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Sex disparities in COVID-19 outcomes in the United States: Quantifying and contextualizing variation

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ABSTRACT

This paper presents the first longitudinal study of sex disparities in COVID-19 cases and mortalities across U.S. states, derived from the unique 13-month dataset of the U.S. Gender/Sex COVID-19 Data Tracker. To analyze sex disparities, weekly case and mortality rates by sex and mortality rate ratios were computed for each U.S. state, and a multilevel crossed-effects conditional logistic binomial regression model was fitted to estimate the variation of the sex disparity in mortality over time and across states. Results demonstrate considerable variation in the sex disparity in COVID-19 cases and mortalities over time and between states. These data suggest that the sex disparity, when present, is modest, and likely varies in relation to context-sensitive variables, which may include health behaviors, preexisting health status, occupation, race/ethnicity, and other markers of social experience.

1. Introduction

Early in the COVID-19 pandemic, researchers noted a pattern of much higher mortality among men compared to women. In Wuhan, China, and Lombardy, Italy, men were reported to be dying at rates as much as twice that of women (Grasselli et al., 2020; Jin et al., 2020). Biomedical researchers seized on this finding, arguing that a robust, stable, cross-contextual pattern of sex differences in COVID-19 mortality supported a primary role of biological sex-related factors in susceptibility to the SARS-CoV-2 virus (Gebhard et al., 2020; Peckham et al., 2020; Pivonello et al., 2020; Scully et al., 2020). On this basis, researchers proposed a number of endocrinological and immunological mechanisms by which sex differences might contribute to mortality, suggesting that these mechanisms offer promising candidates for the design of sex-specific clinical and public health interventions (Bunders and Altfeld, 2020; Giagulli et al., 2021; Klein et al., 2020; Takahashi et al., 2020; Wolfe et al., 2021).

This paper presents the first longitudinal study of sex disparities in the U.S. across states, derived from a 13-month dataset of COVID-19 cases and mortality collected by the U.S. Gender/Sex COVID-19 Data Tracker at Harvard University ("U.S. Gender/Sex COVID-19 Data Tracker" 2020). The Tracker reveals considerable variation in sex differences in COVID-19 cases and mortality over time and between states. While men, in aggregate, experience higher mortality from COVID-19

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than women, this is not true for all men, in all localities, and at all time points across the pandemic. Specifically, findings from the Tracker challenge the view that the sex disparity is large, stable, and context-independent. Rather, data are more consistent with the interpretation that the sex disparity, when present, is modest, and varies, likely in relation to context-sensitive variables, such as age, race/-ethnicity, occupation, immigration status, educational attainment, zip code, health behaviors, health status, and other social markers, continuous with the broader literature on social determinants of COVID-19 vulnerability (Krieger, 2020; Lopez and Neely, 2020).

In the following, we use the term "sex disparities" to describe differences between people categorized as men/males and women/females in U.S. state COVID-19 data. These data do not accurately classify individuals whose gender identity differs from their sex assigned at birth or who identify with categories beyond the gender/sex binary (Jillson and Shattuck-Heidorn, 2021; Perret et al., 2021). Generally speaking, "sex" refers to biological characteristics enabling sexual reproduction, such as gonads and chromosomes, while "gender" refers to cultural conventions, roles, and behaviors for, as well as relations between and among, women and men and boys and girls. However, our use of the term "sex disparities" is intended to sustain an understanding that social inequities may play a role in structuring differential outcomes and that differences in case or mortality outcomes between "male" and "female" groups do not necessarily result from biological traits related to sexual reproduction. Where appropriate, we also employ the term "gender/sex" to highlight cases in which disentangling gender and sex-related factors is challenging (van Anders, 2015).

Sex disparities can result from sex-related biological variables, gendered norms and behaviors, non-gender/sex related variables that are differentially distributed across sexes, or a combination of these (Homan, 2019; Springer et al., 2012). Despite ongoing study, there is presently no empirical evidence, controlling for key interacting variables such as age, body size, and comorbidity status, that sex-related biological mechanisms predict differential outcomes specific to the SARS-CoV-2 virus in humans. The data that we present, demonstrating substantial contextual heterogeneity in COVID-19 sex disparities, adds to this picture, suggesting little reason to expect that interventions centering sex-related biological factors will play a primary or sizable role in explaining and ameliorating sex disparities. Rather, we argue that the variation observed in COVID-19 sex disparities is likely largely explained by a combination of variations in data collection practices and gendered patterns in health behaviors, occupational exposures, and pre-existing health conditions, all in interaction with other salient socially-relevant variables, patterned by socioeconomic status, geography, and race/ethnicity.

2. Methodology

2.1. Data collection and validation

We analyze fifty-five weeks (April 27, 2020 through May 10, 2021) of data from the U.S. Gender/Sex COVID-19 Data Tracker, which records weekly sex-disaggregated COVID-19 cases and mortality from 50 U.S. states as well as the District of Columbia. Data were collected from state public health websites every Monday to create a longitudinal public dataset for analyses of sex-disaggregated mortality and case data, thereby addressing a significant lag in reporting between state and federal levels. All data were collected and validated, then publicly shared in graphical and tabular forms online. Data used in this analysis were publicly available and de-identified and are exempt from IRB oversight. Detailed descriptions of data collection, validation methods, and limitations of the dataset can be found in the Supplemental.

2.2. Data analysis

Tracker data was compiled for these analyses using R (versions 3.6.2 and 4.0.5) (R Core Team, 2019, 2021) and RStudio (RStudio Team, 2020). A complete list of R-packages used is available in the Supplemental. Each weekly data spreadsheet was imported separately, and weekly raw counts of cases and deaths were calculated by subtracting previous weeks' counts from the latest data.

We computed crude case and mortality rates by sex for each state. While age is a critical determinant of COVID-19 vulnerability, direct age standardization was not possible because most states do not report sex-by-age COVID-19 cases and mortalities (as of April 2021, only 4 states reported sex-by-age mortality rates). Indirect standardization is sometimes used to approximate direct standardization. However, indirect standardization is inappropriate for analysis of longitudinal Tracker data, as discussed in the Supplemental. Total population counts for women and men were derived from the 2015–2019 5-year American Community Survey (ACS) Estimates and downloaded from the U.S. Census API using tidycensus (Walker and Herman, 2021) to calculate case and mortality rates by sex per 100,000 individuals in the corresponding sex stratum for each state. The overall U.S. data for monthly cases and mortality included in visualizations were accessed from the National Center for Health Statistics and used for comparative purposes (National Center for Health "National COVID-19 Statistics, 2021). ACS 2015–2019 population estimates were used as denominators when calculating rates.

