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RESEARCH ARTICLE

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Treatment patterns in US patients hospitalized with COVID-19 and pulmonary involvement

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Abstract

This study describes the baseline characteristics and treatment patterns of US patients hospitalized with a diagnosis of coronavirus disease 2019 (COVID-19) and pulmonary involvement. Patients hospitalized with pulmonary involvement due to COVID-19 (first hospitalization) were identified in the IBM Explorys® electronic health records database. Demographics, baseline clinical characteristics, and in-hospital medications were assessed. For evaluation of in-hospital medications, results were stratified by race, geographic region, age, and month of admission. Of 6564 hospitalized patients with COVID-19-related pulmonary involvement, 50.4% were male, and mean (*SD*) age was 62.6 (16.4) years; 75.2% and 23.6% of patients were from the South and Midwest, respectively, and 50.2% of patients were African American. Compared with African American patients, a numerically higher proportion of White patients received dexamethasone (19.7% vs. 31.8%, respectively), nonsteroidal anti-inflammatory drugs (NSAIDs; 27.1% vs. 34.9%), bronchodilators (19.8% vs. 29.5%), and remdesivir (9.3% vs. 21.0%). Numerically higher proportions of White patients than African American patients received select medications in the South but not in the Midwest. Compared with patients in the South, a numerically higher proportion of patients in the Midwest received dexamethasone (20.1% vs. 34.5%, respectively), NSAIDs (19.6% vs. 55.7%), bronchodilators (15.9% vs. 41.3%), and remdesivir (10.6% vs. 23.1%). Inpatient use of hydroxychloroquine decreased over time, whereas the use of dexamethasone and remdesivir increased over time. Among US patients predominantly from the South and Midwest hospitalized with COVID-19 and pulmonary involvement, differences were seen in medication use between different races, geographic regions, and months of hospitalization.

KEYWORDS

antiviral agents, cytokine/chemokine, disease control, immune responses, immunodulators, inflammation, respiratory tract, SARS coronavirus

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first reported in China in December 2019 and quickly spread globally,[1] with the first known case in the United States (US) confirmed in January 2020.[2] After initial outbreaks in US states in the Northeast and West, outbreaks in the South followed, with spread to areas throughout the country over the course of the pandemic.[3] As of March 22, 2021, the United States had the most confirmed cases of COVID-19 and COVID-19-related deaths of any country in the world, with over 29 000 000 confirmed cases and over 540 000 deaths.[4]

Patients with COVID-19 may present with mild to critical, life-threatening illnesses. Severe COVID-19 cases often progress to acute respiratory distress syndrome (ARDS)-related respiratory failure, septic shock, and/or multiple organ dysfunction and failure, which are associated with high mortality rates.[5,6] Patients with severe and critical COVID-19 illness have been shown to have elevated levels of multiple pro-inflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor α (TNF-α),[7] which are thought to play a role in the pathogenesis of the disease.

The risk of severe infection increases with age and is higher in those with underlying conditions, such as obesity, diabetes, and hypertension.[8-11] In addition, racial and ethnic minority populations have been shown to have an increased risk of hospitalization and death due to COVID-19.[10,12-14] It is important to consider the underlying reasons related to these differences, which are not well understood, but may include health and socioeconomic inequalities.[12,15]

As of December 2020, only one medication, remdesivir, is approved for the treatment of COVID-19; however, treatment of severe COVID-19 currently involves several therapies, including corticosteroids, antiviral drugs, immunomodulatory drugs, and others, to help manage symptoms and to prevent respiratory failure. Results from studies of therapies in patients with COVID-19 pneumonia are published daily, and government and professional organization treatment guidelines and recommendations have changed regularly as new evidence and data are published.

Awareness of the demographics, baseline clinical characteristics, and patterns of treatments of patients with COVID-19 is important to gain a better understanding of evolving standard of care in hospitalized patients with COVID-19 pneumonia and of potential differences by region or patient demographics. This study used the IBM Explorys® database, which includes a racially diverse group of patients primarily from the Midwest and South, to evaluate demographics, baseline characteristics, and medication use of patients hospitalized with COVID-19 and pulmonary involvement.

