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Does SLE widen or narrow race/ethnic disparities in the risk of five comorbid conditions? Evidence from a community-based outpatient care system

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Abstract

Objective.—The heterogeneous spectrum of systemic lupus erythematosus (SLE) often presents with secondary complications such as cardiovascular disease (CVD), infections and neoplasms. Our study assessed whether the presence of SLE independently increases or reduces the disparities, accounting for the already higher risk of these outcomes among racial/ethnic minority groups without SLE.

Methods.—We defined a cohort using electronic health records data (2005–2016) from a mixed-payer community-based outpatient setting in California serving patients of diverse racial/ethnic backgrounds. The eligible population included adult patients with SLE and matched non-SLE patients (≥18 years old). SLE was the primary exposure. The following outcomes were identified: pneumonia, other infections, CVD, and neoplasms. For each racial/ethnic group, we calculated the proportion of incident comorbidities by SLE exposure, followed by logistic regression for each outcome with SLE as the exposure. We evaluated interaction on the additive and multiplicative scales by calculating the relative excess risk due to interaction and estimating the cross-product term in each model.

Results.—We identified 1,036 SLE cases and 8,875 controls. The incidence for all outcomes was higher among the SLE exposed. We found little difference in the odds of the outcomes associated with SLE across racial/ethnic groups, even after multivariable adjustment. This finding was consistent on the multiplicative and additive scales.

Conclusion.—We demonstrated that SLE status does not independently confer substantial interaction or heterogeneity by race/ethnicity toward the risk of pneumonia, other infections, cardiovascular disease, or neoplasms. Further studies in larger datasets are necessary to validate this novel finding.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease whose clinical management is often complex and multifaceted. In the rheumatology literature, there have been some calls for SLE researchers and clinicians to shift their efforts from addressing the control of the primary disease to becoming more mindful of managing the constellation of secondary complications or outcomes in SLE such as cardiovascular disease[1–3], cerebrovascular manifestation[4] and infections[5]. In the United States, racial minorities (i.e., blacks, Hispanics, Native Americans, and Asians) experience higher rates of these outcomes in the general population compared with whites[6] - health disparities that are also particularly pathognomonic of SLE. In addition to a much higher incidence and prevalence of SLE among female patients[7,8], consistent across multiple studies is the finding that racial and ethnic minorities experience certain clinical phenotypes[9–11]. For example, a recent prevalence estimate indicates that women and non-whites comprise approximately 90% and 70% of prevalent SLE in the United States, respectively[12].

In general, racial and ethnic minorities with SLE also have more severe disease activity and worse outcomes[13–15]. Within the past decade, important insights have emerged regarding the differential distribution of key comorbidities or outcomes by race/ethnicity among patients with SLE. Medicaid data demonstrated that blacks and Native Americans with SLE had 13–37% increased risk of serious infections compared to whites with SLE[16]. Interestingly, a Hispanic and Asian paradox has been described within the Medicaid population, wherein these patients with SLE were found to have decreased mortality[17] and risk of myocardial infarction[18] compared to their white counterparts. Less well-explored is the contribution of race/ethnicity to the risk of malignancy in SLE. While one study identified non-Hispanic whites as having the highest risk of neoplasms[19], a subsequent larger study of patients in California found higher rates among Hispanic patients with SLE[20].

Prior studies have mainly focused on comparing secondary complications or outcomes by race/ethnicity among patients with SLE. However, we know that some of these same outcomes occur with increased frequency among minority populations without SLE compared to their white counterparts. A key question with relevance to the clinician emerges: does the presence of SLE independently increase or reduce the disparities in the frequency of these co-morbid conditions among racial/ethnic minorities compared to that already seen within the non-SLE population? The findings of this inquiry could improve the understanding of the heterogeneous spectrum of SLE by enabling better phenotyping of patients at risk of key outcomes or complications. In addition, understanding whether SLE contributes substantially to existing white-racial minority gap in outcomes can guide efforts aimed at minimizing racial disparities in this realm. With this in mind, we assessed the independent contribution of SLE on numerous outcomes separately across different racial/ethnic groups in a large, well-defined racially diverse cohort of adults in Northern California. We explore the interaction between race/ethnicity and SLE on the risk of five outcomes and specifically assess whether the magnitude of health disparities in these outcomes is greater or lesser than would be expected for patients with SLE compared to controls. This study was funded as a supplement to the Cardiovascular Disease among

