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Prevalence of Systemic Lupus Erythematosus in the United States: Estimates From a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries

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Objective. Epidemiologic data on systemic lupus erythematosus (SLE) are limited, particularly for racial/ethnic subpopulations in the US. This meta-analysis leveraged data from the Centers for Disease Control and Prevention (CDC) National Lupus Registry network of population-based SLE registries to estimate the overall prevalence of SLE in the US.

Methods. The CDC National Lupus Registry network includes 4 registries from unique states and a fifth registry from the Indian Health Service. All registries defined cases of SLE according to the American College of Rheumatology (ACR) 1997 revised classification criteria for SLE. Case findings spanned either 2002–2004 or 2007–2009. Given the heterogeneity across sites, a random-effects model was used to calculate the pooled prevalence of SLE. An estimate of the number of SLE cases in the US was generated by applying sex/race-stratified estimates to the 2018 US Census population.

Results. In total, 5,417 cases were identified as fulfilling the ACR SLE classification criteria. The pooled prevalence of SLE from the 4 state-specific registries was 72.8 per 100,000 person-years (95% confidence interval [95% CI] 65.3–81.0). The prevalence estimate was 9 times higher among females than among males (128.7 versus 14.6 per 100,000), and highest among Black females (230.9 per 100,000), followed by Hispanic females (120.7 per 100,000), White females (84.7 per 100,000), and Asian/Pacific Islander females (84.4 per 100,000). Among males, the prevalence of SLE was highest in Black males (26.7 per 100,000), followed by Hispanic males (18.0 per 100,000), Asian/Pacific Islander males (11.2 per 100,000), and White males (8.9 per 100,000). The American Indian/Alaska Native population had the highest race-specific SLE estimates, both among females (270.6 per 100,000) and among males (53.8 per 100,000). In 2018, an estimated 204,295 individuals (95% CI 160,902–261,725) in the US fulfilled the ACR classification criteria for SLE.

Conclusion. A coordinated network of population-based SLE registries provides more accurate estimates of the prevalence of SLE and the numbers of individuals affected with SLE in the US in 2018.

INTRODUCTION

The heterogeneity of the clinical manifestations of systemic lupus erythematosus (SLE) and lack of a singular diagnostic test make SLE difficult for epidemiologists to study (1). Previous estimates of the rates of SLE in the US have been predominantly derived from tertiary care settings and relatively small, homogeneous patient populations, for which limited data are available on key demographic groups in the US (1). Other explanations for the varied estimates, which range from 19 to 241 per 100,000, include racial/ethnic disparities in SLE susceptibility and mortality, differing case definitions, heterogeneous sources for case ascertainment,

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small populations, possible inaccuracy of self-report, unreliability in coding in health system databases, and variable access to health care for high-risk populations (2,3).

The Centers for Disease Control and Prevention (CDC) funded a network of 5 population-based SLE registries, each using similar active surveillance methods, to determine the incidence and prevalence of SLE in populations reflecting a broad distribution of racial/ethnic demographics in the US. Data from these 5 registries have provided overall prevalence and incidence rates of SLE, as well as estimates focused on the major US demographic groups, including White and Black populations (3,4), Asian/Pacific Islander and Hispanic populations (5,6), and American Indian/Alaska Native (AI/AN) populations (7). Leveraging these data, we performed a meta-analysis to estimate the overall prevalence of SLE and to provide an estimate of the number of SLE cases in the US in 2018.

METHODS

Data sources and study selection. The CDC-supported and SLE-dedicated registries were based in the following source populations, which contained a mix of urban and rural areas. Areas with a large Black population (~50%) included Fulton County and DeKalb County in Georgia (the Georgia Lupus Registry [GLR]) (3) and Washtenaw County and Wayne County in Michigan (the Michigan Lupus Epidemiology and Surveillance Program [MILES]) (4). Areas with populations having substantial representation of Asian/Pacific Islander and Hispanic individuals included San Francisco County in California (the California Lupus Surveillance Program [CLSP]) (5) and New York County in New York (the Manhattan Lupus Surveillance Program [MLSP]) (6). Estimates for the AI/AN population were derived from the Indian Health Service (IHS) (with facilities in Alaska, Phoenix, Arizona, and Oklahoma City, Oklahoma) (7).