2 | METHODS

2.1 | Study design and patient population

This retrospective analysis identified patients hospitalized with COVID-19-related pulmonary involvement using data from the IBM Explorys database from December 1, 2019, through August 27, 2020. The Explorys database, a convenience sample of health systems containing data on approximately 70 million patients (since 2000), comprises data from approximately 400 hospitals and 400 000 providers in 39 large US health systems, including electronic health record (EHR) data, outgoing billing, and adjudicated claims from commercial and public payers. Most patients in the database are from the Midwest (39%) and South (33%), followed by the West (18%) and Northeast (5%). Institutional Review Board (IRB) approval was not required because study data were deidentified and fully compliant with the Health Insurance Portability and Accountability Act of 1996.

Variables were measured using International Classification of Diseases, Clinical Modification (ICD-9-CM and/or ICD-10-CM) diagnosis codes, and additional EHR terminology and drug coding systems, including Systemized Nomenclature of Medicine, Healthcare Common Procedure Coding System, and National Drug Codes. Hospitalized patients with a diagnosis code for COVID-19 or other coronavirus and a diagnosis code for at least 1 of 6 conditions representing pulmonary involvement, including pneumonia (J12.89), acute bronchitis (J20.8), bronchitis not otherwise specified (J40), lower respiratory infection (J22), associated with a respiratory infection not otherwise specified (J98.8), and acute respiratory distress syndrome (J80), based on the Centers for Disease Control and Prevention coding guidelines[16] for patients with COVID-19, were included (Table S1). If a patient had multiple hospitalizations for COVID-19 with pulmonary involvement, only the first hospitalization was analyzed.

2.2 | Outcomes

Patient demographics, including age, sex, self-reported race/ethnicity, and geographic region; comorbidities, including Charlson Comorbidity Index (CCI)[17] conditions and additional selected conditions; and selected prescribed medications from the baseline period of up to 12 months through 14 days before hospital admission were assessed. Body mass index (BMI), self-reported smoking status, the month of first hospital admission, and select inpatient medications during hospitalization were captured; medications were selected based on the published literature of emerging therapeutic options. For inpatient medications, results were stratified by race, geographic region, age (<60 or ≥60 years), and month of hospitalization (patients hospitalized from December 2019 through March 2020 were grouped together). Results are descriptive, and all comparisons were qualitative in nature.

This was a retrospective, observational study, and all study data were deidentified and fully compliant with Health Insurance Portability and Accountability Act regulations (45 CFR 164.514e); therefore, approval from an IRB was not required, and informed consent was not obtained.

TABLE 1 Baseline demographics among hospitalized patients in the United States with COVID-19 and pulmonary involvement

	Total patients (*N* = 6564)
Age, mean (*SD*), years	62.6 (16.4)
Median, years	64.0
Age group, *n* (%), years	
<18	14 (0.2)
18–29	177 (2.7)
30–39	427 (6.5)
40–49	757 (11.5)
50–59	1303 (19.9)
60–69	1532 (23.3)
70–79	1264 (19.3)
80–89	774 (11.8)
≥90	311 (4.7)
Missing	5 (0.1)
Sex, *n* (%)	
Male	3306 (50.4)
Female	3258 (49.6)
Region, *n* (%)	
Northeast	48 (0.7)
Midwest	1549 (23.6)
South	4936 (75.2)
West	22 (0.3)
Unknown/missing	9 (0.1)
Race, *n* (%)	
Hispanic/Latino	6 (0.1)
African American	3297 (50.2)
White	2281 (34.8)
Asian	73 (1.1)
Other	592 (9.0)
Unknown/refused	315 (4.8)
Insurance plan type, *n* (%)	
Private	1321 (20.1)
Medicare	1240 (18.9)
Medicaid	318 (4.8)
Self-pay	421 (6.4)
Other	92 (1.4)
Unknown	3172 (48.3)
Month of hospital admission, *n* (%)	
December 2019	3 (<0.05)
January 2020	6 (0.1)
February 2020	5 (0.1)
March 2020	1134 (17.3)
April 2020	2000 (30.5)
May 2020	1061 (16.2)
June 2020	608 (9.3)
July 2020	1396 (21.3)
August 2020	351 (5.3)

