JAMA Network Open

Original Investigation | Infectious Diseases

Risk Factors Associated With In-Hospital Mortality in a US National Sample of Patients With COVID-19

Ning Rosenthal, MD, MPH, PhD; Zhun Cao, PhD; Jake Gundrum, MS; Jim Sianis, PharmD, MBA; Stella Safo, MD, MPH

Abstract

IMPORTANCE Coronavirus disease 2019 (COVID-19) has infected more than 8.1 million US residents and killed more than 221 000. There is a dearth of research on epidemiology and clinical outcomes in US patients with COVID-19.

OBJECTIVES To characterize patients with COVID-19 treated in US hospitals and to examine risk factors associated with in-hospital mortality.

DESIGN, SETTING, AND PARTICIPANTS This cohort study was conducted using Premier Healthcare Database, a large geographically diverse all-payer hospital administrative database including 592 acute care hospitals in the United States. Inpatient and hospital-based outpatient visits with a principal or secondary discharge diagnosis of COVID-19 (*International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis code, U07.1) between April 1 and May 31, 2020, were included.

EXPOSURES Characteristics of patients were reported by inpatient/outpatient and survival status. Risk factors associated with death examined included patient characteristics, acute complications, comorbidities, and medications.

MAIN OUTCOMES AND MEASURES In-hospital mortality, intensive care unit (ICU) admission, use of invasive mechanical ventilation, total hospital length of stay (LOS), ICU LOS, acute complications, and treatment patterns.

RESULTS Overall, 64 781 patients with COVID-19 (29 479 [45.5%] outpatients; 35 302 [54.5%] inpatients) were analyzed. The median (interquartile range [IQR]) age was 46 (33-59) years for outpatients and 65 (52-77) years for inpatients; 31 968 (49.3%) were men, 25 841 (39.9%) were White US residents, and 14 340 (22.1%) were Black US residents. In-hospital mortality was 20.3% among inpatients (7164 patients). A total of 5625 inpatients (15.9%) received invasive mechanical ventilation, and 6849 (19.4%) were admitted to the ICU. Median (IQR) inpatient LOS was 6 (3-10) days. Median (IQR) ICU LOS was 5 (2-10) days. Common acute complications among inpatients included acute respiratory failure (19 706 [55.8%]), acute kidney failure (11 971 [33.9%]), and sepsis (11 910 [33.7%]). Older age was the risk factor most strongly associated with death (eg, age ≥80 years vs 18-34 years: odds ratio [OR], 16.20; 95% CI, 11.58-22.67; $P < .001$). Receipt of statins (OR, 0.60; 95% CI, 0.56-0.65; $P < .001$), angiotensin-converting enzyme inhibitors (OR, 0.53; 95% CI, 0.46-0.60; $P < .001$), and calcium channel blockers (OR, 0.73; 95% CI, 0.68-0.79; $P < .001$) was associated with decreased odds of death. Compared with patients with no hydroxychloroquine or azithromycin, patients with both azithromycin and hydroxychloroquine had increased odds of death (OR, 1.21; 95% CI, 1.11-1.31; $P < .001$).

(continued)

Key Points

Question What are the epidemiologic characteristics of patients with coronavirus disease 2019 (COVID-19) treated in US hospitals, and what risk factors are associated with mortality?

Findings In this cohort study of 64 781 patients with COVID-19 treated in 592 US hospitals during April and May 2020, the in-hospital mortality rate was 20.3% among inpatients, and severe complications were common. Receipt of statin, angiotensin-converting enzyme inhibitors, and calcium channel blockers were associated with decreased odds of mortality, but the combination use of hydroxychloroquine and azithromycin was associated with increased odds of mortality.

Meaning In this study, COVID-19 was associated with severe complications and deaths among patients hospitalized in the United States; certain medications may be associated with decreased odds of mortality.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

CONCLUSIONS AND RELEVANCE In this cohort study of patients with COVID-19 infection in US acute care hospitals, COVID-19 was associated with high ICU admission and in-hospital mortality rates. Use of statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers were associated with decreased odds of death. Understanding the potential benefits of unproven treatments will require future randomized trials.

JAMA Network Open. 2020;3(12):e2029058.
Corrected on January 14, 2021. doi:10.1001/jamanetworkopen.2020.29058

Introduction

Since the first case of coronavirus disease 2019 (COVID-19) was confirmed in the United States in January 2020, more than 12 million US residents have become ill, and more than 250 000 have died.[1,2] The pandemic has affected the lives of all US residents, disrupted business operations, and overwhelmed hospitals. Despite its tremendous impact, there is a dearth of research on the epidemiology and clinical outcomes of patients with COVID-19 in the United States. Earlier literature has mainly focused on epidemiologic insights from China and the European Union,[3-7] with difficulty extrapolating these findings to the US patient population due to different demographic, socioeconomic, and clinical characteristics as well as different health care delivery systems that affect utilization patterns.

To date, most studies from the United States use either surveillance data with minimal clinical information or data from single health care facilities.[8-10] A study of 5700 patients with confirmed COVID-19 who were hospitalized in a large New York City health system during March 2020 showed that hypertension, obesity, and diabetes were the most common comorbidities; 14.2% of patients with COVID-19 required care in the intensive care unit (ICU); 12.2% of patients received invasive mechanical ventilation; and 21.0% of patients died.[11] However, the overall treatment patterns and risk factors associated with in-hospital mortality among patients treated in hospitals across the United States remain largely unknown.

Using data from 592 hospitals included in the largest hospital discharge database in the United States, the Premier Healthcare Database (PHD), this study aimed to examine the epidemiology, clinical outcomes, and treatment patterns of patients with COVID-19 who were discharged between April 1 and May 31, 2020. It also aimed to identify potential risk factors associated with in-hospital mortality.

Methods

Study Design and Data Source

A retrospective cohort study was conducted to address the study objectives using the most up-to-date PHD data. The PHD is a large, geographically diverse, hospital-based, service-level, all-payer database containing discharge information from inpatient and hospital-based outpatient visits.[12] PHD data were obtained from the Premier hospital quality improvement technology solution, Quality Advisor. It represents approximately 20% of all inpatient admissions in the United States since 2000. As of June 1, 2020, there were more than 1 billion inpatient and outpatient discharges from 1057 hospitals included in the PHD. All data are statistically deidentified and compliant with the Health Insurance Portability and Accountability Act. Patients can be tracked within the hospital through a unique identifier. The PHD contains patient-level and visit-level data from standard hospital discharge files, including patient demographic characteristics, disease states, and a time-stamped log of billed items, including procedures, medications, and laboratory, diagnostic, and therapeutic services. Information on hospital geographic location, rural/urban populations served, teaching

status, and bed capacity are available. Given the timing of the study, an early-release version of the PHD database with a 2-week time lag was used for the current analysis. The early-release data included all data elements from the standard PHD from a subset of 592 hospitals, and all clinical data have been validated. Only cost reconciliation remained incomplete, and that information was not included in this study. Institutional review board approval for this study was not required, based on US Title 45 Code of Federal Regulations, Part 46, because the study used existing deidentified hospital discharge data and recorded information could not be identified directly or through identifiers linked to individuals. No informed consent of study participants was pursued due to the nature of the deidentified data. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study Population

According to the US Centers for Disease Control and Prevention's Official Coding and Reporting Guidelines,[13] all inpatient hospitalization or hospital-based outpatient visits with a principal or secondary discharge diagnosis of COVID-19 (*International Classification of Diseases, 10th revision, Clinical Modification* [*ICD-10-CM*] diagnosis code U07.1) between April 1 and May 31, 2020, were identified as confirmed cases of COVID-19 for study inclusion. For patients who had both inpatient and outpatient visits with a discharge diagnosis of COVID-19, only inpatient visits were included in the current analysis. If a patient had multiple inpatient or outpatient visits with a discharge diagnosis of COVID-19 during the study period, only the first inpatient or outpatient visit was included in the analysis.

