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The Incidence and Prevalence of Systemic Lupus Erythematosus

The California Lupus Surveillance Project

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1

Abstract

Objective: Estimates of SLE incidence and prevalence in the United States have varied widely. The California Lupus Surveillance Project (CLSP) is funded by the Centers for Disease Control and Prevention (CDC) to determine credible estimates of SLE incidence and prevalence, with a special focus on Hispanics and Asians.

Methods: The CLSP is a population-based registry of individuals with SLE residing in San Francisco County, California from 2007 - 2009. Data sources included hospitals, rheumatologists, nephrologists, commercial laboratories, and a state hospital discharge database. We abstracted medical records to define SLE cases as patients with documentation of $\geq$ 4/11 of the American College of Rheumatology (ACR) Classification Criteria for SLE. We estimated crude and age-standardized incidence and prevalence, stratified by sex and race/ethnicity.

Results: Overall age-standardized annual incidence rate was 4.6 per 100,000 person-years. The average annual period prevalence was 84.8 per 100,000 persons. The age-standardized incidence rate was 8.6 and 0.7 per 100,000 person-years in women and men respectively. It was highest among Black women (30.5), followed by Hispanic women (8.9), Asian women (7.2), and White women (5.3). The age-standardized prevalence in women per 100,000 was 458.1 in Blacks, 177.9 in Hispanics, 149.7 in Asians, and 109.8 in Whites. C-RC modeling estimated 33 additional incident and 147 additional prevalent cases.

Conclusions: Comprehensive methods including intensive case finding provide more credible estimates of SLE in Hispanics and Asians, and confirm racial and ethnic disparities in SLE with the highest burden of disease in Black women, followed by Hispanic, Asian, and white women.

2

Historical estimates of the incidence and prevalence of systemic lupus erythematosus (SLE) in the U.S. have varied widely (1). These differences stem from a variety of factors including the definition of SLE used, completeness of case ascertainment, geographic area, and racial/ethnic composition of the study population. The heterogeneity of disease manifestations and the lack of an accurate, reliable diagnostic test result in substantial challenges and costs to conducting large-scale epidemiologic studies in SLE. In an effort to develop more authoritative estimates of the incidence and prevalence of SLE, the Centers for Disease Control and Prevention (CDC) initially provided funding for two population-based lupus surveillance registries in Georgia (Georgia Lupus Registry) and Michigan (Michigan Lupus Epidemiology and Surveillance Program). These two registries have been successfully finished and focused primarily on Whites and Blacks (2, 3). To increase the reliability of SLE estimates in other racial/ethnic groups, the CDC funded two similar registries in California and New York to focus on Hispanics and Asians, and a third registry with the Indian Health Service to focus on American Indians and Alaskan Natives (4).

In collaboration with the CDC and the California Department of Public Health, we conducted the California Lupus Surveillance Project to determine contemporary, population-based estimates of the incidence and prevalence of SLE in San Francisco County during the period 2007 through 2009 using multiple methods of case ascertainment. A secondary goal was to describe the clinical and serologic spectrum of incident SLE in the population. To the greatest extent possible, we aligned our methodology with that of the Georgia and Michigan registries (2,3) to promote consistent data collection and optimal case ascertainment.

PATIENTS AND METHODS

3

The California Lupus Surveillance Project (CLSP). The CLSP was conducted under the statutory authority of the California Department of Public Health (CDPH). Patients were not contacted for this study. A partnership between the CDPH and the University of California, San Francisco (UCSF), allowed medical records to be collected using the health surveillance exemption to the Health Insurance Portability and Accountability Act (HIPAA) privacy rules (45 CFR parts 160 and 164). The use of protected health information was essential in the conduct of this project in order to increase potential case finding, perform unbiased case ascertainment and prevent duplicate patients in the registry. The CDPH subcontracted with the UCSF to conduct this project. The State of California Institutional Review Board (IRB) granted a waiver for this public health surveillance activity, but the project was reviewed and approved by the UCSF IRB.

Source population/catchment criteria. The source population consisted of residents of San Francisco County during 2007 – 2009. According to United States Census estimates, the San Francisco County source population in 2007 – 2009 averaged 790,582 residents, 56% of whom identified as White, 35% Asian or Pacific Islander, 7% Black, and 1% American Indian/Alaskan Native (5). Of note, Hispanic ethnicity is considered a distinct concept from race and is therefore collected and reported separately from race; 15% of residents identified with Hispanic ethnicity.

Case definitions. SLE is currently diagnosed in clinical practice by an expert clinician on the basis of characteristic symptoms and signs in conjunction with supportive serologic and histologic data. For the purposes of this surveillance project in which clinical information was ascertained through review of medical records, we used various case definitions to classify a patient as having SLE. To maintain consistency with the Georgia and Michigan Lupus Registries (2,3), we report estimates using two case-finding definitions:

4

1) <u>American College of Rheumatology (ACR)</u>: This definition included patients who met $\geq$ 4 of

   the 11 ACR revised classification criteria defined in 1982 and updated in 1997 (6,7); this is a

   standard case definition used for research.

2) <u>Combined</u>: This definition was satisfied if any of the following three criteria were met:

   a. ACR case-finding definition, described above.

   b. Patients who had a documented diagnosis of SLE by the treating rheumatologist who

       met three of the 11 ACR classification criteria. This definition was chosen to allow

       for the possibility of missing data and inability to confirm criteria in the available

       medical records for prevalent cases with longstanding disease.

   c. Patients with lupus-related kidney disease defined either by presence of World Health

       Organization class II-VI lupus nephritis biopsy findings, or by the presence in the

       medical record of SLE (ICD-9-CM 710.0) along with either dialysis or renal

       transplantation.

Case ascertainment. The three primary sources of potential SLE cases were: 1) community

rheumatology and nephrology clinics (office based practices), 2) community hospitals (non-

academic hospitals), and 3) integrated healthcare systems (integrated hospitals and clinics)

within the catchment area including the University of California at San Francisco, Kaiser

Permanente Northern California, and the San Francisco Veterans Administration Medical Center

(Figure 1).

We queried these sources over the period 2000-2009 using International Classification of

Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes 710.0 (SLE),

695.4 (discoid lupus), 710.8 (other specified connective tissue disease), and 710.9 (unspecified

5

connective tissue disease).   A secondary source was a commercial laboratory, which we queried

for the following serologic tests: anti-nuclear antibodies (ANAs), anti-dsDNA antibodies, anti-

Smith antibodies, anti-phospholipid antibodies, and low complement levels. Another secondary

source was the California Office of Statewide Health Planning and Development (OSHPD)

hospital discharge database, which we queried for discharges using the ICD-9-CM diagnostic

codes 710.0 (SLE), 695.4 (discoid lupus), 710.8 (other specified connective tissue disease), and

710.9 (unspecified connective tissue disease). We added patients identified from the OSHPD

query to the roster of the appropriate primary source hospitals and integrated healthcare systems.

After compiling a list of potential SLE patients from all sources using the queries described

above, we determined catchment criteria for each patient (proof of residence in San Francisco

County during the period 2007 – 2009). The primary methods for verifying catchment criteria

were via the LexisNexis on-line database service, hospital billing databases, and clinic medical

records. We then abstracted medical records for each of the potential SLE patients who met

catchment criteria to identify those patients who had a physician diagnosis in the medical record

of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or a related

connective tissue disorder such as mixed connective tissue disease.

Data collection. Four trained field staff abstracted medical charts for each potential SLE patient

who met catchment criteria. Training of the staff included lectures by physicians, extensive

reading about SLE clinical manifestations and terminology, and practice abstractions of patient

charts that were then reviewed in detail by the principal investigator (M.D.). The field

abstractors accessed all available medical records (paper charts and electronic medical records)

at each source location, collecting more than 200 data elements. Laboratory records were

reviewed for presence or absence of antibodies and for presence or absence of low complement.

6

 The abstractors recorded whether the source was a community clinic, community hospital, or integrated health care system as described above. Abstractors contacted the principal investigator (M.D.) in real time as questions arose about the information in the medical records, to obtain clarifications. Demographic information was obtained from the medical record. For quality control, a second field abstractor and the principal investigator reviewed five of every 100 charts for each abstractor, and data entry errors identified by discordant responses between abstractors were identified and corrected. Overall, we calculated 98% concordance between abstractors for required data elements (those used to define ACR criteria) and 93% concordance for all other data elements.

Statistical Analysis.

We derived all denominators for incidence and prevalence using the 2007 – 2009 San Francisco population estimates from revised 2000-2009 bridged-race intercensal files (5). The average annual incidence rate (cases/100,000 person-years) was the number of newly diagnosed SLE cases that resided in San Francisco County at the time they were diagnosed with SLE (defined as the earliest date as recorded in the medical record that the physician first stated the diagnosis of SLE, possible SLE, undifferentiated connective tissue disease, or mixed connective tissue disease) during 2007 – 2009 divided by the sum of the annual population of San Francisco for 2007, 2008, and 2009.We calculated annual period prevalence (cases/100,000 persons) for each year separately, dividing the number of SLE cases diagnosed before or during that year and residing in San Francisco County during the year by the San Francisco County population of that year. We then averaged the three annual prevalence estimates to yield the average annual

7

prevalence for 2007 - 2009. Our next step was to calculate exact 95% confidence intervals (CIs) (8) for the incidence rate and average annual prevalence.

We calculated age-standardized incidence and prevalence using the direct method, based on the 2000 US projected population (distribution #2) (9). In addition, we computed age-specific estimates using 10-year age groups, as well as sex-specific estimates. The Census Bureau's intercensal database codes race and Hispanic ethnicity using two variables. One collapses all persons into four mutually exclusive categories defined by bridged race, without accounting for Hispanic ethnicity: Black, White, Asian/Pacific Islander, and American Indian/Alaskan Native (10). The other codes Hispanic ethnicity as a separate construct.

Similar to the Georgia registry (2), we used capture-recapture (C-RC) methods to estimate underascertainment of cases. Specifically, we developed log-linear models that estimated the number of missing cases predicted by the overlap among the three primary sources (community rheumatology and nephrology clinics, community hospitals, and integrated healthcare systems). We evaluated the results of all log-linear models possible for a three-source C-RC analysis and then chose the best-fitting model based on chi-square goodness-of-fit criteria (11). Using the estimated number of undercounted cases from best-fitting model, we calculated C-RC-revised incidence and prevalence estimates for the ACR definition. We considered results significant if P< 0.05.

We compared differences between estimates by case definition using 95% confidence intervals (CIs) of the age-adjusted rates, with non-overlapping CIs considered to be significantly different.

RESULTS

Study population. As shown in Figure 1, among 15,210 potential SLE patients identified from primary and secondary sources, 4,859 met the geographical and temporal catchment criteria

8

(residency in San Francisco County from 2007 through 2009). Abstraction was completed for

4,832 patients because 27 patients did not have any available medical records. Of the abstracted

patients, 1,257 satisfied the catchment criteria and had a physician recorded diagnosis in the

medical record of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or a

related connective tissue disorder such as mixed connective tissue disease. Of these 1,257 cases,

121 incident and 796 prevalent cases met the ACR definition while 137 incident and 909

prevalent cases met the combined definition. All cases were confirmed using primary data

sources, including those initially ascertained from state hospital discharge data. Commercial lab

queries did not provide any additional cases.

Incidence.

