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MAJOR ARTICLE

Timing of Infection as a Key Driver of Racial/Ethnic Disparities in Coronavirus Disease 2019 Mortality Rates During the Prevaccine Period

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Disparities in coronavirus disease 2019 mortality are driven by inequalities in group-specific incidence rates (IRs), case fatality rates (CFRs), and their interaction. For emerging infections, such as severe acute respiratory syndrome coronavirus 2, group-specific IRs and CFRs change on different time scales, and inequities in these measures may reflect different social and medical mechanisms. To be useful tools for public health surveillance and policy, analyses of changing mortality rate disparities must independently address changes in IRs and CFRs. However, this is rarely done. In this analysis, we examine the separate contributions of disparities in the timing of infection—reflecting differential infection risk factors such as residential segregation, housing, and participation in essential work—and declining CFRs over time on mortality disparities by race/ethnicity in the US state of Michigan. We used detailed case data to decompose race/ethnicity-specific mortality rates into their age-specific IR and CFR components during each of 3 periods from March to December 2020. We used these estimates in a counterfactual simulation model to estimate that that 35% (95% credible interval, 30%–40%) of deaths in black Michigan residents could have been prevented if these residents were infected along the timeline experienced by white residents, resulting in a 67% (61%–72%) reduction in the mortality rate gap between black and white Michigan residents during 2020. These results clearly illustrate why differential power to "wait out" infection during an infectious disease emergency—a function of structural racism—is a key, underappreciated, driver of inequality in disease and death from emerging infections.

Keywords. infection inequity; structural racism; mortality; SARS-CoV-2; social epidemiology.

A core principle of social epidemiology has been realized in the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the United States and around the world. Transmission of a virus that is agnostic about who it might infect has nevertheless been powerfully shaped by the social circumstances it travels within, resulting in robust social inequalities in morbidity and mortality rates [1–3]. Lying beneath this general principle is a more specific puzzle: exactly how did this social shaping of pandemic morbidity and mortality rates occur [3]? In this analysis we show that disparities in SARS-CoV-2 outcomes can be understood as emerging from the confluence of 2 critical factors: (1) when in the epidemic members of marginalized populations were at the greatest risk of infection and (2) how likely individuals belonging to these groups were to die when these infections occurred.

Most analyses of disparities in coronavirus disease 2019 (COVID-19) mortality have been cross-sectional, focusing on a single period in which policy and medical responses to SARS-CoV-2 infection remained relatively consistent [4] or cumulative infection and death from March 2020 onward [5]. They often draw on the differential role of inequity within stages of susceptibility, exposure, and recovery [6]. Some of these analyses show that large racial and socioeconomic disparities in COVID-19 mortality observed in the United States are attributable to differential rates of infection, while inequity in case fatality rates (CFRs) stemming from comorbid conditions, such as obesity or heart disease and differential access to care, played an important but less pivotal role [4, 7, 8]. These findings ran counter to early scientific and media speculation that inequities in mortality rates were likely attributable to disparities in comorbid conditions and care that increased the risk of

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death following SARS-CoV-2 infection [9]. Critically, many of these analyses also include age-specific breakdowns of incidence rates (IRs) and mortality rates to ensure that estimates of social disparity are not confounded by differences in age structure—and corresponding age-specific risks of death—between racial, ethnic, and socioeconomic subgroups.

Longitudinal analyses have shed light on the dynamics of inequity over the course of the pandemic: Van Dyke et al [10] analyzed national data cover the period from summer 2020 to winter 2021. They determined that declining relative risk for young minoritized populations (aged <25 years), compared with same-age white populations, primarily reflected growth in the rates of infection and death among white populations rather than sharp decreases among minoritized populations. This suggests that shrinking disparities throughout 2020 resulted from worsening pandemic conditions rather than reflecting positive policy outcomes. Aschmann et al [11] analyzed all-cause mortality rates by racial-ethnic group over 4 years and observed that indigenous groups continue to experience mortality rate disparities greater than their prepandemic levels. Their findings highlight the importance of longitudinal analyses when examining and identifying disparities caused by systems of exposure or structural causes [12].

In the current analysis, we used detailed individual-level incidence and mortality data from the state of Michigan to estimate age- and race/ethnicity-specific per-capita COVID-19 IRs and CFRs over 3 critical periods during 2020. (IRs are population-level rates of cases among all susceptible individuals in the population, while CFRs are population-level rates of death among cases.) Our core proposition is that gaps in mortality rates between racial/ethnic groups during the prevaccination period of the COVID-19 pandemic were driven by differences in infection risk early in the pandemic, when lifesaving knowledge was sparse and population-wide CFRs were high. These differences in exposure reflect inequalities in social power often [13], though by no means exclusively [14], reflected along lines of race and ethnicity. This analysis is differentiated from previous analyses of the drivers of variation in disparities in COVID-19 mortality rates over time by its focus on the joint impact of changing infection IRs and CFRs on disease outcomes, rather than focusing on mortality rates as the sole outcome.

Michigan has a large, racially and socioeconomically diverse population. According to the Michigan Division of Vital Records and Statistics, 75.4% of Michigan residents identified as non-Hispanic white, 14.5% as non-Hispanic black, 5.7% as Hispanic or Latino, and 3.6% as non-Hispanic Asian American or Pacific Islander (AAPI) [15]. However, the state is also among the most racially segregated and economically unequal states in the United States [16]. Michigan also implemented one of the strongest nonpharmaceutical intervention (NPI) strategies early in the pandemic, reaching an Oxford Stringency Index (OSI) score of 50, second in the United States only to Delaware [17]. Michigan also experienced a nearly 7-fold disparity in all-cause excess mortality rates for black versus white residents during 2020, the largest recorded in the United States [18]. This combination of a comprehensive approach to limiting community spread in a context characterized by stark racial/ethnic inequality make Michigan an ideal context to investigate the mechanisms by which structural racism contributes to unequal outcomes even under a "best case" scenario of public health response.