Asians and Pacific Islanders (CASPER) study (funded by grant HL 126172 from NHLBI to Drs. Waitzfelder, Palaniappan, and Fortmann)[21].

Methods

Setting and study population

Our study population was derived from a mixed-payer community-based outpatient care setting which serves approximately one million patients each year in Northern California. We defined a cohort of patients who were diagnosed with SLE and non-SLE-comparators. The eligible population included adult patients with SLE and demographically matched non-SLE patients receiving care (i.e., those with ≥2 recorded visits) in the same setting between 2005 and 2016. Patients without SLE (referred to as controls throughout) were frequency-matched 10:1 to SLE subjects by calendar year of diagnosis (for cases) or first service date (for controls), age, and sex. The earliest date where an SLE diagnosis is found in the electronic health records is the index date for each SLE case (aged ≥18 years on index date and did not die before 2005). The earliest date on or after 1/1/2005 when a subject meets all eligibility criteria (i.e., aged ≥18, in care) is the index date for controls. We used calendar year of index date (index year), sex, and birth year as the predictors to calculate a propensity score and matched based on the value of the propensity score [22,23]. In the first round of 1:10 matching, 8 matched controls died before 7 cases' index date. Another two rounds of matching were conducted to find 8 replacements for 8 controls. We initially identified 1,290 SLE cases who were matched by sex, age, and index year to 12,900 controls. After excluding patients without race/ethnicity profiles, there were 1,036 SLE cases and 8,875 controls. The study was approved by the Sutter Health Institutional Review Board under the project ID number 976421-2.

Systemic lupus erythematosus

SLE was the primary exposure and was defined as having ≥2 clinic visits from January 1, 2005 onwards with an ICD9 code of 710.0 or an ICD10 code of M32.1, M32.8, M32.9 [16]. We were underpowered to restrict to incident SLE, therefore have included prevalent and incident SLE.

Outcomes

We identified five separate comorbidities/outcomes: pneumonia, other infections, CVD, and neoplasms (all and malignancies, separately) using ICD codes for inpatient and outpatient visits, (Supplementary Table 1). We included the records of patients with outcomes that were diagnosed after SLE diagnosis (for SLE cases) and after the index date (for controls). For each analysis, individuals with a history of the specific outcome in the medical record according to ICD codes and the problems list at baseline (SLE diagnosis or index date) were identified and then subsequently were excluded from the specific analysis to remove potential prevalent cases and focus on incident outcomes. Only the first event after SLE diagnosis or the index date was counted. Since there are multiple outcomes, an individual patient may have been counted under more than one outcome (e.g., CVD and infection). For each of the outcomes we noted the first time that they have that outcome –thus, the underlying population for each outcome was slightly different. For example, for CVD

incidence, we counted instances among those who have never had a history of CVD (i.e., those at risk) in the codes or problem list before the start of follow-up, but, these individuals could have had infections or other outcomes. Participants were followed until death, loss to follow-up (primarily leaving the health care system), or 31 December 2016.

Additional covariates

Additional covariates extracted from the electronic health records included: self-reported biological sex (male or female), race/ethnicity and baseline values of age, body mass index (BMI) in kg/m^2(categorized as: underweight ≤18.5, 18.5<normal weight≤25, 25<overweight≤30, or obese>30), smoking status (categorized as: current, former, or never), and diagnoses of diabetes, hypertension and dyslipidemia. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Hispanic, Asian (including Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese and other Asian). Potential confounders were different for each exposure-outcome model.

