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# BMJ Open

## Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan

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## Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan

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## ABSTRACT

### OBJECTIVE

To describe patient characteristics, symptoms, patterns of care and outcomes for COVID-19 patients across Michigan.

### DESIGN

Multi-center retrospective cohort study.

### SETTING AND PARTICIPANTS

Patients discharged (March 16 to May 11, 2020) with suspected or confirmed COVID-19 infection from 32 Michigan hospitals were identified. Trained abstractors collected demographic information on all patients, and detailed clinical data on a subset of COVID-19 positive patients.

### MEASUREMENTS

Patient characteristics, treatment, and outcomes including cardiopulmonary resuscitation, mortality, and venous thromboembolism within and across hospitals.

### RESULTS

Among 1,024 cases with detailed data, median age was 63 years, median BMI 30.6, and 51.4% were black. Cough, fever, and shortness of breath were the top symptoms. 37.2% reported a known COVID-19 contact, 7.0% were healthcare workers, and 16.1% presented from congregated living facilities.

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3 During hospitalization, 232 (22.7%) patients were treated in an ICU, 558 (54.9%)  
4 in a “cohorted” unit, 161 (15.7%) received mechanical ventilation, and 90 (8.8%)  
5 received high-flow nasal cannula. ICU patients more often received hydroxychloroquine  
6 (66% vs. 46%), corticosteroids (34% vs 18%), and antibiotic therapy (92% vs 71%) than  
7 general ward patients ( $p < 0.05$  for all). Overall, 219 (21.4%) patients died, with in-  
8 hospital mortality ranging from 7.9% to 45.7% across hospitals. 73% received at least  
9 one COVID-19-specific treatment, ranging from 32% to 96% across sites.  
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## 21 **LIMITATIONS**

22 Rationales for management decisions could not be determined; findings may be  
23 biased by patients who remain hospitalized; implications of variability of clinical care on  
24 outcomes is unknown.  
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## 33 **CONCLUSIONS**

34 During the Michigan outbreak of COVID-19, patient characteristics, treatment,  
35 and outcomes varied widely within and across hospitals.  
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## Article Summary

### Strengths and Limitations of this Study

- Ours is the first multi-hospital study to examine clinical aspects related to COVID-19 in Michigan. Through a rigorous data collection structure including a well-defined sampling strategy and trained data abstractors, we provide novel and detailed insights into clinical care during the pandemic.
- We were able to examine variation across sites finding substantial differences in clinical care and outcomes across hospitals. To our knowledge, this is the first study to examine differences in these important care processes, treatment approaches and outcomes across sites.
- We report a high rate of use of non-evidence-based therapies for treating COVID-19. This finding has significant safety, economic and policy implications for the most critically ill subsets in the hospital.
- Given the observational nature of the study, rationales for treatment or management decisions cannot be determined. Our study depends on available documentation, so symptoms, comorbidities, or treatments not documented in the medical record may be omitted.
- Because our sampling frame included patients that were discharged or deceased, our findings may be biased as patients who remain hospitalized may not be included in our cohort (potentially explaining lower duration of mechanical ventilation and hospital stay). However, COVID-19 hospitalizations in Southeastern Michigan have been declining since mid-April—limiting the degree of bias from exclusion of patients still in the hospital.

## INTRODUCTION

Since detection in Wuhan, China,<sup>1 2</sup> over 4.5 million cases of COVID-19, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been reported.<sup>3</sup> The United States (US) leads the world in the total number of cases, with over 1.5 million cases and 92,000 deaths reported as of May 20, 2020.<sup>4</sup> Within the US, Michigan remains one of the hardest hit states, with over 52,000 cases and 5,000 deaths as of May 20, 2020.<sup>5</sup>

Michigan has a long history of collaborative quality improvement work that spans several disciplines including cardiovascular medicine, emergency medicine and hospital medicine, among others.<sup>6</sup> These consortia collect detailed clinical variables from hospitals to populate a central registry, allowing benchmarking and comparisons of care and outcomes. As the COVID-19 pandemic unfolded in Southeast Michigan, several consortia came together to focus data collection on patients hospitalized with COVID-19. We describe clinical and epidemiologic findings from Michigan hospitals made possible through these efforts.

## METHODS

A retrospective cohort design was used. Data were collected from medical records of patients discharged between March 16, 2020 and May 11, 2020 from one of 32 Michigan hospitals who participate in collaborative quality initiatives sponsored by Blue Cross Blue Shield of Michigan and Blue Care Network. Trained abstractors at each hospital identified adult patients  $\geq 18$  years of age that underwent testing for COVID-19 via reverse-transcriptase polymerase chain reaction, including both positive cases and

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3 persons under investigation (PUI) who eventually had a negative test. Demographic  
4 data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all  
5 confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was  
6 selected for detailed abstraction. Positive cases were sorted by day of admission (e.g.,  
7 Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge)  
8 was used to select patients for detailed abstraction. Patients who were pregnant,  
9 transitioned to hospice within 3 hours of hospital admission, or discharged against  
10 medical advice were excluded. All data were entered into a registry (Mi-COVID19) using  
11 a structured data collection template.  
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24 Patient characteristics including comorbidities, home medications, presenting  
25 symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare  
26 worker) were collected. Clinical data during hospitalization including location of care  
27 (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body  
28 mass index (BMI), laboratory and radiology findings and therapeutics were abstracted.  
29 Organ supports such as mechanical ventilation and other respiratory support,  
30 vasopressor use, renal replacement therapy (continuous renal replacement therapy  
31 [CRRT] and intermittent hemodialysis [iHD]) were also collected.  
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42 The primary outcomes of interest included hospital mortality, receipt of  
43 cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or  
44 pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric  
45 therapy for presumed thrombosis). In addition, we performed pre-specified exploratory  
46 analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine  
47 variation in patient characteristics, management and outcomes. Specifically, we  
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3 assessed variation in use of COVID-19 specific treatments (defined as  
4 hydroxychloroquine, combination hydroxychloroquine plus azithromycin, Vitamin C [oral  
5 or intravenous], IL-6 inhibitors or remdesivir), antibiotic therapy, use of organ support  
6 (e.g., use of vasopressors, mechanical ventilation and CPR), occurrence of venous  
7 thrombosis and in-hospital mortality.  
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12 Descriptive statistics (e.g., mean, median, proportion) with measures of  
13 dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize  
14 data. Data that were not documented in medical records (e.g., values of certain  
15 laboratory tests) were reported as missing. Pairwise comparisons were made using t-  
16 tests for continuous data and chi-square tests for categorical data, respectively.  
17  
18 Differences across hospitals were tested using the Kruskal–Wallis test for continuous  
19 variables and Pearson chi-square test for categorical variables. All statistical tests were  
20 two-sided with  $p < 0.05$  considered statistically significant. The study was reviewed by the  
21 Institutional Review Board and deemed “not regulated”. It was not appropriate or  
22 possible to involve patients or the public in the design, or conduct, or reporting, or  
23 dissemination plans of our research.  
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## 42 **RESULTS**

### 43 **DEMOGRAPHIC DATA**

44  
45 Demographic-only data from 1,593 COVID-19 positive and 1,259 PUI discharges  
46 from 32 Michigan hospitals were collected. PUIs had a median age of 64.4 years,  
47 52.6% were male and 32.0% Black. COVID-19 positive patients had similar age and  
48 gender as PUIs (63.9 years, and 52.1% male, respectively), but were more commonly  
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3 Black (57.1% vs. 32.0%,  $p<0.01$ ). In the demographic-only cohort, 398 (25.0%) COVID-  
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5 19 positive patients died during hospitalization.  
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8 Detailed data were abstracted on 1,024 (64.3%) randomly-selected COVID-19  
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10 positive patients. The most prevalent comorbidities were hypertension (65.4%),  
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12 diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%);  
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14 14.9% of patients had no comorbidities. Though 12.8% of patients had a diagnosis of  
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16 asthma and 11.2% had a diagnosis of chronic obstructive pulmonary disease, pre-  
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18 hospital use of inhaled steroids, long-acting beta-agonists and long-acting  
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20 antimuscarinic agents was low at 4.2%, 2.9%, and 0.5%, respectively. Current smoking  
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22 or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former  
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24 vaping. 115 (11.3%) patients were on immunosuppressive medications prior to  
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26 hospitalization, including 62 (6.1%) who were on oral steroids. Essential workers  
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28 comprised 12.8% of the cohort, including healthcare workers (7.0%) and service  
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30 workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of  
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32 patients resided in congregated living facilities, including nursing homes and homeless  
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34 shelters (Table 1).  
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## 42 **CLINICAL PRESENTATION AND INITIAL EVALUATION**

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44 In the detailed abstraction cohort ( $n=1,024$ ), median duration of symptoms prior  
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46 to hospitalization was 6 days (IQR 3-9). The most common presenting symptoms were  
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48 cough (73.3%), fever (71.8%), and shortness of breath (72.2%); only 8% of patients did  
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50 not report one of these 3 complaints (Table 1). Gastrointestinal symptoms including  
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52 nausea, vomiting and diarrhea occurred in 39.4% of patients. Over a third of patients  
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3 (37.2%) reported sick contacts at the time of admission, and 23.8% reported contact  
4 with a patient known to have COVID-19. The location of diagnostic testing for COVID-19  
5 varied: 67.5% of patients were tested in hospital laboratories, 23.2% in commercial  
6 laboratories, and 8.0% in the state laboratory. Patients were most commonly admitted  
7 to a general medical/surgical ward (59.5%), but 15.7% were admitted to intermediate  
8 care, 13.5% were admitted directly to ICU, and 11.3% were admitted to an observation  
9 unit (**Figure 1**). A total of 419 (40.9%) of patients were admitted to a “cohorted”  
10 (COVID-19 only) unit. At admission, 6.3% of patients had do not resuscitate/do not  
11 intubate orders, which increased to 13.8% by discharge.

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Common laboratory testing on admission included white blood cell count (93.7%), absolute lymphocyte count (75.8%), troponin (57.4%), lactate (57.2%), CRP (44.9%) and procalcitonin (42.4%) (missingness by laboratory test are reported in the e-Appendix). Among those with available laboratory data, patients who received ICU treatment had higher levels of inflammatory markers at admission including d-dimer (2.88mg/L vs. 1.65mg/L), ferritin (872ng/mL vs. 559ng/mL), CRP (24.3mg/dL vs. 13.8mg/dL) and LDH (476U/L vs. 346U/L) (**Table 2**). Chest imaging (X-ray or CT) was performed in 528 (51.6%) patients within 1 day of admission and was more common in ICU than general care patients (59.9% vs 49.1%,  $p=0.004$ ). ICU patients were more likely to have radiographic abnormalities on presentation. Viral respiratory panels, blood cultures and sputum cultures were collected in 722 (51.0%) patients, but were positive in only 48 (4.7%) patients; 9.5% of ICU patients vs. 3.3% of general care patients had a viral or bacterial pathogen identified ( $p<0.001$ ).

## CRITICAL CARE TREATMENT

Overall, 232 patients (22.7%) were treated in an ICU, including 138 (13.5%) who were admitted directly to an ICU, and 94 (9.2%) who were transferred to ICU a median of 2 days following admission. Median length of ICU stay was 6 days (IQR 3-9), which was similar in survivors vs. non-survivors (5 vs 6 days,  $p=0.790$ ). Among 1,024 patients with detailed abstraction, the maximum respiratory support received was invasive mechanical ventilation in 161 patients (15.7%), non-invasive positive pressure ventilation in 15 (1.5%), heated high-flow nasal cannula in 60 (5.9%), oxygen mask ( $>40\%$   $FiO_2$  or  $>6L/min$ ) in 88 (8.6%), and nasal cannula oxygen (1-6L/min) in 441 (43.1%) (**Table 3**). 259 (25.3%) patients received no respiratory support or oxygen therapy during hospitalization. Among 78 patients initiated on HHFNC, 13 (16.7%) progressed to invasive mechanical ventilation. Among 25 patients initiated on NIPPV, 10 (40.0%) progressed to invasive mechanical ventilation. An additional 12 patients and 2 patients, respectively, used HHFNC and NIPPV after extubation.

Upon initiation of mechanical ventilation, patients were predominantly treated with a volume control mode (75%), with high  $FIO_2$  ( $\geq 80\%$  in 49.1% of ventilated patients), and modest tidal volumes (median tidal volume 7.0 ml/kg predicted body weight, [IQR 6.2-8.0]). The median duration of mechanical ventilation was 6 days (IQR 3-8 days). Prone positioning was documented in 18 patients, pulmonary vasodilators in 2 patients, and extra corporeal membrane oxygenation in 2 patients. CPR was administered to 41 patients (4.0%), with only one patient surviving to hospital discharge.

Vasopressors were used in 141 patients (13.8%), dialysis in 53 (5.2%), and corticosteroids in 222 (21.7%) patients. 771 (75.3%) patients received broad-spectrum

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3 antibiotics, with use being more common in the ICU than general wards (91.8% vs  
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5 70.5%,  $p<0.001$ ).  
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## 10 COVID-19 SPECIFIC THERAPIES

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12 A total of 747 (72.9%) patients were treated with therapies targeting COVID-19,  
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14 or the body's response to COVID-19, most commonly hydroxychloroquine (51%),  
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16 hydroxychloroquine plus azithromycin (36%), and Vitamin C (10%). Treatment with IL-6  
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18 inhibitors and remdesivir was infrequent (27 and 17 patients, respectively). Use of  
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20 COVID-19 treatments was more common in ICU than general care patients (88% vs.  
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22 69%,  $p<0.001$ ). No patients in our sample received convalescent plasma. The  
23  
24 proportion of patients treated with COVID-19 specific therapies decreased over time  
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26 from 78.1% of patients admitted during March 8 to March 31 to 65.0% of patients  
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28 admitted during April 1 to May 11 ( $p<0.001$ ). Only 21 (2.0%) patients were enrolled into  
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30 a clinical trial (**Table 2**).  
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## 38 CLINICAL OUTCOMES

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40 The in-hospital mortality rate for the full cohort of COVID-19 positive patients  
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42 (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age,  
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44 ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years  
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46 (**Figure 2**). Among 219 decedents with detailed abstraction, 134 (61.5%) died following  
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48 ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219  
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50 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were  
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52 transitioned to comfort care prior to death. The most common causes of death were  
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3 refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock  
4 (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9  
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6 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both  
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8 DVT and PE.  
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12 Among the 805 patients that survived to hospital discharge, 86% were  
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14 discharged home and 8% were discharged to a skilled nursing facility or rehabilitation  
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16 center. Only 1 patient (0.1%) was discharged to the Detroit field hospital (**Table 3**).  
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## 21 **VARIATION ACROSS HOSPITALS**

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23 Among 14 hospitals with at least 25 detailed abstractions, substantial variation in  
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25 demographics, illness severity, care processes, treatments, and outcomes of COVID-19  
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27 positive patients were observed (**Table 4**). The proportion of patients over 65 years of  
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29 age ranged from 30.2% to 65.5%, while the proportion of Black patients ranged from 0%  
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31 to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from  
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33 0% to 43.8%, while the proportion of patients who were transferred to an ICU after  
34  
35 admission ranged from 0% to 24.1%. Treatment in “cohorted” units ranged from 0% to  
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37 100%. Mechanical ventilation on admission ranged from 0% to 12.8% while use of  
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39 vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness  
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41 on presentation (defined as admission to an ICU with receipt of vasopressors or  
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43 mechanical ventilation on admission) varied from 0% to 7.7%.  
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50 72.9% of patients received at least one COVID-19 specific therapy (e.g.,  
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52 hydroxychloroquine, hydroxychloroquine plus azithromycin, interleukin-6 inhibitor,  
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54 antiviral therapy), but use varied from 32% to 96.3% across sites. Similarly, 65% of  
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3 patients received concurrent antibiotics and COVID-19 specific treatment during  
4 hospitalization, with frequency varying from 50% to 100% in ICU patients vs. 17% to  
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6 95% in general care patients.  
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10 Mortality across hospitals varied from 7.9% to 45.7% of patients, and rates of  
11 CPR before death ranged from 0% to 66.7%. Finally, rates of VTE also varied, occurring  
12 in 0 to 11% of patients across hospitals.  
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## 16 17 18 19 **DISCUSSION**

20  
21 While reports of COVID-19 patients from New York, Washington, and California  
22 exist,<sup>7-9</sup> this is the first multi-center study to examine epidemiology, treatment and  
23 outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-  
24 hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients  
25 treated at a diverse set of 32 academic and community hospitals.  
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33 The demographics of our cohort differ from other cohorts. First, patients with  
34 confirmed COVID-19 in Michigan are disproportionately Black (over half of our cohort).  
35 This is in contrast to 32% of PUIs—indicating that the predominance of black patients  
36 with COVID-19 is not a reflection of local demographics, but rather disproportionate  
37 impact of COVID-19 on black patients. Second, in contrast to prior studies,<sup>1 7 10</sup> our  
38 cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this  
39 difference are unclear.  
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49 Consistent with prior reports, the main presenting symptoms were cough,  
50 dyspnea and fever. Similar to other studies,<sup>11</sup> a substantial proportion of patients had  
51 multiple comorbidities; but notably, 15% of our cohort had no known medical  
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3 problems.<sup>12</sup> We found that a substantial proportion of patients reported contact with a  
4 known COVID-19 positive patient prior to developing symptoms. These findings mirror  
5 those of a study from Shenzhen, China, where contacts of those with disease  
6 experienced a significantly higher rate of infection than the general public.<sup>13</sup> Additionally,  
7 patients underwent COVID-19 testing through a number of venues including hospital,  
8 commercial and state-run laboratories, illustrating the myriad ways in which diagnosis  
9 was obtained early in the outbreak when testing was limited.<sup>14</sup> Although only 14% of the  
10 sample was admitted directly to an ICU, an additional 9% were transferred to an ICU  
11 later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%,  
12 but increased with age, consistent with prior studies.<sup>15</sup>  
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26 A key finding of our study is that a majority of patients hospitalized for COVID-19  
27 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the  
28 body's immune response. More than half of patients were treated with  
29 hydroxychloroquine, and an additional 6% were treated with antivirals or immune  
30 modulating agents. Experts have increasingly questioned the use of unproven COVID-  
31 19 therapies outside of a clinical trial,<sup>16</sup> and have argued that supportive care and trial  
32 enrollment are the best options until data regarding efficacy of therapies accrues.<sup>17 18</sup>  
33 Accumulating observational and trial data now suggest no benefit from  
34 hydroxychloroquine,<sup>19-21</sup> and concerns regarding harm from empiric use remain.<sup>22</sup>  
35 Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of  
36 experimental COVID-19 therapies outside empiric studies represents a lost opportunity  
37 for learning. It is also emblematic of the strong desire—particularly early in the  
38 pandemic—to use therapies with a theoretical potential to target the virus even though  
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3 improved survival from critical illness is largely attributed to improvements in supportive  
4 care.<sup>23</sup> Notably, we still do not have targeted therapies for sepsis or acute respiratory  
5 distress syndrome, which are the major mechanisms by which patients die from COVID-  
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10 19 infection.