Study Variables

Patient, Hospital, and Visit Characteristics

The demographic characteristics examined included age, sex, patients' self-reported race and ethnicity, and primary insurance payer. Hospital characteristics included urban and rural populations served, teaching status, US census geographical regions (ie, Midwest, Northeast, South, or West), and bed size (ie, 1-199, 200-499, or ≥500 beds). Hospital visit information, such as admission type, point of origin, and discharge disposition, was assessed. All of this information was provided by the participating hospitals.

Clinical Characteristics

Clinical characteristics included baseline comorbidities and COVID-19–related complications. The Charlson-Deyo Comorbidity Index (CCI) was used to assess the baseline comorbidities of patients with COVID-19.[14] In addition to CCI comorbidities, hypertension and hyperlipidemia were assessed. Acute complications assessed included acute respiratory failure, acute respiratory distress syndrome (ARDS), shock, sepsis, acute kidney failure, venous thromboembolism (VTE), cerebrovascular disease, metabolic abnormalities (ie, hypokalemia, hyperkalemia, hyponatremia, acidosis), acute liver damage, and neurological disorders (ie, epileptic seizures, rhabdomyolysis, Guillain-Barre syndrome, necrotizing hemorrhagic encephalopathy, acute encephalitis, myelitis, and encephalomyelitis) as defined by *ICD-10-CM* diagnosis codes listed in eTable 1 and eTable 2 in the Supplement.

Pharmacological Therapies

Common medications and supplements used for the target patient population were examined using hospital chargemaster descriptions. Medications assessed included angiotensin-converting enzyme (ACE) inhibitors, albumins, antiarrhythmics, anticoagulants, antiemetics, azithromycin and other antibiotics, β blockers, calcium channel blockers, blood growth factors, bronchodilators, corticosteroids, HIV antiretroviral therapies, hydroxychloroquine, immunoglobulin, immunomodulators, narcotic analgesics, other antihypertensives, remdesivir and other antiviral drugs, smoking deterrents, and statins. Use of zinc and vitamin C or D was also evaluated. To assess

the joint association of hydroxychloroquine and azithromycin with outcomes, a variable was created to indicate the use of both drugs with the following 4 categories: azithromycin only, hydroxychloroquine only, both azithromycin and hydroxychloroquine, and neither azithromycin nor hydroxychloroquine.

Clinical Outcomes

Clinical outcomes assessed included in-hospital mortality, ICU admission, use of invasive mechanical ventilation, total hospital length of stay (LOS), and ICU LOS. In-hospital mortality was defined as percentage of patients with COVID-19 who died in the hospital. Prevalence of ICU admission was defined as percentage of patients with COVID-19 who had any ICU service charge during the index hospitalization. Invasive mechanical ventilation use status was assessed using *ICD-10* procedure codes (ie, 5A1935Z, 5A1945Z, and 5A1955Z) or *Current Procedural Terminology* (*CPT*) codes (ie, 94002, 94003, 94004, and 94005). The prevalence of invasive mechanical ventilation was reported.

Statistical Analysis

A descriptive analysis was performed to assess the distribution of patient demographic characteristics, hospital characteristics, clinical characteristics, medication use, and clinical outcomes by treatment setting (inpatient vs outpatient) and survival status (survived vs deceased). Continuous data were expressed as mean (SD) or median (interquartile range [IQR]). Categorical variables were expressed as counts and percentages. We used χ^2 tests to test for statistical differences between groups for categorical variables. Two-sample comparisons were evaluated using a Wilcoxon rank sum test for continuous variables. A 2-sided $P < .05$ was considered statistically significant.

Multivariable logistic regression was used to assess the association between potential risk factors and the in-hospital mortality rate among all adult inpatients with known sex, adjusting for known confounders. The hospital-based outpatient visits were not included in the multivariable analysis. Variables assessed included demographic characteristics (ie, age, sex, race, ethnicity, payer type), visit characteristics (ie, type of admission, admission point of origin), hospital characteristics (ie, geographic region, size, rural/urban status, teaching status), clinical characteristics (ie, comorbidities, complications), medications (ie, ACE inhibitors, statins, hydroxychloroquine and/or azithromycin use, β blockers, calcium channel blockers), and supplements (ie, Vitamin C or D and Zinc) used during index hospitalization. A stepwise selection method was used. A significance level of $P < .20$ was required to allow a variable into the model, and a significance level of $P < .10$ was required for a variable to stay in the model. The C statistic was used to assess model goodness of fit. All analyses were done by SAS version 9.4 (SAS Institute).

Results

Patient Characteristics

A total of 64 781 patients with confirmed COVID-19, including 29 479 (45.5%) outpatients and 35 302 (54.5%) inpatients, were analyzed. The median (IQR) age was 46 (33-59) years for outpatients, 65 (52-77) years for inpatients, and 76 (66-84) years for those who died. Patients aged 65 years and older accounted for 35.4% of the total sample (22 903 patients) and 77.5% of all deaths (5704 of 7355). Among all patients with confirmed COVID-19, 31 968 (49.3%) were male, 25 841 (39.9%) were White individuals, 14 340 (22.1%) were Black individuals, 13 776 (21.3%) were Hispanic individuals, 22 945 (35.4%) had Medicare, 11 928 (18.4%) had Medicaid, and 21 698 (33.5%) had commercial insurance.

More than 80% of all patients were admitted emergently or urgently (52 406 patients [80.9%]); 51 163 (79.0%) were admitted from non–health care facility, and 2396 (3.7%) were admitted from long-term care facilities. More than 70% of patients were discharged to home or home health care (46 913 [72.4%]), 6949 (10.7%) were discharged to long-term care or

rehabilitation facilities, and 7355 (11.4%) died. More than half of all patients (34 612 [53.4]%) were from hospitals in the Northeast region, 33 887 (52.3%) were from hospitals with 200 to 499 beds, 38 145 (58.9%) were from teaching hospitals, and 58 398 (90.1%) were from urban hospitals. All patient characteristics significantly varied between outpatient and inpatient settings and between patients who survived and those died (**Table 1**).

Baseline Comorbidities

In the overall COVID-19 patient sample, the most common comorbidities included hypertension (30 236 [46.7%]), hyperlipidemia (18 744 [28.9%]), diabetes (18 091 [27.9%]), and chronic pulmonary disease (10 434 [16.1%]). The mean (SD) CCI score was 1.3 (2.0) for the overall sample, 2.1 (2.3) for inpatients, and 3.1 (2.5) for those who died. Overall, 26 351 patients (40.7%) had CCI scores between 1 and 4, and 5852 (9.0%) had scores greater than 5. Inpatients had a higher level of all comorbidities than outpatients, and those who died had a higher level of all comorbidities (except for metastatic solid tumor) than who survived (Table 1).

Acute Complications

In the overall patient sample, the most common acute complication was acute respiratory failure (19 960 [30.8%]), followed by acute kidney failure (12 181 [18.8%]) and sepsis (12 039 [18.6%]). Among inpatients, 2871 (8.1%) had ARDS, 4028 (11.4%) had shock, 2857 (8.1%) had acute ischemic heart disease, 2606 (7.4%) had neurological disorders, 1446 (4.1%) had VTE, and 810 (2.3%) had cerebrovascular disease. Inpatients and those who died had significantly higher prevalence of all complications than outpatients and those who survived (**Table 2**).

