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ABSTRACT:

The 1918 influenza pandemic stands out for its extreme virulence and unusual age pattern of mortality. Here, we aim to elevate a third unusual feature of its course through United States cities to the same level of scientific prominence: the pandemic produced strikingly small racial disparities in mortality, against a backdrop of extreme racial inequality in the era. We provide the most complete account of racial disparities in influenza and pneumonia mortality in U.S. cities in 1918, showing that they were almost uniformly small. We also advance and evaluate four hypotheses as to why racial disparities in the 1918-1919 pandemic were so small relative to those in proximate years. In particular, we assess hypotheses related to socio-demographic characteristics like segregation, city-level implementation of non-pharmaceutical interventions, racial differences in exposure to the 1918 herald wave, and racial differences in early-life exposures to other influenza strains that could have resulted in differences in immunological vulnerability to the 1918 flu. The results suggest the importance of considering in depth the interactions between the natural history of a particular microbial agent and the social history of the populations it infects.

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Among influenza pandemics, the 1918 "Spanish flu" pandemic was distinctive for at least three reasons. Two of those reasons are well known. First, the pandemic was immensely destructive. The 1918 flu was extremely virulent, with estimates indicating that it killed between 50–100 million globally and roughly 675,000 in the United States. A second distinctive feature of the 1918 pandemic was the unique "W-shaped" age pattern of those it killed, hitting young adults in their late 20s and early 30s particularly hard, alongside the more universally vulnerable very young and very old. The third factor that distinguishes the 1918 pandemic from other pandemics, particularly in the context of the United States, is less well known. Against a backdrop of extreme racial inequality in the early twentieth century, racial disparities in influenza mortality during the 1918 pandemic were notably small. This is surprising for several reasons. During the early twentieth century, racial disparities in infectious disease mortality were extraordinarily large (Feigenhaum et al. 2019; Wrigley-Field 2020). Socially marginalized and oppressed groups, including poor people and communities of color, were also likely to experience comparatively high mortality rates during epidemics. And cities' responses to the 1918 pandemic were explicitly racist. For example, some cities in both Northern and Southern states organized whites-only clinics and pandemic hospitals (Bristow 2012:72). Given this historical context, what explains the small racial disparities in 1918?

The unique racial impact of the pandemic was widely recognized in 1918. Health officials in Chicago noted that race-specific incidence counts were "quite contrary to what would have been expected" (Schlabach 2019, 41), and one prominent Black reverend proclaimed that God had been trying "to show [the white man] the folly of the empty conceit of his vaunted race superiority, by dealing with him just as he dealt with the peoples of darker hue" (Bristow 2012:73). Mortality tables constructed in the immediate wake of the pandemic also noted large excess white mortality and low racial disparities (Frankel and Dublin 1919). However, these racial disparities have received little attention in the subsequent scholarly literature despite being so distinctive. Studies tend to rely on anecdotal evidence from newspapers and public health reports but do not systematically measure racial disparities during the 1918 pandemic (Gamble 2010; Schlabach 2019). The most comprehensive survey of race-specific 1918 mortality rates (Økland and Mamelund 2019) finds that Black individuals likely experienced lower mortality rates but higher morbidity rates than whites during the critical fall 1918 months, when that pandemic was most severe in the United States (Økland and Mamelund 2019).

The causes of such disparities largely remain unclear. Building on a hypothesis originally advanced by Crosby (2003), Økland and Mamelund (2019) suggest that Black individuals may have been disproportionately exposed to a less deadly "herald wave" in the spring of 1918, which could have provided partial immunity against the deadlier fall wave. Segregation may also have functioned as an accidental *cordon sanitaire* that spatially insulated nonwhite communities against centers of infection (Schlabach 2019). But "shockingly sparse" data has prevented the empirical verification of such speculative hypotheses and has restricted scientific studies of the patterning and determinants of disparities induced by the 1918 pandemic (Krishnan et al. 2020, 474; Gamble 2010).

In this study, we aim to elevate scientific understanding of the distinctive racial patterning of influenza mortality in 1918-1919 to the same level of prominence as the other distinctive traits of that pandemic. To do this, we advance two aims. First, we provide the most complete account of racial disparities in influenza and pneumonia mortality in U.S. cities in 1918. Second, we advance and evaluate four hypotheses as to why racial disparities in the 1918-1919 pandemic were so small relative to those in proximate years. In particular, we assess hypotheses related to socio-demographic characteristics like segregation, city-level implementation of non-pharmaceutical interventions, racial differences in exposure to the 1918 herald wave, and racial differences in early-life exposures to other influenza strains that could have resulted in differences in immunological vulnerability to the 1918 flu. We describe the models used to evaluate each hypothesis below and include a detailed discussion of our city-specific data in the appendix.

Consistent with previous findings (Gamble 2010; Schlabach 2019; Økland and Mamelund 2019; Krishnan et al. 2020), we show that racial disparities in influenza and pneumonia mortality were, indeed, strikingly low for the period. Our results further seem to rule out the hypotheses that segregation and non-pharmaceutical interventions—like school closures and quarantines—reduced disparities. Instead, our findings tentatively support two competing immunological hypotheses that draw on the unique migration and public health experiences of Black and white urban populations as well as the specific virology of the 1918 influenza to produce racial differences in influenza mortality.

Our results offer a basic framework for analyzing racial disparities in infectious disease mortality that is widely applicable to a variety of periods, contexts, and microbes. We argue that

the mortality signature observed in the 1918 pandemic reflects the intersection of racially patterned social exposures in the population with the contingent natural history of the particular microbe. We thus treat racial categories not as ready-made facts but as social and political constructs that serve as proxies for the distinctive social histories of different groups. And we suggest that understanding the patterns and drivers of racial disparities in infectious disease mortality requires examining how structural and institutions arrangements shape social and microbial exposures over time in ways that produce differential risk of mortality to infectious agents.

Describing Black and White Influenza and Pneumonia Morality in 1918

The 1918 pandemic occurred in the context of extreme racial inequality in infectious disease mortality in the United States. Prior to 1918, nonwhite residents across U.S. cities were more than twice as likely to die from influenza and pneumonia as white residents. But during the 1918-1919 pandemic, the ratio of nonwhite to white mortality was around three-fourth smaller than in previous years. This sudden decline in mortality disparity reflects the fact that, on average, non-white flu deaths in 1918 were around three times the pre-pandemic average—while white flu deaths were five times the pre-pandemic average.