Our goals in this analysis are 2-fold: (1) to characterize age-specific and population-wide disparities in IRs and mortality rates during each of these periods and second and (2) to estimate the impact of each period on overall patterns of mortality rate inequality throughout the period from March to December 2020.

METHODS

IR and Mortality Rate Data

Data on SARS-CoV-2 infection and mortality rates were obtained from the Michigan Disease Surveillance System (MDSS) maintained by the Michigan Department of Health and Human Services. The current analysis includes all probable and polymerase chain reaction (PCR)–confirmed SARS-CoV-2 cases recorded in MDSS from 8 March to 31 December 2020. Probable cases were determined using the criteria outlined in the Michigan State and Local Public Health COVID-19 Standard Operating Procedures [19]. Deaths were attributed when COVID-19 was the primary or secondary cause of death on the death certificate. Further information about these data can be found elsewhere [4]. For all cases, we obtained the date of case identification and patient age, sex, and racial/ethnic category. This data set consists of 508 648 individually linked probable and PCR-confirmed COVID-19 cases and 13 078 COVID-19 deaths. It includes an onset date, which generally corresponds to the date of testing, and whether the individual eventually died of the infection. The death date we use corresponds to the diagnosis date and not the actual date of death. Probable cases were determined using the Michigan State and Local Public Health COVID-19 standard operating procedures [20].

We binned case data into 10-year age groups, with individuals aged ≥80 years in a single group. The race/ethnicity of case patients was categorized to match census population groups, including black/African American, Latino, AAPI, Native American, white, and other (this comprised the census category of "other" and those who identified as ≥2 racial/ethnic categories). In Michigan, race (eg, black/African American or white) and ethnicity (eg, Latino) were classified separately, as in the US Census approach to data collection. We obtained statewide population estimates stratified by age, sex, and race/ethnicity from the 2018 American Community Survey [21].

When comparing risks, we used the white population as the reference group and looked at contrasts for each of the racial-ethnic categories identified above for which census population data were available. Although Michigan has a large Arab-American population, we could not include this group in our analyses, as the US Census does not recognize Arab populations as a separate racial/ethnic group, and they are categorized as white [19]. This lack of group-specific population denominators makes it impossible to calculate reliable crude or age-specific IRs and mortality rates for this group.

Prevaccine Pandemic Phases

To understand how changing group-specific IRs and CFRs affected inequity in infection and mortality rates in Michigan, we divided the prevaccine period of the COVID-19 pandemic into 3 periods representing distinct phases of the early pandemic and the policy response to COVID-19 in Michigan. Period 1, March–June 2020, included the emergence of SARS-CoV-2 and the most restrictive lockdown interval, with an OSI score of 73 of 100. This period includes sparse personal protective equipment, low supply of ventilators and oximeters, minimal medical knowledge about treatment protocols, and marginalized groups more likely to be in essential work categories (meat packing, grocery store workers, etc) [22–24]. The pandemic hit marginalized communities hard without protection against death, while other, nonmarginalized communities benefited from stay-at-home orders for most office-based workplaces [23–27]. For example, the Occupational Information Network, an analysis of essential frontline workers in census data and the US Department of Labor data set, revealed that >70% of male workers from minoritized groups (Latino, black, Native American, or Asian American/Pacific Islander) were considered frontline workers [26].

Period 2, July–August 2020, was a summer of moderately eased contact restrictions accompanied by a suite of NPIs, including indoor mask mandates and social distancing policies [28], reflecting a 27% decrease in the OSI score. This period included incidence spread to other nonmarginalized groups, protective gear becoming more available, growing medical knowledge, and ventilator supply increased to prevent death in all groups.

Period 3, September–December 2020, was characterized by a further easing of restrictions, along with limited vaccination rollout to high-risk populations beginning in December, with a further 21% decrease in the OSI score. This period includes the availability of the first Food and Drug Administration–approved antiviral drug, Veklury (remdesivir), for widespread use [29], lifting of nearly all stay-at-home orders for most office-based workplaces, widespread high community transmission within all groups, and increased availability of personal protective equipment to the general population.

Statistical Models

Our statistical analysis is focused on estimating age- and race/ethnicity-specific IRs (denoted by λ) and corresponding CFRs (denoted by ρ), which are the composite parts of mortality rates ($\rho\lambda$). This 2-step approach allows us to disaggregate the relative contribution of the risk of infection versus the risk of death following infection from the period-specific mortality rate for each group. Finally, to understand the implications of differential timing of infection by race/ethnicity against a backdrop of falling CFRs, we conduct a counterfactual simulation analysis, described below, in which we compare observed inequities in mortality rates with a scenario in which the timing of infection is equalized for all groups.

IRs. For each period (l), we estimated per-capita rates of COVID-19 in each age (i), sex (j) and racial/ethnic category (k), using a Poisson regression model with a population-offset term, $\log(n_{ijk})$, where n_{ijk} is the size of population in each ijk group within the 2018 American Community Survey data set. The model included several interaction terms to obtain the full spectrum of potential heterogeneity in the outcome data, including age × sex, sex × race and race × age. The observed number of cases in each group are y_{ijkl}, and the per-capita IR in each bin is denoted by λ_{ijkl}. This model included a weakly informative log-Gaussian prior distribution with a mean of 0 and standard deviation of 0.1. Further model specifications are included in the Supplementary Materials, along with empirical coverage of the posterior predictive intervals.

