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Research article

Déjà vu all over again: racial, ethnic and age disparities in mortality from influenza 1918–19 and COVID-19 in the United States

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ABSTRACT

Background: Examination of the mortality patterns in the United States among racial, ethnic, and age groups attributed to the 1918–19 influenza pandemic revealed stark disparities, causes for which could have been addressed and rectified this past century. However, these disparities have been amplified during the current COVID-19 pandemic.
We have ignored the lessons of the past, and were destined to repeat its failings.
Objectives: Compare and contrast mortality patterns by age, race, and ethnicity attributable to the 1918–19 influenza pandemic in the United States with corresponding patterns during the COVID-19 pandemic.
Methods: This is a retrospective study, establishing mortality rates according to age, race and ethnicity attributable to the 1918–19 influenza pandemic in the United States and to the current COVID-19 pandemic, using mortality data published by the U.S. Public Health Service and the Centers for Disease Control and Prevention. Negative binomial regression models were used to establish rate ratios, that is, ratios of mortality rates across the various racial/ethnic groups, and associated 95% confidence intervals.
Results: Mortality patterns by age differ significantly between the 1918–19 influenza pandemic and the COVID-19 pandemic: with infant and young adult (25–40 years old) mortality substantially higher in the former. Disparities in mortality between racial and ethnic groups are amplified in the COVID-19 pandemic compared to the 1918–19 experience.
Conclusions: As we evaluate our nation's response to COVID-19 and design public policy to prepare better for coming pandemics, we cannot ignore the stark disparities in mortality rates experienced by different racial and ethnic groups. This will require a sustained resolve by society and government to delineate and remedy the causative factors, through science devoid of political interpretation and exploitation.

1. Introduction

The current COVID-19 pandemic brought on by widespread circulation of the SAR-CoV-2 virus and variants is the greatest acute health crisis world-wide since the influenza pandemic of 1918–19. That pandemic resulted in upwards of 50 million deaths globally and about 675,000 deaths (0.7% of population) in the United States [1, 2, 3, 4, 5]. The 1918-19 pandemic was also marked by vastly different mortality rates in various countries, with up to 30-fold observed differences [6, 7, 8]. Similarly, the COVID-19 pandemic is not uniform in its impact on society, but in the United States has been reported to affect certain ethnic and racial groups disproportionately [9]. The purpose of this note is to document racial, ethnic and age disparities in influenza mortality in the United States during the 1918-19 pandemic, and compare these outcomes with the corresponding COVID-19 mortality experience.

2. Methods

2.1. 1918-19 Influenza pandemic

Death rates by age, race, and sex in the United States between 1900 and 1953 attributable to influenza and pneumonia (except pneumonia in newborns) have been tabulated by the U.S. National Office of Vital Statistics [10]. We extracted death rates for 1918 and 1919 from this source. There are a number of limitations and qualifications relating to these data:

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(1) Age is grouped into 11 categories: under 1 year; 1–4 years; 5–14 years; 15–24 years; 25–34 years; 35–44 years; 45–54 years; 55–64 years; 65–74 years; 75–84 years; and, 85 years and older.
(2) Mortality statistics were available only from states enrolled in the death registration system maintained by the federal government. By the end of 1919, these comprised 32 states and the District of Columbia, and are enumerated in Table A of the Vital Statistics report [10].
(3) Race was dichotomized into white (also including Mexican or Puerto Rican) and nonwhite (African American, Chinese, Japanese, Native American, and other small nonwhite or mixed race groups).

The population base for these rates is available from Table X of Linder and Grove [11], which conveniently lists population sizes for the death-registration states by the same age x race x sex classification scheme as was used in the Vital Statistics report [10] for the tabulation of mortality rates in 1918 and 1919.

