

UC San Diego

UC San Diego Previously Published Works

Title

Examination of Medication Use Patterns by Age Group, Comorbidity, and Month in COVID-19 Positive Patients in a Large Statewide Health System During the Pandemic in 2020.

Permalink

<https://escholarship.org/uc/item/7sp8880f>

Journal

The Journal of pharmacy technology : jPT : official publication of the Association of Pharmacy Technicians, 38(2)

ISSN

8755-1225

Authors

Watanabe, Jonathan H
Kwon, Jimmy
Nan, Bin
et al.

Publication Date


2022-04-01

DOI

10.1177/87551225211068675

Peer reviewed

Examination of Medication Use Patterns by Age Group, Comorbidity, and Month in COVID-19 Positive Patients in a Large Statewide Health System During the Pandemic in 2020

Journal of Pharmacy Technology
2022, Vol. 38(2) 75–87
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/87551225211068675
journals.sagepub.com/home/pmt


Jonathan H. Watanabe, PharmD, PhD¹ , Jimmy Kwon, MS², Bin Nan, PhD², Shira R. Abeles, MD³, and Sanjay R. Mehta, MD³

Abstract

Background: Understanding medication use patterns for patients with COVID-19 will provide needed insight into the evolution of COVID-19 treatment over the course of the SARS-CoV-2 pandemic and aid clinical management considerations. **Objectives:** To systematically determine most frequently used medications among COVID-19 patients overall and by hospitalization status. Secondary objective was use measurement of medications considered potential therapeutic options. **Methods:** Retrospective cohort study was performed using data from the University of California COVID Research Data Set (UC CORDS) patients between March 10, 2020, and December 31, 2020. Main outcomes were percentages of patients prescribed medications, overall, by age group, and by comorbidity based on hospitalization status for COVID-19 patients. Use percentage by month of COVID-19 diagnosis was measured. Cumulative count of potential therapeutic options was measured over time. **Results:** Dataset included 22 896 unique patients with COVID-19 (mean [SD] age, 42.4 [20.4] years; 12 154 [53%] women). Most frequently used medications in patients overall were acetaminophen (21.2%), albuterol (14.9%), ondansetron (13.9%), and enoxaparin (10.8%). Dexamethasone use increased from fewer than 50 total hospitalized patients through April who had received the medication, to more than 500 patients by mid-August. Cumulative count of enoxaparin users was the largest throughout the study period. **Conclusion and Relevance:** In this retrospective cohort study, across age and comorbidity groups, predominant utilization was for supportive care therapy. Dexamethasone and remdesivir experienced large increases in use. Conversely, hydroxychloroquine and azithromycin use markedly dropped. Medication utilization rapidly shifted toward more evidence-concordant treatment of patients with COVID-19 as rigorous study findings emerged.

Keywords

COVID-19, medications, medication utilization

Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Awareness of the SARS-CoV-2 infectious capacity coupled with a case fatality rate greater than 0.6%¹ has led to global efforts to reduce transmission and identify effective treatment approaches. As of September 10, 2021, there have been more than 223.6 million confirmed cases and in excess of 4.6 million deaths worldwide.²

Understanding medication use patterns for patients with confirmed COVID-19 will provide needed insight into the evolution of COVID-19 treatment over the course of the SARS-CoV-2 pandemic and provide evidence for clinical

management considerations. The goal for this analysis was to characterize the frequency of medications used based on

¹Department of Clinical Pharmacy Practice, UC Irvine School of Pharmacy & Pharmaceutical Sciences, Irvine, CA, USA

²Department of Statistics, UC Irvine Donald Bren School of Information & Computer Sciences, Irvine, CA, USA

³Department of Medicine, UC San Diego School of Medicine, La Jolla, CA, USA

Corresponding Author:

Jonathan H. Watanabe, Associate Dean of Assessment and Quality, Professor of Clinical Pharmacy, Department of Clinical Pharmacy Practice, UC Irvine School of Pharmacy & Pharmaceutical Sciences, 101 Theory, Suite 100, Irvine, CA 92697, USA.
Email: jonathan.watanabe@uci.edu

percentage of COVID-19 positive individuals receiving the medications overall, by age group, and by comorbid condition for both hospitalized and nonhospitalized patients. To examine how this pattern has changed since the pandemic began, medication use based on month of diagnosis was tracked. To quantify use of medications considered as possible treatments that affect the clinical course by shortening the duration of symptoms or preventing complications (referred hereafter as “potential therapeutic options” [PTOs]), dexamethasone, remdesivir, enoxaparin, heparin, colchicine, hydrocortisone, tocilizumab, azithromycin, hydroxychloroquine and medication classes of angiotensin-2 converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs),³⁻⁹ and number of hospitalized patients in the cohort that used each PTO were counted over the pandemic.

Methods

The University of California COVID Research Data Set (UC CORDS) was constructed to be a timely data set for research purposes distributed weekly, containing SARS-CoV-2 testing results and COVID-19 treatment information collected from across University of California (UC) Health. It is a Health Insurance Portability and Accountability Act (HIPAA) Limited Data Set generated from all 5 UC Health medical centers (Davis, Irvine, Los Angeles, San Diego, San Francisco). In 2019, UC Health had 1 092 522 inpatient days. This was equivalent to 6.6% of the total inpatient days in the state. Care was provided to 1.8 million unique patients by UC Health in 2019 which is 4.6% of the population of California that year.¹⁰⁻¹² UC CORDS was operationalized by UC Health as “non-human subjects research,” and analyses are considered institutional review board exempt. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline was followed for this analysis.¹³

Data for 22 897 patients confirmed positive with COVID-19 by SARS-CoV-2 RNA nucleic acid amplification with probe detection were extracted for the period of March 10, 2020, through December 31, 2020. Consistent with UC Health reporting, patients were categorized as experiencing a COVID-19-related hospitalization if they were admitted to the hospital within 30 days of confirmed test or tested positive during their hospitalization.

Generation of Comorbidities From Electronic Health Records

Patients with COVID-19 with comorbid conditions of hypertension, hyperlipidemia, type 2 diabetes, chronic obstructive pulmonary disease (COPD)/Asthma, heart disease, chronic kidney disease (CKD), cancer, obesity, and the respiratory diseases asthma and COPD, and those receiving dialysis are at increased risk for poor outcomes.¹⁴⁻¹⁶ To

examine medication utilization in patients diagnosed with COVID-19 with these risk factors at baseline, we first determined the presence of these conditions using the *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) codes in the patient electronic health record (EHR). Given the possibility that preexisting conditions would not be reported at COVID-19 diagnosis, ICD-10-CM codes up to 1-year preceding diagnosis were included. Self-reported sex and race/ethnicity were extracted from EHR as well as body mass index (BMI) for hospitalized patients. Age was estimated based on patient birth year as birthdate was removed from UC CORDS for de-identification. Uses of mechanical ventilation and extracorporeal membrane oxygen (ECMO) were extracted for each hospitalized patient using affiliated *International Classification of Diseases, Tenth Revision, Procedure Coding System* codes and Current Procedural Terminology, 4th Edition codes.

Medications used for each patient were determined from the UC Health EHR by measurement of all medication active ingredients used within 30 days of COVID-19 positive test based on the RxNorm standardized nomenclature for clinical drugs from the National Library of Medicine.¹⁷ Medication utilization that occurred outside of UC Health was not included in this dataset. Given the assumption, in context of COVID-19, of a similar therapeutic class effect of ACEIs and ARBs, usage of these medications was collapsed to the overall category of “ACEIs/ARBs.” Monthly utilization was based on month in which patient was confirmed for COVID-19.

Statistical Analysis

Descriptive measurement of demographic and clinical characteristics was performed for COVID-19 positive patients in the sample overall and by hospitalization status. Continuous data were expressed as mean \pm SD or median and interquartile range [IQR] values. Use was quantified by percentage of patients with corresponding 95% confidence interval. All confidence intervals and subgroup sample sizes are included in the affiliated tables.

Data were extracted with module pyodbc, version 4.0.30 in Python, version 3.8.3 (Python Software Foundation). All analyses were performed in R, version 3.6.3 (R Project for Statistical Computing). Statistical significance defined using 2-sided significance level of $\alpha = 0.05$.

Results

Descriptive Statistics

The dataset contained 22 896 unique patients confirmed positive for COVID-19 between March 10, 2020, and December 31, 2020 (mean [SD] age, 42.4 [20.4] years; 12 154 [53%] women; median [25th, 75th percentile] BMI for hospitalized patients, 28.5 [23.8, 32.9]). Among the

sample, 6326 (28%) were non-Hispanic White, 8475 (37%) were Hispanic, 1562 (7%) Asian, 1313 (6%) Black, and 3100 (14%) reported as “other.” Of the 22896 unique COVID-19 test confirmed patients, 3546 patients had a COVID-related hospitalization. Of the hospitalized patients, the most common comorbidity was hypertension (48%). Greater than 20% of hospitalized patients had hyperlipidemia (37%), type 2 diabetes (35%), heart disease (24%), and CKD (22%). The rates of asthma/COPD and cancer in hospitalized patients were 17% and 13%, respectively (Table 1).