The ACR definition. The overall crude and age-standardized incidence rates were 5.1 (95% CI

4.3-6.1) and 4.6 (95% CI 3.8-5.5) per 100,000 person-years (Table 1). The 121 incident cases

consisted of 112 women and nine men. Race for these cases was identified as White (n=43),

Asian/Pacific Islander (n=39), Black (n=27), and American Indian/Alaskan native (n=1); 11 had

no race identified. Hispanic ethnicity was identified for 17 patients; 18 had no ethnicity

identified. Among the Asian/Pacific Islander subgroup, the predominant race was Chinese (21

patients, of which 17 were identified as Chinese only, with the remaining four including another

Asian/Pacific Islander racial category) followed by Japanese (three patients, two of which were

exclusively Japanese), Filipino (two patients, all of whom also had another Asian/Pacific

Islander racial category), and one each of Korean, Vietnamese, Asian Indian, Samoan, and

Hawaiian. The remaining seven cases were classified as "other Asian", a category including

Burmese, Indonesian, and Asian not otherwise specified. (Data not shown.)

9

The age-standardized incidence rates were about 12 times higher among women than men, 8.6 versus 0.7 per 100,000 person-years respectively. The age-standardized incidence rate was highest among Black women (30.5 [95% CI 20.7-44.9]), followed by Hispanic women (8.9 [95% CI 5.3-14.8]), Asian women (7.2 [95% CI 5.1-10.2]), and finally White women (5.3 [3.8-7.5]). The age-standardized incidence rate among Black women was approximately six times higher than among White women.

Among Black women, the age-specific incidence rate peaked at 61.2 per 100,000 in the 40-49 year old age group. Among the other racial/ethnic groups, incidence rates were relatively constant across the age groups (Figure 2). There were too few incident cases in men (nine cases) to enable age stratification. Overall mean age at diagnosis was 43.9 years. Mean age at diagnosis stratified by bridged race/ethnicity was: Black (40.1 years), White (46.5 years), Asian (45.1 years), and Hispanic (36.6 years); all CIs for race/ethnicity mean age estimates overlapped. (Data not shown.)

Our C-RC modeling estimated 33 (95% CI 8-130) additional incident cases in the population, yielding CRC-inflated crude rate of 6.5 per 100,000 person-years.

The combined definition. The combined definition yielded an additional 16 cases (15 from the three ACR criteria + rheumatologist diagnosis criterion and a single case from the lupus-related kidney disease criterion) for a total of 137 incident cases (Table 1). The overall crude and age-standardized incidence rates were 5.8 (95% CI 4.9-6.8) and 5.2 (95% 4.3-6.2) per 100,000 person-years. Incident cases' sex and racial/ethnic disparities were similar to those observed for the ACR cases.

Prevalence.

10

The ACR definition. The ACR definition yielded overall crude and age-standardized

prevalence proportions of 96.0 (95% CI 89.4-103.1) and 84.8 (95% CI 78.6-91.5) per 100,000

persons (Table 2). The 796 unique prevalent cases over the three-year period consisted of 708

women and 88 men. We identified race for these cases as White (n=294), Asian/Pacific Islander

(n=290), Black (n=160), and American Indian/Alaskan native (n=4); 48 had no race identified.

Hispanic ethnicity was identified for 118 patients. Similar to the incident cases, the majority of

the Asian/Pacific Islander subgroup was composed of Chinese patients (137, of which 101 were

identified as Chinese and no other race) followed by "other Asian" (56 patients), Filipino (42

patients, of whom 26 were not identified with any other race), Vietnamese (18, of whom 12 had

no other race identified), Japanese (10, of which eight were not identified with any other race),

Korean (five, of whom three had no other race identified), Thai and Pakistani (four each), and

Asian Indian and Samoan (three each), and other South Asian, Cambodian and Pacific

Islander—not otherwise specified (two each), and Hawaiian and Laotian (one each) (Data not

shown).

        Age-standardized prevalence was about eight times higher among women than men,

155.6 versus 19.3 per 100,000 persons respectively. The age-standardized prevalence was

highest among Black women (458.1 [95% CI 385.4-544.5]), followed by Hispanic women

(177.9 [145.9-217.0]), Asian women (149.7 [131.4-170.7]), and finally white women (109.8

[96.5-124.9]). The age-standardized prevalence among Black women was over four times higher

than among White women.   The age-standardized prevalence among Black men was over five

times higher than among White men.

11

Age-specific prevalence in the ACR defined cases were statistically significantly higher in Black women compared with women from the other racial groups for ages (years) 30 – 59, with whites and Asians for ages 69- 79, and with whites only for ages 20 - 29. Among Black women, age-specific prevalence began to increase at age 20 years and peaked at 954.5 per 100,000 in the 40-49 years group (Figure 3).   Among Black men, age-specific prevalence peaked in the 50-69 year range. Age-specific prevalence was higher in Black men compared to the other racial/ethnic groups (Figure 3). Among men, 95% CIs overlapped within each age group with the following exception: In the 50 to 59 group, prevalence for Black men was statistically significantly higher than for white men.

Overall mean age at diagnosis was 34.8 years. Age at diagnosis stratified by bridged race and ethnicity was as follows: Black (35.5 years), White (34.4 years), Asian (34.6 years), and Hispanic (33.9 years). Once again, the 95% CIs for these estimates overlapped. (Data not shown.)

Our C-RC modeling estimated 147 (95% CI 93-225) additional prevalent cases in the population, yielding CRC-inflated average annual crude prevalence of 113.7 per 100,000 persons.

The combined definition. By including an additional 113 individuals (89 from the three ACR criteria + rheumatologist diagnosis criterion and 24 from the lupus-related kidney disease criterion), the combined definition yielded a total of 909 unique individuals over the three-year period (Figure 1), or 869 average annual prevalent cases (Table 2). The overall crude and age-standardized prevalence proportions were 109.9 (95% CI 102.8 – 117.4) and 96.8 (95% 90.2-103.9) per 100,000 persons. Age-standardized prevalence proportions were nine times higher

12

Arthritis & Rheumatology

among women than men, 179.4 versus 20.6 per 100,000 person-years respectively. The age-standardized prevalence was highest among Black women (498.4 [95% CI 422.3-588.2]), followed by Hispanic women (209.9 [174.9-252.0]), Asian/Pacific Islander women (171.0 [151.3-193.2]), and finally White women (130.0 [115.5-146.4]). The age-standardized prevalence among Black women was approximately 4 times higher than among White women.

Clinical manifestations

Among the incident 2007-2009 cases meeting the ACR definition, the most common manifestations were hematologic (84%), immunologic, (80%), arthritis (57%), renal disorder (45%), pleuritis or pericarditis (41%), and malar rash (33%) (Table 3). Neurologic disorder was the least common manifestation (8%). Renal disorder occurred more commonly in the Black (52%), Asian/Pacific Islander (51%), and Hispanic (47%) patients compared with White patients (40%). Discoid rash was highest among Black patients (22%) compared to the other groups and was least common in the Asian (5%) and Hispanic (0%) patients. Similar trends in frequencies of the clinical manifestations across the racial and ethnic groups were observed among the prevalent cases meeting the ACR definition (data not shown).

DISCUSSION

The California Lupus Surveillance Project had the opportunity to extend previous CDC-funded epidemiologic work to include two additional racial/ethnic groups and confirm striking racial and ethnic disparities in SLE incidence and prevalence. San Francisco County is diverse, with substantial numbers of Asian and Hispanic patients. We found that, in addition to African Americans, Asian/Pacific Islanders and Hispanics (of any race) have been disproportionately affected by SLE when compared to Whites (regardless of Hispanic ethnicity). Of the Hispanic

13

cases included in analyses, the majority were identified as White or had no race identified, e.g., race categories for ACR definition prevalent cases of Hispanic ethnicity were White (69%), no race identified (25%), Asian/Pacific Islander (5%), and Black (1%).

Hispanics currently comprise 16% and Asians 5% of the United States population. By 2050, these numbers are expected to rise to 30% and 8%, respectively (12). Thus, a reliable estimate of the burden of SLE in these growing populations is essential for health care planning. A major challenge in advancing knowledge in this area has been the paucity of large-scale, population-based surveillance studies with rigorously defined case definitions and case finding procedures. Up until the recent completion of the Georgia and Michigan surveillance projects, most previous epidemiologic studies were limited by small geographic areas, homogenous populations, varying case definitions, and incomplete case ascertainment that relied on administrative codes or patient self-reported diagnosis. Such historical studies provided estimates ranging from 2.0-7.6/100,000 for overall incidence and 19-241/100,000 for overall prevalence (13,14). The methodologies utilized in the CDC-funded registries, including the CLSP, have enabled us to determine more accurate and contemporary estimates of the incidence and prevalence of SLE in the United States.

The study has several limitations. The first is the potential for incomplete case ascertainment. Although we utilized the HIPAA exemption for obtaining informed consent, each clinic and hospital had to voluntarily agree to participate in the CLSP. This issue led to the potential for incomplete case ascertainment. For example, two small community hospitals in San Francisco chose not to participate in the CLSP. Based on the proportion of discharges from these two hospitals to the total number of discharges for San Francisco residents in 2007 – 2009 (16%) and the number of cases identified solely by community-based hospitals (9), we estimate

14

that the lack of participation of these two hospitals resulted in potentially only two missed

prevalent cases, using the ACR definition. Incomplete case ascertainment might also have

occurred because we did not conduct field work in primary care clinics. Thus, it is possible that

there were diagnosed cases of SLE in the community that never reached the attention of a

specialist or had not been seen by a specialist for many years. Although C-RC analysis estimated

an additional 33 incident cases and 147 prevalent cases, these estimates are imprecise as

indicated by the wide CIs. A second limitation is that data were collected from review of medical

records rather than from direct patient interview and evaluation. The quality of medical record

documentation of SLE manifestations varied widely.. For longstanding, prevalent cases, it was

sometimes difficult to retrieve the initial medical records that may have documented early

manifestations of disease. Third, race and ethnicity were determined from the medical record,

and were not always well documented. This led to missing data for race and ethnicity as well as

potential for misclassification. Lastly, our denominator data was extracted from the Census files,

which provides population totals at the Federal Information Processing Standards (FIPS) level

separately for race and ethnicity. Therefore, it was not possible for us to estimate prevalence and

incidence for mutually exclusive combined categories of these variables (e.g., non-Hispanic

White).

One of the major strengths of the CLSP was the ability to conduct widespread case

ascertainment by using a variety of sources including university and community clinics,

hospitals, regional laboratories, and state administrative databases. The abstractors

comprehensively reviewed patient medical records, thereby minimizing   underreporting bias in

case ascertainment. The CDC funded this project with a specific intent to develop credible and

complete estimates of the incidence and prevalence of lupus in Asians and Hispanics.   Asians

15

and Hispanics are generally smaller populations that we thought might access healthcare through alternative routes. To identify these patients, case-finding efforts were refined by working with physicians who were focused on those populations. For example, we partnered with a physician who cares for many of the Chinese patients in San Francisco at Chinese Hospital. To access the Hispanic population in San Francisco, we performed extensive case finding at San Francisco General Hospital and the associated community health network clinics. Our approach of partnering with the community and engaging culturally and linguistically concordant community members led to successful case ascertainment of these traditionally understudied populations. Had we not taken these extra steps, we would have missed SLE cases in the Asian and Hispanic populations.

SLE is a complex and heterogeneous disease for which there is no gold standard diagnostic test (15). One of the challenges of large, epidemiologic studies is the need to designate a diagnosis of SLE based on documentation in the medical record without the benefit of evaluating the patient in the clinical setting. For the purposes of CLSP, we used case definitions identical to those utilized by other CDC-funded surveillance registries. In this way, consistent methodology across the registries was achieved. The primary case-finding definition used for the study was meeting $\geq$ 4 of the 11 revised classification criteria for SLE as defined by the American College of Rheumatology. Because case-ascertainment relied on patient medical records and sometimes not all medical records for a given patient were available, there was a potential for under diagnosis of SLE if we only relied on the ACR criteria definition. Therefore, we also used the combined case definition that was used by the Georgia Lupus Registry.

