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Race/Ethnicity and Cardiovascular Events among Patients with Systemic Lupus Erythematosus

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Abstract

Objective: Systemic Lupus Erythematosus (SLE) is more prevalent with more severe outcomes among Blacks, Asians, and Hispanics than Whites. Cardiovascular disease (CVD) is the leading cause of death among SLE patients. We examined racial/ethnic variation in risk of CVD events among SLE patients.

Methods: Within Medicaid Analytic eXtract (2000–2010), we identified patients aged 18–65 with SLE (≥ 3 ICD-9 710.0 codes, ≥30 days apart) and ≥12 months of continuous enrollment. Subjects were followed from index date to first CVD event (myocardial infarction [MI] or stroke), death, disenrollment, or end of follow-up. Race/ethnicity-specific annual CVD event rates were calculated. Cox regression models estimated hazard ratios (HR), accounting for competing risk of death, adjusting for baseline demographics and comorbidities.

Results: Of 65,788 SLE patients, 93.1% were female and approximately 42% Black, 38% White, 16% Hispanic, 3% Asian and 1% American Indian/Alaska Native. Mean follow-up was 3.8 ±3.1 years. CVD event rates were highest among Blacks (IR 10.57 [95% CI 9.96–11.22]) and lowest among Asians (IR 6.63 [95% CI 4.97–8.85]). After multivariable adjustment, risk of CVD events was increased among Blacks (HR 1.14 [95%CI 1.03–1.26]) compared to Whites. Hispanics and Asians had lower MI risk (HR 0.61 [95% CI 0.48–0.77] and HR 0.57 [95% CI 0.34–0.96], respectively), whereas Blacks and Hispanics had higher stroke risk (HR 1.31 [95% CI 1.15–1.49] and HR 1.22 [95% CI 1.03–1.44]).

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Conclusion: Among SLE patients enrolled in Medicaid, MI risk was lower among Hispanics and Asians, while stroke risk was elevated among Blacks and Hispanics compared to Whites.

Keywords

Systemic lupus erythematosus; SLE; Cardiovascular; Race/Ethnicity

Introduction

Systemic lupus erythematosus (SLE) is more common among non-White than White racial/ethnic groups in the U.S. Non-White patients also have been shown to have poorer SLE-specific long-term outcomes than Whites (1–5). In particular, lupus nephritis (LN) is more prevalent and rates of ESRD due to LN are over seven times higher among Black than White Americans (1, 5–7). In a prior study of SLE patients enrolled in U.S. Medicaid, a poor and racially/ethnically diverse, high-risk population, risk of death was significantly elevated among American Indian/Alaska Natives (by 40%) and Blacks (by 21%) compared to Whites (8). Conversely and surprisingly, however, a “Hispanic and Asian Paradox” was observed: Hispanic and Asian patients had significantly (52% and 41%) lower mortality risks compared to Whites (8).

Cardiovascular disease (CVD) is the leading cause of death among SLE patients and atherosclerosis develops at younger ages (9–11). Cohort studies have reported elevated risks of myocardial infarction (MI), stroke, and heart failure among SLE patients compared to age-matched controls, particularly among women under age 45 (9, 10, 12–15). SLE itself remains an independent CVD risk factor after controlling for known CVD risk factors (16). In a population-based study of over 90,000 U.S. hospitalizations for SLE, Blacks had younger age at CVD admission than Whites, suggesting important disparities (17). Furthermore, CVD morbidity and mortality may be especially high among LN patients, who have high rates of hypertension, hyperlipidemia, and high-dose glucocorticoid use (18–20). However, relatively little is known about variation in rates of CVD by race/ethnicity among SLE and LN patients.

To address these significant knowledge gaps, we examined rates and relative risks of CVD events overall and by race/ethnicity among SLE and LN patients in a multiracial cohort of 65,788 SLE patients. We hypothesized that CVD event rates and relative risks would be elevated among Blacks and American Indian/Alaska Natives compared to White SLE patients.

Patients and Methods

Study Population:

Medicaid is the U.S. health insurance program for individuals with low-income and limited resources, providing coverage for medical expenses and prescription drugs. We analyzed data from the Medicaid Analytic eXtract (MAX), an administrative database containing all billing claims for Medicaid patients from the 29 most populated U.S. states (21). We included adults aged ≥18 to 65 years between January 1, 2000 and December 31, 2010. We

excluded patients >65 years old as > 90% are dually enrolled in Medicare and thus not all claims are captured in Medicaid.

