Multi-Model Insights into Racial and Ethnic Heterogeneities in Early COVID-19 Transmission and Severity in the U.S.

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Abstract

The COVID-19 pandemic was marked by unequal disease burden across racial and ethnic groups in the US. Using a multi-model ensemble framework, we retrospectively assessed the impact of racial and ethnic heterogeneities in COVID-19 transmission and disease severity on mortality during the winter 2020–2021 surge in California and North Carolina. Models incorporating race and ethnicity projected mortality more accurately than null models, while the ensemble outperformed all individual models on average by weighted interval scores. Eliminating transmission heterogeneities produced larger mortality reductions than eliminating severity differences alone, particularly for Latino populations in California (55% reduction) and Black populations in North Carolina (28% reduction). Reducing severity heterogeneity also lowered mortality, with the greatest benefit among Black populations in both states (21% and 16% reductions in California and North Carolina, respectively). Eliminating both transmission and severity heterogeneity yielded the largest reductions overall, predicting 49–70% lower mortality across racial and ethnic groups in California and 23–40% in North Carolina. Mitigating transmission inequities also produced indirect benefits for non-targeted populations, highlighting the broad impact of reducing disparities in exposure risk and access to protective resources.

Key words: Infectious disease modeling, social epidemiology, health disparities

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Introduction

The COVID-19 pandemic was marked by unequal impacts across population groups driven by multiple factors, including age, presence of comorbidities, geography, and other determinants of health[1,2]. These patterns echo a long history of health inequalities reported across chronic and infectious diseases, such as cancer, smallpox, tuberculosis, and pandemic influenza, often associated with socioeconomic status, race, and ethnicity[3–5]. The mechanisms underlying these inequalities are varied. In the initial phase of the COVID-19 pandemic, differences in exposure risk across racial and ethnic groups, shaped by factors such as the resources and flexibility to practice social distancing and living conditions, were recognized as important contributors to unequal infection risk[6,7]. Further, communities with limited access to healthcare were more likely to experience worse clinical outcomes through delayed care, higher rates of comorbidities, and decreased access to health information[8,9]. Together, these factors contributed to higher rates of COVID-19 infection and mortality among some racial and ethnic populations[9]. While some sources of heterogeneity in infectious disease dynamics, such as age differences in risk of infection, are routinely incorporated in transmission models[10,11], less attention has been focused on other determinants of health. Recent calls have emphasized the need for greater representation of racial and ethnic groups in infectious disease models, the quantification of how socio-economic factors affect disease dynamics, and the collection of more granular and representative data across population groups[12].

Since 2021, the US Scenario Modeling Hub (SMH) has convened multiple modeling teams to generate months-ahead projections of cases, hospitalizations, and deaths for COVID-19 and other respiratory viruses[13,14]. Across 19 rounds of COVID-19 projections, SMH has explored a range of scenarios assessing the impact of various public health measures and epidemiological and behavioral uncertainties, providing evidence to guide policy[13]. An open-door policy for participation in the Hub enabled a diversity of modeling approaches and scientific perspectives to be represented[13,15], with four to nine modeling teams contributing to each round. Building on this collaboration, SMH undertook a retrospective analysis of the early phase of the COVID-19 pandemic to examine racial and ethnic heterogeneities in contacts and severity of infection, and their contribution to differential disease burden. As with prior SMH work, this analysis relied on ensemble approaches that aggregate results from multiple, independent models. These approaches offer greater reliability than individual models and are well-suited to situations of high uncertainty and complex biological mechanisms, such as heterogeneities in disease risk[16,17].

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The goals of this modeling analysis were threefold. First, we aimed to build capacity for disease models to generate projections stratified by racial and ethnic groups and represent the experience of different populations. Second, we wanted to evaluate how racial and ethnic heterogeneities in disease transmission and severity contributed to unequal COVID-19 mortality burden across population groups. Third, we aimed to understand how COVID-19 death burden may have differed if heterogeneities in disease risk were eliminated for populations experiencing disproportionate disease burden under hypothetical scenarios. We focused the analysis on the first year of the pandemic, a period where differences in disease burden by race and ethnicity were exacerbated, and considered two US states (California and North Carolina) due to the availability of epidemiological data stratified by race and ethnicity[18–21].

Methods

The process for each round of the Scenario Modeling Hub is that the coordination team first defines the modeling task through various conferrals with stakeholders and modeling teams, then solicits modeled projections from participating modeling teams[15]. For this round, the coordination team structured the modeling effort into two distinct phases. Seven modeling teams participated in Phase I and six in Phase II.

Phase I: Building capacity to model heterogeneities in transmission and severity and forecasting outcomes by race and ethnicity

Modeling teams calibrated models to race- and ethnicity-stratified serology, case, and death data from March to November of 2020 ("calibration period"), and generated projections for November 2020 - April 2021 ("projection period"). Teams were encouraged to incorporate processes that may generate differences in transmission and severity into their modeling frameworks and were allowed to use data available for the projection period on variant prevalence, non-pharmaceutical interventions (NPI), behavioral trends, vaccination, and other epidemic drivers. However, teams were directed not to validate model projections against case and death observations reported for the projection period.

Of the six modeling teams that participated in both phases, five models were compartmental SEIR-type models and one was agent-based. All models explicitly represented race and ethnicity in transmission and severity processes; three also incorporated age structure. Heterogeneities in transmission were modeled through differences in contact patterns and/or calibration to serology data, while heterogeneities in severity were informed by mortality, serology, and demographic structure. All models incorporated parameter uncertainty, and three additionally included stochastic epidemiological transitions.