Statistical analysis

We compared demographic and clinical characteristics between SLE cases and controls using frequencies and proportions for categorical variables, and medians with interquartile ranges for continuous variables. These characteristics were compared using Pearson Chi-square test for categorical variables and Student's t-test for continuous variables. We found that overall approximately 22% of BMI and smoking data were missing. This was relatively similar between SLE cases and controls for smoking but different for BMI (11% SLE and 23% non-SLE). We used multiple imputation to estimate missing values of smoking and BMI[24]. We calculated the proportion of newly diagnosed (incident) pneumonia, infections, CVD and neoplasms among SLE cases and controls by race/ethnicity. Separate logistic regression models estimated odds ratios (OR) and 95% confidence intervals (CI) for the association between SLE and outcome adjusting for potential confounding by sex, age, smoking status, BMI, and history of diabetes by racial/ethnic group.

Evaluation of additive and multiplicative interactions

We evaluated interaction on additive and multiplicative scales using whites as the reference group because the study sample was not powered to examine multiple comparisons among race/ethnicity groups. We extracted three datasets comprising Asians and whites only (dataset 1), blacks and whites only (dataset 2), and Hispanics and whites only (dataset 3). First, we built five logistic regression models with SLE status (case versus control) as the exposure of interest for each outcome (pneumonia, other infections, CVD, neoplasms, and malignant neoplasms) for each dataset, i.e., we built a model for every outcome for each of the datasets. Thus, there were fifteen models in total (see table 4). In each model, we included potential confounders, as well as an interaction term for race/ethnicity and SLE status. For example, the regression equation modeling malignant neoplasms as the outcome comparing Asians to whites (using dataset 1) would be: $Y(\text{Malignant neoplasms}) = \beta_0 + \beta_1(\text{SLE}) + \beta_2(\text{Asian}) + \beta_3(\text{Gender}) + \beta_4(\text{Age}) + \beta_5(\text{Smoking}) + \beta_6(\text{BMI}) + \beta_7(\text{SLE} * \text{Asian})$. In another example, the regression equation modeling CVD as the outcome comparing blacks to whites (using dataset 2) would be $Y(\text{CVD}) = \beta_0 + \beta_1(\text{SLE}) +$

β_2(Black) + β_3(Gender) + β_4(Age) + β_5(Smoking) + β_6(BMI) + β_7(Diabetes) + β_8 (SLE ∗ Black).

Second, to detect additive interaction, we calculated the Relative Excess Risk due to Interaction (RERI), a measure that assesses whether the risk difference for each outcome between whites and each race/ethnic minority was different from zero[25,26]. We used the following equation: RERI ≈ OR11 - OR10 - OR01 + 1 and estimated the corresponding 95% CIs. For the example of malignant neoplasms in Asians versus whites, the RERI was calculated as: RERI = $\exp^{\beta 7(\text{SLE} * \text{Asian})}$-$\exp^{\beta 1(\text{SLE})}$ — $\exp^{\beta 2(\text{Asian})}$ +1. The RERI for the example of CVD in blacks versus whites was calculated as RERI = $\exp^{\beta 8(\text{SLE} * \text{Black})}$-$\exp^{\beta 1(\text{SLE})}$ — $\exp^{\beta 2(\text{Black})}$ +1. Third, multiplicative interaction was calculated using the cross-product term in each model. We estimated whether the expected OR was greater (for antagonistic interaction) or lesser (for synergistic interaction) than the observed OR for each outcome between whites and each race/ethnic minority group[25,26].

Results

Males comprised 8% of the study population and the median age at baseline was 44 years (Table 1). Nearly half (48%) of SLE cases were non-Hispanic white, 32% were Asian, 16% were Hispanic and 5% were non-Hispanic black. Controls in this study were less likely to be racial minorities compared to SLE cases. Among controls, 58% were white, 11% were Hispanic, 29% were Asian, and 2% were black (Table 1). A majority of the study population reported never smoking. Approximately 43% of SLE cases had normal BMI, while 19% were obese. Controls were less likely to have normal BMI (38%) compared to cases. Diabetes, hypertension, and dyslipidemia were more common in those with SLE, along with history of the outcomes of interest [pneumonia (11% vs 4%), other infections (18% vs 7%), CVD (35% vs 15%), and neoplasms (13% vs 8%)].