We identified prevalent SLE as previously described (≥ 3 International Classification of Diseases, Ninth Revision [(ICD-9) codes for SLE (710.0), from hospital discharge diagnoses or physician visit claims, ≥30 days apart) (5). Among SLE patients, we identified those with LN (≥2 additional ICD-9 claims for nephritis, proteinuria, and/or renal failure on or after index date, ≥30 days apart) (22). We restricted analyses to patients with ≥12 months of continuous Medicaid enrollment prior to index date for collection of baseline covariates. Index date was defined as ≥ 3rd SLE billing code preceded by 12 months of continuous Medicaid enrollment.

Definition of race/ethnicity:

Race/ethnicity in the MAX database is based on self-report, in mutually exclusive categories of White, Black or African American, American Indian/Alaska Natives, Hispanic or Latino, and Asian (including Native Hawaiian or other Pacific Islander)(23). Individuals whose race/ethnicity information was missing or non-classifiable (e.g. “other/unknown” or “more than one race” categories) were excluded.

Outcomes.

The primary outcome was the first CVD event after the index date, defined as a composite measure of the time to either a first acute MI or stroke (Supplementary Table 1) (24–27). As a secondary outcome, we also evaluated the components of the composite CVD outcome, acute MI or stroke, separately.

Outcomes in the primary analysis were based on primary and secondary hospital discharge diagnosis codes, accounting for the possibility that SLE was billed as the primary diagnosis and CVD event as a secondary diagnosis. Patients were followed from the day after index date to first MI or stroke, death, loss to follow-up (no further medical claims in the absence of documented death), Medicaid disenrollment, or end of follow-up period. Deaths were reported directly to Medicaid and are also obtained from the National Death Index. Cause of death was not available.

Covariates:

Baseline data from 12 months prior to index date included demographic, SLE-related, and CVD-related covariates. Demographic variables were age, sex, and U.S. Census-based region of residence (determined by ZIP code) and categorized as Northeast, Midwest, South, or West. For area-based socioeconomic status (SES), we used a validated composite index of seven ZIP code SES indicators from 2000 U.S. Census data (28). We divided area-level SES into quartiles (5).

To characterize SLE-related comorbidities, we utilized the “SLE risk adjustment index”, a validated measure for prediction of in-hospital mortality among SLE patients which utilizes comorbidities specific for SLE (29). We used the median score to divide patients into high or low SLE risk categories. We categorized mean baseline glucocorticoid use (0 to 5mg/day, >5

to 15 mg/day, and >15 mg/day) for interpretability. We also evaluated baseline warfarin use (ever/never), which may serve as proxy for antiphospholipid syndrome (APS). We evaluated baseline CVD comorbidities using validated ICD-9 and/or Current Procedural Terminology (CPT) and/or Diagnosis Related Group (DRG) codes for hypertension, hyperlipidemia, diabetes mellitus, smoking, obesity, acute MI, old MI, angina, percutaneous coronary intervention (PCI), coronary atherosclerosis, and coronary artery bypass graft (Supplementary Table 1) (30–33).

Statistical Analysis:

We calculated unadjusted CVD incidence rates (IRs) and incidence rate ratios (IRRs) overall and by race/ethnicity for SLE per 1,000 person-years, with 95% confidence intervals (95% CIs). To investigate contributions of different sets of factors, we fit three multivariable Cox sub-distribution proportional hazards models, calculating cause-specific risk while accounting for the competing risk of death (34). In each of our models (A-C), while accounting for death as a competing risk, we estimated hazard ratios (HR) for each outcome by race/ethnicity among SLE and LN patients. Model A included age (continuous) and sex. Model B added sociodemographic variables and SLE-related risk factors to model B, including SLE-specific risk adjustment index, glucocorticoid use, and LN. Finally, Model C added cardiac-specific risk comorbidities to model B including history of hypertension, smoking, hyperlipidemia, diabetes mellitus, and obesity. We tested the proportional hazards assumption, using Kaplan-Meier curves as well as time-varying covariates by race/ethnicity, for the variables of interest, and observed no significant deviations in our models.