The CLSP found high age-standardized mean annual incidence rates and prevalence

proportions of 4.6 and 84.8 per 100,000 respectively (ACR definition) and 5.2 and 96.8 per 100,000 respectively (combined definition). The data confirmed and quantified a higher burden of SLE in women and in racial and ethnic minorities. Using the ACR definition, the age-standardized female to male incidence ratio was 12:1 and prevalence ratio was 8:1. The highest age-standardized mean annual incidence rates and prevalence proportions per 100,000 were in Black women (30.5 and 458.1, respectively), followed by Hispanic women (8.9 and 177.9, respectively), Asian women (7.2 and 149.7, respectively) and then White women (5.3 and 109.8, respectively). Age-specific incidence rates and prevalence proportions were highest in Black women, with peak incidence and prevalence in the 40-59 age group.   The findings confirm previous studies that observed an increased burden of SLE among Black women. For example, a population based study in Allegheny County, PA determined a threefold higher incidence rate among Black woman compared to White woman in the years 1985-1990 (16). The Georgia and Michigan registries also showed higher incidence and prevalence estimates among Black women (2,3).

Interestingly, while the age-standardized incidence rate per 100,000 for the ACR definition in CLSP was slightly lower (4.6) than those of the Georgia (5.6) and Michigan (5.5) registries, the CLSP age-standardized prevalence per 100,000 (84.8) was statistically significantly higher than either Georgia's (73.0) or Michigan's (72.8). While the reasons for the higher prevalence but lower incidence of SLE in CLSP are not clear, factors such as better access to healthcare and awareness of the disease in San Francisco compared to the other registries may be playing a role. Also, among Black women, the age-standardized annual incidence rate and average annual prevalence per 100,000 (30.5 and 458.1) were > 2 times higher in California compared to Georgia (13.4 and 196.2, respectively) and Michigan (12.8 and 186.3 respectively).

17

Among White women, the age-standardized mean annual incidence rates were more similar among the three registries, although prevalence was still statistically significantly higher in CLSP. The reasons for the higher incidence and prevalence in CLSP for Black women compared with the other registries are not known, but may relate to several factors. With regard to the observed increased incidence, it is possible that the genetic ancestry of the Black population in San Francisco is different from that in Georgia and Michigan, portending greater risk for disease. In addition, there may be environmental influences that increase risk for SLE. Future studies will be required to address these important questions and further examine these possibilities.

There is a paucity of population-based studies estimating the incidence and prevalence of SLE among Hispanics and Asians in the United States. Increased SLE disease activity and organ damage among U.S. Hispanics versus non-Hispanic Caucasians have been previously noted by studies conducted within the Lupus in Minorities: Nature versus Nurture (LUMINA) longitudinal cohort. LUMINA studies have also showed differing disease outcomes among various Hispanic subgroups, with worse outcomes occurring among Hispanics in Texas compared to Hispanics in Puerto Rico (17, 18, 19). Because of reliance on medical record documentation of ethnicity in CLSP, we were unable to differentiate various Hispanic subgroups in the estimates of incidence and prevalence. Fewer studies have examined differences in SLE frequency and severity in Asian patients. One recent study from the Monash Lupus Clinic in Melbourne, Australia showed increased disease severity and serologic activity among Asian patients compared with White patients (20). The CLSP contributes to an improved understanding of the burden of SLE among Asians and highlights the need for further work on disease phenotypes, outcomes and drug responses which are likely to differ among patients from

18

different racial and ethnic backgrounds.

In conclusion, the CLSP confirmed the increased burden of SLE in Black, Asian, and

Hispanic women compared to White women. Future studies will be necessary to broaden our

understanding of the underlying etiologies for this disparity, including attempting to unravel the

contributions of genetic and biologic factors versus social and environmental factors in order to

improve patient outcomes.

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Table 1: Crude and age-standardized* average annual incidence rates (per 100,000 person-years) of SLE overall and categorized by race/ethnicity† and sex, by ACR and combined case definitions, San Francisco County, 2007 – 2009.

Race/ethnicity, sex	Study population (person-years)	ACR definition				Combined case definition			
		# cases	Crude rate (95% CI)		Age-standardized rate (95% CI)	# cases	Crude rate (95% CI)		Age-standardized rate (95% CI)
Overall‡	2,371,747	121	5.1	(4.3 – 6.1)	4.6 (3.8 – 5.5)	137	5.8	(4.9 – 6.8)	5.2 (4.3 – 6.2)
Women	1,170,817	112	9.6	(8.0 – 11.5)	8.6 (7.1 – 10.5)	127	10.8	(9.1 – 12.9)	9.8 (8.2 – 11.8)
Men	1,200,930	9	0.7	(0.4 – 1.4)	0.7 (0.4 – 1.4)	10	0.8	(0.5 – 1.5)	0.8 (0.4 – 1.5)
Black	170,035	27	15.9	(10.9 – 23.1)	15.5 (10.6 – 22.6)	28	16.5	(11.4 – 23.8)	16.0 (11.1 – 23.3)
Women	83,535	25	29.9	(20.3 – 44.2)	30.5 (20.7 – 44.9)	26	31.1	(21.2 – 45.6)	31.9 (21.8 – 46.5)
Men	86,500	2	2.3	(0.6 – 8.4)	2.1 (0.6 – 8.2)	2	2.3	(0.6 – 8.4)	2.1 (0.6 – 8.2)
White	1,338,200	43	3.2	(2.4 – 4.3)	2.8 (2.1 – 3.9)	50	3.7	(2.8 – 4.9)	3.3 (2.4 – 4.4)
Women	629,158	38	6.0	(4.4 – 8.3)	5.3 (3.8 – 7.5)	44	7.0	(5.2 – 9.4)	6.1 (4.5 – 8.4)
Men	709,042	5	0.7	(0.3 – 1.7)	0.6 (0.3 – 1.6)	6	0.8	(0.4 – 1.8)	0.8 (0.3 – 1.7)
Asian/Pacific Islander	840,386	39	4.6	(3.4 – 6.3)	4.1 (2.9 – 5.7)	43	5.1	(3.8 – 6.9)	4.6 (3.3 – 6.3)
Women	447,855	37	8.3	(6.0 – 11.4)	7.2 (5.1 – 10.2)	41	9.2	(6.7 – 12.4)	8.1 (5.8 – 11.2)
Men	392,531	2	0.5	(0.1 – 1.9)	0.6 (0.2 – 1.9)	2	0.5	(0.1 – 1.9)	0.6 (0.2 – 1.9)
Hispanic†	347,911	17	4.9	(3.1 – 7.8)	4.2 (2.5 – 7.0)	22	6.3	(4.2 – 9.6)	5.6 (3.6 – 8.7)
Women	163,586	16	9.8	(6.0 – 15.9)	8.9 (5.3 – 14.8)	21	12.8	(8.4 – 19.6)	12.0 (7.7 – 18.6)
Men	184,325	1	0.5	(0.1 – 3.1)	0.3 (0.0 – 2.7)	1	0.5	(0.1 – 3.1)	0.3 (0.0 – 2.7)

*Age-standardized to the 2000 projected Census population.

†Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number of cases missing ethnicity information: 18 for ACR definition and 21 for the combined definition.

‡Overall represents the entire population, including persons whose race/ethnicity was not known (n=11 for ACR definition, n=15 for combined definition) or was American Indian/Alaskan native (n=1 for both definitions).

21

Table 2: Crude and age-standardized* average annual prevalence (per 100,000 persons) of SLE, overall and categorized by race/ethnicity† and sex, for ACR and combined case definitions, San Francisco County, 2007 – 2009.

Race/ethnicity†, sex	ACR definition				Combined case definition			
	# cases§	Crude prevalence (95% CI)		Age-standardized prevalence (95% CI)	# cases§	Crude prevalence (95% CI)		Age-standardized prevalence (95% CI)
Overall‡	759	96.0	(89.4 – 103.1)	84.8 (78.6 – 91.5)	869	109.9	(102.8 – 117.4)	96.8 (90.2 – 103.9)
Women	675	172.9	(160.3 – 186.4)	155.6 (143.7 – 168.5)	778	199.4	(185.9 – 213.9)	179.4 (166.6 – 193.2)
Men	84	21.1	(17.0 – 26.1)	19.3 (15.4 – 24.1)	91	22.6	(18.4 – 27.8)	20.6 (16.6 – 25.6)
Black	150	264.1	(225.1 – 309.8)	241.0 (203.9 – 284.9)	163	287.0	(246.2 – 334.5)	261.0 (222.3 – 306.5)
Women	133	476.6	(402.3 – 564.6)	458.1 (385.4 – 544.5)	145	519.7	(441.9 – 611.2)	498.4 (422.3 – 588.2)
Men	17	58.9	(36.8 – 94.4)	52.3 (31.7 – 86.2)	18	62.4	(39.5 – 98.6)	54.8 (33.7 – 89.3)
White	282	63.3	(56.3 – 71.1)	55.2 (48.7 – 62.6)	333	74.7	(67.1 – 83.2)	64.9 (57.8 – 72.8)
Women	256	121.9	(107.8 – 137.7)	109.8 (96.5 – 124.9)	303	144.6	(129.2 – 161.8)	130.0 (115.5 – 146.4)
Men	27	11.3	(7.7 – 16.5)	10.0 (6.7 – 14.9)	30	12.7	(8.9 – 18.1)	11.4 (7.8 – 16.5)
Asian/Pacific Islander	279	99.7	(88.7 – 112.1)	90.5 (80.0 – 102.3)	317	113.1	(101.4 – 126.3)	102.5 (91.3 – 115.1)
Women	247	165.2	(145.8 – 187.1)	149.7 (131.4 – 170.7)	282	189.1	(168.3 – 212.4)	171.0 (151.3 – 193.2)
Men	33	25.0	(17.7 – 35.1)	22.9 (16.1 – 32.7)	35	26.5	(19.0 – 36.9)	24.3 (17.2 – 34.3)
Hispanic‡	111	95.7	(79.4 – 115.2)	94.7 (78.5 – 114.1)	131	112.6	(94.9 – 133.6)	110.5 (93.0 – 131.3)
Women	98	179.0	(146.8 – 218.1)	177.9 (145.9 – 217.0)	115	211.3	(176.1 – 253.5)	209.9 (174.9 – 252.0)
Men	13	21.7	(12.8 – 36.9)	20.1 (11.6 – 34.9)	15	25.0	(15.2 – 41.0)	22.2 (13.1 – 37.5)

*Age-standardized to the 2000 projected Census population.

†Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number cases missing ethnicity information: 178 for ACR definition and 235 for combined definition.

‡Overall represents the entire population, including persons whose race/ethnicity was not known (n=134 for ACR definition, n=158 for combined definition) or was American Indian/Alaskan native (n=10 for both definitions).

§These columns report the average annual cases (sum of prevalent cases for 2007 - 2009 divided by 3).