Graphs of weekly and cumulative case and mortality rates in U.S. states and D.C. show a centered 3-week rolling average. Gaps and empty graphs indicate missing data. Monthly U.S. data was divided by four to adjust for the difference in elapsed time when plotted alongside weekly rolling averages. Weekly rate ratios were calculated with standard methods using women as the reference group (Krieger, Chen, and Waterman, 2020a). Maps show the mortality rate ratio for each of three waves and over the total observation period. Although there is no consensus about the exact dates to distinguish waves of the pandemic in the U.S., we follow media convention in defining the end of Wave 1 as May 25, 2020, Wave 2 as May 26 through August 31, 2020, and Wave 3 as August 31, 2020 through May 10, 2021 (Leatherby, 2021; Wilson, 2021). Code for all data aggregation, analyses, and visualizations is archived (Lee and Rushovich, 2021).

Using mortality data from the Tracker, we fit a multilevel crossed-effects conditional logistic binomial regression model for the proportion of all COVID-19 mortalities that were male mortalities in each state. Arkansas, Florida, New Mexico, North Dakota, and West Virginia were excluded from regression analysis because they do not provide summarized sex-disaggregated data. We fit three hierarchical linear models. Model 1 included a random effect for state, model 2 included a random effect for week, and model 3 included crossed random effects for both week and state. All three models included an additional random effect for individual observation to account for overdispersion in the data (Gelman and Hill, 2007). To assess variation in the relative rates of male to female mortality across time and across states, we used two likelihood ratio tests comparing models 1 and 3 and models 2 and 3; model 3 fit the data significantly better than model 1 or model 2 ($p < 0.001$ for both likelihood ratio tests of model comparisons). We then used model 3 to calculate predicted percentages of male COVID-19 mortality using empirical Bayes estimates of the random effects. Finally, we transformed

these predicted percentages to calculate mortality rate ratios by adjusting for the proportion of women in each state using population estimates from the 2015–2019 ACS (U.S. Census Bureau, 2021).

Our final model, model 3, has the probability of a given COVID-19 mortality for men in week j in state k as

$$y_{jk} = \mathrm{Bin}\left(n_{jk}, p_{jk}\right)$$

$$\mathrm{Logit}\left(p_{jk}\right) = \beta_0 + u_j + v_k + r_{jk}$$

where y_{jk} are the total male COVID-19 mortalities on week j in state k, n_{jk} are total mortalities overall, and p_{jk} is the proportion of total mortalities that are men. The u_j, v_k, and r_{jk} are the random effects for weeks, states, and observations, respectively. We fit this model to data aggregated by state and week.

3. Results

The analysis of sex-disaggregated data from the U.S. Gender/Sex COVID-19 Tracker shows extensive heterogeneity in the magnitude and direction of sex disparities in COVID-19 outcomes, both across states and over time. Over fifty-five weeks of observation (April 27, 2020 through May 10, 2021), the total cases recorded by the Tracker for men and women were 14,889,007 and 15,383,226, respectively. For mortalities, the numbers were 273,455 and 227,863 for men and women respectively.

In the following, we document and characterize heterogeneity in COVID-19 sex disparities using several visualizations and analyses. First, we present sex-disaggregated case rates across U.S. states and over the course of the pandemic (Fig. 1a and b). These are also characterized as case rate ratios in Fig. 2a. We then present data about sex disparities in COVID-19 mortality across U.S. states in three distinct ways: 1) weekly and cumulative mortality rates by sex (Fig. 3a and b); 2) weekly mortality rate ratios for men compared to women (Fig. 2b, Supplemental Fig. S1); 3) maps of mortality rate ratios in U.S. states, by pandemic waves and over the entire period of observation (Fig. 4a–d). Finally, we present the results of a multilevel model analysis that shows significant variation in sex disparities in COVID-19 mortality across both time and U.S state (Fig. 5). These data and analyses highlight how case and mortality rates and mortality rate ratios vary across time and geographic location.

3.1. Cases

Weekly cases. Weekly fluctuations in case rates (Fig. 1a) for men and women reveal variation in the timing of surges across states, as well as variation in case sex disparities over time. In the initial week of data collection, the weekly case rate ratio for men compared to women was greater than one (i.e. the case rate was higher among men) in thirteen jurisdictions. However, in the final week of data collection, that number decreased to eleven jurisdictions. Notably, in Texas, the weekly case rate ratio for men compared to women was greater than one in all but two weeks (Fig. 2a).

Cumulative cases. Tracker data shows considerable heterogeneity in cumulative cases by sex across states and time (Fig. 1b). In the initial week of data collection, the rate ratio for cases among men compared to women was greater than one (i.e. the rate was higher among men) in fourteen jurisdictions. However, in the final week of data collection, that number decreased to just six jurisdictions. Those jurisdictions were: Texas, Hawaii, Vermont, Alaska, District of Columbia, and New York. The corresponding case rate ratios and 95% confidence intervals were: 1.94 (1.93–1.94), 1.11 (1.09–1.14), 1.06 (1.03–1.09), 1.06 (1.04–1.07), 1.01 (1.0–1.03) and 1.01 (1.0–1.01), respectively.

3.2. Mortality

Until July 31, 2020, six U.S. states did not report sex-disaggregated data for mortalities ("U.S. State COVID-19 Data Report Card" 2021). As of May 10, 2021, three jurisdictions (Arkansas, North Dakota and West Virginia) still do not report these data. Furthermore, two jurisdictions (Florida, New Mexico) do not report summarized sex-disaggregated data, and are thus not included in the analysis.

Weekly mortality. Weekly mortality rates (Fig. 3a) demonstrate differences in the timing of COVID-19 deaths across states as well as changes in sex disparity trends. In the initial week of data collection, the mortality rate ratio for men compared to women was greater than one (i.e. the mortality rate was higher among men) in all but two jurisdictions (Kentucky, South Carolina). In the final week of data collection, the rate ratio was greater than one in all but seven jurisdictions (District of Columbia, Maine, Delaware, Kentucky, Connecticut, Arizona, Virginia) (Fig. 2b).