The incidence for all outcomes was higher among patients with SLE compared to controls among those at risk (Table 2). This trend was consistent within race/ethnic groups. For pneumonia among patients with SLE, Hispanics had the highest incidence (41%) while Asians, whites, and blacks had the lowest incidence (33%−34%). Nearly half of all patients with SLE had newly diagnosed other infections, compared with about 25%−30% of controls. For CVD among patients with SLE, the highest incidence was among whites (51%) and blacks (50%), while Asians (42%) had the lowest incidence. For all neoplasms among patients with SLE, whites had the highest incidence (43%), while Asians had the lowest incidence (23%). These trends were also consistent for malignant neoplasms.

Generally, we found little difference in the magnitude of the association of the outcomes between SLE cases and controls across racial/ethnic groups, which was consistent after adjusting for possible confounders (Table 3). SLE cases had approximately two times the odds of pneumonia and other infectious diseases compared to the non-SLE group. For CVD, black patients with SLE had almost 4 times the odds compared to controls while white SLE cases had 2.5 times the odds compared to controls. We found that SLE cases had 1.3 times the odds of all neoplasms compared to controls regardless of race/ethnicity, however, these estimates were only significant for whites but not for racial minorities. We did not

find significantly increased odds for malignant neoplasms. There appeared to be little to no evidence of interaction on either the additive or multiplicative scales (Table 4) in our multivariable adjusted assessments. Almost all of the 95% CI around the RERIs crossed zero indicating a lack of statistically significant additive interaction (with the exception of pneumonia and other infections in Asians and Hispanics). We also found no evidence of interaction on the multiplicative scale (Table 4) after controlling for confounders as the 95% CI around the cross-product ORs overlapped one.

Discussion

Overall, we found that patients with SLE had more CVD, pneumonia, infections, and neoplasms than the control population across all racial/ethnic groups in our study. There were also some differences in incidence of these outcomes across racial/ethnic groups within patients with SLE. However, when addressing our central clinical question of the independent association between SLE and these outcomes by racial/ethnic group, we found there was almost no evidence for substantial interaction or heterogeneity by race/ethnicity. This finding was generally consistent across both multiplicative and additive scales.

The reasoning behind the lack of an independent disease-mediated effect on the risk of outcomes by race/ethnicity in SLE is unknown but is an intriguing finding that warrants further study. We could not identify similar studies- limiting our ability to contextualize our findings in the literature. There are two ways to answer the questions that arise in these analyses. One way would be to explore whether the health disparities found in the outcomes in racial/ethnic minorities with SLE may be due to the disease uniformly activating pathways that already predispose racial minorities to outcomes. Another way would be to explore whether the heterogeneity in these outcomes has nothing to do with SLE pathogenesis but rather may be a consequence of underlying pathways present in the background risk within the general population. The findings of these inquiries would help anticipate the degree to which the white-racial minority gap may widen or narrow in the future because of shifting trends in SLE. Such knowledge may be useful in planning and targeting systems to deliver care to a growing population of patients with SLE.

There is an abundance of studies in the SLE literature comparing race/ethnic groups, with whites as the reference categories. Oftentimes, the regression models in these studies treat race/ethnicity as a confounder of the associations between the exposure(s) and outcome(s) of interest. For example, although the Medicaid studies found significant differences among the patients with SLE by race, they were not necessarily comparing patients with SLE to the general population or examining the effect of SLE on those outcomes for each racial group separately[8,16,18]. The questions that arise in these settings are variations of the following: assuming that we have a population of patients with SLE, which racial/ethnic groups do worse? Our current work instead dissects this from a different angle and asks: given that we know that some of these outcomes are more common in certain racial/ethnic groups, are the racial differences still apparent when one factors out the increased incidence in the non-SLE minority populations? Thus, we suggest that future studies of racial disparities in SLE outcomes need to include general population comparators so that inferences can be made about the extent that SLE widens the gaps in existing inequalities.