CFRs. We used a binomial regression model to estimate age-specific CFRs for each racial/ethnic group in each period. Our modeled outcome was the number of deaths (z_{ijkl}) as a function of the total number of cases (y_{ijkl}) in each age, sex, and racial/ethnic stratum, with the CFR for each group denoted as ρ_{ijkl}. Therefore, $z_{ijkl} \sim Binomial(y_{ijkl}, \rho_{ijkl})$.

Standardization. We present raw and standardized IRs and CFRs in our results to highlight both the aggregate burden of illness and death and to facilitate comparison between groups. IRs were age and sex standardized [30], using direction standardization to reflect group-specific IRs under a scenario of uniform age and sex distributions across all racial/ethnic groups. Standardized CFRs were weighted to present a measure in which the proportion of cases contributed by each racial/ethnic group during 2020 was held constant across time periods to facilitate comparison across epidemic phases [31].

Alternate Infection Timeline. Declines in IR and mortality rate disparities over time have been presented as indications of progress in addressing causes of disparate infection outcomes during the COVID-19 pandemic [32]. While a narrowing of these gaps may reflect short-term success in reducing inequity, it is

critical not to confuse these changes with substantive improvements to the long-term, structural determinants of infection inequality [33]. During the COVID-19 pandemic, the ability to avoid, or at least delay, infection may have been a function of race/ethnicity and socioeconomic privilege, for example, through the ability to work from home for a sustained period. Findings from studies that observed disparity patterns in the first 10 weeks of the pandemic highlight this point [34]. Low-income counties experienced much higher rates of infection in the first few weeks of the pandemic than high-income counties throughout the United States [34]. By April 2020, this relationship had inverted, and wealthier counties began experiencing higher incidence than poor counties. This change, coupled with declining CFRs across all racial/ethnic and age groups may conceal an underappreciated dimension of COVID-19 disparity that reflects structural inequalities related to occupational inequity and residential segregation [14, 35, 36].

To assess how much the ability to wait out the period of highest CFR before acquiring infection affected disparities in mortality rates, we developed a counterfactual analysis in which the timing of infection experienced by white residents was applied to all of the other racial/ethnic groups in our analysis. To isolate this effect, we kept the overall IR and age/sex distribution of cases fixed, as well as the period-specific CFRs. This way, the only difference between the original and counterfactual data sets was the time when individuals belonging to these racial/ethnic groups were infected. To account for uncertainty in our estimates of the number of deaths attributable to inequities in infection timing, we sampled from the posterior distribution of parameters estimated using the original data set. For each posterior sample, we calculated the difference in the expected number of deaths (z) in each racial/ethnic group (k) in the data versus under a counterfactual scenario (y') (z') within a period (l), to estimate the proportion of deaths that could have been averted in each racial/ethnic group, ζ_k, if all individuals experienced the same infection timeline, as follows:

$$\zeta_k = 1 - \frac{\sum_{ijl} z'_{ijkl}}{\sum_{ijl} z_{ijkl}}$$

We then used the quantiles of this counterfactual posterior distribution of deaths averted to calculate posterior medians and 95% posterior credible intervals (CrIs).

Software. Bayesian regression analysis was completed with R 4.0.5 software, using the rstanarm package [37] and the tidybayes package for postprocessing of model results [38], with a reproducible data processing and analytic pipeline orchestrated using Snakemake [39].

Sensitivity to Missing Data. Dropping cases with missing information on race/ethnicity, as we did in this analysis, may result in biased estimates if rates of missingness vary across racial-ethnic categories [40]. This need for a sensitivity analysis was informed by a recent analysis of COVID-19 case data indicating that rates of missing race/ethnicity were in fact higher among black compared with white individuals in early 2020 [19]. To assess the risk that this bias could have affected both the quantitative and qualitative conclusions of our analysis, we conducted extensive sensitivity analyses.

Specifically, we generated numerous synthetic data sets in which data on race/ethnicity were dropped for black and white residents under (1) a baseline scenario of equal likelihood of missingness for both groups (odds ratio [OR], 1) as well as scenarios of (2) moderate (OR, 2) and (3) extreme (OR, 3) differences in missingness for black compared with white residents. We also varied the baseline rate of missingness by race/ethnicity to ensure that the impact of these group-specific rates of missingness was robust across different levels of overall missingness. The results of this analysis show that neither the qualitative conclusions nor the quantitative results of our analysis are likely to be strongly affected by nondifferential missingness of data on race/ethnicity.

Patient Consent and Institutional Review Board Approval

All analyses presented in this paper used deidentified data collected in the course of a public health response, which does not require patient consent. The data used in this analysis were collected by the Michigan Department of Health and Human Services as part of an ongoing public health response and therefore were deemed "not regulated" by the University of Michigan Health Sciences institutional review board.

RESULTS

The MDSS data set included 68 413, 64 377, and 375 858 probable and PCR-confirmed cases in the first, second, and third periods of 2020, respectively. In addition, 6415, 874, and 5789 deaths were recorded during the first, second and third periods, respectively. Across all 3 periods, 59 514 cases and 3173 deaths were among those who identified as African American or black; 28 350 cases and 376 deaths, among those identified as Latino; 1819 cases and 38 deaths, among those identified as Native American or Alaskan Native; 7392 cases and 134 deaths, among those identified as AAPI; 291 247 cases and 8386 deaths, among those identified as white; and 20 051 cases and 265 deaths, among those identified as belonging to any other racial/ethnic group. Figure 1 presents these group-specific IRs and mortality rates over time.