A negative binomial regression model was used to assess racial and gender differences in influenza mortality rates over the period 1918–19, while adjusting for the known effects of age and year. Negative binomial regression is akin to ordinary linear regression, but is used specifically for modeling count variables, particularly when the count outcomes are over-dispersed relative to a Poisson assumption. Generically, the negative binomial regression model in our context may be written

$$\log(rate_i) = \sum_{j=1}^{k} \beta_j x_{ji},$$

where $rate_i$ represents the mortality rate for a particular subgroup during the i^{th} time epoch, the x's are a set of k regressor variables, and the regression coefficients β_j are unknown parameters estimated from the data.

The negative binomial model was selected rather than a Poisson model because variability in the rates exceeded that expected under a Poisson distribution. Our model for 1918–19 includes main effects (regressor variables) year (1918 or 1919), age group (categorical, as enumerated above), gender (male or female), and race (white or nonwhite), and also included interaction terms (additional regressor variables) age group x year and age group x race. We reproduced counts of influenza deaths from the tabulated rates and population bases, and fit the negative binomial regression with dependent variable rate = count/population. Lack of fit of the regression model was assessed with the dispersion deviance, distributed as a chi-squared random variable with the residual degrees of freedom if the model is adequate (so that large values of the deviance would be indicative of lack of fit of the model). Significance of the predictors in the model (here, the main effects and the interaction terms) were assessed with analysis of deviance, the analog of analysis of variance tables in linear regression.

The outcomes of primary interest, rate ratios for the main effects in the model (i.e., ratios of mortality rates for 1919 relative to 1918, females relative to males, and nonwhites relative to whites) and associated 95% confidence intervals were calculated from the regression coefficients of the negative binomial model.

2.2. COVID-19

We took mortality data attributable to COVID-19 in the United States as of July 24, 2021 from Table 2 of the CDC compilation [12], a total of 603,500 deaths. The tabulation consists of the numbers of deaths in slightly different age categories (i.e., 1–4 years; 5–17 years; 18–29 years; 30–39 years; 40–49 years; 50–64 years; 65–74 years; 75–84 years; and, 85 years and older) from the 1918-19 data, but with a finer categorization of race and ethnicity: Hispanic or Latino; Non-Hispanic Whites; Non-Hispanic Blacks or African Americans; Non-Hispanic American Indian or Alaska Native (Native Americans); Non-Hispanic Asian Americans; Non-Hispanic Native Hawaiian and Other Pacific Islanders; Non-Hispanic More than One Race; and Unknown. There was no breakdown by gender. We excluded the "More" and "Other" categories (together, less than 1% of the total number of deaths), and determined population bases for the age x racial/ethnic categories as of the end of 2019 from the CDC Wonder database [13].

We again chose a negative binomial model to assess how mortality varied by race and ethnicity, after adjusting for the known effect of age. As with the 1918-19 data, over-dispersion in counts precluded the adoption of a Poisson model. The negative binomial model regressed counts on the main effects, age group and racial/ethnic category. Note that inclusion of an interaction term age group x race would have exhausted the degrees of freedom in the model and let to a perfect fit, but would have allotted no degrees of freedom to residual error (hence no parameter error estimates). Lack of fit was assessed with the residual deviance, and the significance of the predictors was determined from analysis of deviance.

The primary outcomes of interest, rate ratios (ratios of mortality rates for the racial/ethnic groups relative to whites, the reference group) and associated 95% confidence intervals were calculated from the estimated coefficients of the regression model. We also used joinpoint regression [14] to compare the ages across racial/ethnic groups at which COVID-19 mortality rates begin to deviate substantially from the low baseline levels detected in the young. 95% confidence intervals for locations of these transition points are rather wide and imprecise because of the relative paucity of distinct age categories.

3. Results

3.1. 1918-19 Influenza pandemic

The negative binomial regression model provided a reasonable representation of the mortality data, with no indication of lack of fit: the residual deviance was 17.18 with 54 degrees of freedom, p = 0.99. An analysis of deviance table (Table 1) indicates the significance of the various factors included in the regression model. Note that gender is of borderline significance, especially in comparison with the other factors.