We found higher prevalence of more “upstream” risk factors such as diabetes, hypertension, and dyslipidemia among patients with SLE compared to controls and these conditions are often precursors to CVD and neoplasms. When we adjusted for these risk factors in the regression models, the significant associations between SLE and the outcomes did not change. It is not clear how these traditional risk factors and those specific to SLE (e.g., autoantibodies, interferon signatures) impact CVD outcomes in racial minorities with SLE. In the general population, CVD risk algorithms such as the Framingham Risk Score and the American College of Cardiology/American Heart Association have been shown to validate well in racial minorities[27,28], however, these algorithms may underestimate CVD risk in patients with SLE[29]. The extent to which risk algorithms (and their constituents) can accurately predict CVD risk in individual race/ethnic groups with SLE is currently unknown and warrants research resources. The extent to which diabetes influences CVD and cancer among patients with SLE and how this association is patterned along race/ethnic groups is not well understood in rheumatology. In addition, one question we ask clinicians to ponder is whether the severe clinical phenotypes observed in racial minorities with SLE have correlates within the general population, and if the severe manifestations of these outcomes are due to the underlying predisposition of race/ethnic minorities for these conditions, and not SLE. There is increasing evidence that these risk factors are patterned differently for race/ethnic groups; for example, a 10 mm Hg higher systolic blood pressure level is associated with 24% increase in stroke risk for blacks and only an 8% increase in stroke risk for whites.[30].

The increased incidence of key medical outcomes among patients with SLE in our study – across all racial/ethnic groups – reinforces the health challenges faced by these patients beyond their autoimmune condition. It also presents an opportunity for healthcare providers who care for these patients to enhance current efforts at disease prevention within this patient population. This is certainly true for rheumatologists, who are tasked with the chronic management of these patients’ underlying SLE. At the same time, primary care physicians are often the first point of contact prior to referral to a rheumatologist, and they remain essential to patients’ long-term health maintenance. Close partnership between the rheumatologist and primary care provider is thus critical, ensuring that appropriate screening and treatment of these outcomes occur in a timely manner that conforms with accepted guidelines and recommendations. Whether an updated screening and management approach toward these outcomes among patients with SLE is needed, in light of the increased risk within this patient population, is worthy of further discussion.

To our knowledge, this is one of a few studies to investigate heterogeneity by race/ethnicity in the association between SLE status and outcomes in a diverse U.S. sample. Our study has a few limitations. We were unable to assess severity of these outcomes. Additional research is needed to understand whether there is interaction between race/ethnicity and SLE status on mortality and comorbidity progression over time, and to understand the underlying biological mechanisms. Our findings may have limited generalizability due to the study sample being comprised of individuals who are insured, likely skewing the population by socioeconomic status. In contrast, several recent epidemiologic studies assessing the impact of race/ethnicity on cardiovascular and infectious outcomes in SLE were drawn from the Medicaid population. Therefore, it is difficult to compare our findings with respect to these

outcomes of interest in particular. Due to the study location in California, our sample may not represent the general population of patients with SLE in the U.S. as blacks comprise 43% of the national prevalence estimates, compared to 6% in our study [12]. However, our study was enriched with Hispanic and Asian patients (32% and 16%, respectively) while these groups comprise 16% and 13% of the national prevalent estimates [12]. We also cannot exclude the possibility that differences in the risk of outcomes by race/ethnicity exist at a population-level and had small within-group sample sizes for some race/ethnic groups. We were underpowered to examine differences among more granular groupings of race/ethnicity. Future analyses include Pacific Islanders and parse out Asian subgroups. We were also unable to account for person time, disease duration, clinical phenotypes, or treatment consideration due to the limited ability to ascertain when clinical manifestations first showed in the electronic health records. Thus, there may be some misclassification of prevalent outcomes being labeled as incident and we cannot predict whether this is differential or nondifferential.

