Unraveling Race, Socioeconomic Factors, and Geographical Context in the Heterogeneity of Lupus Mortality in the United States

Titilola Falasinnu,1 Yashaar Chaichian,1 Latha Palaniappan,2 and Julia F. Simard1

Objective. Systemic lupus erythematosus (SLE) is a chronic autoimmune disease disproportionately affecting women and racial/ethnic minorities. We examined SLE-related mortality over time to assess whether the impact of race is attenuated when social economic status (SES) and geographic context are also considered.

Methods. This study examined whether social environment attenuates racial disparities in SLE-related mortality using race-geographical combinations of the US population known as the “Eight Americas.” This framework jointly characterizes race, SES, and geographical location in relation to health disparities in the United States. Using National Vital Statistics and US Census data, we estimated mortality parameters for each of the Eight Americas.

Results. We identified 24,773 SLE deaths (2003-2014). Average annual mortality rates were highest among blacks in three race-geographical contexts: average-income blacks, southern low-income blacks, and high-risk urban blacks (14 to 15 deaths per million population) and lowest among nonblacks living in average-income settings (3 to 4 deaths per million population). Age at death was lowest (~47.5 years) for blacks and Asians and highest among low-income rural whites (~64.8 years).

Conclusion. Blacks sharing the same social and geographical contexts as whites were disproportionately more likely to die young. Although blacks inhabited three vastly different contexts, SLE-related mortality parameters did not vary among socially advantaged and disadvantaged blacks. These findings suggest that race may transcend SES and geographical parameters as a key determinant of SLE-related mortality.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that is a source of significantly decreased life expectancy. Hallmarks of the disease course are multisystemic manifestations, including dermatologic, musculoskeletal, and internal organ involvement as well as premature cardiovascular damage (1). Women of childbearing age are disproportionately impacted as well as racial/ethnic minorities (eg, blacks, Asian and Pacific Islanders, Native Americans, and Hispanics) (1,2). For example, the prevalence of SLE per 100,000 Medicaid-enrolled adults was 111.6 in whites, 223.4 in blacks, 126.6 in Hispanics, and 174.1 in Asians (2). This race/ethnic disparity was most evident in lupus nephritis, a severe manifestation of SLE affecting the kidneys—Asian and African American females had the highest prevalence (80.7 and 75.6 per 100,000 population, respectively) compared with white females (20.1 per 100,000 population). Another study using the Centers for Disease Control and Prevention–funded epidemiologic studies of the incidence and prevalence of SLE in different geographic regions estimated that blacks, Asians, and Hispanics comprise nearly 70% of prevalent SLE cases in the United States (3). The etiological rationale for these disparities in SLE burden have been attributed to genetic, hormonal, and environmental factors (4).

In the United States, although there are ongoing debates in the literature about the pathophysiological factors that drive SLE risk and disease severity (4), little research has elucidated how sociocultural determinants, especially geographical disparities, contribute to the natural history of SLE. Social factors—from income and occupation to ethnicity and culture—influence...
where we live and shape our individual experiences and health outcomes within these local contexts (5). Disparities in social factors, from one geographical setting to the other, impact disease states, from cancer to heart disease to human immunodeficiency virus rates (5). Social determinants, such as the concentration of racial minorities in areas of concentrated poverty and low-wage jobs with exposure to hazardous substances, and harmful working environments, translate to deleterious health outcomes among racial minority populations (6). Failing to acknowledge the role of place in producing variations in social and environmental exposures may lead to spurious and inadequate inferences when making comparisons between racial and demographic groups about SLE outcomes (7). Moreover, detailed attention to context could reveal the reasons why SLE outcomes vary within and across locations and help inform population health interventions to best address these systematic disparities at the population level.