We performed four sensitivity analyses: First, we only included primary discharge diagnosis codes for all outcomes. Second, we excluded patients with a history of CVD (PCI, CABG, coronary atherosclerosis, acute MI, heart failure, stroke, or ‘past MI’) at baseline. Third, we separately examined risks among Hispanics who self-reported ≥1 race and those who only reported Hispanic ethnicity. Lastly, we examined the effect of additional adjustment of baseline warfarin use on our final models for CVD, MI, and stroke.

All statistical analyses were conducted using SAS version 9.3. Data were obtained from Centers for Medicare and Medicaid Services (CMS) through an approved Data Use Agreement and presented in accordance with CMS policies (cell sizes <11 were suppressed). The Partners Institutional Review Board approved all aspects of this study.

Results

We included 65,788 cases of prevalent SLE from 2000–2010. Baseline characteristics are shown in Table 1. The mean (± SD) age was 40.8 (± 12.1) years; 93.1% were female and the largest proportion resided in the South (40%). Racial/ethnic breakdown was: 42% Black, 38% White, 16% Hispanic, 3% Asian, 1% American Indian/Alaska Natives. Black SLE patients had a higher prevalence of hypertension and heart failure than all other race/ethnicities. Compared to Whites, Hispanics had lower baseline rates of angina, coronary atherosclerosis, stroke, MI, smoking, heart failure, obesity, CABG, and PCI, but similar rates of diabetes and hypertension. Asians had the lowest prevalence of coronary atherosclerosis, diabetes, hypertension, obesity, stroke, and smoking, but had the highest proportion of lupus

nephritis and rates of mean glucocorticoid use >5 mg/day, compared to all other race/ethnicities. The prevalence of DM, obesity, and MI at index date was highest among American Indian/Alaska Natives compared to other race/ethnicities. The SLE risk adjustment index was highest among Blacks and lowest among Hispanics and Asians.

Mean follow-up was 3.8 ± 3.1 years and there were 2,259 first CVD events, including 901 hospitalized MIs and 1,441 hospitalized strokes (and 83 events with both MI and stroke). Among all SLE patients, the annual CVD event IR per 1,000 person-years was 9.31 (95%CI 8.93–9.70). Annual rates of MI were 3.65 (95%CI 3.42–3.90) and 5.88 (95%CI 5.58–6.19) for stroke. Blacks had the highest rate of CVD events (IR 10.57 [95%CI 9.96–11.22]) whereas Asians had the lowest CVD event rate (IR 6.63 [95%CI 4.97–8.85]). Compared to Whites, Blacks (IRR 1.18 [95%CI 1.13–1.23]) had increased CVD event rates, whereas CVD event rates were lower among Hispanics (IRR 0.84 [95%CI 0.79–0.90]) and Asians (IRR 0.75 [95% CI 0.65–0.86]).

After multivariable adjustment for sociodemographic factors, as well as SLE- and CVD-specific factors, and accounting for the competing risk of death, racial/ethnic variation in CVD event risks among Black SLE patients persisted. The multivariable hazard ratios (HR) from models A-C for the primary outcome of CVD, in addition to CVD components of MI and stroke separately, are shown in Table 3. Among SLE patients overall, in age- and sex-adjusted models, Blacks with SLE had a significantly increased risk of CVD (HR 1.31 [95%CI 1.19–1.43]); however, this risk was slightly attenuated after sequential adjustment for sociodemographic factors, SLE- and CVD- comorbidities (HR 1.14 [95%CI 1.03–1.26]). After adjustment, no significant association with CVD risk was demonstrated among Hispanics (HR 0.93 [95%CI 0.81–1.07], Asians (HR 0.78 [95%CI 0.58–1.06], or American Indian/Alaska Natives (HR 1.04 [95%CI 0.70–1.56]) compared to Whites.

Secondary outcomes: MI and stroke

When evaluating the secondary outcomes of MI and stroke separately (Table 3), no significant elevation in MI risk was demonstrated among Blacks compared to Whites (HR 0.97 [95%CI 0.83–1.12]). However, among Hispanics compared to Whites, MI risk was significantly reduced after age- and sex-adjustment (HR 0.65 [95%CI 0.51–0.81]) and persisted after additional adjustment for sociodemographic factors, and SLE and CVD-comorbidities (HR 0.61 [95%CI 0.48–0.77]). Similarly, MI risk was significantly reduced among Asians compared to Whites (HR 0.57 [95% CI 0.34–0.96]) after multivariable adjustment.