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12 Another strength of our study is the variation in clinical presentation and  
13 outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19  
14 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals.  
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16 While we are unable to ascertain reasons for such variation, we anecdotally observed  
17 that practice evolved across hospitals over time. For example, at some Michigan  
18 hospitals, routine use of hydroxychloroquine was common in the first few weeks of the  
19 pandemic but curbed as trial data became available. In contrast, use of  
20 hydroxychloroquine continues to be encouraged at other hospitals even today.<sup>24</sup> While it  
21 is unclear if these practice changes influenced outcomes, future studies exploring the  
22 rationale and impact of these changes on patients will be valuable.  
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35 Our study has limitations. First, given the observational nature of the study,  
36 rationales for treatment or management decisions cannot be determined. Second,  
37 because our sampling frame included patients that were discharged or deceased, our  
38 findings may be biased as patients who remain hospitalized may not be included in our  
39 cohort (potentially explaining lower duration of mechanical ventilation and hospital stay).  
40 However, COVID-19 hospitalizations in Southeastern Michigan have been declining  
41 since mid-April—limiting the degree of bias from exclusion of patients still in the  
42 hospital. Third, while variation in care was observed, the implications of such variability  
43 on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are  
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3 scarce and not without risks, reducing variation may improve patient safety and  
4 resource use. Fourth, our study depends on available documentation, so symptoms,  
5 comorbidities, or treatments not documented in the medical record may be omitted. For  
6 example, it is possible that the low use of prone positioning observed in our cohort may  
7 be due to incomplete documentation of this practice. Finally, we did not collect patient  
8 identifiers, so inter-hospital transfers could be reported as two separate hospitalizations.  
9 However, we did collect admission and discharge locations, and only 6% of the cohort  
10 was transferred from another hospital.  
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21 Our study also has strengths. Ours is the first multi-hospital study to examine  
22 clinical aspects related to COVID-19 in Michigan. Through a rigorous data collection  
23 structure including a well-defined sampling strategy and trained data abstractors, we  
24 provide novel and detailed insights into clinical care during the pandemic. Second, we  
25 were able to examine variation across sites finding substantial differences in clinical  
26 care and outcomes across hospitals. To our knowledge, this is the first study to examine  
27 differences in these important care processes, treatment approaches and outcomes  
28 across sites. Third, we report a high rate of use of non-evidence-based therapies for  
29 treating COVID-19. This finding has significant safety, economic and policy implications  
30 for the most critically ill subsets in the hospital. Finally, data collection for this effort  
31 remains ongoing, including longitudinal monitoring of patients after discharge. These  
32 data will help shed new light on the post hospital sequelae of COVID-19.  
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49 Michigan remains one of the regions most affected by COVID-19. This multi-  
50 center study provides granular clinical data regarding patients, care practices and  
51 clinical outcomes in the state. The wide variation in observed practices and outcomes  
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3 suggests caution when interpreting findings from single center studies. Our study also  
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5 demonstrates the value of hospital collaboratives to help inform best practices.  
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For peer review only

**BIBLIOGRAPHY**

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2002032 [published Online First: 2020/02/29]
2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020;382(8):727-33. doi: 10.1056/NEJMoa2001017 [published Online First: 2020/01/25]
3. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Available online at: <https://coronavirus.jhu.edu/maphtml> Accessed April 20, 2020
4. Centers for Disease Control Cases of Coronavirus Disease (COVID-19) in the US. Available online at: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>. Accessed April 20, 2020.
5. Michigan.gov. Coronavirus Resources - Confirmed cases by Jurisdiction. Available online at: <https://www.michigan.gov/coronavirus/0,9753,7-406-98163-520743--,00.html>. Accessed April 20, 2020.
6. Blue Cross Blue Shield Collaborative Quality Initiatives. Available online at: <https://www.bcbsm.com/providers/value-partnerships/collaborative-quality-initiatives.html>. Accessed April 20, 2020.
7. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical Characteristics of Covid-19 in New York City. *N Engl J Med* 2020 doi: 10.1056/NEJMc2010419 [published Online First: 2020/04/18]

- 1  
2  
3 8. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the  
4  
5 Seattle Region - Case Series. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2004500  
6  
7 [published Online First: 2020/04/01]  
8  
9
- 10 9. Myers LC, Parodi SM, Escobar GJ, et al. Characteristics of Hospitalized Adults With  
11  
12 COVID-19 in an Integrated Health Care System in California. *JAMA* 2020 doi:  
13  
14 10.1001/jama.2020.7202 [published Online First: 2020/04/25]  
15  
16
- 17 10. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of  
18  
19 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy  
20  
21 Region, Italy. *JAMA* 2020 doi: 10.1001/jama.2020.5394 [published Online First:  
22  
23 2020/04/07]  
24  
25
- 26 11. Xie J, Tong Z, Guan X, et al. Clinical Characteristics of Patients Who Died of  
27  
28 Coronavirus Disease 2019 in China. *JAMA Netw Open* 2020;3(4):e205619. doi:  
29  
30 10.1001/jamanetworkopen.2020.5619 [published Online First: 2020/04/11]  
31  
32
- 33 12. Gold JAW, Wong KK, Szablewski CM, et al. Characteristics and Clinical Outcomes  
34  
35 of Adult Patients Hospitalized with COVID-19 - Georgia, March 2020. *MMWR*  
36  
37 *Morb Mortal Wkly Rep* 2020;69(18):545-50. doi: 10.15585/mmwr.mm6918e1  
38  
39 [published Online First: 2020/05/08]  
40  
41
- 42 13. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases  
43  
44 and 1286 of their close contacts in Shenzhen, China: a retrospective cohort  
45  
46 study. *Lancet Infect Dis* 2020 doi: 10.1016/S1473-3099(20)30287-5 [published  
47  
48 Online First: 2020/05/01]  
49  
50
- 51 14. Sharfstein JM, Becker SJ, Mello MM. Diagnostic Testing for the Novel Coronavirus.  
52  
53 *JAMA* 2020 doi: 10.1001/jama.2020.3864 [published Online First: 2020/03/10]  
54  
55  
56  
57  
58  
59  
60



- 1  
2  
3 15. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,  
4  
5 Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19  
6  
7 in the New York City Area. *JAMA* 2020 doi: 10.1001/jama.2020.6775 [published  
8  
9 Online First: 2020/04/23]  
10  
11  
12 16. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America  
13  
14 Guidelines on the Treatment and Management of Patients with COVID-19. *Clin*  
15  
16 *Infect Dis* 2020 doi: 10.1093/cid/ciaa478 [published Online First: 2020/04/28]  
17  
18  
19 17. Rice TW, Janz DR. In Defense of Evidence-Based Medicine for the Treatment of  
20  
21 COVID-19 ARDS. *Ann Am Thorac Soc* 2020 doi: 10.1513/AnnalsATS.202004-  
22  
23 325IP [published Online First: 2020/04/23]  
24  
25  
26 18. Waterer GW, Rello J, Wunderink RG. SARS-CoV-2: First Do No Harm. *Am J Respir*  
27  
28 *Crit Care Med* 2020 doi: 10.1164/rccm.202004-1153ED [published Online First:  
29  
30 2020/04/21]  
31  
32  
33 19. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to  
34  
35 moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ*  
36  
37 2020;369:m1849. doi: 10.1136/bmj.m1849 [published Online First: 2020/05/16]  
38  
39  
40 20. Mahevas M, Tran VT, Roumier M, et al. Clinical efficacy of hydroxychloroquine in  
41  
42 patients with covid-19 pneumonia who require oxygen: observational  
43  
44 comparative study using routine care data. *BMJ* 2020;369:m1844. doi:  
45  
46 10.1136/bmj.m1844 [published Online First: 2020/05/16]  
47  
48  
49 21. Rosenberg ES, Dufort EM, Udo T, et al. Association of Treatment With  
50  
51 Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 COVID-19 in New York State. *JAMA* 2020 doi: 10.1001/jama.2020.8630

4  
5 [published Online First: 2020/05/12]

- 6  
7  
8 22. Bessiere F, Rocchia H, Deliniere A, et al. Assessment of QT Intervals in a Case  
9  
10 Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated  
11  
12 With Hydroxychloroquine Alone or in Combination With Azithromycin in an  
13  
14 Intensive Care Unit. *JAMA Cardiol* 2020 doi: 10.1001/jamacardio.2020.1787  
15  
16 [published Online First: 2020/05/02]

- 17  
18  
19 23. Angus DC. Optimizing the Trade-off Between Learning and Doing in a Pandemic.  
20  
21 *JAMA* 2020 doi: 10.1001/jama.2020.4984 [published Online First: 2020/04/01]

- 22  
23  
24 24. Wells K. Hospitals Vary Treatment for Coronavirus Patients. *National Public Radio*  
25  
26 2020; Available online at: [https://www.npr.org/2020/05/18/857727140/hospitals-](https://www.npr.org/2020/05/18/857727140/hospitals-vary-treatment-for-coronavirus-patients)  
27  
28 [vary-treatment-for-coronavirus-patients](https://www.npr.org/2020/05/18/857727140/hospitals-vary-treatment-for-coronavirus-patients). Accessed May 19, 2020.  
29  
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**Table 1. Demographic and Clinical Characteristics of COVID-19 Positive Patients (n=1,024)**

Residence prior to hospitalization - no. (%)		
	Home	824 (80.5%)
	Congregated living facility <sup>1</sup>	165 (16.1%)
	Sub-acute rehabilitation facility	9 (0.9%)
	Unknown	18 (1.8%)
Admission location - no. (%)		
	Emergency department	951 (92.9%)
	Transfer from Another Hospital	60 (5.9%)
	Direct admission	7 (0.7%)
Median age (IQR) - yr		63.3 (50.9-74.4)
Male Sex - no. (%)		533 (52.1%)
Race - no. (%)		
	Black	526 (51.4%)
	White	390 (38.1%)
	Unknown	45 (4.4%)
	Asian	30 (2.9%)
	Other	26 (2.5%)
	Native	4 (0.4%)
	Islander	3 (0.3%)
Ethnicity - no. (%)		
	Non-Hispanic	873 (85.3%)
	Hispanic	30 (2.9%)
	Unknown	117 (11.4%)
Insurance – no. (%)		
	Medicare	497 (48.5%)
	Commercial	251 (24.5%)
	Medicaid	128 (12.5%)
	Self-pay	29 (2.8%)
	Other <sup>2</sup>	117 (11.4%)
BMI - median (IQR)		30.6 (25.9-37.1)
Smoking history - no. (%)		
	Never	615 (60.2%)
	Former	279 (27.3%)
	Current	61 (6.0%)
	Unknown	65 (6.4%)
Vaping history - no. (%)		
	Never	645 (63.2%)
	Former	366 (35.8%)
	Current	6 (0.6%)
	Unknown	3 (0.3%)
Coexisting disorder - no. (%)		
	Hypertension	670 (65.4%)
	Diabetes	377 (36.8%)
	Cardiovascular Disease	266 (26.0%)
	Moderate/ Severe Kidney Disease	239 (23.3%)
	Asthma	132 (12.9%)
	CHF/Cardiomyopathy	131 (12.8%)
	Dementia	123 (12.0%)
	Chronic Obstructive Pulmonary Disease	115 (11.2%)
	Cerebrovascular disease/ paraplegia	97 (9.5%)

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3	Cancer <sup>3</sup>	77 (7.5%)
4	Peripheral Vascular Disorders	41 (4.0%)
5	Chronic Pulmonary Disease (non-asthma/COPD)	35 (3.4%)
6	Rheumatoid Arthritis	29 (2.8%)
7	Peptic Ulcer Disease	10 (1.0%)
8	HIV/AIDS	7 (0.7%)
9	Organ transplant	8 (0.8%)
10	Inflammatory Bowel Disease	8 (0.8%)
11	No reported comorbidities	152 (14.9%)
12	Home Medications	
13	ACE Inhibitors	180 (17.6%)
14	Steroids/immunosuppressive therapy	115 (11.3%)
15	ARBs	136 (13.3%)
16	NSAIDs	182 (17.8%)
17	Statins	378 (37.0%)
18	Beta Blockers	298 (29.2%)
19	Anticoagulants	149 (14.6%)
20	Oral Steroids <sup>4</sup>	62 (6.1%)
21	Inhaled steroids	43 (4.2%)
22	Inhaled long-acting beta-agonist	30 (2.9%)
23	Inhaled long-acting anti-cholinergic	5 (0.5%)
24	Home oxygen therapy	36 (3.5%)
25	Duration of symptoms before admission, days - median (IQR)	6 (3-9)
26	Respiratory symptoms - no. (%)	
27	Cough (New or Worsening)	751 (73.3%)
28	Fever - no. (%)	735 (71.8%)
29	Fever (99.0 - 100.4 [F])	151 (14.7%)
30	Fever ( >100.4 [F])	390 (38.1%)
31	Subjective fever	194 (18.9%)
32	Dyspnea / shortness of breath	739 (72.2%)
33	Nausea/vomiting or diarrhea	403 (39.4%)
34	Fatigue	361 (35.3%)
35	Myalgias	264 (25.8%)
36	Weakness	253 (24.7%)
37	Sputum production	146 (14.3%)
38	Altered Mental Status	144 (14.1%)
39	Non-pleuritic chest pain	100 (9.8%)
40	Generalized malaise	91 (8.9%)
41	Rhinorrhea	75 (7.3%)
42	Pleuritic chest pain	75 (7.3%)
43	No reported symptoms	14 (1.4%)
44	Sick contacts - no. (%)	381 (37.2%)
45	Known COVID-19 positive	244 (23.8%)
46	Unknown COVID-19 status	236 (23.0%)
47	Healthcare worker - no. (%)	72 (7.0%)
48	Service worker - no. (%) <sup>5</sup>	59 (5.8%)
49	Initial location of admission - no. (%)	
50	General Medical/Surgical ward	608 (59.5%)
51	ICU	138 (13.5%)
52	Step-down unit	160 (15.7%)
53	Observation unit	115 (11.3%)
54	Missing/Unknown	3 (0.3%)
55	Admitted to COVID-19 specific (i.e., cohorted) unit	419 (40.9%)
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<i>Advanced Directives on admission</i>		
	DNR/DNI	64 (6.3%)
	No CPR (intubation OK)	19 (1.9%)
	No intubation (CPR OK)	3 (0.3%)

Abbreviations: COVID-19, coronavirus disease 2019; SE=standard error; IQR, inter-quartile range

<sup>1</sup> *Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.*

<sup>2</sup> *Includes other payers, Michigan, out-of-state and government.*

<sup>3</sup> *Includes leukemia, lymphoma, hematologic cancer and any malignancy.*

<sup>4</sup> *Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.*

<sup>5</sup> *Service workers include food service, transportation, postal/delivery and other related fields.*