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Phase II: Exploring hypothetical scenarios where race and ethnicity differences in disease risk are removed

In Phase II, teams generated scenario projections to estimate the impact of eliminating differences in transmission and severity between racial and ethnic groups on COVID-19 death burden. We designed four scenarios, described in **Table 1**. Scenario A represented the baseline scenario, where teams were permitted to calibrate models to epidemiological observations throughout the full study period (from March 2020 to April 2021), ensuring that differences by race and ethnicity were accurately captured. Scenario A served as a reference for comparison with three counterfactual scenarios (Scenarios B–D).

In counterfactual Scenario B, we projected the impact of eliminating differences in transmission risk by race and ethnicity in non-household settings by setting transmission risk equal to that estimated for the White population, as this segment of the population has experienced overall low infection and death rates across diverse infectious diseases, and has a sufficient population size to generate stable risk estimates[22]. Household transmission was left unchanged, given that public health interventions could hypothetically reduce differential transmission in the community, while household composition is generally not actionable by these interventions. Counterfactual Scenario C eliminated disparities in disease severity, represented by age-adjusted infection fatality ratios (IFR), by assigning all racial and ethnic groups the severity profile estimated for the White population. Scenario D simultaneously eliminated disparities in both transmission and severity. In counterfactual Scenarios B-D, we specified that differences in transmission and severity should be removed at the start of the projection period on November 15, 2020, so that the initial conditions in Scenarios A-D were the same for a given simulation. To capture uncertainty, participating modeling teams submitted 100-300 paired projection trajectories of weekly infections and deaths for each scenario, location, and race and ethnicity over the 20-week projection period. More information on the modeling process can be found in **Appendix S1.**

Data for model calibration

Modeling teams calibrated to weekly state-level mortality data stratified by race and ethnicity from the National Center for Health Statistics (NCHS)[23]. We aggregated population groups differently in each state to be consistent with how race and ethnicity was reported by location, resulting in 5 population categories for California and 4 for North Carolina (**Table 2**). NCHS censored death counts below 10; a default dataset replaced censored observations with a value of 1 to ensure that teams could use the minimum number of deaths consistent with the public

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use data, though teams could apply alternative approaches. Censored death data represented <5% of total reported data in both states.

Teams were provided additional publicly available datasets for calibration, including race- and ethnicity- and age-specific serology[24], case and hospitalization data[25,26], census-tract level mobility data (SafeGraph)[27], and synthetic contact matrices by race and ethnicity[28], and further information on each data source is provided in **Appendix S2**. Detailed information about each model can be found in **Table S1.**

Analysis of data and projections

Patterns of observed SARS-CoV-2 infections by race and ethnicity
To assess empirical differences in the risk of severe COVID-19 infection by race and ethnicity, we estimated infection-fatality and case-fatality ratios using race-specific serological, case, and mortality data over the projection period[24–26].

Ensemble Calculations and Scenario Projection Analysis:
Multi-model ensembles have been found to perform consistently better than any individual model in disease modeling contexts, particularly in situations with high epidemiological uncertainty[13,29]. Weekly projections from individual models were aggregated probabilistically into an ensemble using the Vincent method, where quantiles of individual models are averaged[30]. In **Appendix S3**, we also aggregated trajectories using a different aggregation approach, the Linear Opinion Pool (untrimmed)[30].

Phase I: Evaluation of accuracy in prediction of weekly disease burden by race and ethnicity
The goals of Phase I evaluation were two-fold: 1) to determine whether individual models that consider differential transmission/severity by race and ethnicity outperformed null models that did not account for these dynamics, and 2) to determine whether a multi-model ensemble outperformed individual models in predicting the racial and ethnic distribution of a large COVID-19 outbreak. To assess the first goal, we compared each model's predicted proportion of cumulative deaths to two null distributions: the first assumed deaths would occur proportionally to population size and the second assumed that the distribution of deaths would follow that which was observed in the month preceding the projection period (**Figure S1**).

We evaluated the projection performance of each model compared to the distribution of deaths by race and ethnicity that was observed over the projection period using the weighted interval

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score (WIS), a relative metric representing both the accuracy and precision of a model's prediction[13], and coverage (**Figure S2**). We calculated 95% bootstrapped intervals for differences in WIS between the ensemble and individual models by systematically omitting one projection week across locations and racial and ethnic populations and then resampling with replacement using a jackknife approach (n = 1000 replicates)[13].

Phase II: Evaluation of accuracy in calibration of weekly disease burden by race and ethnicity
To ensure that modeling teams captured the observed distribution of deaths by race and ethnicity over the study period during the calibration phase *before* implementing counterfactual scenarios B-D, we again evaluated calibration Scenario A using coverage (**Figure S3**) and WIS (**Figure S4)**. Next, we evaluated the deaths that could have been averted if heterogeneities in transmission and severity were eliminated. For each paired trajectory, we estimated the relative percent difference in projected cumulative deaths over the study period for Scenarios B-D relative to baseline Scenario A.

