The incidence and prevalence of Systemic Lupus Erythematosus in New York County (Manhattan), New York:

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The Incidence and Prevalence of Systemic Lupus Erythematous: The Manhattan Lupus Surveillance Program

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The Incidence and Prevalence of Systemic Lupus Erythematous: The Manhattan Lupus Surveillance Program

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Running Title: Incidence and Prevalence Manhattan Lupus Surveillance Program

Word Count: 4191

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The findings and conclusions in this report are those of the authors and do not

necessarily represent the official position of the Centers for Disease Control and

Prevention.

Abstract

Objective: The Manhattan Lupus Surveillance Program (MLSP) is a population-based registry designed to determine the prevalence of Systemic Lupus Erythematosus (SLE) in 2007 and incidence from 2007 to 2009 among Manhattan residents and characterize cases by race/ethnicity, including Asians and Hispanics for whom data are lacking.

Methods: We identified possible SLE cases from hospitals, rheumatologists, and administrative databases and defined cases using the American College of Rheumatology (ACR) classification criteria, the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, or a treating rheumatologist's diagnosis. Rates among Manhattan residents were age-standardized, and capture-recapture (C-RC) analyses were conducted to assess case under-ascertainment.

Results: By the ACR definition, the age-standardized prevalence and incidence rates of SLE were 62.2 and 4.6 per 100,000 person-years. Rates were approximately nine times higher in women than men for prevalence (107.4 vs. 12.5) and incidence (7.9 vs. 1.0). Compared with non-Hispanic (NH) white women (64.3), prevalence was higher among NH-black (210.9), Hispanic (138.3), and NH-Asian women (91.2). Incidence rates were higher among NH-black women (15.7) compared with NH-Asian (6.6), Hispanic (6.5), and NH-white women (6.5). C-RC adjustment increased prevalence and incidence rates (75.9 and 6.0). Alternate SLE definitions without C-RC adjustment found higher age-standardized prevalence and incidence rates (SLICC: 73.8 and 6.2; rheumatologist: 72.6 and 5.0) than the ACR definition, with similar patterns by sex and race/ethnicity.

Conclusion: The MLSP confirms findings from other registries on disparities by sex and race/ethnicity, provides new estimates among Asians and Hispanics, and also provides estimates using the SLICC criteria.

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Introduction:

Systemic Lupus Erythematosus (SLE) is a potentially fatal, heterogeneous, chronic, systemic autoimmune disease of unknown etiology [1]. Given widely varying estimates of the incidence and prevalence of SLE in the United States (US) [2] and the absence of data available for certain demographic groups, we sought to obtain a fundamental epidemiologic understanding of SLE across racial/ethnic groups. Under the auspices of the National Arthritis Action Plan [3], the Centers for Disease Control and Prevention (CDC) funded four state or city health departments as well as the Indian Health Service (IHS) to more robustly define the incidence and prevalence of SLE. Results from the two initial sites, the Georgia Lupus Registry (GLR) and the Michigan Lupus Epidemiology and Surveillance Program (MILES Program), and the IHS site have been recently published [4-6]. However, their estimates for Asians and Hispanics were limited. The Manhattan Lupus Surveillance Program (MLSP) was designed, along with the California Lupus Surveillance Project (CLSP), to provide estimates of the incidence and prevalence of SLE overall and specifically among Hispanic and Asian populations.

We launched the MLSP in 2009 as a collaboration between the New York City Department of Health and Mental Hygiene (DOHMH) and New York University School of Medicine (NYUSoM). Following methods similar to those of the other CDC-funded sites [2, 5, 6], we designed the MLSP as a retrospective descriptive project to identify all cases of diagnosed SLE among Manhattan residents from 2007 to 2009 to determine the prevalence and incidence of SLE in this population.

Patients and Methods

The Manhattan Lupus Surveillance Program

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The MLSP was designed to be similar to the GLR and MILES program and, as described elsewhere [5, 6], was conducted as a public health surveillance project by the DOHMH with NYUSoM acting as a public health agent on behalf of the DOHMH. No patients were contacted for this project. Medical records were collected under the health surveillance exemption to the Health Insurance Portability and Accountability Act (HIPAA) privacy rules (45 CFR § 164.512(b)) and as authorized by New York City Charter Sections 556(c)(2) and (d)(2). The CDC deemed the MLSP public health practice not requiring review by the CDC Institutional Review Board (IRB). IRBs at both the DOHMH and NYUSoM reviewed and deemed the MLSP a surveillance activity. Additional IRB applications were completed and submitted to independent case finding sources as requested.

Study Population and Period

The MLSP surveillance period was January 1, 2007, through December 31, 2009. Manhattan was selected as the program catchment area due to its racial/ethnic diversity and because it is an island on which inhabitants largely remain for their health care, thus making access to medical records easier. We used data from specialty lupus clinics across NYC during initial planning for the MLSP and found that few Manhattan residents seek care in outer boroughs and that residents from other boroughs were more likely to seek care across a wide geographic range. Based on United States Census data, there were 1,611,581 persons residing in Manhattan in 2010 (48% non-Hispanic (NH) white, 13% NH-black, 25% Hispanic, 11% NH-Asian) [7].

Case Definitions

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Our primary American College of Rheumatology (ACR) case definition required ≥ 4 of 11 ACR classification criteria for SLE [8, 9]. Under the ACR classification criteria, patients with evidence of lupus nephritis (by biopsy report or specific documentation by a rheumatologist and/or nephrologist) are considered to have met renal criteria for SLE, even without information on the degree of proteinuria or description of the sediment. We also used two secondary case definitions for SLE: 1) the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification criteria, which requires a case to have at least four criteria, including at least one clinical and one immunologic criterion or having biopsy-proven lupus nephritis in the presence of antinuclear antibodies or anti-double-stranded DNA antibodies, or 2) a treating rheumatologist's diagnosis of SLE. The SLICC case definition was included as a recently derived classification criteria with greater sensitivity and less specificity than the ACR classification criteria [10]. The rheumatologist case definition was included because there is no gold standard for diagnosing SLE and diagnosis is usually made by a physician familiar with the disease, often a rheumatologist.

Initial Case Finding

We used information from administrative databases, hospitals, and private rheumatologists to identify possible cases from as far back as 2004 when records were available. Administrative databases included the New York State Department of Health Statewide Planning and Research Cooperative System with information on hospitalization discharges in New York State and DOHMH Vital Records with information on all deaths in NYC. We included only hospitals and private rheumatologists based in Manhattan. We queried these sources to identify records with

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International Classification of Disease (Ninth Revision, Clinical Modification) diagnosis codes indicating SLE (710.0), discoid lupus (695.4), or a related condition that may evolve into SLE or have related symptoms (710.8, other specified connective tissue disease; 710.9, unspecified connective tissue disease; 710.2, Sicca syndrome). If residence information was available from the case finding source, we further restricted these records to include only those with evidence of Manhattan residence. Final screening of records was completed by trained MLSP abstractors to confirm physician diagnosis or suspicion of SLE or a related connective tissue disease and Manhattan residence during the surveillance period.

Data collection

After initial case finding, abstractors collected and entered information from the medical records into a DOHMH database, with database and data dictionary materials adapted from those used by the GLR. When necessary, we corroborated Manhattan residence using the LexisNexis on-line database service [11]. Our abstractors entered any ambiguous information into open text notes which were later reviewed with the NYUSoM principal investigator to correctly code in the database.

All MLSP abstractors were trained under the GLR model [5] before abstraction began and underwent routine quality assurance reviews throughout the project. These reviews provided the opportunity for abstractors and the NYUSoM principal investigator to discuss any issues arising in the field and to address questions from the abstractors. Each abstractor had a medical degree and consistently achieved the required minimum inter-observer agreement of 90% on all elements and 95% on ACR classification criteria using abstraction by the NYUSoM principal investigator as the gold standard. The

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average performance of the abstractors during training and reviews was 95.6% on all elements, 97.2% on ACR classification criteria elements, and 97.5% on the unique elements in the SLICC classification criteria that were not already captured as part of the ACR classification criteria.

Statistical Analysis

We defined prevalent cases as new or existing cases meeting the ACR, SLICC, or rheumatologist case definition and residing in Manhattan at some time from January 1, 2007, through December 31, 2007. We defined incident cases as those meeting at least one of the case definitions, first diagnosed from January 1, 2007, through December 31, 2009, and residing in Manhattan. Population denominators were taken from the DOHMH interpolated intercensal population estimates for Manhattan [12]. We calculated rates overall, by sex, and by race/ethnicity per 100,000 person-years and age-standardized to the United States 2000 standard population using 10 year age groups for each racial/ethnic group [13]. Information on race was collected separately from Hispanic ethnicity during abstraction. For analysis, we assigned cases to one of five mutually exclusive race/ethnicity categories: NH-white, NH-black, NH-Asian, Hispanic, and NH-other. NH-cases identified with more than one race were categorized as other.

We conducted capture-recapture (C-RC) analyses [14, 15] to estimate case under-ascertainment from our primary ACR case definition. We fit log-linear models separately for incident and prevalent cases by sex and race/ethnicity to estimate the number of cases missed in our catchment area. Specifically, we fit various models that addressed potential violation of the homogeneity assumption of capture probability and

identified the best fitting model using the Akaike Information Criteria. We then used estimates from these models to calculate revised prevalence and incidence rates.

We used chi-square tests, or Fisher's exact tests when needed, to assess univariate differences in SLE and ACR manifestations by race/ethnicity and sex. We compared differences between estimates by case definition using 95% confidence intervals (CIs) of the age-standardized rates, with non-overlapping CIs considered to be significantly different. All analyses were completed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) and R version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results:

Case Finding

Case finding and abstraction was completed in 19 out of 21 hospitals (90.5%, Figure 1), with two hospitals declining to participate (a cancer specialty hospital, and a Veteran's Administration Hospital). Case finding and abstraction was performed from records of 94 out of 124 (75.8%) private rheumatologists identified in the catchment area. Of the 30 rheumatologists who did not participate, 19 did not respond to repeated requests or declined to participate, two died, two had retired and relocated, and seven agreed to participate but abstraction could not be arranged despite repeated attempts before data abstraction ended.

Initial lists provided from the various case finding sources identified 76,220 records (Figure 1). We deduplicated and removed records that did not have a Manhattan address, resulting in 5,065 possible cases with records for abstraction. During abstraction and data cleaning, we deemed 1,184 cases ineligible due to

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miscoded diagnosis or non-Manhattan residence. Of the remaining 3,881 possible cases, 1,859 met at least one of the case definitions.

Primary ACR Case Definition: Prevalence

In 2007 a total of 1,078 cases (307 NH-white, 282 NH-black, 344 Hispanic, 111 NH-Asian, and 34 NH-other race/ethnicity) fulfilled the ACR case definition for SLE (Table 1). The overall crude and age-standardized prevalence was 68.2 (95% CI 64.1-72.2) and 62.2 (95% CI 58.4-66.0) per 100,000 person-years. Age-standardized rates were approximately nine times higher for women compared with men (107.4 vs. 12.5). Age-standardized rates also differed by race/ethnicity among both women and men. The highest age-standardized prevalence was seen among NH-black women (210.9) followed by Hispanic women (138.3), NH-Asian women (91.2), and NH-white women (64.3). The age-standardized prevalence among men followed a similar pattern with the highest estimate among NH-blacks (26.7) followed by Hispanics (19.4), NH-Asians (14.2), and NH-whites (3.7). C-RC estimated an additional 122 cases of SLE, indicating that 10% of cases may have been missed. Almost two-thirds (62.5%) of the estimated cases missed were NH-white women. With C-RC adjustment, the prevalence increased to 75.9 per 100,000 person-years (95% CI 70.6-81.2).