22

Table 3: ACR clinical manifestations among incident ACR-defined SLE cases, categorized by race/Hispanic ethnicity*, San Francisco County, 2007-2009

	Overall	Race			Hispanic Ethnicity
	(n=121)	Black (n=27)	White (n=43)	Asian or Pacific Islander (n=39)	(n=17)
Characteristic	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Malar Rash	33.1 (24.6 − 41.6)	18.5 (3.7 − 33.4)	32.6 (18.4 − 46.8)	41.0 (25.4 − 56.7)	41.2 (17.4 − 64.9)
Discoid rash	12.4 (6.4 − 18.4)	22.2 (6.3 − 38.1)	16.3 (5.1 − 27.5)	5.1 (0.0 − 12.2)	0.0 (0.0 − 0.0)
Photosensitivity	29.8 (21.5 − 38.0)	25.9 (9.2 − 42.7)	32.6 (18.4 − 46.8)	25.6 (11.7 − 39.5)	35.3 (12.3 − 58.3)
Oral ulcers	19.0 (11.9 − 26.1)	11.1 (0.0 − 23.1)	16.3 (5.1 − 27.5)	25.6 (11.7 − 39.5)	23.5 (3.1 − 44.0)
Nonerosive arthritis	57.0 (48.1 − 66.0)	66.7 (48.6 − 84.7)	65.1 (50.7 − 79.6)	38.5 (23.0 − 53.9)	64.7 (41.7 − 87.7)
Pleuritis or pericarditis	40.5 (31.6 − 49.4)	48.1 (29.0 − 67.3)	39.5 (24.7 − 54.4)	41.0 (25.4 − 56.7)	58.8 (35.1 − 82.6)
Renal disorder	44.6 (35.6 − 53.6)	51.9 (32.7 − 71.0)	39.5 (24.7 − 54.4)	51.3 (35.4 − 67.2)	47.1 (23.0 − 71.1)
Neurologic disorder	8.3 (3.3 − 13.2)	11.1 (0.0 − 23.1)	9.3 (0.5 − 18.1)	5.1 (0.0 − 12.2)	11.8 (0.0 − 27.3)
Hematologic disorder	83.5 (76.8 − 90.2)	85.2 (71.6 − 98.8)	76.7 (63.9 − 89.6)	89.7 (80.1 − 99.4)	88.2 (72.7 − 100.0)
Immunologic disorder	80.2 (73.0 − 87.4)	88.9 (76.9 − 100.0)	72.1 (58.5 − 85.7)	84.6 (73.1 − 96.1)	70.6 (48.6 − 92.6)
Positive antinuclear antibody	98.3 (96.0 − 100.0)	96.3 (89.1 − 100.0)	97.7 (93.1 − 100.0)	100.0 (100.0 − 100.0)	94.1 (82.8 − 100.0)

*Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number of cases missing ethnicity information: 18 for ACR definition and 21 for the combined definition.

Figure 1: Flow diagram of case ascertainment process, San Francisco County,

 2007 - 2009

Figure 2: Average annual age-specific incidence rates* of ACR-defined SLE among women, by race†

and Hispanic ethnicity†, San Francisco County, 2007 – 2009

* Within each age group 95% CIs overlapped with the following exceptions: In the 30 to 39 and 40 to 49 groups,

rates for Black women were statistically significantly higher than those of the other racial groups or Hispanics.

†Race categories are mutually exclusive. Hispanic ethnicity is recorded separately from race; therefore, persons in

this ethnicity category are also represented in the race categories (mostly White).

Figure 3: Average annual age-specific* prevalence of ACR-defined SLE among women and men, by
race† and Hispanic ethnicity†, San Francisco County, 2007 – 2009.

 *Among men, 95% CIs overlapped within each age group with the following exception: In the 50 to 59 group,
prevalence for Black men was statistically significantly higher than for White men.

†Race categories are mutually exclusive. Hispanic ethnicity is recorded separately from race; therefore, persons in

this ethnicity category are also represented in the race categories (mostly White).

24

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The Incidence and Prevalence of Systemic Lupus Erythematosus

The California Lupus Surveillance Project

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1

Abstract

Objective: Estimates of SLE incidence and prevalence in the United States have varied widely. The California Lupus Surveillance Project (CLSP) is funded by the Centers for Disease Control and Prevention (CDC) to determine credible estimates of SLE incidence and prevalence, with a special focus on Hispanics and Asians.

Methods: The CLSP is a population-based registry of individuals with SLE residing in San Francisco County, California from 2007 - 2009. Data sources included hospitals, rheumatologists, nephrologists, commercial laboratories, and a state hospital discharge database. We abstracted medical records to define SLE cases as patients with documentation of $\geq$ 4/11 of the American College of Rheumatology (ACR) Classification Criteria for SLE. We estimated crude and age-standardized incidence and prevalence, stratified by sex and race/ethnicity.

Results: Overall age-standardized annual incidence rate was 4.6 per 100,000 person-years. The average annual period prevalence was 84.8 per 100,000 persons. The age-standardized incidence rate was 8.6 and 0.7 per 100,000 person-years in women and men respectively. It was highest among Black women (30.5), followed by Hispanic women (8.9), Asian women (7.2), and White women (5.3). The age-standardized prevalence in women per 100,000 was 458.1 in Blacks, 177.9 in Hispanics, 149.7 in Asians, and 109.8 in Whites. C-RC modeling estimated 33 additional incident and 147 additional prevalent cases.

Conclusions: Comprehensive methods including intensive case finding provide more credible estimates of SLE in Hispanics and Asians, and confirm racial and ethnic disparities in SLE with the highest burden of disease in Black women, followed by Hispanic, Asian, and white women.

2

Historical estimates of the incidence and prevalence of systemic lupus erythematosus (SLE) in the ~~United States (U.S.)~~U.S. have varied widely (1). These differences stem from a variety of factors including the definition of SLE used, completeness of case ascertainment, geographic area, and racial/ethnic composition of the study population. The heterogeneity of disease manifestations and the lack of an accurate, reliable diagnostic test result in substantial challenges and costs to conducting large-scale epidemiologic studies in SLE. In an effort to develop more authoritative estimates of the incidence and prevalence of SLE, the Centers for Disease Control and Prevention (CDC) initially provided funding for two population-based lupus surveillance registries in Georgia (Georgia Lupus Registry) and Michigan (Michigan Lupus Epidemiology and Surveillance Program). These two registries have been successfully finished and focused primarily on Whites and Blacks (2, 3). To increase the reliability of SLE estimates in other racial/ethnic groups, the CDC funded two similar registries in California and New York to focus on Hispanics and Asians, and a third registry with the Indian Health Service to focus on American Indians and Alaskan Natives (4). ~~These groups have been underrepresented in previous epidemiological studies of SLE.~~

In collaboration with the CDC and the California Department of Public Health, we conducted the California Lupus Surveillance Project to determine contemporary, population-based estimates of the incidence and prevalence of SLE in San Francisco County during the period 2007 through 2009 using multiple methods of case ascertainment. A secondary goal was to describe the clinical and serologic spectrum of incident SLE in the population. To the greatest extent possible, we aligned our methodology with that of the Georgia and Michigan registries (2,3) to promote consistent data collection and optimal case ascertainment.

3

PATIENTS AND METHODS

The California Lupus Surveillance Project (CLSP). The CLSP was conducted under the statutory authority of the California Department of Public Health (CDPH). Patients were not contacted for this study. A partnership between the CDPH and the University of California, San Francisco (UCSF), allowed medical records to be collected using the health surveillance exemption to the Health Insurance Portability and Accountability Act (HIPAA) privacy rules (45 CFR parts 160 and 164). The use of protected health information was essential in the conduct of this project in order to increase potential case finding, perform unbiased case ascertainment and prevent duplicate patients in the registry. The CDPH subcontracted with the UCSF to conduct this project. The State of California Institutional Review Board (IRB) granted a waiver for this public health surveillance activity, but the project was reviewed and approved by the UCSF IRB.

Source population/catchment criteria. The source population consisted of residents of San Francisco County during 2007 – 2009. According to United States Census estimates, the San Francisco County source population in 2007 – 2009 averaged 790,582 residents, 56% of whom identified as White, 35% Asian or Pacific Islander, 7% Black, and 1% American Indian/Alaskan Native (5). Of note, Hispanic ethnicity is considered a distinct concept from race and is therefore collected and reported separately from race; and 15% of residents identified with Hispanic ethnicity.

Case definitions. SLE is currently diagnosed in clinical practice by an expert clinician on the basis of characteristic symptoms and signs in conjunction with supportive serologic and histologic data. For the purposes of this surveillance project in which clinical information was ascertained retrospectively through review of medical records, we used various case definitions

4

to classify a patient as having SLE. ~~For~~ To maintain consistency with the Georgia and Michigan Lupus Registr~~iesy~~ (2,3), we report estimates using two case-finding definitions:

1) American College of Rheumatology (ACR): This definition included patients who met $\geq$ 4 of the 11 ACR revised classification criteria defined in 1982 and updated in 1997 (6,7); this is a standard case definition used for research.

2) Combined: This definition was satisfied if any of the following three criteria were met:

    a. ACR case-finding definition, described above.

    b. Patients who had a documented diagnosis of SLE by the treating rheumatologist who met three of the 11 ACR classification criteria. This definition was chosen to allow for the possibility of missing data and inability to confirm criteria in the available medical records for prevalent cases with longstanding disease.

    c. Patients with lupus-related kidney disease defined either by presence of World Health Organization class II-VI lupus nephritis biopsy findings, or by the presence in the medical record of SLE (ICD-9-CM 710.0) along with either dialysis or renal transplantation.

Case ascertainment. The three primary sources of potential SLE cases were: 1) community rheumatology and nephrology clinics (office based practices), 2) community hospitals (non-academic hospitals), and 3) integrated healthcare systems (integrated hospitals and clinics) within the catchment area including the University of California at San Francisco, Kaiser Permanente Northern California, and the San Francisco Veterans Administration Medical Center (Figure 1)~~.~~

5

We queried these sources over the period 2000-2009 using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes 710.0 (SLE), 695.4 (discoid lupus), 710.8 (other specified connective tissue disease), and 710.9 (unspecified connective tissue disease).   A secondary source was a commercial laboratory, which we queried for the following serologic tests: anti-nuclear antibodies (ANAs), anti-dsDNA antibodies, anti-Smith antibodies, anti-phospholipid antibodies, and low complement levels. Another secondary source was the California Office of Statewide Health Planning and Development (OSHPD) hospital discharge database, which we queried for discharges using the ICD-9-CM diagnostic codes 710.0 (SLE), 695.4 (discoid lupus), 710.8 (other specified connective tissue disease), and 710.9 (unspecified connective tissue disease). We added patients identified from the OSHPD query to the roster of the appropriate primary source hospitals and integrated healthcare systems. After compiling a list of potential SLE patients from all sources using the queries described above, we determined catchment criteria for each patient (proof of residence in San Francisco County during the period 2007 – 2009). The primary methods for verifying catchment criteria were via the LexisNexis on-line database service, hospital billing databases, and clinic medical records. We then abstracted medical records for each of the potential SLE patients who met catchment criteria to identify those patients who had a physician diagnosis in the medical record of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or a related connective tissue disorder such as mixed connective tissue disease.

Data collection. Four trained field staff abstracted medical charts for each potential SLE patient who met catchment criteria. Training of the staff included lectures by physicians, extensive reading about SLE clinical manifestations and terminology, and practice abstractions of patient charts that were then reviewed in detail by the principal investigator (M.D.). The field

6

abstractors accessed all available medical records (paper charts and electronic medical records) at each source location, collecting more than 200 data elements. Laboratory records were reviewed for presence or absence of antibodies and for presence or absence of low complement.

The abstractors recorded whether the source was a community clinic, community hospital, or integrated health care system as described above. Abstractors contacted the principal investigator (M.D.) in real time as questions arose about the information in the medical records, to obtain clarifications. Demographic information was obtained from the medical record. For quality control, a second field abstractor and the principal investigator reviewed five of every 100 charts for each abstractor, and data entry errors identified by discordant responses between abstractors were identified and corrected. Overall, we calculated 98% concordance between abstractors for required data elements (those used to define ACR criteria) and 93% concordance for all other data elements.

Statistical Analysis.