Cumulative mortality. Tracker data shows considerable heterogeneity in cumulative mortality by sex across states and time. Among the cumulative mortality graphs (Fig. 3b), there are four broad patterns. Rates for men (red line) and women (blue line) are either: (1) largely the same over time (e.g., Connecticut); (2) different but parallel (e.g., New York); or (3) start off similar but then modestly diverge either quite early in the pandemic (e.g., Texas) or only in the most recent wave (e.g., Maryland). In the initial week of data collection, the mortality rate was higher among men in all but three jurisdictions (Alaska, Rhode Island, Kentucky). In the final week of data collection, the cumulative mortality rate was higher for men in all but two jurisdictions (Massachusetts, Rhode Island), and was very similar to that for women in nine additional jurisdictions (Connecticut, Maine, New Hampshire, Kentucky, Delaware, Pennsylvania, Indiana, Vermont, Iowa). Large sex disparities accrued at specific points in time can permanently affect cumulative mortality data, as can be seen in the comparison between weekly and cumulative rates for New York, New Jersey, and D.C. For example, the consistent gap between sex-disaggregated cumulative mortality rates in New York (Fig. 3b) is driven by a large sex disparity at the beginning of the pandemic that ceases to be observed over time in weekly rates (Fig. 3a).

Geography of mortality. Mapping mortality rate ratios by wave highlights improvements in the availability of sex-disaggregated data over the course of the pandemic and changes in the mortality rate ratio in U.S. states over time. During the first wave, among states that reported sex-disaggregated mortality data, the mortality rate ratio ranged from 0.34 (0.07–1.70) in Vermont to 2.06 (1.63–2.60) in Colorado (Fig. 4a). During the second and third waves, the mortality rate ratio ranged from 0.69 (0.52–0.93) in New Hampshire to 2.17 (0.95–4.96) in Alaska in wave 2, and from 1.02 (0.76–1.35) in Vermont to 2.01 (1.89–2.15) in Nevada in wave 3 (Fig. 4b and c). By the end of wave 3, most states are either close to parity (mortality rate ratio equal to one) or show a higher mortality rate for men (Fig. 4d).

Regression Model Results. The best-fitting model (Model 3) incorporates state and week (Table 1). Model 3 predicts that in a typical state, the odds of a death being a man compared to a woman is $e^{0.13}$, or 1.14 (1.10–1.18). Of the total variation in this sex disparity across states and time, 10% is attributable to between-week, within-state variation,

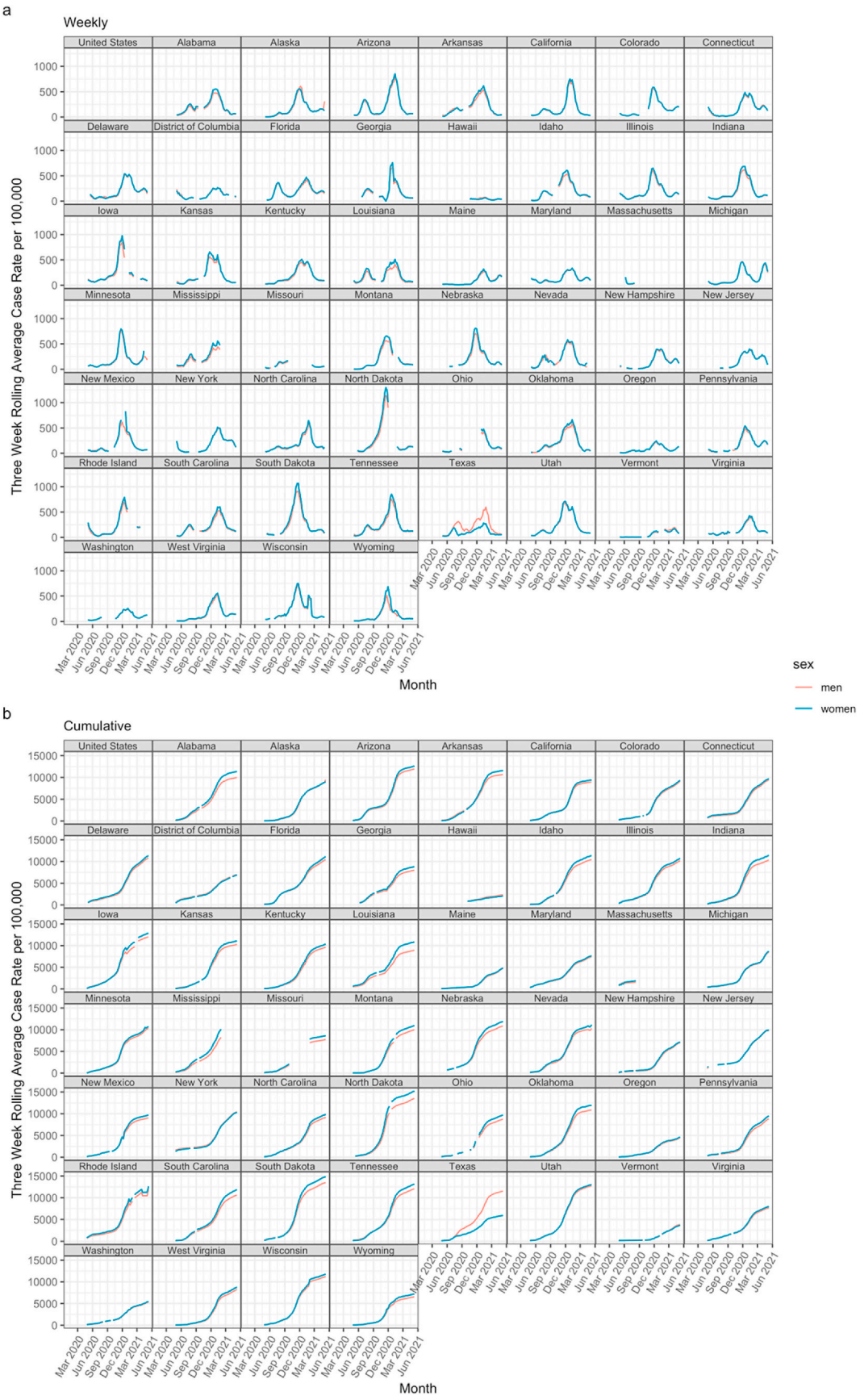

Fig. 1. Case rates per 100,000 people shown weekly (a) and cumulatively (b). Men are the red line, women are the green line. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