**Table 2 – Clinical and Laboratory Data in COVID-19 Positive Patients by ICU-status (n=1,024)**

	Ever ICU (n = 232)	General Ward (n = 792)	p
<b>Vital signs on day of hospital admission, no. (%)</b>			
Fever (>100.4 [F])	95 (40.9%)	295 (37.2%)	0.3073
Hypoxia / new or escalated O2 requirement	142 (61.2%)	257 (32.4%)	<.0001
Supplemental oxygen use	96 (41.4%)	145 (18.3%)	<.0001
Respiratory rate > 20	139 (59.9%)	306 (38.6%)	<.0001
Heart rate > 100 per minute	99 (42.7%)	321 (40.5%)	0.5596
Systolic blood pressure < 100 mmHg	27 (11.6%)	45 (5.7%)	0.0018
<b>Day 1 laboratory measures, median (IQR)</b>			
Hemoglobin	13.2 (11.4-14.7)	13.2 (12.0-14.6)	0.4573
White blood cell count, K/uL	7.3 (5.5-9.7)	6.5 (4.8-8.4)	<.0001
Absolute lymphocyte count, K/uL	0.80 (0.60-1.20)	1.00 (0.70-1.30)	0.3440
Platelet count, K/uL	197 (149-256)	204 (159-268)	0.4875
ALT, IU/L	32.0 (20.0-60.0)	27.0 (18.0-41.0)	0.2228
Lactate, mmol/L	1.6 (1.2-2.5)	1.4 (1.0-1.8)	0.0010
Troponin pg/mL	9 (0-38)	0 (0-12)	0.5872
Brain Natriuretic Peptide (BNP), pg/mL	79 (34-236)	49 (18-157)	0.0088
Procalcitonin, ng/mL	0.30 (0.17-0.94)	0.12 (0.06-0.29)	0.5054
D-dimer, mg/L	2.88 (1.19-35.00)	1.65 (0.59-368.00)	0.8240
Ferritin, ng/mL	872 (379-1531)	559 (237-1019)	0.1074
CRP, mg/dL	24.3 (12.0-107.1)	13.8 (5.8-66.2)	0.0031
LDH, IU/L	476 (337-668)	346 (254-455)	<.0001
Creatinine, mg/dL	1.3 (1.0-2.0)	1.1 (0.8-1.5)	0.5736
Total Bilirubin, mg/dL	0.6 (0.4-0.9)	0.5 (0.4-0.8)	0.7147
Respiratory viral panel positive for non-COVID-19 respiratory virus	2 (0.9%)	7 (0.9%)	0.9443
Positive blood culture within 1 day of admission	7 (3.0%)	9 (1.1%)	0.0422
Positive respiratory culture within 1 day of admission	4 (1.7%)	4 (0.5%)	0.0636
Any Chest imaging <sup>1</sup>	139 (59.9%)	389 (49.1%)	0.0038
Chest X-ray	118 (50.9%)	322 (40.7%)	0.0058
Chest Computed Tomography	34 (14.7%)	106 (13.4%)	0.6201
<b>Imaging findings - no. (%)</b>			
Pneumonia	61 (26.3%)	100 (12.6%)	<.0001
Non-specified opacities/air-space disease	84 (36.2%)	161 (20.3%)	<.0001
Pleural effusion	32 (13.8%)	37 (4.7%)	<.0001
Normal/no abnormalities	5 (2.2%)	30 (3.8%)	0.2287
Pulmonary Edema	25 (10.8%)	29 (3.7%)	<.0001
CT with Ground Glass Infiltrates	14 (6.0%)	58 (7.3%)	0.4995

<b>Respiratory support on day of admission - no. (%)</b>				
	Invasive mechanical ventilation	46 (19.8%)	2 (0.3%)	<.0001
	Non-invasive positive pressure	5 (2.2%)	2 (0.3%)	0.0020
	HHFNC	5 (2.2%)	5 (2.2%)	0.1905
	Oxygen mask (>40% <i>fio</i> <sub>2</sub> )	17 (7.3%)	20 (2.6%)	0.0006
	Nasal cannula oxygen, 1-6L	76 (32.8%)	261 (33.0%)	0.9555
	No supplemental oxygen	83 (8.1%)	502 (49.0%)	<.0001
<b>Treatments during hospitalization - no. (%)</b>				
<i>Covid-19 Specific treatment(s)</i>				
	Hydroxychloroquine	154 (66.4%)	364 (46.0%)	<.0001
	Hydroxychloroquine + Azithromycin	112 (48.3%)	260 (32.8%)	<.0001
	Vitamin C (PO or IV)	35 (15.1%)	68 (8.6%)	0.0038
	Remdesivir	7 (3.0%)	10 (1.3%)	0.0658
	IL-6 receptor inhibitor	27 (11.6%)	. (.%)	<.0001
	<i>Corticosteroids</i> <sup>2</sup>	79 (34.1%)	143 (18.1%)	<.0001
	<i>Antibiotics</i>	213 (91.8%)	558 (70.5%)	<.0001
	Azithromycin	149 (64.2%)	415 (52.4%)	0.0014
	Ceftriaxone	124 (53.4%)	345 (43.6%)	0.0079
	Cefepime	90 (38.8%)	79 (10.0%)	<.0001
	Doxycycline	37 (15.9%)	111 (14.0%)	0.4615
	Vancomycin	115 (49.6%)	106 (13.4%)	<.0001
	Linezolid	12 (5.2%)	8 (1.0%)	<.0001
	Anti-pseudomonals <sup>3</sup>	123 (53.0%)	115 (14.5%)	<.0001
	<i>Antivirals</i> <sup>4</sup>	1 (0.4%)	13 (1.6%)	0.1626
	<i>Enrolled in clinical trial</i>	10 (4.3%)	12 (1.5%)	0.0098
Abbreviations: COVID-19=coronavirus disease 2019; HHFNC=heated high flow nasal cannula; SE=standard error.				
1 Includes chest imaging results 7 days before hospital encounter				
2 Hydrocortisone, Methylprednisolone, prednisolone or prednisone				
3 Cefepime, gentamicin, imipenem, meropenem, piperacillin-tazobactam, ceftazadime, aztreonam or tobramycin				
4 Non-remdesivir antivirals including Oseltamivir, Lopinavir/Ritonavir, Ribavirin, others				

**Table 3. Organ support for COVID-19 Positive Patients by Discharge Status (n=1,024)**

	All patients (n =1,024)	Discharged Alive n = 805	Died in Hospital n = 219
Treated in an ICU	232 (22.7%)	101 (12.5%)	131 (59.8%)
<i>Respiratory support ever received, no. (%)*</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure ventilation	27 (2.6%)	10 (1.2%)	17 (7.8%)
HHFNC	90 (8.8%)	57 (7.1%)	33 (15.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	159 (15.5%)	76 (9.4%)	83 (37.9%)
<i>Maximum respiratory support received, no. (%)**</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure	15 (1.5%)	6 (0.7%)	9 (4.1%)
HHFNC	60 (5.9%)	40 (5.0%)	20 (9.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	88 (8.6%)	48 (6.0%)	40 (18.3%)
Nasal canula oxygen, 1-6L/min	441 (43.1%)	415 (51.6%)	26 (11.9%)
No respiratory support	259 (25.3%)	249 (30.9%)	10 (4.6%)
<i>Max FIO<sub>2</sub> received, no. (%)</i>			
91-100%	126 (12.3%)	34 (4.2%)	92 (42%)
81-90%	30 (2.9%)	13 (1.6%)	17 (7.8%)
71-80%	86 (8.4%)	42 (5.2%)	44 (20.1%)
61-70%	16 (1.6%)	9 (1.1%)	7 (3.2%)
51-60%	26 (2.5%)	14 (1.7%)	12 (5.5%)
41-50%	24 (2.3%)	20 (2.5%)	4 (1.8%)
31-40%	170 (16.6%)	144 (17.9%)	26 (11.9%)
21-30%	287 (28%)	280 (34.8%)	7 (3.2%)
<i>Non-respiratory organ support received, no. (%)</i>			
Vasopressor	141 (13.8%)	35 (4.3%)	106 (48.4%)
Any dialysis***	53 (5.2%)	17 (2.1%)	36 (16.4%)
CRRT only	17 (1.7%)	1 (0.1%)	16 (7.3%)
iHD only	28 (2.7%)	15 (1.9%)	13 (5.9%)
CPR	41 (4.0%)	1 (0.1%)	40 (18.3%)
Abbreviations: SE=standard error; ECMO=extra-corporeal membrane oxygenation; HHFNC=heated high flow nasal cannula; FiO <sub>2</sub> =fraction of inspired oxygen; L= liters/min; ICU=intensive care unit; PE=pulmonary embolism; DVT=deep vein thrombosis; CPR=cardiopulmonary resuscitation; CRRT=continuous renal replacement therapy; iHD=intermittent hemodialysis;			
* Represents any use of respiratory support. Numbers are greater than 100% as one patient may have received multiple treatments.			
** Represents the highest level of respiratory support a patient received during hospitalization.			
*** Includes Intermittent Hemodialysis (iHD), dialysis and ultrafiltration			



**Table 4. Variation in Clinical Care and Outcomes in COVID-19 Positive Patients Across Hospitals**

	Range across Hospitals							<i>p</i> <sup>†</sup>
	Min	10 <sup>th</sup> Pctl	25 <sup>th</sup> Pctl	Median	75 <sup>th</sup> Pctl	90 <sup>th</sup> Pctl	Max	
Patient characteristics								
Age >65, %	30.2	35.3	39.6	51.3	56.8	64.4	65.5	<.0001
Black, %	0.0	17.7	29.7	46.2	76.4	93.7	94.6	<.0001
Male, %	39.2	45.6	47.1	53.0	56.8	72.4	73.8	0.07
Charlson comorbidity index, median	0.0	1.0	1.0	1.0	1.0	2.0	2.0	0.01
BMI, median	24.3	28.4	29.5	31.1	33.3	36.5	36.9	0.09
Age, median in years	39.0	46.5	60.8	62.4	66.4	73.5	76.0	<.0001
Admission information, %								
Hospital-to-hospital transfer	0.0	0.0	0.0	0.00	2.8	10.7	20.9	<.0001
Admitted directly to ICU	0.0	0.0	2.9	6.15	14.8	20.5	43.8	<.0001
Transferred from floor to ICU	0.0	0.0	0.0	8.4	17.6	18.8	24.1	0.09
Admitted to a Cohorted unit	0.0	2.1	18.6	67.9	85.71	96.3	97.1	<.0001
Severe illness on presentation <sup>2</sup>	0.0	0.00	0.00	0.0	3.7	7.1	7.7	0.09
Vasopressor use on day 1	0.0	0.00	0.00	2.1	6.4	10.3	14.8	0.04
Mechanical ventilation on day 1	0.0	0.00	0.00	2.51	8.6	11.1	12.8	0.03
Treatment, %								
Treated in a Cohorted Unit	0.0	0.00	6.3	57.1	90.9	100.0	100.0	<.0001
Treated in an ICU	4.2	5.4	14.0	19.1	31.0	38.5	62.5	<.0001
COVID-19 Specific treatment	32.4	57.1	69.2	76.4	81.4	90.2	96.3	<.0001
Concurrent antibiotic and COVID-19 specific treatment(s)	24.3	42.9	59.4	69.8	76.7	84.3	96.3	<.0001
Hydroxychloroquine	13.5	31.4	42.3	59.7	65.5	81.5	82.4	<.0001
Mechanical ventilation	2.1	2.7	6.4	10.9	31.0	38.5	40.6	<.0001
Vasopressors	2.2	2.9	7.0	12.1	25.0	32.1	32.5	<.0001
CPR before death	0.0	0.0	8.3	14.3	33.3	40.0	66.7	0.0102
Outcomes, %								
Days of mechanical ventilation, median <sup>3</sup>	1.0	1.0	1.0	5.0	8.0	8.0	9.0	0.01
Length of stay, median	2.0	3.0	3.0	4.5	6.0	8.0	8.5	<.0001
ICU length of stay, median <sup>4</sup>	1.0	2.0	3.5	5.0	6.5	7.5	9.5	0.01
DVT	0.0	0.0	0.0	0.0	2.1	3.5	7.1	0.05
VTE	0.0	0.0	0.0	2.9	5.2	6.3	10.7	0.20
PE	0.0	0.0	0.0	1.8	3.9	6.3	7.1	0.72
Discharge status, %								
Death	7.9	8.3	14.6	21.3	31.0	41.4	45.7	<.0001
Transferred to another hospital	0.0	0.0	0.0	0.0	1.6	2.7	5.1	0.07

Discharged home	42.3	48.2	62.1	67.5	72.9	80.0	82.5	<.0001
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<sup>1</sup> Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.

<sup>2</sup> Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.

<sup>3</sup> For patients ever on mechanical ventilation

<sup>4</sup> For patients ever in ICU

\* Variables marked with asterisk represent variation from the demographic cohort

Abbreviations: BMI=body mass index; ICU=intensive care unit; CPR=cardiopulmonary resuscitation; DVT=deep vein thrombosis; VTE=venous thromboembolism; PE=pulmonary embolism

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3 **Figure Legend 1**  
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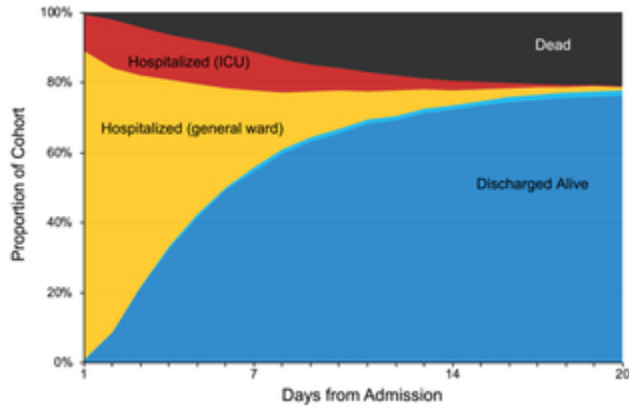
5 *Legend. Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on*  
6 *general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a*  
7 *new hospital (light blue) and deceased over time to day 20 of hospital admission.*  
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10 **Figure Legend 2**  
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12 *Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital*  
13 *by decade of age. Black shading indicates death whereas blue shading indicates discharge*  
14 *alive.*  
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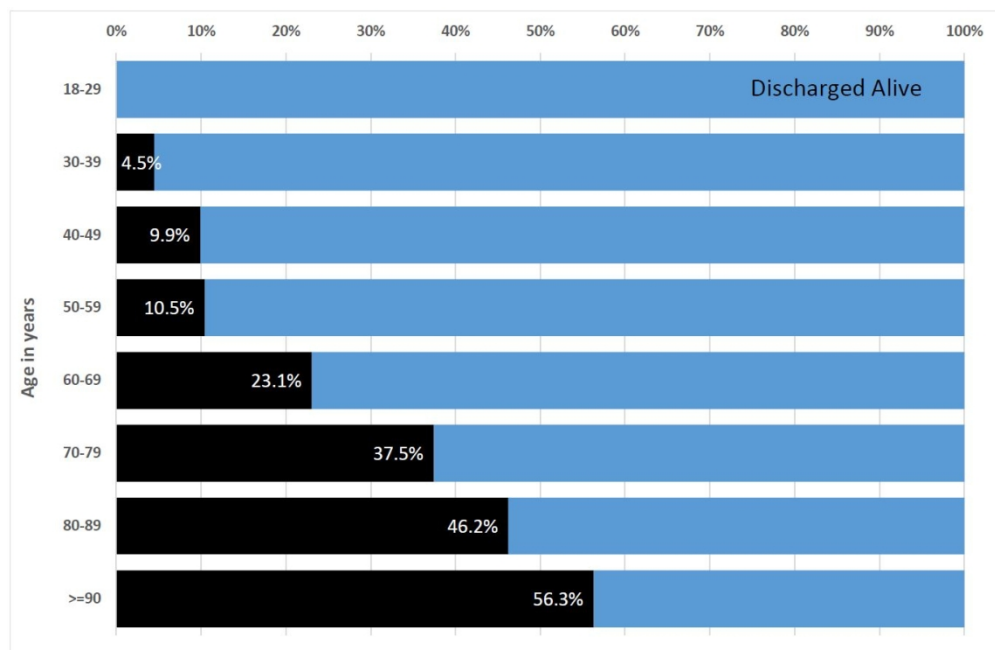
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Caption : Figure 1. Proportion of COVID-19 Positive Patients in hospital, ICU, dead, and discharged over time (n=1,024). Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a new hospital (light blue) and deceased over time to day 20 of hospital admission.

27x17mm (300 x 300 DPI)



Caption : Figure 2. Mortality rate for COVID-19 positive patients by decade of age (demographic data cohort, n=1,593) Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital by decade of age. Black shading indicates death whereas blue shading indicates discharge alive.