We derived all denominators for incidence and prevalence using the 2007 – 2009 San Francisco population estimates from revised 2000-2009 bridged-race intercensal files (5). The average annual incidence rate (cases/100,000 person-years) was the number of newly diagnosed SLE cases that resided in San Francisco County at the time they were diagnosed with SLE (defined as the earliest date as recorded in the medical record that the physician first stated the diagnosis of SLE, possible SLE, undifferentiated connective tissue disease, or mixed connective tissue disease) during 2007 – 2009 divided by the sum of the annual population of San Francisco for 2007, 2008, and 2009. We calculated annual period prevalence (cases/100,000 persons) for each year separately, dividing the number of SLE cases diagnosed before or during that year and residing in San Francisco County during the year by the San Francisco County population of that

7

year. We then averaged the three annual prevalence estimates to yield the average annual prevalence for 2007 - 2009. Our next step was to calculate exact 95% confidence intervals (CIs) (8) for the incidence rate and average annual prevalence.

We calculated age-standardized incidence and prevalence using the direct method, based on the 2000 US projected population (distribution #2) (9). In addition, we computed age-specific estimates using 10-year age groups, as well as sex-specific estimates. The Census Bureau's intercensal database codes race and Hispanic ethnicity using two variables. One collapses all persons into four mutually exclusive categories defined by bridged race, without accounting for Hispanic ethnicity: Black, White, Asian/Pacific Islander, and American Indian/Alaskan Native (10). The other codes Hispanic ethnicity as a separate construct.

Similar to the Georgia registry (2), we used capture-recapture (C-RC) methods to estimate underascertainment of cases. Specifically, we developed log-linear models that estimated the number of missing cases predicted by the overlap among the three primary sources (community rheumatology and nephrology clinics, community hospitals, and integrated healthcare systems). We evaluated the results of all log-linear models possible for a three-source C-RC analysis and then chose the best-fitting model based on chi-square goodness-of-fit criteria (11). Using the estimated number of undercounted cases from best-fitting model, we calculated C-RC-revised incidence and prevalence estimates for the ACR definition. We considered results significant if p P< 0.05.

We compared differences between estimates by case definition using 95% confidence intervals (CIs) of the age-adjusted rates, with non-overlapping CIs considered to be significantly different.

RESULTS

8

Study population. As shown in Figure 1, among 15,210 potential SLE patients identified from primary and secondary sources, 4,859 met the geographical and temporal catchment criteria (residency in San Francisco County from 2007 through 2009). Abstraction was completed for 4,832 patients because 27 patients did not have any available medical records. Of the abstracted patients, 1,257 satisfied the catchment criteria and had a physician recorded diagnosis in the medical record of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or a related connective tissue disorder such as mixed connective tissue disease. Of these 1,257 cases, 121 incident and 796 prevalent cases met the ACR definition while 137 incident and 909 prevalent cases met the combined definition. All cases were confirmed using primary data sources, including those initially ascertained from state hospital discharge data. Commercial lab queries did not provide any additional cases.

Incidence.

The ACR definition. The overall crude and age-standardized incidence rates were 5.1 (95% CI 4.3-6.1) and 4.6 (95% CI 3.8-5.5) per 100,000 person-years (Table 1). The 121 incident cases consisted of 112 women and nine men. Race for these cases was identified as White (n=43), Asian/Pacific Islander (n=39), Black (n=27), and American Indian/Alaskan native (n=1); 11 had no race identified. Hispanic ethnicity was identified for 17 patients; 18 had no ethnicity identified. Among the Asian/Pacific Islander subgroup, the predominant race was Chinese (21 patients, of which 17 were identified as Chinese only, with the remaining four including another Asian/Pacific Islander racial category) followed by Japanese (three patients, two of which were exclusively Japanese), Filipino (two patients, all of whom also had another Asian/Pacific Islander racial category), and one each of Korean, Vietnamese, Asian Indian, Samoan, and

9

Hawaiian. The remaining seven cases were classified as "other Asian", a category including Burmese, Indonesian, and Asian not otherwise specified. (Data not shown.)

The age-standardized incidence rates were about 12 times higher among women than men, 8.6 versus 0.7 per 100,000 person-years respectively. The age-standardized incidence rate was highest among Black women (30.5 [95% CI 20.7-44.9]), followed by Hispanic women (8.9 [95% CI 5.3-14.8]), Asian women (7.2 [95% CI 5.1-10.2]), and finally White women (5.3 [3.8-7.5]). The age-standardized incidence rate among Black women was approximately six times higher than among White women.

Among Black women, the age-specific incidence rate peaked at 61.2 per 100,000 in the 40-49 year old age group. Among the other racial/ethnic groups, incidence rates were relatively constant across the age groups (Figure 2). There were too few incident cases in men (nine cases) to enable age stratification. Overall mean age at diagnosis was 43.9 years. Mean age at diagnosis stratified by bridged race/ethnicity was: Black (40.1 years), White (46.5 years), Asian (45.1 years), and Hispanic (36.6 years); all CIs for race/ethnicity mean age estimates overlapped. (Data not shown.)

Our C-RC modeling estimated 33 (95% CI 8-130) additional incident cases in the population, yielding CRC-inflated crude rate of 6.5 per 100,000 person-years.

The combined definition. The combined definition yielded an additional 16 cases (15 from the three ACR criteria + rheumatologist diagnosis criterion and a single case from the lupus-related kidney disease criterion) for a total of 137 incident cases (Table 1). The overall crude and age-standardized incidence rates were 5.8 (95% CI 4.9-6.8) and 5.2 (95% 4.3-6.2) per 100,000

10

person-years. Incident cases' sex and racial/ethnic disparities were similar to those observed for the ACR cases.

Prevalence.

The ACR definition. The ACR definition yielded overall crude and age-standardized prevalence proportions of 96.0 (95% CI 89.4-103.1) and 84.8 (95% CI 78.6-91.5) per 100,000 persons (Table 2). The 796 unique prevalent cases over the three-year period consisted of 708 women and 88 men. We identified race for these cases as White (n=294), Asian/Pacific Islander (n=290), Black (n=160), and American Indian/Alaskan native (n=4); 48 had no race identified. Hispanic ethnicity was identified for 118 patients. Similar to the incident cases, the majority of the Asian/Pacific Islander subgroup was composed of Chinese patients (137, of which 101 were identified as Chinese and no other race) followed by "other Asian" (56 patients), Filipino (42 patients, of whom 26 were not identified with any other race), Vietnamese (18, of whom 12 had no other race identified), Japanese (10, of which eight were not identified with any other race), Korean (five, of whom three had no other race identified), Thai and Pakistani (four each), and Asian Indian and Samoan (three each), and other South Asian, Cambodian and Pacific Islander—not otherwise specified (two each), and Hawaiian and Laotian (one each) (Data not shown).

Age-standardized prevalence was about eight times higher among women than men, 155.6 versus 19.3 per 100,000 persons respectively. The age-standardized prevalence was highest among Black women (458.1 [95% CI 385.4-544.5]), followed by Hispanic women (177.9 [145.9-217.0]), Asian women (149.7 [131.4-170.7]), and finally white women (109.8 [96.5-124.9]). The age-standardized prevalence among Black women was over four times higher

11

than among White women.   The age-standardized prevalence among Black men was over five times higher than among White men.

Age-specific prevalence in the ACR defined cases were statistically significantly higher in Black women compared with women from the other racial groups for ages (years) 30 – 59, with whites and Asians for ages 69- 79, and with whites only for ages 20 - 29. Among Black women, age-specific prevalence began to increase at age 20 years and peaked at 954.5 per 100,000 in the 40-49 years group (Figure 3).   Among Black men, age-specific prevalence peaked in the 50-69 year range. Age-specific prevalence was higher in Black men compared to the other racial/ethnic groups (Figure 3). Among men, 95% CIs overlapped within each age group with the following exception: In the 50 to 59 group, prevalence for Black men was statistically significantly higher than for white men.

Overall mean age at diagnosis was 34.8 years. Age at diagnosis stratified by bridged race and ethnicity was as follows: Black (35.5 years), White (34.4 years), Asian (34.6 years), and Hispanic (33.9 years). Once again, the 95% CIs for these estimates overlapped. (Data not shown.)

Our C-RC modeling estimated 147 (95% CI 93-225) additional prevalent cases in the population, yielding CRC-inflated average annual crude prevalence of 113.7 per 100,000 persons.

The combined definition.

By including an additional 113 individuals (89 from the three ACR criteria + rheumatologist diagnosis criterion and 24 from the lupus-related kidney disease criterion), the combined

12

definition yielded a total of 909 unique individuals over the three-year period (Figure 1), or 869

average annual prevalent cases (Table 2). The overall crude and age-standardized prevalence

proportions were 109.9 (95% CI 102.8 – 117.4) and 96.8 (95% 90.2-103.9) per 100,000 persons.

Age-standardized prevalence proportions were nine times higher among women than men, 179.4

versus 20.6 per 100,000 person-years respectively. The age-standardized prevalence was highest

among Black women (498.4 [95% CI 422.3-588.2]), followed by Hispanic women (209.9

[174.9-252.0]), Asian/Pacific Islander women (171.0 [151.3-193.2]), and finally White women

(130.0 [115.5-146.4]). The age-standardized prevalence among Black women was

approximately 4 times higher than among White women.

Clinical manifestations

Among the incident 2007-2009 cases meeting the ACR definition, the most common

manifestations were hematologic (84%), immunologic, (80%), arthritis (57%), renal disorder

(45%), pleuritis or pericarditis (41%), and malar rash (33%) (Table 3). Neurologic disorder was

the least common manifestation (8%). Renal disorder occurred more commonly in the Black

(52%), Asian/Pacific Islander (51%), and Hispanic (47%) patients compared with White patients

(40%).   Discoid rash was highest among Black patients (22%) compared to the other groups and

was least common in the Asian (5%) and Hispanic (0%) patients. Similar trends in frequencies

of the clinical manifestations across the racial and ethnic groups were observed among the

prevalent cases meeting the ACR definition (data not shown).

DISCUSSION

        The California Lupus Surveillance Project had the opportunity to extend previous CDC-

funded epidemiologic work to include two additional racial/ethnic groups and confirm striking

13

racial and ethnic disparities in SLE incidence and prevalence. San Francisco County is diverse, with substantial numbers of Asian and Hispanic patients. We found that, in addition to African Americans, Asian/Pacific Islanders and Hispanics (of any race) have been disproportionately affected by SLE when compared to Whites (regardless of Hispanic ethnicity). ~~Note that because the Census Bureau reports race and ethnicity separately, it was not possible for us to estimate prevalence and incidence for mutually exclusive and exhaustive categories of these variables (e.g., non-Hispanic white). However, of~~ Of the Hispanic cases included in analyses, the majority were identified as White or had no race identified, e.g., race categories for ACR definition prevalent cases of Hispanic ethnicity were White (69%), no race identified (25%), Asian/Pacific Islander (5%), and Black (1%).

Hispanics currently comprise 16% and Asians 5% of the United States population. By 2050, these numbers are expected to rise to 30% and 8%, respectively (12). Thus, a reliable estimate of the burden of SLE in these growing populations is essential for health care planning. A major challenge in advancing knowledge in this area has been the paucity of large-scale, population-based surveillance studies with rigorously defined case definitions and case finding procedures. Up until the recent completion of the Georgia and Michigan surveillance projects, most previous epidemiologic studies were limited by small geographic areas, homogenous populations, varying case definitions, and incomplete case ascertainment that relied on administrative codes or patient self-reported diagnosis. Such historical studies provided estimates ranging from 2.0-7.6/100,000 for overall incidence and 19-241/100,000 for overall prevalence (13,14). The methodologies utilized in the CDC-funded registries, including the CLSP, have enabled us to determine more accurate and contemporary estimates of the incidence and prevalence of SLE in the United States.