Medications and Supplements

Among all medications assessed in the overall sample, narcotic analgesic medications were most commonly used (35 377 [54.6%]), followed by antibiotics (azithromycin, 19 411 [30.0%]; other antibiotics, 27 123 [41.9%]), and anticoagulants (24 867 [38.4%]). Hydroxychloroquine was used for 18 751 inpatients (53.1%) and 187 outpatients (0.6%). More than one-third of inpatients (12 084 [34.2%]) used both hydroxychloroquine and azithromycin. For antihypertensive drugs, 3023 inpatients (8.6%) used ACE inhibitors and 8017 (22.7%) used other antihypertensive drugs. Other common cardiovascular drugs used among inpatients included β blockers (10 960 [31.0%]), calcium channel blockers (8372 [23.7%]), and statins (11 970 [33.9%]). Corticosteroids and vitamin C or D were used by 12 342 inpatients (35.0%) and 8631 inpatients (24.4%), respectively (**Table 3**).

Clinical Outcomes

The in-hospital mortality rate was 11.4% for the overall sample (7355 of 64 781) and 20.3% for inpatients (7164 of 35 302). Nearly one-sixth of inpatients (5625 [15.9%]) used invasive mechanical ventilation, and 6849 (19.4%) were admitted to the ICU. The mean (SD) total LOS for inpatients was 7.7 (10.8) days, and the median (IQR) was 6 (3-10) days. Among inpatients with an ICU admission, the mean (SD) ICU LOS was estimated to be 7.3 (6.8) days, and the median (IQR) was 5 (2-10) days (**Table 4**).

Risk Factors Associated With In-Hospital Mortality

Multivariable logistic regression results showed that older age was the risk factor most strongly associated with death. The odds of death were 16.2 times higher in inpatients aged 80 years or older than among those aged 18 to 34 years (odds ratio [OR], 16.20; 95% CI, 11.58-22.67; $P < .001$). Male inpatients had 18% greater odds of death than female inpatients (OR, 1.18; 95% CI, 1.10-1.26; $P < .001$). Compared with White inpatients, Black inpatients had 25% lower odds of death (OR, 0.75; 95% CI, 0.69-0.82; $P < .001$). Compared with inpatients who were admitted from non–health care facilities, those who were transferred from long-term care facilities had 50% higher odds of death

Table 1. Characteristics and Comorbidities for Patients With Confirmed Coronavirus Disease 2019 in Premier Healthcare Database, April to May 2020

Characteristics	No. (%)			P value	No. (%)		P value
	Overall sample (N = 64 781)	Outpatients (n = 29 479)	Inpatients (n = 35 302)		Survived (n = 57 426)	Deceased (n = 7355)	
Age, y							
Mean (SD)	56.1 (19.9)	47.1 (18.5)	63.6 (17.7)	<.001	53.7 (19.3)	74.2 (13.4)	<.001
Median (IQR)	57 (41-71)	46 (33-59)	65 (52-77)		54 (39-67)	76 (66-84)	
0-17	1071 (1.7)	888 (3.0)	183 (0.5)	<.001	1067 (1.9)	4 (0.1)	<.001
18-34	9483 (14.6)	7211 (24.5)	2272 (6.4)		9434 (16.4)	49 (0.7)	
35-49	13 340 (20.6)	8428 (28.6)	4912 (13.9)		13 057 (22.7)	283 (3.8)	
50-64	17 984 (27.8)	7929 (26.9)	10 055 (28.5)		16 669 (29.0)	1315 (17.9)	
65-79	14 170 (21.9)	3343 (11.3)	10 827 (30.7)		11 285 (19.7)	2885 (39.2)	
≥80	8733 (13.5)	1680 (5.7)	7053 (20.0)		5914 (10.3)	2819 (38.3)	
Sex							
Men	31 968 (49.3)	13 107 (44.5)	18 861 (53.4)	<.001	27 701 (48.2)	4267 (58.0)	<.001
Women	32 475 (50.1)	16 150 (54.8)	16 325 (46.2)		29 394 (51.2)	3081 (41.9)	
Unknown	338 (0.5)	222 (0.8)	116 (0.3)		331 (0.6)	7 (0.1)	
Race							
White	25 841 (39.9)	12 116 (41.1)	13 725 (38.9)	<.001	22 659 (39.5)	3182 (43.3)	<.001
Black	14 340 (22.1)	6073 (20.6)	8267 (23.4)		12 764 (22.2)	1576 (21.4)	
Other	24 600 (38.0)	11 290 (38.3)	13 310 (37.7)		22 003 (38.3)	2597 (35.3)	
Ethnicity							
Hispanic	13 776 (21.3)	7445 (25.3)	6331 (17.9)	<.001	12 832 (22.3)	944 (12.8)	<.001
Non-Hispanic	35 731 (55.2)	14 947 (50.7)	20 784 (58.9)		31 228 (54.4)	4503 (61.2)	
Other or unknown	15 274 (23.6)	7087 (24.0)	8187 (23.2)		13 366 (23.3)	1908 (25.9)	
Payer type							
Medicare	22 945 (35.4)	5352 (18.2)	17 593 (49.8)	<.001	17 595 (30.6)	5350 (72.7)	<.001
Medicaid	11 928 (18.4)	5557 (18.9)	6371 (18.0)		11 134 (19.4)	794 (10.8)	
Commercial insurance	21 698 (33.5)	12 676 (43.0)	9022 (25.6)		20 737 (36.1)	961 (13.1)	
Self-pay	4528 (7.0)	3630 (12.3)	898 (2.5)		4431 (7.7)	97 (1.3)	
Other or unknown	3682 (5.7)	2264 (7.7)	1418 (4.0)		3529 (6.1)	153 (2.1)	
Type of admission							
Emergency	47 529 (73.4)	16 406 (55.7)	31 123 (88.2)	<.001	40 883 (71.2)	6646 (90.4)	<.001
Urgent	4877 (7.5)	1940 (6.6)	2937 (8.3)		4370 (7.6)	507 (6.9)	
Elective	7057 (10.9)	5947 (20.2)	1110 (3.1)		6937 (12.1)	120 (1.6)	
Other or unknown	5318 (8.2)	5186 (17.6)	132 (0.4)		5236 (9.1)	82 (1.1)	
Admission point of origin							
Non-health care facility	51 163 (79.0)	22 666 (76.9)	28 497 (80.7)	<.001	45 802 (79.8)	5361 (72.9)	<.001
Clinic	6075 (9.4)	4399 (14.9)	1676 (4.7)		5806 (10.1)	269 (3.7)	
Transferred from acute care facility	3185 (4.9)	187 (0.6)	2998 (8.5)		2309 (4.0)	876 (11.9)	
Transferred from long-term care facility	2396 (3.7)	414 (1.4)	1982 (5.6)		1587 (2.8)	809 (11.0)	
Other or unknown	1962 (3.0)	1813 (6.2)	149 (0.4)		1922 (3.3)	40 (0.5)	
Discharge status							
Home or home health	46 913 (72.4)	27 593 (93.6)	19 320 (54.7)	<.001	46 913 (81.7)	0	NA
Long-term care or rehabilitation facility	6949 (10.7)	417 (1.4)	6532 (18.5)		6949 (12.1)	0	
Transferred to another acute care facility	417 (0.6)	73 (0.2)	344 (1.0)		417 (0.7)	0	
Died	7355 (11.4)	191 (0.6)	7164 (20.3)		0	7355 (100)	
Other or unknown	3147 (4.9)	1205 (4.1)	1942 (5.5)		3147 (5.5)	0	
Hospital region							
Midwest	11 577 (17.9)	6446 (21.9)	5131 (14.5)	<.001	10 672 (18.6)	905 (12.3)	<.001
Northeast	34 612 (53.4)	12 279 (41.7)	22 333 (63.3)		29 450 (51.3)	5162 (70.2)	
South	15 989 (24.7)	9430 (32.0)	6559 (18.6)		14 912 (26.0)	1077 (14.6)	
West	2603 (4.0)	1324 (4.5)	1279 (3.6)		2392 (4.2)	211 (2.9)	