This corresponds to unstandardized race/ethnicity-specific COVID-19 mortality rates of 233 deaths per 100 000 people for black residents, 75/100 000 for Latino residents, 82/100 000 for Native American or Alaskan Native residents, 44/100 000

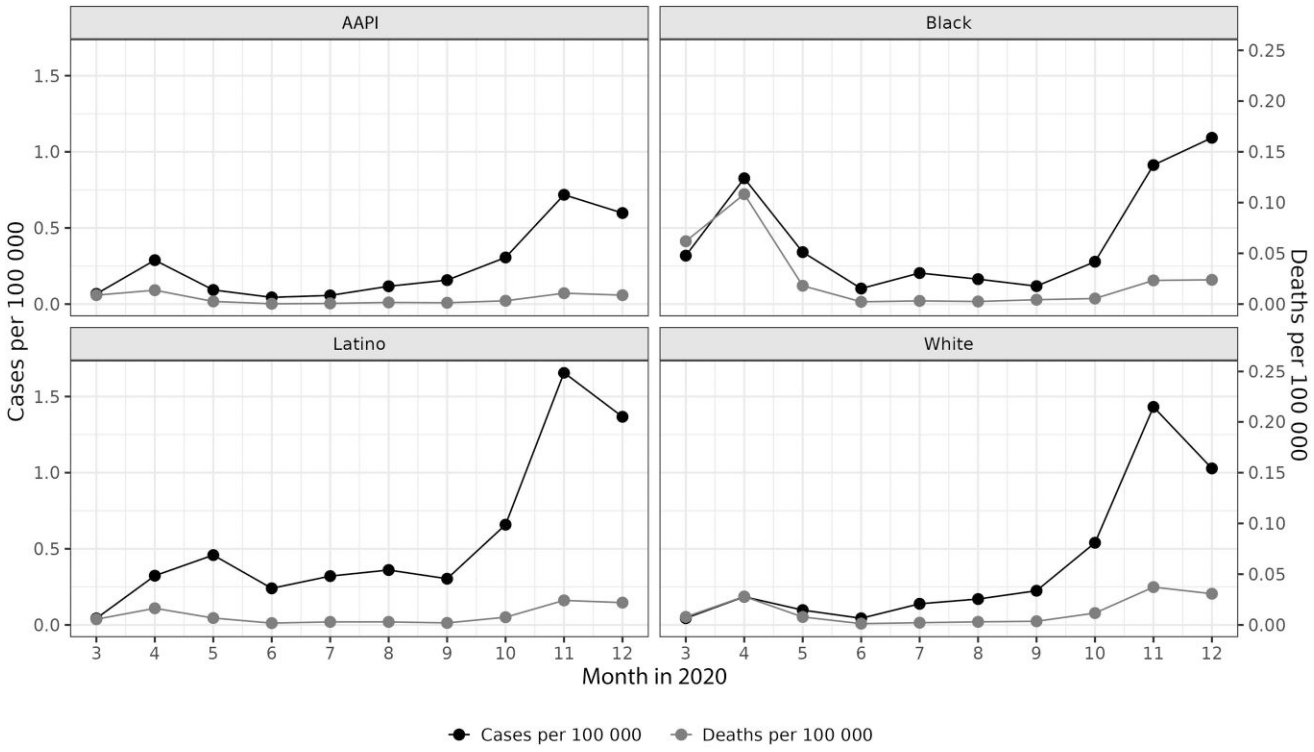

Figure 1. Incidence and mortality rates of coronavirus disease 2019 by race/ethnicity among Michigan residents by month in 2020. The y-axis on the left is on a scale from 0 to 1.75 for cases per 100 000 (*in black*), and the y-axis on the right, on a scale from 0 to 0.25 for deaths per 100 000 (*in gray*). The x-axes show the calendar month (by number) in 2020. All values reflect crude, unstandardized incidence and mortality rates. Abbreviation: AAPI, Asian American or Pacific Islander.

for AAPI residents, 112/100 000 for white residents, and 103/100 000 for individuals identified as belonging to any other racial/ethnic group. The 100 275 cases and 706 deaths that did not have an identified racial/ethnic group were dropped from subsequent analyses (see Supplementary Materials for additional information). Cases with missing racial/ethnic group identification varied across periods, with 9564 in the first period, 7639 in the second, and 83 072 in the third. This reflects an unstandardized population IR of SARS-CoV-2 infection for all groups—232/100 000 in the first period, 217/100 000 in the second, and 1277/100 000 in the third.

Change in IR Disparities Over Time

During the first period, age- and sex-standardized analyses show that black and Latino residents experienced 5.0 (95% CrI, 4.9–5.1) and 3.5 (3.4–3.6) times the IR of white residents, respectively. These values are characterized as IR ratios (IRRs), where the IR of the "exposed" group (in this case those exposed to racism) is compared with that of the "unexposed" group. By the second and third periods, most of these differences in IR were at or near 0.

However, the narrowing of IRRs does not reflect a monotonic decline in IR. In fact, there is a clear temporal shift in age- and sex-standardized IR among black residents from 1789/100 000 people (95% CrI, 1764–1812) in the first period to 497/100 000 (486–509) in the second before rebounding to 2334/100 000 (2308–2359) in the last period (Figure 2). A closer look at age-specific IR in period 3 among black residents reveals that there was a marked increase in infection among working age persons—as high as 2929/100 000 (95% CrI, 2849–3010) among 40–50-year-olds and 3827/100 000 (3733–3925) cases among 30–40-year-olds.