Medication Utilization Overall and for Patients by Hospitalization Status by Age Group, Comorbidity, and Hospital Procedure Status

All patients who tested positive for COVID-19. The 10 medications used in the largest percentage of confirmed COVID-19 patients over the study period overall were acetaminophen (21.2%), albuterol (14.9%), ondansetron (13.9%), enoxaparin (10.8%), sennosides (9.3%), lidocaine (8.5%), polyethylene glycol (PEG) 3350 (8.4%), dexamethasone 8.1%, azithromycin (7%), and insulin lispro (6.8%). Acetaminophen, ondansetron, albuterol, enoxaparin, and sennosides were part of the top 5 medications for every age category except for those under 50 years old where lidocaine was present rather than sennosides (Table 2). Across comorbidities, medications were consistent with those observed in the age group analysis. For any of the baseline comorbidities, the medication used in the largest proportion was acetaminophen. Usage of acetaminophen ranged from 39.6% in patients with cancer to 61.5% for patients with CKD. Enoxaparin or heparin was a top 10 medication for all comorbidities. For patients who received dialysis at baseline, most frequent medications were acetaminophen, heparin, insulin lispro, ondansetron, lidocaine, sennosides, albuterol, pantoprazole, vancomycin, and PEG 3350 (Table 3).

Hospitalized patients with COVID-19. The 10 medications used in the largest percentage of confirmed COVID-19 hospitalized patients were acetaminophen (88.6%), enoxaparin (62.1%), ondansetron (59%), sennosides (54.1%), albuterol (53.3%), PEG 3350 (49.2%), lidocaine (42.5%), dexamethasone (40.1%), heparin (38.8%), and insulin lispro (38.4%). Medications were similar across age groups. Dexamethasone was among the top 10 medications for all age groups (Table 2). Heparin was among the top 10 for all comorbidities except for COPD/asthma. For patients who received dialysis at baseline, top medications were heparin, acetaminophen, insulin lispro, lidocaine, sennosides, vancomycin, ondansetron, albuterol, pantoprazole, and PEG 3350. For obese patients, the medications in the top 10 were consistent with the overall list for hospitalized patients (Table 4).

For hospitalized COVID-19 patients who had mechanical ventilation, top medications were acetaminophen, fentanyl, sennosides, PEG 3350, furosemide, propofol, heparin, vancomycin, lidocaine, and albuterol. For patients who received ECMO, top medications were fentanyl, heparin, furosemide, sennosides, albumin, vancomycin, dexmedetomidine, PEG 3350, propofol, and midazolam (Table 4).

Nonhospitalized patients with COVID-19. The proportion of individuals receiving each medication was substantially lower in nonhospitalized patients. The 10 medications used in the most patients were acetaminophen (8.8%), albuterol (7.8%), ondansetron (5.7%), azithromycin (3.7%), ACEIs/ARBs (3.6%), benzonatate (3.2%), ibuprofen (2.8%), fluticasone (2.7%), atorvastatin (2.5%), and guaifenesin (2.3%). Among all age groups, acetaminophen was the most common ranging from 7.4% in those under 50 years old to 13.4% for those 65 years old and above. Albuterol and ondansetron were among the top 10 for all age groups (Table 2). For all comorbidities studied, ACEIs/ARBs were among the 6 most commonly used medications and were the first or second most common for hypertension (19.1%), hyperlipidemia (13.3%), type 2 diabetes (18.3%), heart disease (16.4%), and CKD (16.4%). Ondansetron was among the 10 most commonly used medications for all comorbidities. For patients who had baseline dialysis, top medications were acetaminophen, heparin, atorvastatin, ondansetron, albuterol, carvedilol, sevelamer, insulin lispro, pantoprazole, and albumin (Table 5).

Medication Utilization by Month of COVID-19 Diagnosis

All patients who tested positive for COVID-19. In March, among all patients COVID-19 test confirmed, the most common medications were acetaminophen (21.3%), albuterol (20.5%), azithromycin (16.2%), ondansetron (12.5%), guaifenesin (11.7%), enoxaparin (11.2%), PEG 3350 (10.5%), hydroxychloroquine (10.2%), sennosides (9.6%), and ceftriaxone (9.6%). By April, while the most common medications were similar, use of azithromycin and hydroxychloroquine decreased. Consequently, March was the only month in which hydroxychloroquine appeared among the top 10. April was the last month in which ceftriaxone was among the top 10. Enoxaparin was the sixth most commonly used medication in March at 11.2%, but increased in May to the third most used medication at 22.8%. Enoxaparin remained in the top 5 medications through December. Dexamethasone was observed as a top 10 medication for the first time in July (8.3% of patients), increasing to 11.1% in August, and remained among the top 8 prescribed meds thereafter. Heparin was not among the top 10 medications after September (Table 6).

Table 1. Descriptive Characteristics of the COVID-19 Test Confirmed Patients.

	Tested COVID-19 positive n (%)	Nonhospitalized n (%)	Hospitalized n (%)
Age			
Sample size	22 896	19 350	3546
Mean (SD)	42.35 ± 20.40	39.92 ± 19.36	55.63 ± 20.84
Under 50	14 378 (63)	13 120 (68)	1258 (35)
50 to <65	4985 (22)	4014 (21)	971 (27)
65 or older	3533 (15)	2216 (11)	1317 (37)
Sex			
Female	12 154 (53)	10 573 (55)	1581 (45)
Race and ethnicity			
Non-Hispanic White	6326 (28)	5416 (28)	910 (26)
Hispanic	8475 (37)	6768 (35)	1707 (48)
Black	1313 (6)	1041 (5)	272 (8)
Asian	1562 (7)	1262 (7)	300 (8)
Native Hawaiian/Other Pacific Islander/American Indian/Alaska Native	252 (1)	200 (1)	52 (1)
Other	3100 (14)	2378 (12)	722 (20)
Not reported	7012 (31)	6316 (33)	696 (20)
Body mass index of hospitalized patients			
Median (25th, 75th)	NA	NA	28.5 (23.8, 32.9)
<18.5	NA	NA	98 (3)
18.5 to <25.0	NA	NA	849 (26)
25 to <30.0	NA	NA	1004 (30)
30 or more	NA	NA	1364 (38)
Variable			
Hypertension	4199 (18)	2502 (13)	1697 (48)
Hyperlipidemia	3720 (16)	2410 (12)	1310 (37)
Type 2 diabetes	2685 (12)	1427 (7)	1258 (35)
Asthma/COPD	1794 (8)	1197 (6)	597 (17)
Heart disease	1520 (7)	670 (3)	850 (24)
Chronic kidney disease	1326 (6)	548 (3)	778 (22)
Cancer	1394 (6)	921 (5)	473 (13)
Baseline dialysis	190 (1)	46 (0)	144 (4)
Hospital procedures			
Mechanical ventilation	661 (3)	0 (0)	661 (19)
ECMO	54 (0)	0 (0)	54 (2)
Positive Covid test month			
March	591 (3)	478 (2)	113 (3)
April	921 (4)	699 (4)	222 (6)
May	709 (3)	467 (2)	242 (7)
June	1915 (8)	1542 (8)	373 (11)
July	3789 (17)	3202 (17)	587 (17)
August	2027 (9)	1617 (8)	410 (12)
September	1108 (5)	863 (4)	245 (7)
October	1083 (5)	880 (5)	203 (6)
November	3200 (14)	2872 (15)	328 (9)
December	7553 (33)	6730 (35)	823 (23)

Abbreviations: COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygen.

Hospitalized patients with COVID-19. In March, the most common medications for those hospitalized were acetaminophen (85.8%), enoxaparin (56.6%), albuterol (56.6%), azithromycin (54%), PEG 3350 (51.3%), ondansetron (48.7%), ceftriaxone (48.7%), guaifenesin (47.8%),

sennosides (45.1%), and hydroxychloroquine (43.4%). The top 2 medications were acetaminophen and either enoxaparin or ondansetron for every month. From March to April, azithromycin use dropped from 54 to 40.5%. Hydroxychloroquine declined rapidly from a high of 43.4% in March and

Table 2. Medication Utilization by Age Group.