The possibility of confounding by race/ethnicity is eliminated in the study design because we are interested in the heterogeneity and therefore are looking by groups. Stratified analyses such as these also implicitly account for confounding because they reduce the variability of that factor within strata.[32] We acknowledge that there may be some measurement error around the reporting of race/ethnicity. Studies of heterogeneity by race/ethnicity are often misleading as race categories are social constructs that often do not reflect the genomic diversity in population subgroups. Thus, we cannot rule out that there is misclassification/measurement error of the race/ethnicity effect modifier and that this may impact the validity of our findings. The race/ethnicity categories reflected in the EHR are based on self-report, although it is possible that on rare occasions, some are simply entered by clinic intake staff based on appearance. However, it is our understanding that this practice is relatively uncommon.

In summary, we demonstrated that while SLE increases the risk of secondary complications, it does not independently confer substantial heterogeneity by race/ethnicity toward the risk of pneumonia, other infections, cardiovascular disease, or neoplasms. Further studies in larger datasets are necessary to validate this novel finding. At the same time, our work confirms the higher risk of these important outcomes among patients with SLE overall – similar to prior studies – and also within each race/ethnicity category compared to controls. Future research should also include exploration of mental health (e.g., depression, schizophrenia, etc), kidney disease, and pregnancy/birth outcomes as these conditions are associated with SLE and racial/ethnic minorities are at increased risk for these diseases. Our study brings further awareness toward the increased burden of medical outcomes among patients with SLE, and is a call to arms to rheumatologists and primary care providers alike to enhance preventative health efforts to reduce the incidence and severity of these outcomes within this at-risk patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1.

Baseline characteristics of study participants by SLE status in the PAMF population, 2005–2016

	SLE		Controls		All	
	N	Median or %	N	Median or %	N	Median or %
Sex						
Females	954	92.1	8203	92.4	9157	92.4
Males	82	7.9	672	7.6	754	7.6
Median age at baseline	1036	44	8875	44	9911	44
Race/ethnicity						
Non-Hispanic White	492	47.5	5181	58.4	5673	57.2
Non-Hispanic Black	55	5.3	200	2.3	255	2.6
Hispanic	162	15.6	931	10.5	1093	11
Asian	327	31.6	2563	28.9	2890	29.2
Smoking status						
Non-smoker	612	59.1	5574	62.8	6186	62.4
Former smoker	120	11.6	972	11	1092	11
Current smoker	37	3.6	436	4.9	473	4.8
Missing	267	25.8	1893	21.3	2160	21.8
Baseline body mass index *#						
Underweight	46	4.4	172	1.9	218	2.2
Normal weight	447	43.1	3367	37.9	3814	38.5
Overweight	227	21.9	1899	21.4	2126	21.5
Obese	200	19.3	1394	15.7	1594	16.1
Missing	116	11.2	2043	23	2159	21.8
Prevalent diabetes *	76	7.3	455	5.1	531	5.4
Prevalent hypertension *	424	40.9	2214	24.9	2638	26.6
Prevalent dyslipidemia *	313	30.2	2325	26.2	2638	26.6
Prevalent pneumonia *	112	10.8	341	3.8	453	4.6
Prevalent infections *	185	17.9	652	7.3	837	8.4
Prevalent cardiovascular diseases *	357	34.5	1365	15.4	1722	17.4
Prevalent neoplasms *	133	12.8	714	8	847	8.5
Prevalent malignant neoplasms *^	42	4.1	235	2.6	277	2.8

* $p<0.05$

Body mass index was categorized (kg/m^2) as: underweight ≤18.5, 18.5<normal weight≤25, 25<overweight≤30, or obese>30

^ Malignant neoplasms are a subset of all neoplasms

Table 2.