In contrast, Latino residents experienced a lower age- and sex-standardized IR of 1261/100 000 (95% CrI, 1223–1301) that remained relatively constant during the first 2 time periods, before increasing to 4085/100 000 (4016–4157) in the last period. This dramatic increase was not isolated to working-age groups for Latino residents. The IR among white and AAPI residents, on the other hand, was minimal in the first and second periods (see the Supplementary Materials for age-specific IRs in all racial-ethnic categories). White residents experienced incidence levels closer to their black counterparts during the last period, for an age- and sex-standardized IR of 2946/100 000 (95% CrI, 2934–2958)

Change in CFRs Over Time

Age-specific CFRs for all racial/ethnic groups fell sharply after an initial period of high CFR during the first period (see

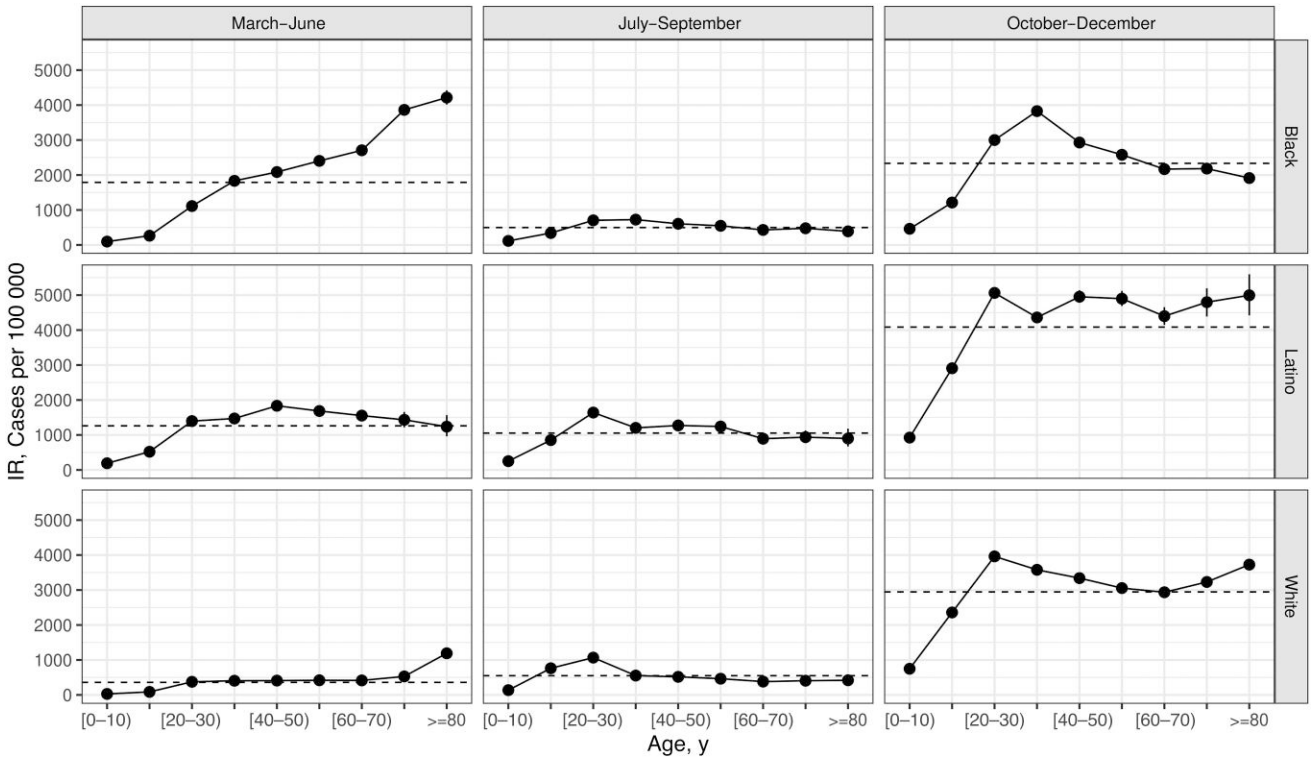

Figure 2. Age-specific incidence rates (IRs) of coronavirus disease 2019 (COVID-19) by race/ethnicity among Michigan residents over 3 periods during 2020. Each panel represents age-specific IR of COVID-19 by racial/ethnic group (rows) for each of 3 time periods during the first year of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (columns). Dashed lines represent the age-standardized IR of SARS-CoV-2 infection for each racial/ethnic group during each time period, and vertical lines around the points indicate the width of the 95% posterior credible interval of the age-specific IR. The x-axes increments reflect 10-year age bins; alternating age group labels are presented to ensure readability.

Figure 3) For example, black residents 50–60 years old experienced CFRs of 7.8% (95% CrI, 7.0%–8.7%) in the first period, which decreased to 2.0% (1.23%–3.0%) and 1.23% (.92%–1.58%) in the second and third periods, respectively.

Disparities in the risk of death from COVID-19 among individuals with a recorded infection, as measured by case fatality risk ratios, were small but did change over time. For example, black residents experienced CFRs 1.3, (95% CrI, 1.3–1.4), 1.5 (1.3–1.8), and 1.5 (1.3–1.6) times higher than their white counterparts in the first, second and third periods, respectively. However, marked age-specific CFR disparities by race/ethnicity were observed across all periods among those aged ≥30 years. For Latino residents, change over time in case fatality risk ratios relative to white residents was more dramatic. For detailed illustration of these results, see Supplementary Fgures 1–3.