The average age (± standard deviation [SD]) among women and men with SLE living in Manhattan in 2007 was 43.3 (± 15.5) and 40.7 (± 16.9) years respectively. The average age by race/ethnicity was 47.0 (± 16.5) years among NH-whites, 42.9 (± 15.6) years among Hispanics, 41.5 (± 13.7) years among NH-blacks, and 37.3 (± 15.4) years among NH-Asians. Figures 2A shows age-specific prevalence for women by race/ethnicity. Prevalence was higher among NH-black and Hispanic women ages 20 to

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59 years old compared to similarly-aged NH-white women. Prevalence among NH-Asian women was not significantly different than those among NH-white women for any age group. Numbers among men were too small to assess age-specific rates by race/ethnicity.

Among the 344 Hispanic cases, 82.9% were also identified as white, 11.3% as black, and 5.8% as other race/ethnicity. Information on Hispanic ethnicity was often absent, with 239 (69.5%) having no further details, but Hispanic case ethnicities included Central or South American, Cuban, Dominican, Mexican, Puerto Rican, and Spanish. There were 111 NH-Asian cases as well as five identified as NH-other due to multiple race/ethnicity but with evidence of Asian race. More than a quarter (26.7%) of these cases had no further classification for Asian ethnicity, but ethnicities among cases with information available included Chinese, Filipino, Hawaiian, Indian or Pakistani, Japanese, Korean, Pacific Islander not otherwise specified, South Asian, and Vietnamese.

Table 2 shows the occurrence of the 11 ACR criteria overall and by race/ethnicity among prevalent ACR cases. Renal disease was more common among NH-Asians (53.2%), NH-blacks (50.7%), and Hispanics (49.4%) compared with NH-whites (25.4%). Neurologic manifestations were more common among Hispanics (26.2%) and NH-blacks (24.5%) compared with NH-whites (16.6%). Also compared with NH-whites, discoid lesions were more commonly seen among NH-blacks (25.9% vs. 8.8%) and malar rash was more commonly seen among Hispanics (50.0% vs. 35.8%).

Primary ACR Case Definition: Incidence Rates

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From 2007-2009, 232 incident cases met the ACR case definition (Table 3) for

SLE (92 NH-white, 62 NH-black, 49 Hispanic, 22 NH-Asian, and 7 NH-other

race/ethnicity). The overall crude and age-standardized incidence rates were 4.9 (95%

CI 4.3-5.5) and 4.6 (95% CI 4.0-5.2) per 100,000 person-years respectively. Age-

standardized rates differed by sex, and were almost 8 times higher for women

compared with men (7.9 vs. 1.0). Age-standardized rates also differed by race/ethnicity

among both women and men. The highest age-standardized incidence rates among

women were among NH-blacks (15.7) followed by NH-Asians (6.6), Hispanics (6.5), and

NH-whites (6.5). Similarly, the highest age-standardized incidence rates among men

were among NH-blacks (2.4) followed by Hispanics (1.3), NH-Asians (0.5), and NH-

whites (0.5). C-RC adjustment estimated 284 incident cases of SLE, indicating that 18%

of cases were missed and 67.0% of these were NH-white women. The resulting C-RC

adjusted incidence rate increased to 6.0 per 100,000 person-years (95% CI 4.6-7.4).

The average age (±SD) at diagnosis was 40.4 (± 16.6) years among women and

42.9 (± 20.4) years among men. The average age (±SD) at diagnosis was 42.2 (± 17.7)

years among NH-whites, 39.2 (± 16.6) years among NH-blacks, 39.6 (± 17.0) years

among Hispanics, and 37.9 (± 16.0) years among NH-Asians. Figure 2B shows age-

specific incidence rates for women by race/ethnicity. The only age-specific difference

was between NH-black and NH-white women aged 20 to 39 years old. Otherwise, due

to small numbers within each strata, no age-specific differences were found.

Among the 49 incident Hispanic cases, 77.6% were also identified as NH-white,

16.3% as NH-black, and 6.1% as NH-other race/ethnicity. As with prevalent cases,

Hispanic ethnicity information for incident cases was often absent, with 71.4% having no

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further ethnicity information available. Among the 22 incident NH-Asian cases, 32% had no further data available.

Table 2 shows the occurrence of the 11 ACR criteria overall and by race/ethnicity among incident ACR cases. Evidence of renal disease was found among 34.9% of incident cases, but was more common among NH-Asians (45.5%), NH-blacks (43.5%), and Hispanics (42.9%) compared with NH-whites (23.9%). Discoid lesions were more common among NH-blacks (25.8%) compared with NH-whites (9.8%).

Secondary Case Definitions

Prevalence and incidence rates calculated using the SLICC case definition for SLE were significantly higher than those calculated with the primary case ACR definition. Using the SLICC case definition generated crude and age-standardized prevalence of 80.1 (95% CI 75.7-84.5) and 73.8 (95% CI 69.6-77.9) per 100,000 years respectively, which were 17-19% higher than those calculated with the ACR case definition. The SLICC crude and age-standardized incidence rates (6.6, 95% CI 5.8-7.3; 6.2, 95% CI 5.5-6.9) were nearly 35% higher than the ACR incidence rates.

The rheumatologist case definition yielded crude and age-standardized prevalence that was approximately 17% higher than those from the ACR case definition (79.4, 95% CI 75.0-83.8; 72.6, 95% CI 68.5-76.7). Crude and age-standardized incidence rates using the rheumatologist case definition were similar to rates using the ACR case definition (5.3, 95% CI 4.7-6.0; 5.0, 95% CI 4.4-5.7). For both secondary case definitions differences in rates by sex and race/ethnicity were similar to those identified by the ACR case definition.

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Of the 1,538 incident and prevalent cases meeting either the ACR or SLICC case definition, 75.6% met both ACR and SLICC definitions, 4.3% only met the ACR definition, and 20.2% met the SLICC definition only. Table 4 displays information on the unique SLICC criteria that are not part of the ACR classification criteria among incident and prevalent cases meeting the SLICC case definition only. The most common unique SLICC criteria among these cases were low complement levels, alopecia, and different definitions for lymphopenia. In addition, 5.5% of cases meeting the SLICC case definition had an ANA and/or anti–double-stranded DNA antibody and a biopsy consistent with lupus nephritis. Reasons that cases met the ACR and not the SLICC case definition were largely due to having $\geq$ 4 clinical criteria but no immunologic criteria, differences in categorization of photosensitivity and malar rash (which were separated in the ACR and combined in the SLICC criteria), and differences in defining lymphopenia and anti-cardiolipin antibody (data not shown).

Discussion

Our analysis of the MLSP provides prevalence and incidence rate estimates of SLE among Manhattan residents using methods similar to other CDC-funded SLE registries. Our analysis confirms evidence for higher prevalence of SLE among NH-blacks compared with NH-whites and adds evidence for higher prevalence of SLE among Hispanics and NH-Asians as well. The MLSP is also the first among the CDC-funded SLE registry sites to report using the SLICC classification criteria, which were recently validated, to describe cases of SLE [10].

The age-standardized prevalence and incidence of SLE in Manhattan were 62.2 (95% CI 58.4-66.0) and 4.6 (95% CI 4.0-5.2) using the ACR case definition. Compared

with previous reports by the CDC-funded sites , we estimated slightly lower overall age-standardized prevalence than the GLR (73.0, 95% CI 68.9-77.4) [5] and MILES (72.8, 95% CI 70.8-74.8) [6], but found similar disparities by sex and race/ethnicity for NH-whites and NH-blacks. MLSP prevalence estimates increased with C-RC adjustment and were comparable to C-RC adjusted estimates from the GLR (75.8, 95% CI 70.3-81.2 vs. 83.0, 95% CI 78.6-87.7). Our age-standardized incidence rates using the ACR case definition were similar to those from the GLR and MILES.

We found the highest prevalence and incidence rates among NH-blacks, in line with the GLR and MILES and with preliminary data from the CLSP. However, unlike the GLR and MILES we found elevated prevalence among NH-Asians and Hispanics compared with NH-whites. Compared with preliminary crude estimates from the CLSP [16] the MLSP showed similar elevated rates among Hispanics (84.2, 95% CI 75.3-93.1 vs 87.7 95% CI 72.1-106.8) but slightly lower rates among NH-Asians (64.0, 95% CI 52.1-75.9 vs 95.8 95% CI 84.9-108.1). These MLSP findings are particularly important, given the few published studies on prevalence and incidence of SLE among Asians and Hispanics in the United States. A 1973 review presented estimates among NYC residents from 1956 to 1965 but focused only on whites, blacks, and Puerto Ricans [17]. Another study published in 2001 estimated the prevalence of SLE among Hispanics in Arizona to be 103 per 100,000, slightly higher than the rate found by the MLSP among Hispanics in Manhattan [18]. A more recent study using Medicaid data estimated an even higher prevalence of SLE among Hispanics (126.5 per 100,000) with Medicaid coverage in the United States from 2000 to 2004 [19].

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The study using Medicaid data is one of the few to estimate rates of SLE among Asians in the United States, reporting a prevalence almost four times that estimated by the MLSP (175.1 per 100,000 vs. 45.7) [19]. The only other studies known to assess rates SLE among Asians in the United States focused on SLE prevalence. One study identified cases in Hawaii based on physician diagnosis at five medical centers and outpatient practices in 1989. The overall SLE prevalence identified in that study (41.8 per 100,000) was similar to the MLSP estimate for NH-Asians, and the age-standardized rates for women from specific Asian ethnic groups (Chinese, Filipino, Hawaiian, Japanese) was found to be higher compared with that among white women [20]. Another study, using hospital discharge data, reported that Asian/Pacific Islander women had a lower rate of prevalent SLE compared with white women [21]. Less is known about the incidence of SLE among Asians. In England, new diagnoses of SLE are more common among Asians, specifically South Asians from India and Pakistan, compared with whites [22, 23], but to our knowledge there are no other published reports on the incidence of SLE among Asians in the United States.

In this analysis, we also provide information on manifestations among SLE cases. Clinical or serologic manifestations among prevalent cases approximated those from the GLR and MILES registries. The MLSP found a high burden of nephritis overall with nearly half (42.4%) of prevalent cases developing nephritis. The proportion of those with nephritis was higher among non-white prevalent cases, specifically 50.7% among NH-blacks, 49.4% among Hispanics, and 53.2% among NH-Asians, compared with 25.4% among NH-whites, in line with other studies [5, 6, 19, 24, 25].