14

The study has several limitations. The first is the potential for incomplete case ascertainment. Although we utilized the HIPAA exemption for obtaining informed consent, each clinic and hospital had to voluntarily agree to participate in the CLSP. This issue led to the potential for incomplete case ascertainment. For example, two small community hospitals in San Francisco chose not to participate in the CLSP. Based on the proportion of discharges from these two hospitals to the total number of discharges for San Francisco residents in 2007 – 2009 (16%) and the number of cases identified solely by community-based hospitals (9), we estimate that the lack of participation of these two hospitals resulted in potentially only two missed prevalent cases, using the ACR definition. Incomplete case ascertainment might also have occurred because we ~~focused our surveillance efforts on rheumatology clinics and~~ did not conduct field work in primary care clinics. Thus, it is possible that there were diagnosed cases of SLE in the community that never reached the attention of a specialist or had not been seen by a specialist for many years. Although C-RC analysis estimated an additional 33 incident cases and 147 prevalent cases, these estimates are imprecise as indicated by the wide CIs. A second limitation is that data were collected ~~retrospectively~~ from review of medical records rather than from direct patient interview and evaluation. The quality of medical record documentation of SLE manifestations ~~and criteria~~ varied widely ~~. from clinic to clinic~~. For longstanding, prevalent cases, it was sometimes difficult to retrieve the initial medical records that may have documented early manifestations of disease~~, particularly serologic laboratory results~~. Third, race and ethnicity were determined from the medical record, and ~~and not patient self-report. We found that race and ethnicity~~ were not always well documented. ~~in the medical records.~~ This led to missing data for race and ethnicity as well as potential for misclassification. ~~Lastly, we used non-overlapping confidence intervals rather than p values to assess differences.~~ Lastly, our

15

denominator data was extracted from the Census files, which provides population totals at the

Federal Information Processing Standards (FIPS) level separately for race and ethnicity.

Therefore, it was not possible for us to estimate prevalence and incidence for mutually exclusive

combined categories of these variables (e.g., non-Hispanic White).

One of the major strengths of the CLSP was the ability to conduct widespread case ascertainment

by using a variety of sources including university and community clinics, hospitals, regional

laboratories, and state administrative databases. The abstractors comprehensively reviewed

patient medical records, thereby minimizing. Thus, underreporting bias in case ascertainment.

was minimized. The CDC funded this project with a specific intent to develop credible and

complete estimates of the incidence and prevalence of lupus in Asians and Hispanics. Asians

and Hispanics are generally smaller populations that we thought might access healthcare through

alternative routes. To identify Asian and Hispanic patients who might not have had access to or

might not have chosen to receive specialty care through the traditional health-care systems in the

catchment area,these patients, case-finding efforts were refined by working with physicians who

were focused on those populations. For example, we partnered with a physician who cares for

many of the Chinese patients in San Francisco at Chinese Hospital. Also, one of our abstractors

speaks both Cantonese and Mandarin and has strong ties to the Chinese community in San

Francisco. Her connections and skills were very helpful in accessing the Chinese population.

To access the Hispanic population in San Francisco, we performed extensive case finding at San

Francisco General Hospital and the associated community health network clinics. Our approach

of partnering with the community and engaging culturally and linguistically concordant

community members led to successful case ascertainment of these traditionally understudied

16

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populations. Had we not taken these extra steps, we would have missed SLE cases in the Asian and Hispanic populations.

SLE is a complex and heterogeneous disease for which there is no gold standard diagnostic test (15). One of the challenges of large, epidemiologic studies is the need to designate a diagnosis of SLE based on documentation in the medical record without the benefit of evaluating the patient in the clinical setting. For the purposes of CLSP, we used agreed upon case definitions that wereidentical to those utilized by other CDC-funded surveillance registries. In this way, consistent methodology across the registries was achieved. The primary case-finding definition used for the study was meeting ≥ 4 of the 11 revised classification criteria for SLE as defined by the American College of Rheumatology. Because case-ascertainment relied on patient medical records and sometimes not all medical records for a given patient were available, there was a potential for under diagnosis of SLE if we only relied on the ACR criteria definition. Therefore, we also used the combined case definition that was used by the Georgia Lupus Registry.

The CLSP found high age-standardized mean annual incidence rates and prevalence proportions of 4.6 and 84.8 per 100,000 respectively (ACR definition) and 5.2 and 96.8 per 100,000 respectively (combined definition). The data confirmed and quantified a higher burden of SLE in women and in racial and ethnic minorities. Using the ACR definition, the age-standardized female to male incidence ratio was 12:1 and prevalence ratio was 8:1. The highest age-standardized mean annual incidence rates and prevalence proportions per 100,000 were in Black women (30.5 and 458.1, respectively), followed by Hispanic women (8.9 and 177.9, respectively), Asian women (7.2 and 149.7, respectively) and then White women (5.3 and 109.8,

17

respectively). Age-specific incidence rates and prevalence proportions were highest in Black women, with peak incidence and prevalence in the 40-59 age group.   The findings confirm previous studies that observed an increased burden of SLE among Black women. For example, a population based study in Allegheny County, PA determined a threefold higher incidence rate among Black woman compared to White woman in the years 1985-1990 (16). The Georgia and Michigan registries also showed higher incidence and prevalence estimates among Black women (2,3).

Interestingly, while the age-standardized incidence rate per 100,000 for the ACR definition in CLSP was slightly lower (4.6) than those of the Georgia (5.6) and Michigan (5.5) registries, the CLSP age-standardized prevalence per 100,000 (84.8) was statistically significantly higher than either Georgia's (73.0) or Michigan's (72.8). While the reasons for the higher prevalence but lower incidence of SLE in CLSP are not clear, factors such as better access to healthcare and awareness of the disease in San Francisco compared to the other registries may be playing a role. Also, among Black women, the age-standardized annual incidence rate and average annual prevalence per 100,000 (30.5 and 458.1) were > 2 times higher in California compared to Georgia (13.4 and 196.2, respectively) and Michigan (12.8 and 186.3 respectively). Among White women, the age-standardized mean annual incidence rates were more similar among the three registries, although prevalence was still statistically significantly higher in CLSP. The reasons for the higher incidence and prevalence in CLSP for Black women compared with the other registries are not known, but may relate to several factors.   With regard to the observed increased incidence, it is possible that the genetic ancestry of the Black population in San Francisco is different from that in Georgia and Michigan, portending greater risk for disease. In addition, there may be environmental influences that increase risk for SLE.

18

Future studies will be required to address these important questions and further examine these possibilities.

There is a paucity of population-based studies estimating the incidence and prevalence of SLE among Hispanics and Asians in the United States. Increased SLE disease activity and organ damage among U.S. Hispanics versus non-Hispanic Caucasians have been previously noted by studies conducted within the Lupus in Minorities: Nature versus Nurture (LUMINA) longitudinal cohort. LUMINA studies have also showed differing disease outcomes among various Hispanic subgroups, with worse outcomes occurring among Hispanics in Texas compared to Hispanics in Puerto Rico (17, 18, 19). Because of reliance on medical record documentation of ethnicity in CLSP, we were unable to differentiate various Hispanic subgroups in the estimates of incidence and prevalence. Fewer studies have examined differences in SLE frequency and severity in Asian patients. One recent study from the Monash Lupus Clinic in Melbourne, Australia showed increased disease severity and serologic activity among Asian patients compared with White patients (20). The CLSP contributes to an improved understanding of the burden of SLE among Asians and highlights the need for further work on disease phenotypes, outcomes and drug responses which are likely to differ among patients from different racial and ethnic backgrounds.

In conclusion, the CLSP confirmed the increased burden of SLE in Black, Asian, and Hispanic women compared to White women. Future studies will be necessary to broaden our understanding of the underlying etiologies for this disparity, including attempting to unravel the contributions of genetic and biologic factors versus social and environmental factors in order to improve patient outcomes.

19

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20

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21

Table 1: Crude and age-standardized* average annual incidence rates (per 100,000 person-years) of SLE overall and categorized by race/ethnicity† and sex, by ACR and combined case definitions, San Francisco County, 2007 – 2009.

Race/ethnicity, sex	Study population (person-years)	ACR definition			Combined case definition		
		# cases	Crude rate (95% CI)	Age-standardized rate (95% CI)	# cases	Crude rate (95% CI)	Age-standardized rate (95% CI)
Overall‡	2,371,747	121	5.1 (4.3 – 6.1)	4.6 (3.8 – 5.5)	137	5.8 (4.9 – 6.8)	5.2 (4.3 – 6.2)
Women	1,170,817	112	9.6 (8.0 – 11.5)	8.6 (7.1 – 10.5)	127	10.8 (9.1 – 12.9)	9.8 (8.2 – 11.8)
Men	1,200,930	9	0.7 (0.4 – 1.4)	0.7 (0.4 – 1.4)	10	0.8 (0.5 – 1.5)	0.8 (0.4 – 1.5)
Black	170,035	27	15.9 (10.9 – 23.1)	15.5 (10.6 – 22.6)	28	16.5 (11.4 – 23.8)	16.0 (11.1 – 23.3)
Women	83,535	25	29.9 (20.3 – 44.2)	30.5 (20.7 – 44.9)	26	31.1 (21.2 – 45.6)	31.9 (21.8 – 46.5)
Men	86,500	2	2.3 (0.6 – 8.4)	2.1 (0.6 – 8.2)	2	2.3 (0.6 – 8.4)	2.1 (0.6 – 8.2)
White	1,338,200	43	3.2 (2.4 – 4.3)	2.8 (2.1 – 3.9)	50	3.7 (2.8 – 4.9)	3.3 (2.4 – 4.4)
Women	629,158	38	6.0 (4.4 – 8.3)	5.3 (3.8 – 7.5)	44	7.0 (5.2 – 9.4)	6.1 (4.5 – 8.4)
Men	709,042	5	0.7 (0.3 – 1.7)	0.6 (0.3 – 1.6)	6	0.8 (0.4 – 1.8)	0.8 (0.3 – 1.7)
Asian/Pacific Islander	840,386	39	4.6 (3.4 – 6.3)	4.1 (2.9 – 5.7)	43	5.1 (3.8 – 6.9)	4.6 (3.3 – 6.3)
Women	447,855	37	8.3 (6.0 – 11.4)	7.2 (5.1 – 10.2)	41	9.2 (6.7 – 12.4)	8.1 (5.8 – 11.2)
Men	392,531	2	0.5 (0.1 – 1.9)	0.6 (0.2 – 1.9)	2	0.5 (0.1 – 1.9)	0.6 (0.2 – 1.9)
Hispanic†	347,911	17	4.9 (3.1 – 7.8)	4.2 (2.5 – 7.0)	22	6.3 (4.2 – 9.6)	5.6 (3.6 – 8.7)
Women	163,586	16	9.8 (6.0 – 15.9)	8.9 (5.3 – 14.8)	21	12.8 (8.4 – 19.6)	12.0 (7.7 – 18.6)
Men	184,325	1	0.5 (0.1 – 3.1)	0.3 (0.0 – 2.7)	1	0.5 (0.1 – 3.1)	0.3 (0.0 – 2.7)

*Age-standardized to the 2000 projected Census population.

†Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number of cases missing ethnicity information: 18 for ACR definition and 21 for the combined definition.

‡Overall represents the entire population, including persons whose race/ethnicity was not known (n=11 for ACR definition, n=15 for combined definition) or was American Indian/Alaskan native (n=1 for both definitions).

22

Table 2: Crude and age-standardized* average annual prevalence (per 100,000 persons) of SLE, overall and categorized by race/ethnicity† and sex, for ACR and combined case definitions, San Francisco County, 2007 – 2009.