Here, we present an examination of SLE-related mortality rates across eight groups of race-county combinations of the population in the United States, which was developed by Murray et al in 2006, and are referred to as the “Eight Americas” (8). These Eight Americas were defined “based on race, location of the county of residence, population density, race-specific county-level per capita income, and cumulative homicide rate” and yielded notable disparities in mortality rates and life expectancy (8). These contextual factors—such as neighborhood deprivation and disadvantage, everyday occurrences of social and economic distress, and ongoing experiences of marginalization—influence individuals’ health both by offering differential social influences on health-related views and behaviors and by restraining access to resources (9).

SLE-related mortality across the Eight Americas over time assessed whether the impact of race is attenuated when the social and geographic context is also considered. In addition, we examined whether age at death in decedents with SLE differed across the Eight Americas and explicated patterns of disease comorbidities among decedents whose deaths were attributed to SLE on their death certificates in the Eight Americas.

METHODS

Study population. Using death certificate data from the National Center for Health Statistics Multiple Cause of Death (MCOD) database, SLE-related deaths were identified via International Classification of Diseases, 10th revision (ICD-10) codes: M32.1, M32.9, and M32.8. We obtained county-level mortality data (2003-2014) by race using MCOD and county-level population estimates by race from the US Census Bureau. We merged the Eight Americas file, which included a list of all of the counties from the original paper, the US Census population files (2003-2014), and the mortality data by county identification number to obtain estimates of SLE-related deaths and the corresponding underlying population for each county, year, and race category. We use the terms “SLE-related deaths” and “decedents with SLE” to mean deaths attributed to SLE on death certificates, either as an underlying or contributory cause.

The Eight Americas. Table 1 describes the socio-demographic characteristics of the Eight Americas (8,10). Americas 7 and 8 consist of low-income blacks living in southern rural areas and blacks living in high-risk urban settings, respectively. America 6 is comprised of blacks living outside of Americas 7 and 8. Americas 2 and 4 consist of low-income whites living in the northern plains and low-income whites living in the Appalachian and the Mississippi Valley, respectively. America 1 is comprised of only Asians, whereas America 5 is comprised of Native Americans living on reservations. America 3 is comprised of average-income whites and a few Asians and Native Americans living outside of Americas 1 and 5. The Eight Americas provide the opportunity to examine whether differences exist when race is held constant and social context is varied (i.e., America 6 vs America 7 vs America 8 for blacks). In order to explore what happens when race is varied and social context is held constant, blacks in Middle America (i.e., America 6) could be compared with whites in America 3.

Statistical analysis. Annual SLE-related mortality rates were calculated for each of the Eight Americas by dividing the number of decedents with SLE (as the underlying or contributory cause of death) by the population of the corresponding America along with change in mortality rates between 2003 and 2014. We estimated the annualized percent change by calculating the geometric mean of the proportional changes (year over year) in the mortality rates over the 13-year period. Similarly, we calculated annual mean and median age at death for each of the Eight Americas and the change between 2003 and 2014. Crude mortality rate ratios were estimated for each America using America 3 or middle America as the reference (11). Logistic regression models estimated the odds of premature death (i.e, dying before age 50) for each America relative to America 3.