Elevated stroke risk was found among Blacks (HR 1.48 [95%CI 1.31–1.66] and Hispanics (HR 1.25 [95% CI 1.07–1.46]) compared to Whites in age- and sex-adjusted models. This elevated risk remained significant after multivariable adjustment for sociodemographic factors, SLE and CVD-comorbidities among Blacks (HR 1.31 [95%CI 1.15–1.49]) and Hispanics (HR 1.22 [95% CI 1.03–1.44]). No association was demonstrated among Asians or American Indian/Alaska Natives with SLE for stroke risk.

Lupus Nephritis Subgroup

Patients with LN (n=13,966, 21.2%) comprised a younger subset, mean age 37.6 (± 12.5) years, with higher prevalence of many baseline CVD risk factors, including angina, coronary atherosclerosis, diabetes, hyperlipidemia, hypertension, stroke, heart failure, MI, PCI and CABG. LN patients also had increased use of warfarin and higher mean daily glucocorticoid doses compared to the overall SLE group. Furthermore, the SLE risk adjustment index was nearly two-fold higher among LN patients compared to that among all prevalent SLE cases (3.83 [±3.29] versus 1.64 [±2.59]). Among patients with LN, annual CVD event rates per 1,000 years were higher than the SLE cohort overall (IR 13.89 [95%CI 12.83–15.04) and also by race/ethnicity (data not shown).

No significant association was demonstrated for CVD risk by race/ethnicity in age- and sex- or multivariable-adjusted models among the LN subgroup. Hispanics with LN had a significant reduction in MI risk after age- and sex-adjustment (HR 0.61 [95%CI 0.40–0.93]) compared to Whites, however this was no longer significant after multivariable adjustment (HR 0.66 [95%CI 0.43–1.03]). In age- and sex- adjusted models, Hispanics also had a significantly elevated risk of stroke (HR 1.46 [95% CI 1.06–2.02]), which remained elevated but no longer significant after multivariable adjustment (HR 1.41 [95% CI 1.00–1.99]). Asians also had a potentially reduced MI risk (HR 0.47 [95%CI 0.21–1.08], whereas Blacks had a potentially increased risk of stroke (HR 1.21 [95% CI 0.92–1.57]) after age-and sex-adjustment, although these findings were not significant.

Sensitivity Analyses

In a sensitivity analysis restricting to primary discharge diagnoses, results remained consistent with the main analysis: after multivariable adjustment, MI risk among SLE patients remained significantly lower among Hispanics (HR 0.61 [95%CI 0.47–0.80) and was lower, although not significantly, among Asians (HR 0.61 [95% CI 0.35–1.06]). Risk of stroke remained significantly increased among Blacks (HR 1.32 [95%CI 1.15–1.51]) and Hispanics (HR 1.23 [95% CI 1.04–1.47] compared to Whites.

After excluding SLE patients with baseline CVD, MI risk was similarly significantly lower among Hispanics (HR 0.62 [95%CI 0.46–0.84) and not significantly among Asians (HR 0.59 [95% CI 0.31–1.12]) and stroke risk was increased among Blacks (HR 1.40 [95%CI 1.18–1.66] and Hispanics (HR 1.32 [95% CI 1.07–1.63]) compared to Whites after multivariable adjustment.

In a sensitivity analysis separately examining Hispanics reporting ≥1 race from those only reporting Hispanic ethnicity, we found similar results to our main analysis. MI risk was reduced among Hispanics reporting ≥1 race (HR 0.43 [95% CI 0.25–0.71] and those only reporting Hispanic ethnicity (HR 0.68 [95% CI 0.52–0.87]) compared to Whites. Hispanics in both groups also had increased risk of stroke (HR of 1.34 [95% CI 1.00–1.80] among Hispanics reporting ≥1 race and HR 1.19 [95% CI 0.99–1.42] among Hispanics reporting ethnicity only).