Race/ethnicity†, sex	ACR definition					Combined case definition				
	# cases§	Crude prevalence (95% CI)		Age-standardized prevalence (95% CI)		# cases§	Crude prevalence (95% CI)		Age-standardized prevalence (95% CI)	
Overall‡	759	96.0	(89.4 – 103.1)	84.8	(78.6 – 91.5)	869	109.9	(102.8 – 117.4)	96.8	(90.2 – 103.9)
Women	675	172.9	(160.3 – 186.4)	155.6	(143.7 – 168.5)	778	199.4	(185.9 – 213.9)	179.4	(166.6 – 193.2)
Men	84	21.1	(17.0 – 26.1)	19.3	(15.4 – 24.1)	91	22.6	(18.4 – 27.8)	20.6	(16.6 – 25.6)
Black	150	264.1	(225.1 – 309.8)	241.0	(203.9 – 284.9)	163	287.0	(246.2 – 334.5)	261.0	(222.3 – 306.5)
Women	133	476.6	(402.3 – 564.6)	458.1	(385.4 – 544.5)	145	519.7	(441.9 – 611.2)	498.4	(422.3 – 588.2)
Men	17	58.9	(36.8 – 94.4)	52.3	(31.7 – 86.2)	18	62.4	(39.5 – 98.6)	54.8	(33.7 – 89.3)
White	282	63.3	(56.3 – 71.1)	55.2	(48.7 – 62.6)	333	74.7	(67.1 – 83.2)	64.9	(57.8 – 72.8)
Women	256	121.9	(107.8 – 137.7)	109.8	(96.5 – 124.9)	303	144.6	(129.2 – 161.8)	130.0	(115.5 – 146.4)
Men	27	11.3	(7.7 – 16.5)	10.0	(6.7 – 14.9)	30	12.7	(8.9 – 18.1)	11.4	(7.8 – 16.5)
Asian/Pacific Islander	279	99.7	(88.7 – 112.1)	90.5	(80.0 – 102.3)	317	113.1	(101.4 – 126.3)	102.5	(91.3 – 115.1)
Women	247	165.2	(145.8 – 187.1)	149.7	(131.4 – 170.7)	282	189.1	(168.3 – 212.4)	171.0	(151.3 – 193.2)
Men	33	25.0	(17.7 – 35.1)	22.9	(16.1 – 32.7)	35	26.5	(19.0 – 36.9)	24.3	(17.2 – 34.3)
Hispanic‡	111	95.7	(79.4 – 115.2)	94.7	(78.5 – 114.1)	131	112.6	(94.9 – 133.6)	110.5	(93.0 – 131.3)
Women	98	179.0	(146.8 – 218.1)	177.9	(145.9 – 217.0)	115	211.3	(176.1 – 253.5)	209.9	(174.9 – 252.0)
Men	13	21.7	(12.8 – 36.9)	20.1	(11.6 – 34.9)	15	25.0	(15.2 – 41.0)	22.2	(13.1 – 37.5)

*Age-standardized to the 2000 projected Census population.

†Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number cases missing ethnicity information: 178 for ACR definition and 235 for combined definition.

‡Overall represents the entire population, including persons whose race/ethnicity was not known (n=134 for ACR definition, n=158 for combined definition) or was American Indian/Alaskan native (n=10 for both definitions).
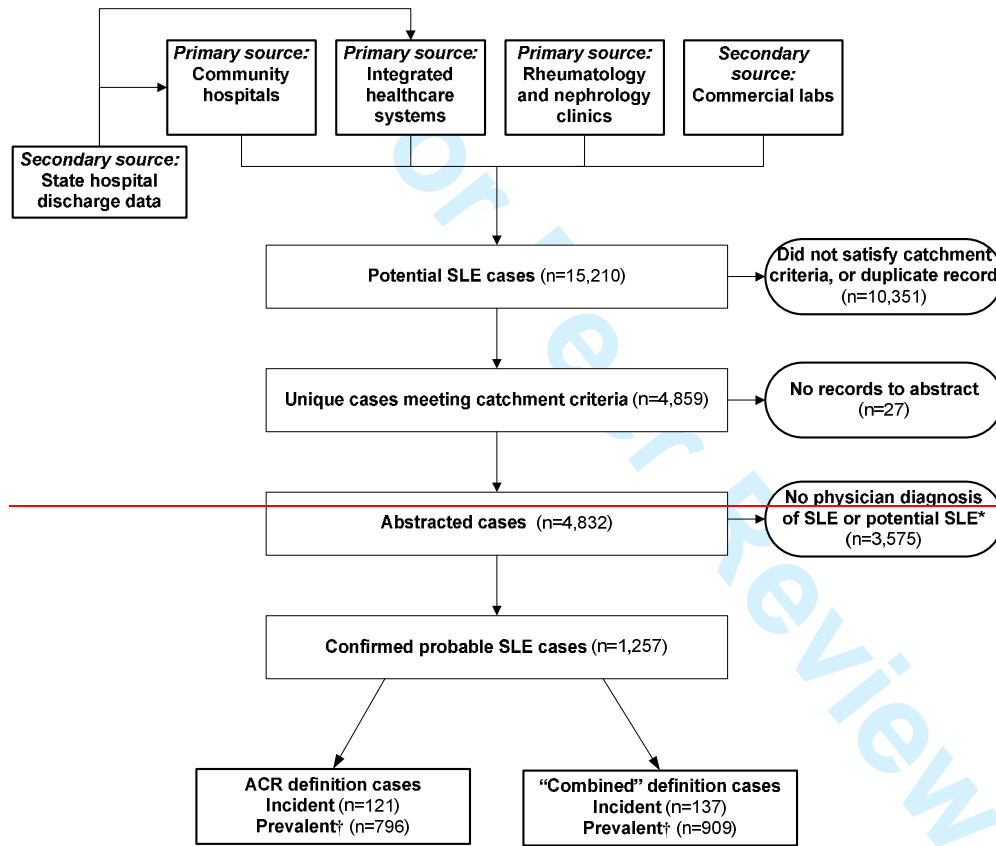
§These columns report the average annual cases (sum of prevalent cases for 2007 - 2009 divided by 3).

23

Table 3: ACR clinical manifestations among incident ACR-defined SLE cases, categorized by race/Hispanic ethnicity*, San Francisco County, 2007-2009

	Overall		Race					Hispanic Ethnicity	
	(n=121)		Black (n=27)		White (n=43)		Asian or Pacific Islander (n=39)		(n=17)	
Characteristic	% (95% CI)		% (95% CI)		% (95% CI)		% (95% CI)		% (95% CI)	
Malar Rash	33.1	(24.6 − 41.6)	18.5	(3.7 − 33.4)	32.6	(18.4 − 46.8)	41.0	(25.4 − 56.7)	41.2	(17.4 − 64.9)
Discoid rash	12.4	(6.4 − 18.4)	22.2	(6.3 − 38.1)	16.3	(5.1 − 27.5)	5.1	(0.0 − 12.2)	0.0	(0.0 − 0.0)
Photosensitivity	29.8	(21.5 − 38.0)	25.9	(9.2 − 42.7)	32.6	(18.4 − 46.8)	25.6	(11.7 − 39.5)	35.3	(12.3 − 58.3)
Oral ulcers	19.0	(11.9 − 26.1)	11.1	(0.0 − 23.1)	16.3	(5.1 − 27.5)	25.6	(11.7 − 39.5)	23.5	(3.1 − 44.0)
Nonerosive arthritis	57.0	(48.1 − 66.0)	66.7	(48.6 − 84.7)	65.1	(50.7 − 79.6)	38.5	(23.0 − 53.9)	64.7	(41.7 − 87.7)
Pleuritis or pericarditis	40.5	(31.6 − 49.4)	48.1	(29.0 − 67.3)	39.5	(24.7 − 54.4)	41.0	(25.4 − 56.7)	58.8	(35.1 − 82.6)
Renal disorder	44.6	(35.6 − 53.6)	51.9	(32.7 − 71.0)	39.5	(24.7 − 54.4)	51.3	(35.4 − 67.2)	47.1	(23.0 − 71.1)
Neurologic disorder	8.3	(3.3 − 13.2)	11.1	(0.0 − 23.1)	9.3	(0.5 − 18.1)	5.1	(0.0 − 12.2)	11.8	(0.0 − 27.3)
Hematologic disorder	83.5	(76.8 − 90.2)	85.2	(71.6 − 98.8)	76.7	(63.9 − 89.6)	89.7	(80.1 − 99.4)	88.2	(72.7 − 100.0)
Immunologic disorder	80.2	(73.0 − 87.4)	88.9	(76.9 − 100.0)	72.1	(58.5 − 85.7)	84.6	(73.1 − 96.1)	70.6	(48.6 − 92.6)
Positive antinuclear antibody	98.3	(96.0 − 100.0)	96.3	(89.1 − 100.0)	97.7	(93.1 − 100.0)	100.0	(100.0 − 100.0)	94.1	(82.8 − 100.0)

*Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories. Number of cases missing ethnicity information: 18 for ACR definition and 21 for the combined definition.
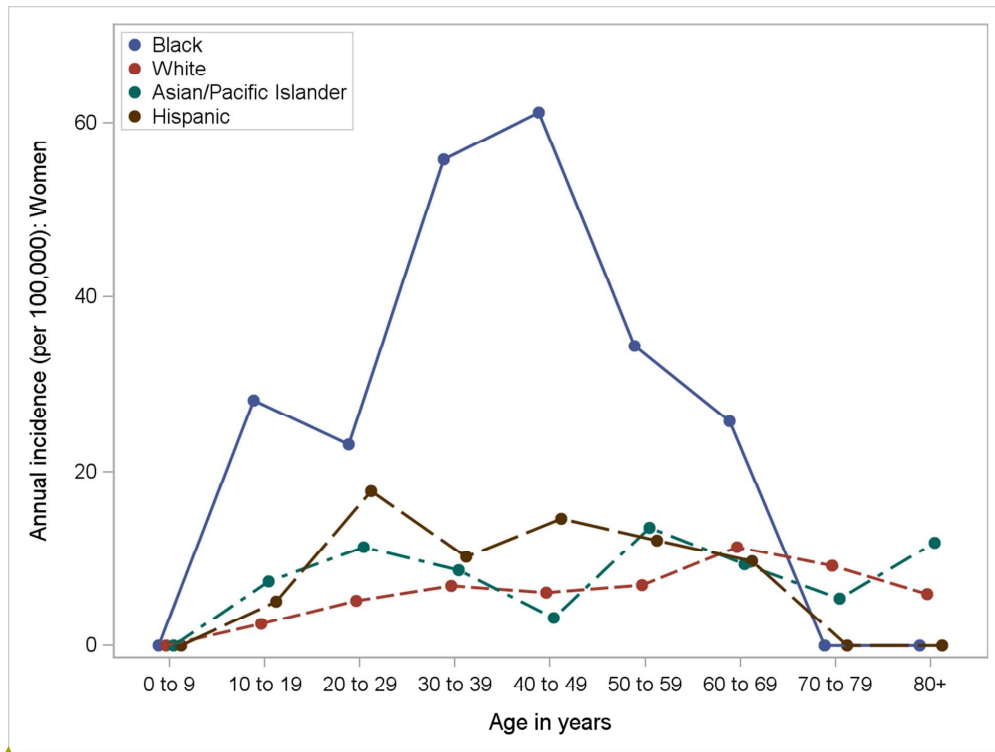
24

Figure 1: Flow diagram of case ascertainment process, San Francisco County, 2007 - 2009

* Medical record diagnosis of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or related connective tissue disorder

† These cases represent unique persons over the 3-year time period.