Proportionate mortality ratios (PMRs) for the top causes of death (derived from the literature) among SLE patients (12) were calculated by dividing the proportion of observed deaths from a specific cause in each America by the proportion of deaths observed in the reference America (i.e, America 3). PMRs are crude risk ratios and are unadjusted measures of disease burden. PMRs estimate the relative importance of a specific cause, such as renal disease, as a cause of death in decedents with SLE. For example, in the renal disease scenario, if a decedent in low-income white America has a PMR of three, this means they are three times as likely to die of renal disease compared with decedents in middle America. Statistical analyses were performed using SAS version 9.4.
| America     | General Description                      | Population (Millions) | Average Income per Capita | % Completing High School | Definition                                                                 | Calculation of SLE Mortality Ratesb |
|-------------|------------------------------------------|-----------------------|---------------------------|--------------------------|-----------------------------------------------------------------------------|--------------------------------------|
| 1           | Asian                                    | 10.4                  | $21,566                   | 80                       | Asians living in counties where Pacific Islanders make up less than 40% of total Asian population | SLE decedents reported as “Asians and Pacific Islanders” across counties in America 1 |
| 2           | Northland low-income rural white         | 3.6                   | $17,758                   | 83                       | Whites in northern plains and Dakotas with 1990 county-level per capita income below $11,775 and population density less than 100 persons/km² | SLE decedents reported as “Whites, non-Hispanic” and “Hispanics” across counties in America 2 |
| 3           | Middle America                           | 214.0                 | $24,640                   | 84                       | All other whites not included in Americas 2 and 4, Asians not in America 1, and Native Americans not in America 5 | SLE decedents reported as “Asians and Pacific Islanders,” “Whites, Non-Hispanic,” “Hispanics,” and “American Indians and Alaska Natives,” excluding those in America 1, America 2, America 4, and America 5. |
| 4           | Low-income whites in Appalachia and the Mississippi Valley | 16.6                  | $16,390                   | 72                       | Whites in Appalachia and the Mississippi Valley with 1990 county-level per capita income below $11,775 | SLE decedents reported as “Whites, non-Hispanic” and “Hispanics” across counties in America 4 |
| 5           | Western Native American                  | 1.0                   | $10,029                   | 69                       | Native American populations in the mountain and plains areas, predominantly on reservations | SLE decedents reported as “American Indians and Alaska Natives” across counties in America 5 |
| 6           | Black Middle America                     | 23.4                  | $15,412                   | 75                       | All other black populations living in counties not included in Americas 7 and 8 | SLE decedents reported as “Blacks, Non-Hispanic” across counties in America 6 |
| 7           | Southern low-income rural black          | 5.8                   | $10,463                   | 61                       | Blacks living in counties in the Mississippi Valley and the Deep South with population density below 100 persons/km², 1990 county-level per capita income below $7,500, and total population size above 1000 persons (to avoid small numbers) | SLE decedents reported as “Blacks, Non-Hispanic” across counties in America 7 |
| 8           | High-risk urban black                    | 7.5                   | $14,800                   | 72                       | Urban populations of more than 150,000 blacks living in counties with cumulative probability of homicide death between 15 and 74 y > 1.0% | SLE decedents reported as “Blacks, Non-Hispanic” across counties in America 8 |

Abbreviation: SLE, systemic lupus erythematosus.

a Table 1 (except final column) was obtained directly from Murray et al (8).

b The final column “Calculation of SLE Mortality rates” describes how the numerator of the SLE mortality rate (number of SLE deaths) was calculated. The denominator (number of people) was calculated using analogous population estimates.
RESULTS

There were 24,773 SLE-related deaths in the United States between 2003 and 2014, of which 85% were female (Table 2). There were no differences in the demographic characteristics between males and females. A majority of deaths occurred among those 45-64 years, and the mean age at death was 57 years. More than 60% of deaths occurred among whites and approximately 40% of decedents were high school graduates. Most decedents with SLE resided in Middle America, ie, America 3.

Table 2. Demographic characteristics of decedents with systemic lupus erythematosus in the United States, 2003-2014