(continued)

Table 1. Characteristics and Comorbidities for Patients With Confirmed Coronavirus Disease 2019 in Premier Healthcare Database, April to May 2020 (continued)

Characteristics	No. (%)			P value	No. (%)		P value
	Overall sample (N = 64 781)	Outpatients (n = 29 479)	Inpatients (n = 35 302)		Survived (n = 57 426)	Deceased (n = 7355)	
Hospital beds, No.							
1-199	9934 (15.3)	5526 (18.7)	4408 (12.5)	<.001	9246 (16.1)	688 (9.4)	<.001
200-499	33 887 (52.3)	16 396 (55.6)	17 491 (49.5)		29 842 (52.0)	4045 (55.0)	
≥500	20 960 (32.4)	7557 (25.6)	13 403 (38.0)		18 338 (31.9)	2622 (35.6)	
Hospital teaching status							
Teaching	38 145 (58.9)	13 847 (47.0)	24 298 (68.8)	<.001	33 023 (57.5)	5122 (69.6)	<.001
Nonteaching	26 636 (41.1)	15 632 (53.0)	11 004 (31.2)		24 403 (42.5)	2233 (30.4)	
Population served							
Urban	58 398 (90.1)	25 373 (86.1)	33 025 (93.5)	<.001	51 477 (89.6)	6921 (94.1)	<.001
Rural	6383 (9.9)	4106 (13.9)	2277 (6.5)		5949 (10.4)	434 (5.9)	
Charlson comorbidities[a]							
Myocardial infarction	3717 (5.7)	404 (1.4)	3313 (9.4)	<.001	2392 (4.2)	1325 (18.0)	<.001
Congestive heart failure	6045 (9.3)	744 (2.5)	5301 (15.0)	<.001	4173 (7.3)	1872 (25.5)	<.001
Peripheral vascular disease	1661 (2.6)	222 (0.8)	1439 (4.1)	<.001	1180 (2.1)	481 (6.5)	<.001
Cerebrovascular disease	2892 (4.5)	327 (1.1)	2565 (7.3)	<.001	2019 (3.5)	873 (11.9)	<.001
Dementia	6201 (9.6)	718 (2.4)	5483 (15.5)	<.001	4119 (7.2)	2082 (28.3)	<.001
Chronic pulmonary disease	10 434 (16.1)	2907 (9.9)	7527 (21.3)	<.001	8615 (15.0)	1819 (24.7)	<.001
Rheumatologic disease	821 (1.3)	127 (0.4)	694 (2.0)	<.001	649 (1.1)	172 (2.3)	<.001
Peptic ulcer disease	385 (0.6)	59 (0.2)	326 (0.9)	<.001	299 (0.5)	86 (1.2)	<.001
Mild liver disease	348 (0.5)	50 (0.2)	298 (0.8)	<.001	269 (0.5)	79 (1.1)	<.001
Diabetes							
Without complications	10 855 (16.8)	2974 (10.1)	7881 (22.3)	<.001	9274 (16.1)	1581 (21.5)	<.001
With chronic complications	7236 (11.2)	822 (2.8)	6414 (18.2)	<.001	5201 (9.1)	2035 (27.7)	<.001
Hemiplegia or paraplegia	524 (0.8)	49 (0.2)	475 (1.3)	<.001	377 (0.7)	147 (2.0)	<.001
Kidney disease	9069 (14.0)	968 (3.3)	8101 (22.9)	<.001	6291 (11.0)	2778 (37.8)	<.001
Any malignancy, including leukemia or lymphoma	1788 (2.8)	315 (1.1)	1473 (4.2)	<.001	1311 (2.3)	477 (6.5)	<.001
Moderate or severe liver disease	348 (0.5)	30 (0.1)	318 (0.9)	<.001	205 (0.4)	143 (1.9)	<.001
Metastatic solid tumor	506 (0.8)	82 (0.3)	424 (1.2)	<.001	365 (0.6)	141 (1.9)	<.001
AIDS/HIV	252 (0.4)	61 (0.2)	191 (0.5)	<.001	215 (0.4)	37 (0.5)	0.09
Charlson Comorbidity Index score, mean (SD)[a]	1.3 (2.0)	0.5 (1.1)	2.1 (2.3)	<.001	1.1 (1.8)	3.1 (2.5)	<.001
Charlson comorbidities, No.[a]							
0	32 578 (50.3)	22 036 (74.8)	10 542 (29.9)	<.001	31 650 (55.1)	928 (12.6)	<.001
1-4	26 351 (40.7)	6875 (23.3)	19 476 (55.2)		21 876 (38.1)	4475 (60.8)	
≥5	5852 (9.0)	568 (1.9)	5284 (15.0)		3900 (6.8)	1952 (26.5)	
Hypertension	30 236 (46.7)	6803 (23.1)	23 433 (66.4)	<.001	24 376 (42.4)	5860 (79.7)	<.001
Hyperlipidemia	18 744 (28.9)	3553 (12.1)	15 191 (43.0)	<.001	14 844 (25.8)	3900 (53.0)	<.001

Abbreviations: IQR, interquartile range; NA, not applicable.

[a] Comorbidities were assessed during both index visit and 6 months prior to index.

(OR, 1.50; 95% CI, 1.33-1.68; $P < .001$). Patients from hospitals in the Northeast had 59% higher odds of death than patients from hospitals in the Midwest (OR, 1.59; 95% CI, 1.44-1.76; $P < .001$) (**Table 5**).

Among all medications and supplements assessed, statins (OR, 0.60; 95% CI, 0.56-0.65; $P < .001$), vitamin C or D (OR, 0.89; 95% CI, 0.82-0.97; $P = .005$), ACE inhibitors (OR, 0.53; 95% CI, 0.46-0.60; $P < .001$), and calcium channel blockers (OR, 0.73; 95% CI, 0.68-0.79; $P < .001$) were associated with decreased odds of death. Compared with patients who did not use hydroxychloroquine or azithromycin, patients who used azithromycin only (OR, 1.02; 95% CI, 0.92-1.13; $P = .71$) or hydroxychloroquine only (OR, 1.08; 95% CI, 0.98-1.19; $P = .13$) had similar odds of death, while patients who received both azithromycin and hydroxychloroquine had increased odds of death (OR, 1.21; 95% CI, 1.11-1.31; $P < .001$) (Table 5).

Acute complications including sepsis (OR, 3.34; 95% CI, 3.12-3.57; *P* < .001), acute kidney failure (OR, 2.46; 95% CI, 2.30-2.63; *P* < .001), hyperkalemia (OR, 2.28; 95% CI, 2.09-2.48; *P* < .001), acidosis (OR, 1.85; 95% CI, 1.70-2.00; *P* < .001), acute liver damage (OR, 3.58; 95% CI, 2.95-4.35; *P* < .001), and neurological disorders (OR, 1.23; 95% CI, 1.10-1.38; *P* < .001) were associated with increased odds of death compared with patients without such complications (Table 5).