Results

Observed heterogeneities in disease severity
In the 2020-2021 winter, California and North Carolina experienced large COVID-19 outbreaks, with cases and deaths peaking in January 2021 in both states (**Figure 1a-b**). Overall deaths per 100,000 persons were highest for Latino and Black populations in California, and Black and White populations in North Carolina (**Figure 1a**). Using state-level serology (**Figure 1c**), we estimated infection fatality ratios (IFR) as of April 2021 (**Figure 1d).** Finally, we reported case fatality ratios (CFR) as of April 2021 using reported case and mortality data (**Figure 1e**), finding that the highest CFRs were observed in Asian and White populations (California) and Black and White populations (North Carolina). After adjusting for age (**Appendix S4, Figure S5)**, we found that the CFR was highest for Asian and Black populations (California), but the relative ordering of CFR remained unchanged for North Carolina. Differences in the relative scale of IFR vs. CFR across racial and ethnic groups may be attributable to variable reporting rates across groups, case definitions, the representation of groups in serological data, and the relatively high portion of missingness present in case data **(Figures S6-S7)**.

Phase I Results
Seven modeling teams contributed Phase I projections meant to simulate true forward projections. Compared to a null distribution that assumed the distribution of deaths by race and ethnicity followed the population distribution, all seven models explicitly incorporating

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demographics in the transmission process more accurately projected the distribution of deaths across racial and ethnic populations and both states (**Figure S1**). When compared to an alternative null model that assumed the distribution of deaths followed the pattern observed in the month preceding the outbreak, we found that in California, all models outperformed the null for all racial and ethnic populations, with the exception of the Other population. In North Carolina, all seven models more accurately predicted the distribution of deaths by race and ethnicity for the White and Black populations, while 4 and 1 models outperformed the null for the Other and Asian populations. Despite sub-optimal performance for small populations in each state, the transmission models more accurately captured the distribution of disease for the majority of racial and ethnic populations across both states.

Ensembled Phase I projections were well aligned with observations for all racial groups except the Other racial and ethnic group in California (**Figure 2a**). We found that ensemble projections were more accurate than individual model estimates overall in both California (median relative WIS = 0.66 (IQR: 0.59, 0.70) for the ensemble compared to an average 1.01 (IQR: 0.76, 1.22) across individual models) and North Carolina (median relative WIS = 0.51 (IQR: 0.47, 0.58) for the ensemble compared to 0.94 (IQR: 0.58, 1.44) for individual models). Using a bootstrapped analysis, we determined that the difference between the ensemble and average individual model performance was statistically significant (mean difference in relative WIS between the ensemble and individual models was -0.34 (95% PI: -0.40, -.29) in California and -0.44 (95% PI: -0.46, -0.39) in North Carolina) (**Figure 2b**). The ensemble also had more consistent performance than individual models; even when models did outperform the ensemble in some cases (e.g., model A in North Carolina), the same model often underperformed in other locations (as model A did in California). Additional comparison of projection interval coverage is provided in **Figure S2.**

Phase II Results

Six teams contributed projections to Phase II. In Phase II, we assessed the calibration accuracy of Scenario A, in which teams were permitted to use the full time series to capture death burden by race and ethnicity. Calibration performance was assessed to ensure that disease burden was accurately captured before assessing how putative differences in transmission/severity impacted disease distribution. Individual model calibration is provided in **Appendix S5, Figure S8.** We found that the ensemble model similarly significantly outperformed individual models in this round for both states (mean difference in relative WIS between ensemble and individual models was -0.67 (95% PI: -0.73, -.64) in California and -0.46 (95% PI: -0.49, -0.43) in North Carolina (**Figure S4**).

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In Phase II Scenarios B-D, we assessed the impact of heterogeneities in transmission and/or disease severity on mortality by racial and ethnic group. We focused our analysis on predicted death burden given low missingness in observed NCHS data used for validation, but additionally provided modeled infections (**Figure S9**) and IFRs for each model (**Figure S10**) in **Appendix S6.** We found that the scenarios focused on eliminating differences in transmission (Scenario B and D) resulted in the largest reductions in overall deaths (**Figure 3a**). Over the projection period in California, cumulative deaths across all groups were reduced from 42,400 (95% PI: 27,800, 62,400) in baseline scenario A to 18,300 (95% PI: 5,700, 47,300) in the scenario where heterogeneities in transmission were eliminated (Scenario B), 36,500 (95% PI: 23,000, 53,700) in the scenario where heterogeneities in severity were eliminated (Scenario C), and 15,400 (95% PI: 4,900, 40,600) when heterogeneities in both transmission and severity (Scenario D) were eliminated. In North Carolina, targeting transmission heterogeneities was associated with 4,700 predicted deaths (95% PI: 2,600, 10,300), targeting severity heterogeneities was associated with 7,000 predicted deaths (95% PI: 5,300, 9,600), and targeting both was associated with 4,500 predicted deaths (95% PI: 2,500, 9,900), compared to 7,400 deaths (95% PI: 5,400, 10,100) in baseline Scenario A. Reductions in absolute deaths by race and ethnicity and state are provided in **Figure S11** (**Appendix S7)** for the ensemble and individual models.