| Characteristics | Females | | | Males | | |
|-----------------|---------|---|---|-------|---|---|
| Age group (years) | N | % | N | % |
| <15             | 74 | 0.4 | 20 | 0.5 |
| 15-44           | 5327 | 25.3 | 924 | 25.0 |
| 45-64           | 8113 | 38.5 | 1332 | 36.0 |
| ≥65             | 7562 | 35.9 | 1421 | 38.4 |
| Mean age (years) | 57.0 | | 59.0 | |
| Race            | | | | |
| White           | 13,342 | 63.3 | 2543 | 68.8 |
| Black           | 6723 | 31.9 | 997 | 27.0 |
| Native American | 238 | 1.1 | 35 | 0.9 |
| Asian           | 773 | 3.7 | 122 | 3.3 |
| Ethnicity       | | | | |
| Non-Hispanic    | 18,504 | 87.8 | 3233 | 87.4 |
| Hispanic        | 2523 | 12.0 | 455 | 12.3 |
| Unknown         | 49 | 0.2 | 9 | 0.2 |
| Educational attainment | | | | |
| Less than high school | 3823 | 18.1 | 744 | 20.1 |
| High school graduate | 8508 | 40.4 | 1525 | 41.2 |
| Some college    | 4978 | 23.6 | 708 | 19.2 |
| College graduate and above | 3099 | 14.7 | 589 | 15.9 |
| Unknown         | 668 | 3.2 | 131 | 3.5 |

The overall mortality rate was 6.11 deaths per million population (Table 3). Blacks had the highest mortality rates regardless of their geographical location (Americas 6-8 had rates of 15-16 deaths per million population), whereas Asians living in America 1 and Northland Whites living in America 2 had the lowest mortality rates (~4 deaths per million population). (Figure 1, Table 3). Compared with other race groups living in America 3, blacks were more than three times as likely to die because of SLE. Low-income whites in the Appalachia and Mississippi valleys (America 4) and Native Americans living on reservations (America 5) were also at increased risk of death attributable to SLE compared with Middle America (Table 3). There was an overall 17% decrease in mortality rates attributed to SLE between 2003 and 2017 (Table 3). The highest decrease was among Native Americans on reservations (America 5), experiencing a 36% decrease in mortality rate, whereas Northland whites (America 2) experienced a 5% increase in mortality rate (Table 3, Figure 1). This group had only 176 deaths during that period, so this increase may not be statistically significant.

The mean age at death for decedents with SLE was 57.0 years (Table 3, Figure 2). Patterns across the Eight Americas for age at death were generally consistent with mortality rate findings. In other words, the groups with the highest mortality rates had the youngest average age at death. The one notable exception was Asians in America 1 who had low mortality rates but young mean age at death, with individuals in this group dying in their late 40s (Table 3). Overall, 36.1% of decedents with SLE died prematurely (younger than 50 years of age). Decedents living in Americas 1, 6, 7, and 8 were more than three times as likely as those living in America 3 to die prematurely (odds ratio [OR]: 3.27, 95% confidence interval [CI]: 2.80-3.80; 3.21, 95% CI: 3.00-3.43; 3.71, 95% CI: 3.30-4.16; 3.65, 95% CI: 3.27-4.08, respectively).

Cardiovascular disease (CVD) (~49% of all SLE-related deaths), renal manifestations (~20% of all SLE-related deaths), and infections (~20%) were among the most frequently associated causes of death. Proportionate mortality for CVD did not seem to vary across Americas. However, there were differences by racial group for specific categories of CVD, such as ischemic heart disease, hypertensive heart disease, and arrhythmia (Table 4).

Differences by race were also observed for noncardiovascular causes of death among decedents with SLE (Table 4). Racial minority groups (ie, black, Asian, and Native American) had higher proportionate mortality for renal conditions compared with individuals living in America 3, and these disparities were particularly pronounced for Asians in America 1 and blacks in Americas 6-8. Furthermore, Asians in America 1 and Native Americans living on reservations in America 5 had greater proportionate mortality for infectious diseases than those in America 3 (PMR: 1.53, 95% CI: 1.35-1.73; 1.47, 95% CI: 1.09-1.98, respectively). Blacks in Americas 6-8 also had greater proportionate mortality for infectious diseases relative to America 3 (PMR: 1.23, 95% CI: 1.15-1.31; 1.33, 95% CI: 1.20-1.48, and 1.29, 95% CI: 1.17-1.43, respectively) (Table 4).
DISCUSSION

The disparities in reported SLE-related mortality across the Eight Americas were similar to those described in the original study (8). In the original study, mortality rates were higher with increasing social deprivation; that is, America 1 had some of the lowest level of social deprivation and the highest level of life expectancy, whereas America 8 had the highest level of social deprivation and the lowest level of life expectancy. In our study, SLE-related mortality rates were generally lower in Americas 1-4 than in Americas 5-8. In contrast, average age at death among decedents with SLE was higher in Americas 2-4 than for those in Americas 1, 5, 6, 7, and 8.