25

Figure 2: Average annual age-specific incidence rates* of ACR-defined SLE among women, by race† and Hispanic ethnicity†, San Francisco County, 2007 – 2009
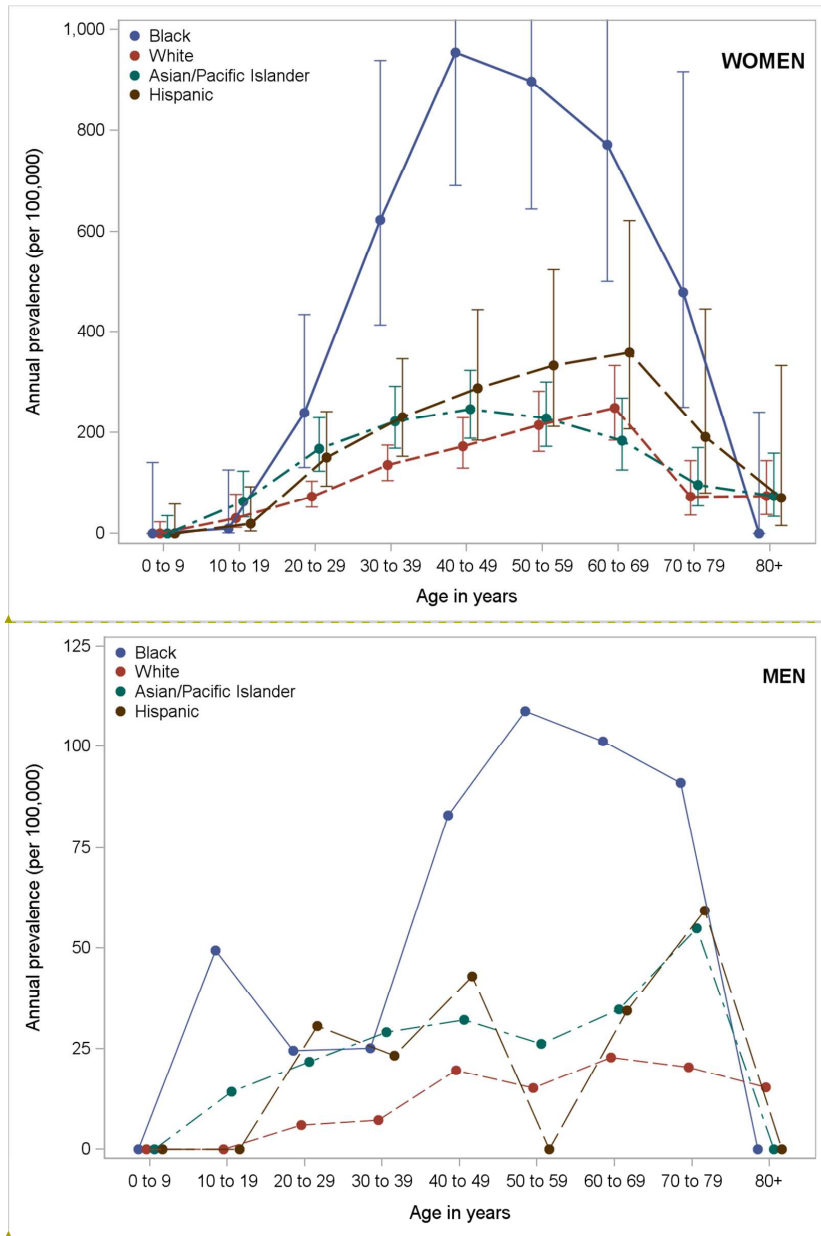
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* Within each age group 95% CIs overlapped with the following exceptions: In the 30 to 39 and 40 to 49 groups, rates for Black women were statistically significantly higher than those of the other racial groups or Hispanics.

†Race categories are mutually exclusive. Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories (mostly White).

26

Figure 3: Average annual age-specific* prevalence of ACR-defined SLE among women and men, by race† and Hispanic ethnicity†, San Francisco County, 2007—2009.
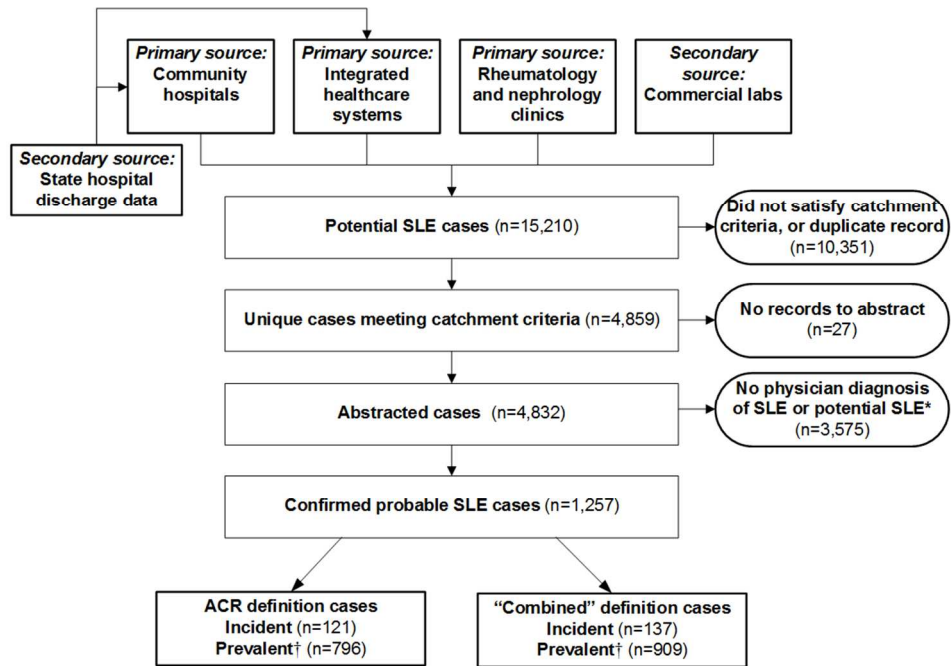
27

*Among men, 95% CIs overlapped within each age group with the following exception: In the 50 to 59 group, prevalence for Black men was statistically significantly higher than for white men.

†Race categories are mutually exclusive. Hispanic ethnicity is recorded separately from race; therefore, persons in this ethnicity category are also represented in the race categories (mostly white).
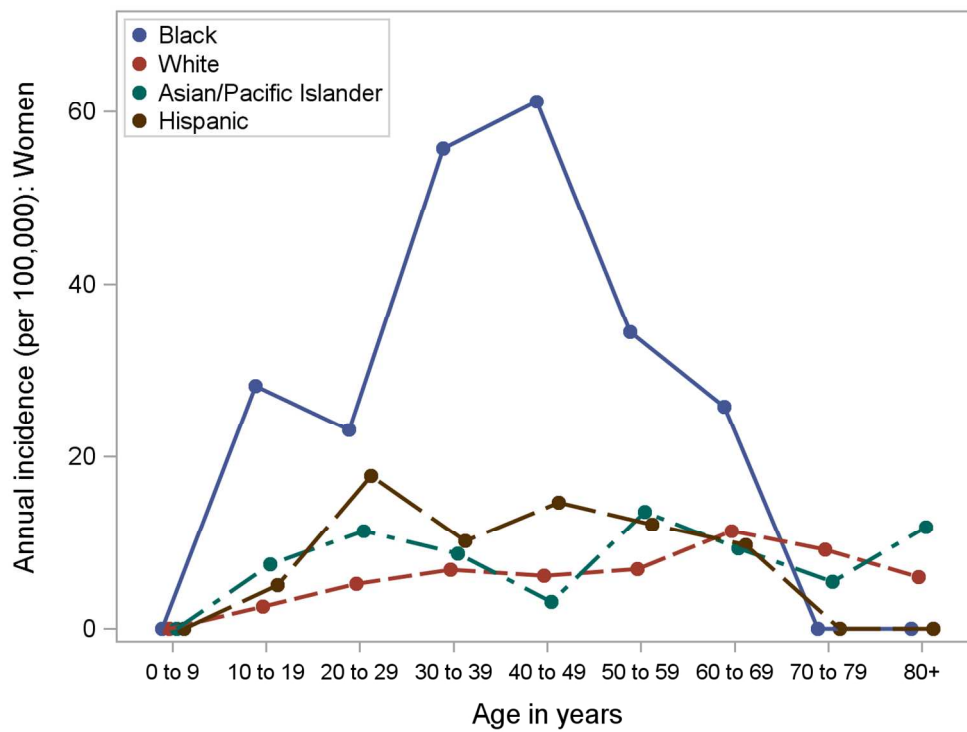
28

* Medical record diagnosis of SLE, possible SLE, undifferentiated/unspecified connective tissue disease, or related connective tissue
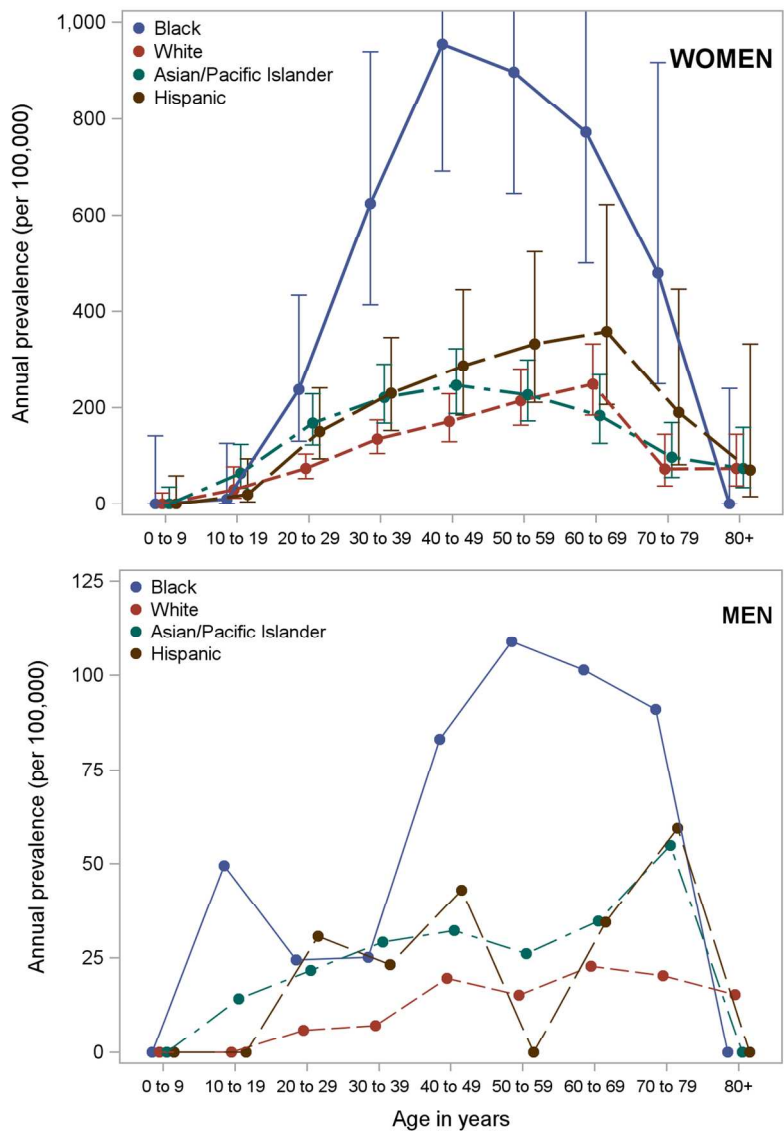 disorder

† These cases represent unique persons over the 3-year time period.

100x78mm (300 x 300 DPI)

381x285mm (100 x 100 DPI)

127x190mm (300 x 300 DPI)