We also evaluated the role of warfarin use on CVD risk. During baseline, prevalence of warfarin use was 6.9% in SLE overall, with similar rates by race/ethnicity. Additional

adjustment for warfarin use yielded unchanged results compared to our final model (Model C) for the outcomes of CVD, MI, or stroke among SLE patients by race/ethnicity (data not shown).

Discussion

Within a cohort of >65,000 racially, ethnically- and geographically-diverse SLE patients from the 29 most populated U.S. states, we observed marked racial/ethnic variation in CVD event rates and relative risks. Blacks had a 14% *increased* CVD risk. We also found reduced MI risk among Hispanics by 39% and Asians by 43%, compared to White SLE patients. Risk of stroke was increased by 31% among Blacks and 22% among Hispanics with SLE, compared to Whites. Sequential adjustment for sociodemographic factors, SLE and CVD comorbidities attenuated the increased stroke risk among Blacks, suggesting that these factors may explain some of this excess risk. In a sensitivity analysis excluding those with prior CVD events during baseline, similar racial and ethnic disparities in outcomes related to Hispanics, Asians and Blacks compared to Whites were observed, suggesting that history of prior CVD does not alter subsequent CVD event risk.

The demonstration of substantially reduced MI risks in Hispanics and Asians compared to White SLE patients is novel. SLE has been reported to be more prevalent, more severe, and to result in more end-organ damage in Hispanics and Asians compared to White patients (35, 36). However, we have previously reported a 52% and 41% lower adjusted all-cause mortality risk among Hispanic and Asian patients compared to Whites within this Medicaid SLE cohort (8). The current results suggest a similar “Hispanic and Asian paradox” for reduced MI risk, possibly contributing to the lower mortality risk. Hispanics in the general U.S. population have a high prevalence of many CVD risk factors, including hypertension, diabetes, physical inactivity, obesity, and metabolic syndrome (37). Nonetheless, paradoxically lower rates of coronary death, vascular death and total mortality have been demonstrated among Hispanics vs. non-Hispanics in the general population (37, 38).

CVD risk is less well-characterized among Asians in the U.S. National prevalence rates for coronary heart disease among Asian adults are lower compared to non-Hispanic Whites (2.9% versus 6.5%)(39). Although Asians are shown to have similar rates of classical CVD risk factors compared to Whites overall, this risk can vary substantially by subgroup (40). Furthermore, studies examining CVD risk among aggregate Asians versus Whites have typically demonstrated no association, largely thought to be due to varied risks among Asian subgroups (41).

Possible explanations for the observed reduced MI risk among Hispanics and Asians includes incomplete ascertainment of MI events as immigrants may return to their countries of origin during illness or at end of life, and thus are not captured in claims data, potentially leading to under-ascertainment of adverse outcomes (42). However, we previously investigated this possibility and did not demonstrate the existence of differential loss to follow-up among Hispanics or Asians in our SLE Medicaid cohort (8). Additionally, immigrants who do not “acculturate” may follow a healthier lifestyle than U.S. Whites, with healthier diets and less smoking (43). Hispanics and Asians in our cohort were slightly

younger and had lower SLE risk index (SLE severity indicator) than White or Black patients, but adjustment for these and other CVD risk factors did not influence the reduced MI risk observed. Despite having the highest proportion of LN and use of moderate-to-high dose glucocorticoids, Asians still had reduced MI risk in age- and sex-adjusted models. Additionally, although Asians and Hispanics had lower rates of CVD risk factors compared to Whites, adjustment for these factors did not account for the reduced risk. Claims data do not contain granular data such as smoking duration/intensity, systolic blood pressure, cholesterol levels, or hemoglobin a1c values, which may all be potential contributors to CVD risk. The observed “paradox” may be the result of complex interactions between environmental, cultural, socioeconomic, psychosocial, genetic and other clinical factors. Further studies, possibly with more clinical and sociodemographic data are needed to delve deeper into this question.