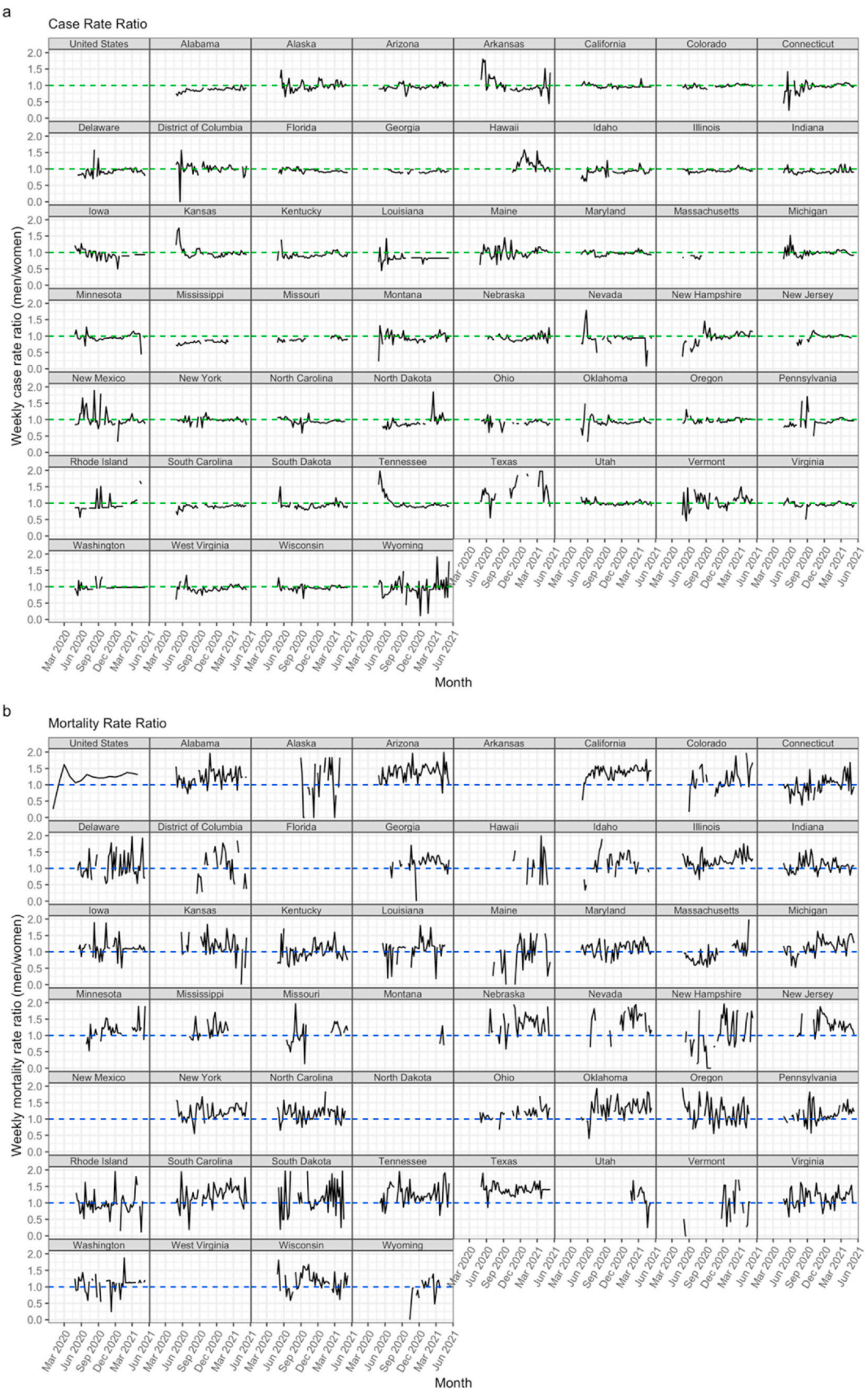

Fig. 2. Weekly case rate ratio (a) and weekly mortality rate ratio (b). For both rate ratios, the horizontal line at 1.0 indicates where the rate of male and female cases or deaths are equal. Rate ratios for some states are missing because not all states publish sex-disaggregated mortality data. Additionally, we do not have U.S. case rate ratios.