The incidence of major outcomes comparing SLE with non-SLE controls, 2005–2016*

	Pneumonia (N, %)		Other infections (N, %)		CVD (N, %)		All Neoplasms (N, %)		Malignant neoplasms^ (N, %)	
	N	%	N	%	N	%	N	%	N	%
All										
SLE	924	34.4	851	48.1	679	47.6	903	33.1	994	7.3
Non-SLE	8534	21.5	8223	30.4	7510	25.9	8161	27.6	8640	7.1
Asian										
SLE	291	33.0	266	44.0	229	42.4	289	23.2	317	3.2
Non-SLE	2449	21.6	2392	26.6	2283	19.0	2420	18.6	2532	2.7
NH Black										
SLE	49	32.7	45	46.7	30	50.0	53	28.3	55	5.5
Non-SLE	192	20.8	179	27.9	148	31.1	183	23.5	196	3.6
Hispanic										
SLE	135	40.7	137	49.6	109	47.7	146	27.4	159	5.0
Non-SLE	900	24.0	862	33.3	790	22.0	874	22.7	914	3.8
NH White										
SLE	449	33.6	403	50.4	311	51.1	415	42.7	463	11.2
Non-SLE	4993	21.0	4790	31.8	4289	30.2	4684	33.4	4998	10.1

NH Black=Non-Hispanic Black; NH White=Non-Hispanic White

*The denominators are not the same across outcomes because the analyses was restricted to those without a history of these outcomes

^Malignant neoplasms are a subset of all neoplasms

Table 3.

Odds Ratios of having outcomes comparing SLE cases to controls stratified by race/ethnicity

	All	Asian	NH Black	Hispanic	NH White
Pneumonia					
OR (95% CI)	1.92 (1.66, 2.22)	1.79 (1.37, 2.32)	1.84 (0.92, 3.68)	2.18 (1.50, 3.17)	1.91 (1.55, 2.35)
aOR (95% CI)	1.92 (1.66, 2.22)	1.79 (1.37, 2.32)	2.03 (1.00, 4.14)	2.20 (1.51, 3.21)	1.89 (1.54, 2.33)
Other infections					
OR (95% CI)	2.12 (1.84, 2.44)	2.16 (1.67, 2.80)	2.26 (1.16, 4.41)	1.97 (1.37, 2.84)	2.17 (1.77, 2.67)
aOR (95% CI)	2.12 (1.84, 2.44)	2.14 (1.65, 2.78)	2.50 (1.25, 5.00)	1.97 (1.37, 2.83)	2.16 (1.76, 2.65)
CVD					
OR (95% CI)	2.59 (2.21, 3.04)	3.14 (2.37, 4.16)	2.22 (1.00, 4.91)	3.23 (2.14, 4.87)	2.42 (1.92, 3.05)
aOR (95% CI)	2.98 (2.52, 3.53)	3.64 (2.70, 4.90)	3.90 (1.57, 9.63)	3.61 (2.30, 5.67)	2.53 (1.98, 3.23)
All Neoplasms					
OR (95% CI)	1.30 (1.12, 1.50)	1.33 (0.99, 1.77)	1.29 (0.65, 2.56)	1.29 (0.87, 1.92)	1.49 (1.21, 1.82)
aOR (95% CI)	1.31 (1.13, 1.53)	1.30 (0.97, 1.75)	1.44 (0.71, 2.93)	1.29 (0.86, 1.93)	1.47 (1.19, 1.81)
Malignant neoplasms					
OR (95% CI)	1.03 (0.80, 1.34)	1.18 (0.60, 2.32)	1.56 (0.39, 6.23)	1.33 (0.61, 2.92)	1.12 (0.83, 1.52)
aOR (95% CI)	1.05 (0.81, 1.36)	1.20 (0.61, 2.38)	1.39 (0.30, 6.50)	1.37 (0.61, 3.06)	1.06 (0.77, 1.45)

NH Black=Non-Hispanic Black; NH White=Non-Hispanic White

* non-SLE groups are reference categories

Covariates in each multivariate model

Outcome: Pneumonia

Covariates: Gender, SLE status, Baseline age, Smoking status

Outcome: Other infectious and parasitic diseases

Covariates: Gender, SLE status, Baseline age, Smoking status

Outcome: Cardiovascular disease

Covariates: Gender, SLE status, Baseline age, Smoking status, BMI category, Diabetes

Outcome: Neoplasms

Covariates: Gender, SLE status, Baseline age, Smoking status, BMI category

Outcome: Malignant Neoplasms

Covariates: Gender, SLE status, Baseline age, Smoking status, BMI category

Table 4.