We measured the percent of cumulative deaths averted by race and ethnicity by estimating the difference between paired trajectories (**Figure 3b**). We found that all populations benefit from eliminating differences in transmission risk, even those not directly targeted by the modeled interventions. Further, every racial and ethnic population benefited relatively more from reducing transmission heterogeneities than from reducing severity heterogeneities. When transmission differences are eliminated (Scenario B), relative reductions in deaths were highest for the Latino population in California and the Black population in North Carolina, showing 55% (95% confidence interval (CI): 41, 67), and 28% (95% CI: 13, 43) reduced mortality, respectively. This amounted to 8,500 deaths (95% PI: 2,600, 20,200) predicted for the Latino population in California in Scenario B compared to a baseline value of 20,800 deaths (95% PI: 13,600, 28,900). In North Carolina, reducing heterogeneities in transmission in Scenario B reduced predicted deaths from 1,900 (95% PI: 1,300, 2,700) to 1,100 (600, 2,200) for the Black population. Indirect effects were more pronounced in California; for example, we predicted that White populations in California experienced 49% (95% CI: 39, 67) reduced mortality when transmission-related differences are eliminated, compared to 23% (95% CI: 11, 34) in North Carolina. We additionally explored the impact of reducing heterogeneities in household-based transmission (**Appendix S8**), finding this could result in a 4-19% and 4-8% additional reduction in predicted infections across racial and ethnic populations in California and North Carolina relative to Scenario B, respectively (**Figure S12**). We found that eliminating differences in

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disease severity (Scenario C) was a beneficial intervention for Asians, Blacks, and Latino populations in California and for the Black population in North Carolina. The greatest relative benefit of eliminating severity differences was found for the Black population, reducing deaths by 21% (95% CI: 12, 27) in California and 16% (95% CI: 9, 22) in North Carolina.

The greatest overall percent reductions in mortality were observed for Scenario D, in which heterogeneities in transmission and severity were both eliminated. For California, this resulted in 49-70% reductions in mortality on average across racial and ethnic groups, with the Latino population seeing the largest relative reduction. In North Carolina, we predicted less pronounced effects, corresponding to between 23-40% reductions in mortality on average across racial and ethnic groups, with the highest reduction being predicted for the Black population. We assessed how differences in disease burden between broader population groups changed on a weekly basis in each of the scenarios in **Figure S13 (Appendix S9).**

Discussion

We developed a multi-model framework to incorporate racial and ethnic heterogeneities in COVID-19 transmission and severity and evaluated the mortality burden that could be averted if these differences were eliminated. Across both states, models incorporating differential transmission and severity more accurately projected deaths by race and ethnicity than null models where disease occurred proportionally to population size or followed pre-outbreak distributions. Our work demonstrates that including these complexities in modeling frameworks can improve epidemic projections and better reflect population-specific experiences during pandemics. Importantly, though, we could not identify a single modeling feature that consistently explained predictive performance across settings. Performance was generally strongest for ensemble approaches that aggregated projections from individual models with diverse structures and assumptions. Most high-performing individual models stratified the population by both age and race and ethnicity and incorporated mobility data to modulate contact patterns, although exceptions to these trends were observed (**Appendix S1**). Nevertheless, across models, counterfactual scenarios suggested that eliminating heterogeneity in transmission would have led to larger reductions in mortality than eliminating heterogeneity in severity alone, although both had substantial impacts. Given that the analysis was conducted retrospectively with access to known epidemic drivers such as mobility and variant data, Phase I results likely represent an upper bound on current predictive capacity. Improving real-time projections under greater epidemiological uncertainty will be a key focus for future research.

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Eliminating disparities in transmission and severity would require substantial long-term structural changes. Differences in infection risk between racial and ethnic groups are multifactorial, but differential contact patterns may be an important contributor. National contact surveys found higher contact rates among Black and Hispanic populations early in the pandemic[22], particularly in occupational settings where access to personal protective equipment was insufficient[31–33]. Existing workplace regulations have limited ability to protect against workplace hazards such as COVID-19 that also occur outside of the workplace, requiring long-term policy change to reduce occupational infectious disease risk[34]. Additional relevant public health interventions could reduce transmission disparities through both limiting the number of contacts, such as by limiting crowding in congregate occupational settings or enabling increased flexibility for remote work, and also by reducing the probability of infection upon exposure. This could be achieved through modifying workplace settings during periods of high infectious disease transmission by improving ventilation, increasing capacity for social distancing, and widening access to personal protective equipment.

Moreover, we acknowledge that reducing transmission differences early in a pandemic may delay rather than fully prevent infections without additional measures. For example, countries such as China and the United Kingdom implemented successful stringent control efforts in the early pandemic, but when lifted, observed a high burden of infections, likely due to combined impacts of low coverage in high-risk groups and large underlying susceptible populations[35,36]. While the period studied here predates the large-scale COVID-19 vaccination program in the United States, early interventions to reduce transmission could delay infections long enough for vaccination campaigns to begin, provided that vaccination coverage is widespread. However, if the marked disparities in vaccination coverage across racial and ethnic groups in the United States that were observed during the pandemic persist[37], this could further compound differential disease burden. Reducing differences in severity would similarly require long-standing infrastructure policy changes. For example, severe COVID-19 outcomes were more common among individuals with underlying comorbidities, which are more prevalent among racial and ethnic minority populations[38,39]. Focusing on efforts to treat and prevent existing comorbidities, in conjunction with improving access and affordability to medical care, represents a potential pathway for sustainably mitigating differences in disease severity.

Although directly addressing structural inequities requires long-term efforts, explicitly incorporating race and ethnicity into infectious disease models is immediately actionable and can improve public-health decision-making. While most early COVID-19 modeling studies considered age as the sole demographic driver of disease[40], the pandemic instigated greater investment in modeling additional subpopulation dynamics. These studies often employed

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stratified compartmental and agent-based models, and primarily focused on projecting or explaining disproportionate infections and mortality among marginalized populations in the United States[7,41–43]. Many studies dynamically linked disproportionate disease burden among subpopulations to factors such as mobility, population density, and geography, although major limitations were cited regarding unknown case reporting, testing access, and population mixing patterns[12]. Consistent with our analysis, a study based in Michigan found that unequal transmission risk drove disparate health outcomes among racial and ethnic populations[7]. Our study extends this by quantifying mortality reductions that could hypothetically be achieved by designing interventions that target sources of heterogeneous transmission and severity.