The median non-white/white flu mortality ratio was 1.35 in 1918, compared with 2.33 over the pooled years 1910-1917. Equally striking to the small disparities is their notably small variation across cities. We illustrate this in Figure 1. Racial disparities in 1918 were uniformly small. The 1910-1917 median standard deviation in nonwhite/white ratios across 71 cities was 1.11, yet it shrunk to 0.32 in 1918.

The reduction in disparities occurred across the age distribution, as shown in Figure 2. There was one exception: the oldest 70+ years age category, where there was little racial disparity in flu deaths in either pre-pandemic years or in 1918. This mortality convergence with age might reflect the operation of selective mortality, particularly given the high nonwhite mortality rates of this era. Still, the decline in overall disparities was driven especially by a mortality convergence among those aged 10-19, 20-29 and 30-39. These three groups had the highest pre-pandemic disparities—with the nonwhite/white ratio scale measuring 4.48, 4.15 and 3.39 respectively—but had among the smallest disparities in 1918. Compared to 1910-1917, racial disparities in 1918 declined by 78 percent in the 10-19 age group, by 95 percent in the 20-

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29 age group, and by 98 percent in the 30-39 age group. This decline in racial mortality disparities is especially striking because nonwhites were over-represented in age groups that experienced a notably high mortality in 1918, while whites were over-represented among the very young and the very old — age groups that had high pre-pandemic mortality but did not experience comparable mortality spikes during the pandemic.

In absolute terms, children aged 0-10 and seniors aged 60-69 and 70+ had the highest mortality in pre-pandemic years, as well as in 1918. For seniors, nonwhite mortality was roughly comparable to white mortality. But nonwhite children aged 0-10 were more likely to die from influenza and pneumonia than white children in pre-pandemic years, and remained at greater risk in 1918. Because of this high absolute mortality, most of the relative nonwhite/white disparity can also be traced to absolute mortality differences among the very young. Nonwhite children aged 0-10 experienced a median of 890 deaths per 100,000 during the pooled 1910-1917 years and a median 1571 deaths per 100,000 in 1918, compared to a pre-pandemic median of 268 deaths and a pandemic median of 608 deaths for white children.

In contrast, high mortality for those aged 10-39 was a distinctive feature of the 1918 flu, regardless of race. Figure 3 shows that average non-white mortality in this age range grew from 156 deaths per 100,000 people in pre-pandemic years to 732 deaths in 1918, and average white mortality increased from a negligible 42 deaths per 100,000 people to 627 deaths. In the group that experienced the largest proportional mortality increase during the 1918 pandemic—whites aged 20-29—mortality was almost 20 times higher in 1918 than in the pooled 1910-1917 years.

Potential Explanations: City-Level Organization and Action

A. Segregation: Levels of infectious disease mortality are widely understood to depend on local socio-demographic characteristics, although the exact associations and causal mechanisms vary by disease and location (Waitzman and Smith 1998; Hart et al. 1998; Bonds et al. 2010; Valleron et al. 2020). Building on this literature, several studies suggest that residential segregation may have offered temporary protection to nonwhite communities during the 1918 pandemic if they were physically and socially distanced from hotspots of community transmission (Schlabach 2019; Krishnan et al. 2020). Because viral transmission was often localized during the pandemic (Grantz et al. 2016), such distancing may have been sufficient to reduce nonwhite exposure and subsequent nonwhite deaths, thereby driving down mortality disparities.

We assess the association between socio-demographic indicators and mortality during the 1918 pandemic as well as during pre- and post-pandemic years. For each year between 1910 and 1930, we construct a series of race-independent and race-specific bivariate and multivariate linear models that include logged mortality, logged baseline mortality (in 1918 only), city- and race-specific measurements of illiteracy and residential density, and city-specific segregation indices. Because our priors suggest that infectious disease mortality may have been generally correlated with factors like poverty and residential density in the early twentieth century, we test not only whether such associations existed during the pandemic but also whether they were significantly different in 1918 than in other years.

We find that total and race-specific mortalities during pre-pandemic years are strong predictors of 1918 mortality and excess mortality. Cities and racial communities that were generally vulnerable to infectious diseases remained so during the pandemic. Yet we find no evidence that segregation or residential density predict race-specific mortality or excess mortality during the pandemic. Race-specific illiteracy rates have some predictive power in 1918, but their regression coefficients are statistically indistinguishable from coefficients recorded during non-pandemic years. This suggests that city characteristics and socio-demographic indicators may be more useful for explaining the general levels of infectious disease mortality in a given city, rather than the specific mortality patterns and mortality disparities of the 1918 pandemic.

B. Non-pharmaceutical interventions (NPIs): During the fall 1918, many American cities implemented non-pharmaceutical interventions (NPIs) to contain the spread of infections. These included the closure of schools, theaters, and bars, bans on gatherings in public places, and the forced quarantine of infected persons. Cities that implemented NPIs early and sustained them until the end of the pandemic tended to experience lower weekly mortality peaks and lower overall mortality than cities that delayed NPIs or lifted them prematurely (Markel et al. 2007; Hatchett et al. 2007).

Because nonwhite populations had a much higher baseline risk of infectious disease mortality, those NPIs may have disproportionately benefitted nonwhites, thereby driving down mortality disparities. This hypothesis is similar to Troesken's (2004) argument that water and sewage improvements in Southern cities disproportionately benefitted Black individuals due to their higher risk, absent such improvements, of waterborne disease. We that cities with early and

sustained NPIs experienced lower mortality disparities (measured once again in ratio scale) in addition to lower total mortality.

We assemble a dataset of city-specific quarantine orders, school closures, and bans on public gatherings from historical newspaper data. We then construct race-independent and race-specific models with logged 1918 mortality, the duration of NPIs in days, the delay of NPI implementation from the first locally recorded infection in days, and the counterfactual baseline mortality for each city, calculated from 1910-1017 mortality trends for each city. Like prior studies (Markel et al. 2007; Hatchett et al. 2007), we find that lower NPI delays were associated with lower total mortality. Yet we find no statistically significant effect of NPI onset or NPI duration on mortality disparities or race-specific mortality (FIG. 4) This finding holds when substituting NPI data gathered by Markel et al. (2007) for our original data, when using monthly mortality measures instead of annual mortality, and when controlling for the age composition of each city. It thus appears unlikely that the unexpectedly low mortality disparities during the 1918 pandemic were due to the racially disparate impact of ostensibly race-neutral measures like NPIs.