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The SLICC case definition for SLE yielded higher incidence and prevalence estimates than the ACR case definition. Unique criteria which substantiated the classification of SLE based on SLICC but not ACR criteria, included low complements, alopecia, and different definitions for lymphopenia [10]. The small number of cases that met the ACR but not the SLICC case definition is reassuring as it suggests that few cases met ACR criteria for SLE without the presence of autoantibodies. However, given the descriptive nature of the MLSP and the absence of a gold standard test that would unambiguously identify SLE, this project cannot assess which set of classification criteria is more sensitive or specific. In addition, non-overlapping confidence intervals were used to conservatively assess differences among rates (26).

There were several limitations to this project. First, we may have underestimated cases as two hospitals and one quarter of rheumatologists in the catchment area declined to participate. Most of the practices that did not participate were in neighborhoods with a majority white population, which is in line with our C-RC analysis that estimated 67.3% of prevalent cases and 70.0% of incident cases missed were NH-white. However, the exclusion of the Veteran's Administration Hospital may have resulted in under-identification of males diagnosed with SLE. We also did not include nephrology, dermatology, or primary or alternative care practices among our case finding sources. Though when possible we did query hospital pathology databases for relevant kidney or skin biopsies, we still may have missed milder cases that were not hospitalized or seen by a rheumatologist during the surveillance period. It is also possible that we missed cases if they lived in Manhattan but sought care in other boroughs or a neighboring state.

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Second, medical systems differed tremendously, and any difficulty navigating different electronic medical records or with the legibility of paper charts could have led to missed or miscoded data. Additionally, medical records are designed for physician use, not for data abstraction and surveillance. Thus, some information of interest may have been missing or ambiguous, depending on what was collected and recorded by the case finding source.

Third, abstracting occurred several years after the surveillance period, which could have led to missing information if records were put into storage or data elements were lost during a facility's migration from paper to electronic records. This lag time may have also affected our ability to find all prevalent cases of SLE, as some newer systems were unable to query past certain dates. Additionally, many private practices did not retain information on patients' prior addresses, so we may not have abstracted cases who moved outside of Manhattan since the surveillance period. However, when possible the software LexisNexis was used to verify patient residence within the catchment area.

Finally, data on race and ethnicity was abstracted from administrative and medical records, which may not accurately represent the patient's own racial or ethnic identification. Additionally, information on ethnicity was often missing or did not include detail such as country of origin, which limited our ability to describe rates of SLE among specific ethnic groups. Though available information did reflect the major ethnic groups in Manhattan, ethnicity information was missing for most Hispanic cases and more than one quarter of NH-Asian cases. Categorized broadly, Hispanic or Asian race encompasses a number of heterogeneous groups and SLE rates among them may

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differ. Given the already limited number of published studies on SLE among Asians and

Hispanics, additional work is needed to better describe and understand the experience

of SLE among specific ethnic subpopulations.

Despite these limitations, our analysis benefitted from the design and

composition of the MLSP. First, the MLSP was designed as a population-based registry

with methods similar to four other CDC-funded SLE registries, which allowed us to

compare rates across sites. Second, the diverse population within our catchment area

allowed us to estimate rates of SLE among the major racial categories, particularly

Asians and Hispanics. Third, given the recent publication of the SLICC classification

criteria, we were able to estimate rates of SLE by this case definition and compare them

to the ACR case definition. Fourth, the partnership with the DOHMH allowed us to

collect information from a number of case finding sources and find complete clinical

information on most cases. Finally, our abstractors all had a medical background, which

helped during training and also provided an advantage during extensive review of

medical records to identify SLE criteria.

In conclusion, we found substantial disparities in prevalence, incidence, and

manifestations of SLE by sex and race/ethnicity among Manhattan residents. Women

consistently had higher prevalence and incidence rates of SLE compared with men, and

NH-blacks, Hispanics, and NH-Asians had higher rates of diagnosed SLE and a higher

proportion lupus nephritis compared with NH-whites. The highest rates of SLE were

seen among NH-black women followed by Hispanic, NH-Asian, and NH-white women.

Using the SLICC criteria for SLE provided higher prevalence and incidence rates than

the ACR criteria.

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Table 1: Crude and age-standardized prevalence of SLE among Manhattan residents, 2017, according to the ACR, SLICC, and rheumatologist case definitions overall and by race/ethnicity and sex

	ACR					SLICC			Rheumatologist		
	N	Crude rate (95% CI)	Age-standardized rate (95% CI)	Capture-recapture N missed	Adjusted rate (95% CI)	N	Crude rate (95% CI)	Age-standardized rate (95% CI)	N	Crude rate (95% CI)	Age-standardized rate (95% CI)
Overall	1,078	68.2 (64.1-72.2)	62.2 (58.4-66.0)	122.4	75.9 (70.6-81.2)	1,267	80.1 (75.7-84.5)	73.8 (69.6-77.9)	1,256	79.4 (75.0-83.8)	72.6 (68.5-76.7)
Male	101	13.6 (10.9-16.2)	12.5 (10.0-15.0)	8.3	14.7 (12.5-16.9)	110	14.8 (12.0-17.6)	13.8 (11.1-16.4)	98	13.2 (10.7-16.1)	12.0 (9.7-14.7)
Female	977	116.7 (109.3-124.0)	107.4 (100.5-114.4)	114.1	130.3 (122.1-138.4)	1,157	138.2 (130.2-146.1)	128.3 (120.7-135.9)	1,158	138.3 (130.3-146.2)	127.5 (119.9-135.1)
Non-Hispanic White	307	40.5 (36.0-45.0)	34.7 (30.7-38.8)	389.4	51.4 (45.0-57.7)	373	49.2 (44.2-54.2)	42.7 (38.1-47.3)	352	46.4 (41.6-51.3)	39.7 (35.3-44.0)
Male	17	4.7 (2.7-7.5)	3.7 (2.2-6.0)	22.9	6.3 (3.2-9.4)	23	6.3 (4.0-9.5)	5.3 (3.3-8.0)	24	6.6 (4.2-9.8)	5.3 (3.4-7.8)
Female	290	73.4 (64.9-81.8)	64.3 (56.4-72.2)	366.5	92.7 (83.4-102.1)	350	88.6 (79.3-97.8)	78.2 (69.4-86.9)	328	83.0 (74.0-92.0)	72.0 (63.7-80.4)
Non-Hispanic Black	282	131.4 (116.1-146.8)	124.9 (110.3-139.6)	285.6	133.1 (130.6-135.7)	326	151.9 (135.5-168.4)	144.7 (128.9-160.5)	312	145.4 (129.3-161.6)	137.7 (122.3-153.1)
Male	28	28.5 (18.9-41.2)	26.7 (17.7-38.7)	28.0	28.5 (28.1-28.9)	31	31.6 (21.4-44.8)	29.7 (20.2-42.3)	24	24.4 (15.7-36.4)	22.6 (14.5-33.7)
Female	254	218.4 (191.5-245.2)	210.9 (184.8-237.1)	257.6	221.4 (217.1-225.8)	295	253.6 (224.7-282.5)	244.4 (216.3-272.6)	288	247.6 (219.0-276.2)	237.2 (209.5-264.8)
Hispanic	344	84.2 (75.3-93.1)	82.8 (74.0-91.7)	345.4	84.6 (83.8-85.3)	372	91.1 (81.8-100.3)	90.2 (81.0-99.5)	396	97.0 (87.4-106.5)	96.2 (86.7-105.8)
Male	38	19.7 (13.9-27.0)	19.4 (13.6-26.9)	38.1	19.7 (19.4-20.0)	38	19.7 (13.9-27.0)	19.5 (13.7-26.9)	33	17.1 (11.8-24.0)	16.7 (11.4-23.6)
Female	306	142.1 (126.2-158.0)	138.3 (122.7-153.9)	307.3	142.7 (141.5-143.9)	334	155.1 (138.4-171.7)	151.7 (135.3-168.1)	363	168.5 (151.2-185.9)	165.3 (148.2-182.5)
Non-Hispanic Asian	111	64.0 (52.1-75.9)	56.2 (44.7-67.7)	131.0	75.5 (66.0-85.0)	145	83.6 (70.0-97.2)	75.1 (61.7-88.5)	118	68.0 (55.7-80.3)	62.2 (49.7-74.6)
Male	15	19.3 (10.8-31.9)	14.2 (7.6-24.0)	17.3	22.3 (17.0-27.6)	15	19.3 (10.8-31.9)	14.2 (7.6-24.0)	13	16.8 (8.9-28.7)	12.5 (6.2-22.6)
Female	96	100.0 (81.0-122.2)	91.2 (72.1-113.8)	113.7	118.5 (105.6-131.3)	130	135.5 (112.2-158.7)	125.9 (102.0-149.9)	105	109.4 (88.5-130.3)	103.6 (81.5-125.8)
Non-Hispanic Other	34			49.0		51			78		

Case definitions: ACR: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE; SLICC: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification; Rheumatologist: have been diagnosed with SLE by a treating rheumatologist

Rates are per 100,000 Manhattan resident person-years. Denominator data is based on 2007 intercensal population estimates from the NYC DOHMH Bureau of Epi Services (2000-2014 files). Data are standardized for age and race/ethnicity to the US 2000 Standard Population. Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

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Table 2: Frequency of 11 ACR manifestations of SLE among prevalent and incident cases by the ACR case definition, overall and by race/ethnicity

| | Prevalent cases (2007) | | | | | Incident cases (2007-2009) | | | | |
| | Overall | Non-Hispanic White | Non-Hispanic Black | Hispanic | Non-Hispanic Asian | Overall | Non-Hispanic White | Non-Hispanic Black | Hispanic | Non-Hispanic Asian |
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Overall	1,078	307 (28.5)	282 (26.2)	344 (31.9)	111 (10.3)	232	92 (39.7)	62 (26.7)	49 (21.1)	22 (9.5)
Antinuclear antibody	996 (92.4)	284 (92.5)	262 (92.9)	316 (91.9)	103 (92.8)	213 (91.8)	82 (89.1)	58 (93.5)	47 (95.9)	22 (100.0)
Hematologic disorder	893 (82.8)	255 (83.1)	238 (84.4)	278 (80.8)	98 (88.3)	188 (81.0)	71 (77.2)	56 (90.3*)	37 (75.5)	19 (86.4)
Arthritis	813 (75.4)	246 (80.1)	204 (72.3)	255 (74.1)	80 (72.1)	159 (68.5)	66 (71.7)	41 (66.1)	30 (61.2)	17 (77.3)
Immunologic disorder	781 (72.4)	213 (69.4)	204 (72.3)	253 (73.5)	89 (80.2*)	170 (73.3)	66 (71.7)	46 (74.2)	37 (75.5)	18 (81.8)
Renal disorder	457 (42.4)	78 (25.4)	143 (50.7*)	170 (49.4*)	59 (53.2*)	81 (34.9)	22 (23.9)	27 (43.5*)	21 (42.9*)	10 (45.5*)
Serositis	449 (41.7)	117 (38.1)	127 (45.0)	156 (45.3)	36 (32.4)	84 (36.2)	25 (27.2)	33 (53.2*)	18 (36.7)	5 (22.7)
Malar rash	428 (39.7)	110 (35.8)	82 (29.1)	172 (50.0*)	46 (41.4)	86 (37.1)	31 (33.7)	20 (32.3)	22 (44.9)	8 (36.4)
Photo sensitivity	370 (34.3)	121 (39.4)	76 (27.0*)	132 (38.4)	30 (27.0*)	74 (31.9)	32 (34.8)	11 (17.7*)	21 (42.9)	7 (31.8)
Oral ulcers	333 (30.9)	104 (33.9)	64 (22.7*)	115 (33.4)	37 (33.3)	81 (34.9)	42 (45.7)	16 (25.8*)	12 (24.5*)	7 (31.8)
Neurologic disorder	230 (21.3)	51 (16.6)	69 (24.5*)	90 (26.2*)	11 (9.9)	43 (18.5)	15 (16.3)	15 (24.2)	11 (22.4)	1 (4.5)
Discoid rash	179 (16.6)	27 (8.8)	73 (25.9*)	58 (16.9*)	17 (15.3)	32 (13.8)	9 (9.8)	16 (25.8*)	5 (10.2)	1 (4.5)

ACR case definition: meets ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE.

Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

* Univariate logistic regression indicates the proportion with this manifestation is significantly different than the proportion among non-Hispanic whites (p<0.05).

Table 3: Crude and age-standardized incidence rates of SLE among Manhattan residents, 2007-2009, according to the ACR, SLICC, and rheumatologist case definitions overall and by race/ethnicity and sex

	ACR N	Crude rate (95% CI)	Age-standardized rate (95% CI)	Capture-recapture N missed	Adjusted rate (95% CI)	SLICC N	Crude rate (95% CI)	Age-standardized rate (95% CI)	Rheumatologist N	Crude rate (95% CI)	Age-standardized rate (95% CI)
Overall	232	4.9 (4.3-5.5)	4.6 (4.0-5.2)	284.4	6.0 (4.6-7.4)	312	6.6 (5.8-7.3)	6.2 (5.5-6.9)	253	5.3 (4.7-6.0)	5.0 (4.4-5.7)
Male	23	1.0 (0.7-1.5)	1.0 (0.6-1.5)	26.3	1.2 (0.7-1.7)	38	1.7 (1.2-2.3)	1.7 (1.2-2.3)	28	1.3 (0.8-1.8)	1.2 (0.8-1.8)
Female	209	8.3 (7.2-9.4)	7.9 (6.8-9.0)	258.1	10.3 (8.0-12.5)	274	10.9 (9.6-12.2)	10.3 (9.1-11.6)	225	8.9 (7.8-10.1)	8.6 (7.4-9.7)
Non-Hispanic White	92	4.0 (3.2-4.9)	3.6 (2.8-4.5)	128.7	5.6 (4.2-7.1)	124	5.4 (4.5-6.4)	4.8 (3.9-5.8)	94	4.1 (3.3-5.0)	3.8 (3.0-4.8)
Male	7	0.6 (0.3-1.3)	0.5 (0.2-1.0)	8.6	0.8 (0.4-1.2)	13	1.2 (0.6-2.0)	1.0 (0.5-1.7)	9	0.8 (0.4-1.6)	0.7 (0.3-1.3)
Female	85	7.1 (5.7-8.8)	6.5 (5.0-8.3)	120.1	10.1 (7.7-12.5)	111	9.3 (7.6-11.1)	8.5 (6.7-10.3)	85	7.1 (5.7-8.8)	6.8 (5.2-8.6)
Non-Hispanic Black	62	9.8 (7.5-12.6)	9.3 (7.1-12.0)	63.8	10.1 (9.1-11.0)	79	12.5 (9.9-15.5)	12.0 (9.5-15.0)	61	9.6 (7.4-12.4)	9.2 (7.0-11.8)
Male	7	2.4 (1.0-5.0)	2.4 (1.0-5.0)	8.0	2.8 (1.6-3.9)	11	3.8 (1.9-6.8)	3.8 (1.9-6.8)	7	2.4 (1.0-5.0)	2.3 (0.9-4.7)
Female	55	16.0 (12.1-20.9)	15.7 (11.8-20.5)	55.8	16.3 (15.5-17.0)	68	19.8 (15.4-25.1)	19.3 (14.9-24.5)	54	15.7 (11.8-20.5)	15.5 (11.6-20.3)
Hispanic	49	4.0 (3.0-5.3)	4.0 (3.0-5.4)	50.3	4.1 (3.8-4.5)	64	5.2 (4.0-6.7)	5.3 (4.1-6.7)	50	4.1 (3.0-5.4)	4.2 (3.1-5.5)
Male	7	1.2 (0.5-2.5)	1.3 (0.5-2.7)	7.4	1.3 (1.0-1.5)	8	1.4 (0.6-2.7)	1.6 (0.7-3.2)	6	1.0 (0.4-2.3)	1.1 (0.4-2.5)
Female	42	6.5 (4.7-8.8)	6.5 (4.7-8.8)	42.9	6.7 (6.2-7.1)	56	8.7 (6.6-11.3)	8.6 (6.5-11.2)	44	6.8 (5.0-9.2)	7.0 (5.1-9.4)
Non-Hispanic Asian	22	4.2 (2.6-6.3)	3.8 (2.3-6.0)	28.7	5.4 (3.3-7.5)	31	5.8 (4.0-8.3)	5.3 (3.4-7.7)	27	5.1 (3.4-7.4)	4.5 (2.9-6.9)
Male	1	0.4 (0.0-2.4)	0.5 (0.0-2.7)	1.3	0.6 (0.0-1.1)	2	0.8 (0.1-3.1)	1.0 (0.1-3.5)	2	0.8 (0.1-3.1)	1.0 (0.1-3.7)
Female	21	7.1 (4.4-10.9)	6.6 (3.8-10.5)	27.4	9.3 (6.0-12.7)	29	9.9 (6.6-14.2)	8.8 (5.6-13.1)	25	8.5 (5.5-12.6)	7.5 (4.5-11.6)
Non-Hispanic Other	7			12.9		14			21		

Case definitions: ACR: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE; SLICC: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification; Rheumatologist: have been diagnosed with SLE by a treating rheumatologist

Rates are per 100,000 Manhattan resident person-years. Denominator data is based on 2007-2009 intercensal population estimates from the NYC DOHMH Bureau of Epi Services (2000-2014 files). Data are standardized for age and race/ethnicity to the US 2000 Standard Population.Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

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Table 4: Unique manifestations among SLE incident and prevalent cases meeting SLICC but not ACR case definitions

	N	%
Overall	310	
Immunologic criteria		
Low complements	151	48.7%
Anti-Beta2 Glycoprotein Antibodies (IgG, or IgM)	16	5.2%
Direct Coombs test in the absence of hemolytic anemia	5	1.6%
Clinical criteria		
Acute cutaneous lupus		
Bullous lupus	1	0.3%
Toxic epidermal necrolysis variant of SLE	0	0.0%
Maculopapular lupus rash	13	4.2%
Subacute cutaneous lupus	4	1.3%
Chronic cutaneous lupus		
Hypertrophic (verrucous) lupus	3	1.0%
Lupus Panniculitis (profundus)	4	1.3%
Mucosal lupus	0	0.0%
Lupus erythematosus tumidus	1	0.3%
Chilblains lupus	1	0.3%
Discoid lupus/Lichen planus overlap	4	1.3%
Non-scarring alopecia	122	39.4%
Neurologic criteria		
Mononeuritis multiplex	3	1.0%
Myelitis	2	0.6%
Peripheral or cranial neuropathy	53	17.1%
Acute confusional state	3	1.0%
Lymphopenia	147	47.4%
Antinuclear antibody or anti-double stranded DNA and biopsy proven lupus nephritis and renal biopsy only	17	5.5%

SLICC: Systemic Lupus Erythematosus Collaborating Clinics

ACR: American College of Rheumatology

Criteria are not mutually exclusive; a case may have more than one criteria listed above.

Data on IgA isotypes for anti–B2glycoprotein I and anti-cardiolipin antibodies were not collected. Anti-dsDNA when done by ELISA was only reported as positive or negative so it is possible that is some cases this criterion was over counted in the SLICC if the positive was not specifically double the upper cutoff for the negative value. Finally, CH50 was not captured and thus it is possible that the SLICC criterion for complement could be under-counted.

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Figure 1. Flow chart showing the Manhattan Lupus Surveillance Program case-finding procedure for Systemic Lupus Erythematosus

ACR case definition: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE
SLICC case definition: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification
Rheumatologist definition: have been diagnosed with SLE by a treating rheumatologist

Figure 2. Age-specific prevalence and incidence rates of SLE among Manhattan residents in 2007 and from 2007-2009 by ACR case definition, by age group among females

ACR case definition: meets ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE
Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other.
Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other and are not shown in this figure.

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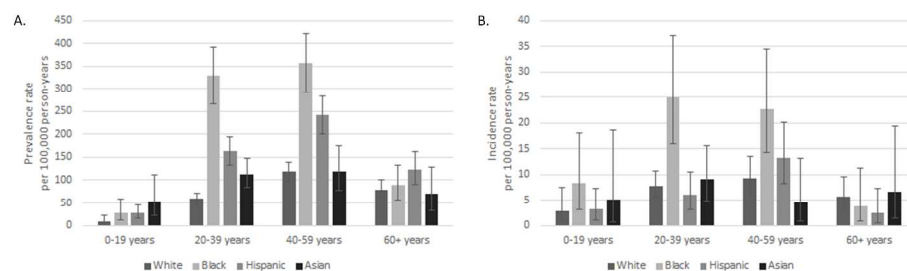
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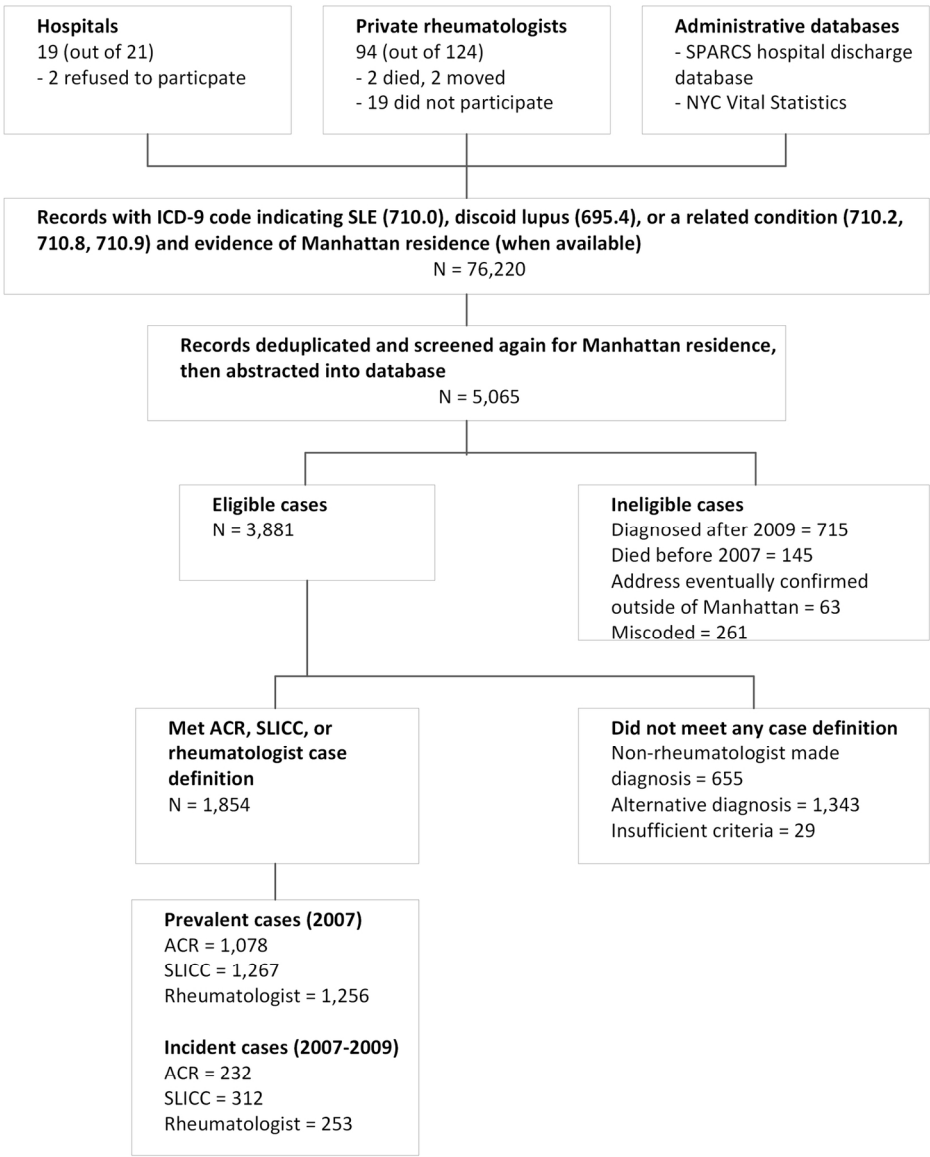
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The Incidence and Prevalence of Systemic Lupus Erythematous:

