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Declining COVID-19 case-fatality in Georgia, USA, March 2020 to March 2021: a sign of real improvement or a broadening epidemic?

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A B S T R A C T

Purpose: To examine whether declines in the crude U.S. COVID-19 case fatality ratio is due to improved clinical care and/or other factors.
Methods: We used multivariable logistic regression, adjusted for age and other individual-level characteristics, to examine associations between report month and mortality among confirmed and probable COVID-19 cases and hospitalized cases in Georgia reported March 2, 2020 to March 31, 2021.
Results: Compared to August 2020, mortality risk among cases was lowest in November 2020 (OR = 0.84; 95% CI: 0.78–0.91) and remained lower until March 2021 (OR = 0.86; 95% CI: 0.77–0.95). Among hospitalized cases, mortality risk increased in December 2020 (OR = 1.16, 95% CI: 1.07–1.27) and January 2021 (OR = 1.25; 95% CI: 1.14–1.36), before declining until March 2021 (OR = 0.90, 95% CI: 0.78–1.04).
Conclusions: After adjusting for other factors, including the shift to a younger age distribution of cases, we observed lower mortality risk from November 2020 to March 2021 compared to August 2020 among cases. This suggests that improved clinical management may have contributed to lower mortality risk. Among hospitalized cases, mortality risk increased again in December 2020 and January 2021, but then decreased to a risk similar to that among all cases by March 2021.

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Despite stay-at-home orders and other extraordinary public health efforts, COVID-19 was the third leading cause of death in the United States in 2020 [1]. While U.S. case counts have followed complex patterns, the crude case fatality ratio (CFR), or the proportion of identified cases who died, declined between May 2020 and January 2021 [2]. One possible explanation for this decline is that improved clinical management led to increased survival among cases. However, because the crude CFR is not adjusted for other variables, additional factors must be considered before concluding that declines are a result of improved clinical care. First, the COVID-19 case distribution in the United States shifted to a younger demographic [3], and younger individuals are less susceptible to severe disease. Second, the number of cases among long-term care facility (LTCF) residents, who have an increased risk of severe illness [4], declined over time. Third, the social determinants of COVID-19 mortality, including race and occupation of cases, may have changed over time. For instance, essential work-

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ers, a population disproportionately comprised of racial minorities [5], were likely among the first to become infected. These populations may also have been more vulnerable to severe illness and death [5,6]. Lastly, testing among the general population increased as the pandemic progressed, leading to an increased detection of less severe cases [7].

While previous studies have examined trends in COVID-19 case-fatality in the United States, these studies included hospitalized cases only and did not consider changes in the proportion of cases that were LTCF residents [8–10]. In this analysis, we examine the risk of COVID-19 death among reported cases in the state of Georgia. The first case of COVID-19 was reported in Georgia on March 2, 2020 [11]. On April 5, 2020, COVID-19 became a nationally notifiable condition in the United States, after which all cases or suspected cases were legally required to be reported by physicians, laboratories, and other health providers to the Georgia Department of Public Health (GDPH) [12,13]. However, cases were being reported to the GDPH prior to this date. As of June 1, 2021, there have been nearly 900,000 confirmed cases of COVID-19 and 18,000 deaths reported in the state [14]. The primary aim of this study is to examine temporal changes in the risk of COVID-19 mortality among cases in Georgia, and to determine the extent to which trends can be explained by shifts in case demographics and setting over time as opposed to improved survival. A second aim of this study is to examine individual-level risk factors for COVID-19 mortality. Lastly, because mortality trends among hospitalized cases, compared to all cases, are less affected by changes in testing and reporting, as only more severe cases are hospitalized, we also examine temporal changes in risk and individual-level risk factors for COVID-19 mortality among hospitalized cases in Georgia.

Materials and methods

Data description

We used individual-level COVID-19 surveillance data collected by the GDPH. Data were downloaded on June 13, 2021 and restricted to confirmed and probable cases reported March 2, 2020 to March 31, 2021, approximately 2.5 months prior to data download to account for lags in reporting and death. Cases with positive results from reverse-transcription polymerase chain reaction (PCR) tests were classified as confirmed, and cases lacking PCR results but meeting other testing, clinical, epidemiologic, and/or vital records criteria were classified as probable [14]. Confirmed cases were classified as COVID-19 deaths if they: 1) died within 60 days of their most recent positive PCR specimen collection date and had symptoms compatible with COVID-19 indicated as contributors to death on death certificates, 2) died with 21 days of their most recent positive PCR specimen collection date and had natural causes of death indicated on death certificates, 3) had COVID-19 indicated as the cause of death on death certificates, or 4) had evidence that COVID-19 contributed to death [14]. We also used information from the following datasets: 1) GDPH PCR testing data, which was used to examine trends in the number of PCR tests reported and the percent that were positive for SARS-CoV-2 by month, 2) 2010 census data from the U.S. Census Bureau [15] and rural-urban continuum codes from the U.S. Department of Agriculture [16], which were used to classify cases' counties as metro-urban, nonmetro-urban, or nonmetro-rural, and 3) COVID-19 Reported Patient Impact and Hospital Capacity by State Timeseries data, which was used to examine the percent of hospital beds occupied by COVID-19 patients in Georgia by month [17].