Notably, racial and ethnic differences in infectious disease burden are not unique to COVID-19. Racial and ethnic minority populations also experienced disproportionate hospitalization burden during the 2009 H1N1 influenza pandemic, and disparities have been observed for endemic influenza and respiratory syncytial virus[44–46]. These findings suggest that the framework developed here may be useful for understanding unequal disease burden for other pathogens and in endemic settings. Continued investment in detailed epidemiological surveillance, particularly serological and severe outcome (hospitalizations, mortality) data jointly stratified by age, race and ethnicity, and other sociodemographic factors, as well as improved tools to infer contact mixing patterns for relevant subpopulations, would improve understanding of disparate disease risk and improve model parameterization.

This analysis examined COVID-19 disease burden by race and ethnicity, given the extensive literature reporting considerable differential disease burden during the early pandemic and the availability of epidemiological data stratified by race and ethnicity. However, racial and ethnic groups are not homogeneous populations, and various social determinants of health, such as socioeconomic status, essential worker status, and access to healthcare, play a crucial role in shaping disease dynamics[47–50]. The broad racial and ethnic populations studied in this analysis represent diverse populations, and the generalizations made here will not apply to all individuals within any given subgroup. Of note, the “Other” population in California represented American Indian/Alaskan Native populations, Native Hawaiian and Pacific Islander populations, and multiracial individuals, while the “Other” population in North Carolina comprised these populations and the Hispanic population. While suboptimal to aggregate multiple racial and ethnic groups into an “Other” category, as they may experience divergent challenges in mitigating COVID-19 disease risk, a lack of granular data available for smaller racial and ethnic populations necessitated this step for our modeling approach. Thus, direct comparisons of racial and ethnic populations across states are discouraged in our analysis. While we focused on race and ethnicity in this work, other sociodemographic variables may be similarly useful for

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understanding the underlying transmission processes that lead to unequal health outcomes; we encourage continued analysis in this area.

Lastly, there were several data limitations given the scarcity of demographic disease data in the US. In the absence of joint age and racial and ethnic disease data for both states, teams developed different approaches and made simplifying assumptions to estimate age-adjusted severity, which may impact scenarios C-D (**Appendix S1**). Second, reporting inconsistencies and data gaps introduced substantial challenges for data interpretation. NCHS mortality data were censored for populations with <10 reported deaths in a single time point, suggesting predicted death burden for smaller populations may be underestimated. The Other population in California and Asian population in North Carolina, which comprise 3.6 and 2.2% of the state population, respectively, were particularly impacted by data reporting restrictions and thus had limited calibration data available. To better capture small subpopulation dynamics, future efforts may focus on more intense surveillance efforts and improved methods for inferring subpopulation dynamics when data is sparse. This impacted the performance of smaller population projections, and we were not able to run posterior predictive checks on the individual models, as models were fitted using different approaches. However, we were able to show that models incorporating race and ethnicity explicitly outperformed approaches that did not across most racial and ethnic populations. We also utilized serology from a donor-based surveillance system. Recruitment practices and eligibility criteria for blood donations may lead to lower-risk individuals being overrepresented in serological data[51], yet, given high missingness of demographic information in many case reporting systems[52], serology may provide a more accurate picture of infection burden among the data that was available. Further, we only considered differences in contacts between racial and ethnic groups as a driver of heterogeneity in infection risk, and did not consider potential differences in susceptibility to infection. Relatedly, in counterfactual scenarios B and D, the transmission risk from non-household contacts was removed while household contacts remained unchanged. This was based on the logic that household contacts may not be as easily actionable, and also so that we could isolate the effect of mitigating occupational and community transmission, which has been shown to have driven a majority of the disparities in early COVID-19 transmission[22,31–33]. We did not consider a completely equal risk of transmission between population groups, although this could potentially be achieved by limiting secondary household transmission, such as promoting household masking[53], reducing household crowding[54], and improving housing material quality and ventilation[55]. Modeling the impact of reducing disparities in the household setting remains an important area of future work. Finally, we focused on California and North Carolina as examples of US states with significant population diversity and disease burden differences; however, our results are not necessarily generalizable to other states with different

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population makeup, COVID-19 control policies, and health behavior.

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Data availability: The data underlying this article are available at: https://github.com/midas-network/covid19-smh-research_resources
Code availability: Code used in this manuscript is publicly available at: https://github.com/sbents/COVID19-Heterogeneities-Race-Ethnicity/tree/main
Links to individual modeling code are available in Table S1.
Disclaimer: The findings and conclusions in this article are those of the author(s) and do not necessarily represent the views or opinions of the California Department of Public Health, the California Health and Human Services Agency, or the US National Institutes of Health.