Potential Explanations: Social Immunology

We consider a variety of potential explanations for small racial disparities drawing on the unique life course histories of infectious disease exposure among urban white and non-white populations of this era. These potential explanations are elaborated in Table 2 as six hypotheses that fall into two broad types. The first three hypotheses in Table 2 (H1-H3) posit that disparities in 1918 are small because nonwhite populations were more likely to have had a prior exposure that was protective; the second three (H4-H6) posit that disparities in 1918 are small because white populations were more likely to have had a prior exposure that was harmful. Collectively, these hypotheses build on the distinctive social histories of exposure of each racial group. The urban white population of this era was a mixture of immigrants from abroad, children (many now grown) of earlier immigrants, and some internal migrants, particularly through westward expansion. In contrast, nonwhite urban residents had often migrated from rural Southern areas (low exposure) where they spent their childhood, into Southern and Northern cities where they were forced, by law and by violence, into intensely crowded, filthy, and dangerous conditions (very high exposure). This combination of relatively low early exposure followed by intense exposure after urban migration, allows for the mix of protective and harmful exposures hypothesized in Table 2.

The partial immunity hypotheses (H1-H3) are organized in Table 2 in order of how early that exposure may have begun. Among this class of hypotheses, we focus on testing H1 since its predictions are the most clearly delineated, as well as being the focus of prior literature; we use this hypothesis as a stand-in for the broader mechanism of protective immunity that may have operated over prior years in some cities, where flu and pneumonia measures would capture a mixture of the 1918 virus (if in fact it was there) with other seasonal strains.

The immunological imprinting hypotheses, and more broadly the hypotheses that small racial disparities reflect greater early-life exposure to the 1890 flu among whites (H4-H6), are organized in Table 2 by how old the cohorts who may have been affected were. Because these hypotheses make distinctive predictions about which cohorts should have been affected, they can be partially tested through analyses of the age pattern of mortality in 1918, and they offer the enticing possibility of a consilience between two of the most striking features of the 1918 pandemic: its unusual age shape and its small racial disparities.

C. Partial immunity: Although the overwhelming majority of 1918 influenza deaths occurred in the United States between September and December, several studies have suggested that a less lethal flu strain began circulating during an earlier "herald wave." Beginning in February or March, this wave led to a mortality increase in excess of normal seasonal mortality fluctuations (Patterson and Pyle 1991; Olson et al. 2005; Hoffman 2011). Crosby (2003) has speculated that exposure to this herald wave may have primed the immune system for a more efficient response during the fall. Nonwhite communities may also have been disproportionately exposed to this herald wave because they were more likely to live in overcrowded housing and had lower access to medical care than white communities (Mamelund 2018; Økland and Mamelund 2019). In this scenario, partial immunity induced by the herald wave would also explain the comparatively small mortality disparities during the fall because it made nonwhite individuals disproportionally resistant (Crosby 2003, 229).

While the partial immunity hypothesis has been widely cited as a potential explanation for low racial disparities in 1918, it has – to our knowledge – never "been theoretically or empirically substantiated" (Økland and Mamelund 2019, p. 1). We test it by answering two questions: First, were nonwhite communities more affected by the herald wave than white communities? Second, was greater exposure to the herald wave associated with lower mortality during the main

pandemic? We expect to find high nonwhite/white disparities during the spring as a result of differential spring exposure, and we also expect a race-independent association between spring and fall mortality. Cities with a more severe herald wave should have experienced a less severe pandemic.

C.1 Differential spring exposure: Cities that experienced high influenza mortality during the 1910-1917 period were significantly more likely to experience high mortality during the 1918 herald wave. This finding is robust to changing definitions of the herald wave's onset and duration, and it holds for total mortality and separately for nonwhite and white mortality. But in addition to this city-specific mortality penalty, nonwhites also experienced a more severe herald wave than whites. Compared to the period 1910-1917, median nonwhite mortality increased by 50% while median white mortality increased by 30%. As a result, the median nonwhite/white mortality disparity in the spring of 1918 was 2.79, compared to 2.43 during the period 1910-1917. This made the spring of 1918 among the most unequal periods recorded in our pre-pandemic data, tying mortality disparities observed during the 1912 spring wave and exceeding disparities during the (least unequal) 1915 spring wave by 42%. This disproportionate exposure of nonwhite communities may be due to overcrowded living conditions and poor health, both of which disproportionately affected nonwhites during the early twentieth century (Crosby 2003). We do not systematically explore the causes of differential spring exposure but note a statistically significant association between illiteracy and herald wave mortality. This broadly tracks with Crosby's (2003) emphasis on community-specific social conditions as a key driver of mortality levels, as well as with the findings by Grantz et al. (2016) that higher mortality in Chicago was associated with greater illiteracy at the census-tract level.

C.2 Spring/fall association: The partial immunity hypothesis predicts that cities that experienced greater mortality in the spring should experience lower excess mortality during the fall because their populations were partially immune to the pandemic viral strain. Yet we find the association between spring and fall mortality to be small and statistically indistinguishable from zero. This finding holds when controlling for two factors that may have affected pandemic mortality within each city: the onset and duration of NPIs and the percentage of residents aged 20-39, which was the age group that was experienced the greatest excess mortality in 1918. Our null finding is also robust to changes in the dependent variable, e.g. using absolute mortality rather than

excess mortality; to a substitution of NPI data taken from Markel et al. (2007) for our original data; and to a stratification of our model into multiple tiers of herald wave severity.