3 | RESULTS

3.1 | Baseline demographics and clinical characteristics

Of 6564 hospitalized patients who had a diagnosis of COVID-19 and pulmonary involvement, 50.4% were male, and mean (*SD*) age was 62.6 (16.4) years; most patients were from the South (75.2%) or Midwest (23.6%), and 50.2% of patients self-identified as African American and 34.8% as White (Table 1). The months of admission with the highest proportion of patients were April 2020 (30.5%), July 2020 (21.3%), and March 2020 (17.3%). The mean (*SD*) Deyo CCI was 0.91 (1.92), and the most common select comorbidities were hypertension (29.8%), hyperlipidemia (18.6%), and diabetes (17.8%; Table 2). Mean (*SD*) BMI was 32.25 (8.69), and 26.2% had a history of smoking or tobacco use. Private insurance (20.1%) and Medicare (18.9%) were the most common insurance plan types; however, for almost half of patients, insurance data were unknown.

3.2 | Inpatient medications

Overall, the most common inpatient medications were corticosteroids (including dexamethasone and methylprednisolone; 31.3%), nonsteroidal anti-inflammatory drugs (NSAIDs; 28.2%), bronchodilators (22.1%), hydroxychloroquine (19.6%), and remdesivir (13.5%; Table 3). Compared with African American patients, a numerically higher proportion of White patients received dexamethasone (19.7% vs. 31.8%, respectively), NSAIDs (27.1% vs. 34.9%, respectively), bronchodilators (19.8% vs. 29.5%), and remdesivir (9.3% vs. 21.0%). A comparable proportion of African American and White patients received hydroxychloroquine (21.9% vs. 20.4%, respectively; Table 3).

Compared with patients in the South, a higher proportion of patients in the Midwest received dexamethasone (20.1% vs. 34.5%, respectively), NSAIDs (19.6% vs. 55.7%), bronchodilators (15.9% vs. 41.3%), and remdesivir (10.6% vs. 23.1%; Table 3). The proportion of

TABLE 2 Twelve-month baseline clinical characteristics before hospitalization[a]

	Total patients (*N* = 6564)
Deyo CCI	
Mean (*SD*)	0.91 (1.92)
Median	0
Deyo CCI comorbidities, *n* (%)	
Mild to moderate diabetes	763 (11.6)
Renal disease	673 (10.3)
Chronic pulmonary disease	570 (8.7)
Diabetes with chronic complications	512 (7.8)
Congestive heart failure	442 (6.7)
Primary cancer	247 (3.8)
Cerebrovascular disease	200 (3.0)
Peripheral vascular disease	164 (2.5)
Dementia	145 (2.2)
Myocardial infarction	125 (1.9)
Rheumatologic disease	84 (1.3)
Metastatic solid tumor	59 (0.9)
Mild liver disease	33 (0.5)
Hemiplegia and paraplegia	30 (0.5)
Peptic ulcer disease	27 (0.4)
HIV infection	17 (0.3)
Moderate to severe liver disease	13 (0.2)
Select comorbidities, *n* (%)	
Hypertension	1958 (29.8)
Hyperlipidemia	1222 (18.6)
Diabetes	1169 (17.8)
Obesity	761 (11.6)
Coronary artery disease	505 (7.7)
Respiratory conditions	
COPD	468 (7.1)
Sleep apnea	397 (6.0)
Asthma	265 (4.0)
Pulmonary fibrosis	104 (1.6)
Organ transplant	107 (1.6)
Influenza	87 (1.3)
Pregnancy	43 (0.7)
History of smoking/tobacco use, *n* (%)	1721 (26.2)
Has BMI measurement, *n* (%)	4629 (70.5)
BMI, mean (*SD*)	32.25 (8.69)
BMI, median	31.00

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease.