Our study shows empirically how race and the social context may function separately or together to produce disparities in SLE. Overall, blacks had the highest mortality rate and lowest age at death, regardless of their sociodemographic heterogeneity (8). Although mortality rates were highest among blacks in the original Eight Americas study, the rates increased between Americas 6-8 (8). Hypothetically, if the social environment is a necessary or sufficient source of this disparity, then our findings would have reflected an attenuation or amplification in mortality parameters between Americas 6-8. The absence of differences (and the consistency in these measures) between blacks in varying social contexts suggests that social context alone may not be the key determinant of SLE-related mortality.

Racial minorities, especially Asians and blacks, often present with more aggressive disease than whites, and it is thought that var-

Table 3. Trends in mortality rate and mean age at death among decedents with systemic lupus erythematosus, eight Americas, 2003-2014

| America | Average mortality rate | Mortality rate ratio (95% CI) | % Change in mortality rates between 2003-2014 | Mean age at death | % Change in mean age between 2003-2014 | % Premature mortality | Odds ratio for premature mortality (95% CI) |
|---------|------------------------|-------------------------------|-----------------------------------------------|------------------|----------------------------------------|-----------------------|------------------------------------------|
| 1       | 4.16                   | 0.88 (0.81, 0.94)             | −13.6%                                        | 47.6             | 12.9%                                  | 54.3%                 | 3.27 (2.80, 3.80)                        |
| 2       | 4.11                   | 0.88 (0.75, 1.02)             | 5.2%                                          | 68.6             | 4.8%                                   | 16.5%                 | 0.54 (0.36, 0.81)                        |
| 3       | 4.70                   | Ref                           | −18.3%                                        | 62.3             | 4.9%                                   | 26.7%                 | Ref                                      |
| 4       | 6.58                   | 1.40 (1.33, 1.48)             | −27.4%                                        | 64.8             | −7.5%                                  | 21.5%                 | 0.75 (0.66, 0.86)                        |
| 5       | 8.67                   | 1.83 (1.53, 2.19)             | −35.9%                                        | 49.2             | 3.9%                                   | 49.6%                 | 2.70 (1.89, 3.86)                        |
| 6       | 15.10                  | 3.20 (3.10, 3.30)             | −11.3%                                        | 49.0             | 15.2%                                  | 53.9%                 | 3.21 (3.00, 3.43)                        |
| 7       | 17.50                  | 3.72 (3.51, 3.93)             | −22.1%                                        | 47.5             | 2.1%                                   | 57.4%                 | 3.71 (3.30, 4.16)                        |
| 8       | 16.14                  | 3.44 (3.26, 3.63)             | −11.5%                                        | 47.9             | 6.3%                                   | 57.1%                 | 3.65 (3.27, 4.08)                        |
| All     | 6.11                   | −16.9%                        |                                               | 57.0             | 5.1%                                   | 36.1%                 |                                          |

Abbreviation: CI, confidence interval.

* Premature mortality was defined as deaths at <50 years.
iations in disease phenotypes and interferon signature seen among Blacks and Asians could partially explain some of these disparities, apart from SES and race (13,14). Another commonality among racial minorities may include cultural beliefs and health behaviors. Distrust of medical care providers and systems among blacks has been cited to account for poor adherence to care and medications, in addition to limited access to quality care (3). There are also indications that cultural and health beliefs similarly are not favorable toward long-term need for medications among Asian immigrants, specially if there is no perceptible physical evidence of illness (15). Dependence on fate, spirituality, and by modifying eating behaviors are often seen in these groups as means to cope with chronic illness (15).