The Manhattan Lupus Surveillance Program

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Running Title: Incidence and Prevalence Manhattan Lupus Surveillance Program

Word Count: 4199 4191

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The findings and conclusions in this report are those of the authors and do not

necessarily represent the official position of the Centers for Disease Control and

Prevention.

2

Abstract

Objective: The Manhattan Lupus Surveillance Program (MLSP) is a population-based registry designed to determine the prevalence of Systemic Lupus Erythematosus (SLE) in 2007 and incidence from 2007 to 2009 among Manhattan residents and characterize cases by race/ethnicity, including Asians and Hispanics for whom data are lacking.

Methods: We identified possible SLE cases from hospitals, rheumatologists, and administrative databases and defined cases using the American College of Rheumatology (ACR) classification criteria, the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, or a treating rheumatologist's diagnosis. Rates among Manhattan residents were age-~~adjusted~~standardized, and capture-recapture (C-RC) analyses were conducted to assess case under-ascertainment.

Results: By the ACR definition, the age-~~adjusted~~ standardized prevalence and incidence rates of SLE were 62.2 and 4.6 per 100,000 person-years. Rates were approximately nine times higher in women than men for prevalence (107.4 vs. 12.5) and incidence (7.9 vs. 1.0). Compared with non-Hispanic (NH) white women (64.3), prevalence ~~rates were~~ was higher among NH-black (210.9), Hispanic (138.3), and NH-Asian women (91.2). Incidence rates were higher among NH-black women (15.7) compared with NH-Asian (6.6), Hispanic (6.5), and NH-white women (6.5). C-RC adjustment increased prevalence and incidence rates (75.9 and 6.0). Alternate SLE definitions without C-RC adjustment found higher age-~~adjusted~~ standardized prevalence and incidence rates (SLICC: 73.8 and 6.2; rheumatologist: 72.6 and 5.0) than the ACR definition, with similar patterns by sex and race/ethnicity.

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Conclusion: The MLSP confirms findings from other registries on disparities by sex and race/ethnicity, provides new estimates among Asians and Hispanics, and also provides estimates using the SLICC criteria.

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Introduction:

Systemic Lupus Erythematosus (SLE) is a potentially fatal, heterogeneous, chronic, systemic autoimmune disease of unknown etiology [1]. Given widely varying estimates of the incidence and prevalence of SLE in the United States (US) [2] and the absence of data available for certain demographic groups, we sought to obtain a fundamental epidemiologic understanding of SLE across racial/ethnic groups. Under the auspices of the National Arthritis Action Plan [3], the Centers for Disease Control and Prevention (CDC) funded four state or city health departments as well as the Indian Health Service (IHS) to more robustly define the incidence and prevalence of SLE. Results from the two initial sites, the Georgia Lupus Registry (GLR) and the Michigan Lupus Epidemiology and Surveillance Program (MILES Program), and the IHS site have been recently published [4-6]. However, their estimates for Asians and Hispanics were limited. The Manhattan Lupus Surveillance Program (MLSP) was designed, along with the California Lupus Surveillance Project (CLSP), to provide estimates of the incidence and prevalence of SLE overall and specifically among Hispanic and Asian populations.

We launched the MLSP in 2009 as a collaboration between the New York City Department of Health and Mental Hygiene (DOHMH) and New York University School of Medicine (NYUSoM). Following methods similar to those of the other CDC-funded sites [2, 5, 6], we designed the MLSP as a retrospective descriptive project to identify all cases of diagnosed SLE among Manhattan residents from 2007 to 2009 to determine the prevalence and incidence of SLE in this population.

Patients and Methods

The Manhattan Lupus Surveillance Program

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The MLSP was designed to be similar to the GLR and MILES program and, as described elsewhere [5, 6], was conducted as a public health surveillance project by the DOHMH with NYUSoM acting as a public health agent on behalf of the DOHMH. No patients were contacted for this project. Medical records were collected under the health surveillance exemption to the Health Insurance Portability and Accountability Act (HIPAA) privacy rules (45 CFR § 164.512(b)) and as authorized by New York City Charter Sections 556(c)(2) and (d)(2). The CDC deemed the MLSP public health practice not requiring review by the CDC Institutional Review Board (IRB). IRBs at both the DOHMH and NYUSoM reviewed and deemed the MLSP a surveillance activity. Additional IRB applications were completed and submitted to independent case finding sources as requested.

Study Population and Period

The MLSP surveillance period was January 1, 2007, through December 31, 2009. Manhattan was selected as the program catchment area due to its racial/ethnic diversity and because it is an island on which inhabitants largely remain for their health care, thus making access to medical records easier. We used data from specialty lupus clinics across NYC during initial planning for the MLSP and found that few Manhattan residents seek care in outer boroughs and that residents from other boroughs were more likely to seek care across a wide geographic range. Based on United States Census data, there were 1,611,581 persons residing in Manhattan in 2010 (48% non-Hispanic (NH) white, 13% NH-black, 25% Hispanic, 11% NH-Asian) [7].

Case Definitions

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Our primary American College of Rheumatology (ACR) case definition required ≥ 4 of 11 ACR classification criteria for SLE [8, 9]. Under the ACR classification criteria, patients with evidence of lupus nephritis (by biopsy report or specific documentation by a rheumatologist and/or nephrologist) are considered to have met renal criteria for SLE, even without information on the degree of proteinuria or description of the sediment. We also used two secondary case definitions for SLE: 1) the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification criteria, which requires a case to have at least four criteria, including at least one clinical and one immunologic criterion or having biopsy-proven lupus nephritis in the presence of antinuclear antibodies or anti-double-stranded DNA antibodies, or 2) a treating rheumatologist's diagnosis of SLE. The SLICC case definition was included as a recently derived classification criteria with greater sensitivity and less specificity than the ACR classification criteria [10]. The rheumatologist case definition was included because there is no gold standard for diagnosing SLE and diagnosis is usually made by a physician familiar with the disease, often a rheumatologist.

Initial Case Finding

We used information from administrative databases, hospitals, and private rheumatologists to identify possible cases from as far back as 2004 when records were available. Administrative databases included the New York State Department of Health Statewide Planning and Research Cooperative System with information on hospitalization discharges in New York State and DOHMH Vital Records with information on all deaths in NYC. We included only hospitals and private rheumatologists based in Manhattan. We queried these sources to identify records with

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International Classification of Disease (Ninth Revision, Clinical Modification) diagnosis codes indicating SLE (710.0), discoid lupus (695.4), or a related condition that may evolve into SLE or have related symptoms (710.8, other specified connective tissue disease; 710.9, unspecified connective tissue disease; 710.2, Sicca syndrome). If residence information was available from the case finding source, we further restricted these records to include only those with evidence of Manhattan residence. Final screening of records was completed by trained MLSP abstractors to confirm physician diagnosis or suspicion of SLE or a related connective tissue disease and Manhattan residence during the surveillance period.

Data collection

After initial case finding, abstractors collected and entered information from the medical records into a DOHMH database, with database and data dictionary materials adapted from those used by the GLR. When necessary, we corroborated Manhattan residence using the LexisNexis on-line database service [11]. Our abstractors entered any ambiguous information into open text notes which were later reviewed with the NYUSoM principal investigator to correctly code in the database.

All MLSP abstractors were trained under the GLR model [5] before abstraction began and underwent routine quality assurance reviews throughout the project. These reviews provided the opportunity for abstractors and the NYUSoM principal investigator to discuss any issues arising in the field and to address questions from the abstractors. Each abstractor had a medical degree and consistently achieved the required minimum inter-observer agreement of 90% on all elements and 95% on ACR classification criteria using abstraction by the NYUSoM principal investigator as the gold standard. The

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average performance of the abstractors during training and reviews was 95.6% on all

elements, ~~and~~ 97.2% on ACR classification criteria elements, and 97.5% on the unique

elements in the SLICC classification criteria that were not already captured as part of

the ACR classification criteria.

Statistical Analysis

We defined prevalent cases ~~~~as new or existing cases meeting the ACR, SLICC,

or rheumatologist case definition and residing in Manhattan at some time from January

1, 2007, through December 31, 2007. We defined incident cases as those meeting at

least one of the case definitions, first diagnosed from January 1, 2007, through

December 31, 2009, and residing in Manhattan. Population denominators were taken

from the DOHMH interpolated intercensal population estimates for Manhattan [12]. We

calculated rates overall, by sex, and by race/ethnicity per 100,000 person-years and

age-~~adjusted~~ standardized to the United States 2000 standard population using 10 year

age groups for each racial/ethnic group [13]. Information on race was collected

separately from Hispanic ethnicity during abstraction. For analysis, we assigned cases

to one of five mutually exclusive race/ethnicity categories: NH-white, NH-black, NH-

Asian, Hispanic, and NH-other. NH-cases identified with more than one race were

categorized as other.

We conducted capture-recapture (C-RC) analyses [14, 15] to estimate case

under-ascertainment from our primary ACR case definition. We fit log-linear models

separately for incident and prevalent cases by sex and race/ethnicity to estimate the

number of cases missed in our catchment area. Specifically, we fit various models that

addressed potential violation of the homogeneity assumption of capture probability and

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identified the best fitting model using the Akaike Information Criteria. We then used estimates from these models to calculate revised prevalence and incidence and prevalence rates.