116x75mm (300 x 300 DPI)

**Appendix: Availability of Laboratory Tests**

Variable	N	% missing
Hemoglobin (Hgb)	959	6.3%
WBC *	959	6.3%
Absolute Lymphocyte Count *	776	24.2%
Platelet	957	6.5%
ALT *	803	21.6%
Lactate	586	42.8%
Troponin	588	42.6%
Brain Natriuretic Peptide (BNP)	282	72.5%
Procalcitonin	434	57.6%
D-dimer	333	67.5%
Ferritin *	419	59.1%
CRP *	460	55.1%
Lactic Acid Dehydrogenase (LDH)	392	61.7%
pH* (imputed)	326	68.2%
Creatinine *	956	6.6%
Total Bilirubin	777	24.1%

## STROBE (Strengthening The Reporting of OBServational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	
<b>Introduction</b>			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
<b>Methods</b>			
Study Design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed  <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study Size	10	Explain how the study size was arrived at	
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical Methods	12	(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	



Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key Results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
<b>Other Information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.**

# BMJ Open

## Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-044921.R1
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Date Submitted by the Author:	21-Jan-2021
Complete List of Authors:	Chopra, Vineet; University of Michigan Michigan Medicine, General Internal Medicine Flanders, Scott A.; University of Michigan, Vaughn, Valerie ; University of Michigan, Petty, Lindsay; University of Michigan Medical School, Division of Infectious Diseases Gandhi, Tejal; University of Michigan Michigan Medicine McSparron, Jakob; University of Michigan Health System Malani, Anurag; St Joseph Mercy Health System O'Malley, Megan; University of Michigan Michigan Medicine Kim, Tae; University of Michigan Michigan Medicine McLaughlin, Elizabeth; University of Michigan Michigan Medicine Prescott, Hallie; University of Michigan Michigan Medicine, Internal Medicine
<b>Primary Subject Heading</b>:	Infectious diseases
Secondary Subject Heading:	Epidemiology, Infectious diseases, Intensive care
Keywords:	COVID-19, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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3 **Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An**  
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5 **Observational Study in 32 Hospitals**  
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**ABSTRACT****OBJECTIVES**

To describe patient characteristics, symptoms, patterns of care and outcomes for patients hospitalized with COVID-19 in Michigan.

**DESIGN**

Multi-center retrospective cohort study.

**SETTING**

32 acute care hospitals in the state of Michigan.

**PARTICIPANTS**

Patients discharged (March 16 to May 11, 2020) with suspected or confirmed COVID-19 were identified. Trained abstractors collected demographic information on all patients, and detailed clinical data on a subset of COVID-19 positive patients.

**PRIMARY OUTCOME MEASUREMENTS**

Patient characteristics, treatment, and outcomes including cardiopulmonary resuscitation, mortality, and venous thromboembolism within and across hospitals.

**RESULTS**

Demographic-only data from 1,593 COVID-19 positive and 1,259 persons under investigation discharges were collected. Among 1,024 cases with detailed data, the

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3 median age was 63 years, median BMI was 30.6, and 51.4% were black. Cough, fever,  
4 and shortness of breath were the top symptoms. 37.2% reported a known COVID-19  
5 contact, 7.0% were healthcare workers, and 16.1% presented from congregated living  
6 facilities.  
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12 During hospitalization, 232 (22.7%) patients were treated in an ICU, 558 (54.9%)  
13 in a “cohorted” unit, 161 (15.7%) received mechanical ventilation, and 90 (8.8%)  
14 received high-flow nasal cannula. ICU patients more often received hydroxychloroquine  
15 (66% vs. 46%), corticosteroids (34% vs 18%), and antibiotic therapy (92% vs 71%) than  
16 general ward patients ( $p < 0.05$  for all). Overall, 219 (21.4%) patients died, with in-  
17 hospital mortality ranging from 7.9% to 45.7% across hospitals. 73% received at least  
18 one COVID-19-specific treatment, ranging from 32% to 96% across sites.  
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28 Across 14 hospitals, the proportion of patients admitted directly to an ICU ranged from  
29 0% to 43.8%; mechanical ventilation on admission from 0% to 12.8%; mortality from  
30 7.9% to 45.7%. Use of at least one COVID-19 specific therapy varied from 32% to  
31 96.3% across sites.  
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## 40 CONCLUSIONS

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42 During the early days of the Michigan outbreak of COVID-19, patient  
43 characteristics, treatment, and outcomes varied widely within and across hospitals.  
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## Article Summary

### Strengths and Limitations of this Study

- Using rigorous data collection including a well-defined sampling strategy and trained data abstractors, our paper is the largest multi-hospital study to examine clinical aspects related to COVID-19 in Michigan.
- This is the first study to examine variations in clinical care processes, treatment approaches and outcomes across hospitals.
- The high rate of use of non-evidence-based therapies for treating COVID-19 has significant safety, economic and policy implications for the most critically ill subsets in the hospital.
- Given the observational nature of the study and potential missing documentation on symptoms, comorbidities, or treatments in the medical record, rationales for treatment or management decisions cannot be determined.
- Our sampling frame may be biased as patients who remain hospitalized may not be included in our cohort.

## INTRODUCTION

Since detection in Wuhan, China,<sup>1 2</sup> over 4.5 million cases of COVID-19, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been reported.<sup>3</sup> The United States (US) leads the world in the total number of cases, with over 1.5 million cases and 92,000 deaths reported as of May 20, 2020.<sup>4</sup> Within the US, Michigan remains one of the hardest hit states, with over 52,000 cases and 5,000 deaths as of May 20, 2020.<sup>5</sup>

In the early days of the pandemic, data regarding patient characteristics, symptoms and signs and presentation and care strategies including aspects such as oxygenation, laboratory testing, and therapeutics were unclear. As well, short and long-term outcomes of patients exposed to these varying approaches was unknown. Some studies reported substantial variation in patient characteristics and treatment modalities across hospitals. But the extent of such variation and impact on outcomes remained unknown.

Michigan has a long history of collaborative quality improvement work that spans several disciplines including cardiovascular medicine, emergency medicine and hospital medicine, among others.<sup>6</sup> These consortia collect detailed clinical variables from hospitals to populate a central registry, allowing benchmarking and comparisons of care and outcomes. As the COVID-19 pandemic unfolded in Southeast Michigan, several consortia came together to focus data collection on patients hospitalized with COVID-19.

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3 Using a well-established data collection strategy, we examined variations in  
4 clinical care processes, treatment approaches, and clinical outcomes across Michigan  
5 hospitals.  
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## 10 **METHODS**

11  
12 A retrospective cohort design was used. Data were collected from medical  
13 records of patients discharged between March 16, 2020 and May 11, 2020 from one of  
14 32 Michigan hospitals who participate in collaborative quality initiatives sponsored by  
15 Blue Cross Blue Shield of Michigan and Blue Care Network. Trained abstractors at each  
16 hospital identified adult patients  $\geq 18$  years of age that underwent testing for COVID-19  
17 via reverse-transcriptase polymerase chain reaction, including both positive cases and  
18 persons under investigation (PUI) who eventually had a negative test. Demographic  
19 data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all  
20 confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was  
21 selected for detailed abstraction. Positive cases were sorted by day of admission (e.g.,  
22 Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge)  
23 was used to select patients for detailed abstraction. Patients who were pregnant,  
24 transitioned to hospice within 3 hours of hospital admission, or discharged against  
25 medical advice were excluded. All data were entered into a registry (Mi-COVID19) using  
26 a structured data collection template.  
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47 Patient characteristics including comorbidities, home medications, presenting  
48 symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare  
49 worker) were collected. Clinical data during hospitalization including location of care  
50 (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body  
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3 mass index (BMI), laboratory and radiology findings and therapeutics were abstracted.  
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5 Organ supports such as mechanical ventilation and other respiratory support,  
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7 vasopressor use, renal replacement therapy (continuous renal replacement therapy  
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9 [CRRT] and intermittent hemodialysis [iHD]) were also collected.  
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12 The primary outcomes of interest included hospital mortality, receipt of  
13  
14 cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or  
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16 pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric  
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18 therapy for presumed thrombosis). In addition, we performed pre-specified exploratory  
19  
20 analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine  
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22 variation in patient characteristics, management and outcomes. Specifically, we  
23  
24 assessed variation in use of COVID-19 specific treatments (defined as  
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26 hydroxychloroquine, combination hydroxychloroquine plus azithromycin, Vitamin C [oral  
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28 or intravenous], IL-6 inhibitors or remdesivir), antibiotic therapy, use of organ support  
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30 (e.g., use of vasopressors, mechanical ventilation and CPR), occurrence of venous  
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32 thrombosis and in-hospital mortality.  
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38 Descriptive statistics (e.g., mean, median, proportion) with measures of  
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40 dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize  
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42 data. Data that were not documented in medical records (e.g., values of certain  
43  
44 laboratory tests) were reported as missing. Pairwise comparisons were made using t-  
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46 tests for continuous data and chi-square tests for categorical data, respectively.  
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48 Differences across hospitals were tested using the Kruskal–Wallis test for continuous  
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50 variables and Pearson chi-square test for categorical variables. All statistical tests were  
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52 two-sided with  $p < 0.05$  considered statistically significant. The study was reviewed by the  
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3 Institutional Review Board of the University of Michigan and deemed “not regulated”. It  
4 was not appropriate or possible to involve patients or the public in the design, or  
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8 conduct, or reporting, or dissemination plans of our research.  
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## 10 11 12 **RESULTS**

### 13 14 **DEMOGRAPHIC DATA**

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17 Demographic-only data from 1,593 COVID-19 positive and 1,259 PUI discharges  
18 from 32 Michigan hospitals were collected. PUIs had a median age of 64.4 years,  
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21 52.6% were male and 32.0% Black. COVID-19 positive patients had similar age and  
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23  
24 gender as PUIs (63.9 years, and 52.1% male, respectively), but were more commonly  
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26  
27 Black (57.1% vs. 32.0%,  $p<0.01$ ). In the demographic-only cohort, 398 (25.0%) COVID-  
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30 19 positive patients died during hospitalization.

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32 Detailed data were abstracted on 1,024 (64.3%) randomly-selected COVID-19  
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35 positive patients. The most prevalent comorbidities were hypertension (65.4%),  
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38 diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%);  
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41 14.9% of patients had no comorbidities. Though 12.8% of patients had a diagnosis of  
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44 asthma and 11.2% had a diagnosis of chronic obstructive pulmonary disease, pre-  
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47 hospital use of inhaled steroids, long-acting beta-agonists and long-acting  
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50 antimuscarinic agents was low at 4.2%, 2.9%, and 0.5%, respectively. Current smoking  
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53 or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former  
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56 vaping. 115 (11.3%) patients were on immunosuppressive medications prior to  
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59 hospitalization, including 62 (6.1%) who were on oral steroids. Essential workers  
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62 comprised 12.8% of the cohort, including healthcare workers (7.0%) and service

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3 workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of  
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5 patients resided in congregated living facilities, including nursing homes and homeless  
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7 shelters (**Table 1**).  
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## 10 11 12 **CLINICAL PRESENTATION AND INITIAL EVALUATION** 13

14  
15 In the detailed abstraction cohort (n=1,024), median duration of symptoms prior  
16  
17 to hospitalization was 6 days (IQR 3-9). The most common presenting symptoms were  
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19 cough (73.3%), fever (71.8%), and shortness of breath (72.2%); only 8% of patients did  
20  
21 not report one of these 3 complaints (**Table 1**). Gastrointestinal symptoms including  
22  
23 nausea, vomiting and diarrhea occurred in 39.4% of patients. Over a third of patients  
24  
25 (37.2%) reported sick contacts at the time of admission, and 23.8% reported contact  
26  
27 with a patient known to have COVID-19. The location of diagnostic testing for COVID-19  
28  
29 varied: 67.5% of patients were tested in hospital laboratories, 23.2% in commercial  
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31 laboratories, and 8.0% in the state laboratory. Patients were most commonly admitted  
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33 to a general medical/surgical ward (59.5%), but 15.7% were admitted to intermediate  
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35 care, 13.5% were admitted directly to ICU, and 11.3% were admitted to an observation  
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37 unit (**Figure 1**). A total of 419 (40.9%) of patients were admitted to a “cohorted”  
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39 (COVID-19 only) unit. At admission, 6.3% of patients had do not resuscitate/do not  
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41 intubate orders, which increased to 13.8% by discharge.  
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48 Common laboratory testing on admission included white blood cell count  
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50 (93.7%), absolute lymphocyte count (75.8%), troponin (57.4%), lactate (57.2%), CRP  
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52 (44.9%) and procalcitonin (42.4%) (missingness by laboratory test are reported in the e-  
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54 Appendix). Among those with available laboratory data, patients who received ICU  
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3 treatment had higher levels of inflammatory markers at admission including d-dimer  
4 (2.88mg/L vs. 1.65mg/L), ferritin (872ng/mL vs. 559ng/mL), CRP (24.3mg/dL vs.  
5 13.8mg/dL) and LDH (476U/L vs. 346U/L) (**Table 2**). Chest imaging (X-ray or CT) was  
6 performed in 528 (51.6%) patients within 1 day of admission and was more common in  
7 ICU than general care patients (59.9% vs 49.1%,  $p=0.004$ ). ICU patients were more  
8 likely to have radiographic abnormalities on presentation. Viral respiratory panels, blood  
9 cultures and sputum cultures were collected in 722 (51.0%) patients, but were positive  
10 in only 48 (4.7%) patients; 9.5% of ICU patients vs. 3.3% of general care patients had a  
11 viral or bacterial pathogen identified ( $p<0.001$ ).  
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## 26 **CRITICAL CARE TREATMENT**

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28 Overall, 232 patients (22.7%) were treated in an ICU, including 138 (13.5%) who  
29 were admitted directly to an ICU, and 94 (9.2%) who were transferred to ICU a median  
30 of 2 days following admission. Median length of ICU stay was 6 days (IQR 3-9), which  
31 was similar in survivors vs. non-survivors (5 vs 6 days,  $p=0.790$ ). Among 1,024 patients  
32 with detailed abstraction, the maximum respiratory support received was invasive  
33 mechanical ventilation in 161 patients (15.7%), non-invasive positive pressure  
34 ventilation in 15 (1.5%), heated high-flow nasal cannula in 60 (5.9%), oxygen mask  
35 (>40% FiO<sub>2</sub> or >6L/min) in 88 (8.6%), and nasal cannula oxygen (1-6L/min) in 441  
36 (43.1%) (**Table 3**). 259 (25.3%) patients received no respiratory support or oxygen  
37 therapy during hospitalization. Among 78 patients initiated on HHFNC, 13 (16.7%)  
38 progressed to invasive mechanical ventilation. Among 25 patients initiated on NIPPV,  
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3 10 (40.0%) progressed to invasive mechanical ventilation. An additional 12 patients and  
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5 2 patients, respectively, used HHFNC and NIPPV after extubation.  
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8 Upon initiation of mechanical ventilation, patients were predominantly treated  
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10 with a volume control mode (75%), with high FIO<sub>2</sub> (≥80% in 49.1% of ventilated  
11  
12 patients), and modest tidal volumes (median tidal volume 7.0 ml/kg predicted body  
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14 weight, [IQR 6.2-8.0]). The median duration of mechanical ventilation was 6 days (IQR  
15  
16 3-8 days). Prone positioning was documented in 18 patients, pulmonary vasodilators in  
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18 2 patients, and extra corporeal membrane oxygenation in 2 patients. CPR was  
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20 administered to 41 patients (4.0%), with only one patient surviving to hospital discharge.  
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24 Vasopressors were used in 141 patients (13.8%), dialysis in 53 (5.2%), and  
25  
26 corticosteroids in 222 (21.7%) patients. 771 (75.3%) patients received broad-spectrum  
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28 antibiotics, with use being more common in the ICU than general wards (91.8% vs  
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30 70.5%, p<0.001).  
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### 33 34 35 **COVID-19 SPECIFIC THERAPIES** 36

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38 A total of 747 (72.9%) patients were treated with therapies targeting COVID-19,  
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40 or the body's response to COVID-19, most commonly hydroxychloroquine (51%),  
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42 hydroxychloroquine plus azithromycin (36%), and Vitamin C (10%). Treatment with IL-6  
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44 inhibitors and remdesivir was infrequent (27 and 17 patients, respectively). Use of  
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46 COVID-19 treatments was more common in ICU than general care patients (88% vs.  
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48 69%, p<0.001). No patients in our sample received convalescent plasma. The  
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50 proportion of patients treated with COVID-19 specific therapies decreased over time  
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52 from 78.1% of patients admitted during March 8 to March 31 to 65.0% of patients  
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3 admitted during April 1 to May 11 ( $p < 0.001$ ). Only 21 (2.0%) patients were enrolled into  
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5 a clinical trial (**Table 2**).  
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## 10 **CLINICAL OUTCOMES**

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12 The in-hospital mortality rate for the full cohort of COVID-19 positive patients  
13 (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age,  
14 ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years  
15 (**Figure 2**). Among 219 decedents with detailed abstraction, 134 (61.5%) died following  
16 ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219  
17 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were  
18 transitioned to comfort care prior to death. The most common causes of death were  
19 refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock  
20 (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9  
21 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both  
22 DVT and PE.  
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37 Among the 805 patients that survived to hospital discharge, 86% were  
38 discharged home and 8% were discharged to a skilled nursing facility or rehabilitation  
39 center. Only 1 patient (0.1%) was discharged to the Detroit field hospital (**Table 3**).  
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## 47 **VARIATION ACROSS HOSPITALS**

48  
49 Among 14 hospitals with at least 25 detailed abstractions, substantial variation in  
50 demographics, illness severity, care processes, treatments, and outcomes of COVID-19  
51 positive patients were observed (**Table 4**). The proportion of patients over 65 years of  
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3 age ranged from 30.2% to 65.5%, while the proportion of Black patients ranged from 0%  
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5 to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from  
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7 0% to 43.8%, while the proportion of patients who were transferred to an ICU after  
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9 admission ranged from 0% to 24.1%. Treatment in “cohorted” units ranged from 0% to  
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11 100%. Mechanical ventilation on admission ranged from 0% to 12.8% while use of  
12  
13 vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness  
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15 on presentation (defined as admission to an ICU with receipt of vasopressors or  
16  
17 mechanical ventilation on admission) varied from 0% to 7.7%.