The following individual-level variables were included in our study: COVID-19 death, case report month, race/ethnicity, age, gender, LTCF residency status (LTCF resident or non-LTCF resident) and metro-urban status (metro-urban, nonmetro-urban or nonmetro-

rural). If cases were missing information on COVID-19 death, we assumed they did not die from COVID-19. Cases with COVID-19 death listed as "Under Review" were excluded from all analyses. We categorized reported race/ethnicity as Hispanic/Latino (any race), and non-Hispanic/Latino Black, Asian, White or Other. The Other race/ethnicity category included American Indian/Alaska Native (1.6%), Native Hawaiian/Pacific Islander (2.4%), and "other" (96%). To determine LTCF residency status, cases were first categorized as LTCF-associated and then as residents or staff based on a decision tree (Supplementary Fig. 1). Lastly, metro-urban status was determined using cases' county of residence (usual residence at time of exposure/infection; 98.9%), when available, and current county (location at time of initial report; 1.1%) otherwise.

Risk factors for COVID-19 death: all cases

To identify temporal and demographic factors associated with COVID-19 death among cases in Georgia, we used univariable and multivariable logistic regression. The following independent variables were included in the multivariable analysis: report month, race/ethnicity, age, gender, LTCF residency status and metro-urban status. Due to uncertainty in testing and reporting early in the pandemic, we compared the odds of death for each month to that of August 2020, a mid-point in the study period.

Cases missing report month and/or LTCF residency status were excluded from analyses, as these variables were rarely missing (<0.05%). A total of 155,756 cases (14.9%) were missing information for other variables in the analysis: race/ethnicity (14.5%), age (0.4%), gender (1%), and/or metro-urban status (0.2%). These missing variables were imputed using multivariate imputation by chained equations (MICE) [18]. All variables included in the multivariable analysis, and also hospitalization, were included in imputation models. Variables for interactions between report month and age and race and age were included in imputation models using a transform–impute–transform approach [19]. These interaction terms were identified prior to imputations by performing interaction assessments of all pairs of independent variables for cases and hospitalized cases with complete information. Using the "mice" package in R [20], we created 15 imputed datasets with 20 iterations each. Imputation models were checked by comparing distributions of imputed variables and regression coefficients for individual datasets. The "mice" package was then used to perform regression analyses on individual imputed datasets and to pool results using "Rubin's Rules" (i.e., the mean point estimates were calculated and within- and between-dataset variances were incorporated into confidence interval estimates) [21]. However, for the interaction assessment, because the "mice" package could not be used to combine regression results for models with interaction terms, we performed regression analyses separately for each imputed dataset, used contrast statements to estimate coefficients and standard errors, and then combined results using "Rubin's Rules." Lastly, because multiple imputation can produce invalid results [22], we also performed a sensitivity analysis in which we excluded cases missing any information from the model (i.e., complete case analysis).

Risk factors for COVID-19 death: hospitalized cases

To identify temporal and demographic factors associated with COVID-19 death among hospitalized cases, we again used univariable and multivariable logistic regression models. We used the same 15 imputed datasets from the analysis of all cases, but restricted the data to cases that were reported as hospitalized in the original, non-imputed dataset. The same variables included in the multivariable regression analysis for all cases were included in the analysis for hospitalized cases.
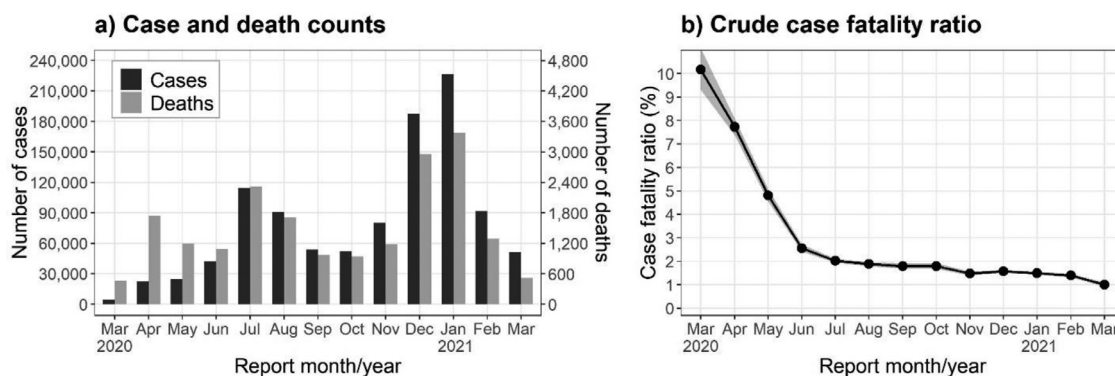
Fig. 1. Confirmed and probable COVID-19 case[1] and death[2] counts and crude case fatality ratio[3] by report month in Georgia, USA: March 2, 2020 – March 31, 2020.
[1]Confirmed cases were lab-confirmed by polymerase chain reaction (PCR); probable cases lacked PCR results but met other testing, clinical, epidemiologic, and/or vital records criteria.
[2]COVID-19 deaths were confirmed cases that were reported as deceased by healthcare providers or medical examiners/coroners, identified by death certificates with COVID-19 indicated as the cause of death, or had evidence that COVID-19 contributed to death.
[3]The crude case fatality ratio was calculated by dividing the number of COVID-19 deaths reported in a given month by the number of confirmed and probable cases reported that month.