We used chi-square tests, or Fisher's exact tests when needed, to assess univariate differences in SLE and ACR manifestations by race/ethnicity and sex. We compared differences between estimates by case definition using 95% confidence intervals (CIs) of the age-adjusted standardized rates, with non-overlapping CIs considered to be significantly different. All analyses were completed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) and R version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results:

Case Finding

Case finding and abstraction was completed in 19 out of 21 hospitals (90.5%, Figure 1), with two hospitals declining to participate (a cancer specialty hospital, and a Veteran's Administration Hospital). Case finding and abstraction was performed from records of 94 out of 124 (75.8%) private rheumatologists identified in the catchment area. Of the 30 rheumatologists who did not participate, 19 did not respond to repeated requests or declined to participate, two died, two had retired and relocated, and seven agreed to participate but abstraction could not be arranged despite repeated attempts before data abstraction ended.

Initial lists provided from the various case finding sources identified 76,220 records (Figure 1). We deduplicated and removed records that did not have a Manhattan address, resulting in 5,065 possible cases with records for abstraction.

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During abstraction and data cleaning, we deemed 1,184 cases ineligible due to

miscoded diagnosis or non-Manhattan residence. Of the remaining 3,881 possible

cases, 1,859 met at least one of the case definitions.

Primary ACR Case Definition: Prevalence ~~Rates~~

In 2007 a total of 1,078 cases (307 NH-white, 282 NH-black, 344 Hispanic, 111

NH-Asian, and 34 NH-other race/ethnicity) fulfilled the ACR case definition for SLE

(Table 1). The overall crude and age-~~adjusted~~ standardized prevalence ~~rates were~~ was

68.2 (95% CI 64.1-72.2) and 62.2 (95% CI 58.4-66.0) per 100,000 person-years. Age-

~~adjusted~~ standardized rates were approximately nine times higher for women compared

with men (107.4 vs. 12.5). Age-~~adjusted~~ standardized rates also differed by

race/ethnicity among both women and men. The highest age-~~adjusted~~ standardized

prevalence ~~rates were~~ was seen among NH-black women (210.9) followed by Hispanic

women (138.3), NH-Asian women (91.2), and NH-white women (64.3). The age-

~~adjusted~~ standardized prevalence ~~rates~~ among men followed a similar pattern with the

highest ~~rate~~ estimate among NH-blacks (26.7) followed by Hispanics (19.4), NH-Asians

(14.2), and NH-whites (3.7). C-RC estimated an additional 122 cases of SLE, indicating

that 10% of cases may have been missed. Almost two-thirds (62.5%) of the estimated

cases missed were NH-white women. With C-RC adjustment, the prevalence ~~rate~~

increased to 75.9 per 100,000 person-years (95% CI 70.6-81.2).

The average age (± standard deviation [SD]) among women and men with SLE

living in Manhattan in 2007 was 43.3 (± 15.5) and 40.7 (± 16.9) years respectively. The

average age by race/ethnicity was 47.0 (± 16.5) years among NH-whites, 42.9 (± 15.6)

years among Hispanics, 41.5 (± 13.7) years among NH-blacks, and 37.3 (± 15.4) years

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among NH-Asians. Figures 2A shows age-specific prevalence ~~rates~~ for women by race/ethnicity. Prevalence ~~rates were~~ was higher among NH-black and Hispanic women ages 20 to 59 years old compared to similarly-aged NH-white women. Prevalence ~~rates~~ among NH-Asian women ~~were~~ was not significantly different than those among NH-white women for any age group. Numbers among men were too small to assess age-specific rates by race/ethnicity.

Among the 344 Hispanic cases, 82.9% were also identified as white, 11.3% as black, and 5.8% as other race/ethnicity. Information on Hispanic ethnicity was often absent, with 239 (69.5%) having no further details, but Hispanic case ethnicities included Central or South American, Cuban, Dominican, Mexican, Puerto Rican, and Spanish. There were 111 NH-Asian cases as well as five identified as NH-other due to multiple race/ethnicity but with evidence of Asian race. More than a quarter (26.7%) of these cases had no further classification for Asian ethnicity, but ethnicities among cases with information available included Chinese, Filipino, Hawaiian, Indian or Pakistani, Japanese, Korean, Pacific Islander not otherwise specified, South Asian, and Vietnamese.

Table 2 shows the occurrence of the 11 ACR criteria overall and by race/ethnicity among prevalent ACR cases. Renal disease was more common among NH-Asians (53.2%), NH-blacks (50.7%), and Hispanics (49.4%) compared with NH-whites (25.4%). Neurologic manifestations were more common among Hispanics (26.2%) and NH-blacks (24.5%) compared with NH-whites (16.6%). Also compared with NH-whites, discoid lesions were more commonly seen among NH-blacks (25.9% vs. 8.8%) and malar rash was more commonly seen among Hispanics (50.0% vs. 35.8%).

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Primary ACR Case Definition: Incidence Rates

From 2007-2009, 232 incident cases met the ACR case definition (Table 3) for

SLE (92 NH-white, 62 NH-black, 49 Hispanic, 22 NH-Asian, and 7 NH-other

race/ethnicity). The overall crude and age- ~~adjusted~~ standardized incidence rates were

4.9 (95% CI 4.3-5.5) and 4.6 (95% CI 4.0-5.2) per 100,000 person-years respectively.

Age- ~~adjusted~~ standardized rates differed by sex, and were almost 8 times higher for

women compared with men (7.9 vs. 1.0). Age- ~~adjusted~~ standardized rates also differed

by race/ethnicity among both women and men. The highest age- ~~adjusted~~ standardized

incidence rates among women were among NH-blacks (15.7) followed by NH-Asians

(6.6), Hispanics (6.5), and NH-whites (6.5). Similarly, the highest age- ~~adjusted~~

standardized incidence rates among men were among NH-blacks (2.4) followed by

Hispanics (1.3), NH-Asians (0.5), and NH-whites (0.5). C-RC adjustment estimated 284

incident cases of SLE, indicating that 18% of cases were missed and 67.0% of these

were NH-white women. The resulting C-RC adjusted incidence rate increased to 6.0 per

100,000 person-years (95% CI 4.6-7.4).

The average age (±SD) at diagnosis was 40.4 (± 16.6) years among women and

42.9 (± 20.4) years among men. The average age (±SD) at diagnosis was 42.2 (± 17.7)

years among NH-whites, 39.2 (± 16.6) years among NH-blacks, 39.6 (± 17.0) years

among Hispanics, and 37.9 (± 16.0) years among NH-Asians. Figure 2B shows age-

specific incidence rates for women by race/ethnicity. The only age-specific difference

was between NH-black and NH-white women aged 20 to 39 years old. Otherwise, due

to small numbers within each strata, no age-specific differences were found.

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Among the 49 incident Hispanic cases, 77.6% were also identified as NH-white, 16.3% as NH-black, and 6.1% as NH-other race/ethnicity. As with prevalent cases, Hispanic ethnicity information for incident cases was often absent, with 71.4% having no further ethnicity information available. Among the 22 incident NH-Asian cases, 32% had no further data available.

Table 2 shows the occurrence of the 11 ACR criteria overall and by race/ethnicity among incident ACR cases. Evidence of renal disease was found among 34.9% of incident cases, but was more common among NH-Asians (45.5%), NH-blacks (43.5%), and Hispanics (42.9%) compared with NH-whites (23.9%). Discoid lesions were more common among NH-blacks (25.8%) compared with NH-whites (9.8%).

Secondary Case Definitions

Prevalence and incidence rates calculated using the SLICC case definition for SLE were significantly higher than those calculated with the primary case ACR definition. Using the SLICC case definition generated crude and age-adjusted standardized prevalence rates of 80.1 (95% CI 75.7-84.5) and 73.8 (95% CI 69.6-77.9) per 100,000 years respectively, which were 17-19% higher than those calculated with the ACR case definition. The SLICC crude and age-adjusted standardized incidence rates (6.6, 95% CI 5.8-7.3; 6.2, 95% CI 5.5-6.9) were nearly 35% higher than the ACR incidence rates.

The rheumatologist case definition yielded crude and age-adjusted standardized prevalence rates that were was approximately 17% higher than those from the ACR case definition (79.4, 95% CI 75.0-83.8; 72.6, 95% CI 68.5-76.7). Crude and age-adjusted standardized incidence rates using the rheumatologist case definition were

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similar to rates using the ACR case definition (5.3, 95% CI 4.7-6.0; 5.0, 95% CI 4.4-5.7). For both secondary case definitions differences in rates by sex and race/ethnicity were similar to those identified by the ACR case definition.

Of the 1,538 incident and prevalent cases meeting either the ACR or SLICC case definition, 75.6% met both ACR and SLICC definitions, 4.3% only met the ACR definition, and 20.2% met the SLICC definition only. Table 4 displays information on the unique SLICC criteria that are not part of the ACR classification criteria among incident and prevalent cases meeting the SLICC case definition only. The most common unique SLICC criteria among these cases were low complement levels, alopecia, and different definitions for lymphopenia. In addition, 5.5% of cases meeting the SLICC case definition had an ANA and/or anti–double-stranded DNA antibody and a biopsy consistent with lupus nephritis. Reasons that cases met the ACR and not the SLICC case definition were largely due to having $\geq$ 4 clinical criteria but no immunologic criteria, differences in categorization of photosensitivity and malar rash (which were separated in the ACR and combined in the SLICC criteria), and differences in defining lymphopenia and anti-cardiolipin antibody (data not shown).

Discussion

Our analysis of the MLSP provides prevalence and incidence rate estimates of SLE among Manhattan residents using methods similar to other CDC-funded SLE registries. Our analysis confirms evidence for higher prevalence of SLE among NH-blacks compared with NH-whites and adds evidence for higher prevalence of SLE among Hispanics and NH-Asians as well. The MLSP is also the first among the CDC-

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funded SLE registry sites to report using the SLICC classification criteria, which were recently validated, to describe cases of SLE [10].

~~Based on case finding and data abstraction from administrative databases, hospitals, and private rheumatology practices, we identified 1,078 prevalent cases of SLE in Manhattan in 2007 and 232 incident cases from 2007-2009,~~ The ~~resulting in~~ age-~~adjusted~~ standardized prevalence and incidence ~~rates~~ of SLE in Manhattan were 62.2 (95% CI 58.4-66.0) and 4.6 (95% CI 4.0-5.2) using the ACR case definition. Compared with previous reports by the CDC-funded sites , we estimated slightly lower overall age-~~adjusted~~ standardized prevalence ~~rates~~ than the GLR (73.0, 95% CI 68.9-77.4) [5] and MILES (72.8, 95% CI 70.8-74.8) [6], but found similar disparities by sex and race/ethnicity for NH-whites and NH-blacks. MLSP prevalence estimates increased with C-RC adjustment and were comparable to C-RC adjusted estimates from the GLR (75.8, 95% CI 70.3-81.2 vs. 83.0, 95% CI 78.6-87.7). Our age-~~adjusted~~ standardized incidence rates using the ACR case definition were similar to those from the GLR and MILES.