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22 72.9% of patients received at least one COVID-19 specific therapy (e.g.,  
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24 hydroxychloroquine, hydroxychloroquine plus azithromycin, interleukin-6 inhibitor,  
25  
26 antiviral therapy), but use varied from 32% to 96.3% across sites. Similarly, 65% of  
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28 patients received concurrent antibiotics and COVID-19 specific treatment during  
29  
30 hospitalization, with frequency varying from 50% to 100% in ICU patients vs. 17% to  
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32 95% in general care patients.

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36 Mortality across hospitals varied from 7.9% to 45.7% of patients, and rates of  
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38 CPR before death ranged from 0% to 66.7%. Finally, rates of VTE also varied, occurring  
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40 in 0 to 11% of patients across hospitals.

## 44 45 **DISCUSSION**

46  
47 While reports of COVID-19 patients from New York, Washington, and California  
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49 exist,<sup>7-9</sup> this is the first multi-center study to examine epidemiology, treatment and  
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51 outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-  
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3 hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients  
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5 treated at a diverse set of 32 academic and community hospitals.  
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8 The demographics of our cohort differ from other cohorts. First, patients with  
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10 confirmed COVID-19 in Michigan are disproportionately Black (over half of our cohort).  
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12 This is in contrast to 32% of PUIs—indicating that the predominance of black patients  
13  
14 with COVID-19 is not a reflection of local demographics, but rather disproportionate  
15  
16 impact of COVID-19 on black patients. Second, in contrast to prior studies,<sup>1 7 10</sup> our  
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18 cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this  
19  
20 difference are unclear.  
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24 Consistent with prior reports, the main presenting symptoms were cough,  
25  
26 dyspnea and fever. Similar to other studies,<sup>11</sup> a substantial proportion of patients had  
27  
28 multiple comorbidities; but notably, 15% of our cohort had no known medical  
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30 problems.<sup>12</sup> We found that a substantial proportion of patients reported contact with a  
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32 known COVID-19 positive patient prior to developing symptoms. These findings mirror  
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34 those of a study from Shenzhen, China, where contacts of those with disease  
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36 experienced a significantly higher rate of infection than the general public.<sup>13</sup> Additionally,  
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38 patients underwent COVID-19 testing through a number of venues including hospital,  
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40 commercial and state-run laboratories, illustrating the myriad ways in which diagnosis  
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42 was obtained early in the outbreak when testing was limited.<sup>14</sup> Although only 14% of the  
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44 sample was admitted directly to an ICU, an additional 9% were transferred to an ICU  
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46 later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%,  
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48 but increased with age, consistent with prior studies.<sup>15</sup>  
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3 A key finding of our study is that a majority of patients hospitalized for COVID-19  
4 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the  
5 body's immune response. More than half of patients were treated with  
6 hydroxychloroquine, and an additional 6% were treated with antivirals or immune  
7 modulating agents. Experts have increasingly questioned the use of unproven COVID-  
8 19 therapies outside of a clinical trial,<sup>16</sup> and have argued that supportive care and trial  
9 enrollment are the best options until data regarding efficacy of therapies accrues.<sup>17 18</sup>  
10 Accumulating observational and trial data now suggest no benefit from  
11 hydroxychloroquine,<sup>19-21</sup> and concerns regarding harm from empiric use remain.<sup>22</sup>  
12 Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of  
13 experimental COVID-19 therapies outside empiric studies represents a lost opportunity  
14 for learning. It is also emblematic of the strong desire—particularly early in the  
15 pandemic—to use therapies with a theoretical potential to target the virus even though  
16 improved survival from critical illness is largely attributed to improvements in supportive  
17 care.<sup>23</sup> Notably, we still do not have targeted therapies for sepsis or acute respiratory  
18 distress syndrome, which are the major mechanisms by which patients die from COVID-  
19 19 infection.

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42 Another strength of our study is the variation in clinical presentation and  
43 outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19  
44 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals.  
45 While we are unable to ascertain reasons for such variation, we anecdotally observed  
46 that practice evolved across hospitals over time. For example, at some Michigan  
47 hospitals, routine use of hydroxychloroquine was common in the first few weeks of the  
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3 pandemic but curbed as trial data became available. In contrast, use of  
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5 hydroxychloroquine continues to be encouraged at other hospitals even today.<sup>24</sup> While it  
6  
7 is unclear if these practice changes influenced outcomes, future studies exploring the  
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9 rationale and impact of these changes on patients will be valuable.  
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12 Our study has limitations. First, given the observational nature of the study,  
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14 rationales for treatment or management decisions cannot be determined. Second,  
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16 because our sampling frame included patients that were discharged or deceased, our  
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18 findings may be biased as patients who remain hospitalized may not be included in our  
19  
20 cohort (potentially explaining lower duration of mechanical ventilation and hospital stay).  
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22 However, COVID-19 hospitalizations in Southeastern Michigan have been declining  
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24 since mid-April—limiting the degree of bias from exclusion of patients still in the  
25  
26 hospital. Third, while variation in care was observed, the implications of such variability  
27  
28 on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are  
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30 scarce and not without risks, reducing variation may improve patient safety and  
31  
32 resource use. Fourth, our study depends on available documentation, so symptoms,  
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34 comorbidities, or treatments not documented in the medical record may be omitted. For  
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36 example, it is possible that the low use of prone positioning observed in our cohort may  
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38 be due to incomplete documentation of this practice. Finally, we did not collect patient  
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40 identifiers, so inter-hospital transfers could be reported as two separate hospitalizations.  
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42 However, we did collect admission and discharge locations, and only 6% of the cohort  
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44 was transferred from another hospital.  
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51 Our study also has strengths. Ours is the first multi-hospital study to examine  
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53 clinical aspects related to COVID-19 in Michigan. Through a rigorous data collection  
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3 structure including a well-defined sampling strategy and trained data abstractors, we  
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5 provide novel and detailed insights into clinical care during the pandemic. Second, we  
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7 were able to examine variation across sites finding substantial differences in clinical  
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9 care and outcomes across hospitals. To our knowledge, this is the first study to examine  
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11 differences in these important care processes, treatment approaches and outcomes  
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13 across sites. Third, we report a high rate of use of non-evidence-based therapies for  
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15 treating COVID-19. This finding has significant safety, economic and policy implications  
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17 for the most critically ill subsets in the hospital. Finally, data collection for this effort  
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19 remains ongoing, including longitudinal monitoring of patients after discharge. These  
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21 data will help shed new light on the post hospital sequelae of COVID-19.  
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26 Michigan remains one of the regions most affected by COVID-19. This multi-  
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28 center study provides granular clinical data regarding patients, care practices and  
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30 clinical outcomes in the state. The wide variation in observed practices and outcomes  
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32 suggests caution when interpreting findings from single center studies. Our study also  
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34 demonstrates the value of hospital collaboratives to help inform best practices.  
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**BIBLIOGRAPHY**

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2002032 [published Online First: 2020/02/29]
2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020;382(8):727-33. doi: 10.1056/NEJMoa2001017 [published Online First: 2020/01/25]
3. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Available online at: <https://coronavirus.jhu.edu/maphtml> Accessed April 20, 2020
4. Centers for Disease Control Cases of Coronavirus Disease (COVID-19) in the US. Available online at: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>. Accessed April 20, 2020.
5. Michigan.gov. Coronavirus Resources - Confirmed cases by Jurisdiction. Available online at: <https://www.michigan.gov/coronavirus/0,9753,7-406-98163-520743--00.html>. Accessed April 20, 2020.
6. Blue Cross Blue Shield Collaborative Quality Initiatives. Available online at: <https://www.bcbsm.com/providers/value-partnerships/collaborative-quality-initiatives.html>. Accessed April 20, 2020.

- 1  
2  
3 7. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical Characteristics of Covid-19 in New York  
4  
5 City. *N Engl J Med* 2020 doi: 10.1056/NEJMc2010419 [published Online First:  
6  
7 2020/04/18]  
8  
9
- 10 8. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the  
11  
12 Seattle Region - Case Series. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2004500  
13  
14 [published Online First: 2020/04/01]  
15  
16
- 17 9. Myers LC, Parodi SM, Escobar GJ, et al. Characteristics of Hospitalized Adults With  
18  
19 COVID-19 in an Integrated Health Care System in California. *JAMA* 2020 doi:  
20  
21 10.1001/jama.2020.7202 [published Online First: 2020/04/25]  
22  
23
- 24 10. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of  
25  
26 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy  
27  
28 Region, Italy. *JAMA* 2020 doi: 10.1001/jama.2020.5394 [published Online First:  
29  
30 2020/04/07]  
31  
32
- 33 11. Xie J, Tong Z, Guan X, et al. Clinical Characteristics of Patients Who Died of  
34  
35 Coronavirus Disease 2019 in China. *JAMA Netw Open* 2020;3(4):e205619. doi:  
36  
37 10.1001/jamanetworkopen.2020.5619 [published Online First: 2020/04/11]  
38  
39
- 40 12. Gold JAW, Wong KK, Szablewski CM, et al. Characteristics and Clinical Outcomes  
41  
42 of Adult Patients Hospitalized with COVID-19 - Georgia, March 2020. *MMWR*  
43  
44 *Morb Mortal Wkly Rep* 2020;69(18):545-50. doi: 10.15585/mmwr.mm6918e1  
45  
46 [published Online First: 2020/05/08]  
47  
48
- 49 13. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases  
50  
51 and 1286 of their close contacts in Shenzhen, China: a retrospective cohort  
52  
53  
54  
55  
56  
57  
58  
59  
60



- 1  
2  
3 study. *Lancet Infect Dis* 2020 doi: 10.1016/S1473-3099(20)30287-5 [published  
4  
5 Online First: 2020/05/01]  
6  
7
- 8 14. Sharfstein JM, Becker SJ, Mello MM. Diagnostic Testing for the Novel Coronavirus.  
9  
10 *JAMA* 2020 doi: 10.1001/jama.2020.3864 [published Online First: 2020/03/10]  
11
- 12 15. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,  
13  
14 Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19  
15  
16 in the New York City Area. *JAMA* 2020 doi: 10.1001/jama.2020.6775 [published  
17  
18 Online First: 2020/04/23]  
19  
20
- 21 16. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America  
22  
23 Guidelines on the Treatment and Management of Patients with COVID-19. *Clin*  
24  
25 *Infect Dis* 2020 doi: 10.1093/cid/ciaa478 [published Online First: 2020/04/28]  
26  
27
- 28 17. Rice TW, Janz DR. In Defense of Evidence-Based Medicine for the Treatment of  
29  
30 COVID-19 ARDS. *Ann Am Thorac Soc* 2020 doi: 10.1513/AnnalsATS.202004-  
31  
32 325IP [published Online First: 2020/04/23]  
33  
34
- 35 18. Waterer GW, Rello J, Wunderink RG. SARS-CoV-2: First Do No Harm. *Am J Respir*  
36  
37 *Crit Care Med* 2020 doi: 10.1164/rccm.202004-1153ED [published Online First:  
38  
39 2020/04/21]  
40  
41
- 42 19. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to  
43  
44 moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ*  
45  
46 2020;369:m1849. doi: 10.1136/bmj.m1849 [published Online First: 2020/05/16]  
47  
48
- 49 20. Mahevas M, Tran VT, Roumier M, et al. Clinical efficacy of hydroxychloroquine in  
50  
51 patients with covid-19 pneumonia who require oxygen: observational  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 comparative study using routine care data. *BMJ* 2020;369:m1844. doi:  
4 10.1136/bmj.m1844 [published Online First: 2020/05/16]  
5  
6  
7  
8 21. Rosenberg ES, Dufort EM, Udo T, et al. Association of Treatment With  
9  
10 Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With  
11  
12 COVID-19 in New York State. *JAMA* 2020 doi: 10.1001/jama.2020.8630  
13  
14 [published Online First: 2020/05/12]  
15  
16  
17 22. Bessiere F, Rocchia H, Deliniere A, et al. Assessment of QT Intervals in a Case  
18  
19 Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated  
20  
21 With Hydroxychloroquine Alone or in Combination With Azithromycin in an  
22  
23 Intensive Care Unit. *JAMA Cardiol* 2020 doi: 10.1001/jamacardio.2020.1787  
24  
25 [published Online First: 2020/05/02]  
26  
27  
28 23. Angus DC. Optimizing the Trade-off Between Learning and Doing in a Pandemic.  
29  
30 *JAMA* 2020 doi: 10.1001/jama.2020.4984 [published Online First: 2020/04/01]  
31  
32  
33 24. Wells K. Hospitals Vary Treatment for Coronavirus Patients. *National Public Radio*  
34  
35 2020; Available online at: [https://www.npr.org/2020/05/18/857727140/hospitals-](https://www.npr.org/2020/05/18/857727140/hospitals-vary-treatment-for-coronavirus-patients)  
36  
37 [vary-treatment-for-coronavirus-patients](https://www.npr.org/2020/05/18/857727140/hospitals-vary-treatment-for-coronavirus-patients). Accessed May 19, 2020.  
38  
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**Table 1. Demographic and Clinical Characteristics of COVID-19 Positive Patients (n=1,024)**

Residence prior to hospitalization - no. (%)		
	Home	824 (80.5%)
	Congregated living facility <sup>1</sup>	165 (16.1%)
	Sub-acute rehabilitation facility	9 (0.9%)
	Unknown	18 (1.8%)
Admission location - no. (%)		
	Emergency department	951 (92.9%)
	Transfer from Another Hospital	60 (5.9%)
	Direct admission	7 (0.7%)
Median age (IQR) - yr		63.3 (50.9-74.4)
Male Sex - no. (%)		533 (52.1%)
Race - no. (%)		
	Black	526 (51.4%)
	White	390 (38.1%)
	Unknown	45 (4.4%)
	Asian	30 (2.9%)
	Other	26 (2.5%)
	Native	4 (0.4%)
	Islander	3 (0.3%)
Ethnicity - no. (%)		
	Non-Hispanic	873 (85.3%)
	Hispanic	30 (2.9%)
	Unknown	117 (11.4%)
Insurance – no. (%)		
	Medicare	497 (48.5%)
	Commercial	251 (24.5%)
	Medicaid	128 (12.5%)
	Self-pay	29 (2.8%)
	Other <sup>2</sup>	117 (11.4%)
BMI - median (IQR)		30.6 (25.9-37.1)
Smoking history - no. (%)		
	Never	615 (60.2%)
	Former	279 (27.3%)
	Current	61 (6.0%)
	Unknown	65 (6.4%)
Vaping history - no. (%)		
	Never	645 (63.2%)
	Former	366 (35.8%)
	Current	6 (0.6%)
	Unknown	3 (0.3%)
Coexisting disorder - no. (%)		
	Hypertension	670 (65.4%)
	Diabetes	377 (36.8%)
	Cardiovascular Disease	266 (26.0%)
	Moderate/ Severe Kidney Disease	239 (23.3%)
	Asthma	132 (12.9%)
	CHF/Cardiomyopathy	131 (12.8%)
	Dementia	123 (12.0%)
	Chronic Obstructive Pulmonary Disease	115 (11.2%)
	Cerebrovascular disease/ paraplegia	97 (9.5%)