All positive COVID-19 patients												
Rank	Overall (n = 22 896)	%	95% CI	<50 (n = 14 378)	%	95% CI	50 to <65 (n = 4985)	%	95% CI	65 or older (n = 3533)	%	95% CI
1	Acetaminophen	21.2	(20.6-21.7)	Acetaminophen	14.3	(13.7-14.9)	Acetaminophen	26.2	(25.0-27.4)	Acetaminophen	41.8	(40.2-43.4)
2	Albuterol	14.9	(14.4-15.3)	Albuterol	9.4	(8.9-9.9)	Albuterol	20.7	(19.6-21.8)	Albuterol	28.8	(27.3-30.3)
3	Ondansetron	13.9	(13.5-14.4)	Ondansetron	9.4	(8.9-9.9)	Ondansetron	17.6	(16.5-18.7)	Ondansetron	27.1	(25.6-28.6)
4	Enoxaparin	10.8	(10.4-11.2)	Enoxaparin	5.6	(5.2-6.0)	Enoxaparin	15.5	(14.5-16.5)	Senosides, USP	25.8	(24.4-27.2)
5	Senosides, USP	9.3	(8.9-9.7)	Lidocaine	5.4	(5.0-5.8)	Senosides, USP	12.4	(11.5-13.3)	Enoxaparin	25.3	(23.9-26.7)
6	Lidocaine	8.5	(8.1-8.9)	Ibuprofen	5.0	(4.6-5.4)	Dexamethasone	11.7	(10.8-12.6)	Polyethylene glycol 3350	23.2	(21.8-24.6)
7	Polyethylene glycol 3350	8.4	(8.1-8.8)	Senosides, USP	4.2	(3.9-4.5)	ACEIs/ARBs	11.2	(10.3-12.1)	Atorvastatin	21.3	(19.9-22.7)
8	Dexamethasone	8.1	(7.8-8.5)	Polyethylene glycol 3350	4.0	(3.7-4.3)	Insulin lispro	11.0	(10.1-11.9)	Dexamethasone	20.3	(19.0-21.6)
9	Azithromycin	7.0	(6.6-7.3)	Azithromycin	4.0	(3.7-4.3)	Polyethylene glycol 3350	10.8	(9.9-11.7)	ACEIs/ARBs	19.1	(17.8-20.4)
10	Insulin lispro	6.8	(6.5-7.1)	Benzonatate	4.0	(3.7-4.3)	Benzonatate	10.7	(9.8-11.6)	Heparin	19.0	(17.7-20.3)
Hospitalized patients												
Rank	Overall (n = 3546)	%	95% CI	<50 (n = 1258)	%	95% CI	50 to <65 (n = 971)	%	95% CI	65 or older (n = 1317)	%	95% CI
1	Acetaminophen	88.6	(87.5-89.6)	Acetaminophen	86.8	(84.9-88.7)	Acetaminophen	89.5	(87.6-91.4)	Acetaminophen	89.6	(87.9-91.3)
2	Enoxaparin	62.1	(60.5-63.7)	Ondansetron	61.9	(59.2-64.6)	Enoxaparin	70.5	(67.6-73.4)	Senosides, USP	63.0	(60.4-65.6)
3	Ondansetron	59.0	(57.3-60.6)	Enoxaparin	56.6	(53.9-59.3)	Albuterol	62.1	(59.0-65.2)	Enoxaparin	61.2	(58.6-63.8)
4	Senosides, USP	54.1	(52.4-55.7)	Senosides, USP	43.2	(40.5-45.9)	Ondansetron	59.1	(56.0-62.2)	Albuterol	58.2	(55.5-60.9)
5	Albuterol	53.3	(51.7-54.9)	Lidocaine	42.8	(40.1-45.5)	Senosides, USP	56.0	(52.9-59.1)	Polyethylene glycol 3350	57.5	(54.8-60.2)
6	Polyethylene glycol 3350	49.2	(47.5-50.8)	Albuterol	41.3	(38.6-44.0)	Polyethylene glycol 3350	48.9	(45.8-52.0)	Ondansetron	56.0	(53.3-58.7)
7	Lidocaine	42.4	(40.8-44.1)	Polyethylene glycol 3350	40.7	(38.0-43.4)	Insulin lispro	47.7	(44.6-50.8)	Heparin	47.8	(45.1-50.5)
8	Dexamethasone	40.1	(38.5-41.7)	Docusate	35.1	(32.5-37.7)	Dexamethasone	44.4	(41.3-47.5)	Dexamethasone	45.9	(43.2-48.6)
9	Heparin	38.7	(37.1-40.4)	Fentanyl	30.8	(28.2-33.4)	Lidocaine	40.0	(36.9-43.1)	Insulin lispro	45.6	(42.9-48.3)
10	Insulin lispro	38.4	(36.8-40.0)	Dexamethasone	30.6	(28.1-33.1)	Heparin	39.0	(35.9-42.1)	Lidocaine	43.9	(41.2-46.6)
Nonhospitalized patients												
Rank	Overall (n = 19 350)	%t	95% CI	<50 (n = 13 120)	%	95% CI	50 to <65 (n = 4014)	%	95% CI	65 or older (n = 2216)	%	95% CI
1	Acetaminophen	8.8	(8.4-9.2)	Acetaminophen	7.4	(7.0-7.8)	Acetaminophen	10.9	(9.9-11.9)	Acetaminophen	13.4	(12.0-14.8)
2	Albuterol	7.8	(7.5-8.2)	Albuterol	6.3	(5.9-6.7)	Albuterol	10.7	(9.7-11.7)	ACEIs/ARBs	11.6	(10.3-12.9)
3	Ondansetron	5.7	(5.3-6.0)	Ondansetron	4.4	(4.0-4.8)	Ondansetron	7.5	(6.7-8.3)	Albuterol	11.4	(10.1-12.7)
4	Azithromycin	3.7	(3.4-4.0)	Ibuprofen	3.0	(2.7-3.3)	ACEIs/ARBs	7.3	(6.5-8.1)	Ondansetron	9.9	(8.7-11.1)
5	ACEIs/ARBs	3.6	(3.3-3.8)	Azithromycin	2.7	(2.4-3.0)	Azithromycin	5.6	(4.9-6.3)	Atorvastatin	9.5	(8.3-10.7)
6	Benzonatate	3.1	(2.9-3.4)	Benzonatate	2.3	(2.0-2.6)	Benzonatate	5.1	(4.4-5.8)	Azithromycin	6.4	(5.4-7.4)
7	Ibuprofen	2.8	(2.6-3.0)	Fluticasone	2.1	(1.9-2.3)	Atorvastatin	5.1	(4.4-5.8)	Amlodipine	5.2	(4.3-6.1)
8	Fluticasone	2.7	(2.5-2.9)	Lidocaine	1.8	(1.6-2.0)	Metformin	4.6	(4.0-5.2)	Dexamethasone	5.1	(4.2-6.0)
9	Atorvastatin	2.5	(2.3-2.7)	Guafenesin	1.6	(1.4-1.8)	Fluticasone	3.9	(3.3-4.5)	Aspirin	5.1	(4.2-6.0)
10	Guafenesin	2.3	(2.1-2.5)	Codeine	1.6	(1.4-1.8)	Guafenesin	3.8	(3.2-4.4)	Metoprolol	5.0	(4.1-5.9)

Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval.

Table 3. Medication Utilization by Baseline Comorbidity and Hospital Procedure (All COVID-19 Positive Patients).

All positive COVID-19 patients

Rank	Hypertension (n = 4199)			Hyperlipidemia (n = 3720)			Type 2 diabetes (n = 2685)			COPD/asthma (n = 1794)			Heart disease (n = 1520)			Chronic kidney disease (n = 1326)
	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI	
1	Acetaminophen	46.5	(45-48)	Acetaminophen	40.2	(38.6-41.8)	Acetaminophen	52.0	(50.1-53.8)	Albuterol	41.8	(39.5-44)	Acetaminophen	59.0	(56.5-61.5)	Acetaminophen
2	Albuterol	32.2	(30.7-33.6)	Albuterol	29.5	(28.1-31)	Insulin lispro	40.7	(38.9-42.6)	Acetaminophen	39.9	(37.6-42.1)	Albuterol	39.9	(37.5-42.4)	Heparin
3	Ondansetron	30.2	(28.8-31.6)	Ondansetron	26.6	(25.1-28)	Albuterol	35.0	(33.2-36.8)	Ondansetron	25.9	(23.9-27.9)	Ondansetron	37.2	(34.7-39.6)	Ondansetron
4	ACEIs/ARBs	28.5	(27.1-29.8)	Atorvastatin	25.2	(23.8-26.6)	Ondansetron	33.5	(31.7-35.3)	Enoxaparin	22.6	(20.6-24.5)	Sennosides, USP	36.6	(34.2-39)	Albuterol
5	Enoxaparin	27.2	(25.9-28.5)	Sennosides, USP	23.2	(21.8-24.5)	Insulin glargine	30.9	(29.2-32.7)	Sennosides, USP	20.8	(18.9-22.7)	Aspirin	34.9	(32.5-37.3)	Sennosides, USP
6	Sennosides, USP	25.8	(24.5-27.1)	Enoxaparin	22.9	(21.5-24.2)	Sennosides, USP	30.5	(28.7-32.2)	Polyethylene glycol 3350	20.3	(18.4-22.2)	Atorvastatin	34.3	(31.9-36.7)	Insulin lispro
7	Polyethylene glycol 3350	23.6	(22.3-24.9)	ACEIs/ARBs	22.3	(20.9-23.6)	Enoxaparin	30.1	(28.4-31.8)	Ipratropium	17.7	(16-19.5)	Polyethylene glycol 3350	33.0	(30.7-35.4)	Pantoprazole
8	Insulin lispro	22.5	(21.2-23.8)	Insulin lispro	21.5	(20.2-22.8)	ACEIs/ARBs	29.0	(27.3-30.7)	Dexamethasone	17.7	(15.9-19.4)	Heparin	32.3	(29.9-34.7)	Polyethylene glycol 3350
9	Atorvastatin	21.0	(19.7-22.2)	Polyethylene glycol 3350	20.1	(18.8-21.4)	Polyethylene glycol 3350	27.3	(25.6-29)	Lidocaine	17.1	(15.3-18.8)	Enoxaparin	30.6	(28.3-32.9)	Lidocaine
10	Dexamethasone	20.7	(19.5-21.9)	Dexamethasone	18.3	(17.1-19.6)	Atorvastatin	26.2	(24.5-27.8)	Pantoprazole	15.3	(13.7-17)	Insulin lispro	30.5	(28.1-32.8)	Atorvastatin

Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygen.

Table 4. Medication Utilization by Baseline Comorbidity and Hospital Procedure (Hospitalized COVID-19 Patients).