All statistical analyses were performed using R software version 4.0.5. This activity was determined by the Georgia Department of Public Health Institutional Review Board to be nonresearch and consistent with public health surveillance as per title 45 code of Federal Regulations 46.102(1)(2).

Results

After excluding cases with COVID-19 mortality listed as "Under Review" (n = 1801; 8.4% of confirmed or possible COVID-19 deaths) and cases missing report month (n = 326; 0.03% of cases) and/or LTCF residency status (n = 21; 0.002% of cases), a total of 1043,407 confirmed and probable COVID-19 cases, 65,870 hospitalizations (6.3% of cases) and 19,754 deaths (1.9% of cases) were included in the analyses. Cases with COVID-19 mortality listed as "Under Review" were slightly less likely to be Black or Hispanic/Latino and more likely to be female or LTCF residents compared to confirmed deaths (Supplementary Table 1). The crude CFR, or the number of COVID-19 deaths divided by the number of cases reported in a given month, was an average of 1.9%. COVID-19 case counts peaked in July 2020 and January 2021, and then decreased sharply from January to March 2021 (Fig. 1). Death counts followed a similar pattern, but with an additional peak in April 2020. The crude CFR declined sharply from 10.2% in March 2020 to 2.0% in July 2020, then decreased gradually to a minimum of 1.1% in March 2021 (Fig. 1). The number of reported PCR tests was greatest in July/August 2020 and December 2020/January 2021 (Fig. 2). Finally, monthly percent positivity peaked in March 2020 (31.5%), June 2020 (17.2%) and January 2021 (16.3%) (Fig. 2).

In a crude analysis comparing COVID-19 deaths to all cases and hospitalized cases, COVID-19 deaths were older, less likely to be Hispanic/Latino or female and more likely to be LTCF residents (Table 1). They were also more likely than all cases but about as likely as hospitalized cases to be in nonmetro-rural counties. Finally, COVID-19 deaths were more likely than all cases but less likely than hospitalized cases to be Black.

The distributions of race/ethnicity, age and LTCF residency status changed over the study period (Fig. 3). The proportion of cases that were Black was highest in March 2020 (52.7%) and then generally decreasing until September 2020, and the proportion of cases that were Hispanic/Latino increased substantially from 5% in March 2020 to 24.7% in June 2020 before declining. The proportion of cases that were less than 40 years of age increased each month until June 2020 and then plateaued. Lastly, the proportion of cases

that were LTCF residents peaked early at 16.1% in April 2020 before declining. Similar trends were seen among COVID-19 deaths, however there was no obvious trend in the age distribution, with the majority of deaths being ≥70 years throughout the study period (Supplementary Fig. 2).

Finally, we examined trends in hospital capacity by plotting the percentages of hospital inpatient beds and adult intensive care unit (ICU) beds that were occupied by COVID-19 patients by month in Georgia. The percent of COVID-19-occupied inpatient beds peaked three distinct times in April 2020 (14.2%), July 2020 (18.7%) and January 2021 (25.7%) (Supplementary Fig. 3). The percent of COVID-19-occupied ICU beds was highest in August 2020 (40.2%), when the data first became available, and January 2021 (46.5%).

Risk factors for COVID-19 death: all cases

To examine associations between COVID-19 mortality and report month among cases, we imputed missing values for race/ethnicity (14.5%), gender (1.0%), age (0.4%) and metro-urban status (0.2%). We found that the distributions of imputed variables and regression results were consistent across the 15 imputed datasets (Supplementary Figs. 4–6). After accounting for case demographics/location, we found that the odds of death, compared to the August 2020 reference, was highest in March 2020 (OR = 3.58; 95% CI: 3.17–4.04) and lowest in November 2020 (OR = 0.84; 95% CI: 0.78–0.91), but did not decrease monotonically during this time (Table 2, Fig. 4). Instead, the odds of death increased in June 2020 (OR = 1.21; 95% CI: 1.11–1.32) and July 2020 (OR = 1.27; 95% CI: 1.18–1.36). After November 2020, the odds of death remained consistently low until the end of the study period.