Interaction between SLE status and race/ethnicity on the risk of outcomes

	NH White compared with…		
	Asian[1]	**NH Black**[2]	**Hispanic**[3]
Pneumonia			
Relative excess risk due to interaction (95% CI)	−1.02 (−1.71, −0.33) *	−0.87 (−2.00, 0.25)	−0.95 (−1.81, −0.09) *
Multiplicative interaction parameter (95% CI)	0.94 (0.67, 1.31)	1.02 (0.49, 2.10)	1.16 (0.76, 1.79)
Infections			
Relative excess risk due to interaction (95% CI)	−1.00 (−1.72, −0.27) *	−1.07 (−2.21, 0.08)	−1.35 (−2.12, −0.58) *
Multiplicative interaction parameter (95% CI)	0.99 (0.71, 1.38)	1.07 (0.53, 2.15)	0.92 (0.60, 1.39)
Cardiovascular diseases			
Relative excess risk due to interaction (95% CI)	−0.85 (−1.93, 0.23)	−1.41 (−2.97, 0.15)	−1.02 (−2.56, 0.53)
Multiplicative interaction parameter (95% CI)	1.42 (0.97, 2.08)	1.23 (0.52, 2.90)	1.35 (0.82, 2.23)
Neoplasms			
Relative excess risk due to interaction (95% CI)	−0.07 (−0.65, 0.51)	−0.22 (−1.14, 0.70)	−0.23 (−0.88, 0.41)
Multiplicative interaction parameter (95% CI)	0.91 (0.64, 1.30)	0.90 (0.44, 1.86)	0.89 (0.57, 1.40)
Malignant neoplasms			
Relative excess risk due to interaction (95% CI)	0.78 (−0.33, 1.88)	1.24 (−1.44, 3.92)	0.83 (−0.55, 2.21)
Multiplicative interaction parameter (95% CI)	1.18 (0.56, 2.49)	1.66 (0.40, 6.99)	1.34 (0.57, 3.17)

NH Black=Non-Hispanic Black; NH White=Non-Hispanic White

*RERI appear to be statistically significant

**To calculate interaction on the additive and multiplicative scales, we extracted three datasets comprising Asians and whites only (dataset 1), blacks and whites only (dataset 2), and Hispanics and whites only (dataset 3).

[1]Dataset 1;

[2]Dataset 2;

[3]Dataset 3. In each model, we included potential confounders, as well as an interaction term for race/ethnicity and SLE status. For example, the regression equation modeling malignant neoplasms as the outcome comparing Asians to whites (using dataset 1) would be: $Y(\text{Malignant neoplasm}) = \beta_0 + \beta_1(\text{SLE}) + \beta_2(\text{Asian}) + \beta_3(\text{Gender}) + \beta_4(\text{Age}) + \beta_5(\text{Smoking}) + \beta_6(\text{BMI}) + \beta_7(\text{SLE} * \text{Asian})$. In another example, the regression equation modeling CVD as the outcome comparing blacks to whites (using dataset 2) would be $Y(\text{CVD}) = \beta_0 + \beta_1(\text{SLE}) + \beta_2(\text{Black}) + \beta_3(\text{Gender}) + \beta_4(\text{Age}) + \beta_5(\text{Smoking}) + \beta_6(\text{BMI}) + \beta_7(\text{Diabetes}) + \beta_8(\text{SLE} * \text{Black})$.