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3	Cancer <sup>3</sup>	77 (7.5%)
4	Peripheral Vascular Disorders	41 (4.0%)
5	Chronic Pulmonary Disease (non-asthma/COPD)	35 (3.4%)
6	Rheumatoid Arthritis	29 (2.8%)
7	Peptic Ulcer Disease	10 (1.0%)
8	HIV/AIDS	7 (0.7%)
9	Organ transplant	8 (0.8%)
10	Inflammatory Bowel Disease	8 (0.8%)
11	No reported comorbidities	152 (14.9%)
12	Home Medications	
13	ACE Inhibitors	180 (17.6%)
14	Steroids/immunosuppressive therapy	115 (11.3%)
15	ARBs	136 (13.3%)
16	NSAIDs	182 (17.8%)
17	Statins	378 (37.0%)
18	Beta Blockers	298 (29.2%)
19	Anticoagulants	149 (14.6%)
20	Oral Steroids <sup>4</sup>	62 (6.1%)
21	Inhaled steroids	43 (4.2%)
22	Inhaled long-acting beta-agonist	30 (2.9%)
23	Inhaled long-acting anti-cholinergic	5 (0.5%)
24	Home oxygen therapy	36 (3.5%)
25	Duration of symptoms before admission, days - median (IQR)	6 (3-9)
26	Respiratory symptoms - no. (%)	
27	Cough (New or Worsening)	751 (73.3%)
28	Fever - no. (%)	735 (71.8%)
29	Fever (99.0 - 100.4 [F])	151 (14.7%)
30	Fever ( >100.4 [F])	390 (38.1%)
31	Subjective fever	194 (18.9%)
32	Dyspnea / shortness of breath	739 (72.2%)
33	Nausea/vomiting or diarrhea	403 (39.4%)
34	Fatigue	361 (35.3%)
35	Myalgias	264 (25.8%)
36	Weakness	253 (24.7%)
37	Sputum production	146 (14.3%)
38	Altered Mental Status	144 (14.1%)
39	Non-pleuritic chest pain	100 (9.8%)
40	Generalized malaise	91 (8.9%)
41	Rhinorrhea	75 (7.3%)
42	Pleuritic chest pain	75 (7.3%)
43	No reported symptoms	14 (1.4%)
44	Sick contacts - no. (%)	381 (37.2%)
45	Known COVID-19 positive	244 (23.8%)
46	Unknown COVID-19 status	236 (23.0%)
47	Healthcare worker - no. (%)	72 (7.0%)
48	Service worker - no. (%) <sup>5</sup>	59 (5.8%)
49	Initial location of admission - no. (%)	
50	General Medical/Surgical ward	608 (59.5%)
51	ICU	138 (13.5%)
52	Step-down unit	160 (15.7%)
53	Observation unit	115 (11.3%)
54	Missing/Unknown	3 (0.3%)
55	Admitted to COVID-19 specific (i.e., cohorted) unit	419 (40.9%)
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<i>Advanced Directives on admission</i>		
	DNR/DNI	64 (6.3%)
	No CPR (intubation OK)	19 (1.9%)
	No intubation (CPR OK)	3 (0.3%)

Abbreviations: COVID-19, coronavirus disease 2019; SE=standard error; IQR, inter-quartile range

<sup>1</sup> Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.

<sup>2</sup> Includes other payers, Michigan, out-of-state and government.

<sup>3</sup> Includes leukemia, lymphoma, hematologic cancer and any malignancy.

<sup>4</sup> Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.

<sup>5</sup> Service workers include food service, transportation, postal/delivery and other related fields.

**Table 2 – Clinical and Laboratory Data in COVID-19 Positive Patients by ICU-status (n=1,024)**

	Ever ICU (n = 232)	General Ward (n = 792)	p
<b>Vital signs on day of hospital admission, no. (%)</b>			
Fever (>100.4 [F])	95 (40.9%)	295 (37.2%)	0.3073
Hypoxia / new or escalated O2 requirement	142 (61.2%)	257 (32.4%)	<.0001
Supplemental oxygen use	96 (41.4%)	145 (18.3%)	<.0001
Respiratory rate > 20	139 (59.9%)	306 (38.6%)	<.0001
Heart rate > 100 per minute	99 (42.7%)	321 (40.5%)	0.5596
Systolic blood pressure < 100 mmHg	27 (11.6%)	45 (5.7%)	0.0018
<b>Day 1 laboratory measures, median (IQR)</b>			
Hemoglobin	13.2 (11.4-14.7)	13.2 (12.0-14.6)	0.4573
White blood cell count, K/uL	7.3 (5.5-9.7)	6.5 (4.8-8.4)	<.0001
Absolute lymphocyte count, K/uL	0.80 (0.60-1.20)	1.00 (0.70-1.30)	0.3440
Platelet count, K/uL	197 (149-256)	204 (159-268)	0.4875
ALT, IU/L	32.0 (20.0-60.0)	27.0 (18.0-41.0)	0.2228
Lactate, mmol/L	1.6 (1.2-2.5)	1.4 (1.0-1.8)	0.0010
Troponin pg/mL	9 (0-38)	0 (0-12)	0.5872
Brain Natriuretic Peptide (BNP), pg/mL	79 (34-236)	49 (18-157)	0.0088
Procalcitonin, ng/mL	0.30 (0.17-0.94)	0.12 (0.06-0.29)	0.5054
D-dimer, mg/L	2.88 (1.19-35.00)	1.65 (0.59-368.00)	0.8240
Ferritin, ng/mL	872 (379-1531)	559 (237-1019)	0.1074
CRP, mg/dL	24.3 (12.0-107.1)	13.8 (5.8-66.2)	0.0031
LDH, IU/L	476 (337-668)	346 (254-455)	<.0001
Creatinine, mg/dL	1.3 (1.0-2.0)	1.1 (0.8-1.5)	0.5736
Total Bilirubin, mg/dL	0.6 (0.4-0.9)	0.5 (0.4-0.8)	0.7147
Respiratory viral panel positive for non-COVID-19 respiratory virus	2 (0.9%)	7 (0.9%)	0.9443
Positive blood culture within 1 day of admission	7 (3.0%)	9 (1.1%)	0.0422
Positive respiratory culture within 1 day of admission	4 (1.7%)	4 (0.5%)	0.0636
Any Chest imaging <sup>1</sup>	139 (59.9%)	389 (49.1%)	0.0038
Chest X-ray	118 (50.9%)	322 (40.7%)	0.0058
Chest Computed Tomography	34 (14.7%)	106 (13.4%)	0.6201
<b>Imaging findings - no. (%)</b>			
Pneumonia	61 (26.3%)	100 (12.6%)	<.0001
Non-specified opacities/air-space disease	84 (36.2%)	161 (20.3%)	<.0001
Pleural effusion	32 (13.8%)	37 (4.7%)	<.0001
Normal/no abnormalities	5 (2.2%)	30 (3.8%)	0.2287
Pulmonary Edema	25 (10.8%)	29 (3.7%)	<.0001
CT with Ground Glass Infiltrates	14 (6.0%)	58 (7.3%)	0.4995

<b>Respiratory support on day of admission - no. (%)</b>				
	Invasive mechanical ventilation	46 (19.8%)	2 (0.3%)	<.0001
	Non-invasive positive pressure	5 (2.2%)	2 (0.3%)	0.0020
	HHFNC	5 (2.2%)	5 (2.2%)	0.1905
	Oxygen mask (>40% <i>fio</i> <sub>2</sub> )	17 (7.3%)	20 (2.6%)	0.0006
	Nasal cannula oxygen, 1-6L	76 (32.8%)	261 (33.0%)	0.9555
	No supplemental oxygen	83 (8.1%)	502 (49.0%)	<.0001
<b>Treatments during hospitalization - no. (%)</b>				
<i>Covid-19 Specific treatment(s)</i>				
	Hydroxychloroquine	154 (66.4%)	364 (46.0%)	<.0001
	Hydroxychloroquine + Azithromycin	112 (48.3%)	260 (32.8%)	<.0001
	Vitamin C (PO or IV)	35 (15.1%)	68 (8.6%)	0.0038
	Remdesivir	7 (3.0%)	10 (1.3%)	0.0658
	IL-6 receptor inhibitor	27 (11.6%)	. (.%)	<.0001
	<i>Corticosteroids</i> <sup>2</sup>	79 (34.1%)	143 (18.1%)	<.0001
	<i>Antibiotics</i>	213 (91.8%)	558 (70.5%)	<.0001
	Azithromycin	149 (64.2%)	415 (52.4%)	0.0014
	Ceftriaxone	124 (53.4%)	345 (43.6%)	0.0079
	Cefepime	90 (38.8%)	79 (10.0%)	<.0001
	Doxycycline	37 (15.9%)	111 (14.0%)	0.4615
	Vancomycin	115 (49.6%)	106 (13.4%)	<.0001
	Linezolid	12 (5.2%)	8 (1.0%)	<.0001
	Anti-pseudomonals <sup>3</sup>	123 (53.0%)	115 (14.5%)	<.0001
	<i>Antivirals</i> <sup>4</sup>	1 (0.4%)	13 (1.6%)	0.1626
	<i>Enrolled in clinical trial</i>	10 (4.3%)	12 (1.5%)	0.0098
Abbreviations: COVID-19=coronavirus disease 2019; HHFNC=heated high flow nasal cannula; SE=standard error.				
1 Includes chest imaging results 7 days before hospital encounter				
2 Hydrocortisone, Methylprednisolone, prednisolone or prednisone				
3 Cefepime, gentamicin, imipenem, meropenem, piperacillin-tazobactam, ceftazadime, aztreonam or tobramycin				
4 Non-remdesivir antivirals including Oseltamivir, Lopinavir/Ritonavir, Ribavirin, others				



**Table 3. Organ support for COVID-19 Positive Patients by Discharge Status (n=1,024)**

	All patients (n =1,024)	Discharged Alive n = 805	Died in Hospital n = 219
Treated in an ICU	232 (22.7%)	101 (12.5%)	131 (59.8%)
<i>Respiratory support ever received, no. (%)*</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure ventilation	27 (2.6%)	10 (1.2%)	17 (7.8%)
HHFNC	90 (8.8%)	57 (7.1%)	33 (15.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	159 (15.5%)	76 (9.4%)	83 (37.9%)
<i>Maximum respiratory support received, no. (%)**</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure	15 (1.5%)	6 (0.7%)	9 (4.1%)
HHFNC	60 (5.9%)	40 (5.0%)	20 (9.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	88 (8.6%)	48 (6.0%)	40 (18.3%)
Nasal canula oxygen, 1-6L/min	441 (43.1%)	415 (51.6%)	26 (11.9%)
No respiratory support	259 (25.3%)	249 (30.9%)	10 (4.6%)
<i>Max FIO<sub>2</sub> received, no. (%)</i>			
91-100%	126 (12.3%)	34 (4.2%)	92 (42%)
81-90%	30 (2.9%)	13 (1.6%)	17 (7.8%)
71-80%	86 (8.4%)	42 (5.2%)	44 (20.1%)
61-70%	16 (1.6%)	9 (1.1%)	7 (3.2%)
51-60%	26 (2.5%)	14 (1.7%)	12 (5.5%)
41-50%	24 (2.3%)	20 (2.5%)	4 (1.8%)
31-40%	170 (16.6%)	144 (17.9%)	26 (11.9%)
21-30%	287 (28%)	280 (34.8%)	7 (3.2%)
<i>Non-respiratory organ support received, no. (%)</i>			
Vasopressor	141 (13.8%)	35 (4.3%)	106 (48.4%)
Any dialysis***	53 (5.2%)	17 (2.1%)	36 (16.4%)
CRRT only	17 (1.7%)	1 (0.1%)	16 (7.3%)
iHD only	28 (2.7%)	15 (1.9%)	13 (5.9%)
CPR	41 (4.0%)	1 (0.1%)	40 (18.3%)
Abbreviations: SE=standard error; ECMO=extra-corporeal membrane oxygenation; HHFNC=heated high flow nasal cannula; FiO <sub>2</sub> =fraction of inspired oxygen; L= liters/min; ICU=intensive care unit; PE=pulmonary embolism; DVT=deep vein thrombosis; CPR=cardiopulmonary resuscitation; CRRT=continuous renal replacement therapy; iHD=intermittent hemodialysis;			
* Represents any use of respiratory support. Numbers are greater than 100% as one patient may have received multiple treatments.			
** Represents the highest level of respiratory support a patient received during hospitalization.			
*** Includes Intermittent Hemodialysis (iHD), dialysis and ultrafiltration			



**Table 4. Variation in Clinical Care and Outcomes in COVID-19 Positive Patients Across Hospitals**

	Range across Hospitals							<i>p</i> <sup>†</sup>
	Min	10 <sup>th</sup> Pctl	25 <sup>th</sup> Pctl	Median	75 <sup>th</sup> Pctl	90 <sup>th</sup> Pctl	Max	
Patient characteristics								
Age >65, %	30.2	35.3	39.6	51.3	56.8	64.4	65.5	<.0001
Black, %	0.0	17.7	29.7	46.2	76.4	93.7	94.6	<.0001
Male, %	39.2	45.6	47.1	53.0	56.8	72.4	73.8	0.07
Charlson comorbidity index, median	0.0	1.0	1.0	1.0	1.0	2.0	2.0	0.01
BMI, median	24.3	28.4	29.5	31.1	33.3	36.5	36.9	0.09
Age, median in years	39.0	46.5	60.8	62.4	66.4	73.5	76.0	<.0001
Admission information, %								
Hospital-to-hospital transfer	0.0	0.0	0.0	0.00	2.8	10.7	20.9	<.0001
Admitted directly to ICU	0.0	0.0	2.9	6.15	14.8	20.5	43.8	<.0001
Transferred from floor to ICU	0.0	0.0	0.0	8.4	17.6	18.8	24.1	0.09
Admitted to a Cohorted unit	0.0	2.1	18.6	67.9	85.71	96.3	97.1	<.0001
Severe illness on presentation <sup>2</sup>	0.0	0.00	0.00	0.0	3.7	7.1	7.7	0.09
Vasopressor use on day 1	0.0	0.00	0.00	2.1	6.4	10.3	14.8	0.04
Mechanical ventilation on day 1	0.0	0.00	0.00	2.51	8.6	11.1	12.8	0.03
Treatment, %								
Treated in a Cohorted Unit	0.0	0.00	6.3	57.1	90.9	100.0	100.0	<.0001
Treated in an ICU	4.2	5.4	14.0	19.1	31.0	38.5	62.5	<.0001
COVID-19 Specific treatment	32.4	57.1	69.2	76.4	81.4	90.2	96.3	<.0001
Concurrent antibiotic and COVID-19 specific treatment(s)	24.3	42.9	59.4	69.8	76.7	84.3	96.3	<.0001
Hydroxychloroquine	13.5	31.4	42.3	59.7	65.5	81.5	82.4	<.0001
Mechanical ventilation	2.1	2.7	6.4	10.9	31.0	38.5	40.6	<.0001
Vasopressors	2.2	2.9	7.0	12.1	25.0	32.1	32.5	<.0001
CPR before death	0.0	0.0	8.3	14.3	33.3	40.0	66.7	0.0102
Outcomes, %								
Days of mechanical ventilation, median <sup>3</sup>	1.0	1.0	1.0	5.0	8.0	8.0	9.0	0.01
Length of stay, median	2.0	3.0	3.0	4.5	6.0	8.0	8.5	<.0001
ICU length of stay, median <sup>4</sup>	1.0	2.0	3.5	5.0	6.5	7.5	9.5	0.01
DVT	0.0	0.0	0.0	0.0	2.1	3.5	7.1	0.05
VTE	0.0	0.0	0.0	2.9	5.2	6.3	10.7	0.20
PE	0.0	0.0	0.0	1.8	3.9	6.3	7.1	0.72
Discharge status, %								
Death	7.9	8.3	14.6	21.3	31.0	41.4	45.7	<.0001
Transferred to another hospital	0.0	0.0	0.0	0.0	1.6	2.7	5.1	0.07

Discharged home	42.3	48.2	62.1	67.5	72.9	80.0	82.5	<.0001
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<sup>1</sup> Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.

<sup>2</sup> Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.