Table 2 displays rate ratios for the main effects: the mortality rate for 1919 was about 42% that of 1918 (95% confidence interval (CI) 29.3%–59.9%), while holding the other variables in the model constant; the mortality rate for females was 91.6% that of males (95% CI 82.2%–102.1%), while holding the other variables in the model constant; and, most relevant, the mortality rate for nonwhites was about 1.76 times that of whites (95% CI 1.23 to 2.52), while holding the other variables in the model constant. Summarizing, there was a significant decline in mortality in 1919 compared to 1918; the mortality rate for females did not appear to differ significantly from that of males; and nonwhites experienced significantly greater mortality than whites.

In Figure 1 we display the observed influenza mortality rates by race and gender, for 1918 and separately 1919, across the age spectrum. The graphs reflect the main points summarized above: a decline in mortality rates in 1919 compared to 1918; little difference between male and female mortality rates within the two race categories; and clear differences between nonwhites and whites across the age spectrum.

3.2. COVID-19

Again, the negative binomial regression model showed little evidence of lack of fit: residual deviance = 43.94, error degrees of freedom = 40, p = 0.69. The analysis of deviance table (Table 3) indicates that the two main effects, namely age group and race, were highly significant predictors of mortality.

Table 4 presents the mortality rate ratios (relative to whites) for the racial/ethnic categories. Mortality rates for Asians did not differ significantly from whites: rate ratio = 1.10, 95% CI 0.76 to 1.58. The other four

groups had significantly greater mortality rates than whites: African Americans, rate ratio = 2.53, 95% CI 1.78 to 3.60; Hispanics or Latinos, rate ratio = 2.75, 95% CI 1.94 to 3.90; Hawaiians and Pacific Islanders, rate ratio = 3.50, 95% CI 2.38 to 5.13; and Native Americans, rate ratio = 4.17, 95% CI 2.89 to 6.02.

In Figure 2 we display the differences in the observed COVID-19 mortality rates by race/ethnicity (Native Americans, Hawaiians and Pacific Islanders, Hispanics and Latinos, African Americans, Asian Americans, and whites) this time across the age spectrum. The differences in the curves are even more striking than the 1918/19 data in Figure 1 and uphold Table 4 quantification. Beyond the ages of youth showing minimal levels across the board, whites and Asian Americans nearly always show concordant and lower mortality rates at each age than the other groups.

Figure 2 also shows that, in contradistinction to the 1918–19 influenza pandemic (Figure 1), mortality rates in the young are near zero, and there is no "hump" in the 25–40 year age range. On the other hand, in accord with the 1918 experience, mortality rates are clearly highest for seniors, age 65 and above, regardless of race and ethnicity. These distinctions between pandemics is made more clear in Figure 3 where all data were combined from each group/sex/year to yield a single curve compiled for each pandemic in toto. This composite puts on view two markedly different age-dependency curves easily compared to reveal the greater and more broadly indiscriminate devastation of the earlier pandemic across all ages. Simply put, COVID-19 mortality rates are skewed heavily to the aged and so far clearly fall far short of the 1918-19 pandemic, even among seniors.

From Figure 2, the earliest significant rise in COVID-19 mortality rates from near nil levels occurs sooner in age for several groups relative to whites. Joinpoint regression analysis of this data quantifies this observation and shows the mortality rate for African Americans, Hispanics, and Hawaiians and Pacific Islanders begins to ascend at about age 40 (95% confidence interval 10 to 40 for each group) compared to whites at age 50 (95% CI 40 to 70), and Asian Americans, at age 60 (95% CI 50 to 70), with a second joinpoint at about age 70. Native Americans are even earlier at age 30 (95% CI 20 to 40). Nonetheless the mortality burden of COVID-19 disease is borne primarily by the elderly, about age 65 onwards.