[a]Diagnoses and prescriptions using available data from up to 12 months through 14 days before hospital admission.

patients who received hydroxychloroquine was comparable in the South and Midwest.

After analysis of select medication use by US region, numerically higher proportions of White patients than African American patients in the South received multiple select medications, including dexamethasone (30.0% vs. 16.0%) and remdesivir (20.6% vs. 5.7%), but select medication use was generally comparable among White and African American patients in the Midwest (Table 4). When patients were stratified by age (<60 or ≥60 years), numerically higher proportions of White patients than African American patients in both age groups received multiple select medications, including dexamethasone (<60 years: 35.6% vs. 23.0%; ≥60 years, 30.1% vs. 17.3%) and remdesivir (<60 years: 24.7% vs. 11.2%; ≥60 years, 19.3% vs. 7.9%; Table 4).

Inpatient use of hydroxychloroquine decreased over time from a peak of 54.0% in December 2019 through March 2020 to 2.0% in August 2020, whereas the use of dexamethasone and remdesivir increased over the same period, from 11.9% to 59.8% and 0.8% to 36.5%, respectively. Methylprednisone use remained relatively constant (Table 5; Figure 1). The proportion of patients who received NSAIDs and bronchodilators also remained generally comparable over time.

4 | DISCUSSION

This study evaluated the baseline characteristics, clinical characteristics, and treatment patterns of US patients hospitalized with COVID-19 and pulmonary involvement. Of 6564 hospitalized patients, the proportions of males and females were comparable, mean age was >60 years, and most patients were from the South or Midwest. The most common select comorbidities were hypertension, diabetes, and hyperlipidemia. The months of admission with the highest proportion of patients (April and July) likely reflect the peaks of hospitalization in the Midwest and South, where the majority of patients in the Explorys database are located.

Overall, 50.2% of patients in this study self-identified as African American. This percentage is not due to an overrepresentation in the Explorys database in which approximately 10% of patients in all regions and 16% of patients in the South identify as African American. The Explorys database is reflective of the US population, which is 13% Black or African American and 60% non-Hispanic White based on the latest US Census data.[18] Higher rates of COVID-19 infection and pulmonary involvement in African American patients in this study may be due to a multitude of factors, including increased rates of infection in some areas of the country, as well as the increased numbers of African American or Black people who work in essential jobs that cannot be performed remotely and who have living situations that increase their potential exposure to COVID-19. The complex effect of race in COVID-19 disease also involves socioeconomic, health, and healthcare disparities, which are often the result of systemic inequities.[12,15]

TABLE 3 Inpatient medications used during first hospitalization stratified by race or ethnicity and US region[a]