<sup>3</sup> For patients ever on mechanical ventilation

<sup>4</sup> For patients ever in ICU

\* Variables marked with asterisk represent variation from the demographic cohort

Abbreviations: BMI=body mass index; ICU=intensive care unit; CPR=cardiopulmonary resuscitation; DVT=deep vein thrombosis; VTE=venous thromboembolism; PE=pulmonary embolism

For peer review only

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3 **Figure Legend 1**  
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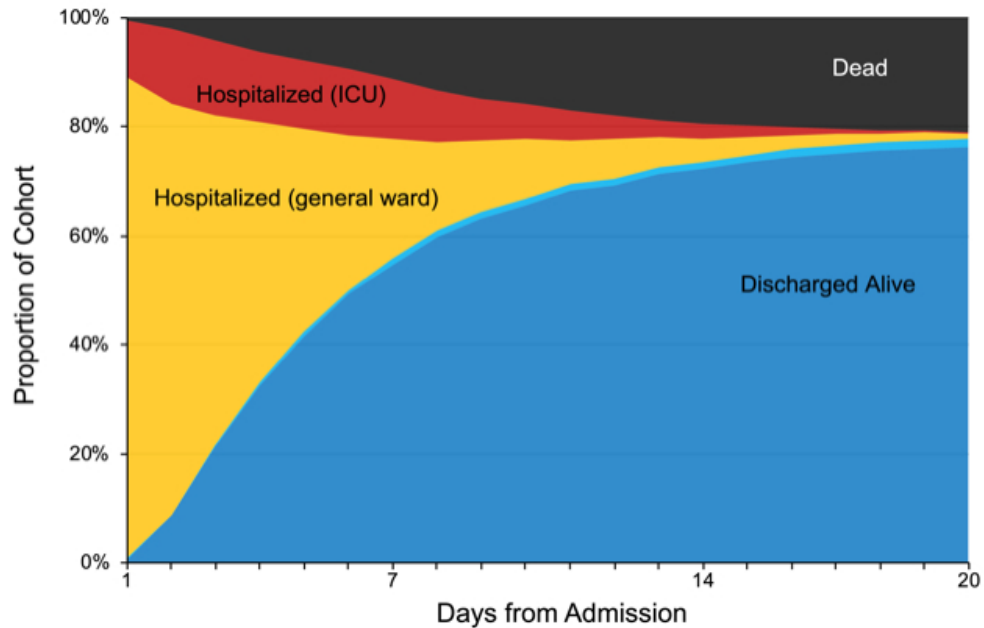
5 *Legend. Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on*  
6 *general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a*  
7 *new hospital (light blue) and deceased over time to day 20 of hospital admission.*  
8

9  
10 **Figure Legend 2**  
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12 *Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital*  
13 *by decade of age. Black shading indicates death whereas blue shading indicates discharge*  
14 *alive.*  
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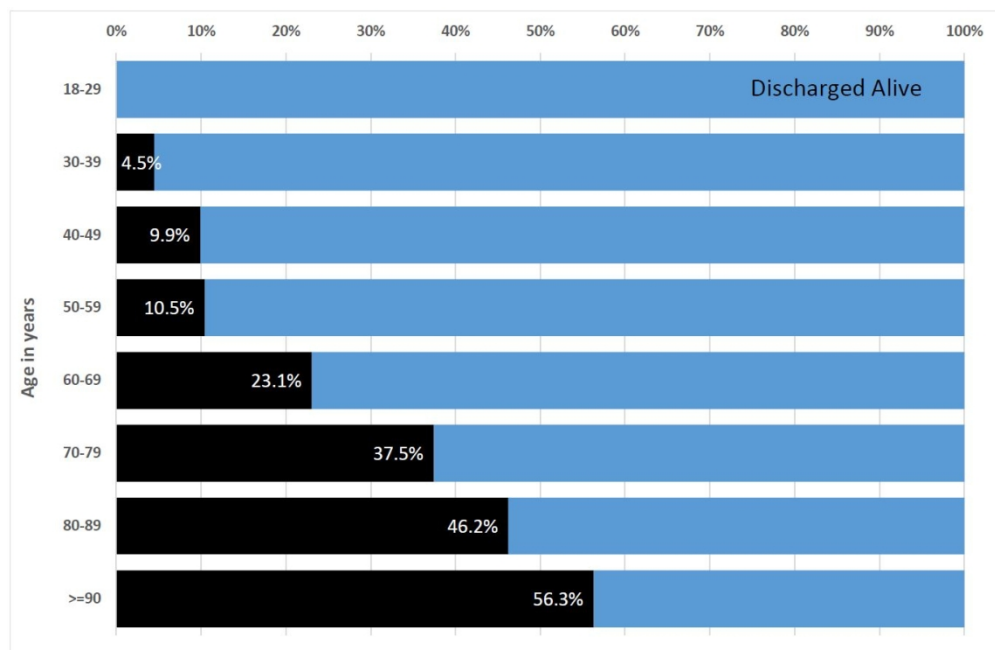
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For peer review only



Caption : Figure 1. Proportion of COVID-19 Positive Patients in hospital, ICU, dead, and discharged over time (n=1,024). Legend. Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a new hospital (light blue) and deceased over time to day 20 of hospital admission.

27x17mm (600 x 600 DPI)



Caption : Figure 2. Mortality rate for COVID-19 positive patients by decade of age (demographic data cohort, n=1,593) Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital by decade of age. Black shading indicates death whereas blue shading indicates discharge alive.

116x75mm (300 x 300 DPI)

**Appendix: Availability of Laboratory Tests**

Variable	N	% missing
Hemoglobin (Hgb)	959	6.3%
WBC *	959	6.3%
Absolute Lymphocyte Count *	776	24.2%
Platelet	957	6.5%
ALT *	803	21.6%
Lactate	586	42.8%
Troponin	588	42.6%
Brain Natriuretic Peptide (BNP)	282	72.5%
Procalcitonin	434	57.6%
D-dimer	333	67.5%
Ferritin *	419	59.1%
CRP *	460	55.1%
Lactic Acid Dehydrogenase (LDH)	392	61.7%
pH* (imputed)	326	68.2%
Creatinine *	956	6.6%
Total Bilirubin	777	24.1%

## STROBE (Strengthening The Reporting of OBServational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	
<b>Introduction</b>			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
<b>Methods</b>			
Study Design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed  <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study Size	10	Explain how the study size was arrived at	
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical Methods	12	(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	



Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key Results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
<b>Other Information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.**

# BMJ Open

## Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-044921.R2
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Keywords:	COVID-19, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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## Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals

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33 60 Detroit Receiving, Detroit Medical Center-Harper Hutzell, Detroit Medical Center-Detroit-34  
35 61 Huron Valley Sinai, Henry Ford, Henry Ford Allegiance, Henry Ford Macomb, Henry36  
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50 68 Mary Mercy Livonia.51  
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8 72 drafting/revisions; final approval to be published  
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10 73 Scott A. Flanders MD – manuscript planning; manuscript drafting/revisions; final  
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12 74 approval to be published  
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3 **93 ABSTRACT**

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5 **95 OBJECTIVES**

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8 96 To describe patient characteristics, symptoms, patterns of care and outcomes for  
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10 97 patients hospitalized with COVID-19 in Michigan.

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14 **99 DESIGN**

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17 100 Multi-center retrospective cohort study.

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21 **102 SETTING**

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24 103 32 acute care hospitals in the state of Michigan.

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28 **105 PARTICIPANTS**

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31 106 Patients discharged (March 16 to May 11, 2020) with suspected or confirmed  
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33 107 COVID-19 were identified. Trained abstractors collected demographic information on all  
34  
35 108 patients, and detailed clinical data on a subset of COVID-19 positive patients.

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40 **110 PRIMARY OUTCOME MEASUREMENTS**

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42 111 Patient characteristics, treatment, and outcomes including cardiopulmonary  
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44 112 resuscitation, mortality, and venous thromboembolism within and across hospitals.

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49 **114 RESULTS**

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51 115 Demographic-only data from 1,593 COVID-19 positive and 1,259 persons under  
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53 116 investigation discharges were collected. Among 1,024 cases with detailed data, the



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3 117 median age was 63 years, median BMI was 30.6, and 51.4% were black. Cough, fever,  
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5 118 and shortness of breath were the top symptoms. 37.2% reported a known COVID-19  
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7 119 contact, 7.0% were healthcare workers, and 16.1% presented from congregated living  
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9 120 facilities.

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12 121 During hospitalization, 232 (22.7%) patients were treated in an ICU, 558 (54.9%)  
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14 122 in a “cohorted” unit, 161 (15.7%) received mechanical ventilation, and 90 (8.8%)  
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16 123 received high-flow nasal cannula. ICU patients more often received hydroxychloroquine  
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18 124 (66% vs. 46%), corticosteroids (34% vs 18%), and antibiotic therapy (92% vs 71%) than  
19  
20 125 general ward patients ( $p < 0.05$  for all). Overall, 219 (21.4%) patients died, with in-  
21  
22 126 hospital mortality ranging from 7.9% to 45.7% across hospitals. 73% received at least  
23  
24 127 one COVID-19-specific treatment, ranging from 32% to 96% across sites.

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26 128 Across 14 hospitals, the proportion of patients admitted directly to an ICU ranged from  
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28 129 0% to 43.8%; mechanical ventilation on admission from 0% to 12.8%; mortality from  
29  
30 130 7.9% to 45.7%. Use of at least one COVID-19 specific therapy varied from 32% to  
31  
32 131 96.3% across sites.

## 33 34 35 36 37 38 39 133 **CONCLUSIONS**

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42 134 During the early days of the Michigan outbreak of COVID-19, patient  
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44 135 characteristics, treatment, and outcomes varied widely within and across hospitals.

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3 136 **Article Summary**  
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5 137 **Strengths and Limitations of this Study**  
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- 7
- 8 138 • Using rigorous data collection including a well-defined sampling strategy and  
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10 139 trained data abstractors, our paper is the largest multi-hospital study to examine  
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12 140 clinical aspects related to COVID-19 in Michigan.  
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- 14 141 • This is the first study to examine variations in clinical care processes, treatment  
15  
16 142 approaches and outcomes across hospitals.  
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- 18 143 • The high rate of use of non-evidence-based therapies for treating COVID-19 has  
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20 144 significant safety, economic and policy implications for the most critically ill  
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22 145 subsets in the hospital.  
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- 24 146 • Given the observational nature of the study and potential missing documentation  
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26 147 on symptoms, comorbidities, or treatments in the medical record, rationales for  
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28 148 treatment or management decisions cannot be determined.  
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30 149 • Our sampling frame may be biased as patients who remain hospitalized may not  
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32 150 be included in our cohort.  
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## 152 INTRODUCTION

153 Since detection in Wuhan, China,<sup>1 2</sup> over 4.5 million cases of COVID-19, caused  
154 by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been  
155 reported.<sup>3</sup> The United States (US) leads the world in the total number of cases, with  
156 over 1.5 million cases and 92,000 deaths reported as of May 20, 2020.<sup>4</sup> Within the US,  
157 Michigan remains one of the hardest hit states, with over 52,000 cases and 5,000  
158 deaths as of May 20, 2020.<sup>5</sup>

159 In the early days of the pandemic, data regarding patient characteristics,  
160 symptoms and signs and presentation and care strategies including aspects such as  
161 oxygenation, laboratory testing, and therapeutics were unclear. As well, short and long-  
162 term outcomes of patients exposed to these varying approaches was unknown. Some  
163 studies reported substantial variation in patient characteristics and treatment modalities  
164 across hospitals. But the extent of such variation and impact on outcomes remained  
165 unknown.

166 Michigan has a long history of collaborative quality improvement work that spans  
167 several disciplines including cardiovascular medicine, emergency medicine and hospital  
168 medicine, among others.<sup>6</sup> These consortia collect detailed clinical variables from  
169 hospitals to populate a central registry, allowing benchmarking and comparisons of care  
170 and outcomes. As the COVID-19 pandemic unfolded in Southeast Michigan, several  
171 consortia came together to focus data collection on patients hospitalized with COVID-  
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3 173 Using a well-established data collection strategy, we examined variations in  
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5 174 clinical care processes, treatment approaches, and clinical outcomes across Michigan  
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8 175 hospitals.  
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12 177 **METHODS**  
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14 178 A retrospective cohort design was used. Data were collected from medical  
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17 179 records of patients discharged between March 16, 2020 and May 11, 2020 from one of  
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19 180 32 Michigan hospitals who participate in collaborative quality initiatives sponsored by  
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21 181 Blue Cross Blue Shield of Michigan and Blue Care Network. Trained abstractors at each  
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23 182 hospital identified adult patients  $\geq 18$  years of age that underwent testing for COVID-19  
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25 183 via reverse-transcriptase polymerase chain reaction, including both positive cases and  
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27 184 persons under investigation (PUI) who eventually had a negative test. Abstractors were  
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29 185 asked to abstract as many eligible cases as possible for their hospital. Demographic  
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31 186 data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all  
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33 187 confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was  
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35 188 selected for detailed abstraction. Positive cases were sorted by day of admission (e.g.,  
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37 189 Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge)  
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39 190 was used to select patients for detailed abstraction. Patients who were pregnant,  
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41 191 transitioned to hospice within 3 hours of hospital admission, or discharged against  
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43 192 medical advice were excluded. All data were entered into a registry (Mi-COVID19) using  
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45 193 a structured data collection template. Of the 92 noncritical access, nonfederal hospitals  
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47 194 in Michigan, data from 32 hospitals (34.8%) was included in the sample. Included  
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3 195 hospitals are diverse in terms of size, teaching status, and ownership structure  
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5 196 (Appendix 1).  
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10 198 Patient characteristics including comorbidities, home medications, presenting  
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12 199 symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare  
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14 200 worker) were collected. Clinical data during hospitalization including location of care  
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16 201 (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body  
17  
18 202 mass index (BMI), laboratory and radiology findings and therapeutics were abstracted.  
19  
20 203 Organ supports such as mechanical ventilation and other respiratory support,  
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22 204 vasopressor use, renal replacement therapy (continuous renal replacement therapy  
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24 205 [CRRT] and intermittent hemodialysis [iHD]) were also collected.  
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28 206 The primary outcomes of interest included hospital mortality, receipt of cardiopulmonary  
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30 207 resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or pulmonary  
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32 208 embolism (PE) (based on positive imaging findings or initiation of empiric therapy for  
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34 209 presumed thrombosis). In addition, we performed pre-specified exploratory analyses in  
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36 210 hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine variation in  
37  
38 211 patient characteristics, management and outcomes. Specifically, we assessed variation  
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40 212 in use of COVID-19 specific treatments (defined as hydroxychloroquine, combination  
41  
42 213 hydroxychloroquine plus azithromycin, Vitamin C [oral or intravenous], IL-6 inhibitors or  
43  
44 214 remdesivir), antibiotic therapy, use of organ support (e.g., use of vasopressors,  
45  
46 215 mechanical ventilation and CPR), occurrence of venous thrombosis and in-hospital  
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48 216 mortality.  
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3 217 Descriptive statistics (e.g., mean, median, proportion) with measures of  
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5 218 dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize  
6  
7 219 data. Data that were not documented in medical records (e.g., values of certain  
8  
9 220 laboratory tests) were reported as missing. Pairwise comparisons were made using t-  
10  
11 221 tests for continuous data and chi-square tests for categorical data, respectively.  
12  
13 222 Differences across hospitals were tested using the Kruskal–Wallis test for continuous  
14  
15 223 variables and Pearson chi-square test for categorical variables. All statistical tests were  
16  
17 224 two-sided with  $p < 0.05$  considered statistically significant. The study was reviewed by the  
18  
19 225 Institutional Review Board of the University of Michigan and deemed “not regulated”. It  
20  
21 226 was not appropriate or possible to involve patients or the public in the design, or  
22  
23 227 conduct, or reporting, or dissemination plans of our research.  
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## 31 229 Patient and Public Involvement

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35 231 No patient involved.  
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## 39 233 Data Availability

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43 235 All data relevant to the study are included in the article or uploaded as supplementary  
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45 236 information.  
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## 50 51 238 **RESULTS**

### 52 53 239 **DEMOGRAPHIC DATA**

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3 240 Demographic-only data from 1,593 COVID-19 positive and 1,259 PUI discharges  
4  
5 241 from 32 Michigan hospitals were collected. PUIs had a median age of 64.4 years,  
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7 242 52.6% were male and 32.0% Black. COVID-19 positive patients had similar age and  
8  
9 243 gender as PUIs (63.9 years, and 52.1% male, respectively), but were more commonly  
10  
11 244 Black (57.1% vs. 32.0%,  $p<0.01$ ). In the demographic-only cohort, 398 (25.0%) COVID-  
12  
13 245 19 positive patients died during hospitalization.  
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17 246 Detailed data were abstracted on 1,024 (64.3%) randomly-selected COVID-19  
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19 247 positive patients. The most prevalent comorbidities were hypertension (65.4%),  
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21 248 diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%);  
22  
23 249 14.9% of patients had no comorbidities. Though 12.8% of patients had a diagnosis of  
24  
25 250 asthma and 11.2% had a diagnosis of chronic obstructive pulmonary disease, pre-  
26  
27 251 hospital use of inhaled steroids, long-acting beta-agonists and long-acting  
28  
29 252 antimuscarinic agents was low at 4.2%, 2.9%, and 0.5%, respectively. Current smoking  
30  
31 253 or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former  
32  
33 254 vaping. 115 (11.3%) patients were on immunosuppressive medications prior to  
34  
35 255 hospitalization, including 62 (6.1%) who were on oral steroids. Essential workers  
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37 256 comprised 12.8% of the cohort, including healthcare workers (7.0%) and service  
38  
39 257 workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of  
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41 258 patients resided in congregated living facilities, including nursing homes and homeless  
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43 259 shelters (**Table 1**).  
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## 50 51 261 **CLINICAL PRESENTATION AND INITIAL EVALUATION**

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3 262 In the detailed abstraction cohort (n=1,024), median duration of symptoms prior  
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5 263 to hospitalization was 6 days (IQR 3-9). The most common presenting symptoms were  
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7 264 cough (73.3%), fever (71.8%), and shortness of breath (72.2%); only 8% of patients did  
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9  
10 265 not report one of these 3 complaints (**Table 1**). Gastrointestinal symptoms including  
11  
12 266 nausea, vomiting and diarrhea occurred in 39.4% of patients. Over a third of patients  
13  
14 267 (37.2%) reported sick contacts at the time of admission, and 23.8% reported contact  
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16  
17 268 with a patient known to have COVID-19. The location of diagnostic testing for COVID-19  
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19 269 varied: 67.5% of patients were tested in hospital laboratories, 23.2% in commercial  
20  
21 270 laboratories, and 8.0% in the state laboratory. Patients were most commonly admitted  
22  
23 271 to a general medical/surgical ward (59.5%), but 15.7% were admitted to intermediate  
24  
25 272 care, 13.5% were admitted directly to ICU, and 11.3% were admitted to an observation  
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28 273 unit (**Figure 1**). A total of 419 (40.9%) of patients were admitted to a “cohorted”  
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30 274 (COVID-19 only) unit. At admission, 6.3% of patients had do not resuscitate/do not  
31  
32 275 intubate orders, which increased to 13.8% by discharge.