4. Discussion

Two pandemics spaced almost exactly 100 years apart have subjected our medical system, society, and government to extraordinary stressors. Despite undisputed medical progress and societal change in the last century, this accumulative stress has unmasked untoward inequities that should no longer exist but clearly do. In this regard, we have found that, after adjusting for age, sex, and year, mortality rates for nonwhites were about 1.76 times greater than the rates for whites during the 1918-19 pandemic in the United States. Disparities between nonwhites and whites are more pronounced with the COVID 19 data, with the distinct

Table 1. Analysis of deviance table from negative binomial regression modeling of influenza mortality in the United States, 1918–19.

Model Term	DF	Deviance	Increase From Model Deviance (Chi^2)	P-Value
Intercept Only	1	314.4097		
year	1	23.0233	5.84	0.0157
age_group	10	239.4719	222.29	0.0000
gender	1	21.0304	3.85	0.0499
race	1	31.3295	14.14	0.0002
age_group*year	10	75.6388	58.45	0.0000
age_group*race	10	53.8132	36.63	0.0001
(Full Model)	34	17.1849		

The p-value is for testing the significance of that term after considering all other terms.

Table 2. Ratios of mortality rates and associated 95% confidence limits from negative binomial modeling of influenza mortality during the 1918–19 influenza pandemic in the United States.

Factor	Rate Ratio	Lower 95% Confidence Limit	Upper 95% Confidence Limit
year (1919/1918)	0.419	0.293	0.599
gender (female/male)	0.916	0.822	1.021
race (nonwhite/white)	1.763	1.232	2.521

Note: The rate ratios correspond to the ratios of 1919 mortality rates to 1918 mortality rates, or female mortality rates to male mortality rates, or nonwhite mortality rates to white mortality rates, as determined from the negative binomial regression model with all terms (including interactions) from Table 1 included in the model.

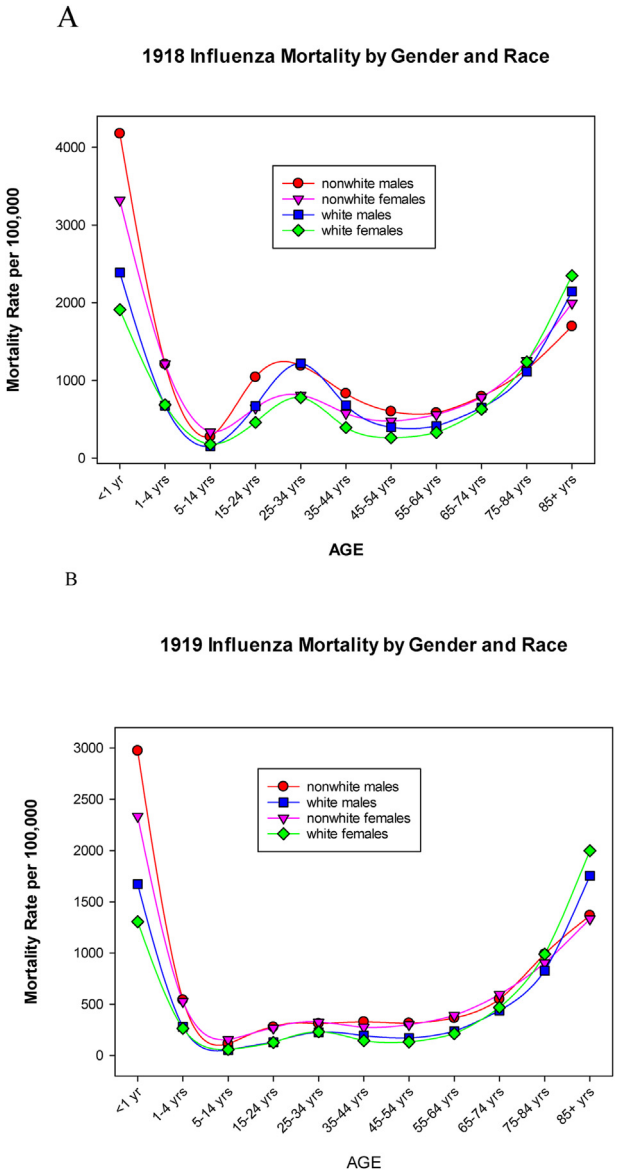

Figure 1. Observed influenza mortality in the United States by race (white or nonwhite) and gender (male or female) for 1918 (Panel A) and 1919 (Panel B). Smoothing splines to the observed values are also depicted.