Furthermore, in the multivariable analysis, we found that Asian, Black and Hispanic/Latino cases had higher odds of death compared to White cases (ORs = 1.39 [95% CI: 1.24–1.55], 1.54 [95% CI: 1.49–1.59], and 1.40 [95% CI: 1.31–1.51], respectively), and cases with other race had lower odds of death (OR = 0.16; 95% CI: 0.13–0.20) (Table 2). Compared to cases less than 40 years, the odds of death increased monotonically with age from an OR of 4.82 (95% CI: 4.27–5.44) for cases 40–49 years to an OR of 255.64 (95% CI: 231.19–282.66) for cases ≥80 years. We also found that females had a lower odd of death compared to males (OR = 0.58; 95% CI: 0.56–0.60) and LTCF residents had a higher odd of death compared to non-LTCF residents (OR = 2.81; 95% CI: 2.70–2.92). Finally, the odds of death for cases in nonmetro-urban and nonmetro-rural
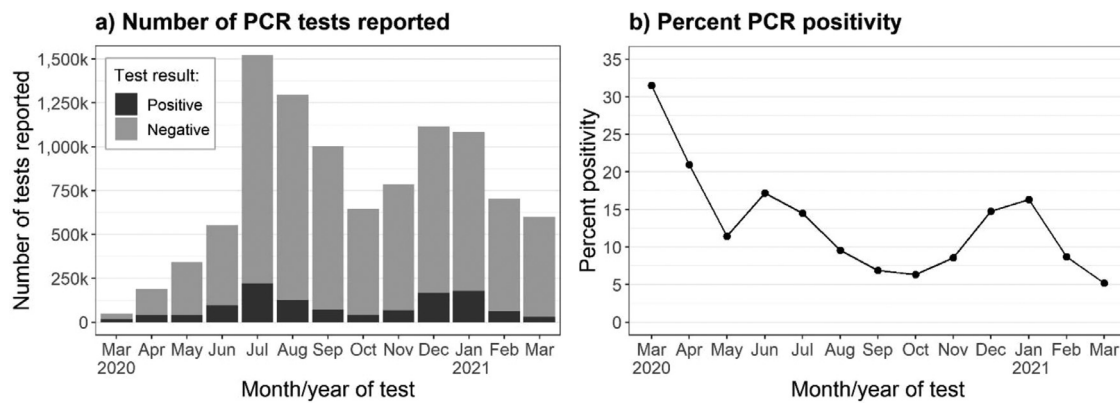
Fig. 2. Number of COVID-19 PCR tests by test result reported to the State of Georgia and COVID-19 percent positivity[1] by month: March 2, 2020 – March 31, 2021. Abbreviations: k = thousand; PCR = polymerase chain reaction.

[1] Percent positivity was calculated by dividing the number of positive PCR tests by the number of total PCR tests reported to the State of Georgia by month, multiplied by 100.

Table 1

Characteristics of confirmed and probable COVID-19 cases[*],[†], hospitalizations, and deaths[‡] in Georgia, USA: March 2, 2020 – March 31, 2020.

Characteristic	All cases (n = 1043,407)	Hospitalized cases (n = 65,870)	Deaths (n = 19,754)
Race/ethnicity (N (%))[§],[‖]			
White	456,995 (51.2)	29,535 (46.0)	11,493 (58.3)
Asian	22,927 (2.6)	1202 (1.9)	371 (1.9)
Black	268,631 (30.1)	25,428 (39.6)	6732 (34.2)
Hispanic/Latino	105,084 (11.8)	6768 (10.5)	1028 (5.2)
Other	38,839 (4.4)	1245 (1.9)	87 (0.4)
Age; years (median (IQR))	39 (24, 55)	62 (48, 74)	75 (65, 84)
Female (N (%))[§]	560,107 (54.2)	33,611 (51.1)	9314 (47.2)
LTCF resident (N (%))	31,956 (3.1)	6941 (10.5)	6097 (30.9)
Metro-urban status (N (%))[§],[¶]			
Metro-urban	852,000 (81.8)	50,267 (76.3)	14,321 (72.5)
Nonmetro-urban	169,527 (16.3)	13,654 (20.7)	4846 (24.5)
Nonmetro-rural	19,623 (1.9)	1929 (2.9)	580 (2.9)

Abbreviations: number, N; interquartile range, IQR; long-term care facility, LTCF.

[*] Cases with missing information were not included in the table (i.e., imputed values were excluded).

[†] Confirmed cases were lab-confirmed by polymerase chain reaction (PCR); probable cases lacked PCR results but met other testing, clinical, epidemiologic and/or vital records criteria.

[‡] COVID-19 deaths were confirmed cases that were reported as deceased by healthcare providers or medical examiners/coroners, identified by death certificates with COVID-19 indicated as the cause of death, or had evidence that COVID-19 contributed to death.

[§] Percentages were calculated by excluding cases with missing information (there was no missingness for LTCF residency status).

[‖] Race/ethnicity was categorized as Hispanic/Latino (any race) and non-Hispanic/Latino Black, Asian, White or Other; Other race/ethnicity included American Indian/Alaska Native, Native Hawaiian/Pacific Islander and those who reported their race as "other".

[¶] Metro-urban status is the classification of a case's county of residence (i.e., usual residence at time of exposure/infection), when available, and current county (i.e., location at time of initial report) otherwise.

counties were greater than that for cases in metro-urban counties (ORs = 1.30 [95% CI: 1.26–1.35] and 1.14 [95% CI: 1.04–1.25], respectively). Of note, age is a likely confounder of the associations between report month, race/ethnicity and LTCF residency status and COVID-19 death, as ORs for these variables changed meaningfully after age was added to the model (Supplementary Fig. 7). Lastly, in a sensitivity analysis excluding cases with missing data, we found that results were comparable to those from our main analysis (Supplementary Table 2).