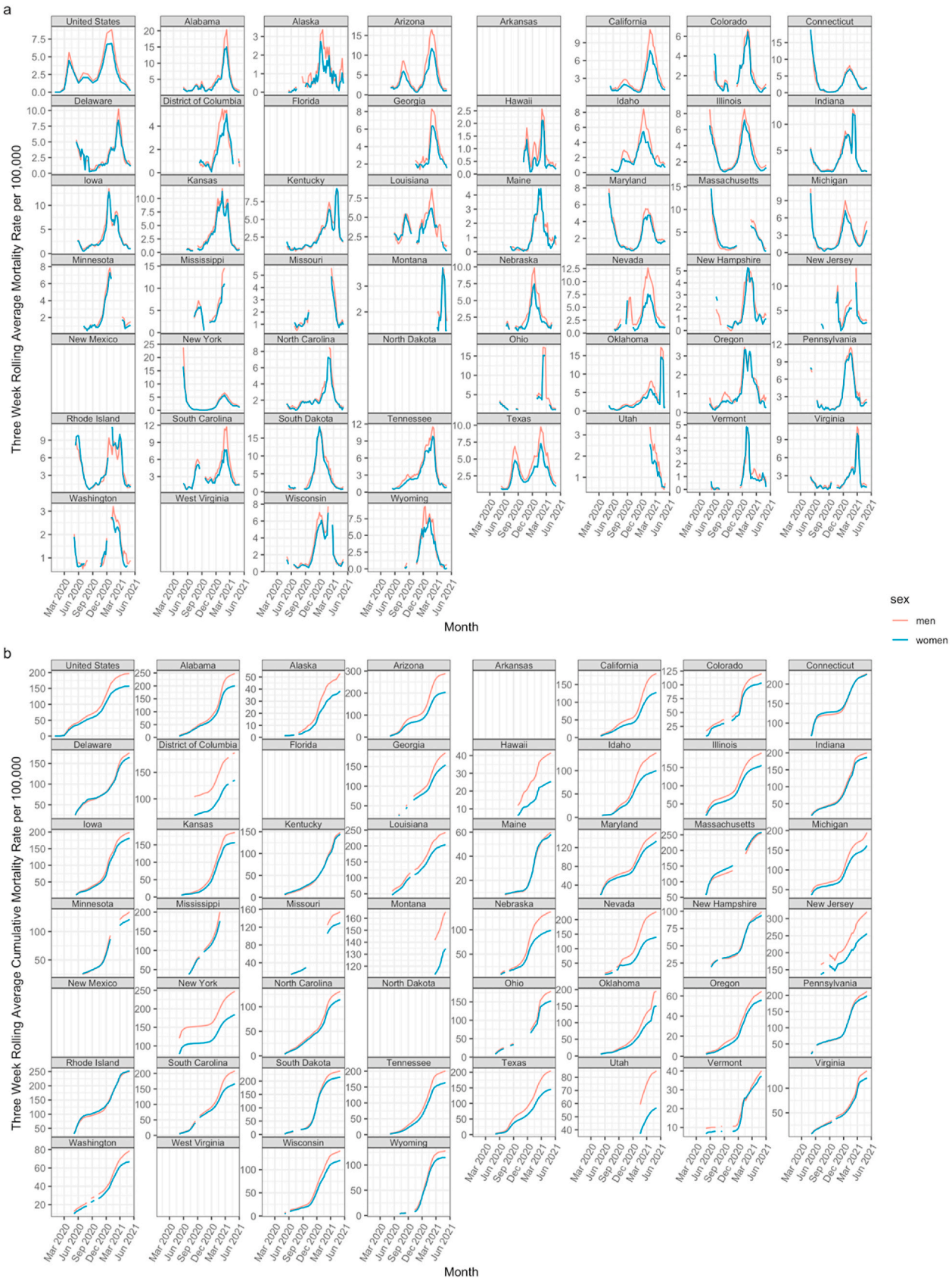

Fig. 3. Mortality rates per 100,000 people shown weekly (a) and cumulatively (b). Note that the scale on the y-axis differs between graphs. The decrease in cumulative mortality in NJ is an artefact of a temporary change to the state data dashboard (see Supplemental).

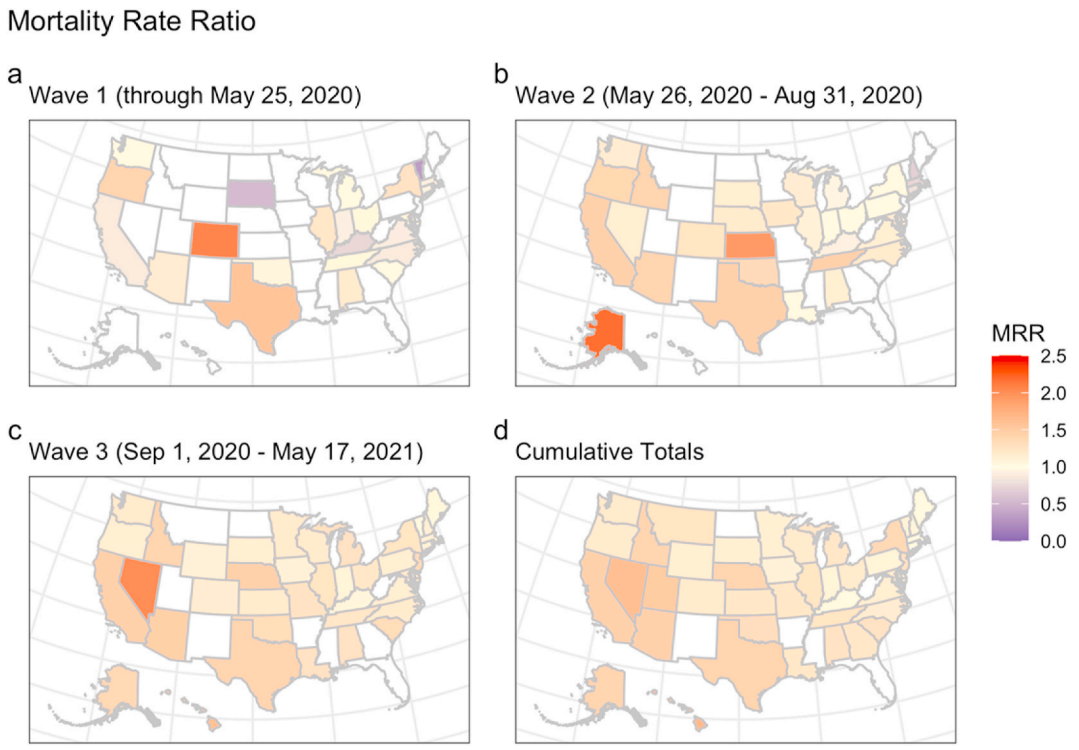

Fig. 4. Male:female mortality rate ratio by pandemic waves (a–c) and cumulatively (d) across states. Orange indicates higher rates among men, blue indicates higher rates among women, and yellow indicates equal rates. White indicates missing data. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

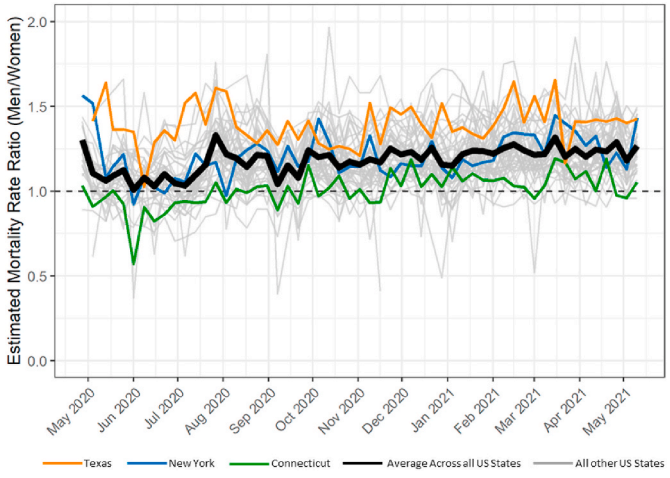

Fig. 5. Predicted weekly mortality rate ratio by state from a multilevel crossed-effects conditional logistic binomial regression model. The black trendline is the average across states at that week. Texas, New York, and Connecticut are emphasized in orange, blue, and green, respectively, to highlight trends. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

and 30% attributable to between-state variation. The remaining 60% is unexplained by either time or state. The state variation includes variation induced by different percentages of men in the population; this is adjusted for in our subsequent step.