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Tables

	Race and ethnicity differences in transmission operate as observed. SARS-CoV-2 infection rates differ by race and ethnicity.	Race and ethnicity differences in transmission outside of the household are eliminated. Transmission rates outside of the household are indexed on the White population as calculated in Scenario A.
Race and ethnicity differences in severity operate as observed. COVID-19 infection fatality rate differs by race and ethnicity.	Scenario A (calibration)	Scenario B (projection)
Race and ethnicity differences in severity are eliminated. Age-adjusted infection fatality rate is indexed on the White population as calculated in Scenario A.	Scenario C (projection)	Scenario D (projection)

Table 1. **Phase II scenario definitions for assessing the impact of reducing race and ethnicity population group differences in COVID-19 transmission and severity risks, November 2020-April 2021, California and North Carolina.** For Scenario A, models were calibrated to observed serology, cases, and deaths by race and ethnicity up until April 2021. In Scenarios B-D, models were calibrated up to November 2020 and then projected until April 2021 under different hypothetical scenarios where racial and ethnic groups have the same risk of B) transmission outside of the household, C) severity, and D) both transmission outside of the household and severity.

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State	Race and ethnicity group in SMH projections	Race and ethnicity reported in the NCHS data
California	Latino	Hispanic or Latino
California	White	non-Hispanic White
California	Black	non-Hispanic Black
California	Asian	non-Hispanic Asian
California	Other	non-Hispanic American Indian or Alaskan Native, non-Hispanic Native Hawaiian or other Pacific Islander, non-Hispanic more than one race
North Carolina	White	non-Hispanic White
North Carolina	Black	non-Hispanic Black
North Carolina	Asian	non-Hispanic Asian
North Carolina	Other	Hispanic or Latino, non-Hispanic Other

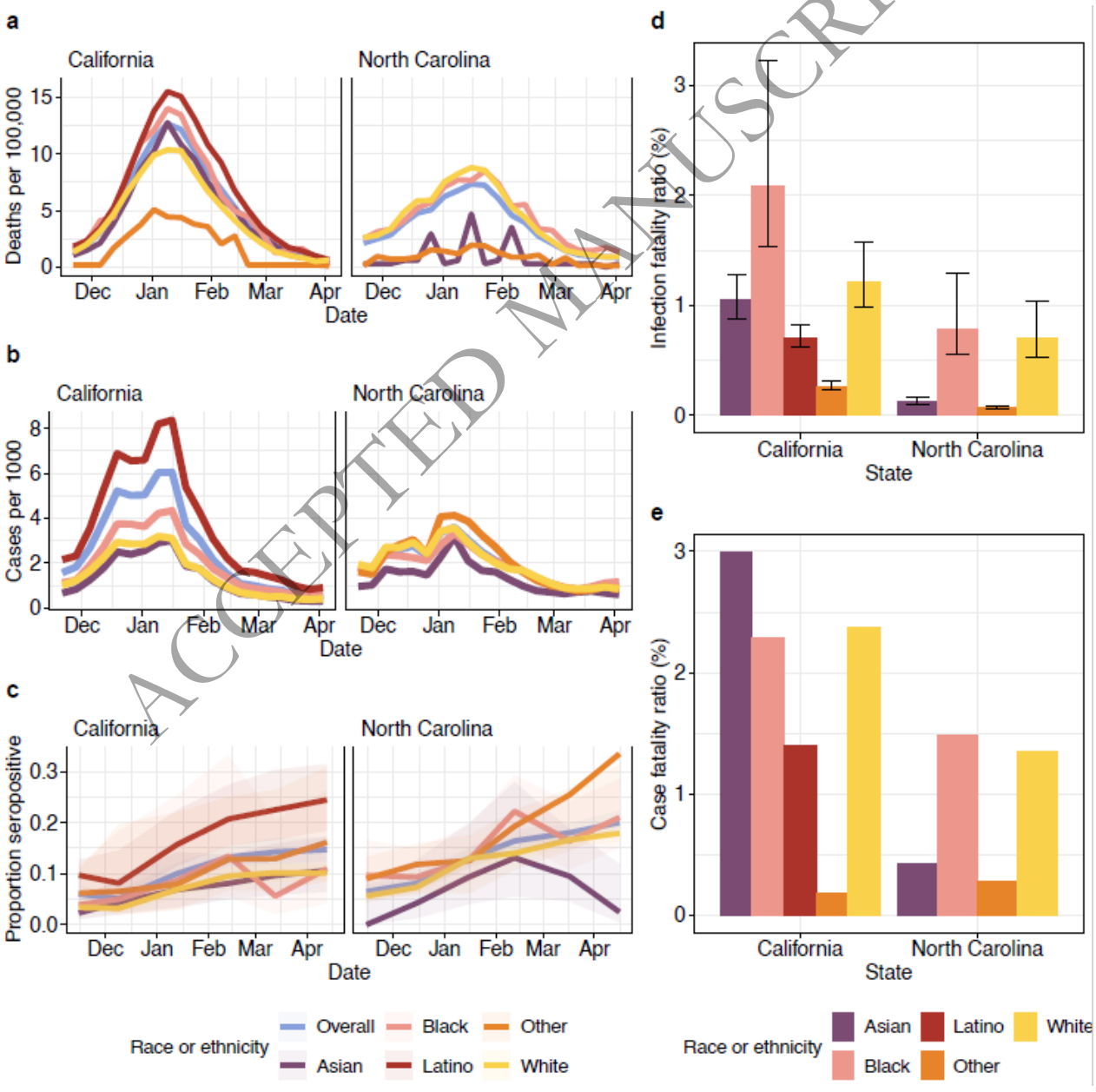
Table 2. Definition of racial and ethnic groups by state. Racial and ethnic groups present in the NCHS COVID-19 death data mapped onto the groups used in the SMH modeling exercise. In California, this resulted in the following racial and ethnic grouping: Latino, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and Other, where Other comprises multiracial, non-Hispanic American Indian or Alaskan Native, and non-Hispanic Native Hawaiian or other Pacific Islander individuals. In North Carolina, racial and ethnic groups were classified as: non-Hispanic Asian, non-Hispanic Black, non-Hispanic White, and Other, where other comprised Hispanic or Latino, multiracial, non-Hispanic American Indian or Alaskan Native, and non-Hispanic Native Hawaiian or other Pacific Islander individuals. Hispanic and Latino individuals were combined with Other in North Carolina to align with how case and hospitalization data are reported by the North Carolina Department of Health and Human Services[56].