Active surveillance for these registries was performed at various times between 2003 and 2015 using the surveillance exemption to the US Health Insurance Portability and Accountability Act (HIPAA) and public health authorization by the respective state or city Health Departments, which allowed access to medical records without individual consent. The case definitions for determination of SLE prevalence varied slightly according to the time period evaluated in each registry, ranging between 2002 and 2009 (3–7). In all registries, the American College of Rheumatology (ACR) 1997 revised classification criteria for SLE was used as the primary case definition for SLE (8,9). The registries employed harmonized methods, including the utilization of a variety of case-finding sources and screening for potential SLE cases using the same core set of International Classification of Diseases, Ninth Revision (ICD-9) codes.

Registries used a consistent approach to capture the relevant clinical and demographic information and core definitions from a standardized data dictionary. Trained medical abstractors, who underwent routine quality assurance monitoring, collected the data. Population denominators were based on intercensal population estimates for the respective source populations. Sex- and race/ethnicity-specific prevalence estimates were calculated per 100,000 person-years and age-adjusted to the 2000 US Standard Population (10) (see Supplementary Figure 1, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.41632/abstract). Data were extracted from the published articles independently by 2 of the authors (PI and HP), who reached agreement with regard to all of the data used.

Data synthesis and analysis. A meta-analysis was conducted to derive pooled prevalence estimates of SLE using data from the 4 similar CDC-funded state registries (the GLR, MILES, CLSP, and MLSP registries) for estimating the age-standardized prevalence of SLE (adjusted to the 2000 US Standard Population) (10) and the rates of SLE stratified by sex and race/ethnicity categories other than AI/AN (3–6). In contrast to the 4 state-based registries, the IHS-based registry (7) was different, as it focused on a single demographic (AI/AN), and therefore was handled separately.

For the meta-analysis, heterogeneity across sites was tested by Cochran's Q and I^2 statistical tests (11,12). Due to significant heterogeneity among the sites, we used a random-effects model, weighted by the population denominator for each site, to calculate the pooled prevalence of SLE (13). Such random-effects models allow an underlying distribution of the effect sizes across different studies. Pooled race- and ethnicity-specific estimates were calculated for each population, except for estimates for the AI/AN population, whose data were derived solely from the IHS registry covering multiple states.

In the report of the MLSP data (6), rates of SLE were presented as those in combined race and ethnicity categories (e.g., Non-Hispanic White). For the present meta-analysis, rates were calculated separately by race and ethnicity for consistency across the registries based in states. Hispanic ethnicity and race categories overlap, so estimates in Hispanic populations include all races, and each race category will include Hispanic (i.e., race and Hispanic ethnicity are not mutually exclusive).

To estimate the number of SLE cases in the US, the pooled age-adjusted, sex- and race-specific prevalence rates from the 4 states and the prevalence in the AI/AN population from the IHS registry were extrapolated separately to 2018 US Census population data; these stratum-specific estimates were then summed for the total population count of SLE cases. The pooled prevalence estimates of SLE do not incorporate the Hispanic SLE prevalence rates, because that would lead to duplicate counting.

RESULTS

Prevalence of SLE in the US. The 5 registries contributed 5,417 SLE cases fulfilling the ACR classification criteria among populations from diverse areas across the country. The random-effects model for the meta-analysis of the estimates of SLE prevalence from the 4 state-based registries yielded an overall SLE prevalence of 72.8 per 100,000 person-years (95% confidence

interval [95% CI] 65.3–81.0) (Figure 1A). The prevalence among female persons was ~9 times higher than among male persons (128.7 versus 14.6 per 100,000) (Table 1).