Crosby's own data produces similar results as well. Using mortality data published in the appendix to Crosby (2003) for 45 cities, we observe a positive relationship between mortality during the first eight months of 1918 – the herald wave – and mortality during the final four months of the pandemic. This is contrary to the negative association predicted by the partial immunity hypotheses and holds, once again, when controlling for age composition and NPIs.These findings make it seem unlikely that higher partial immunity among the nonwhite population as a result of herald wave exposure explains mortality disparities during the pandemic. However, we find a significant difference in the *race-specific* associations between spring and fall for nonwhites and whites (FIG. 5). For nonwhites, the association between spring and fall mortality is smaller than for whites and, depending on the specifications of the model, negative. For whites, it is positive. This variation in the sign of the conditional association between spring and fall wave mortality leads to multiple possible interpretations, particularly in light of the lack of common support visible in Figure 5: the distributions of spring wave mortality in white and nonwhite urban populations barely overlap. This makes it possible that potential immunity mechanisms operate within a restricted range that is only discernible at the population level in nonwhite populations, given their substantially greater exposure. It is also possible that these differences are merely noise, given the relatively small size of our dataset.

But Økland and Mamelund (2019) also hint at an alternative hypothesis that is compatible with the observed race-specific associations. Because the regular hospital system often refused to admit African-Americans or triaged them into sub-standard care during the early decades of the twentieth century, public health campaigns in nonwhite communities tended to rely more heavily on community-based prevention and education (Gamble 2010; Schlabach 2019; Krishnan et al. 2020). So-called "health weeks" sought to raise awareness about sanitation and infectious disease prevention. Those initiatives, as well as the persistent experience of high infectious disease mortality in nonwhite communities, may have contributed to behavioral changes and greater lay knowledge about infectious diseases in urban nonwhite communities. Because mainstream newspaper coverage largely ignored the herald wave and initially played down the severity of the pandemic (Crosby 2003), it is plausible that behavior during the pandemic was shaped by such community knowledge rather than concurrent mainstream media coverage. Thus, herald wave

exposure may have mattered because it precipitated greater vigilance among nonwhite communities that were most heavily affected during the spring of 1918, not necessarily because it conveyed partial immunity.

D. Immunological imprinting

The possibility that early-life exposure to the 1890 influenza virus may have increased the likelihood of cytokine storms following exposure to the 1918 virus has been advanced as a possible explanation of the unusually high mortality among young adults in 1918 (Luk et al. 2001, Mamelund 2011, Gagnon et al. 2013, Hallman 2015). For example, one version of this hypothesis holds that the combination of antigenic similarities and differences between the 1890 and 1918 viruses led those whose immune systems had been "imprinted" through early exposure to the 1890 virus to respond to the 1918 virus with a dysregulated immune response characterized by an abundance of antibodies that could not neutralize that virus, crowded out a more effective immune response, and produced deadly tissue damage. The canonical version of this hypothesis (H5) is an "original antigenic sin" (OAS) account (Francis 1960, Zhang et al. 2019) in that it purportedly occurs specifically among those whose *first* flu exposure (after losing maternal antibodies around six months of age) was to the 1890 flu; an alternative (H6) also allows childhood exposure to the 1890 virus to "refocus" the immune system to produce an OAS-like response even if the 1890 virus was not the individual's first flu exposure (Gagnon et al. 2015). We extend these hypotheses to potentially account for the small racial disparities in 1918 as well as the elevated young adult mortality, in light of the distinctive social and geographic histories of the urban white and nonwhite populations—specifically, the disproportionately rural origins of the urban nonwhite population in 1918.

No direct measure of exposure to the 1890 influenza virus is available, so as an alternative, we conduct several suggestive tests of hypotheses based on the idea that white populations had greater early-life exposure to the 1890 virus. One test uses urban origins as a proxy for greater likelihood of 1890 flu exposure during childhood; another set of suggestive tests exploits the cohort exposure patterns implied by each of hypotheses H4-H6. Broadly, these hypotheses imply that relatively small racial disparities in the aggregate n are driven by small disparities in the age bands that had the most notably high mortality: those in their 20s and 30s in 1918. Figure 2 showed that this is the case: the small disparities are driven by strikingly high

mortality among urban whites in their 20s and 30s. However, H4-H6 make different assumptions about the upper limit on the ages that should be affected; indeed, the hypothesis that small disparities are driven by fetal exposure to the 1890 virus (H4) cannot account for small disparities in 30-39 age category. In what follows, we focus on the immunological imprinting hypotheses (H5-H6).

D1. *City-level variation in urban origins as a proxy for 1890 flu exposure*. It is indeed the case that the urban white population had more urban origins than the urban nonwhite population in 1918. Among cohorts aged 20-39 in 1918 and residing in cities in 1910, we estimated the national proportion born in cities at nearly half of the nonwhite population compared to nearly two-thirds of the white population, and the non-white and white proportion born in cities of at least 100,000 residents (whose flu exposure may have been heightened) at around one-fifth or more than one-third, respectively (though these estimates reflect substantial uncertainty due to a relatively small number of individuals who could be linked through time; details are in the Supplemental Appendix). We tested whether this estimated city-level variation in the portion of the total, white, and nonwhite populations with urban origins was associated with greater 1918 mortality in total and in the 20-29 and 30-39 age groups, with and without controls for NPI timing and duration. This association is in the expected direction (i.e., more residents with urban background is associated with greater mortality) in all twelve models, but is statistically significant only for whites aged 20-39 without adjusting for NPIs (full regression results are reported in the Supplemental Appendix). Given the small samples and imprecise measures, we consider these results to be broadly suggestive but hardly definitive.

D2. *Simulated individual-level effect sizes*. We simulate cohort mixtures of imprinted and non-imprinted individuals to answer two questions, with the aim of deriving implications of the immunological imprinting hypotheses. First, to generate the observed age-group-specific, race-specific mortality rates, how high would the mortality of the imprinted individuals need to be, as a function of how many are imprinted in each cohort? Assuming an upper limit on "reasonable" mortality rates imposes a lower limit on what portion of this age group must have been imprinted. When combined with assumptions about how many cohorts were partially imprinted, this also generates lower limits on within-cohort imprinting. Second, what rates of exposure to previous flus could generate these cohort imprinting rates? High rates of imprinting imply high rates of 1890 exposure and either low rates of prior H1N1 exposure or high rates of

immunological refocusing. The simulated answers to the second question, in particular, are exploratory. Our goal is not to provide any definitive evaluation of these hypotheses, but rather, by clarifying their implications, to construct a foundation that would allow them to be evaluated in future historical virological work.