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Figure 1. Reported COVID-19 deaths and estimated infection fatality ratios by race and ethnicity in California and North Carolina from November 2020 until April 2021. a) Observed weekly COVID-19 deaths per 100,000 population by racial and ethnic groups. **b)** Observed weekly COVID-19 cases per 1,000 population by racial and ethnic groups. **c)** Cumulative proportion of racial and ethnic group seropositive for COVID-19 from November 2020-April 2021 based on infection-based serological markers. **d)** Estimated infection fatality ratio by racial and ethnic group and state for the overall population, estimated over the projection period from November 2020-April 2021. Given differences in how subpopulations are aggregated into broader racial and ethnic populations across states, comparison of groups between states is discouraged. **e)** Estimated case fatality ratio by racial and ethnic group and state for the overall population, estimated over the projection period.

Alt Text: Time series showing differences in the proportion seropositive, case, and death rate, and estimated infection- and case fatality ratio for racial and ethnic populations in California and North Carolina.



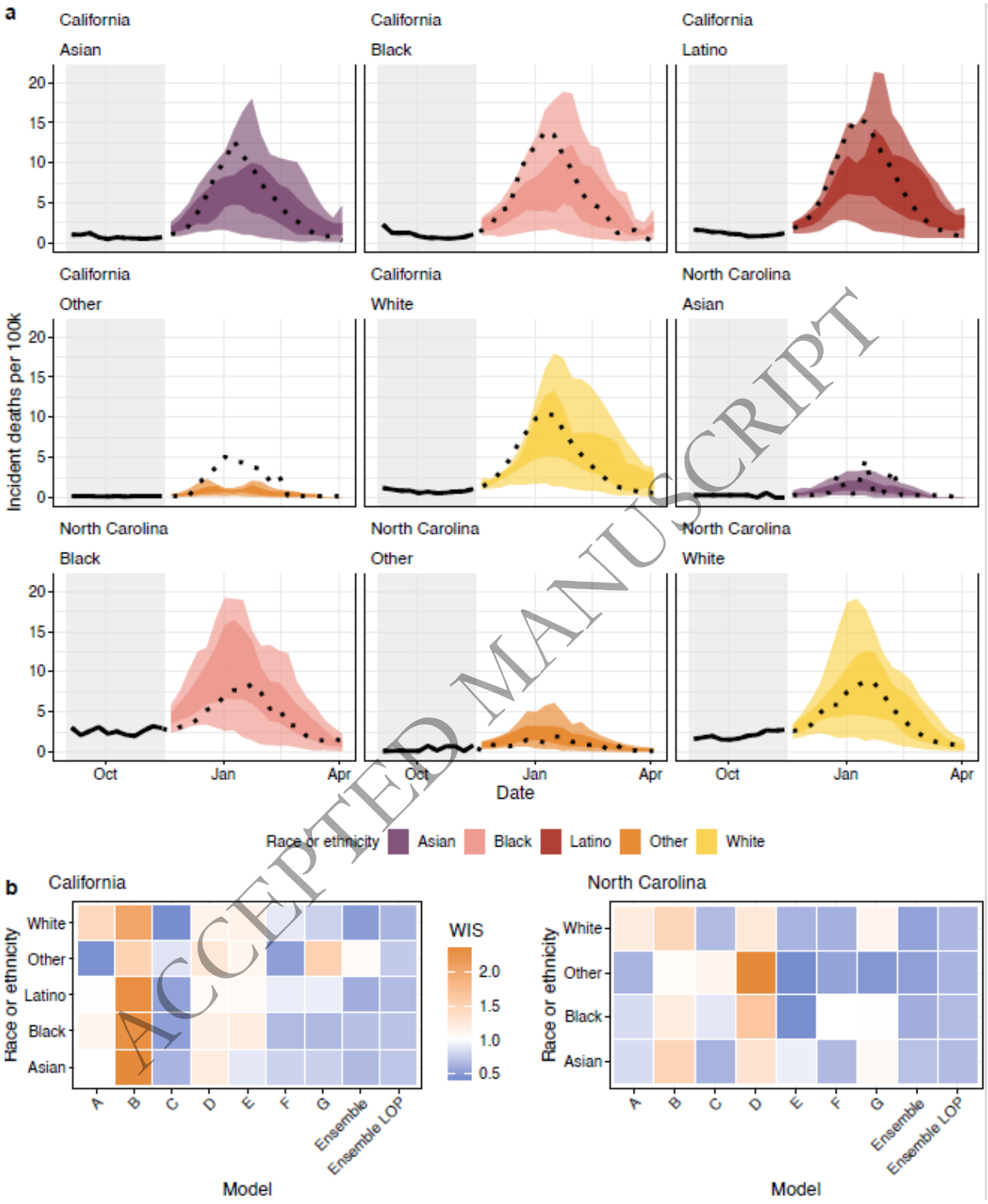
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Figure 2. Phase I predicted COVID-19 weekly deaths by race and ethnicity up until April 2021, assuming that heterogeneities in transmission and severity proceed as observed from a multi-model ensemble and accuracy of individual models and ensemble. a) In Phase I, teams calibrated up until November 2020 (gray box) and predicted deaths by racial and ethnic group until April 2021. Colored ribbons represent the Phase I ensemble 95% projection interval (darker ribbon indicates 50% projection interval) against ground truth weekly death data (solid black line during calibration period, dotted line during projection period) by race and ethnicity and state: California and North Carolina. **b)** We calculated the weighted interval score (WIS) for each model and the ensemble by race and ethnicity, which measures the extent to which projections captured the observed time series while penalizing wide projection intervals. Lower values, shown in blue, indicate higher model accuracy.
Alt Text: Ensembled projections captured observed incident deaths by race and ethnicity, and outperformed individual models as measured by weighted interval score.