		Race or ethnicity			US region		
Select medications, n (%)	All, *N* = 6564	African American, *n* = 3297	White, *n* = 2281	Hispanic/Latino/ Asian/Other/ Unknown, *n* = 986	South, *n* = 4936	Midwest, *n* = 1549	Northeast/ West/ Unknown, *n* = 79
Corticosteroids	2055 (31.3)	898 (27.2)	951 (41.7)	206 (20.9)	1289 (26.1)	748 (48.3)	18 (22.8)
Dexamethasone	1532 (23.3)	650 (19.7)	726 (31.8)	156 (15.8)	991 (20.1)	535 (34.5)	6 (7.6)
Methylprednisolone	407 (6.2)	195 (5.9)	179 (7.8)	33 (3.3)	285 (5.8)	117 (7.6)	5 (6.3)
NSAIDs	1848 (28.2)	894 (27.1)	796 (34.9)	158 (16.0)	969 (19.6)	863 (55.7)	16 (20.3)
Bronchodilators	1450 (22.1)	654 (19.8)	673 (29.5)	123 (12.5)	787 (15.9)	640 (41.3)	23 (29.1)
Hydroxychloroquine	1289 (19.6)	723 (21.9)	466 (20.4)	100 (10.1)	988 (20.0)	296 (19.1)	5 (6.3)
Remdesivir	883 (13.5)	307 (9.3)	479 (21.0)	97 (9.8)	522 (10.6)	358 (23.1)	3 (3.8)
ACE inhibitors	395 (6.0)	159 (4.8)	191 (8.4)	45 (4.6)	145 (2.9)	245 (15.8)	5 (6.3)
Angiotensin II receptor blockers	341 (5.2)	145 (4.4)	156 (6.8)	40 (4.1)	153 (3.1)	184 (11.9)	4 (5.1)
IL-6 inhibitors	206 (3.1)	53 (1.6)	123 (5.4)	30 (3.0)	78 (1.6)	125 (8.1)	3 (3.8)
Tocilizumab	204 (3.1)	53 (1.6)	123 (5.4)	28 (2.8)	78 (1.6)	125 (8.1)	1 (1.3)
Sarilumab	2 (0.0)	0	0	2 (0.2)	0	0	2 (2.5)
Alteplase	279 (4.3)	167 (5.1)	94 (4.1)	18 (1.8)	201 (4.1)	77 (5.0)	1 (1.3)
Lopinavir/ritonavir	11 (0.2)	4 (0.1)	7 (0.3)	0	3 (0.1)	7 (0.5)	1 (1.3)
Dornase alfa	3 (0.0)	3 (0.1)	0	0	2 (0.0)	1 (0.1)	0
Intravenous immunoglobulin	2 (0.0)	1 (0.0)	0	1 (0.1)	1 (0.0)	1 (0.1)	0
TNF inhibitors	1 (0.0)	0	0	0	0	1 (0.1)	0
Infliximab	1 (0.0)	1 (0.0)	0	0	0	1 (0.1)	0

Abbreviations: ACE, angiotensin-converting enzyme; IL-6, interleukin-6; NSAID, nonsteroidal anti-inflammatory drug; TNF, tumor necrosis factor.

[a]No patient in this study received the following drugs: siltuximab, antirejection medications, chloroquine, tofacitinib, filgotinib, baricitinib, etanercept, certolizumab, golimumab, adalimumab, or baloxavir marboxil.

TABLE 4 Proportion of African American and White patients treated with select medications by US region and age group

	US Region				Age group			
	South		Midwest		<60 years		≥60 years	
Select medications, *n* (%)	African American, *n* = 2706	White, *n* = 1495	African American, *n* = 580	White, *n* = 749	African American, *n* = 1429	White, *n* = 721	African American, *n* = 1865	White, *n* = 1558
Corticosteroids	602 (22.2)	556 (37.2)	294 (50.7)	382 (51.0)	441 (30.9)	322 (44.7)	457 (24.5)	629 (40.4)
Dexamethasone	432 (16.0)	448 (30.0)	217 (37.4)	275 (36.7)	328 (23.0)	257 (35.6)	322 (17.3)	469 (30.1)
Methylprednisolone	151 (5.6)	117 (7.8)	44 (7.6)	58 (7.7)	101 (7.1)	43 (6.0)	94 (5.0)	136 (8.7)
NSAIDs	523 (19.3)	378 (25.3)	369 (63.6)	407 (54.3)	447 (31.3)	278 (38.6)	446 (23.9)	517 (33.2)
Bronchodilators	402 (14.9)	318 (21.3)	249 (42.9)	337 (45.0)	287 (20.1)	183 (25.4)	367 (19.7)	490 (31.5)
Hydroxychloroquine	629 (23.2)	292 (19.5)	94 (16.2)	169 (22.6)	320 (22.4)	128 (17.8)	403 (21.6)	338 (21.7)
Remdesivir	154 (5.7)	308 (20.6)	153 (26.4)	170 (22.7)	160 (11.2)	178 (24.7)	147 (7.9)	301 (19.3)

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

TABLE 5 Inpatient medications used during first hospitalization stratified by month of admission between December 2019 and August 2020[a]

