit/loan; on the street/public setting; from the police or in the courts), with 40% experiencing racial discrimination in five or more [24*]. Greater racial discrimination correlated with both higher disease activity and organ damage after adjusting for socioeconomic and health-related factors. The same group of investigators further examined the relationship between vicarious racism and disease activity in the GOAL sample of African-American women with SLE [25]. Vicarious racism is a ‘secondhand’ type of exposure to racism (e.g., hearing about or observing acts of racism or discrimination) that causes psychosocial stress and may contribute to health disparities. Vicarious racism stress was found to be associated with SLE activity after adjusting for socioeconomic and health-related covariates, as well as for everyday discrimination.

As people of color are disproportionately stricken by lupus and also more frequently exposed to racial discrimination, these experiences can lead or accentuate health disparities. The authors suggested that public health interventions directed to eradicate racial discrimination across multiple societal levels, along with policies aimed at combating the structural systems that perpetuate racism are needed to reduce racial disparities in US populations, including those afflicted by SLE.

Childhood trauma
Another psychosocial stressor that has been linked to chronic conditions is childhood trauma [26]. In a racially/ ethnically diverse sample of 269 individuals with SLE, the CLUES cohort underscored a significant association of increasing levels of adverse childhood experiences (ACEs) with higher depression, higher disease activity, and worse physical function [27]. Moreover, women, Latinos or African-Americans, older participants, those without a college degree, and those with lupus nephritis were more likely to reported ACEs. As these subgroups have worse SLE outcomes, these findings support the need for ACE screening and psychological interventions among high-risk patients with SLE.

Quality of lupus nephritis care
Renal involvement occurs in up to 60% of SLE patients and the 5-year cumulative incidence of end-stage renal disease was estimated to be 6.4 and 2.5% among black and white SLE patients, respectively [28]. As early diagnosis and treatment are critical to reducing morbidity and mortality associated with lupus nephritis, the CLUE cohort was used to assess the quality of lupus nephritis care in patients with and without lupus nephritis. Findings indicated that the largest quality gap across 25 different clinical sites was in the screening of SLE patients for renal involvement [29*]. Of 148 patients without lupus nephritis, the overall performance across lupus nephritis screening measures was 54%. While the majority (81%) had the blood pressure checked every 6 months, only 42 and 38% had...
Impact of dietary omega fatty acid intake on health-related quality of life domains

Omega-3 (n-3) polyunsaturated fatty acid (PUFA), which is found in fatty fish, oils, nuts, and seeds, has anti-inflammatory effects. However, it is consumed at relatively low levels in the US diet. In contrast, omega-6 (n-6) PUFA, including linoleic and arachidonic acids, tend to be proinflammatory and are ubiquitous (e.g., soybean and corn oils) in the US diet. A cross-sectional study of 456 SLE participants (51% whites, 45% blacks, 3% Asian, or other races) of the MILES Cohort & Biobank demonstrated a significant association between higher dietary intake of n-3 FAs and lower n-6 : n-3 ratios with lower self-reported lupus activity and better sleep quality [30]. A nonsignificant association was also found between higher n-3 intake and less depressive symptoms, fibromyalgia, and higher quality of life, whereas results for the n-6 : n-3 ratio trended in the opposite direction. The authors suggested that promoting a better balance of FAs from dietary sources, with a higher intake of n-3 PUFA might positively impact the quality of life of SLE individuals through immunomodulatory and anti-inflammatory effects.

Kidney allograft survival in US minorities with systemic lupus erythematosus

A consistent finding of epidemiological studies is the higher incidence of lupus nephritis and end-stage renal disease in Blacks and Hispanics with SLE [1,9,28,37,38]. A US group analyzed records in the United Network for Organ Sharing program and Standard Transplant Analysis and Research files to compare kidney allograft survival in African-American and Hispanic individuals who had SLE and received kidney transplants between 1987 and 2006 [39]. Data from a cohort of 478 pairs of recipients that matched for 16 confounders, including sociodemographic, type of donor, human leukocyte antigen (HLA) mismatch, cold ischemia time, and follow-up time, showed significantly lower allograft survival, higher rates of rejection, and higher allograft failure attributed to rejection in
African-Americans, compared with Hispanics. The overall mortality was similar between African-Americans and Hispanics in the matched cohort (2.7 and 2.3/100 patient-years, respectively). However, the unmatched cohort ($n = 1816$ African-Americans and $n = 901$ Hispanics) revealed that African-Americans were older, had lower frequency of both private insurance and college or technical education, primarily received kidney from deceased donors with higher frequency of kidneys from expanded criteria donors, longer cold ischemia time and higher HLA mismatch level, and had a significantly higher mortality (2.8 deaths/100 patient-years), compared with Hispanics (1.7 deaths/100 patient-years).

**CONCLUSION**

Recent epidemiological studies have made significant contributions to our understanding of the population burden and natural history of individuals with SLE and cutaneous lupus from diverse racial and ethnic backgrounds. While ongoing research is providing new insight into the social and healthcare system factors that shape outcomes in lupus minorities, future studies addressing causal pathways, biologic mechanisms, and mitigating factors will be critical in guiding multilevel interventions to confront the problem of lupus health disparities in the United States, as well as the rest of the world.

Note by the authors: Black and African-American terms are used in this article as in the original article each section is referencing.

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**Conflicts of interest**

There are no conflicts of interest.

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