Furthermore, our finding of elevated stroke risk among Black and Hispanic SLE patients is consistent with the known increased stroke burden among Blacks and Hispanics in the U.S. general population (44). Although Blacks with SLE are shown to have increased CVD event risks (defined as a composite of MI, angina, and/or cardiac procedures) compared to White SLE patients (17), in the current study Blacks did not have an elevated MI risk, but did have a 31% increased stroke risk vs. Whites. The reasons for these discrepant findings are not clear. In our cohort, Black patients had higher SLE risk indices, more hypertension and a higher proportion with LN. However, Hispanics had similar rates of hypertension to Whites but a higher proportion with LN. Additionally, stroke risks remained unchanged despite adjustment for warfarin use; however, given that warfarin prevalence was lower than reported rates of APS in SLE (45), warfarin may not be an accurate APS surrogate in this population. Results of laboratory testing for antiphospholipid antibodies and effective anticoagulation would be more informative, but are unavailable in claims. Thus, while it is impossible to determine the biologic basis of these differences from an administrative cohort such as MAX, possible explanations include residual effects of hypertension or racial differences in the nature and severity of SLE that are not fully captured by the covariates included in the adjusted models.

A main strength of this study is the use of more than a decade of data on over 43,000 SLE patients. Data concerning sociodemographic factors, SLE- and CVD-specific comorbidities were available in administrative claims. We fit several models to adjust for potential confounders and mediators that might contribute to increased CVD risk among SLE patients, while accounting for the competing risk of death. As diagnostic claims for CVD events may cause an underestimation of event rates (46), we used primary and secondary codes in our primary analysis. We also performed sensitivity analyses, which demonstrated even stronger associations for race/ethnicity and CVD risk after excluding participants with baseline CVD history. Furthermore, in an additional sensitivity analysis, we demonstrated that CVD risk among Hispanics reporting other races was similar to Hispanics without additional race data, confirming the robustness of our main results. Additionally, we applied the previously validated SLE risk adjustment index to the Medicaid population to capture SLE severity and SLE-related comorbidities. Finally, our estimates of SLE prevalence among Black women are similar to those published for Centers for Disease Control and

Prevention-funded epidemiology projects in Michigan and Georgia, providing external validation of our methods (8, 47, 48).

There are limitations inherent in utilizing Medicaid data for the study of SLE outcomes by race/ethnicity, including use of an administrative case definition to identify prevalent SLE, potential misclassification of race/ethnicity, in addition to the inability to examine risks among those over age 65 given dual enrollment in Medicare which was not part of this dataset (8). By requiring 12 months of continuous enrollment prior to index date, we reduced the study sample size somewhat. Although adequate to detect associations in the SLE cohort, the analysis may have been underpowered to detect significant associations in the LN subgroup. Body mass index, physical exercise, diet and lifestyle behaviors—which are related to CVD risk—are not adequately captured in administrative data. Moreover, the self-reported U.S. “Hispanic” and “Asian” populations are heterogeneous ethnic groups and genetically admixed populations, and the current data do not include country of origin, genetic ancestry information, or sociocultural experience.

Furthermore, although Medicaid patients may be more ill than privately insured patients in the U.S., we do not suspect that we disproportionately included severe SLE cases. Although we cannot directly measure SLE-related damage or activity in claims data, patients with LN, who typically have more aggressive SLE, comprised 21% of our SLE cohort. The SLE-specific risk adjustment index, a proxy for SLE severity, was low for SLE overall and by race/ethnicity. Use of a prevalent SLE cohort also limited the ability to investigate the effect of SLE duration or cumulative exposure to glucocorticoids. Additionally, we were not able to account for CVD events without hospitalization. Finally, as Medicaid provides health care coverage for low-income U.S. populations, our results may not be generalizable to higher socioeconomic status groups; however, they certainly pertain to a large proportion of the U.S. population. Based on our estimate of approximately 55,500 prevalent adult SLE cases in Medicaid in 2010 among an estimated 161,000 to 322,000 total adult SLE cases in the U.S. (49), Medicaid in 2010 covered approximately 17–35% of the U.S. SLE population. (The Medicaid program in 2010 included approximately 22% of the U.S. population (50)).