Select medications, *n* (%)	December to March, *n* = 1148	April, *n* = 2000	May, *n* = 1061	June, *n* = 608	July, *n* = 1396	August, *n* = 351
Corticosteroids	286 (24.9)	342 (17.1)	134 (12.6)	201 (33.1)	869 (62.2)	223 (63.5)
Dexamethasone	137 (11.9)	147 (7.4)	57 (5.4)	168 (27.6)	813 (58.2)	210 (59.8)
Methylprednisolone	98 (8.5)	108 (5.4)	36 (3.4)	39 (6.4)	103 (7.4)	23 (6.6)
NSAIDs	372 (32.4)	450 (22.5)	221 (20.8)	198 (32.6)	500 (35.8)	107 (30.5)
Bronchodilators	301 (26.2)	348 (17.4)	174 (16.4)	158 (26.0)	392 (28.1)	77 (21.9)
Hydroxychloroquine	620 (54.0)	589 (29.5)	42 (4.0)	14 (2.3)	17 (1.2)	7 (2.0)
Remdesivir	9 (0.8)	5 (0.3)	86 (8.1)	184 (30.3)	471 (33.7)	128 (36.5)
ACE inhibitors	41 (3.6)	98 (4.9)	58 (5.5)	40 (6.6)	125 (9.0)	33 (9.4)
Angiotensin II receptor blockers	47 (4.1)	69 (3.5)	40 (3.8)	43 (7.1)	122 (8.7)	20 (5.7)
IL-6 inhibitors	37 (3.2)	50 (2.5)	30 (2.8)	30 (4.9)	49 (3.5)	10 (2.8)
Tocilizumab	37 (3.2)	50 (2.5)	30 (2.8)	28 (4.6)	49 (3.5)	10 (2.8)
Sarilumab	0	0	0	2 (0.3)	0	0
Alteplase	111 (9.7)	87 (4.4)	25 (2.4)	19 (3.1)	33 (2.4)	4 (1.1)
Lopinavir/ritonavir	9 (0.8)	2 (0.1)	0	0	0	0
Dornase alfa	3 (0.3)	0	0	0	0	0
Intravenous immunoglobulin	0	0	0	0	2 (0.1)	0
TNF inhibitors	0	0	1 (0.1)	0	0	0
Infliximab	0	0	1 (0.1)	0	0	0

Abbreviations: ACE, angiotensin-converting enzyme; IL-6, interleukin-6; NSAID, nonsteroidal anti-inflammatory drug; TNF, tumor necrosis factor.

[a]No patient in this study received the following drugs: siltuximab, antirejection medications, chloroquine, tofacitinib, filgotinib, baricitinib, etanercept, certolizumab, golimumab, adalimumab, or baloxavir marboxil.

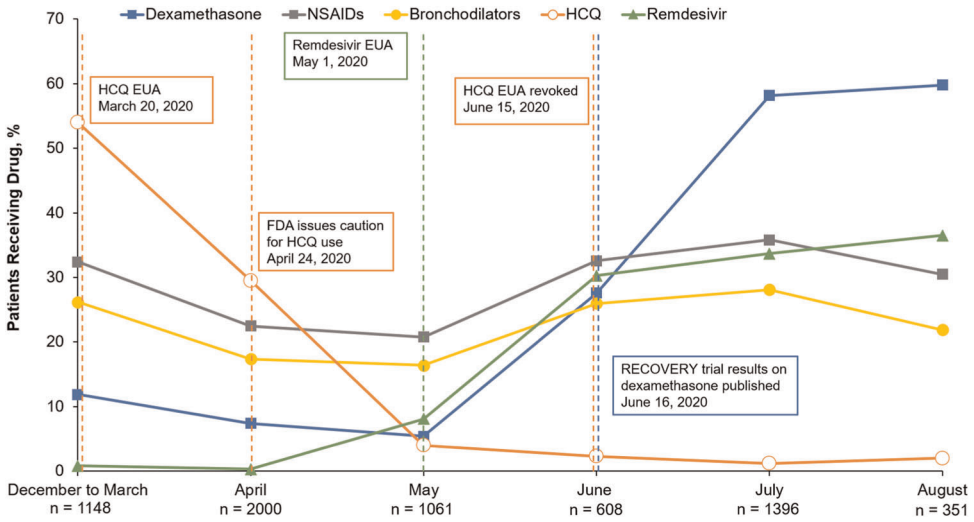

FIGURE 1 Inpatient medications used during first hospitalization by month of admission between December 2019 and August 2020. EUA, emergency use authorization; FDA, US Food and Drug Administration; HCQ, hydroxychloroquine; NSAID, nonsteroidal anti-inflammatory drug