Discussion

COVID-19 presents an unprecedented challenge to the health care systems worldwide due to its complex transmission patterns, our limited understanding of risk factors associated with mortality, and the lack of effective treatments. To our knowledge, this study is the first to examine the demographic and clinical characteristics, treatment patterns, and risk factors associated with mortality using a large national sample of patients with confirmed COVID-19 across all census regions in the United States.

With 15.9% of inpatients receiving invasive mechanical ventilation, 19.4% of inpatients treated in an ICU, and 20.3% in-hospital mortality among inpatients with COVID-19, this study found that COVID-19 may lead to severe clinical outcomes, including death, among a high percentage of patients. The in-hospital mortality rate was highest among patients from the Northeast. The median hospital LOS was 6 days, with an IQR of 3 to 10 days. Severe acute complications, including acute respiratory failure, sepsis, acute kidney failure, and metabolic abnormalities, were common among inpatients. Patients aged 65 years and older disproportionally accounted for more than 75% of all in-hospital deaths. Use of statins, ACE inhibitors, calcium channel blockers, and vitamin C or D supplements were associated with significantly decreased odds of in-hospital mortality among adult inpatients with COVID-19 compared with those without such medication use. The combination use of azithromycin and hydroxychloroquine was associated with increased odds of in-hospital mortality compared with those who received neither drug.

Table 2. Acute Complications Among Patients With Confirmed Coronavirus Disease 2019 in Premier Healthcare Database, April to May 2020

Characteristic	No. (%) Overall sample (N = 64 781)	Outpatient (n = 29 479)	Inpatient (n = 35 302)	*P* value	No. (%) Survived (n = 57 426)	Deceased (n = 7355)	*P* value
Respiratory failure	19 960 (30.8)	254 (0.9)	19 706 (55.8)	<.001	14 662 (25.5)	5298 (72.0)	<.001
Acute respiratory distress syndrome	2905 (4.5)	34 (0.1)	2871 (8.1)	<.001	1314 (2.3)	1591 (21.6)	<.001
Shock	4059 (6.3)	31 (0.1)	4028 (11.4)	<.001	1322 (2.3)	2737 (37.2)	<.001
Sepsis	12 039 (18.6)	129 (0.4)	11 910 (33.7)	<.001	7590 (13.2)	4449 (60.5)	<.001
Acute kidney failure	12 181 (18.8)	210 (0.7)	11 971 (33.9)	<.001	7376 (12.8)	4805 (65.3)	<.001
Venous thromboembolism	1521 (2.3)	75 (0.3)	1446 (4.1)	<.001	1124 (2.0)	397 (5.4)	<.001
Cerebrovascular disease	857 (1.3)	47 (0.2)	810 (2.3)	<.001	529 (0.9)	328 (4.5)	<.001
Acute ischemic heart disease	2897 (4.5)	40 (0.1)	2857 (8.1)	<.001	1649 (2.9)	1248 (17.0)	<.001
Hyperkalemia	4352 (6.7)	62 (0.2)	4290 (12.2)	<.001	2258 (3.9)	2094 (28.5)	<.001
Hypokalemia	6475 (10.0)	377 (1.3)	6098 (17.3)	<.001	5323 (9.3)	1152 (15.7)	<.001
Hyponatremia	6142 (9.5)	185 (0.6)	5957 (16.9)	<.001	4897 (8.5)	1245 (16.9)	<.001
Acidosis	5317 (8.2)	74 (0.3)	5243 (14.9)	<.001	2993 (5.2)	2324 (31.6)	<.001
Acute liver damage	701 (1.1)	15 (0.1)	686 (1.9)	<.001	301 (0.5)	400 (5.4)	<.001
Neurological disorders							
Overall	2847 (4.4)	241 (0.8)	2606 (7.4)	<.001	2062 (3.6)	785 (10.7)	<.001
Epileptic seizures	2133 (3.3)	228 (0.8)	1905 (5.4)	<.001	1633 (2.8)	500 (6.8)	<.001
Rhabdomyolysis	744 (1.1)	9 (<0.1)	735 (2.1)	<.001	442 (0.8)	302 (4.1)	<.001
Guillain-Barre syndrome	25 (<0.1)	5 (<0.1)	20 (0.1)	.01	22 (<0.1)	3 (<0.1)	.92
Necrotizing hemorrhagic encephalopathy	1 (<0.1)	0	1 (<0.1)	.36	0	1 (<0.1)	.005
Acute encephalitis, myelitis, and encephalomyelitis	18 (<0.1)	0 (<0.1)	18 (0.1)	<.001	16 (<0.1)	2 (<0.1)	.97

The in-hospital mortality rate estimated in this study is comparable with what was reported in the study by Richardson et al.[11] However, the prevalence of ICU admissions (19.4% vs 14.2%) and invasive mechanical ventilation use (15.9% vs 12.2%) was much higher in the current study than in the study by Richardson et al.[11] Median total hospital LOS was also 2 days longer than what was reported by Richardson et al.[11] The study by Richardson et al included patients with COVID-19 from 1 large New York hospital during the early stage of the pandemic, which limits the generalizability of its findings to other hospitals in other areas.[11] In comparison, the current study included patients with COVID-19 from 592 hospitals nationwide during the 2 peak months of the pandemic, making its results more reliable and generalizable than single-facility reports. The findings of this study showed that Black US residents accounted for 22.1% of the overall sample, and White patients only accounted for 39.9% of all patients. Compared with the ethnic distribution in the nation as of 2020, with 13.4% of the population identifying as Black individuals and 76.3% as White individuals, our findings are consistent with what several smaller-scale studies and data reported by the US Centers for Disease Control and Prevention have shown, ie, that Black US residents were disproportionally infected with COVID-19. In addition, Black US residents only accounted for 14.4% of total hospital discharges

Table 3. Medications and Supplements Used by Patients With Confirmed Coronavirus Disease 2019 in Premier Healthcare Database, April to May 2020