To address the first question, we first leverage the sharper age cutoff in the 20-29 age group: individuals who were younger than 25 in 1918 were too young to have been exposed to the "Russian" flu, without maternal antibodies, in 1890-1893. Given the enormity of mortality in the 20-29 age group, we estimate that this restriction implies very large effects indeed: to account for the observed aggregate mortality, 1890 imprinting would need to increase mortality by a factor of at least 1.9 in nonwhite populations and 3.75 in white populations. Constraining the individual-level effect to be on the smaller end of the range of effect sizes essentially implies that the cohorts aged 25-29 had close to universal 1890 imprinting among urban white individuals. For example, urban white people aged 25-29 who were imprinted by the 1890 virus in childhood would have had greater mortality than urban white people aged 70+ in 1918, unless at least 85% of urban whites in the 25-29-year-old cohorts had been imprinted. Since the mortality jump in the 20s and 30s, compared with surrounding age groups, is smaller in the nonwhite population, this same constraint is compatible with a far greater range of 1890 cohort imprinting, ranging below 60%.

How many cohorts in the 30-39 age range could have experienced immunological imprinting depends on whether an immunological refocusing mechanism operated (H6 vs. H5), i.e., whether the effect also operated in some children who had already been exposed to a different flu strain. If the substantially elevated white mortality in this age group in 1918 is explained by imprinting without refocusing, we estimate that, for the urban white population, exposure must have been essentially universal in the youngest several cohorts in this age range.

To provide some rough, exploratory calibration of the flu exposure rates implied by these cohort exposures, we simulated annual childhood rates of exposure to H1N1 strains before 1890 for urban and rural populations, exposure to the 1890 virus in 1890-93 for urban and rural populations, and immunological refocusing (including 0%, as implied by H5). Figure 6 shows the exposure rates implied by 85% cohort exposure. These simulations suggest that, for immunological imprinting to account for the dramatic spike in white young adult mortality, the either the rate of exposure during the 1890-1892 pandemic, or the rate of immunological

refocusing given exposure in that pandemic, must have been very high—though not outside the boundaries of pandemic (Matthews et al. 2009:147; Saunders-Hastings and Krewski 2016:7) and seasonal (Chunara et al. 2015) influenza attack rates.

Discussion

Analyses of race-specific city-level mortality data suggest that racial disparities during the 1918 pandemic were uniformly small -- and around three-fourth smaller than during pre-pandemic years -- driven primarily by high excess mortality among whites aged 20-39. While this unique racial signature was well known in the wake of the 1918 pandemic, it remains surprising for several reasons. During the early twentieth century, racial disparities in infectious disease mortality were staggeringly large. The risk of death from infectious disease among Black Americans was so high that it explains much of the observed variation in infectious mortality across US cities during the first decades of the twentieth century (Feigenbaum et al. 2019). Public health responses to the pandemic were also steeped in racism and routinely provided sub-standard care to nonwhite communities (Bristow 2012), which could have translated into high excess mortality among nonwhites.

Prior works present several hypotheses to explain uncommonly low pandemic disparities, although none test these hypotheses systematically. In this study, we are able to leverage race-specific mortality data and city-level variables for up to 70 cities to shrink and refocus the space of plausible explanations. Our findings suggest that two of the most frequently cited hypotheses – disproportionate partial immunity in nonwhite communities as a result of higher exposure to a spring herald wave, and reduced exposure as a result of residential segregation – do not explain city-level disparities during the pandemic. We also find that non-pharmaceutical interventions like school closings, which have been shown to reduce overall mortality, do not explain low mortality disparities.

Instead, our findings suggest that the unique migration and public health histories of nonwhite and white populations may have intersected with the virology of the 1918 influenza strain to produce high excess mortality among whites between the ages of 20 and 39 and partially explain unexpectedly low mortality disparities. The disproportionately urban origins of urban white young adults in 1918, compared to urban non-white young adults who had frequently migrated from rural areas, may have resulted in differential exposure to the 1890 flu pandemic

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during critical childhood developmental windows and produced a unique vulnerability in 1918. However, our simulations suggest that, for this mechanism to have accounted for the extremely high 1918 mortality among white young adults, immunological imprinting must have been extremely widespread in key cohorts. In addition to this hypothesized immunological imprinting in the white population, nonwhite communities may have experienced comparatively low excess mortality as a result of behavioral adjustments that reduced their exposure to infectious disease agents in the fall of 1918. Excluded from the regular public health system but accustomed to high infectious disease mortality, nonwhite populations regularly relied on community-based education and prevention to reduce infections and may have been more circumspect during the pandemic (Schlabach 2019, Krishnan et al. 2020). While our data do not allow us to test this hypothesis directly, our findings of a race-specific association between pre-pandemic exposure and pandemic mortality offer suggestive support to explanations that highlight such behavioral pathways.

In 1918, public health officials attempted to explain low mortality disparities with essentialist logics and racial pseudo-science that cast nonwhite populations as naturally immune to infectious diseases. Subsequent scholarly work takes a very different perspective and focuses on race-specific immunological histories and the spatial geography of urban life. Our findings build on this literature, but they also allow us to sketch a perspective on race and infectious disease mortality that explicitly draws attention to the interplay between the macrosocial histories of different groups and the microbiological characteristics of epidemics. We argue that explaining health outcomes during the 1918 pandemic requires an awareness of the immunities and vulnerabilities that different groups may have accumulated prior to such a pandemic due to disparate exposure or disparate access to healthcare. This also suggests that simplistic comparisons between 2020 and 1918 may be misguided, because the virological features of COVID-19 and the historically rooted vulnerabilities of different social and racial groups may differ from those of the early twentieth century.

Materials and Methods

We integrate several data sources that allow us to examine racial disparities across the United States, including a series of annual race-specific and cause-specific mortality rates for 70

American cities that is based on annual death counts collected by the Department of Commerce (Feigenbaum et al. 2019), supplementary datasets with age-specific and monthly mortality rates for a smaller number of cities (n=21), and measures of an array of city characteristics and public health responses to the pandemic.