In conclusion, marked racial/ethnic variation in CVD event rates and risks was uncovered within a large cohort of racially/ethnically diverse, low-income SLE patients at high risk for adverse outcomes. Compared to White SLE patients, Blacks and Hispanics had an elevated risk of stroke whereas the risk of MI was reduced among Hispanics and Asians despite adjustment for sociodemographics, SLE- and CVD- specific risk factors, in addition to accounting for the competing risk of death. Future research on SLE among racial/ethnic groups should consider the role of diversity in genetic factors, biomarkers, lifestyle and physical activity, other thrombotic risk factors, and socioeconomics among various subpopulations and evaluate potential gene-environment interactions in relation to CVD risk. Improved understanding of race/ethnicity-specific rates and risks of CVD events could allow improved prevention strategies, including risk stratification and earlier diagnosis and management of CVD risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Baseline Characteristics among 65,788 Patients with Systemic Lupus Erythematosus (SLE) enrolled in Medicaid in the 29 most populated U.S. States, 2000–2010

	White	Black	Hispanic	Asian	American Indian/Alaska Native
Total number of patients (N, %)	25,204 (38.31)	27,470 (41.76)	10,562 (16.05)	1,827 (2.78)	725 (1.10)
Female (N, %)	23,401 (92.85)	25,643 (93.35)	9,846 (93.22)	1,663 (91.02)	668 (92.14)
Age, years (Mean, SD)	42.7 (11.98)	39.70 (11.79)	39.24 (12.30)	39.12 (12.72)	41.9 (11.83)
Residential Region (N, %)					
Midwest	6,238 (24.75)	6,060 (22.06)	701 (6.64)	142 (7.77)	89 (12.28)
Northeast	5,151 (20.44)	4.704 (17.12)	2,848 (26.96)	440 (24.08)	74 (10.21)
South	8,874 (35.21)	14,126 (51.42)	2,555 (24.19)	197 (10.78)	271 (37.38)
West	4,941 (19.60)	2,580 (9.39)	4,458 (42.21)	1,048 (57.36)	291 (40.14)
Comorbidities (N, %)*					
Previous Angina	1,203 (4.77)	1,122 (4.08)	398 (3.77)	47 (2.57)	15 (2.07)
Previous CABG	88 (0.35)	85 (0.31)	31 (0.29)	--	--
Previous CVA	1,525 (6.05)	1,668 (6.07)	414 (3.92)	63 (3.45)	37 (5.10)
Coronary atherosclerosis	2,056 (8.16)	1,824 (6.64)	391 (5.81)	80 (4.38)	40 (5.52)
Previous MI	716 (2.84)	742 (2.70)	157 (1.49)	34 (1.86)	25 (3.45)
Previous PCI	211 (0.84)	160 (0.58)	49 (0.46)	--	--
Diabetes mellitus	3,748 (14.87)	4,229 (15.39)	1,566 (14.83)	203 (11.11)	141 (19.45)
Heart failure	1,849 (7.34)	2,988 (10.88)	644 (6.10)	133 (7.28)	44 (6.07)
Hypertension	8,658 (34.35)	13,309 (48.45)	3,444 (32.61)	569 (31.14)	236 (32.55)
Hyperlipidemia	4,241 (16.83)	3,102 (11.29)	1,498 (14.18)	252 (13.79)	84 (11.59)
Obesity	1,618 (6.42)	1,742 (6.34)	556 (5.26)	25 (1.37)	53 (7.31)
Smoking	2,983 (11.84)	1,898 (6.91)	334 (3.16)	37 (2.03)	84 (11.59)
Lupus Nephritis (N, %)	3,263 (12.95)	7,309 (26.61)	2,406 (22.78)	582 (31.86)	136 (18.76)
SLE Risk Adjustment index¥ (Mean, SD)	1.55 (2.59)	1.81 (2.67)	1.44 (2.36)	1.46 (2.38)	1.69 (2.63)
Glucocorticoid Use (N, %)					
0 to 5 mg/day	21,686 (86.04)	21,553 (78.46)	8,289 (78.48)	1,308 (71.59)	623 (85.93)

	White	Black	Hispanic	Asian	American Indian/Alaska Native
>5 to 15 mg/day	2,793 (11.08)	4,517 (16.44)	1,762 (16.68)	411 (22.50)	85 (11.72)
>15 mg/day	725 (2.88)	1,400 (5.10)	511 (4.84)	108 (5.91)	17 (2.34)
Warfarin Use, Ever (N, %)	1,915 (7.60)	1,792 (6.52)	702 (6.65)	112 (6.13)	43 (5.93)

Baseline: 12 months prior to index date; CABG: *coronary artery bypass graft,* CVA: cerebrovascular accident, MI: myocardial infarction, PCI: percutaneous coronary intervention.