Risk factors for COVID-19 death: hospitalized cases

To examine associations between COVID-19 mortality and report month among hospitalized cases, we excluded cases that were not hospitalized (n = 548,453; 52.6%) or had missing hospitalization information (n = 429,084; 41.1%) from the analysis. After ac-

counting for case demographics/location, we found slightly different trends in the risk of COVID-19 death compared to all cases. Most notably, compared to August 2020, the odds of death among hospitalized cases were higher in December 2020, January 2021 and February 2021 (ORs = 1.16 [95% CI: 1.07–1.27], 1.25 [95% CI: 1.14–1.36] and 1.11 [95% CI: 1.00–1.24, respectively), whereas the odds of death among all cases were lower during these months. However, the odds of death among hospitalized cases declined from January to March 2021, and the odds of death in March 2021, compared to August 2020, was again lower (OR = 0.90; 95% CI: 0.78–1.04) (Table 2, Fig. 4). Associations between COVID-19 mortality and case characteristics were similar for all cases and hospitalized cases, with the exceptions of race/ethnicity and metro-urban status. Unlike among all cases, Black and White hospitalized cases had about an equal odd of dying, as did hospitalized cases in nonmetro-rural and metro-urban counties (Table 2).
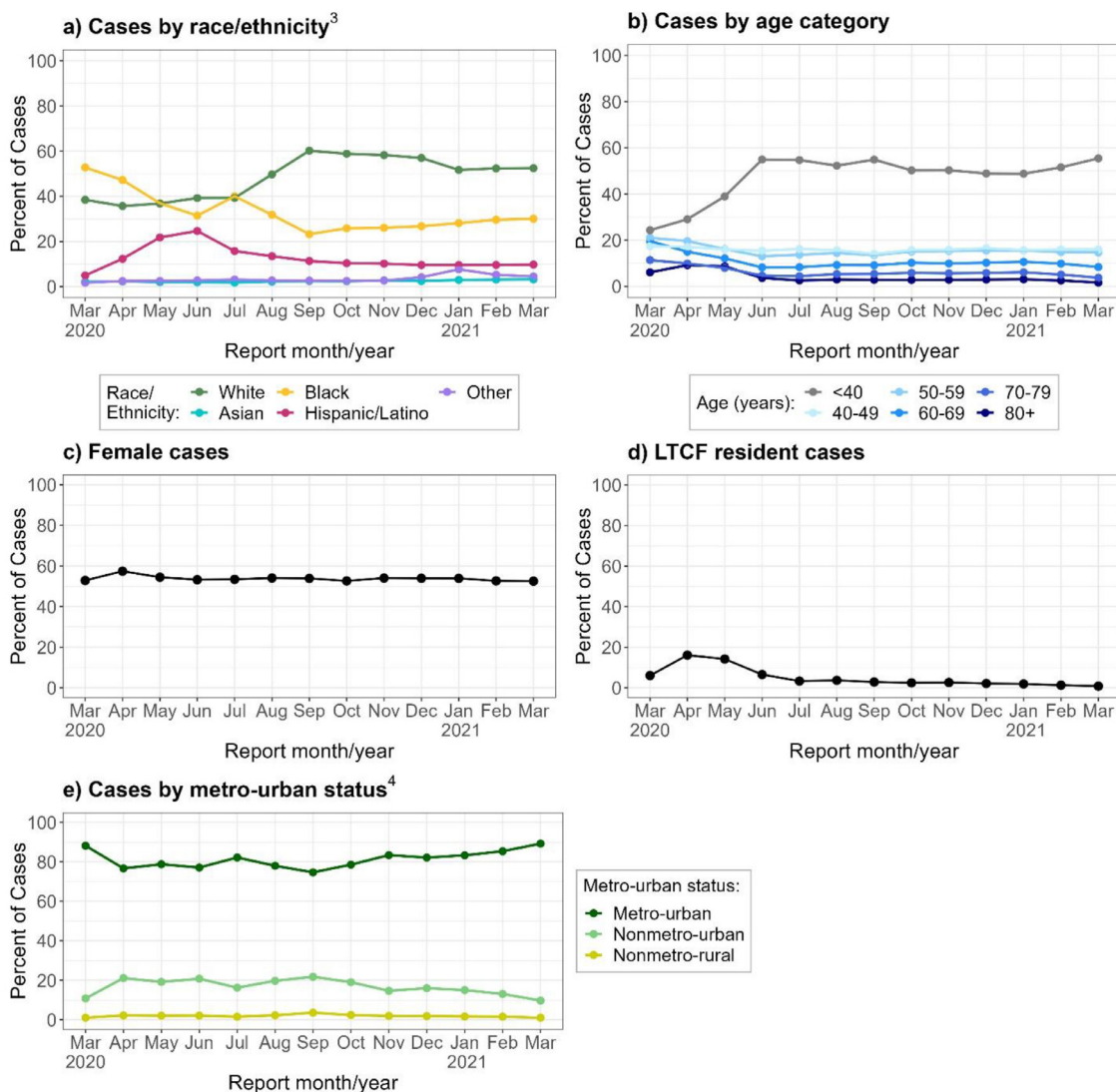
Fig. 3. Characteristics of confirmed and probable COVID-19 cases[1,2] by report month in Georgia, USA: March 2, 2020 – March 31, 2020

Abbreviations: LTCF = long-term care facility.

[1]Cases with missing information were not included in plots (i.e., imputed values were excluded).