Our study showed that across all regions, for most of the select medications evaluated, a numerically smaller proportion of African American patients received the medication than White patients, with a >10% numerical difference for dexamethasone and remdesivir. Notably, when analyzed by region, the difference in medication use by race was seen in the South, but not in the Midwest. The comparisons are unadjusted for disease severity, type of hospital (academic vs. community), insurance status, and other factors, such

as concomitant medications or underlying conditions that may affect the differences noted by race. Racial differences in medication use by region may reflect a multitude of factors, including access to healthcare, access to insurance coverage, and structural inequities. However, insurance coverage is unlikely to account for differences in use of a low-cost therapy, such as dexamethasone. Also, inpatient care (including medications) is reimbursed based on diagnosis-related group codes, so costs may not be a major factor in deciding whether patients receive a particular therapy. Although exploring all the possible reasons for regional differences in medication use by race is beyond the scope of this manuscript, these results raise important questions and warrant further study.

Within this population of patients predominantly from the Midwest and South, we found regional differences in the use of medications. Differences in the patterns of prescriptions may reflect varying treatment guidelines and implementation of evidence-based medicine and differences in practice between hospitals and healthcare systems across regions, and variable access to medications and healthcare resources due to regional surges in COVID-19-related hospitalizations. Further study is warranted with regard to regional differences and potential resulting health outcome disparities.

This study demonstrated notable changes in medication use in patients with COVID-19 and pulmonary involvement over a relatively short period of time. Hydroxychloroquine and chloroquine are approved to treat or prevent malaria, and hydroxychloroquine is approved to treat certain autoimmune conditions, including rheumatoid arthritis and systemic lupus erythematosus, due to their immunomodulatory effects.[19] The US Food and Drug Administration (FDA) granted emergency use authorization to chloroquine and hydroxychloroquine in March 2020 based on in vitro and observational studies in patients with COVID-19. However, this authorization was revoked in June 2020 based on updated scientific evidence, indicating a lack of benefit. Results of our study show a decrease in in-hospital hydroxychloroquine use over time; the highest proportion of patients receiving hydroxychloroquine did so in December 2019 through March 2020 (54.0%) and April (29.5%); in May, only 4.0% of patients received hydroxychloroquine, and the proportion of patients was <2.5% thereafter.

In the Adaptive COVID-19 Treatment Trial (ACTT-1), remdesivir was shown to shorten the time to recovery compared with placebo in patients with COVID-19 pneumonia.[20] In May 2020, remdesivir received emergency use authorization for patients with severe COVID-19 that was expanded in August for all hospitalized adult and pediatric patients; remdesivir received FDA approval in October. This timeline is reflected in the results of our study, which showed a notable increase in the proportion of patients receiving remdesivir, from 8.1% in May to 30.3% in June, 33.7% in July, and 36.5% in August. Dexamethasone has been shown to decrease the mortality rate in patients with COVID-19 who were receiving either invasive mechanical ventilation or oxygen support.[21] Results of the RECOVERY trial were released in June and are reflected in our study, showing 5.4% of patients receiving dexamethasone in May, 27.6% in June, and >58% in July and August.

Research into potential COVID-19 therapies is ongoing with hundreds of COVID-19 clinical trials, including trials examining the safety and efficacy of immunomodulatory therapies, including IL-1, IL-6, and Janus kinase inhibitors, antithrombotic therapies, and interferons, among other medications, as well as large observational studies. Medication use in patients with severe COVID-19 is primarily driven by clinical status (e.g., dexamethasone for patients who require mechanical ventilation or supplemental oxygen). As more study results are published, recommendations based on available scientific evidence and expert opinion from government and national professional societies will continue to be revised and updated to inform healthcare professionals on optimal patient care. In this unprecedented pandemic environment, understanding treatment patterns in light of the frequent and rapid release of scientific information and evaluating medication use in different racial and ethnic, and geographic populations are important to identify potential barriers to access to care.