Table 3. Analysis of deviance table from negative binomial regression modeling of influenza mortality attributable to COVID-19 in the United States.

Model Term	DF	Deviance	Increase From Model Deviance (Chi^2)	P-Value
Intercept Only	1	262.5365		
race	5	105.0818	61.14	0.0000
age_group	8	261.4606	217.52	0.0000
(Full Model)	14	43.9409		

The p-value is for testing the significance of that term after considering all other terms.

Table 4. Ratios of mortality rates and associated 95% confidence limits of various racial/ethnic groups from negative binomial modeling of mortality attributable to COVID-19 in the United States.

Group	Rate Ratio	Lower 95% Confidence Limit	Upper 95% Confidence Limit
Asian Americans	1.098	0.764	1.577
African Americans	2.529	1.779	3.595
Hispanics and Latinos	2.748	1.936	3.900
Hawaiians and Pacific Islanders	3.496	2.384	5.126
Native Americans	4.174	2.893	6.021

Note: The ratios are all relative to the mortality rates for whites, the reference group in the negative binomial regression model. The rate ratios were determined from the negative binomial regression model two main effects (race and age group).

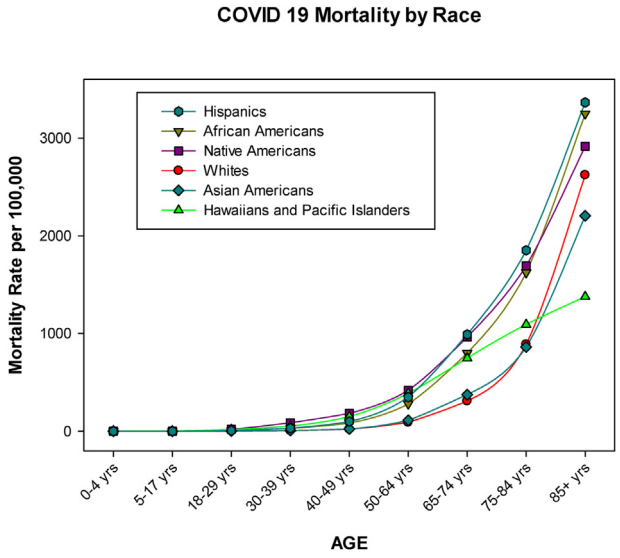

Figure 2. Observed mortality attributable to COVID-19 disease in the United States, by race/ethnicity.

exception of Asian Americans. The mortality ratios (relative to whites) range from just over 2.5 for African Americans and 3 for Hispanics and Latinos to approaching 5 for Native Americans. Recall, however, that the "white" category from the 1918-19 data pooled whites and Hispanics, and the "nonwhite" category pooled African Americans with Asians and Native Americans; this in turn would lead to mortality rates for the two categories to be closer than one might have anticipated.

Our regression methodology was primarily focused on assessing the significance of differential mortality rates attributable to race and ethnicity, after controlling for known or potential confounders. Nevertheless, we would be remiss were we to overlook the intriguing differences in the age vs mortality curves for the two pandemics. The W-shaped