After adjusting for population demographics, the predicted mortality rate ratio averaged across all states ranged from 1.01 during the week of June 1, 2020 to 1.3 during the week of July 27, 2020 (Fig. 5, black trendline). There was considerable variability in the range of the estimated mortality rate ratio across states. For example, in Texas the estimated mortality rate ratio ranged from 1.02 to 1.65 and never fell below 1 (i.e. men consistently had higher rates); in NY, it ranged from 0.92 to 1.56 and fell below 1 for three weeks; while in Connecticut the rate ranged from 0.57 to 1.2 and fell below 1 for 22 weeks.

Table 1
Multilevel crossed-effects conditional logistic binomial regression model results.

	Model 1 (excluding week)	Model 2 (excluding state)	Model 3 (full model)
Intercept (SE)	0.14*** (0.019)	0.13*** (0.011)	0.13*** (0.021)
AIC	14180.36	14372.32	14131.75
BIC	14197.40	14389.36	14154.47
Log Likelihood	−7087.18	−7183.16	−7061.87
Num. obs.	2164.00	2164.00	2164.00
Num. groups: obs	2164.00	2164.00	2164.00
Num. groups: state	47.00		47.00
Var: obs (Intercept)	0.0323	0.0422	0.0278
Var: state (Intercept)	0.0143		0.0677
Num. groups: date.cat		55.00	55.00
Var: date.cat (Intercept)		0.00479	0.00458

***p < 0.001; **p < 0.01; *p < 0.05.

4. Discussion

Tracker data show that sex disparities in case and mortality rates are highly heterogeneous over time both within and between states. The regression model confirms that a significant portion of the variation in the sex disparity is related to the timepoint in the pandemic and can be attributed to underlying state-level factors. This is consistent with the interpretation that multiple social and contextual factors play an important role in shaping sex disparities in COVID-19 outcomes. In this respect, our findings are continuous with research showing geographical variability in patterns of sex disparity (Akter, 2020; Islam et al., 2021), and do not support the interpretation of sex disparities as being stable across contexts (Klein et al., 2020; Peckham et al., 2020).

4.1. Is there a sex disparity in COVID-19 outcomes in the U.S.?

Tracker data suggest modestly higher COVID-19 mortality for men in aggregate. When interpreting the higher aggregate mortality for men compared to women, it should first be noted that U.S. men had persistently higher all-cause mortality rates than women before COVID-19. When disparities in all-cause excess mortality between women and men during the pandemic are considered relative to pre-COVID-19 disparities, there is evidence that COVID-19 has not changed this fundamental dynamic. In Massachusetts, for example, the relative increase in mortality registered during the height of the first COVID-19 surge was identical for women and men, compared to previous years (Krieger, Chen, and Waterman, 2020b). A larger study of excess mortality found a similar pattern: in 2020, the percentage increase in crude excess deaths over time was equivalent for men and women in the U.S. (Islam et al., 2021). This could indicate that the disparity in COVID-19 outcomes between men and women does not have to do with a specific, sex-linked male vulnerability to COVID-19, but reflects the preexisting propensity of men and women to die in any given year, as a result of a diverse set of complexly entangled biosocial factors structured by the differing average age demography of men and women and also long-standing systemic health and social inequities of men and women in different socio-economic groups.

The connections between these biosocial factors and COVID-19 outcomes are particularly evident in the unequal distribution of pre-existing health conditions between women and men across various social groups. For instance, heart conditions and cardiovascular disease are comorbidities associated with poorer COVID-19 outcomes and mortality (Bae et al., 2021; Madjid et al., 2020), and their prevalence is not evenly distributed across age and sex population strata. The 2017 Global Burden of Disease Study found that, in age groups of 50–54 years and up, cardiovascular disease occurred predominantly in men (James et al., 2018). Coronary heart disease also occurs at higher rates among men in nearly every age stratum above 45 years (Mosca et al., 2011). Gender/sex disparities in underlying health conditions such as heart disease may influence the likelihood of death following infection and, thus, pattern outcomes of COVID-19 between men and women.

There are potential sources of bias in COVID-19 data that may lead to distortions in the magnitude of any sex disparity. Early in the pandemic, with low case and mortality counts, small changes in the number of cases or mortalities can create large changes and high variability in sex rate ratios. A consistent finding, replicated by the Tracker, is that women tend to account for a greater share of confirmed COVID-19 infections (Curley, 2020; Griffith et al., 2020; Peckham et al., 2020). The higher numbers of cases among women in the U.S. is likely due in part to well-documented skews in surveillance testing rates linked to several sex- and gender-related factors. For example, pregnant women were prioritized for testing during a period when testing was not widely available because pregnancy is considered a risk factor for severe COVID-19, and universal testing upon admission for delivery is a common practice in the U.S. (The American College of Obstetricians and Gynecologists, 2020). Most healthcare workers, who are disproportionately women, are also tested at high rates (Cheeseman Day and Christnacht, 2019; U.S. Bureau of Labor Statistics, 2020).

Case fatality rates, which represent the number of confirmed deaths divided by the number of confirmed cases, have been inferred to be higher among men and have been used to argue that men have a higher risk of dying from COVID-19 once infected than do women (Gebhard et al., 2020; Scully et al., 2020). Case fatality rates would be an accurate and reliable indicator of sex disparities if cases of all levels of severity among women and men of all ages, classes, health statuses, and occupations were equally likely to be detected. However, if women are more likely to get tested for COVID-19 through routine surveillance, it is plausible that a greater number of cases - especially mild and asymptomatic ones - will be detected among women than among men. Analysis of COVID-19 testing and outcome data in the U.S. demonstrates that differential testing rates by sex are likely linked to observed disparities in case fatality rates, with widespread higher testing among women artificially lowering the case fatality rate in women compared to men (Gompers et al., 2021).