Medication or supplement	No. (%)			*P* value	No. (%)		*P* value
	Overall sample (N = 64 781)	Outpatients (n = 29 479)	Inpatients (n = 35 302)		Survived (n = 57 426)	Deceased (n = 7355)	
ACE inhibitors	3162 (4.9)	139 (0.5)	3023 (8.6)	<.001	2817 (4.9)	345 (4.7)	.42
Albumin	2194 (3.4)	11 (0.0)	2183 (6.2)	<.001	1028 (1.8)	1166 (15.9)	<.001
Antiarrhythmics	1708 (2.6)	21 (0.1)	1687 (4.8)	<.001	691 (1.2)	1017 (13.8)	<.001
Anticoagulants	24 867 (38.4)	573 (1.9)	24 294 (68.8)	<.001	20 659 (36.0)	4208 (57.2)	<.001
Antiemetics	10 264 (15.8)	2154 (7.3)	8110 (23.0)	<.001	9090 (15.8)	1174 (16.0)	.77
Azithromycin	19 411 (30.0)	1544 (5.2)	17 867 (50.6)	<.001	15 638 (27.2)	3773 (51.3)	<.001
β blocker	11 246 (17.4)	286 (1.0)	10 960 (31.0)	<.001	8342 (14.5)	2904 (39.5)	<.001
Blood growth factor	2832 (4.4)	53 (0.2)	2779 (7.9)	<.001	2229 (3.9)	603 (8.2)	<.001
Bronchodilator	12 584 (19.4)	1087 (3.7)	11 497 (32.6)	<.001	9508 (16.6)	3076 (41.8)	<.001
Calcium channel blocker	8590 (13.3)	218 (0.7)	8372 (23.7)	<.001	6841 (11.9)	1749 (23.8)	<.001
Corticosteroids	12 840 (19.8)	498 (1.7)	12 342 (35.0)	<.001	9178 (16.0)	3662 (49.8)	<.001
HIV antiviral therapies	602 (0.9)	4 (0.0)	598 (1.7)	<.001	472 (0.8)	130 (1.8)	<.001
Immunoglobulin	108 (0.2)	3 (0.0)	105 (0.3)	<.001	70 (0.1)	38 (0.5)	<.001
Immunomodulator	1711 (2.6)	2 (0.0)	1709 (4.8)	<.001	1109 (1.9)	602 (8.2)	<.001
Narcotic analgesic	35 377 (54.6)	6899 (23.4)	28 478 (80.7)	<.001	28 818 (50.2)	6559 (89.2)	<.001
Other antibiotics	27 123 (41.9)	1866 (6.3)	25 257 (71.5)	<.001	20 902 (36.4)	6221 (84.6)	<.001
Other antihypertensive	8226 (12.7)	209 (0.7)	8017 (22.7)	<.001	6355 (11.1)	1871 (25.4)	<.001
Other antiviral	723 (1.1)	20 (0.1)	703 (2.0)	<.001	562 (1.0)	161 (2.2)	<.001
Smoking deterrent	345 (0.5)	17 (0.1)	328 (0.9)	<.001	321 (0.6)	24 (0.3)	.009
Statin	12 233 (18.9)	263 (0.9)	11 970 (33.9)	<.001	9807 (17.1)	2426 (33.0)	<.001
Vitamin C or D	8834 (13.6)	203 (0.7)	8631 (24.4)	<.001	7170 (12.5)	1664 (22.6)	<.001
Zinc	6200 (9.6)	153 (0.5)	6047 (17.1)	<.001	5014 (8.7)	1186 (16.1)	<.001
Hydroxychloroquine and azithromycin							
Azithromycin only	7234 (11.2)	1451 (4.9)	5783 (16.4)	<.001	6092 (10.6)	1142 (15.5)	<.001
Hydroxychloroquine and azithromycin	12 177 (18.8)	93 (0.3)	12 084 (34.2)		9546 (16.6)	2631 (35.8)	
Hydroxychloroquine only	6761 (10.4)	94 (0.3)	6667 (18.9)		5382 (9.4)	1379 (18.7)	
Neither hydroxychloroquine nor azithromycin	38 609 (59.6)	27 841 (94.4)	10 768 (30.5)		36 406 (63.4)	2203 (30.0)	
Hydroxychloroquine, azithromycin, and zinc	3209 (5.0)	17 (0.1)	3192 (9.0)	<.001	2524 (4.4)	685 (9.3)	<.001
Remdesivir	100 (0.2)	0	100 (0.3)	<.001	76 (0.1)	24 (0.3)	<.001

Abbreviation: ACE, angiotensin-converting enzyme.

captured in PHD in 2019, which corroborated the disproportionately higher Black representation among COVID-19–related discharges. However, among hospitalized COVID-19 patients, after adjusting for known confounders, Black US residents had 25% lower odds of dying in the hospital (OR, 0.75; 95% CI, 0.69-0.82) compared with White patients. Rentsch et al[15] and Price-Haywood et al[16] found similar associations between race and mortality in a veteran cohort (OR, 0.93; 95% CI, 0.64-1.33)[15] and a patient cohort in an integrated-delivery health system in Louisiana (OR, 0.89; 95% CI, 0.68-1.17).[16] Neither this study nor the referenced studies were able to adjust for socioeconomic status and structural disparities that are potential risk factors associated with overall mortality.

The multivariable regression results showed that the odds of in-hospital mortality increased linearly with age, with the highest odds of death among those aged 80 years and older. Being male and being admitted from long-term care facilities were associated with increased odds of in-hospital mortality compared with reference groups. Patients from the Northeast had increased odds of in-hospital mortality compared with those from the Midwest. Most of these findings are consistent with prior reports.[16,17]

There have been widespread discussions and speculations regarding whether ACE inhibitors, angiotensin receptor blockers (ARBs), and statins have adverse or beneficial associations with outcomes among patients with COVID-19.[15-20] The findings of this study showed that statins, ACE inhibitors, and calcium channel blockers were associated with significantly decreased odds of mortality after adjusting for cardiovascular comorbidities. Such protective associations in multiple drug classes could be an indicator of enhanced accessibility to these drugs among patients who might be socially advantaged compared with those who did not have access to these drugs. Further studies are needed to explore the mechanisms behind the protective associations of these drugs. Meanwhile, it may be important to continue these antihypertensive and antilipidemic treatments in patients with hypertension, hyperlipidemia, or other cardiovascular conditions. In contrast, β blockers were associated with increased odds of death.

Patients with both azithromycin and hydroxychloroquine use had increased odds of mortality after adjusting for confounders. These findings are not only consistent with what was observed in other observational studies conducted in the earlier stage of the COVID-19 pandemic[18-23] but also similar to results of recently published clinical trials in the United States and other countries.[24,25] The multicenter, randomized, open-label trial of 504 patients with confirmed COVID-19 in Brazil by Cavalcanti et al[24] found that neither hydroxychloroquine nor a combination of hydroxychloroquine and azithromycin showed any benefit compared with controls on clinical outcomes at 15 days.[24] A randomized, controlled, open-label trial of more than 4500 patients hospitalized with COVID-19 in the United Kingdom (Horby et al[25]) indicated that 28-day mortality was slightly higher among patients treated with hydroxychloroquine than among those in the control group (OR, 1.09; 95% CI, 0.97-1.23).[25] A randomized, double-masked, placebo-controlled trail across the United States and

Table 4. Clinical Outcomes of Patients With Confirmed COVID-19 in Premier Healthcare Database, April to May 2020

Characteristic	No. (%)			*P* value
	Overall sample (N = 64 781)	Outpatients (n = 29 479)	Inpatients (n = 35 302)	
In-hospital mortality	7355 (11.4)	191 (0.6)	7164 (20.3)	<.001
Use of invasive mechanical ventilation	5651 (8.7)	26 (0.1)	5625 (15.9)	<.001
ICU admission (inpatient only)	NA	NA	6849 (19.4)	NA
No. of days in ICU (inpatient only)				
Mean (SD)	NA	NA	7.27 (6.76)	NA
Median (IQR)	NA	NA	5 (2-10)	NA
Total hospital length of stay (inpatient only), d				
Mean (SD)	NA	NA	7.74 (10.80)	NA
Median (IQR)	NA	NA	6 (3-10)	NA

Abbreviations: ICU, intensive care unit; IQR, interquartile range; NA, not applicable.