[2]Confirmed cases were lab-confirmed by polymerase chain reaction (PCR); probable cases lacked PCR results but met other testing, clinical, epidemiologic, and/or vital records criteria.

[3]Race/ethnicity was categorized as Hispanic/Latino (any race) and non-Hispanic/Latino Black, Asian, White or Other; Other race/ethnicity included American Indian/Alaska Native, Native Hawaiian/Pacific Islander and those who reported their race as "other"; cases with non-missing race information but missing ethnicity information were assumed to be non-Hispanic/Latino.

[4]Metro-urban status is the classification of a case's county of residence (i.e., usual residence at time of exposure/infection), when available, and current county (i.e., location at time of initial report) otherwise.

Evidence for interactions: all cases and hospitalized cases

Among all cases and hospitalized cases, we found evidence for interactions between report month and age and race and age. Of note, Black race/ethnicity appeared to be a greater risk factor for COVID-19 mortality among younger cases and, to a lesser extent, younger hospitalized cases, with the odds of death among all cases decreasing monotonically with age from an OR of 2.84 (95% CI: 2.25–3.59) for cases less than 40 to an OR of 1.29 (95% CI: 1.20–1.37) for cases more than 80 years (Supplementary Figs. 8–9).

Discussion

Similar to national trends, the risk of COVID-19 mortality among cases in Georgia declined between March 2020 and March 2021. We investigated the extent to which this decline could be the result of shifting case characteristics as opposed to improved survival. Indeed, we found that Asian, Black and Hispanic/Latino race/ethnicity, male gender, being a LTCF resident, being in a nonmetro-urban or nonmetro-rural county and, especially, older age was associated with higher mortality among COVID-19 cases. Nevertheless, after adjusting for all these factors, we still observed lower mortality risk from November 2020 to March 2021, compared to August 2020, among cases. Because COVID-19 testing became more widely available in Georgia prior to August 2020, it is unlikely that these trends can be completely explained by changes in testing. This suggests that declines in COVID-19 mortality among cases were due, in part, to improved survival. This may have been due to improvements in clinical care, such as the use of remdesivir [23], dexamethasone [24,25], and monoclonal antibody treatment [26,27], a less overwhelmed healthcare system, and/or early COVID-19 vaccinations, which are more effective against severe

Table 2

Odds ratios (unadjusted and adjusted) for associations between COVID-19 death[*] and report month and case characteristics among all cases[†] and hospitalized cases in Georgia, USA: March 2, 2020 – March 31, 2021.

Variable	All cases (n = 1043,407)		Hospitalized cases (n = 65,870)	
	Univariable OR (95% CI)	Multivariable[‡] OR (95% CI)	Univariable OR (95% CI)	Multivariable[‡] OR (95% CI)
Report month/year				
March 2020	5.88 (5.29, 6.55)	3.58 (3.17, 4.04)	1.35 (1.19, 1.54)	1.44 (1.26, 1.66)
April 2020	4.35 (4.07, 4.66)	1.74 (1.61, 1.88)	1.62 (1.48, 1.77)	1.27 (1.15, 1.40)
May 2020	2.63 (2.44, 2.83)	1.11 (1.02, 1.21)	1.65 (1.48, 1.83)	1.27 (1.12, 1.43)
June 2020	1.37 (1.27, 1.48)	1.21 (1.11, 1.32)	0.95 (0.85, 1.06)	1.03 (0.92, 1.16)
July 2020	1.07 (1.01, 1.14)	1.27 (1.18, 1.36)	0.97 (0.89, 1.06)	1.10 (1.00, 1.20)
August 2020	Ref	Ref	Ref	Ref
September 2020	0.95 (0.88, 1.03)	1.05 (0.97, 1.15)	0.97 (0.87, 1.08)	0.95 (0.85, 1.07)
October 2020	0.95 (0.88, 1.03)	1.03 (0.95, 1.12)	0.96 (0.86, 1.07)	0.95 (0.85, 1.07)
November 2020	0.78 (0.72, 0.84)	0.84 (0.78, 0.91)	0.97 (0.88, 1.08)	0.91 (0.82, 1.02)
December 2020	0.83 (0.78, 0.88)	0.91 (0.86, 0.98)	1.25 (1.16, 1.36)	1.16 (1.07, 1.27)
January 2021	0.79 (0.74, 0.84)	0.84 (0.79, 0.90)	1.36 (1.25, 1.47)	1.25 (1.14, 1.36)
February 2021	0.74 (0.68, 0.79)	0.91 (0.84, 0.98)	1.15 (1.04, 1.27)	1.11 (1.00, 1.24)
March 2021	0.53 (0.48, 0.59)	0.86 (0.77, 0.95)	0.76 (0.66, 0.86)	0.90 (0.78, 1.04)
Race/ethnicity[§,‖]				
White	Ref	Ref	Ref	Ref
Asian	0.63 (0.57, 0.70)	1.39 (1.24, 1.55)	0.97 (0.85, 1.11)	1.47 (1.27, 1.70)
Black	1.00 (0.97, 1.03)	1.54 (1.49, 1.59)	0.67 (0.64, 0.70)	1.03 (0.99, 1.08)
Hispanic/Latino	0.38 (0.36, 0.41)	1.40 (1.31, 1.51)	0.40 (0.37, 0.44)	1.11 (1.02, 1.22)
Other	0.09 (0.07, 0.11)	0.16 (0.13, 0.20)	0.14 (0.11, 0.18)	0.20 (0.15, 0.27)
Age (years)[§]				
< 40	Ref	Ref	Ref	Ref
40–49	4.92 (4.36, 5.55)	4.82 (4.27, 5.44)	2.56 (2.19, 2.98)	2.40 (2.05, 2.80)
50–59	13.81 (12.43, 15.34)	13.37 (12.03, 14.86)	4.92 (4.29, 5.63)	4.50 (3.93, 5.16)
60–69	46.07 (41.70, 50.90)	42.32 (38.28, 46.78)	9.79 (8.60, 11.14)	8.58 (7.53, 9.79)
70–79	125.55 (113.80, 138.52)	109.21 (98.87, 120.62)	16.55 (14.56, 18.81)	13.96 (12.25, 15.91)
≥ 80	352.26 (319.45, 388.43)	255.64 (231.19, 282.66)	30.96 (27.22, 35.21)	23.60 (20.67, 26.94)
Gender[§]				
Male	Ref	Ref	Ref	Ref
Female	0.75 (0.73, 0.77)	0.58 (0.56, 0.60)	0.72 (0.69, 0.75)	0.68 (0.65, 0.70)
LTCF resident status				
Non-resident	Ref	Ref	Ref	Ref
Resident	17.23 (16.67, 17.80)	2.81 (2.70, 2.92)	4.40 (4.18, 4.64)	2.33 (2.20, 2.47)
Metro-urban status[§,¶]				
Metro-urban	Ref	Ref	Ref	Ref
Nonmetro-urban	1.72 (1.67, 1.78)	1.30 (1.26, 1.35)	1.28 (1.22, 1.34)	1.18 (1.12, 1.24)
Nonmetro-rural	1.78 (1.64, 1.94)	1.14 (1.04, 1.25)	1.08 (0.97, 1.21)	0.95 (0.84, 1.07)