Hospitalized patients

Rank	Hypertension (n = 1697)			Hyperlipidemia (n = 1310)			Type 2 diabetes (n = 1258)			COPD/asthma (n = 597)			Heart disease (n = 850)		
	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI	Medication	%	95% CI
1	Acetaminophen	90.4	(89-91.8)	Acetaminophen	91.0	(89.4-92.5)	Acetaminophen	90.9	(89.3-92.5)	Acetaminophen	91.0	(88.6-93.3)	Acetaminophen	90.5	(88.5-92.4)
2	Enoxaparin	62.4	(60.1-64.7)	Sennosides, USP	61.7	(59-64.3)	Insulin lispro	78.5	(76.3-80.8)	Albuterol	77.7	(74.4-81.1)	Sennosides, USP	63.1	(59.8-66.3)
3	Sennosides, USP	59.5	(57.2-61.9)	Enoxaparin	60.0	(57.3-62.7)	Sennosides, USP	60.8	(58.1-63.5)	Enoxaparin	63.3	(59.4-67.2)	Albuterol	60.4	(57.1-63.6)
4	Albuterol	59.1	(56.8-61.4)	Albuterol	59.5	(56.8-62.1)	Enoxaparin	60.3	(57.6-63)	Ondansetron	62.0	(58.1-65.9)	Polyethylene glycol 3350	57.8	(54.4-61.1)
5	Ondansetron	57.8	(55.5-60.2)	Ondansetron	58.2	(55.5-60.8)	Albuterol	59.6	(56.9-62.3)	Sennosides, USP	58.3	(54.3-62.3)	Ondansetron	57.4	(54.1-60.7)
6	Polyethylene glycol 3350	54.6	(52.3-57)	Insulin lispro	55.6	(53-58.3)	Ondansetron	58.0	(55.3-60.8)	Polyethylene glycol 3350	57.3	(53.3-61.3)	Heparin	55.9	(52.5-59.2)
7	Insulin lispro	50.9	(48.5-53.3)	Polyethylene glycol 3350	54.2	(51.5-56.9)	Insulin glargine	57.2	(54.5-60)	Ipratropium	45.1	(41.1-49.1)	Aspirin	55.3	(51.9-58.6)
8	Heparin	46.1	(43.8-48.5)	Atorvastatin	50.5	(47.8-53.2)	Polyethylene glycol 3350	55.2	(52.5-58)	Lidocaine	45.1	(41.1-49.1)	Enoxaparin	53.3	(49.9-56.7)
9	Dexamethasone	43.5	(41.1-45.8)	Heparin	48.6	(45.9-51.3)	Insulin aspart, human	50.6	(47.9-53.4)	Dexamethasone	43.6	(39.6-47.5)	Insulin lispro	52.2	(48.9-55.6)
10	Lidocaine	43.5	(41.1-45.8)	Dexamethasone	44.8	(42.1-47.5)	Heparin	49.8	(47-52.5)	Insulin lispro	42.7	(38.7-46.7)	Atorvastatin	49.2	(45.8-52.5)

Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygen.

%	95% CI	Cancer (n = 1394)		Receives dialysis (n = 190)		BMI 30 or more (n = 6201)		Mechanical ventilation (n = 661)		ECMO (n = 54)		%	95% CI
		%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI		
61.5 (58.8-64.1)		Acetaminophen	39.6 (37-42.2)	Acetaminophen	75.3 (69.1-81.4)	Acetaminophen	29.4 (28.2-30.6)	Acetaminophen	90.6 (88.4-92.8)	Fentanyl	96.3 (91.1-101.4)		
42.9 (40.2-45.6)		Ondansetron	31.1 (28.7-33.6)	Heparin	73.2 (66.8-79.5)	Albuterol	21.9 (20.9-22.9)	Fentanyl	79.6 (76.5-82.7)	Heparin	96.3 (91.1-101.4)		
41.4 (38.7-44.1)		Albuterol	27.4 (25.1-29.7)	Insulin lispro	52.1 (45-59.3)	Ondansetron	18.7 (17.7-19.7)	Sennosides, USP	77.5 (74.3-80.6)	Furosemide	94.4 (88.2-100.7)		
38.4 (35.8-41)		Dexamethasone	22.5 (20.3-24.6)	Ondansetron	49.5 (42.3-56.6)	Enoxaparin	15.5 (14.5-16.5)	Polyethylene glycol 3350	75.8 (72.5-79.1)	Sennosides, USP	92.6 (85.4-99.7)		
36.7 (34.1-39.2)		Lidocaine	22.2 (20.1-24.4)	Lidocaine	48.9 (41.8-56.1)	Sennosides, USP	12.5 (11.7-13.3)	Furosemide	75.0 (71.7-78.3)	Albumin human, USP	90.7 (82.8-98.6)		
35.7 (33.2-38.3)		Heparin	21.6 (19.4-23.8)	Sennosides, USP	48.9 (41.8-56.1)	Polyethylene glycol 3350	11.5 (10.7-12.3)	Propofol	73.2 (69.8-76.6)	Vancomycin	90.7 (82.8-98.6)		
33.0 (30.5-35.6)		Enoxaparin	21.0 (18.9-23.2)	Albuterol	48.4 (41.3-55.6)	Dexamethasone	11.4 (10.6-12.2)	Heparin	69.9 (66.4-73.4)	Dexmedetomidine	88.9 (80.3-97.5)		
32.6 (30.1-35.1)		Sennosides, USP	19.7 (17.6-21.8)	Pantoprazole	45.8 (38.7-52.9)	Lidocaine	11.3 (10.5-12.1)	Vancomycin	69.1 (65.6-72.7)	Polyethylene glycol 3350	88.9 (80.3-97.5)		
31.5 (29-34)		Polyethylene glycol 3350	19.4 (17.3-21.4)	Vancomycin	45.3 (38.1-52.4)	Insulin lispro	10.6 (9.8-11.4)	Lidocaine	69.0 (65.5-72.5)	Propofol	88.9 (80.3-97.5)		
29.2 (26.7-31.6)		Pantoprazole	15.6 (13.7-17.5)	Polyethylene glycol 3350	42.6 (35.6-49.7)	Benzonatate	10.5 (9.7-11.3)	Albuterol	67.5 (63.9-71.1)	Midazolam	85.2 (75.5-94.9)		

Chronic kidney disease (n = 778)	%	95% CI	Cancer (n = 473)		Receives dialysis (n = 144)		BMI 30 or more (n = 1364)		Mechanical ventilation (n = 661)		ECMO (n = 54)		%	95% CI
			%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI		
Acetaminophen	90.5 (88.4-92.6)	Acetaminophen	85.6 (82.5-88.8)	Heparin	88.2 (82.9-93.5)	Acetaminophen	89.0 (87.43-90.6)	Acetaminophen	90.6 (88.4-92.8)	Fentanyl	96.3 (91.1-101.4)			
Heparin	68.1 (64.8-71.4)	Ondansetron	63.8 (59.5-68.2)	Acetaminophen	87.5 (82.1-92.9)	Enoxaparin	63.6 (61.05-66.2)	Fentanyl	79.6 (76.5-82.7)	Heparin	96.3 (91.1-101.4)			
Ondansetron	59.8 (56.3-63.2)	Enoxaparin	55.2 (50.7-59.7)	Insulin lispro	62.5 (54.5-70.5)	Ondansetron	58.4 (55.85-61)	Sennosides, USP	77.5 (74.3-80.6)	Furosemide	94.4 (88.2-100.7)			
Sennosides, USP	58.4 (54.9-61.8)	Albuterol	52.4 (47.9-56.9)	Lidocaine	59.7 (51.6-67.8)	Albuterol	56.5 (53.95-59.1)	Polyethylene glycol 3350	75.8 (72.5-79.1)	Sennosides, USP	92.6 (85.4-99.7)			
Insulin lispro	56.3 (52.8-59.8)	Polyethylene glycol 3350	52.2 (47.7-56.7)	Sennosides, USP	59.7 (51.6-67.8)	Sennosides, USP	52.0 (49.25-54.7)	Furosemide	75.0 (71.7-78.3)	Albumin human, USP	90.7 (82.8-98.6)			
Albuterol	55.5 (52-59)	Sennosides, USP	51.0 (46.4-55.5)	Vancomycin	59.0 (50.9-67.1)	Polyethylene glycol 3350	48.6 (45.85-51.3)	Propofol	73.2 (69.8-76.6)	Vancomycin	90.7 (82.8-98.6)			
Polyethylene glycol 3350	52.8 (49.3-56.3)	Dexamethasone	49.5 (45-54)	Ondansetron	57.6 (49.5-65.8)	Insulin lispro	43.2 (40.65-45.8)	Heparin	69.9 (66.4-73.4)	Dexmedetomidine	88.9 (80.3-97.5)			
Pantoprazole	50.3 (46.7-53.8)	Heparin	49.0 (44.5-53.6)	Albuterol	56.9 (48.8-65.1)	Lidocaine	41.3 (38.75-43.9)	Vancomycin	69.1 (65.6-72.7)	Polyethylene glycol 3350	88.9 (80.3-97.5)			
Lidocaine	48.8 (45.3-52.4)	Lidocaine	47.6 (43.1-52.1)	Pantoprazole	54.2 (46-62.4)	Dexamethasone	41.0 (38.45-43.6)	Lidocaine	69.0 (65.5-72.5)	Propofol	88.9 (80.3-97.5)			
Ceftriaxone	44.2 (40.7-47.7)	Pantoprazole	38.3 (33.9-42.7)	Polyethylene glycol 3350	52.1 (43.9-60.3)	Heparin	36.0 (33.45-38.6)	Albuterol	67.5 (63.9-71.1)	Midazolam	85.2 (75.5-94.9)			

Table 5. Medication Utilization by Baseline Comorbidity (Nonhospitalized COVID-19 Patients).