Table 5. Multivariable Logistic Regression Results for Assessing Factors Associated With In-Hospital Mortality Among Inpatients With Confirmed COVID-19 in Premier Healthcare Database, April to May 2020

	Univariable regression		Multivariable regression	
Covariate	OR (95% CI)	*P* value	aOR (95% CI)[a]	*P* value
Age, y				
18-34	1 [Reference]	NA	1 [Reference]	NA
35-49	2.94 (2.12-4.07)	<.001	2.12 (1.51-2.99)	<.001
50-64	7.56 (5.56-10.28)	<.001	4.38 (3.16-6.06)	<.001
65-79	18.37 (13.54-24.91)	<.001	8.58 (6.16-11.94)	<.001
≥80	33.00 (24.31-44.79)	<.001	16.20 (11.58-22.67)	<.001
Sex, male vs female	1.26 (1.19-1.32)	<.001	1.18 (1.10-1.26)	<.001
Race				
White	1 [Reference]	NA	1 [Reference]	NA
Black	0.78 (0.73-0.84)	<.001	0.75 (0.69-0.82)	<.001
Other/unknown	0.82 (0.77-0.87)	<.001	0.95 (0.88-1.03)	.24
Payer type				
Commercial insurance	1 [Reference]	NA	1 [Reference]	NA
Medicaid	1.21 (1.10-1.34)	<.001	1.29 (1.14-1.45)	<.001
Medicare	3.67 (3.40-3.96)	<.001	1.33 (1.20-1.48)	<.001
Self-pay	1.02 (0.85-1.23)	.83	1.33 (1.00-1.75)	.05
Other or unknown	0.89 (0.71-1.13)	.35	1.12 (0.91-1.39)	.29
Admission point of origin				
Non-health care facility	1 [Reference]	NA	1 [Reference]	NA
Transferred from acute care facility	1.84 (1.69-2.00)	<.001	1.71 (1.54-1.90)	<.001
Clinic	0.83 (0.72-0.95)	.01	1.07 (0.91-1.27)	.39
Transferred from long-term care facility	2.93 (2.66-3.22)	<.001	1.50 (1.33-1.68)	<.001
Other or unknown	1.15 (0.76-1.73)	.51	1.59 (0.96-2.63)	.07
Hospital region				
Midwest	1 [Reference]	NA	1 [Reference]	NA
Northeast	1.39 (1.29-1.51)	<.001	1.59 (1.44-1.76)	<.001
South	0.89 (0.80-0.98)	.02	1.00 (0.88-1.13)	.98
West	0.91 (0.77-1.07)	.25	1.10 (0.89-1.34)	.38
Hospital beds, No.				
1-199	0.76 (0.69-0.83)	<.001	0.72 (0.63-0.81)	<.001
200-499	1.23 (1.16-1.30)	<.001	1.23 (1.14-1.33)	<.001
≥500	1 [Reference]	NA	1 [Reference]	NA
Hospital teaching status, nonteaching vs teaching	0.94 (0.89-0.99)	.03	1.45 (1.34-1.58)	<.001
Statin, yes vs no	0.99 (0.94-1.04)	.68	0.60 (0.56-0.65)	<.001
Vitamin C or D, yes vs no	0.91 (0.86-0.97)	<.001	0.89 (0.82-0.97)	.005
Zinc, yes vs no	0.94 (0.88-1.01)	.09	1.16 (1.05-1.28)	.003
ACE inhibitor, yes vs no	0.48 (0.42-0.54)	<.001	0.53 (0.46-0.60)	<.001
β blocker, yes vs no	1.68 (1.60-1.78	<.001	1.11 (1.04-1.20)	.003
Calcium channel blocker, yes vs no	1.04 (0.98-1.11)	.20	0.73 (0.68-0.79)	<.001
Hydroxychloroquine and azithromycin use				
Neither hydroxychloroquine nor azithromycin	1 [Reference]	NA	1 [Reference]	NA
Azithromycin only	1.04 (0.96-1.13)	.36	1.02 (0.92-1.13)	.71
Hydroxychloroquine only	1.10 (1.02-1.19)	.01	1.08 (0.98-1.19)	.13
Both hydroxychloroquine and azithromycin	1.18 (1.11-1.26)	<.001	1.21 (1.11-1.31)	<.001
Sepsis, yes vs no	4.45 (4.21-4.70)	<.001	3.34 (3.12-3.57)	<.001
Acute kidney failure, yes vs no	5.83 (5.51-6.16)	<.001	2.46 (2.30-2.63)	<.001
Hypokalemia, yes vs no	0.89 (0.83-0.95)	<.001	0.82 (0.75-0.89)	<.001
Hyperkalemia, yes vs no	4.80 (4.49-5.13)	<.001	2.28 (2.09-2.48)	<.001

(continued)

Table 5. Multivariable Logistic Regression Results for Assessing Factors Associated With In-Hospital Mortality Among Inpatients With Confirmed COVID-19 in Premier Healthcare Database, April to May 2020 (continued)

	Univariable regression		Multivariable regression	
Covariate	OR (95% CI)	*P* value	aOR (95% CI)[a]	*P* value
Hyponatremia, yes vs no	1.04 (0.97-1.11)	.29	0.92 (0.84-1.00)	.04
Acidosis, yes vs no	4.08 (3.83-4.34)	<.001	1.85 (1.70-2.00)	<.001
Acute liver damage, yes vs no	5.72 (4.91-6.68)	<.001	3.58 (2.95-4.35)	<.001
Neurological disorder, yes vs no	1.77 (1.62-1.93)	<.001	1.23 (1.10-1.38)	<.001
Baseline comorbidities, yes vs no				
Myocardial infarction	2.89 (2.68-3.11)	<.001	1.47 (1.34-1.62)	<.001
Congestive heart failure	2.47 (2.32-2.63)	<.001	1.37 (1.26-1.49)	<.001
Cerebrovascular disease	2.11 (1.93-2.30)	<.001	1.39 (1.25-1.56)	<.001
Chronic pulmonary disease	1.30 (1.23-1.39)	<.001	1.16 (1.08-1.26)	<.001
Dementia	2.83 (2.66-3.01)	<.001	1.21 (1.11-1.32)	<.001
Diabetes	1.59 (1.50-1.67)	<.001	1.20 (1.12-1.28)	<.001
Any malignant neoplasm	1.90 (1.70-2.13)	<.001	1.27 (1.09-1.47)	.002
Metastatic solid tumor	1.94 (1.59-2.38)	<.001	1.57 (1.20-2.05)	.001
Hemiplegia	1.72 (1.41-2.10)	<.001	1.34 (1.05-1.72)	.02
AIDS	0.90 (0.63-1.30)	.58	0.68 (0.44-1.04)	.07
Hypertension	2.38 (2.24-2.54)	<.001	1.08 (0.99-1.18)	.07
Hyperlipidemia	1.69 (1.60-1.78)	<.001	1.11 (1.03-1.19)	.004

Abbreviations: ACE, angiotensin-converting enzyme; aOR, adjusted odds ratio; NA, not applicable; OR, odds ratio.

[a] C statistic for the multivariable model was 0.862, indicating a strong model.

parts of Canada[26] also concluded that hydroxychloroquine did not help prevent illness when used as postexposure prophylaxis for COVID-19.

Limitations

This study has limitations. First, PHD is a hospital administrative database and does not include as many clinical details as electronic health records would. The identification of clinical conditions, procedures, and medications relied on the accuracy of the hospital-reported diagnosis and procedure codes and chargemaster descriptions. Compassionate use of experimental drugs or medications used in clinical trials, which are not associated with a hospital charge, may not be completely captured, which may result in underreporting of receipt of remdesivir. Second, due to the nature of observational studies, although adjusted analysis was performed to control for patient, hospital, and clinical characteristics, this study was not designed to detect causal relationships between the assessed medications or patient characteristics and in-hospital mortality. Third, the race and ethnicity information captured in PHD was self-reported by patients at time of each hospital visit. Because one-quarter to one-third of patients had other or unknown race or ethnicity, the actual percentage of Black US residents with COVID-19 might be underestimated. The potential misclassification of race due to unknown or omitted values may bias the odds ratio for the comparison of Black and White patients away from the null. The actual racial difference in in-hospital mortality might be smaller than observed. The in-hospital mortality rate reported in this study was estimated in hospitalized patients, who are more likely to have severe COVID-19; therefore, it does not reflect the mortality rate in all patients with COVID-19. The overall mortality rate of COVID-19 is likely to be lower when the mild or moderate cases are included in the denominators.