The historical *Vital Statistics* reports that we draw on for all mortality data report death counts. To convert these into death rates, we estimate race-specific, age-specific populations for each city. Because the 1920 Census likely reflected substantial population distortions resulting from the pandemic, we avoid drawing on that Census in constructing our population denominators. Instead, our main measure interpolates populations from 1910 to 1930. Since that measure may be distorted by altered migration patterns in the 1920s compared to the 1910s, we also construct an alternative measure based on estimating population sizes from non-infectious death counts, which were reported annually. These measures, which make very different assumptions, evince relatively close agreement: for example, the alternative measure estimates the non-white/white ratio of flu and pneumonia mortality at 1.19 in 1918 (vs. 1.35 with our main measure) and 2.17 in 1910-1917 (vs. 2.33).

The *Vital Statistics* report deaths in "White" and "Colored" populations. In this era, the latter non-white populations in cities were overwhelmingly Black, and we interpret them as a measure of Black mortality.

We combine mortality data with a wide array of city- and race-specific measures of segregation, residential density, illiteracy, air pollution, age composition, the percent of urban-born residents, and the onset and duration of NPIs. NPI data were collected from a qualitative survey of historical newspaper records, while other variables come from full-count census microdata (via IPUMS-USA [Ruggles et al. 2020]) and several prior studies (Crosby 2003; Markel et al. 2007; Clay et al. 2018).

We use these data to construct a series of bivariate and multivariate models that specifically test the predictions of each hypotheses and control for variables like illiterary and age composition, which are known to affect infectious disease mortality in the United States. To test the immunological imprinting hypothesis, we also develop a set of simple simulations that evaluate the effects of 1890 flu exposure on the magnitude of age-specific mortality in 1918. Details of all data sources, measures, statistical models, and simulations are given in the

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Supplemental Appendix. Data and software code are available at [posted upon journal submission].

Tables and Figures

TABLE 1:

	log(mortality_1)		log(mortality_ratio_1)
	(1)	(2)	(3)
NPI duration	0.005	0.004	0.0001
NPI delay	0.049*	0.053	0.009
Race dummy		-0.077	
log(city baseline mortality)	0.716***	0.508***	-0.428**
NPI duration * delay	-0.001	-0.001	-0.0001
NPI duration * race		0.004	
NPI delay * race		0.008	
NPI duration * delay * race		-0.0002	
Constant	2.327***	3.387***	2.436**
N	34	68	34
R2	0.618	0.501	0.268
Adjusted R2	0.565	0.433	0.167
Residual Std. Error	0.259 (df = 29)	0.319 (df = 59)	0.321 (df = 29)
F Statistic	11.732*** (df = 4; 29)	7.402*** (df = 8; 59)	2.657 (df = 4; 29)

*p < .05; **p < .01; ***p < .001

Table 1. Results of modeling race-specific mortality (Columns 1 and 2) or racial disparities (Column 3) on non-pharmaceutical interventions.

Hypothesis	Prior exposure protective or harmful?	Which prior exposure?	Exposure in which years?	Youngest cohort likely to be affected	Oldest cohort likely to be affected	Canonical citations
H1: Spring wave	Protective	1918 flu	1918	No limit	No limit	Crosby (2003), Okland and Mamelund (2019)
H2: Early "1918" flu	Protective	1918 flu	1915-1918	No limit	No limit	Worobey (2019)
H3: H1N1 partial immunity	Protective	Any H1N1 virus	1900-1918 and pre-1889	No hard limit, but 1889-99ish; older is more plausible	No hard limit, but younger is generally more plausible	Worobey et al. (2014)
H4: Fetal harms	Harmful	1890 flu ("Russian")	1889-1893	1894 birth	1890 birth	Gagnon et al. (various)
H5: Original antigenic sin (immunological imprinting)	Harmful	1890 flu ("Russian")	1889-1893	1892 or 1893 birth?	~1885 birth? Younger is more plausible	Gagnon et al. (various)
H6: Original antigenic sin plus immunological refocusing	Harmful	1890 flu ("Russian")	1889-1893	1892 or 1893 birth?	1879-1880 birth?	Gagnon et al. (various)