Nonhospitalized patients															
Rank	Hypertension (n = 2502)			Hyperlipidemia (n = 2410)			Type 2 diabetes (n = 1427)			COPD/asthma (n = 1197)			Heart disease (n = 670)		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI
1	ACEIs/ARBs	19.1	(17.6-20.6)	ACEIs/ARBs	13.3	(11.9-14.6)	Metformin	21.2	(19.1-23.4)	Albuterol	23.8	(21.4-26.2)	Acetaminophen	19.1	(16.1-22.1)
2	Acetaminophen	16.8	(15.3-18.3)	Albuterol	13.3	(11.9-14.6)	ACEIs/ARBs	18.3	(16.3-20.3)	Acetaminophen	14.4	(12.4-16.4)	ACEIs/ARBs	16.4	(13.6-19.2)
3	Albuterol	13.9	(12.5-15.2)	Acetaminophen	12.6	(11.2-13.9)	Acetaminophen	17.7	(15.7-19.6)	Fluticasone	11.9	(10-13.7)	Atorvastatin	15.4	(12.6-18.1)
4	Ondansetron	11.5	(10.3-12.8)	Atorvastatin	11.4	(10.1-12.6)	Albuterol	13.2	(11.5-15)	Ondansetron	7.9	(6.4-9.5)	Albuterol	14.0	(11.4-16.7)
5	Atorvastatin	9.8	(8.6-11)	Ondansetron	9.4	(8.2-10.5)	Atorvastatin	12.9	(11.2-14.6)	Prednisone	7.7	(6.2-9.2)	Ondansetron	11.5	(9.1-13.9)
6	Amlodipine	9.4	(8.3-10.6)	Metformin	7.7	(6.7-8.8)	Ondansetron	11.9	(10.2-13.6)	ACEIs/ARBs	7.5	(6-9)	Metoprolol	10.4	(8.1-12.8)
7	Metformin	8.2	(7.1-9.3)	Azithromycin	7.6	(6.5-8.6)	Insulin glargine	7.7	(6.3-9.1)	Azithromycin	6.4	(5-7.8)	Aspirin	9.1	(6.9-11.3)
8	Azithromycin	6.9	(5.9-7.9)	Benzonatate	7.1	(6.1-8.2)	Insulin lispro	7.4	(6.1-8.8)	Montelukast	4.8	(3.6-6.1)	Metformin	8.1	(6-10.1)
9	Benzonatate	6.8	(5.8-7.7)	Amlodipine	6.1	(5.1-7)	Benzonatate	7.3	(5.9-8.6)	Dexamethasone	4.8	(3.6-6)	Amlodipine	7.0	(5.1-9)
10	Metoprolol	6.0	(5-6.9)	Fluticasone	5.5	(4.6-6.4)	Azithromycin	7.2	(5.9-8.6)	Salmeterol	4.8	(3.6-6)	Azithromycin	7.0	(5.1-9)

Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygen.

was not in the 10 most common medications for the duration of the study. Early in the pandemic, ceftriaxone was frequently used (48.7 and 45.9% of patients in March and April, respectively). After April, however, ceftriaxone was no longer found among the 10 most frequently used medications. Heparin was not among the top 10 medications after September. Dexamethasone was used in 43.3% of patients in July with usage exceeding 50% in November and December. Remdesivir, approved under FDA emergency use authorization in May 2020, was among the top 10 medications in October at 39.9% and increased to 52.7% in December (Table 6).

Nonhospitalized patients with COVID-19. In March, the top medications were albuterol (11.9%), azithromycin (7.3%), acetaminophen (6.1%), ACEIs/ARBs (4.8%), ondansetron (4%), codeine (4%), benzonatate (3.8%), guaifenesin (3.1%), fluticasone (2.9%), atorvastatin (2.9%). While azithromycin use decreased after March, it remained among the top 10 in all months except August and September. Albuterol and acetaminophen were among the top 3 medications throughout. Fluticasone was among the top 10 medications in all months besides October and December. Dexamethasone was among the top 10 medications from August through December (Table 6).

Cumulative Use Count in Hospitalized Patients Since March 2020 of Potential Treatment Option Medications in Hospitalized Patients

Throughout the period of March to December 2020, enoxaparin was used in the most patients to that point at any instance. By mid-December, more than 2000 in the analysis cohort of hospitalized patients had received enoxaparin.

Prior to May, dexamethasone was rarely used, with well under 50 COVID-19 patients who had been hospitalized to that point receiving the medication. By mid-August, more than 500 patients to that point had received dexamethasone. By mid-December, dexamethasone use increased to the extent that more than 1000 patients to that point had received it. Hydroxychloroquine use effectively halted in COVID-19 hospitalized patients after May. Azithromycin prescribing slowed from initial heavy use. Among the PTOs studied, it was the third most frequently used in patients as of August 1, but by close of 2020 had fallen to the sixth most commonly used. Increase in counts of heparin, ACEIs/ARBs, and hydrocortisone use was fairly stable over time. Total dexamethasone users exceeded azithromycin users by end of August. Roughly 1000 patients had received remdesivir by close of December (Figure 1).

Discussion

This study is the first comprehensive analysis of medication utilization for COVID-19 patients in a large, diverse, statewide health system overall and by comorbidity, age group, baseline dialysis use, and by month for both the hospitalized and nonhospitalized. Numbers of patients who used medications considered PTOs during the pandemic were also tracked over time.

Initially, in the pandemic, our data show attempts were made to use antimicrobials to manage COVID-19. Azithromycin, ceftriaxone, and hydroxychloroquine were each used in more than 40% of hospitalized patients in March. This quickly abated. By May, none of the 3 were among the top 10 medications for hospitalized patients. Supportive care medications for symptom relief of fever, nausea, pain, cough, constipation, and shortness of breath were heavily used

Chronic kidney disease (n = 548)			Cancer (n = 921)			Receives dialysis (n = 46)			BMI 30 or more (n = 4837)			Mechanical ventilation (n = 0)			ECMO (n = 0)		
	%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI
Acetaminophen	20.3	(16.9-23.6)	Acetaminophen	16.0	(13.6-18.3)	Acetaminophen	37.0	(22.6-51.3)	Acetaminophen	12.6	(11.6-13.6)	None	NA	NA	None	NA	NA
ACEIs/ARBs	16.4	(13.3-19.5)	Albuterol	14.5	(12.3-16.8)	Heparin	26.1	(13.1-39.1)	Albuterol	12.1	(11.1-13.1)	None	NA	NA	None	NA	NA
Ondansetron	15.3	(12.3-18.4)	Ondansetron	14.3	(12.1-16.6)	Atorvastatin	23.9	(11.3-36.6)	Ondansetron	7.6	(6.8-8.4)	None	NA	NA	None	NA	NA
Albuterol	14.1	(11.1-17)	Lidocaine	9.2	(7.4-11.1)	Ondansetron	23.9	(11.3-36.6)	ACEIs/ARBs	6.4	(5.6-7.2)	None	NA	NA	None	NA	NA
Prednisone	14.1	(11.1-17)	Dexamethasone	8.6	(6.8-10.4)	Albuterol	21.7	(9.5-34)	Benzonate	5.0	(4.4-5.6)	None	NA	NA	None	NA	NA
Amlodipine	12.6	(9.8-15.4)	ACEIs/ARBs	8.3	(6.5-10)	Carvedilol	21.7	(9.5-34)	Azithromycin	4.7	(4.1-5.3)	None	NA	NA	None	NA	NA
Atorvastatin	12.2	(9.5-15)	Diphenhydramine	8.1	(6.4-9.9)	Sevelamer	21.7	(9.5-34)	Fluticasone	4.2	(3.6-4.8)	None	NA	NA	None	NA	NA
Tacrolimus	11.9	(9.1-14.6)	Beparin	7.5	(5.8-9.2)	Insulin lispro	19.6	(7.8-31.3)	Ibuprofen	4.0	(3.4-4.6)	None	NA	NA	None	NA	NA
Metoprolol	9.7	(7.2-12.2)	Atorvastatin	6.8	(5.2-8.5)	Pantoprazole	19.6	(7.8-31.3)	Metformin	3.7	(3.1-4.3)	None	NA	NA	None	NA	NA
Pantoprazole	8.6	(6.2-10.9)	Epinephrine	6.8	(5.2-8.5)	Albumin human, USP	17.4	(6.1-28.6)	Atorvastatin	3.5	(2.9-4.1)	None	NA	NA	None	NA	NA

throughout with acetaminophen being used in the largest percentage of all COVID-19 patients followed by albuterol, ondansetron, enoxaparin, and sennosides. Enoxaparin had over 50% use throughout 2020 as enoxaparin serves both as supportive care for deep vein thrombosis prophylaxis and for treatment, given the thrombophilia caused by COVID-19.¹⁸ Examining other PTO over time, dexamethasone and remdesivir use increased substantially. Use of remdesivir likely corresponded with availability, as early in the pandemic, it was only available through trials. On the contrary, hydroxychloroquine use dropped from over 40% in late March and was not observed in top 10 medications beyond that month. Early studies of limited sampled size favored use of these agents,^{19,20} but later larger, controlled studies did not demonstrate clinical benefit in patients.^{7,21}

Treatment for COVID-19 patients has progressed from the initial stages, where treatment decisions were educated based on case series and in vitro data. With little guidance, the early approaches applied by clinicians were best guesses. Remarkably, practice patterns appeared to change in near real-time as quality data became available through landmark trials. The trajectories of medication usage generally corresponded to publication of rigorous studies. The acceleration in use of dexamethasone is reasonably correlated to the publication of findings from the RECOVERY trial.³ The wide accessibility of data, effectively at the moment of publication, to clinicians over the course of the pandemic is unparalleled compared with past public health crises. This was demonstrated by the PTO curves where usage was generally concordant with the emerging evidence over time. A prior study examined outpatient prescriptions for hydroxychloroquine noted a decline after May 2020. However, this analysis was not focused on patients confirmed for COVID-19.²² An analysis over a 2-month period

that examined medication use patterns in COVID-19 hospitalized patients also showed reductions in azithromycin and hydroxychloroquine over time.²³ Differentiating strengths of our study compared with these prior studies was a longer duration (March to December 2020) to observe oscillations in use of these agents. Beyond a small selection of medications, we captured use patterns of the most common medications prescribed by age, high-risk condition, and month.