Conclusions

In this study, COVID-19 was associated with high levels of ICU admission and in-hospital mortality. Severe acute complications were common. Death disproportionately affected older and male patients as well as patients from the Northeast region. With the shift of the pandemic from being heavily concentrated in Northeast in the early months to peaking in the South and Midwest in June and July, regional differences in mortality may change. Use of statins, ACE inhibitors, calcium channel

blockers, and vitamin C or D supplements was associated with lower odds of in-hospital mortality among inpatients with COVID-19. The combination use of azithromycin and hydroxychloroquine was associated with increased odds of in-hospital mortality compared with those who received neither drug. Understanding the potential benefits of unproven treatments will require future randomized trials.

ARTICLE INFORMATION

Accepted for Publication: October 18, 2020.

Published: December 10, 2020. doi:10.1001/jamanetworkopen.2020.29058

Correction: This article was corrected on January 14, 2021, to fix an error in the References section.

Corresponding Author: Ning Rosenthal, MD, PhD, MPH, Premier Applied Sciences, Premier Inc, 13034 Ballantyne Corporate Pl, Charlotte, NC 28277 (ning_rosenthal@premierinc.com).

Author Affiliations: Premier Applied Sciences, Premier Inc, Charlotte, North Carolina.

Author Contributions: Dr Rosenthal and Mr Gundrum had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: Rosenthal, Cao, Gundrum.

Drafting of the manuscript: Rosenthal, Cao.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Rosenthal, Cao, Gundrum.

Administrative, technical, or material support: Rosenthal, Sianis, Safo.

Supervision: Rosenthal, Safo.

Conflict of Interest Disclosures: All authors worked on the study as full-time employees of Premier Inc. No other disclosures were reported.

Funding/Support: This study was funded by Premier Inc.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: The authors would like to thank Bernadette Johnson Flavors, MBA, John House, MS, Teresa Davis, BS, Umang Patel, MS, and the entire PHD development team for making the data available on time for the analysis. The authors would also like to thank Denise Juliano, MS, Myla Maloney, MBA, BCMAS, Carol Cohen, BA, and the Premier Applied Sciences COVID-19 Task Force for their support with the analysis. All of the above individuals are employees of Premier Inc. No payment in addition to their regular salary was provided for their support. Dr Rosenthal has obtained written permission to include the names of individuals in this article.

REFERENCES

1. US Centers for Disease Control and Prevention. CDC COVID data tracker. Accessed on November 19, 2020. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html

2. Holshue ML, DeBolt C, Lindquist S, et al; Washington State 2019-nCoV Case Investigation Team. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382(10):929-936. doi:10.1056/NEJMoa2001191

3. Piva S, Filippini M, Turla F, et al. Clinical presentation and initial management critically ill patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Brescia, Italy. *J Crit Care*. 2020;58:29-33. doi:10.1016/j.jcrc.2020.04.004

4. Rubino S, Kelvin N, Bermejo-Martin JF, Kelvin D. As COVID-19 cases, deaths and fatality rates surge in Italy, underlying causes require investigation. *J Infect Dev Ctries*. 2020;14(3):265-267. doi:10.3855/jidc.12734

5. Xia XY, Wu J, Liu HL, Xia H, Jia B, Huang WX. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. *J Clin Virol*. 2020;127:104360. doi:10.1016/j.jcv.2020.104360

6. Zhai P, Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of COVID-19. *Int J Antimicrob Agents*. 2020;55(5):105955. doi:10.1016/j.ijantimicag.2020.105955

7. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3

8. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(13):382-386. doi:10.15585/mmwr.mm6913e2

9. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(12):343-346. doi:10.15585/mmwr.mm6912e2

10. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): early report from the United States. *Diagnosis (Berl)*. 2020;7(2):91-96. doi:10.1515/dx-2020-0046

11. Richardson S, Hirsch JS, Narasimhan M, et al; the Northwell COVID-19 Research Consortium. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*. 2020;323(20):2052-2059. doi:10.1001/jama.2020.6775

12. Premier. Premier Healthcare Database: data that informs and performs. Published March 2, 2020. Accessed November 6, 2020. https://learn.premierinc.com/white-papers/premier-healthcare-database-whitepaper

13. US Centers for Disease Control and Prevention. *ICD-10-CM* official coding and reporting guidelines, April 1, 2020 through September 30, 2020. Accessed on May 31, 2020. 2020. https://www.cdc.gov/nchs/data/icd/COVID-19-guidelines-final.pdf

14. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619. doi:10.1016/0895-4356(92)90133-8

15. Rentsch CT, Kidwai-Khan F, Tate JP, et al. COVID-19 by race and ethnicity: a national cohort study of 6 million United States veterans. medRxiv. Preprint published May 17, 2020. doi:10.1101/2020.05.12.20099135

16. Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and mortality among Black patients and White patients with COVID-19. *N Engl J Med*. 2020;382(26):2534-2543. doi:10.1056/NEJMsa2011686

17. Imam Z, Odish F, Gill I, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. *J Intern Med*. 2020;288(4):469-476. doi:10.1111/joim.13119

18. Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. *J Med Virol*. 2020;92(7):770-775. doi:10.1002/jmv.25887

19. Chary MA, Barbuto AF, Izadmehr S, Hayes BD, Burns MM. COVID-19: therapeutics and their toxicities. *J Med Toxicol*. 2020;16(3):284-294. doi:10.1007/s13181-020-00777-5

20. Guzik TJ, Mohiddin SA, Dimarco A, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res*. 2020;116(10):1666-1687. doi:10.1093/cvr/cvaa106

21. Lu CC, Chen MY, Lee WS, Chang YL. Potential therapeutic agents against COVID-19: what we know so far. *J Chin Med Assoc*. 2020;83(6):534-536. doi:10.1097/JCMA.0000000000000318

22. Scuccimarri R, Sutton E, Fitzcharles MA. Hydroxychloroquine: a potential ethical dilemma for rheumatologists during the COVID-19 pandemic. *J Rheumatol*. 2020;47(6):783-786. doi:10.3899/jrheum.200369

23. Singh AK, Singh A, Shaikh A, Singh R, Misra A. Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: a systematic search and a narrative review with a special reference to India and other developing countries. *Diabetes Metab Syndr*. 2020;14(3):241-246. doi:10.1016/j.dsx.2020.03.011

24. Cavalcanti AB, Zampieri FG, Rosa RG, et al; Coalition Covid-19 Brazil I Investigators. Hydroxychloroquine with or without azithromycin in mild-to-moderate COVID-19. *N Engl J Med*. 2020. doi:10.1056/NEJMoa2019014

25. Horby P, Mafham M, Linsell L, et al; RECOVERY Collaborative Group. Effect of hydroxychloroquine in hospitalized patients with COVID-19. *N Engl J Med*. 2020.

26. Boulware DR, Pullen MF, Bangdiwala AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. *N Engl J Med*. 2020;383(6):517-525. doi:10.1056/NEJMoa2016638

SUPPLEMENT.

eTable 1. Charlson-Deyo Comorbidities and Related *ICD-10-CM* Diagnosis Codes
eTable 2. *ICD-10* Diagnosis Codes for Defining Acute Complications