In assessing the race- and ethnicity-specific pooled estimates of SLE from the 4 state-specific registries, the prevalence of SLE was the highest among Black females (230.9 per

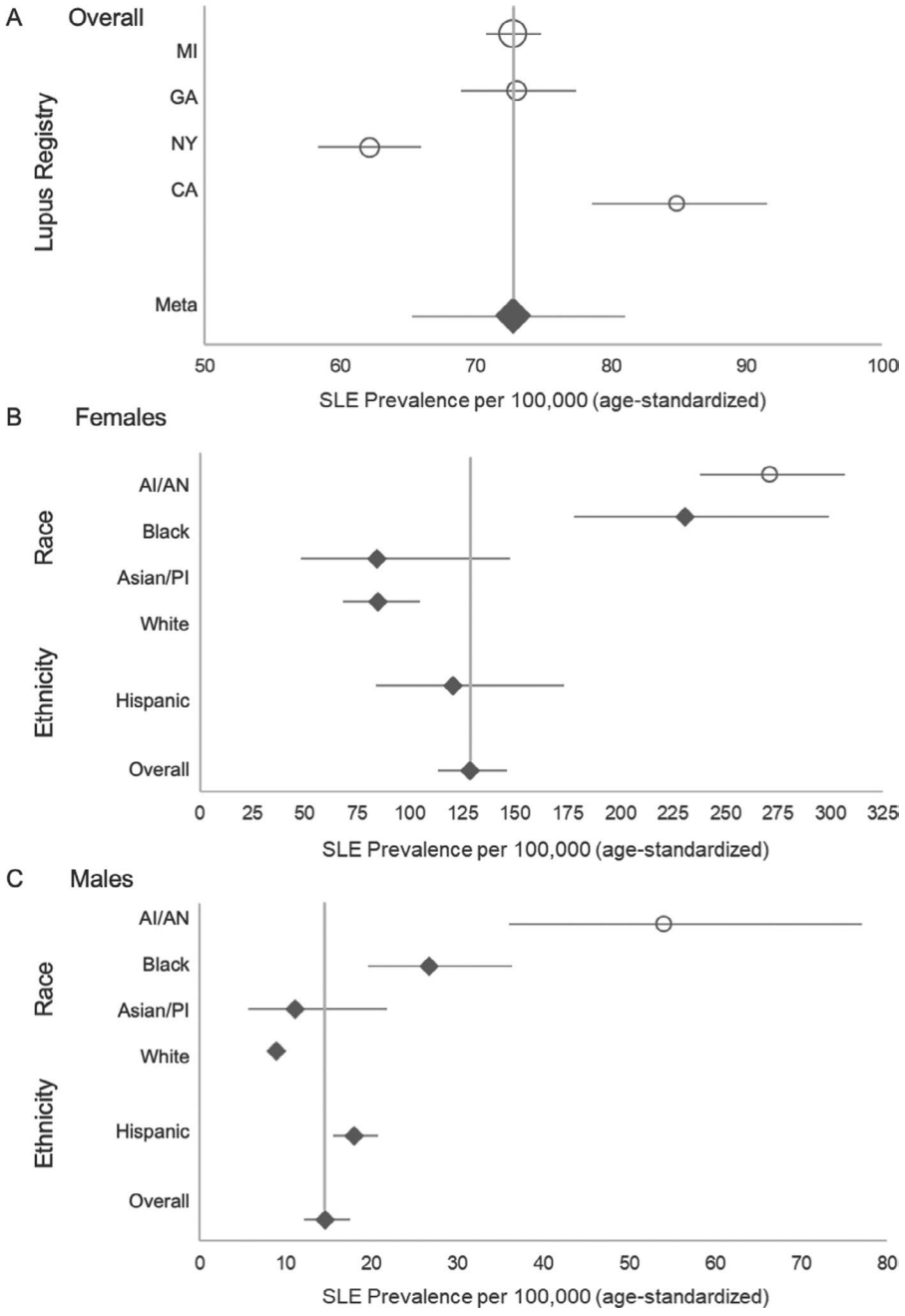

Figure 1. Meta-analysis results showing age-standardized estimates of the prevalence of systemic lupus erythematosus (SLE) in the US from Centers for Disease Control and Prevention population-based registries in 4 states and the Indian Health Service. SLE cases were defined according to the American College of Rheumatology 1997 classification criteria. **A**, SLE prevalence estimates overall and by 4 state-specific registry sites (Michigan, Georgia, New York, and California). The size of each circle corresponds to the weight of the contribution to the meta-analysis. **B** and **C**, SLE prevalence estimates by race and Hispanic ethnicity among females (**B**) and males (**C**). Estimates for Black and White persons are based on the pooled estimates from the 4 state-specific lupus registry sites. Estimates for the Asian/Pacific Islander populations (Asian/PI) are based on pooled estimates from the registries in Michigan, California, and New York. Estimates for the American Indian/Alaska Native populations (AI/AN) are based on data from the Indian Health Service. Estimates for the Hispanic persons are based on pooled estimates from the registries in Michigan, California, and New York. Symbols with horizontal lines represent the prevalence estimates with 95% confidence intervals. Vertical line denotes the overall estimate.

Table 1. Estimated number of persons with SLE living in the US in 2018, by sex and race/ethnicity categories*

	Prevalence of SLE per 100,000 person-years (95% CI)†	US Census population denominator	Estimated no. of SLE cases in US (95% CI)
Females			
Black (4 sites)	230.9 (178.2–299.2)	24,880,722	57,450 (44,337–74,443)
White (4 sites)	84.7 (68.4–104.8)	130,137,989	110,227 (89,014–136,437)
Asian/PI (3 sites)	84.4 (48.3–147.4)	12,544,896	10,588 (6,059–18,491)
AI/AN (1 site)	270.6 (237.5–307.0)	2,238,966	6,059 (5,318–6,874)
Total‡	128.7 (113.3–146.2)	169,802,573	184,323 (144,729–236,245)
Hispanic (3 sites)§	120.7 (84.0–173.4)	30,689,083	37,042 (25,779–53,215)