*Comorbidities collected at any time up to and including index date. Cell sizes < 11 individuals suppressed in accordance with Federal reporting requirements;

¥SLE specific index ranges from 0–46 (Reference: Ward MM, *J Rheumatol.* 2000; 27(6):1408–13)

Table 2.

Annual Rates of Cardiovascular Disease (MI and Stroke), among SLE patients enrolled in Medicaid within the 29 most populated U.S. states, 2000–2010, Overall and by Race/Ethnicity

	Number of Patients	Age at Event, Mean (SD)	Number of Events	Person-years, mean (SD)	IR* (95% CI)	IRR** (95%CI)
Cardiovascular Disease (MI or stroke)						
All patients	65,788	48.00 (11.41)	2,259	3.69 (3.03)	9.31 (8.93–9.70)	-
White	25,204	50.32 (10.93)	814	3.62 (3.00)	8.91 (8.32–9.54)	1.0 (ref)
Black	27,470	46.71 (11.19)	1,070	3.68 (3.02)	10.57 (9.96–11.22)	**1.18 (1.13–1.23)**
Hispanic	10,562	46.73 (12.15)	304	3.85 (3.11)	7.48 (6.68–8.37)	**0.84 (0.79–0.90)**
Asian	1,827	43.67 (12.41)	46	3.80 (3.07)	6.63 (4.97–8.85)	**0.75 (0.65–0.86)**
American Indian/Alaska Native	725	50.60 (12.08)	25	3.66 (3.01)	9.42 (6.37–13.94)	1.06 (0.88–1.28)

* IR = incidence rate, annual CVD event rate per 1,000 person years, IRR: incidence rate ratio, SD: Standard deviation; Cell sizes of < 11 individuals =suppressed in accordance with Federal reporting requirements

Table 3.

Multivariable-Adjusted Hazard Ratios* for Cardiovascular Disease (and components, MI and Stroke) among SLE patients enrolled in Medicaid within the 29 most populated U.S. states, 2000–2010, Overall and by Race/Ethnicity

Race/ Ethnicity	Model A (HRsd [95%CI])	Model B (HRsd [95%CI])	Model C (HRsd [95%CI])
Cardiovascular Disease (MI or Stroke)			
White	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Black	**1.31 (1.19–1.43)**	**1.19 (1.08–1.31)**	**1.14 (1.03–1.26)**
Hispanic	0.96 (0.84–1.10)	0.93 (0.81–1.06)	0.93 (0.81–1.07)
Asian	0.84 (0.62–1.13)	0.78 (0.58–1.05)	0.78 (0.58–1.06)
American Indian/Alaska Native	1.07 (0.72–1.59)	1.03 (0.69–1.54)	1.04 (0.70–1.56)
Myocardial Infarction			
White	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Black	1.15 (1.00–1.32)	0.99 (0.85–1.15)	0.97 (0.83–1.12)
Hispanic	**0.65 (0.51–0.81)**	**0.60 (0.48–0.76)**	**0.61 (0.48–0.77)**
Asian	0.61 (0.37–1.03)	**0.57 (0.34–0.95)**	**0.57 (0.34–0.96)**
American Indian/Alaska Native	0.95 (0.51–1.78)	0.91 (0.48–1.71)	0.92 (0.49–1.73)
Stroke			
White	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Black	**1.48 (1.31–1.66)**	**1.37 (1.21–1.56)**	**1.31 (1.15–1.49)**
Hispanic	**1.25 (1.07–1.46)**	**1.22 (1.04–1.44)**	**1.22 (1.03–1.44)**
Asian	0.99 (0.69–1.42)	0.93 (0.64–1.34)	0.93 (0.64–1.34)
American Indian/Alaska Native	1.12 (0.67–1.88)	1.08 (0.64–1.82)	1.11 (0.66–1.86)

* These are sub-distribution hazard ratios based on competing risk analysis taking competing risk of death into account

Model A: Age (continuous), sex

Model B: Model A + region of residence, year and area-level SES + SLE-specific index, glucocorticoid use (mean dose, grams/day) + lupus nephritis

Model C: Model B + comorbidities at study index date including history of hypertension, hyperlipidemia, diabetes mellitus, smoking and obesity

Bold= p<0.05