Generally, racial minorities had lower age at death and higher odds of premature mortality compared with whites. On average, blacks, Asians, and Native Americans with SLE were found to have died ~20 years earlier compared with whites, and had three times the odds of dying before age 50 years compared with whites. Racial minorities had higher proportionate mortality for infectious diseases and renal manifestations compared with whites, whereas whites had a higher proportionate mortality for CVD and neoplasms. Over 40 years ago, Urowitz et al demonstrated a bimodal mortality pattern in SLE, where early deaths among SLE patients were attributed to active SLE disease and the preponderance of later deaths a result of CVD (16). We posit that racial minorities, either because of social deprivation, other vulnerabilities, or through mechanisms related to genetic susceptibility, are more likely to die in the early death phase than whites. The fact that whites have higher age at death and die of diseases of old age (ie, heart disease and neoplasms), regardless of their geographical location, supports this hypothesis. However, age at death was also higher among low-income, rural whites, compared with blacks, despite the poor access to rheumatologists in rural areas and limited access to care and medications in rural areas (17,18). It is unknown whether this could be explained by less aggressive phenotype of disease in these patients as compared with racial minorities or because rural whites are more receptive of the need for ongoing care and lifelong medications.

Our study has a few limitations. One is the lack of adjustment for disease activity, damage, medications, and comorbidities in the models, all of which are potential sources of unmeasured confounding. We cannot exclude the possibility of disproportionate reporting of deaths among various groups using death certificate data (10). The extent to which SLE-related mortality burden in Americas 6-8 exceeds the SLE-related mortality burden in other Americas would be inflated if SLE-related deaths there are more likely to be reported than SLE-related deaths among other racial groups. Because we were unable to assess date of disease diagnosis or disease duration, our interpretations should be viewed cautiously until additional studies can corroborate these findings. There may also be discordance between a decedent’s self-reported race and the family-reported race on the death certificate. Furthermore, there may be misclassification of other causes of death and unmeasured confounding, such as factors in the social environment that are common across the black Americas, cannot be excluded. We also cannot rule out residual effects of social vulnerabilities and time because the Americas were broadly categorized in 2006. Finally, we quantified SLE-related mortality rates across the Eight Americas, we were unable to identify trends based on ethnicity, particularly since Hispanics are disproportionately affected by SLE compared with non-Hispanic whites.