Males			
Black (4 sites)	26.7 (19.6–36.4)	22,961,129	6,131 (4,500–8,358)
White (4 sites)	8.9 (8.0–10.1)	127,942,583	11,387 (10,235–12,922)
Asian/PI (3 sites)	11.2 (5.7–21.9)	11,660,533	1,306 (665–2,554)
AI/AN (1 site)	53.8 (36.2–77.1)	2,134,870	1,149 (773–1,646)
Total‡	14.6 (12.2–17.5)	164,699,115	19,972 (16,173–25,480)
Hispanic (3 sites)§	18.0 (15.6–20.8)	31,281,605	5,631 (4,880–6,507)

* Systemic lupus erythematosus (SLE) cases were defined according to the American College of Rheumatology 1997 revised classification criteria for SLE. 95% CI = 95% confidence interval.
† Estimates for the Black and White populations are based on pooled estimates from the 4 state-based registries; estimates for the Asian/Pacific Islander (PI) and Hispanic populations are based on pooled estimates from Michigan, California, and New York; estimates for the American Indian/Alaska Native (AI/AN) population are based on the Indian Health Service Registry.
‡ The pooled total SLE prevalence estimates include the Black, White, and Asian/PI populations. Since the prevalence in the AI/AN population was based on a single registry and the values were significantly higher, it was not included in the pooled prevalence per 100,000.
§ Hispanic ethnicity is not mutually exclusive from the race categories, i.e., all Hispanic persons are included in one of the race categories. Thus, the pooled estimates do not incorporate the rates in Hispanic persons, since that would lead to duplicate counting. Estimates for Hispanic persons are based on pooled estimates from Michigan, California, and New York.

100,000, 95% CI 178.2–299.2), followed by Hispanic females (120.7 per 100,000, 95% CI 84.0–173.4), White females (84.7 per 100,000, 95% CI 68.4–104.8), and Asian/Pacific Islander females (84.4 per 100,000, 95% CI 48.3–147.4) (Table 1 and Figure 1B). Among males, the prevalence of SLE followed a similar pattern, with the highest rates among Black males (26.7 per 100,000, 95% CI 19.6–36.4), followed by Hispanic males (18.0 per 100,000, 95% CI 15.6–20.8), Asian/Pacific Islander males (11.2 per 100,000, 95% CI 5.7–21.9), and White males (8.9 per 100,000, 95% CI 8.0–10.1) (Table 1 and Figure 1C).