Impact of Infection Timing on Race/Ethnicity-Specific Mortality Rates

The infection trajectory for black and Latino Michigan residents differed from that for white Michiganders, with the differences in timing most pronounced between black and white residents (Figure 4). Of cases among black residents, 36.7% occurred during the first period, 11.3% in the second, and 52.1% in the third. By contrast, only 9.6% of cases among white residents occurred during the first period and 13.9% in the second, with the large majority, 76.5%, occurring in the third period when CFRs were at their lowest.

Results from our counterfactual simulation analysis illustrate the potential impact these inequities in infection timing may have had on the disparities in SARS-CoV-2 mortality rates observed in Michigan throughout 2020. We found that 35% (95% CrI, 30%–40%) of all deaths in black residents could have been avoided under a scenario in which black residents experienced infection along the same timeline as white residents. This corresponds to a 67% (95% CrI, 61%–73%) reduction in the difference in per-capita mortality rates between black and white residents in 2020. Our results also suggest that a portion of deaths in Latinos (9% [95% CrI, −5% to 21%) might have been prevented as well under this alternate timeline, though the posterior CrI spans the null value of 0.

Sensitivity Analysis

Sensitivity analyses showed that IRR and CFR estimates were robust to differential rates of missing observations by race/ethnicity (see Supplementary Figures 4–12 for additional sensitivity analysis results and Supplementary Figures 13–16 for posterior checks of model fit).

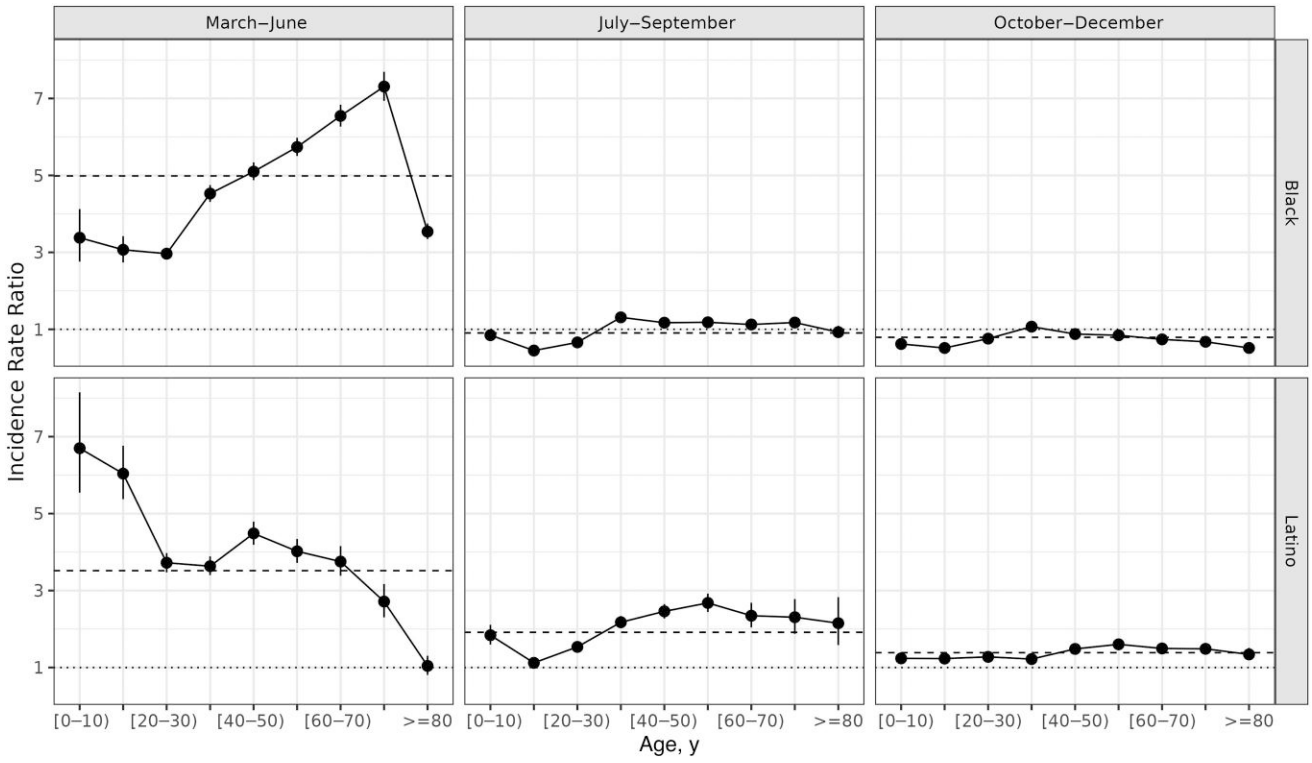

Figure 3. Age-specific incidence rate ratios (IRRs) of coronavirus disease 2019 (COVID-19) infection for black and Latino Michigan residents compared with white residents over 3 periods in 2020. Each panel represents age-specific IRR of COVID-19 by racial/ethnic group (rows) compared with white residents, for each of 3 time periods during the first year of the severe acute respiratory syndrome coronavirus 2 pandemic (columns). Dashed lines represent the age-standardized IRR for each racial/ethnic group during each period; dotted lines indicate an IRR of 1 and are provided as a reference for assessing the magnitude of risk disparity between each racial/ethnic group and white residents during each time period; and vertical lines around each point indicate the width of the 95% posterior credible interval of the age-specific IRR.