Although previous studies have focused on racial disparities in SLE-related morbidity and mortality while accounting for social economic variables and geographical settings, our study is the first to consider these factors combined. The Eight Americas
|                      | America 1 | America 2 | America 3 | America 4 | America 5 | America 6 | America 7 | America 8 | ALL   |
|----------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-------|
| **Pneumonia**        |           |           |           |           |           |           |           |           |       |
| N                    | 705       | 176       | 14,666    | 1,385     | 121       | 4,980     | 1,330     | 1,410     | 24,773|
| %                    | 9.6       | 4.0       | 6.6       | 8.2       | 12.4      | 5.7       | 5.9       | 4.0       | 6.4   |
| PMR                  | 1.45 (1.15, 1.83) | 0.60 (0.29, 1.24) | Ref       | 1.23 (1.02, 1.48) | 1.86 (1.16, 3.01) | 0.85 (0.75, 0.97) | 0.89 (0.72, 1.12) | 0.61 (0.47, 0.79) |       |
| **Infectious diseases** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 27.5      | 5.7       | 18.0      | 16.1      | 26.4      | 22.1      | 24.0      | 23.2      | 19.5  |
| PMR                  | 1.53 (1.35, 1.73) | 0.32 (0.17, 0.58) | Ref       | 0.90 (0.79, 1.01) | 1.47 (1.09, 1.98) | 1.23 (1.15, 1.31) | 1.33 (1.20, 1.48) | 1.29 (1.17, 1.43) |       |
| **Cardiovascular disease** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 43.1      | 52.3      | 48.4      | 53.5      | 41.3      | 50.2      | 51.5      | 44.0      | 48.8  |
| PMR                  | 0.89 (0.82, 0.97) | 1.08 (0.94, 1.25) | Ref       | 1.11 (1.05, 1.17) | 0.85 (0.69, 1.06) | 1.04 (1.00, 1.07) | 1.07 (1.01, 1.13) | 0.91 (0.86, 0.97) |       |
| **Ischemic heart disease** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 11.9      | 22.2      | 15.4      | 19.6      | 14.0      | 12.4      | 13.2      | 14.3      | 14.8  |
| PMR                  | 0.77 (0.63, 0.95) | 1.44 (1.09, 1.90) | Ref       | 1.27 (1.14, 1.42) | 0.91 (0.58, 1.42) | 0.80 (0.74, 0.87) | 0.85 (0.74, 0.98) | 0.93 (0.81, 1.06) |       |
| **Cerebrovascular disease** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 8.8       | 9.1       | 6.9       | 6.2       | 7.4       | 7.1       | 7.2       | 5.3       | 6.9   |
| PMR                  | 1.27 (0.99, 1.62) | 1.31 (0.82, 2.10) | Ref       | 0.89 (0.72, 1.11) | 1.07 (0.57, 2.01) | 1.02 (0.91, 1.15) | 1.04 (0.85, 1.27) | 0.77 (0.61, 0.96) |       |
| **Heart Failure**    |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 5.4       | 10.2      | 7.6       | 12.6      | 7.4       | 6.7       | 7.8       | 5.7       | 7.6   |
| PMR                  | 0.71 (0.52, 0.97) | 1.34 (0.86, 2.08) | Ref       | 1.65 (1.42, 1.92) | 0.97 (0.52, 1.83) | 0.88 (0.78, 0.99) | 1.02 (0.84, 1.24) | 0.74 (0.60, 0.93) |       |
| **Hypertensive heart disease** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 8.7       | 16.5      | 12.1      | 13.9      | 15.4      | 14.1      | 14.8      | 13.0      |       |
| PMR                  | 0.71 (0.56, 0.91) | 1.36 (0.97, 1.90) | Ref       | 1.14 (1.00, 1.31) | 0.61 (0.33, 1.15) | 1.27 (1.17, 1.37) | 1.17 (1.01, 1.34) | 1.22 (1.07, 1.40) |       |
| **Arrhythmia**       |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 3.5       | 6.8       | 5.2       | 6.2       | 4.1       | 4.0       | 3.2       | 2.7       | 4.7   |
| PMR                  | 0.68 (0.46, 1.01) | 1.32 (0.76, 2.28) | Ref       | 1.20 (0.97, 1.49) | 0.80 (0.34, 1.89) | 0.77 (0.66, 0.90) | 0.61 (0.45, 0.83) | 0.52 (0.38, 0.72) |       |
| **Pulmonary embolism** |           |           |           |           |           |           |           |           |       |
| N                    | 2,477     |           |           |           |           |           |           |           |       |
| %                    | 2.6       | 2.3       | 3.4       | 3.0       | 2.5       | 3.6       | 3.8       | 3.8       | 3.5   |
| PMR                  | 0.74 (0.47, 1.18) | 0.66 (0.25, 1.75) | Ref       | 0.88 (0.65, 1.20) | 0.72 (0.24, 2.21) | 1.05 (0.89, 1.24) | 1.12 (0.84, 1.48) | 1.09 (0.83, 1.44) |       |