We found the highest prevalence and incidence rates among NH-blacks, in line with the GLR and MILES and with preliminary data from the CLSP. However, unlike the GLR and MILES we found elevated prevalence ~~rates~~ among NH-Asians and Hispanics compared with NH-whites. Compared with preliminary crude estimates from the CLSP [16] the MLSP showed similar elevated rates among Hispanics (84.2, 95% CI 75.3-93.1 vs 87.7 95% CI 72.1-106.8) ~~and~~ but slightly lower rates among NH-Asians (64.0, 95% CI 52.1-75.9 vs 95.8 95% CI 84.9-108.1). These MLSP findings are particularly important, given the few published studies on prevalence and incidence of SLE among

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Asians and Hispanics in the United States. A 1973 review presented estimates among NYC residents from 1956 to 1965 but focused only on whites, blacks, and Puerto Ricans [17]. Another study published in 2001 estimated the prevalence of SLE among Hispanics in Arizona to be 103 per 100,000, slightly higher than the rate found by the MLSP among Hispanics in Manhattan [18]. A more recent study using Medicaid data estimated an even higher prevalence ~~rate~~ of SLE among Hispanics (126.5 per 100,000) with Medicaid coverage in the United States from 2000 to 2004 [19].

The study using Medicaid data is one of the few to estimate rates of SLE among Asians in the United States, reporting a prevalence ~~rate~~ almost four times that estimated by the MLSP (175.1 per 100,000 vs. 45.7) [19]. The only other studies known to assess rates SLE among Asians in the United States focused on SLE prevalence. One study identified cases in Hawaii based on physician diagnosis at five medical centers and outpatient practices in 1989. The overall SLE prevalence ~~rate~~ identified in that study (41.8 per 100,000) was similar to the MLSP estimate for NH-Asians, and the age-~~adjusted~~ standardized rates for women from specific Asian ethnic groups (Chinese, Filipino, Hawaiian, Japanese) was found to be higher compared with that among white women [20]. Another study, using hospital discharge data, reported that Asian/Pacific Islander women had a lower rate of prevalent SLE compared with white women [21]. Less is known about the incidence of SLE among Asians. In England, new diagnoses of SLE are more common among Asians, specifically South Asians from India and Pakistan, compared with whites [22, 23], but to our knowledge there are no other published reports on the incidence of SLE among Asians in the United States.

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In this analysis, we also provide information on manifestations among SLE cases. Clinical or serologic manifestations among prevalent cases approximated those from the GLR and MILES registries. The MLSP found a high burden of nephritis overall with nearly half (42.4%) of prevalent cases developing nephritis. The proportion of those with nephritis was higher among non-white prevalent cases, specifically 50.7% among NH-blacks, 49.4% among Hispanics, and 53.2% among NH-Asians, compared with 25.4% among NH-whites, in line with other studies [5, 6, 19, 24, 25].

The SLICC case definition for SLE yielded higher incidence and prevalence estimates than the ACR case definition. Unique criteria which substantiated the classification of SLE based on SLICC but not ACR criteria, included low complements, alopecia, and different definitions for lymphopenia [10]. The small number of cases that met the ACR but not the SLICC case definition is reassuring as it suggests that few cases met ACR criteria for SLE without the presence of autoantibodies. However, given the descriptive nature of the MLSP and the absence of a gold standard test that would unambiguously identify SLE, this project cannot assess which set of classification criteria is more sensitive or specific. In addition, non-overlapping confidence intervals were used to conservatively assess differences among rates (26).

There were several limitations to this project. First, we may have underestimated cases as two hospitals and one quarter of rheumatologists in the catchment area declined to participate. Most of the practices that did not participate were in neighborhoods with a majority white population, which is in line with our C-RC analysis that estimated 67.3% of prevalent cases and 70.0% of incident cases missed were NH-white. However, the exclusion of the Veteran's Administration Hospital may have

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resulted in under-identification of males diagnosed with SLE. We also did not include nephrology, dermatology, or primary or alternative care practices among our case finding sources. Though when possible we did query hospital pathology databases for relevant kidney or skin biopsies, we still may have missed milder cases that were not hospitalized or seen by a rheumatologist during the surveillance period. It is also possible that we missed cases if they lived in Manhattan but sought care in other boroughs or a neighboring state.

Second, medical systems differed tremendously, and any difficulty navigating different electronic medical records or with the legibility of paper charts could have led to missed or miscoded data. Additionally, medical records are designed for physician use, not for data abstraction and surveillance. Thus, some information of interest may have been missing or ambiguous, depending on what was collected and recorded by the case finding source.

Third, abstracting occurred several years after the surveillance period, which could have led to missing information if records were put into storage or data elements were lost during a facility's migration from paper to electronic records. This lag time may have also affected our ability to find all prevalent cases of SLE, as some newer systems were unable to query past certain dates. Additionally, many private practices did not retain information on patients' prior addresses, so we may not have abstracted cases who moved outside of Manhattan since the surveillance period. However, when possible the software LexisNexis was used to verify patient residence within the catchment area.

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Finally, data on race and ethnicity was abstracted from administrative and medical records, which may not accurately represent the patient's own racial or ethnic identification. Additionally, information on ethnicity was often missing or did not include detail such as country of origin, which limited our ability to describe rates of SLE among specific ethnic groups. Though available information did reflect the major ethnic groups in Manhattan, ethnicity information was missing for most Hispanic cases and more than one quarter of NH-Asian cases. Categorized broadly, Hispanic or Asian race encompasses a number of heterogeneous groups and SLE rates among them may differ. Given the already limited number of published studies on SLE among Asians and Hispanics, additional work is needed to better describe and understand the experience of SLE among specific ethnic subpopulations.

Despite these limitations, our analysis benefitted from the design and composition of the MLSP. First, the MLSP was designed as a population-based registry with methods similar to four other CDC-funded SLE registries, which allowed us to compare rates across sites. Second, the diverse population within our catchment area allowed us to estimate rates of SLE among the major racial categories, particularly Asians and Hispanics. Third, given the recent publication of the SLICC classification criteria, we were able to estimate rates of SLE by this case definition and compare them to the ACR case definition. Fourth, the partnership with the DOHMH allowed us to collect information from a number of case finding sources and find complete clinical information on most cases. Finally, our abstractors all had a medical background, which helped during training and also provided an advantage during extensive review of medical records to identify SLE criteria.

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In conclusion, we found substantial disparities in prevalence, incidence, and manifestations of SLE by sex and race/ethnicity among Manhattan residents. Women consistently had higher prevalence and incidence rates of SLE compared with men, and NH-blacks, Hispanics, and NH-Asians had higher rates of diagnosed SLE and a higher proportion lupus nephritis compared with NH-whites. The highest rates of SLE were seen among NH-black women followed by Hispanic, NH-Asian, and NH-white women. Using the SLICC criteria for SLE provided higher prevalence and incidence rates than the ACR criteria.

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Table 1: Crude and age-~~adjusted~~ standardized prevalence ~~rates~~ of SLE among Manhattan residents, 2007, according to the ACR, SLICC, and rheumatologist case definitions overall and by race/ethnicity and sex

	ACR N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)	Capture-recapture N missed	Adjusted rate (95% CI)	SLICC N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)	Rheumatologist N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)
Overall	1,078	68.2 (64.1-72.2)	62.2 (58.4-66.0)	122.4	75.9 (70.6-81.2)	1,267	80.1 (75.7-84.5)	73.8 (69.6-77.9)	1,256	79.4 (75.0-83.8)	72.6 (68.5-76.7)
Male	101	13.6 (10.9-16.2)	12.5 (10.0-15.0)	8.3	14.7 (12.5-16.9)	110	14.8 (12.0-17.6)	13.8 (11.1-16.4)	98	13.2 (10.7-16.1)	12.0 (9.7-14.7)
Female	977	116.7 (109.3-124.0)	107.4 (100.5-114.4)	114.1	130.3 (122.1-138.4)	1,157	138.2 (130.2-146.1)	128.3 (120.7-135.9)	1,158	138.3 (130.3-146.2)	127.5 (119.9-135.1)
Non-Hispanic White	307	40.5 (36.0-45.0)	34.7 (30.7-38.8)	389.4	51.4 (45.0-57.7)	373	49.2 (44.2-54.2)	42.7 (38.1-47.3)	352	46.4 (41.6-51.3)	39.7 (35.3-44.0)
Male	17	4.7 (2.7-7.5)	3.7 (2.2-6.0)	22.9	6.3 (3.2-9.4)	23	6.3 (4.0-9.5)	5.3 (3.3-8.0)	24	6.6 (4.2-9.8)	5.3 (3.4-7.8)
Female	290	73.4 (64.9-81.8)	64.3 (56.4-72.2)	366.5	92.7 (83.4-102.1)	350	88.6 (79.3-97.8)	78.2 (69.4-86.9)	328	83.0 (74.0-92.0)	72.0 (63.7-80.4)
Non-Hispanic Black	282	131.4 (116.1-146.8)	124.9 (110.3-139.6)	285.6	133.1 (130.6-135.7)	326	151.9 (135.5-168.4)	144.7 (128.9-160.5)	312	145.4 (129.3-161.6)	137.7 (122.3-153.1)
Male	28	28.5 (18.9-41.2)	26.7 (17.7-38.7)	28.0	28.5 (28.1-28.9)	31	31.6 (21.4-44.8)	29.7 (20.2-42.3)	24	24.4 (15.7-36.4)	22.6 (14.5-33.7)
Female	254	218.4 (191.5-245.2)	210.9 (184.8-237.1)	257.6	221.4 (217.1-225.8)	295	253.6 (224.7-282.5)	244.4 (216.3-272.6)	288	247.6 (219.0-276.2)	237.2 (209.5-264.8)
Hispanic	344	84.2 (75.3-93.1)	82.8 (74.0-91.7)	345.4	84.6 (83.8-85.3)	372	91.1 (81.8-100.3)	90.2 (81.0-99.5)	396	97.0 (87.4-106.5)	96.2 (86.7-105.8)
Male	38	19.7 (13.9-27.0)	19.4 (13.6-26.9)	38.1	19.7 (19.4-20.0)	38	19.7 (13.9-27.0)	19.5 (13.7-26.9)	33	17.1 (11.8-24.0)	16.7 (11.4-23.6)
Female	306	142.1 (126.2-158.0)	138.3 (122.7-153.9)	307.3	142.7 (141.5-143.9)	334	155.1 (138.4-171.7)	151.7 (135.3-168.1)	363	168.5 (151.2-185.9)	165.3 (148.2-182.5)
Non-Hispanic Asian	111	64.0 (52.1-75.9)	56.2 (44.7-67.7)	131.0	75.5 (66.0-85.0)	145	83.6 (70.0-97.2)	75.1 (61.7-88.5)	118	68.0 (55.7-80.3)	62.2 (49.7-74.6)
Male	15	19.3 (10.8-31.9)	14.2 (7.6-24.0)	17.3	22.3 (17.0-27.6)	15	19.3 (10.8-31.9)	14.2 (7.6-24.0)	13	16.8 (8.9-28.7)	12.5 (6.2-22.6)
Female	96	100.0 (81.0-122.2)	91.2 (72.1-113.8)	113.7	118.5 (105.6-131.3)	130	135.5 (112.2-158.7)	125.9 (102.0-149.9)	105	109.4 (88.5-130.3)	103.6 (81.5-125.8)
Non-Hispanic Other	34			49.0		51			78		

Case definitions: ACR: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE; SLICC: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification; Rheumatologist: have been diagnosed with SLE by a treating rheumatologist

Rates are per 100,000 Manhattan resident person-years. Denominator data is based on 2007 intercensal population estimates from the NYC DOHMH Bureau of Epi Services (2000-2014 files). Data are ~~age~~standardized for age and race/ethnicity ~~adjusted~~ to the US 2000 Standard Population.