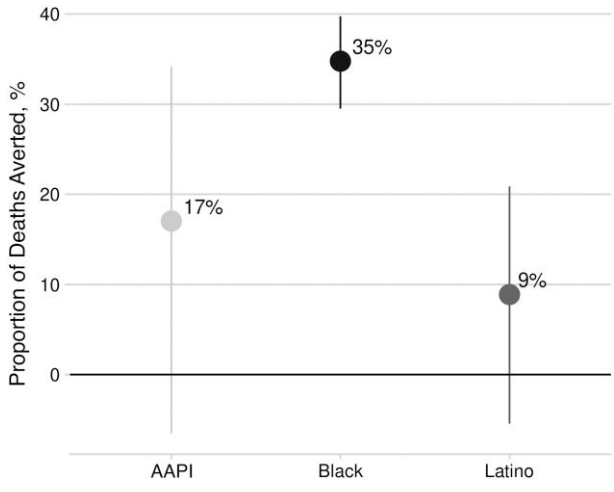

Figure 4. Proportions of deaths that could potentially have been averted if minoritized Michigan residents had experienced the same timing of infection as white residents during 2020. Vertical lines indicate the width of 95% posterior credible intervals. Abbreviation: AAPI, Asian American or Pacific Islander.

DISCUSSION

Our results underscore the importance of understanding inequities in SARS-CoV-2 mortality rates as the product of the interaction between (1) the social processes that drive between-group differences in exposure and infection and (2) the rapidly changing state of medical knowledge about a novel pathogen, as well as differences in access to care, frailties due to comorbid health conditions, and other factors. Specifically, our finding that the timing of infection strongly influenced the magnitude of mortality rate inequities between black and white Michiganders during 2020 highlights a critical but underrecognized mechanism of socioeconomic and racial inequality in the COVID-19 pandemic: white Michigan residents appear to have been more able than black residents to marshal the resources necessary to delay exposure until the first period of greatest uncertainty and highest mortality risk from SARS-CoV-2 was over. Overall, these findings highlight important implications for how we should think about averting infection inequities in the future. When

confronted with a novel, lethal infection about which little is known, equitable protection against exposure and infection—facilitated by housing, occupational, and healthcare policy—is paramount.

Our results for Latino and AAPI residents were more equivocal but are suggestive of similar dynamics at play. While individuals in these groups did not experience higher overall reported SARS-CoV-2 mortality rates than white residents in 2020, our counterfactual analysis suggested that the total number of deaths among members of these groups either could have been slightly reduced or would have remain unchanged under the scenario in which all Michigan residents were infected along the same timeline as white residents. Among Latino residents, the more muted impact of an alternate infection timeline scenario on the overall burden of death from SARS-CoV-2 in 2020 reflects the starkly different patterns of age-specific incidence, illustrated in Figure 2, for Latino compared with white and black residents.

These different age-specific rates may reflect a complex function of inequities in economic and social power, reflected, for example, by the large proportion of minoritized compared with white residents who work in frontline and often precarious jobs and the dynamics of racial residential segregation [23–27, 35]. Our data do not provide information on the specific nature of these risks, but these findings clearly suggest the need for more detailed analysis of how structural determinants—such as housing affordability, migration, labor policy, and other factors—collectively shape racial/ethnic differences in age-specific risks of infection and death from SARS-CoV-2 and other emerging infections. Such a structural approach is also important for future analyses examining intersectional effects, such as variation in occupational exposure associated with the combined effects of racism and sexism, which may, for example, create unique risks for black and Latino women.

Another important explanation for the differences in overall SARS-CoV-2 mortality rates as well as the number of cases potentially averted under an alternate infection timeline relates to the different age compositions of these groups in Michigan. Younger individuals compose a larger proportion of the Hispanic/Latino population in Michigan than any other group. According to the Michigan Division of Vital Records and Statistics, in 2020, approximately 20% of non-Hispanic white, 13% of non-Hispanic black, and 9% of non-Hispanic AAPI residents were aged ≥65 years—those at the highest risk of death from SARS-CoV-2—compared with only 6% of Hispanic/Latino residents [15]. Similarly, 34% of Hispanic or Latino residents were <18 years old, the group at lowest risk of death from SARS-CoV-2, compared with 27%, 23%, and 19% of non-Hispanic black, AAPI, and white residents, respectively.

In this analysis, we leveraged detailed, individual-level data on age- and group-specific IRs and mortality rates to better understand the role of infection timing in inequality in SARS-CoV-2 mortality rates. However, it is important to highlight some potential limitations when interpreting these results. First, a portion of cases were missing information on race/ethnicity (see Supplementary Table 2), which resulted in their removal from our final data set. However, our sensitivity analysis indicated that our IRR and CFR estimates are robust to even large differences in the probability of missing race/ethnicity for cases among black residents, compared with their white counterparts.

If there were systematic differences in the frailty of individuals (regardless of racial/ethnic group) who died in the first versus second and third periods, our counterfactual analysis might overestimate the impact of infection timing on inequalities in mortality rates. However, the use of age-specific comparisons using narrow age bands should mitigate this risk and facilitate a comparison between groups as a function of time. Our findings also echo data from the national level, which showed that differences in CFR between white and black residents were minimal throughout the first period of our analysis [8].

While our results are specific to the state of Michigan, we believe that the overarching insight of our analysis—that prevaccine racial/ethnic disparities in COVID-19 mortality rates were driven by differential timing of infection rather than differences in CFR by race/ethnicity—is likely to apply across state and local contexts, regardless of NPIs and other policies. For example, reports from the Centers for Disease Control and Prevention and other sources from this period echo our findings that CFRs fell dramatically and rapidly during spring 2020 for all racial-ethnic groups and that temporal differences in these risks are considerably larger than between-group differences within any period [4, 10, 30].