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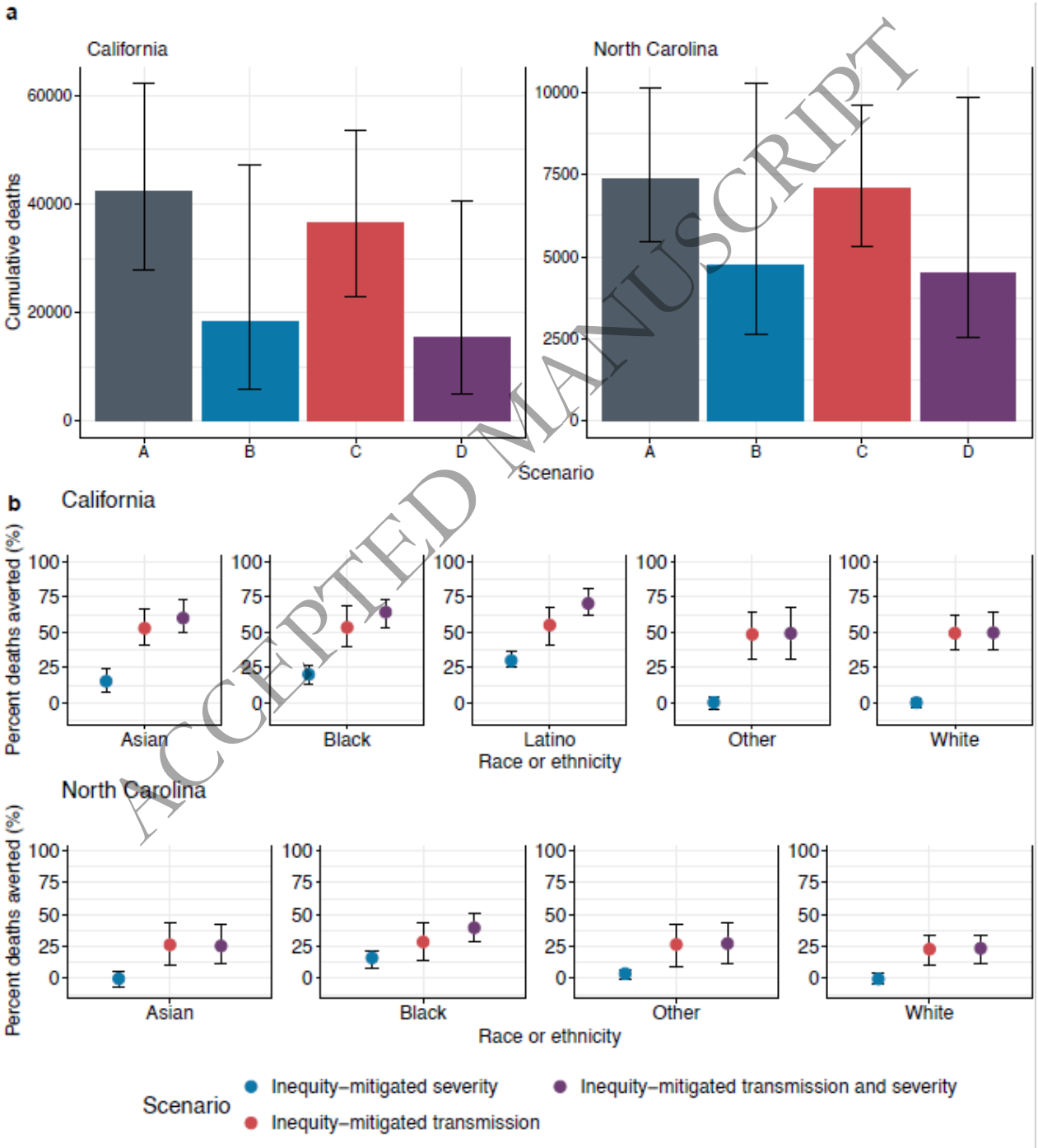
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Figure 3. Cumulative and percent COVID-19 deaths averted by mitigating heterogeneities in transmission, severity, or both, from November 2020-April 2021. a) The median number and 95% prediction interval of cumulative deaths projected for each scenario in California (left) and North Carolina (right). **b)** Percent of cumulative deaths averted in counterfactual Scenarios B-D where heterogeneities in transmission were mitigated (Scenario B, blue), heterogeneities in severity were mitigated (Scenario C, red), and both were mitigated (Scenario D, purple) relative to baseline Scenario A (grey), in which heterogeneities in transmission and severity were present for California (top) North Carolina (bottom).
Alt Text: Reducing heterogeneities in transmission and severity averted deaths across racial and ethnic populations, with the largest impacts associated with inequity-mitigated transmission.



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