Table 2. Social immunology hypotheses purporting to explain small racial disparities in 1918 urban pandemic mortality based on greater non-white protective exposure to earlier flu viruses (H1-H3) or greater white harmful exposure to earlier flu viruses (H4-H6).
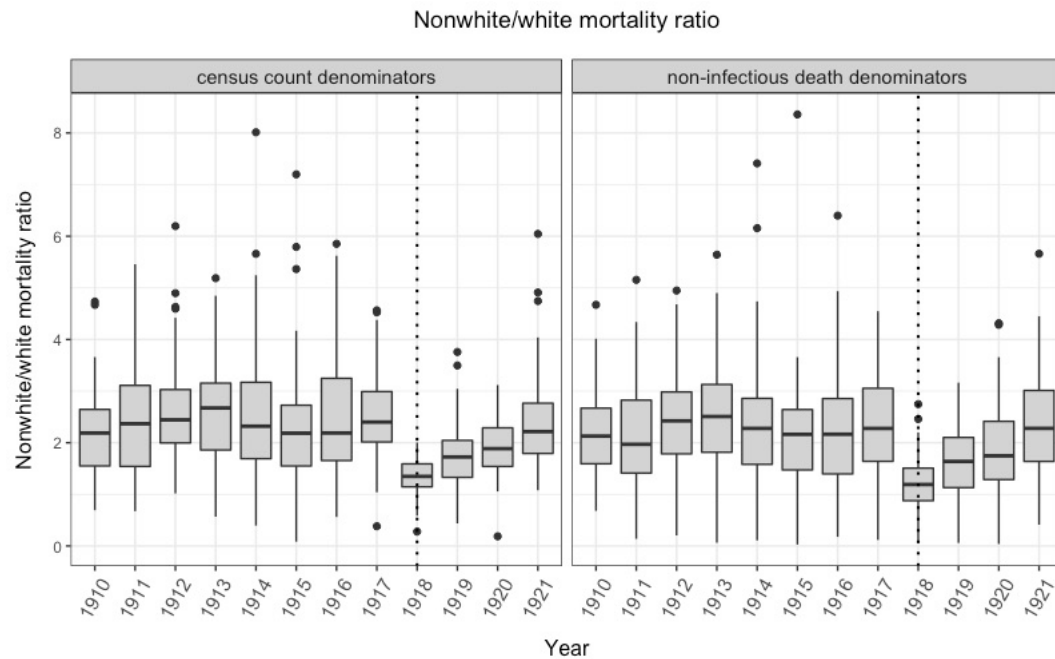
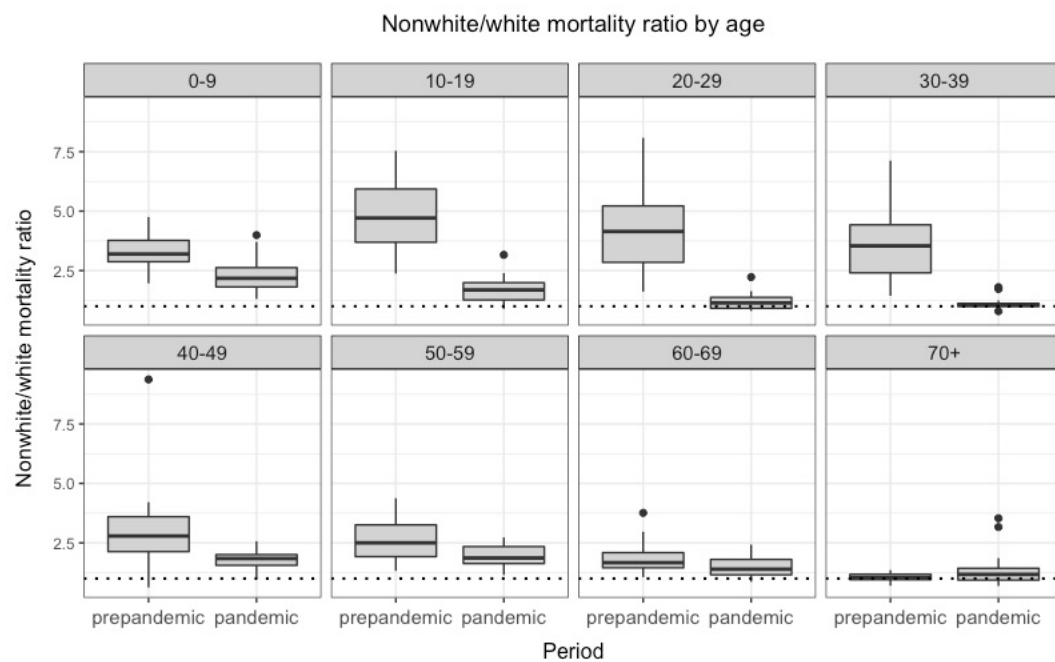Figure 1. Nonwhite/white influenza and pneumonia mortality ratios (with two alternative measures)

Figure 2. Pre-pandemic and 1918 (pandemic) nonwhite/white mortality ratios.
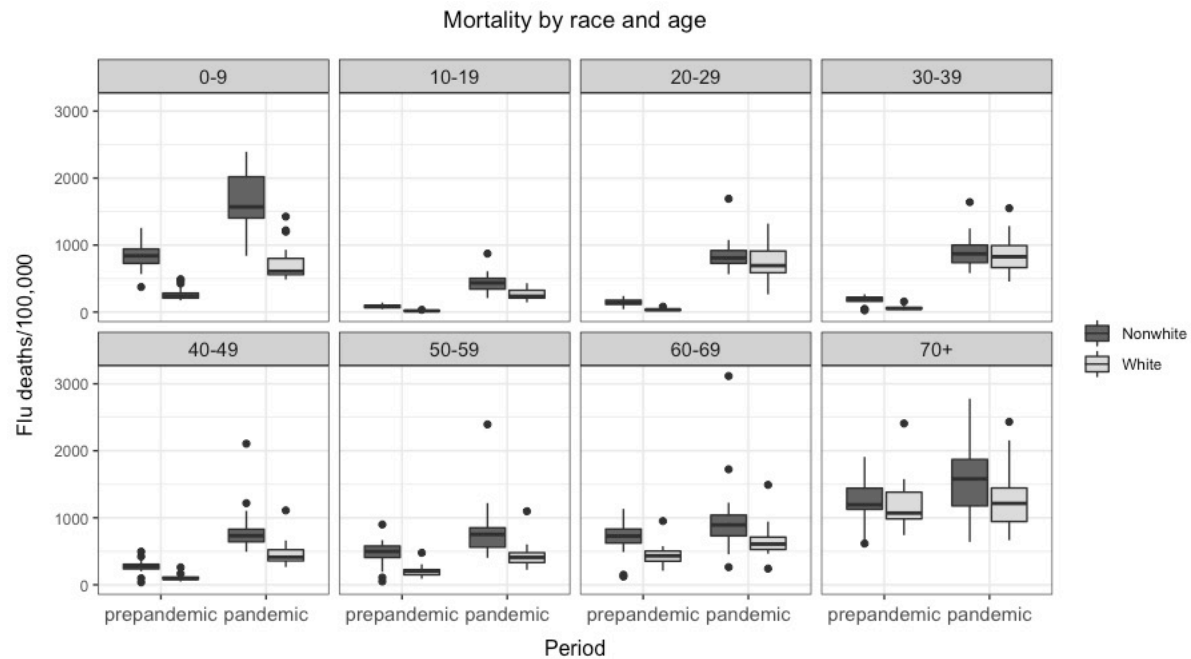
Mortality by race and age

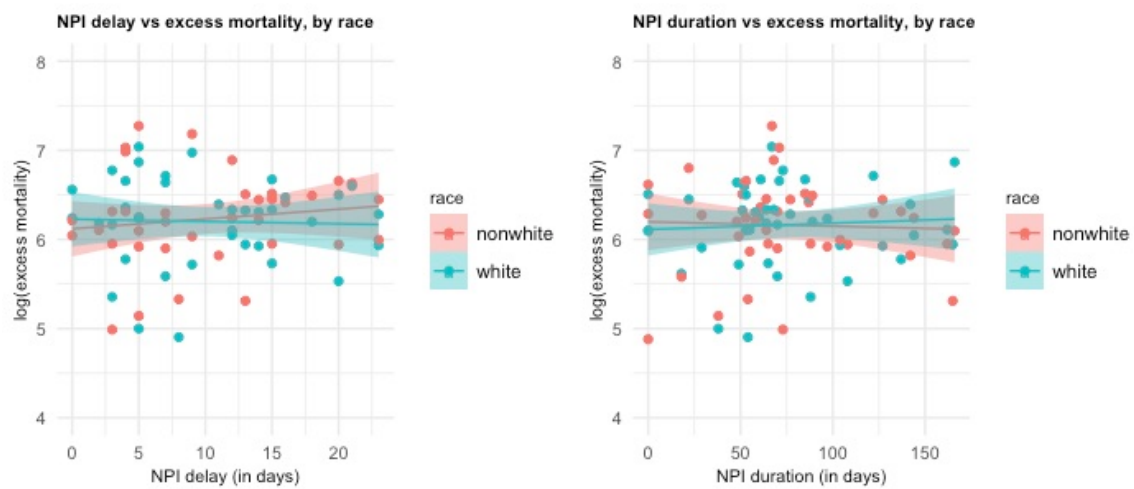Figure 3. Race-specific, age-specific mortality.