Abbreviations: odds ratio, OR; confidence interval, CI; reference, Ref; long-term care facility, LTCF.

[*] COVID-19 deaths were confirmed cases that were reported as deceased by healthcare providers or medical examiners/coroners, identified by death certificates with COVID-19 indicated as the cause of death, or had evidence that COVID-19 contributed to death.

[†] Confirmed and probable cases were included. Confirmed cases were lab-confirmed by polymerase chain reaction (PCR); probable cases lacked PCR results but met other testing, clinical, epidemiologic and/or vital records criteria.

[‡] Multivariable models included the following independent variables: report month, race/ethnicity, age, gender, LTCF residency status and metro-urban status.

[§] Missing values for race/ethnicity, age, gender and metro-urban status were imputed using multivariate imputation by chained equations (MICE).

[‖] Race/ethnicity was categorized as Hispanic/Latino (any race) and non-Hispanic/Latino Black, Asian, White or Other; Other race/ethnicity included American Indian/Alaska Native, Native Hawaiian/Pacific Islander and those who reported their race as "other".

[¶] Metro-urban status is the classification of a case's county of residence (i.e., usual residence at time of exposure/infection), when available, and current county (i.e., location at time of initial report) otherwise.

disease and death than asymptomatic infection or mild disease [28].

However, we also found that trends in mortality risk among hospitalized cases differed from that among all cases. Most notably, mortality risk among hospitalized cases increased again in December 2020 and January 2021. While this difference in risk may be due to changes in testing and reporting, which is more likely to affect trends among all cases compared to hospitalized cases, the increased risk among hospitalized cases coincided with a sharp increase in the percent of hospital beds occupied by COVID-19 patients. Therefore, we hypothesize that the increased risk among hospitalized cases was primarily due to increased COVID-19 hospital occupancy rates, which may have led to increased mortality due to an overwhelmed healthcare system. Indeed, previous studies have similarly found that surges in COVID-19 caseload were associated with increased COVID-19 mortality risk [29,30], possibly due to staff shortages [31,32], staff burnout [32,33], and supply (e.g., ventilator) shortages [32,34]. Furthermore, increases in COVID-19

hospital occupancy rates may also have led to selection bias, with sicker patients being admitted given limited capacity, thus inflating mortality risk. This may explain why a similar increase in risk was not observed among all cases.