(continued)
### Table 4. (Cont’d)

|                  | America 1 | America 2 | America 3 | America 4 | America 5 | America 6 | America 7 | America 8 | ALL |
|------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|------|
| Neoplasm %       | 4.7       | 11.4      | 8.3       | 7.5       | 6.6       | 5.2       | 4.0       | 4.3       | 7.1  |
| PMR              | 0.57 (0.40, 0.79) | 1.38 (0.91, 2.09) | Ref       | 0.91 (0.75, 1.10) | 0.80 (0.41, 1.57) | 0.63 (0.56, 0.72) | 0.48 (0.37, 0.63) | 0.52 (0.41, 0.67) |
| Solid malignant neoplasm % | 3.3 | 9.7 | 6.7 | 6.5 | 6.6 | 4.1 | 3.3 | 3.5 | 5.7 |
| PMR              | 0.49 (0.33, 0.73) | 1.45 (0.92, 2.28) | Ref       | 0.97 (0.79, 1.20) | 0.99 (0.51, 1.94) | 0.61 (0.52, 0.70) | 0.50 (0.37, 0.67) | 0.52 (0.39, 0.69) |
| Hematologic malignancy % | 1.4 | 2.3 | 1.7 | 1.2 | 0.0 | 1.2 | 0.8 | 0.9 | 1.5 |
| PMR              | 0.83 (0.44, 1.55) | 1.32 (0.50, 3.51) | Ref       | 0.67 (0.41, 1.11) | N/A       | 0.72 (0.55, 0.95) | 0.44 (0.23, 0.82) | 0.50 (0.28, 0.88) |
| Respiratory disease % | 16.6 | 13.6 | 20.0 | 25.3 | 17.4 | 15.3 | 14.4 | 14.5 | 18.6 |
| PMR              | 0.83 (0.70, 0.98) | 0.68 (0.47, 0.99) | Ref       | 1.27 (1.15, 1.39) | 0.87 (0.59, 1.28) | 0.77 (0.71, 0.82) | 0.72 (0.63, 0.83) | 0.72 (0.63, 0.82) |
| Renal manifestations % | 28.2 | 18.8 | 17.3 | 15.5 | 18.2 | 26.4 | 25.0 | 22.5 | 20.0 |
| PMR              | 1.64 (1.45, 1.85) | 1.09 (0.80, 1.48) | Ref       | 0.90 (0.79, 1.02) | 1.05 (0.72, 1.54) | 1.53 (1.45, 1.62) | 1.45 (1.31, 1.60) | 1.30 (1.18, 1.44) |

Abbreviation: PMR, proportionate mortality ratios; SLE, systemic lupus erythematosus.

* PMRs for the top causes of death (derived from the literature) among SLE patients were calculated by dividing the proportion of observed deaths from a specific cause in each America by the proportion of deaths observed in the reference America (i.e., America 3). PMRs are crude risk ratios and are unadjusted measures of disease burden. PMRs estimate the relative importance of a specific cause, such as renal disease, as a cause of death in decedents with SLE. For example, in the renal disease scenario, if a decedent in low income white America has a PMR of three, this means they are three times as likely to die of renal disease compared to decedents in middle America.
framework has been well-validated in other contexts, including disparities in sexual health (10) and CVD (11). Long-term cohort studies of SLE patients suggest that the risk of developing SLE and the risk of severe disease has a strong genetic component impacting blacks, Hispanics, and Asians; however, the risk of fulminant disease is complicated by social factors (19–24). These studies are often characterized by small and selective sample sizes, whose generalizability might be limited.

In conclusion, these findings suggest that race may transcend SES and geographical parameters as a key determinant of SLE-related mortality. Although we were unable to examine causes of the disparities in SLE-related mortality rates, we theorize that genetic disposition may disproportionately contribute to these disparities, as well as other shared nongenetic factors within racial groups. Thus, developing research policies that focus on clarifying these factors associated with diagnosis, disease severity, and mortality may reduce disparities in SLE.

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AUTHOR CONTRIBUTIONS

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

Study conception and design. Falasinnu, Simard.

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