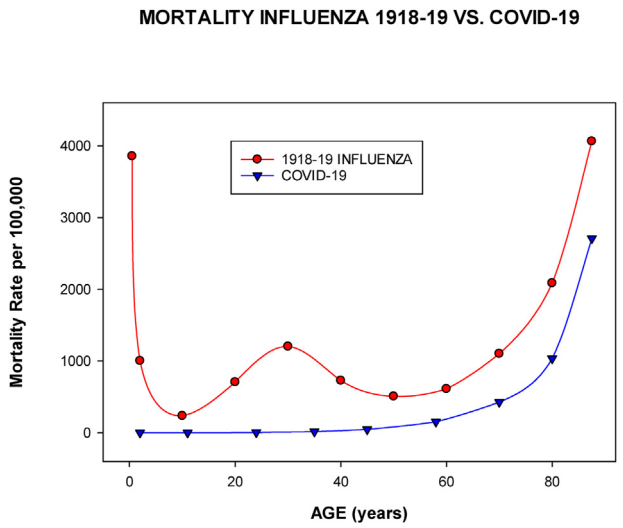

Figure 3. Age-specific mortality rates in the United States attributable to influenza 1918–19 and COVID-19.

mortality rates during the 1918-19 pandemic, with peaks in infants, young adults, and seniors, are unusual and provocative, especially with regard to the high mortality rates experienced by young adults aged 25 to 40: this has engendered considerable speculation and commentary [6, 15, 16, 17, 18, 19, 20, 21] Of comparable interest are the hockey-stick shaped mortality rates by age with COVID-19, and in particular the pronounced diminution of mortality among infants compared to the U-shaped mortality curves generally observed in typical influenza seasons.

On a macro level, Murray and colleagues [6] have examined disparities in influenza mortality in 27 countries during the 1918-19 pandemic, and found that the average income per country explained a large proportion of excess mortality. On a micro level, Grantz and colleagues [22] found literacy, homeownership, and unemployment were associated with influenza mortality. More to the point, social and economic inequalities impacted disease progression and outcomes through decreased access to health care, overcrowding, comorbidities associated with fewer resources, nutritional status, poor hygiene, or understanding of control measures disseminated only in English. As Chowell and Viboud [23] pointed out, the sociodemographic and socioeconomic variables delineated by Grantz and colleagues are surrogates for the effects of poverty and inequity in general.

The shapes of the age-dependency curves between sexes and races appear quite similar for 1918–19, suggesting that the causative factors for the racial bias applied equally across the age spectrum. By contrast, our analysis uncovered the greater risk of death from COVID-19 may occur much earlier in age for many nonwhite groups, possibly reflecting poorer health status with more risk factors and behaviors not being addressed prophylactically through preventive and sustained family medicine. Social determinants of health have been investigated and identified for well over one hundred fifty years. In 1849, Virchow [24] associated typhus epidemics in Silesia with contributing factors such as malnutrition, poverty, and illiteracy among a vulnerable populace. He argued that medical intervention was insufficient to tame the spread of disease, and advocated socioeconomic remedies and interventions to reduce health disparities and outcomes. In 1899, W. E. B. Du Bois [25] attributed increased mortality among African Americans compared to whites in Philadelphia to social factors such as inadequate housing, education, and occupational opportunities, and not to intrinsic biological differences. One might have hoped that the 1918-19 pandemic would have been a wake-up call to rectify documented inequities associated with mortality, but the previous century has been marked by neglect rather than action, with little attempt to address the needs of particularly

vulnerable segments of society [26]. Stark disparities in income, education and opportunities, affordable housing, or ready access to adequate medical care persist, a sad commentary on the struggle for justice and equality in this country.

Churchill (perhaps borrowing from Santayana) wrote that those who fail to learn from history are doomed to repeat it. This aptly summarizes the experience in the United States relative to differential mortality rates across racial and ethnic groups from the 1918–19 influenza pandemic and the current COVID-19 pandemic. As we evaluate our nation's response to COVID-19 and design public policy to prepare better for coming pandemics, we cannot ignore these uncomfortable, unfair and discriminatory realities cogently identified by Virchow, Du Bois and others. This will require a sustained resolve by society and government to delineate **and remedy** the causative factors, through science devoid of political interpretation and exploitation. If not, it will be déjà vu all over again in another 100 years or sooner. Let's do better this time!

Declarations

Author contribution statement

James A. Koziol and Jan E. Schnitzer: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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