Overall, this analysis also demonstrated that most of the medications used to treat COVID-19 patients have been generally inexpensive, generic medications. While this is comforting, more expensive proprietary medications have now been released under emergency use authorization (eg, monoclonal antibodies). Furthermore, generic medications have been increasingly subject to shortages. This compilation of medication use from the COVID-19 experience can serve as a guide for medication needs during future pandemics from respiratory viruses.

The population of COVID-19 patients in the CORDS features a demographic breakdown consistent overall with the State of California. Hispanics were 37% of the study population which is similar to 39% of the state. Non-Hispanic Whites were 28% of COVID-19 positive patients in this study population compared with 37% in the state. Percentages of those in the sample that reported to be black, and Native Hawaiian/Pacific Islander/American Indian/Alaska Native were similar to the demographic breakdown of California (7% and 1%, respectively).¹²

Limitations

Outpatient medications for patients in CORDS may require at least a month for complete capture. Use rates are conservative estimates for the nonhospitalized patients as

Table 6. Medication Utilization by Month.

All positive COVID-19 patients														
Rank	March (n = 591)	%	95% CI	April (n = 921)	%	95% CI	May (n = 709)	%	95% CI	June (n = 1915)	%	95% CI	July (n = 3789)	%
1	Acetaminophen	21.3	(18.0-24.6)	Acetaminophen	29.2	(26.3-32.1)	Acetaminophen	39.1	(35.5-42.7)	Acetaminophen	27.9	(25.9-29.9)	Acetaminophen	22.2
2	Albuterol	20.5	(7.2-23.8)	Albuterol	21.1	(18.5-23.7)	Ondansetron	23.6	(20.5-26.7)	Ondansetron	17.7	(16.0-19.4)	Albuterol	14.5
3	Azithromycin	16.2	(3.2-19.2)	Ondansetron	18.7	(16.2-21.2)	Enoxaparin	22.8	(19.7-25.9)	Albuterol	17.2	(15.5-18.9)	Ondansetron	13.9
4	Ondansetron	12.5	(9.8-15.2)	Enoxaparin	16.4	(14.0-18.8)	Albuterol	22.3	(19.2-25.4)	Enoxaparin	14.4	(12.8-16.0)	Enoxaparin	11.2
5	Guaifenesin	11.7	(9.1-14.3)	Sennosides, USP	14.8	(12.5-17.1)	Sennosides, USP	22.1	(19.0-25.2)	Sennosides, USP	11.2	(9.8-12.6)	Lidocaine	9.1
6	Enoxaparin	11.2	(8.7-13.7)	Azithromycin	13.8	(11.6-16.0)	Lidocaine	17.6	(14.8-20.4)	Lidocaine	11.1	(9.7-12.5)	Sennosides, USP	8.8
7	Polyethylene glycol 3350	10.5	(8.0-13.0)	Polyethylene glycol 3350	13.6	(11.4-15.8)	Polyethylene glycol 3350	16.1	(13.4-18.8)	Polyethylene glycol 3350	9.7	(8.4-11.0)	Dexamethasone	8.3
8	Hydroxychloroquine	10.2	(7.8-12.6)	Heparin	11.8	(9.7-13.9)	Heparin	15.5	(12.8-18.2)	Insulin lispro	9.2	(7.9-10.5)	Polyethylene glycol 3350	8.0
9	Sennosides, USP	9.6	(7.2-12.0)	Ceftriaxone	11.6	(9.5-13.7)	Fentanyl	14.7	(12.1-17.3)	Ipratropium	8.7	(7.4-10.0)	Insulin lispro	8.0
10	Ceftriaxone	9.6	(7.2-12.0)	Furosemide	11.0	(9.0-13.0)	Ascorbic acid	13.4	(10.9-15.9)	Heparin	8.6	(7.3-9.9)	ACEIs/ARBs	7.5
Hospitalized patients														
Rank	March (n = 113)	%	95% CI	April (n = 222)	%	95% CI	May (n = 242)	%	95% CI	June (n = 373)	%	95% CI	July (n = 587)	%
1	Acetaminophen	85.8	(79.3-92.3)	Acetaminophen	90.5	(86.6-94.4)	Acetaminophen	86.0	(81.6-90.4)	Acetaminophen	89.0	(85.8-92.2)	Acetaminophen	90.3
2	Enoxaparin	56.6	(47.4-65.8)	Enoxaparin	64.0	(57.7-70.3)	Enoxaparin	63.2	(57.1-69.3)	Enoxaparin	70.0	(65.3-74.7)	Enoxaparin	66.4
3	Albuterol	56.6	(47.4-65.8)	Ondansetron	62.2	(55.8-68.6)	Sennosides, USP	60.3	(54.1-66.5)	Ondansetron	62.5	(57.6-67.4)	Ondansetron	60.8
4	Azithromycin	54.0	(44.7-63.3)	Albuterol	62.2	(55.8-68.6)	Albuterol	51.7	(45.4-58.0)	Albuterol	57.6	(52.6-62.6)	Albuterol	54.5
5	Polyethylene glycol 3350	51.3	(42.0-60.6)	Sennosides, USP	59.0	(52.5-65.5)	Ondansetron	50.0	(43.7-56.3)	Sennosides, USP	53.1	(48.0-58.2)	Sennosides, USP	52.6
6	Ondansetron	48.7	(39.4-58.0)	Polyethylene glycol 3350	52.7	(46.1-59.3)	Polyethylene glycol 3350	44.6	(38.3-50.9)	Lidocaine	46.4	(41.3-51.5)	Polyethylene glycol 3350	46.7
7	Ceftriaxone	48.7	(39.4-58.0)	Heparin	47.7	(41.1-54.3)	Heparin	43.4	(37.1-49.7)	Polyethylene glycol 3350	45.6	(40.5-50.7)	Insulin lispro	46.3
8	Guaifenesin	47.8	(38.5-57.1)	Ceftriaxone	45.9	(39.3-52.5)	Lidocaine	40.5	(34.3-46.7)	Insulin lispro	44.0	(38.9-49.1)	Lidocaine	44.1
9	Sennosides, USP	45.1	(35.8-54.4)	Furosemide	43.2	(36.6-49.8)	Vancomycin	38.4	(32.2-44.6)	Ipratropium	41.0	(36.0-46.0)	Dexamethasone	43.3
10	Hydroxychloroquine	43.4	(34.2-52.6)	Azithromycin	40.5	(34.0-47.0)	Fentanyl	38.0	(31.9-44.1)	Heparin	40.5	(35.5-45.5)	Ceftriaxone	38.2
Nonhospitalized patients														
Rank	March (n = 478)	%	95% CI	April (n = 699)	%	95% CI	May (n = 467)	%	95% CI	June (n = 1542)	%	95% CI	July (n = 3202)	%
1	Albuterol	11.9	(9.0-14.8)	Acetaminophen	9.7	(7.5-11.9)	Acetaminophen	14.8	(11.6-18.0)	Acetaminophen	13.2	(11.5-14.9)	Acetaminophen	9.7
2	Azithromycin	7.3	(5.0-9.6)	Albuterol	8.0	(6.0-10.0)	Ondansetron	9.9	(7.2-12.6)	Albuterol	7.5	(6.2-8.8)	Albuterol	7.1
3	Acetaminophen	6.1	(3.9-8.3)	ACEIs/ARBs	5.6	(3.9-7.3)	Albuterol	7.1	(4.8-9.4)	Ondansetron	6.9	(5.6-8.2)	Ondansetron	5.2
4	ACEIs/ARBs	4.8	(2.9-6.7)	Azithromycin	5.3	(3.6-7.0)	Lidocaine	5.8	(3.7-7.9)	ACEIs/ARBs	4.2	(3.2-5.2)	ACEIs/ARBs	4.2
5	ondansetron	4.0	(2.2-5.8)	Ondansetron	4.9	(3.3-6.5)	ACEIs/ARBs	5.6	(3.5-7.7)	Ibuprofen	3.9	(2.9-4.9)	Azithromycin	3.8
6	Codeine	4.0	(2.2-5.8)	Atorvastatin	4.4	(2.9-5.9)	Azithromycin	4.5	(2.6-6.4)	Metformin	3.5	(2.6-4.4)	Ibuprofen	3.0
7	Benzonatate	3.8	(2.1-5.5)	Fluticasone	3.4	(2.1-4.7)	Ibuprofen	3.9	(2.1-5.7)	Azithromycin	3.4	(2.5-4.3)	Fluticasone	2.8
8	Guaifenesin	3.1	(1.5-4.7)	Levothyroxine	3.4	(2.1-4.7)	Atorvastatin	3.6	(1.9-5.3)	Benzonatate	2.7	(1.9-3.5)	Lidocaine	2.7
9	Fluticasone	2.9	(1.4-4.4)	Benzonatate	3.3	(2.0-4.6)	Metformin	3.4	(1.8-5.0)	Fluticasone	2.7	(1.9-3.5)	Benzonatate	2.3
10	Atorvastatin	2.9	(1.4-4.4)	Guaifenesin	3.1	(1.8-4.4)	Fluticasone	3.2	(1.6-4.8)	Lidocaine	2.6	(1.8-3.4)	Atorvastatin	2.3

Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval.