The SLE prevalence estimates in the AI/AN population from the IHS Registry (not included in the pooled meta-analysis estimates from the 4 state-based registries) were the highest among all of the races, both in females (270.6 per 100,000, 95% CI 237.5–307.0) and in males (53.8 per 100,000, 95% CI 36.2–77.1) (Table 1 and Figures 1B and C).

Numbers of SLE cases among persons living in the US in 2018. When the sex- and race-specific estimates of SLE prevalence were applied to the corresponding stratum-specific population denominators from the 2018 US Census, we estimated that 204,295 persons (95% CI 160,902–261,725) in the US in 2018 fulfilled the ACR classification criteria for SLE (Table 1).

DISCUSSION

Based on the data from registries in which the ACR classification criteria were used to clinically define SLE, we found that the overall prevalence of SLE in the US was estimated to be 72.8 per 100,000 person-years (95% CI 65.3–81.0) during the calendar years 2002–2009. Prevalence was ~9 times higher in females than in males, and was highest among AI/AN females and Black females. Extrapolating sex- and race-specific estimates to the 2018 US Census data, we estimated that 204,295 individuals (95% CI 160,902–261,725) (184,323 females and 19,972 males) in the US fulfilled the ACR classification criteria for SLE.

Limitations and strengths of our data derived from each of the 5 component registries have been described previously (3–7). There are several limitations. First, although the registries were designed to employ similar methods, there were subtle differences in the comprehensive case-finding sources that were approached by the different registries and differences in the ICD-9 criteria used to identify possible cases.

Second, case findings may have missed some true cases meeting the ACR criteria, so the actual numbers may be slightly higher than these estimates, as demonstrated by the capture-recapture analyses conducted by the state-based registries (3–6).

Third, data on race and ethnicity were abstracted from the medical records, which may not accurately represent the patient's own racial or ethnic identification. Hispanic ethnicity and the different races encompass several heterogeneous groups, and SLE rates among these groups may differ.

Fourth, the prevalence of SLE in the AI/AN population was based on a single registry, although 3 geographic regions with different population characteristics were encompassed in the IHS registry, which improved the generalizability of the results (7). Due to significant heterogeneity across sites, the IHS registry data were not used in the calculations of pooled prevalence in our meta-analysis; however, the estimates of SLE prevalence derived from the AI/AN population in the IHS registry were used for the national estimate calculation of the number of SLE cases.

Fifth, secondary case definitions used by the 5 registries (3–7) (results not shown herein) resulted in slightly higher estimates of SLE in most instances, although these data may have greater sensitivity with lower specificity.

Sixth, our analyses did not include other forms of lupus, such as "early" or "incomplete" lupus, drug-induced lupus, or primary cutaneous lupus (14,15).

Seventh, our prevalence estimates from 2002–2004 and 2007–2009 were applied to the 2018 US Census population. This approach provided a more relevant estimate of the numbers of individuals with SLE, but it might have been slightly affected if the prevalence of lupus had changed significantly during that period.

These analyses also have several strengths. First, case finding likely captured a wider spectrum of SLE than has been captured by previous studies, because of the HIPAA surveillance exemption and case finding that facilitated data collection that extended beyond academic medical centers.

Second, cases were validated through standardized and quality-controlled abstracting and rigid reviews of all available medical records.

Third, the standard ACR 1997 revised classification criteria for SLE (8,9) were used for case definitions.

Fourth, the registries used harmonized methods and data dictionaries, and included a large number of SLE cases from diverse populations across the country, with substantial representation of males and the major racial and ethnic groups found in the US.

Fifth, employing these estimates allowed us to estimate the numbers affected with SLE in the US. This estimate of the number of individuals with SLE approaches the 1983 definition of a rare disease used in the US (i.e., a condition that affects fewer than 200,000 people in the US) (16) and is lower than the widely used estimate of 1.5 million persons (17).

In summary, using estimates from a large, coordinated network of population-based registries in which active surveillance of SLE was conducted, a more accurate estimate of the prevalence of SLE in the US was obtained. This likely represents a lower bound for SLE prevalence in the US.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Izmirly had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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