There may also be important differences in testing rates by race/ethnicity, socioeconomic status, geographic location, and other social categories that intersect with these gendered factors. While data reflecting COVID-19 testing availability and distribution by race/ethnicity are scarce, existing research points to clear barriers in accessing healthcare, both before and during the pandemic (Lopez et al., 2021). Receiving a COVID-19 test often takes significant time investment and can cost money, which may serve as barriers among economically disadvantaged social groups (Betancourt, 2020; Karedes, 2020). How these testing disparities interact with sex disparities remains under-investigated.

Mortality, too, may be differentially counted by sex, potentially amplifying the sex skew of mortality rates. An early study found a correlation between the magnitude of COVID-19 mortality sex disparities in U.S. states and states' healthcare capacity as well as women's access to healthcare, whereby lower healthcare capacity and lower access to healthcare for women correlated with larger disparities in mortality (Akter, 2021). This supports the hypothesis that gender inequities in access to care likely contribute to under-reporting of COVID-19 mortality among women. Data collection and reporting practices in nursing homes and other long-term care facilities (LTCFs) are another area of concern. While less than 1% of the U.S. population lives in these facilities, deaths in LTCFs account for approximately 34% of total COVID-19 deaths on the national scale (The New York Times, 2020). Although identification and reporting of COVID-19 cases and deaths in LTCFs varied significantly between locations, they have been characterized by under-counting and under-reporting, especially early in the pandemic (AARP, 2021; The New York Times, 2020). Women account for approximately 70% of LTCF residents (Harris-Kojetin et al., 2019), and under- or miscounting in these settings could affect overall estimates of COVID-19 deaths disaggregated by sex. The potential impact that such undercounting could have on apparent sex disparities is exemplified by states like Massachusetts and Connecticut. There, mortality rates for women and men have consistently been more similar than in other states, which has been attributed to more complete and timely reporting of COVID-19 deaths in LTCFs throughout the pandemic (Perls, 2020; Ostriker, 2020).

4.2. Social factors in variation in male-female disparities in COVID-19 outcomes

The heterogeneity of sex disparities across geographies and over the course of the pandemic suggests a number of theoretically-grounded hypotheses about the role of gender-related social factors in these patterns. These factors include gender-linked health behaviors and occupational exposures, which intersect with other socially-salient variables such as race/ethnicity and socioeconomic status.

Health Behaviors. Health behaviors vary across context and social

group, and may differ between women and men (Himmelstein and Sanchez, 2016). Multiple survey studies have found women and girls more likely to report mask wearing, hand washing, and compliance with other public health and social distancing recommendations (Chen et al., 2020; Galasso et al., 2020). Observational studies conducted in the U.S. support this finding. In a study of retail shoppers, men were 1.5 times less likely than women to be observed wearing a mask, while a study of pedestrians found that the proportion of women wearing masks was 17% higher than that of men (Haischer et al., 2020; Olcaysoy Okten, Gollwitzer, and Oettingen, 2020). Such gender differences may be expected to be particularly pronounced in the absence of enforced public health mandates (e.g., states that never instituted mask mandates or states that lifted mask mandates earlier than others), explaining some geographical and temporal variation in COVID-19 sex disparities.

Research shows that perceptions of the pandemic and of the importance of adopting protective health behaviors vary by gender and by party affiliation, which skews along many covariates, including geography and gender (Druckman et al., 2021; Niño et al., 2021). In the context of COVID-19, men are less likely to be concerned about their own health and the health of others, and less likely to support implementation of public health measures, including mask mandates and bans on public gatherings (Cassino and Besen-Cassino, 2020; Prichard and Christman, 2020). Men are also more likely than women to perceive masks as infringing on their freedom (Howard, 2021). Overall, these findings indicate that gender is associated with individuals' perceptions of COVID-19 risk and adoption of risk-mitigation behaviors during the pandemic.

Gender-linked occupational and other structural exposures. Evidence from past pandemics, including the 1918 influenza epidemic and other recent coronavirus outbreaks, suggests that apparent sex-related disparities in risk and outcomes were largely explained by geographically specific demographic and gendered structural variables (Bengtsson et al., 2018; Jia et al., 2009; Paskoff and Sattenspiel, 2019; Shattuck-Heidorn et al., 2020; Yang et al., 2017). Gender differences in structural patterns of exposure, including occupation, housing, and incarceration, stand out as especially powerful potential drivers of state-level variation in sex disparities in COVID-19 outcomes. Occupations are highly gender-stratified and are also tightly linked with exposure to COVID-19 and severe disease. In Massachusetts, workers in healthcare support, transportation, food preparation, grounds keeping, and construction experienced higher age-adjusted COVID-19 mortality rates than those for all workers (Hawkins et al., 2021). In California, food and agriculture workers showed the largest increase in mortality, followed by transportation and logistics, facilities, and manufacturing workers (Chen et al., 2021). In the U.S., the meatpacking industry was the site of numerous early pandemic hotspots (Davison, 2021). Differences in state-level paid sick leave policies, the length and reach of business shutdowns, school closures, and other policies likely contribute to variation in gender-linked occupational exposures across state and time (Kaiser Family Foundation, 2021).

Apart from healthcare support, men constitute the overwhelming majority of the labor force in the professions with heightened risk of COVID-19 mortality. For example, men account for 75.6% of agricultural workers and for 96% of construction, maintenance, and repair workers in the U.S. (U.S. Bureau of Labor Statistics, 2020). Gender disparities may also be present across categories of workers that left the workforce due to COVID-related issues, that were required to work remotely (such as teachers) or had access to personal protective equipment (such as healthcare workers), and those who did not, in caregiving, retail, agricultural, and construction occupations (Avdiu and Nayyar, 2020). U.S. women hold the majority of administrative, secretarial and teaching roles that were likely restructured for remote working during the pandemic (Robertson and Gebeloff, 2020; U.S. Bureau of Labor Statistics, 2020), although women are also more likely to provide paid and unpaid cross-household domestic and care-giving labor that increases risk of exposure (Van Houtven, DePasquale, and Coe, 2020; Feinberg et al., 2011; Altintas and Sullivan, 2016).