Geographic, temporal, socioeconomic, and racial/ethnic differences in rates of SARS-CoV-2 testing and case reporting may also have affected our results, as our data set reflects only PCR-confirmed and probable cases. During 2020, the availability of COVID-19 testing may have varied over time, with limited testing available in the first part of 2020 and much wider availability toward the end of the year [41]. The high overall CFRs we observed in the first period could reflect the presence of many unobserved cases which did not result in death [41–43]. Similarly, large geographic and race/ethnicity-specific differences in case ascertainment could also bias our results.

For example, analyses of testing access by race/ethnicity and social conditions across 3 major cities in 2020 suggested that per-capita rates of testing in areas characterized by high social deprivation and/or a high concentration of minoritized residents were slightly lower than in low-deprivation or majority-white areas and that these areas had a higher burden of test positivity, on average [44]. However, our sensitivity analyses (see the Supplementary Materials) suggest that ascertainment biases of this nature would have had to be extremely large to

erase or reverse our qualitative findings about the role of infection timing on mortality rate disparities between black and white residents. While this sensitivity analysis focused specifically on differential ascertainment between black and white residents—due to the disparity between and large contribution to overall burden by these groups—differential ascertainment of cases among Latino and AAPI residents may also have affected our findings for these groups. Nevertheless, CFRs were also documented to have fallen dramatically nationwide across all groups throughout 2020 [43] because of improvements in the clinical management of SARS-CoV-2 infection, which is in keeping with our findings.

These challenges highlight the need for individual-level testing data inclusive of both positive and negative test outcomes during an emerging pandemic, which were difficult if not impossible to attain in 2020 [45]. Such data are essential for assessing and mitigating the extent of potential bias due to differential access and uptake of testing between groups and over time. The urgent need for improved data systems and regulations that allows access to these and other important data to public health departments and researchers is underscored in the ongoing H5N1 avian influenza outbreak in Michigan, in which farmworkers—many of whom are younger Latino migrant workers—have experienced the highest risks of infection [46].

Finally, analyzing racial/ethnic disparities in isolation, as we did due to a lack of information on individual socioeconomic status and other modifiable risk factors, limits the ability to understand the differential contributions of wealth and income inequalities versus structural and interpersonal racism on observed COVID-19 outcomes [14]. For example, Kamis et al [47] showed that the intensity of the relationship between household crowding and COVID-19 mortality risk within US counties strengthened during summer 2020, suggesting that despite a narrowing of some racial/ethnic gaps in reported infection and mortality rates, overarching socioeconomic disparities may have in fact widened during this period. Increasing our understanding of the role played by the socioeconomic factors that put people at risk of risk can only be done if such information is routinely collected by public health and medical information systems.

While attention to health equity in infectious disease preparedness has grown in the wake of COVID-19 [48, 49], our analysis illustrates why taking a sociostructural and historically minded approach to these questions is essential [3, 6, 12, 14]. The stakes associated with these analytic choices are high and fall hardest on the most vulnerable. They shape not only our understanding of the causes of inequity in infection mortality rates but also the universe of policy mechanisms we perceive as capable of addressing them. For example, analyses of cumulative disparities in COVID-19 IRs and mortality rates that collapse 2020 into a single time period [35, 36] are more likely lead to the conclusion that racial/ethnic inequities in COVID-19 mortality rates were attributable to group-specific differences in the risk of death on infection (ie, the CFR) and thus reflecting some characteristic of minoritized individuals (eg, preexisting poor health or limited access to care) that could not have been addressed quickly enough to prevent these outcomes.

Instead, our results suggest that differentials in COVID-19 mortality rates throughout 2020 —at least between black and white Michigan residents—reflect in large part the way that infection timing affected the risk of dying from SARS-CoV-2. This suggests that more equitable protection from infection, in the form of short-to-medium-term income support, housing support, and increased workplace and employment protections for essential workers, were accessible policy levers that could have reduced these differentials. Preventing these outcomes in the future necessitates more proactive disease surveillance to detect inequities as they emerge, as well as social welfare and workplace policies that can preempt these inequitable patterns of exposure in the first instance.

Our results also provide a critical insight that is useful to bear in mind when evaluating progress in tackling inequity during future emergencies. Outbreaks, epidemics, and pandemics should be understood as historical events in which the social patterning of outcomes is strongly shaped, if not overdetermined, by sociostructural conditions at the outset. As a result, it is crucial to not conflate within-pandemic narrowing of incidence disparities with progress against the underlying causes of inequality in SARS-CoV-2 mortality rates. To understand why, a simple thought experiment is instructive: If these inequities are downstream effects of racial capitalism—that is, a system that extracts material benefits from those racialized as nonwhite for the benefit of those considered white [50]—can we expect they will not reappear when the next highly virulent, very transmissible pathogen emerges?

As we continue to confront emerging infections of varying severity, there is no evidence that the structural inequities that set the table for the disparities in death from COVID-19 documented here have lessened since early 2020 [51]. In fact, it is likely that the social and economic inequities that made minoritized communities more vulnerable to SARS-CoV-2 infection in the earliest days of this pandemic have been exacerbated by its effects [52, 53]. Taken as a whole, our results suggest that addressing these inequities using every social and public health policy lever at our disposal must be a key focus of preparedness for future outbreaks, epidemics, and pandemics.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Data availability. All code will be made available on a public GitHub repository. The data used in this analysis are confidential and cannot be shared.

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