	August (n = 2027)			September (n = 1108)			October (n = 1083)			November (n = 3200)			December (n = 7553)		
	95% CI	%	95% CI	%	95% CI	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	
(20.9-23.5)	Acetaminophen	27.1	(25.2-29.0)	Acetaminophen	28.6	(25.9-31.3)	Acetaminophen	23.6	(21.1-26.1)	Acetaminophen	15.9	(14.6-17.2)	Acetaminophen	15.5	(14.7-16.3)
(13.4-15.6)	Ondansetron	18.5	(16.8-20.2)	Ondansetron	18.4	(16.1-20.7)	Albuterol	17.1	(14.9-19.3)	Albuterol	12.1	(11.0-13.2)	Albuterol	12.8	(12.0-13.6)
(12.8-15.0)	Albuterol	15.9	(14.3-17.5)	Albuterol	17.6	(15.4-19.8)	Ondansetron	16.2	(14.0-18.4)	Ondansetron	10.9	(9.8-12.0)	Ondansetron	10.7	(10.0-11.4)
(10.2-12.2)	Enoxaparin	14.2	(12.7-15.7)	Lidocaine	15.3	(13.2-17.4)	Enoxaparin	11.0	(9.1-12.9)	Dexamethasone	7.6	(6.7-8.5)	Dexamethasone	8.8	(8.2-9.4)
(8.2-10.0)	Sennosides, USP	12.7	(11.2-14.2)	Enoxaparin	13.4	(11.4-15.4)	Polyethylene glycol 3350	10.8	(8.9-12.7)	Enoxaparin	7.2	(6.3-8.1)	Enoxaparin	8.0	(7.4-8.6)
(7.9-9.7)	Polyethylene glycol 3350	11.9	(10.5-13.3)	Sennosides, USP	13.0	(11.0-15.0)	Dexamethasone	10.7	(8.9-12.5)	Azithromycin	6.5	(5.6-7.4)	Sennosides, USP	7.1	(6.5-7.7)
(7.4-9.2)	Lidocaine	11.8	(10.4-13.2)	Polyethylene glycol 3350	12.2	(10.3-14.1)	Sennosides, USP	10.2	(8.4-12.0)	Benzonate	6.4	(5.6-7.2)	Remdesivir	6.4	(5.8-7.0)
(7.1-8.9)	Dexamethasone	11.1	(9.7-12.5)	Dexamethasone	12.0	(10.1-13.9)	Lidocaine	10.2	(8.4-12.0)	Lidocaine	6.2	(5.4-7.0)	Polyethylene glycol 3350	6.1	(5.6-6.6)
(7.1-8.9)	Heparin	9.0	(7.8-10.2)	Docusate	9.7	(8.0-11.4)	Insulin lispro	8.1	(6.5-9.7)	Sennosides, USP	6.1	(5.3-6.9)	Benzonate	6.0	(5.5-6.5)
(6.7-8.3)	Insulin lispro	8.7	(7.5-9.9)	Heparin	9.6	(7.9-11.3)	Melatonin	7.9	(6.3-9.5)	Polyethylene glycol 3350	5.9	(5.1-6.7)	Pantoprazole	5.7	(5.2-6.2)

	August (n = 410)			September (n = 245)			October (n = 203)			November (n = 328)			December (n = 823)		
	95% CI	%	95% CI	%	95% CI	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	
(87.9-92.7)	Acetaminophen	89.3	(86.3-92.3)	Acetaminophen	91.8	(88.3-95.3)	Acetaminophen	86.7	(82.0-91.4)	Acetaminophen	86.6	(82.9-90.3)	Acetaminophen	87.7	(85.5-89.9)
(62.6-70.2)	Enoxaparin	63.4	(58.7-68.1)	Ondansetron	61.2	(55.1-67.3)	Ondansetron	58.6	(51.8-65.4)	Ondansetron	59.8	(54.5-65.1)	Enoxaparin	60.6	(57.3-63.9)
(56.8-64.8)	Ondansetron	62.2	(57.5-66.9)	Enoxaparin	54.7	(48.4-61.0)	Enoxaparin	53.2	(46.3-60.1)	Enoxaparin	58.5	(53.1-63.9)	Dexamethasone	59.9	(56.5-63.3)
(50.5-58.5)	Sennosides, USP	55.1	(50.3-59.9)	Lidocaine	53.9	(47.6-60.2)	Polyethylene glycol 3350	51.7	(44.8-58.6)	Dexamethasone	51.8	(46.4-57.2)	Sennosides, USP	56.9	(53.5-60.3)
(48.6-56.6)	Polyethylene glycol 3350	52.7	(47.9-57.5)	Sennosides, USP	51.4	(45.1-57.7)	Sennosides, USP	50.7	(43.8-57.6)	Polyethylene glycol 3350	49.7	(44.3-55.1)	Ondansetron	56.7	(53.3-60.1)
(42.7-50.7)	Albuterol	47.8	(43.0-52.6)	Polyethylene glycol 3350	48.6	(42.3-54.9)	Albuterol	50.2	(43.3-57.1)	Sennosides, USP	48.5	(43.1-53.9)	Albuterol	56.6	(53.2-60.0)
(42.3-50.3)	Lidocaine	46.6	(41.8-51.4)	Albuterol	46.5	(40.2-52.8)	Dexamethasone	43.8	(36.9-50.7)	Remdesivir	48.2	(42.8-53.6)	Remdesivir	52.7	(49.3-56.1)
(40.1-48.1)	Dexamethasone	44.6	(39.8-49.4)	Dexamethasone	42.9	(36.7-49.1)	Lidocaine	43.3	(36.4-50.2)	Albuterol	45.7	(40.3-51.1)	Polyethylene glycol 3350	50.3	(46.9-53.7)
(39.3-47.3)	Heparin	39.8	(35.0-44.6)	Heparin	38.4	(32.3-44.5)	Remdesivir	39.9	(33.1-46.7)	Lidocaine	42.7	(37.3-48.1)	Insulin aspart, human	42.3	(38.9-45.7)
(34.3-42.1)	Insulin lispro	38.8	(34.1-43.5)	Docusate	37.1	(31.0-43.2)	Melatonin	38.9	(32.2-45.6)	Insulin lispro	42.1	(36.7-47.5)	Bisacodyl	40.8	(37.4-44.2)

	August (n = 1617)			September (n = 863)			October (n = 880)			November (n = 2872)			December (n = 6730)		
	95% CI	%	95% CI	%	95% CI	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	
(8.7-10.7)	Acetaminophen	11.4	(9.8-13.0)	Acetaminophen	10.7	(8.6-12.8)	Albuterol	9.4	(7.5-11.3)	Albuterol	8.2	(7.2-9.2)	Albuterol	7.4	(6.8-8.0)
(6.2-8.0)	Albuterol	7.8	(6.5-9.1)	Albuterol	9.4	(7.5-11.3)	Acetaminophen	9.1	(7.2-11.0)	Acetaminophen	7.8	(6.8-8.8)	Acetaminophen	6.6	(6.0-7.2)
(4.4-6.0)	Ondansetron	7.4	(6.1-8.7)	Ondansetron	6.3	(4.7-7.9)	Ondansetron	6.4	(4.8-8.0)	Ondansetron	5.3	(4.5-6.1)	Ondansetron	5.1	(4.6-5.6)
(3.5-4.9)	ACEIs/ARBs	4.0	(3.0-5.0)	Fluticasone	4.5	(3.1-5.9)	Azithromycin	4.5	(3.1-5.9)	Azithromycin	4.4	(3.6-5.2)	Azithromycin	3.3	(2.9-3.7)
(3.1-4.5)	Ibuprofen	4.0	(3.0-5.0)	Lidocaine	4.4	(3.0-5.8)	Benzonate	3.8	(2.5-5.1)	Benzonate	3.9	(3.2-4.6)	Benzonate	3.2	(2.8-3.6)
(2.4-3.6)	Atorvastatin	3.2	(2.3-4.1)	Atorvastatin	4.3	(2.9-5.7)	Atorvastatin	3.8	(2.5-5.1)	ACEIs/ARBs	3.8	(3.1-4.5)	ACEIs/ARBs	2.6	(2.2-3.0)
(2.2-3.4)	Fluticasone	3.0	(2.2-3.8)	Ibuprofen	3.7	(2.4-5.0)	Dexamethasone	3.1	(2.0-4.2)	Fluticasone	3.1	(2.5-3.7)	Dexamethasone	2.5	(2.1-2.9)
(2.1-3.3)	Lidocaine	3.0	(2.2-3.8)	ACEIs/ARBs	3.6	(2.4-4.8)	ACEIs/ARBs	3.0	(1.9-4.1)	Ibuprofen	2.8	(2.2-3.4)	Guaifenesin	2.3	(1.9-2.7)
(1.8-2.8)	Benzonate	2.9	(2.1-3.7)	Benzonate	3.6	(2.4-4.8)	Ibuprofen	3.0	(1.9-4.1)	Dexamethasone	2.5	(1.9-3.1)	Ibuprofen	2.1	(1.8-2.4)
(1.8-2.8)	Dexamethasone	2.6	(1.8-3.4)	Dexamethasone	3.2	(2.0-4.4)	Levothyroxine	3.0	(1.9-4.1)	Codeine	2.4	(1.8-3.0)	Codeine	2.1	(1.8-2.4)