Limitations of this study include those inherent to retrospective EHR data analysis, including potential bias and missing data (e.g., care and medications provided outside of Explorys). For almost half of patients, insurance data were missing; EHR data are not used for administrative and/or billing purposes, so insurance status is more likely to be missing than in claims data. This study included only first hospital admission; however, it is unlikely that including the small number of readmissions would have changed observed treatment patterns. Another potential limitation is that patients were included based on a COVID-19 diagnosis, rather than a positive test. Thus, a few patients may have been presumed to have COVID-19 and given a diagnosis of COVID-19, particularly early in the pandemic when testing was not readily available. Furthermore, the absence of correlation between disease severity/clinical condition and medication use is an important limitation of this study because we cannot demonstrate that patients in all regions and races had equal disease severity when evaluating treatments received.

Most patients in this study were from the South and Midwest, and our results may not be generalizable to the overall US population. However, because the selection criteria included nationally used ICD codes, the selection of these populations was unintentional and likely reflects the geographic distribution of the Explorys database and the pandemic outbreak itself. As the treatment of patients with COVID-19 is evolving in this rapidly changing and unprecedented pandemic environment, it is possible that treatment patterns have changed over time by region and race, and these potential trends were not evaluated. In part due to this ever-changing treatment environment, this study reported on only select medications (based on published literature of emerging therapies), and data on the use of other COVID-19 therapies, including convalescent plasma or anticoagulants, were not evaluated. Despite these limitations, this study using a large database, including a racially diverse group of patients, reveals important information about differences in medication use in patients with COVID-19 and pulmonary involvement. Identification and awareness of disparities in medication use

are the first steps, and additional studies are warranted to further evaluate and understand these study findings.

5 | CONCLUSION

This retrospective EHR study included US patients hospitalized with COVID-19 and pulmonary involvement predominantly from the South and Midwest. These study results, which demonstrate different rates of medication use between geographic regions, in addition to differences in medication use among African American and White patients within some regions and age groups, warrant further study.

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CONFLICT OF INTEREST

Jennie H. Best, Shalini V. Mohan, and James L. Zazzali are employees and shareholders of Genentech, Inc. Amanda M. Kong was an employee of IBM Watson Health at the time of this study and manuscript preparation. Krutika Jariwala-Parikh is an employee of IBM Watson Health. Emma Kaplan-Lewis is a principal investigator for a Genentech-sponsored clinical trial at Elmhurst Hospital Center, with no direct financial support received, and has served on medical advisory boards for ViiV Pharmaceuticals. Otis W. Brawley reports no conflicts of interest. Rachel Baden is a principal investigator for a Genentech-sponsored clinical trial at Highland Hospital, with no direct financial support received. Karen S. Miller is a principal investigator for a Genentech-sponsored clinical trial at St Luke's Health System, with no direct financial support received. James Loveless has served as an investigator for Genentech-sponsored clinical trials, and as an advisor and on a speaker's bureau for Genentech, all outside of the submitted work.

AUTHOR CONTRIBUTIONS

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. All authors had access to the data, provided critical feedback, and contributed to the writing of the manuscript. Jennie H. Best and Shalini V. Mohan conceived and designed the study. Amanda M. Kong provided subject matter expertise, and Krutika Jariwala-Parikh conducted programming and data analysis support. Jennie H. Best, Amanda M. Kong, Emma Kaplan-Lewis, Otis W. Brawley, Rachel Baden, James L. Zazzali, Karen S. Miller, James Loveless, and Shalini V. Mohan contributed to the interpretation of the results.

ETHICS STATEMENT

This was a retrospective, observational study, and all study data were deidentified and fully compliant with Health Insurance Portability and Accountability Act regulations (45 CFR 164.514e); therefore, approval from an Institutional Review Board was not required, and informed consent was not obtained.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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