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Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

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Table 2: Frequency of 11 ACR manifestations of SLE among prevalent and incident cases by the ACR case definition, overall and by race/ethnicity

	Prevalent cases (2007)					Incident cases (2007-2009)				
	Overall	Non-Hispanic White	Non-Hispanic Black	Hispanic	Non-Hispanic Asian	Overall	Non-Hispanic White	Non-Hispanic Black	Hispanic	Non-Hispanic Asian
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Overall	1,078	307 (28.5)	282 (26.2)	344 (31.9)	111 (10.3)	232	92 (39.7)	62 (26.7)	49 (21.1)	22 (9.5)
Antinuclear antibody	996 (92.4)	284 (92.5)	262 (92.9)	316 (91.9)	103 (92.8)	213 (91.8)	82 (89.1)	58 (93.5)	47 (95.9)	22 (100.0)
Hematologic disorder	893 (82.8)	255 (83.1)	238 (84.4)	278 (80.8)	98 (88.3)	188 (81.0)	71 (77.2)	56 (90.3*)	37 (75.5)	19 (86.4)
Arthritis	813 (75.4)	246 (80.1)	204 (72.3)	255 (74.1)	80 (72.1)	159 (68.5)	66 (71.7)	41 (66.1)	30 (61.2)	17 (77.3)
Immunologic disorder	781 (72.4)	213 (69.4)	204 (72.3)	253 (73.5)	89 (80.2*)	170 (73.3)	66 (71.7)	46 (74.2)	37 (75.5)	18 (81.8)
Renal disorder	457 (42.4)	78 (25.4)	143 (50.7*)	170 (49.4*)	59 (53.2*)	81 (34.9)	22 (23.9)	27 (43.5*)	21 (42.9*)	10 (45.5*)
Serositis	449 (41.7)	117 (38.1)	127 (45.0)	156 (45.3)	36 (32.4)	84 (36.2)	25 (27.2)	33 (53.2*)	18 (36.7)	5 (22.7)
Malar rash	428 (39.7)	110 (35.8)	82 (29.1)	172 (50.0*)	46 (41.4)	86 (37.1)	31 (33.7)	20 (32.3)	22 (44.9)	8 (36.4)
Photo sensitivity	370 (34.3)	121 (39.4)	76 (27.0*)	132 (38.4)	30 (27.0*)	74 (31.9)	32 (34.8)	11 (17.7*)	21 (42.9)	7 (31.8)
Oral ulcers	333 (30.9)	104 (33.9)	64 (22.7*)	115 (33.4)	37 (33.3)	81 (34.9)	42 (45.7)	16 (25.8*)	12 (24.5*)	7 (31.8)
Neurologic disorder	230 (21.3)	51 (16.6)	69 (24.5*)	90 (26.2*)	11 (9.9)	43 (18.5)	15 (16.3)	15 (24.2)	11 (22.4)	1 (4.5)
Discoid rash	179 (16.6)	27 (8.8)	73 (25.9*)	58 (16.9*)	17 (15.3)	32 (13.8)	9 (9.8)	16 (25.8*)	5 (10.2)	1 (4.5)

ACR case definition: meets ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE.

Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

* Univariate logistic regression indicates the proportion with this manifestation is significantly different than the proportion among non-Hispanic whites (p<0.05).

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Table 3: Crude and age-~~adjusted~~ standardized incidence rates of SLE among Manhattan residents, 2007-2009, according to the ACR, SLICC, and rheumatologist case definitions overall and by race/ethnicity and sex

	ACR			Capture-recapture		SLICC			Rheumatologist		
	N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)	N missed	Adjusted rate (95% CI)	N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)	N	Crude rate (95% CI)	Age-~~adjusted~~ standardized rate (95% CI)
Overall	232	4.9 (4.3-5.5)	4.6 (4.0-5.2)	284.4	6.0 (4.6-7.4)	312	6.6 (5.8-7.3)	6.2 (5.5-6.9)	253	5.3 (4.7-6.0)	5.0 (4.4-5.7)
Male	23	1.0 (0.7-1.5)	1.0 (0.6-1.5)	26.3	1.2 (0.7-1.7)	38	1.7 (1.2-2.3)	1.7 (1.2-2.3)	28	1.3 (0.8-1.8)	1.2 (0.8-1.8)
Female	209	8.3 (7.2-9.4)	7.9 (6.8-9.0)	258.1	10.3 (8.0-12.5)	274	10.9 (9.6-12.2)	10.3 (9.1-11.6)	225	8.9 (7.8-10.1)	8.6 (7.4-9.7)
Non-Hispanic White	92	4.0 (3.2-4.9)	3.6 (2.8-4.5)	128.7	5.6 (4.2-7.1)	124	5.4 (4.5-6.4)	4.8 (3.9-5.8)	94	4.1 (3.3-5.0)	3.8 (3.0-4.8)
Male	7	0.6 (0.3-1.3)	0.5 (0.2-1.0)	8.6	0.8 (0.4-1.2)	13	1.2 (0.6-2.0)	1.0 (0.5-1.7)	9	0.8 (0.4-1.6)	0.7 (0.3-1.3)
Female	85	7.1 (5.7-8.8)	6.5 (5.0-8.3)	120.1	10.1 (7.7-12.5)	111	9.3 (7.6-11.1)	8.5 (6.7-10.3)	85	7.1 (5.7-8.8)	6.8 (5.2-8.6)
Non-Hispanic Black	62	9.8 (7.5-12.6)	9.3 (7.1-12.0)	63.8	10.1 (9.1-11.0)	79	12.5 (9.9-15.5)	12.0 (9.5-15.0)	61	9.6 (7.4-12.4)	9.2 (7.0-11.8)
Male	7	2.4 (1.0-5.0)	2.4 (1.0-5.0)	8.0	2.8 (1.6-3.9)	11	3.8 (1.9-6.8)	3.8 (1.9-6.8)	7	2.4 (1.0-5.0)	2.3 (0.9-4.7)
Female	55	16.0 (12.1-20.9)	15.7 (11.8-20.5)	55.8	16.3 (15.5-17.0)	68	19.8 (15.4-25.1)	19.3 (14.9-24.5)	54	15.7 (11.8-20.5)	15.5 (11.6-20.3)
Hispanic	49	4.0 (3.0-5.3)	4.0 (3.0-5.4)	50.3	4.1 (3.8-4.5)	64	5.2 (4.0-6.7)	5.3 (4.1-6.7)	50	4.1 (3.0-5.4)	4.2 (3.1-5.5)
Male	7	1.2 (0.5-2.5)	1.3 (0.5-2.7)	7.4	1.3 (1.0-1.5)	8	1.4 (0.6-2.7)	1.6 (0.7-3.2)	6	1.0 (0.4-2.3)	1.1 (0.4-2.5)
Female	42	6.5 (4.7-8.8)	6.5 (4.7-8.8)	42.9	6.7 (6.2-7.1)	56	8.7 (6.6-11.3)	8.6 (6.5-11.2)	44	6.8 (5.0-9.2)	7.0 (5.1-9.4)
Non-Hispanic Asian	22	4.2 (2.6-6.3)	3.8 (2.3-6.0)	28.7	5.4 (3.3-7.5)	31	5.8 (4.0-8.3)	5.3 (3.4-7.7)	27	5.1 (3.4-7.4)	4.5 (2.9-6.9)
Male	1	0.4 (0.0-2.4)	0.5 (0.0-2.7)	1.3	0.6 (0.0-1.1)	2	0.8 (0.1-3.1)	1.0 (0.1-3.5)	2	0.8 (0.1-3.1)	1.0 (0.1-3.7)
Female	21	7.1 (4.4-10.9)	6.6 (3.8-10.5)	27.4	9.3 (6.0-12.7)	29	9.9 (6.6-14.2)	8.8 (5.6-13.1)	25	8.5 (5.5-12.6)	7.5 (4.5-11.6)
Non-Hispanic Other	7			12.9		14			21		

Case definitions: ACR: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE; SLICC: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification; Rheumatologist: have been diagnosed with SLE by a treating rheumatologist

Rates are per 100,000 Manhattan resident person-years. Denominator data is based on 2007-2009 intercensal population estimates from the NYC DOHMH Bureau of Epi Services (2000-2014 files). Data are ~~age~~standardized for age and race/ethnicity ~~adjusted~~ to the US 2000 Standard Population.—

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Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other. Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other.

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Table 4: Unique manifestations among SLE incident and prevalent cases meeting SLICC but not ACR case definitions

	N	%
Overall	310	
Immunologic criteria		
__Low complements	151	48.7%
__Anti-Beta2 Glycoprotein Antibodies (IgG, or IgM)bs	16	5.2%
__Direct Coombs test in the absence of hemolytic anemia	5	1.6%
Clinical criteriacriteria		
Acute cutaneous lupus		
__Bullous lupus	1	0.3%
__Toxic epidermal neocrolysis variant of SLE	0	0.0%
__Maculopapular lupus rash (only if Malar)	13	4.2%
__Subacute cutaneous lupus	4	1.3%
Chronic cutaneous lupus		
__Hypertrophic (verrucous) lupus	3	1.0%
__Lupus Panniculitis (profundus)	4	1.3%
__Mucosal lupus if oral ulcers	0	0.0%
__Lupus erythematosus tumidus	1	0.3%
__Chilblains lupus	1	0.3%
__Discoid lupus/Lichen planus overlap	4	1.3%
Non-scarring alopecia	122	39.4%
Neurologic criteria		
__Mononeuritis multiplex	3	1.0%
__Transverse mMyelitis	2	0.6%
__Peripheral or cranial neuropathy	53	17.1%
__Acute cConfusional Sstate	3	1.0%
Lymphopenia	147	47.4%
Antinuclear antibody or anti-double stranded DNA and biopsy proven lupus nephritis and renal biopsy only	17	5.5%

SLICC: Systemic Lupus Erythematosus Collaborating Clinics

ACR: American College of Rheumatology

Criteria are not mutually exclusive; a case may have more than one criteria listed above.

Data on IgA isotypes for anti–B2glycoprotein I and anti-cardiolipin antibodies were not collected. Anti-dsDNA when done by ELISA was only reported as positive or negative so it is possible that is some cases this criterion was over counted in the SLICC if the positive was not specifically double the upper cutoff for the negative value. Finally, CH50 was not captured and thus it is possible that the SLICC criterion for complement could be under-counted.

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Figure 1. Flow chart showing the Manhattan Lupus Surveillance Program case-finding procedure for Systemic Lupus Erythematosus

ACR case definition: meet ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE
SLICC case definition: have sufficient criteria to meet the Systemic Lupus Erythematosus Collaborating Clinics (SLICC) classification
Rheumatologist definition: have been diagnosed with SLE by a treating rheumatologist

Figure 2. Age-specific prevalence and incidence rates of SLE among Manhattan residents in 2007 and from 2007-2009 by ACR case definition, by age group among females

ACR case definition: meets ≥ 4 of 11 American College of Rheumatology (ACR) classification criteria for SLE
Cases were assigned to one of five mutually exclusive race/ethnicity categories: non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Hispanic, and non-Hispanic other.
Non-Hispanic cases identified with more than one race were categorized as non-Hispanic other and are not shown in this figure.

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