Other structural exposures, such as residential settings, including incarceration and homelessness, may also contribute to observed differences in mortality across states, considering that pandemic protective measures for these populations varied largely across geographies (National COVID bib19 Statistics "National COVID-19 Statistics, 2021). Incarcerated people, among whom Black men are overrepresented in the U.S., face extreme risk of exposure and minimal control over social distancing (Akiyama et al., 2020). Due to lengthy sentences, imprisoned populations are increasingly elderly, and nearly half of people in state prisons have at least one chronic condition (Hawks et al., 2020). Officially reported U.S. state and federal prison COVID-19 death rates dramatically exceed those of the general population, despite undercounting (Saloner et al., 2020). Men also comprise the majority of individuals experiencing homelessness in the U.S. (Moses and Janosko, 2018). In one study, more than a third of residents at a large shelter in Boston tested positive for COVID-19 (Baggett et al., 2020). Invisible in these sex disaggregated analyses are LGBTQ + populations, particularly queer and transgender people of color, who disproportionately experience homelessness and incarceration (ACLU West Virginia, 2020).

4.3. *The importance of intersectional analysis of COVID-19 health disparities*

COVID-19 outcomes vary across many social variables, including race/ethnicity, socioeconomic status, education level, housing status, zip codes, and occupational roles (Bassett et al., 2020; J. T. Chen et al., 2021; J. T. Chen and Krieger, 2021; Hawkins, 2020; Islam et al., 2020; Krieger, 2020; Lopez and Neely, 2021; McClure et al., 2020) and, as we have shown here, gender/sex. As emphasized above, a more nuanced and accurate picture of disparities in COVID-19 risks emerges from analyses of interactions *between* these variables (Laster Pirtle and Wright, 2021; Rushovich et al., 2021; Xu et al., 2021).

Gender/sex variables interact with other social variables to modulate risk and contribute to COVID-19 sex disparities. Analysis of data from Georgia and Michigan demonstrated that the sex disparity in COVID-19 mortality varies in magnitude across social groups defined by race. In Michigan, the sex disparity in COVID-19 mortality was 30% greater among Black Americans than it was among white Americans. Additionally, the COVID-19 mortality rate among Black women was five times larger than that of white women and nearly four times larger than that of white men (Rushovich et al., 2021). Similar findings were recently replicated at the national level (Xu et al., 2021). The root causes of such disparities are complex and linked to the ways that gendered structural factors, racism, and white supremacy have contributed to resource deprivation, differences in comorbidities, and lack of healthcare access.

Disparities in socio-economic status can also interact with gendered occupational exposures to drive variation in sex disparities in COVID-19 outcomes. Among some lower-paid occupations, the necessity of second jobs and unpaid care work increases risk of exposure (Van Houtven, DePasquale, and Coe, 2020). Workers deemed essential for in-person occupations often lacked adequate personal protective equipment, despite high levels of face-to-face interactions (Avdiu and Nayyar, 2020; Schneider and Harknett, 2020). In the U.S., they were also less likely to have health insurance or paid sick leave (Kearney and Muñana, 2020; The Shift Project, 2020).

Comorbidities should be understood as producing biological preconditions that reflect the interaction of gendered social-structural inequities in access to healthcare and access to lifestyle choices conducive to health (e.g., recreation, regular work schedules, etc.). Gender, race, sexuality, and class health disparities in chronic diseases are widely understood as reflections of historical, structural and contextual experiences of racism, discrimination and inequity (Williams et al., 2019). For example, a study of New York City residents found that although women in aggregate had lower prevalence of cardiovascular disease risk

factors than men, this "female protective advantage" was limited mostly to non-Latina white women. In fact, non-Latina Black women exhibited significantly greater prevalence of risk factors (e.g. hypertension and diabetes) than non-Latino white men, non-Latino women, and non-Latino Black men (Kanchi et al., 2018).

Trans, nonbinary, and gender-expansive individuals also face biosocial vulnerabilities to COVID-19 (Gibb et al., 2020). An exclusive focus on sex without consideration for gender contributes to critical gaps in knowledge about how COVID-19 has affected gender-diverse people (Perret et al., 2021). For example, they experience higher prevalence of cardiovascular disease, and bear the disproportionate burden of HIV, which compromises the immune system and if insufficiently treated may lead to higher risk of severe illness from COVID-19 (National Academies of Sciences, 2020; Poteat et al., 2016). These factors, unevenly distributed among gender categories across social groups, should be accounted for when investigating COVID-19 sex disparities.

4.4. Placing sex-related biological variables in their social context

A primary focus on biological sex-related variables in explanations of sex disparities in COVID-19 outcomes (e.g., Klein et al., 2020; Takahashi et al., 2020) sustains two familiar fallacies in reasoning about sex disparities in health outcomes and their causes: (1) sex is emphasized while excluding or minimizing other important variables, such as age, comorbidities, or social context; and (2) gender differences between women and men are improperly attributed to sex (Springer et al., 2012).

Our approach to COVID-19 sex disparities embraces an understanding of SARS-COV-2 as a biological agent embedded in social contexts. The observation that the magnitude and direction of COVID-19 sex disparities varied widely across the course of the pandemic in the U.S. and across states does not disprove a role for biological factors, nor does it prove an overriding role for social ones. But it does discredit single-factor approaches that are not sensitive to contextual variation. The 13 months of pandemic data presented here supports the view that gender-related and other social factors (e.g., age demographics and gendered and racialized occupational stratification and comorbidities) are potentially as or more relevant than biological sex in shaping gender/sex disparities in vulnerability to COVID-19.

5. Conclusion

The U.S. Gender/Sex COVID-19 Data Tracker, which collected available weekly state-level data disaggregated by sex on case and mortality counts throughout the pandemic, offers an important longitudinal dataset for exploring how sex and/or gender may or may not have played a factor in variations in COVID-19 transmission, illness, and death across U.S. states. Here, we use Tracker data to highlight the significant variation present in sex-classified case and mortality rates when analyzed across geographic locality and time, weakening the evidence for a primary causal role for biological sex in these patterns. Future research could leverage this publicly-available dataset, in combination with other data, to explore the effects of policy, investment, vaccine uptake, and other underlying structural inequities on sex disparities in COVID-19 outcomes. We emphasize that understanding the role of gender and sex in COVID-19 disparities requires comprehensive, accessible, and transparent data on COVID-19 outcomes that include not only sex, but also gender identity, race, class, comorbidities, occupation, and other relevant demographic variables, in combination with quantitative and qualitative data on gendered behaviors, occupations, and comorbidities that may be associated with COVID-19 outcomes.

Author contributions

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Declaration of competing interest

None.

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Appendix A. Supplementary data

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