Figure 4. Race-specific 1918 mortality as a function of non-pharmaceutical interventions (NPIs).
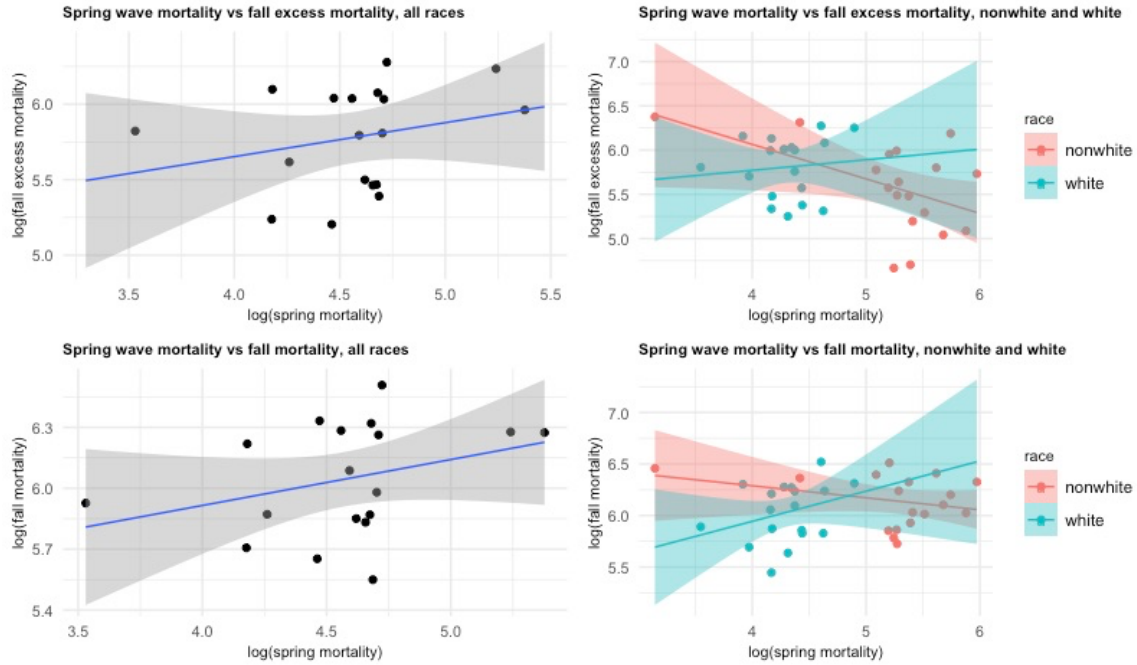
Figure 5. Fall 1918 mortality as a function of spring 1918 mortality, in total and by race.
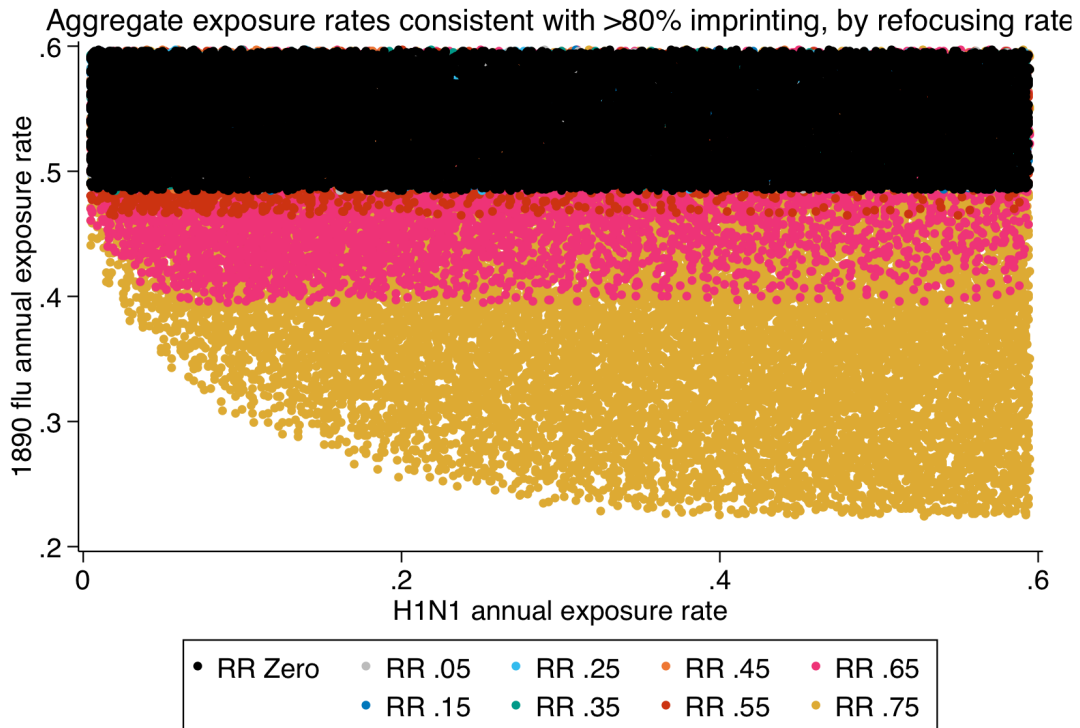

Figure 6. Annual flu exposure and immunological refocusing rates consistent urban white immunological imprinting rate derived from simulations.