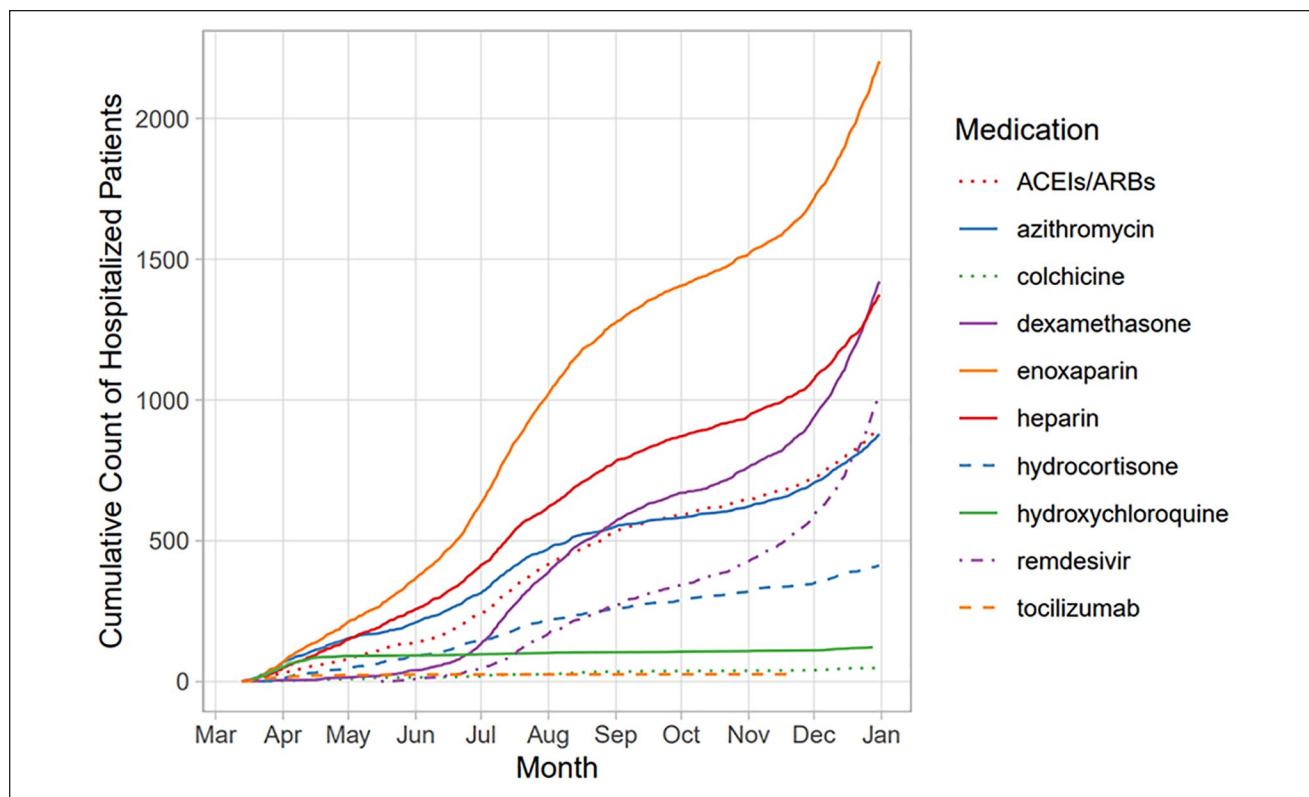


Figure 1. Cumulative count of hospitalized patients using potential therapeutic option over time. Abbreviations: ACEI, angiotensin-2 converting enzyme inhibitor; ARB, angiotensin receptor blocker.

medications for COVID-19 positive patients prescribed medications outside of UC Health are not present in CORDS. While the study demographics were consistent with California overall, given that this state has a large minority population, this may influence generalizability to the United States. Consequently, the percentage of COVID-19 positive cases that were non-Hispanic White in CORDS (28%) was lower than that observed in US national estimates (56%). Hispanics were 37% of the positive cases in our dataset and 21% in the United States. A smaller percentage of COVID-19 positive patients were black (6%) than observed in national estimates (12.2%). Asians were 7% of the COVID-19 positive patients in CORDS compared with 4% in US estimates.²⁴ It is possible that the ICD-10 diagnosis may remain on the EHR of a patient after successful remediation of a chronic condition. Hence, there is a possibility of exaggerated counts of patients by high-risk condition. However, this would not be expected to produce systematic differences in percentages of medications used.

Conclusions

In this retrospective cohort study, across age and comorbidity groups, predominant utilization was for supportive care therapy. Dexamethasone and remdesivir experienced large increases in utilization over time. Conversely, hydroxychloroquine and

azithromycin use rapidly declined. Anticoagulation was recognized early in the pandemic as an important approach for both prophylaxis and in treatment, and was widely applied throughout. Medication utilization has changed, in near real-time, in the direction of evidence-concordant treatment of patients with COVID-19 as quality data became available. Future projects will include comparisons of medication treatment patterns of COVID-19 patients with non-COVID-19 patients.

Authors' Note

Sanjay R. Mehta is now affiliated to Department of Medicine, San Diego Veterans Affairs Medical Center, San Diego, CA.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Jonathan H. Watanabe  <https://orcid.org/0000-0002-2543-5305>

References

1. Meyerowitz-Katz G, Merone L. A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates. *Int J Infect Dis.* 2020;101:138-148. doi:10.1016/j.ijid.2020.09.1464.
2. COVID-19 Map. Johns Hopkins Coronavirus Resource Center. Accessed November 8, 2020. <https://coronavirus.jhu.edu/map.html>.
3. Group TRC. Dexamethasone in hospitalized patients with covid-19—preliminary report. *N Engl J Med.* 2021;384:693-704. doi:10.1056/NEJMoa2021436
4. Barco S, Bingisser R, Colucci G, et al. Enoxaparin for primary thromboprophylaxis in ambulatory patients with coronavirus disease-2019 (the COVID study): a structured summary of a study protocol for a randomized controlled trial. *Trials.* 2020;21(1):770. doi:10.1186/s13063-020-04678-4.
5. Thachil J. The versatile heparin in COVID-19. *J Thromb Haemost.* 2020;18(5):1020-1022. doi:https://doi.org/10.1111/jth.14821
6. Deftereos SG, Giannopoulos G, Vrachatis DA, et al. Effect of colchicine vs standard care on cardiac and inflammatory biomarkers and clinical outcomes in patients hospitalized with coronavirus disease 2019: the GRECCO-19 randomized clinical trial. *JAMA Netw Open.* 2020;3(6):e2013136. doi:10.1001/jamanetworkopen.2020.13136.
7. Group TRC. Effect of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med.* 2020;383:2030-2040. doi:10.1056/NEJMoa2022926
8. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. *N Engl J Med.* 2020;383(24):2333-2344. doi:10.1056/NEJMoa2028836.
9. Li J, Wang X, Chen J, Zhang H, Deng A. Association of renin-angiotensin system inhibitors with severity or risk of death in patients with hypertension hospitalized for coronavirus disease 2019 (COVID-19) infection in Wuhan, China. *JAMA Cardiol.* 2020;5(7):825-830. doi:10.1001/jamacardio.2020.1624
10. University of California Medical Centers Financial Report 2019/2020. https://finreports.universityofcalifornia.edu/index.php?file=/med_ctr/19-20/medical-center-reports-2020.pdf
11. FastStats. Published June 19, 2019. Accessed July 2, 2019. <https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm>.
12. US Census Bureau QuickFacts: California. Accessed February 24, 2021. <https://www.census.gov/quickfacts/CA>.
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med.* 2007;147(8):573-577. doi:10.7326/0003-4819-147-8-200710160-00010.
14. 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.
15. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet.* 2020;395(10239):1763-1770. doi:10.1016/S0140-6736(20)31189-2.
16. Ng JH, Hirsch JS, Wanchoo R, et al. Outcomes of patients with end-stage kidney disease hospitalized with COVID-19. *Kidney Int.* 2020;98(6):1530-1539. doi:10.1016/j.kint.2020.07.030.
17. RxNorm Technical Documentation. Accessed November 12, 2020. https://www.nlm.nih.gov/research/umls/rxnorm/docs/techdoc.html#s1_0
18. Lillicrap D. Disseminated intravascular coagulation in patients with 2019-nCoV pneumonia. *J Thromb Haemost.* 2020;18(4):786-787. doi:10.1111/jth.14781.
19. Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. medRxiv. doi:10.1101/2020.03.22.20040758.
20. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents.* 2020;56(1):105949. doi:10.1016/j.ijantimicag.2020.105949
21. Self WH, Semler MW, Leither LM, et al. Effect of hydroxychloroquine on clinical status at 14 days in hospitalized patients with COVID-19: a randomized clinical trial. *JAMA.* 2020;324(21):2165-2176. doi:10.1001/jama.2020.22240
22. Bull-Otterson L, Gray EB, Budnitz DS, et al. Hydroxychloroquine and chloroquine prescribing patterns by provider specialty following initial reports of potential benefit for COVID-19 treatment—United States, January-June 2020. *Morb Mortal Wkly Rep.* 2020;69(35):1210-1215. doi:10.15585/mmwr.mm6935a4
23. Lin KJ, Schneeweiss S, Tesfaye H, et al. Pharmacotherapy for hospitalized patients with COVID-19: treatment patterns by disease severity. *Drugs.* 2020;80(18):1961-1972. doi:10.1007/s40265-020-01424-7.
24. Centers for Disease Control and Prevention. COVID Data Tracker. Centers for Disease Control and Prevention. Published March 28, 2020. Accessed February 21, 2021. <https://covid.cdc.gov/covid-data-tracker>.