Similar trends in adjusted mortality risk among hospitalized COVID-19 cases were found in national studies of acute care hospitals [8,9] and the Department of Veterans Affairs healthcare system [10]. Other studies have similarly found that older age [35–37], male sex [8,9,35–38], and Asian race/ethnicity [39–41] are associated with increased COVID-19 mortality risk among cases. Our finding that cases in nonmetro-rural counties, compared to cases in metro-urban counties, had a greater risk of COVID-19 death is consistent with evidence that individuals in rural U.S. counties face disparities in access to healthcare [42,43]. However, among hospitalized cases, we found no association between nonmetro-rural county and COVID-19 death, possibly because cases in nonmetro-rural counties were less likely to be tested for COVID-19, therefore inflating mortality risk among all cases, or because cases in
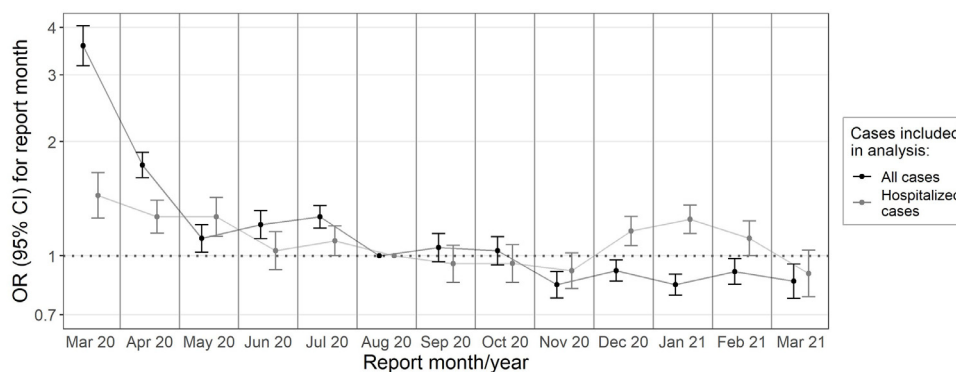
Fig. 4. Adjusted[1] odds ratios for associations between report month and COVID-19 death[2] among all cases[3] and hospitalized cases of COVID-19 in GA, USA: March 2, 2020 – March 31, 2020.

Abbreviations: OR = odds ratio; CI = confidence interval.

[1]Logistic regression models included the following independent variables: report month, race/ethnicity, age, gender, LTCF residency status and metro-urban status; metro-urban status is the classification of a case's county of residence, when available, and current county otherwise.

[2]COVID-19 deaths were confirmed cases that were reported as deceased by healthcare providers or medical examiners/coroners, identified by death certificates with COVID-19 indicated as the cause of death, or had evidence that COVID-19 contributed to death.

[3]Confirmed and probable cases were included. Confirmed cases were lab-confirmed by polymerase chain reaction (PCR); probable cases lacked PCR results but met other testing, clinical, epidemiologic and/or vital records criteria.

nonmetro-rural counties were being transferred to larger, urban hospitals where COVID-19 occupancy rates may have been lower, resulting in improved survival. Without more detailed data on hospitalizations, we were unable to examine this further. Lastly, there is currently mixed evidence for associations between Hispanic/Latino and Black race/ethnicity and increased mortality risk among cases. While some studies have found that Hispanic/Latino and Black cases have an increased mortality risk [40,41], most studies have found no evidence of an increased risk [39,44–46]. Furthermore, among hospitalized cases, we found no association between Black race/ethnicity and COVID-19 death, possibly because Black individuals were less likely to be tested, therefore inflating the mortality risk [40,45], or because Black individuals, who are less likely than White individuals to have health insurance in Georgia [47], had less access to or were less likely to seek non-hospital care [48]. While less access to hospital care could also explain this finding, we found that Black and White cases who died were about equally likely to have been hospitalized or to have missing hospitalization information. Nevertheless, while there is mixed evidence about increased risk of case fatality, Black individuals have clearly experienced disproportionately higher rates of SARS-CoV-2 infection and COVID-19-related mortality [44]. This may be due to type of work (e.g., essential work) [5], access to healthcare [47,48], and racism, the latter of which has been linked to stress and other medical conditions that can increase the risk of severe COVID-19 [49,50].

We note a number of limitations with this analysis. First, limited testing early in the pandemic inflated the risk COVID-19 mortality among reported cases. To address this, we compared the risk of death for each month to that of August 2020, a month in which testing was more widely available in Georgia. Furthermore, we examined trends among hospitalized cases, which are less subject to bias from changes in testing. Similarly, testing and reporting changed over the course of the pandemic, which could not be fully addressed in this analysis. Second, information on hospitalization was missing for almost half of cases, so some cases missing hospitalization information were likely misclassified as having not been hospitalized. For this reason, our main analysis examined COVID-19 mortality among all case, rather than hospitalized cases. Third, race/ethnicity was frequently missing. To address this, we used MICE to impute missing information. Fourth, additional social determinants of health, including occupation, education, and socioeconomic status, could not be controlled for in this analysis due

to data limitations. If these variables were associated with both time of infection and COVID-19 mortality, results may be subject to bias from residual confounding. Fourth, due to missingness, we were unable to include vaccination status in our analyses. Future studies should examine associations between COVID-19 vaccination and mortality risk in Georgia.

Conclusions

After adjusting for individual-level characteristics, the risk of COVID-19 mortality among cases was lower from November 2020 to March 2021 compared to August 2020, suggesting that improved clinical management may have contributed to lower mortality risk. Among hospitalized cases, mortality risk increased again in December 2020 and January 2021, but then decreased to a risk similar to that among all cases by March 2021.

Authors contributions

Benjamin A. Lopman: Conceptualized, Supervision, Writing- Reviewing and Editing. Carly Adams: Data analysis, Writing- Original draft preparation. Pascale Wortley: Subject matter expertise, Writing- Reviewing and Editing. Allison Chamberlain: Subject matter expertise, Writing- Reviewing and Editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.annepidem.2022.05.008.

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