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35 276 Common laboratory testing on admission included white blood cell count  
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37 277 (93.7%), absolute lymphocyte count (75.8%), troponin (57.4%), lactate (57.2%), CRP  
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39 278 (44.9%) and procalcitonin (42.4%) (missingness by laboratory test are reported in the e-  
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41 279 Appendix 2). Among those with available laboratory data, patients who received ICU  
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43 280 treatment had higher levels of inflammatory markers at admission including d-dimer  
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45 281 (2.88mg/L vs. 1.65mg/L), ferritin (872ng/mL vs. 559ng/mL), CRP (24.3mg/dL vs.  
46  
47 282 13.8mg/dL) and LDH (476U/L vs. 346U/L) (**Table 2**). Chest imaging (X-ray or CT) was  
48  
49 283 performed in 528 (51.6%) patients within 1 day of admission and was more common in  
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51 284 ICU than general care patients (59.9% vs 49.1%, p=0.004). ICU patients were more  
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3 285 likely to have radiographic abnormalities on presentation. Viral respiratory panels, blood  
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5 286 cultures and sputum cultures were collected in 722 (51.0%) patients, but were positive  
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7 287 in only 48 (4.7%) patients; 9.5% of ICU patients vs. 3.3% of general care patients had a  
8  
9 288 viral or bacterial pathogen identified ( $p < 0.001$ ).

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## 290 **CRITICAL CARE TREATMENT**

291 Overall, 232 patients (22.7%) were treated in an ICU, including 138 (13.5%) who  
292 were admitted directly to an ICU, and 94 (9.2%) who were transferred to ICU a median  
293 of 2 days following admission. Median length of ICU stay was 6 days (IQR 3-9), which  
294 was similar in survivors vs. non-survivors (5 vs 6 days,  $p = 0.790$ ). Among 1,024 patients  
295 with detailed abstraction, the maximum respiratory support received was invasive  
296 mechanical ventilation in 161 patients (15.7%), non-invasive positive pressure  
297 ventilation in 15 (1.5%), heated high-flow nasal cannula in 60 (5.9%), oxygen mask  
298 ( $>40\%$   $FiO_2$  or  $>6L/min$ ) in 88 (8.6%), and nasal cannula oxygen (1-6L/min) in 441  
299 (43.1%) (**Table 3**). 259 (25.3%) patients received no respiratory support or oxygen  
300 therapy during hospitalization. Among 78 patients initiated on HHFNC, 13 (16.7%)  
301 progressed to invasive mechanical ventilation. Among 25 patients initiated on NIPPV,  
302 10 (40.0%) progressed to invasive mechanical ventilation. An additional 12 patients and  
303 2 patients, respectively, used HHFNC and NIPPV after extubation.

304 Upon initiation of mechanical ventilation, patients were predominantly treated  
305 with a volume control mode (75%), with high  $FIO_2$  ( $\geq 80\%$  in 49.1% of ventilated  
306 patients), and modest tidal volumes (median tidal volume 7.0 ml/kg predicted body  
307 weight, [IQR 6.2-8.0]). The median duration of mechanical ventilation was 6 days (IQR

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3 308 3-8 days). Prone positioning was documented in 18 patients, pulmonary vasodilators in  
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5 309 2 patients, and extra corporeal membrane oxygenation in 2 patients. CPR was  
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7 310 administered to 41 patients (4.0%), with only one patient surviving to hospital discharge.

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10 311 Vasopressors were used in 141 patients (13.8%), dialysis in 53 (5.2%), and  
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12 312 corticosteroids in 222 (21.7%) patients. 771 (75.3%) patients received broad-spectrum  
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14 313 antibiotics, with use being more common in the ICU than general wards (91.8% vs  
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16 314 70.5%,  $p<0.001$ ).

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## 20 21 316 **COVID-19 SPECIFIC THERAPIES**

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24 317 A total of 747 (72.9%) patients were treated with therapies targeting COVID-19,  
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26 318 or the body's response to COVID-19, most commonly hydroxychloroquine (51%),  
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28 319 hydroxychloroquine plus azithromycin (36%), and Vitamin C (10%). Treatment with IL-6  
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30 320 inhibitors and remdesivir was infrequent (27 and 17 patients, respectively). Use of  
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32 321 COVID-19 treatments was more common in ICU than general care patients (88% vs.  
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34 322 69%,  $p<0.001$ ). No patients in our sample received convalescent plasma. The  
35  
36 323 proportion of patients treated with COVID-19 specific therapies decreased over time  
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38 324 from 78.1% of patients admitted during March 8 to March 31 to 65.0% of patients  
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40 325 admitted during April 1 to May 11 ( $p<0.001$ ). Only 21 (2.0%) patients were enrolled into  
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42 326 a clinical trial (**Table 2**).

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## 46 47 328 **CLINICAL OUTCOMES**

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50 329 The in-hospital mortality rate for the full cohort of COVID-19 positive patients  
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52 330 (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age,  
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3 331 ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years  
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5 332 **(Figure 2)**. Among 219 decedents with detailed abstraction, 134 (61.5%) died following  
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7 333 ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219  
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9 334 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were  
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11 335 transitioned to comfort care prior to death. The most common causes of death were  
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13 336 refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock  
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15 337 (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9  
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17 338 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both  
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19 339 DVT and PE.  
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24 340 Among the 805 patients that survived to hospital discharge, 86% were  
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26 341 discharged home and 8% were discharged to a skilled nursing facility or rehabilitation  
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28 342 center. Only 1 patient (0.1%) was discharged to the Detroit field hospital **(Table 3)**.  
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### 33 344 **VARIATION ACROSS HOSPITALS**

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35 345 Among 14 hospitals with at least 25 detailed abstractions, substantial variation in  
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37 346 demographics, illness severity, care processes, treatments, and outcomes of COVID-19  
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39 347 positive patients were observed **(Table 4)**. The proportion of patients over 65 years of  
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41 348 age ranged from 30.2% to 65.5%, while the proportion of Black patients ranged from 0%  
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43 349 to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from  
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45 350 0% to 43.8%, while the proportion of patients who were transferred to an ICU after  
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47 351 admission ranged from 0% to 24.1%. Treatment in “cohorted” units ranged from 0% to  
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49 352 100%. Mechanical ventilation on admission ranged from 0% to 12.8% while use of  
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51 353 vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness  
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3 354 on presentation (defined as admission to an ICU with receipt of vasopressors or  
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5 355 mechanical ventilation on admission) varied from 0% to 7.7%.

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7 356 72.9% of patients received at least one COVID-19 specific therapy (e.g.,  
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9 357 hydroxychloroquine, hydroxychloroquine plus azithromycin, interleukin-6 inhibitor,  
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11 358 antiviral therapy), but use varied from 32% to 96.3% across sites. Similarly, 65% of  
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13 359 patients received concurrent antibiotics and COVID-19 specific treatment during  
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15 360 hospitalization, with frequency varying from 50% to 100% in ICU patients vs. 17% to  
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17 361 95% in general care patients.

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19 362 Mortality across hospitals varied from 7.9% to 45.7% of patients, and rates of  
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21 363 CPR before death ranged from 0% to 66.7%. Finally, rates of VTE also varied, occurring  
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23 364 in 0 to 11% of patients across hospitals.

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## 26 366 **DISCUSSION**

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28 367 While reports of COVID-19 patients from New York, Washington, and California  
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30 368 exist,<sup>7-9</sup> this is the first multi-center study to examine epidemiology, treatment and  
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32 369 outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-  
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34 370 hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients  
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36 371 treated at a diverse set of 32 academic and community hospitals.

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38 372 The demographics of our cohort differ from other cohorts. First, patients with  
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40 373 confirmed COVID-19 in Michigan are disproportionately Black (over half of our cohort).  
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42 374 This is in contrast to 32% of PUIs—indicating that the predominance of black patients  
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44 375 with COVID-19 is not a reflection of local demographics, but rather disproportionate  
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46 376 impact of COVID-19 on black patients. Second, in contrast to prior studies,<sup>1 7 10</sup> our

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3 377 cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this  
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5 378 difference are unclear.

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8 379 Consistent with prior reports, the main presenting symptoms were cough,  
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10 380 dyspnea and fever. Similar to other studies,<sup>11</sup> a substantial proportion of patients had  
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12 381 multiple comorbidities; but notably, 15% of our cohort had no known medical  
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14 382 problems.<sup>12</sup> We found that a substantial proportion of patients reported contact with a  
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16 383 known COVID-19 positive patient prior to developing symptoms. These findings mirror  
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18 384 those of a study from Shenzhen, China, where contacts of those with disease  
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20 385 experienced a significantly higher rate of infection than the general public.<sup>13</sup> Additionally,  
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22 386 patients underwent COVID-19 testing through a number of venues including hospital,  
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24 387 commercial and state-run laboratories, illustrating the myriad ways in which diagnosis  
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26 388 was obtained early in the outbreak when testing was limited.<sup>14</sup> Although only 14% of the  
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28 389 sample was admitted directly to an ICU, an additional 9% were transferred to an ICU  
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31 390 later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%,  
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33 391 but increased with age, consistent with prior studies.<sup>15</sup>

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37 392 A key finding of our study is that a majority of patients hospitalized for COVID-19  
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39 393 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the  
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41 394 body's immune response. More than half of patients were treated with  
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43 395 hydroxychloroquine, and an additional 6% were treated with antivirals or immune  
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45 396 modulating agents. Experts have increasingly questioned the use of unproven COVID-  
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47 397 19 therapies outside of a clinical trial,<sup>16</sup> and have argued that supportive care and trial  
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49 398 enrollment are the best options until data regarding efficacy of therapies accrues.<sup>17 18</sup>  
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52 399 Accumulating observational and trial data now suggest no benefit from  
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3 400 hydroxychloroquine,<sup>19-21</sup> and concerns regarding harm from empiric use remain.<sup>22</sup>  
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5 401 Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of  
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7 402 experimental COVID-19 therapies outside empiric studies represents a lost opportunity  
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9 403 for learning. It is also emblematic of the strong desire—particularly early in the  
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11 404 pandemic—to use therapies with a theoretical potential to target the virus even though  
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13 405 improved survival from critical illness is largely attributed to improvements in supportive  
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15 406 care.<sup>23</sup> Notably, we still do not have targeted therapies for sepsis or acute respiratory  
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17 407 distress syndrome, which are the major mechanisms by which patients die from COVID-  
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19 408 19 infection.

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23 409 Another strength of our study is the variation in clinical presentation and  
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25 410 outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19  
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27 411 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals.  
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29 412 While we are unable to ascertain reasons for such variation, we anecdotally observed  
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31 413 that practice evolved across hospitals over time. For example, at some Michigan  
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33 414 hospitals, routine use of hydroxychloroquine was common in the first few weeks of the  
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35 415 pandemic but curbed as trial data became available. In contrast, use of  
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37 416 hydroxychloroquine continues to be encouraged at other hospitals even today.<sup>24</sup> While it  
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39 417 is unclear if these practice changes influenced outcomes, future studies exploring the  
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41 418 rationale and impact of these changes on patients will be valuable.

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45 419 Our finding provides corroboratory information regarding the first COVID wave  
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47 420 within Michigan. For example, in a single center retrospective study, Imam and  
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49 421 colleagues found that advanced age and increasing number of comorbidities were  
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51 422 independent predictors of in-hospital mortality in hospitalized Michigan patients, just as  
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3 423 we did in our cohort.<sup>25</sup> Similarly, in two national population-level studies led by the  
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5 424 Centers for Disease Prevention and Control, individuals over 65 years of age and those  
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7 425 with  $\geq 3$  comorbidities experienced greater risk of hospitalization and adverse outcomes,  
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9  
10 426 again consistent with our findings.<sup>26 27</sup> Our findings are also similar to others regarding  
11  
12 427 disparities in COVID care and outcomes, especially among minority populations.<sup>28</sup>  
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14 428 Despite these findings, our study also differ from other national studies in important  
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16 429 ways. For example, we observed a low rate of readmissions in our cohort. In contrast,  
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18 430 Donnelly et al. using Veterans Health Affairs (VHA) data reported a readmission rate of  
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20 431 19.9% at 60-days.<sup>29</sup> While the reasons for this discrepancy are unclear, it is possible  
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22 432 that practice pattern differences including variation in threshold for readmission and  
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24 433 differences in patient characteristics may account for these discrepancies. As we begin  
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26 434 to understand and manage the chronic sequelae of acute COVID,<sup>30</sup> studies  
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28 435 understanding reasons for these pattern differences would be important. Another  
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30 436 important difference lies in the use of therapeutics targeting COVID-19. For example,  
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32 437 reports from New York City and Seattle show greater rates of use of remdesivir, and IL-  
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34 438 6 inhibitors.<sup>31 32</sup> Whether these differences were due to practice variation (which  
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36 439 occurred widely in the early US waves of COVID-19), vs. lack of access to therapeutics  
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38 440 which was also reported is unclear.

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40 441 Our study has limitations. First, given the observational nature of the study,  
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42 442 rationales for treatment or management decisions cannot be determined. Second,  
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44 443 because our sampling frame included patients that were discharged or deceased, our  
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46 444 findings may be biased as patients who remain hospitalized may not be included in our  
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48 445 cohort (potentially explaining lower duration of mechanical ventilation and hospital stay).  
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3 446 However, COVID-19 hospitalizations in Southeastern Michigan have been declining  
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5 447 since mid-April—limiting the degree of bias from exclusion of patients still in the  
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7 448 hospital. Third, while variation in care was observed, the implications of such variability  
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9 449 on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are  
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11 450 scarce and not without risks, reducing variation may improve patient safety and  
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13 451 resource use. Fourth, our study depends on available documentation, so symptoms,  
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15 452 comorbidities, or treatments not documented in the medical record may be omitted. For  
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17 453 example, it is possible that the low use of prone positioning observed in our cohort may  
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19 454 be due to incomplete documentation of this practice. Finally, we did not collect patient  
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21 455 identifiers, so inter-hospital transfers could be reported as two separate hospitalizations.  
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23 456 However, we did collect admission and discharge locations, and only 6% of the cohort  
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25 457 was transferred from another hospital.

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31 458 Our study also has strengths. Ours is the first multi-hospital study to examine  
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33 459 clinical aspects related to COVID-19 in Michigan. Through a rigorous data collection  
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35 460 structure including a well-defined sampling strategy and trained data abstractors, we  
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37 461 provide novel and detailed insights into clinical care during the pandemic. Second, we  
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39 462 were able to examine variation across sites finding substantial differences in clinical  
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41 463 care and outcomes across hospitals. To our knowledge, this is the first study to examine  
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43 464 differences in these important care processes, treatment approaches and outcomes  
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45 465 across sites. Third, we report a high rate of use of non-evidence-based therapies for  
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47 466 treating COVID-19. This finding has significant safety, economic and policy implications  
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49 467 for the most critically ill subsets in the hospital. Finally, data collection for this effort  
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3 468 remains ongoing, including longitudinal monitoring of patients after discharge. These  
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5 469 data will help shed new light on the post hospital sequelae of COVID-19.  
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8 470 Michigan remains one of the regions most affected by COVID-19. This multi-  
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10 471 center study provides granular clinical data regarding patients, care practices and  
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12 472 clinical outcomes in the state. The wide variation in observed practices and outcomes  
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14 473 suggests caution when interpreting findings from single center studies. Our study also  
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16 474 demonstrates the value of hospital collaboratives to help inform best practices.  
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## 21 476 Ethics Statement

22  
23  
24 477 The study was deemed “not regulated” by the University of Michigan IRB (HUM  
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26 478 00179611).  
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## 30 480 **BIBLIOGRAPHY**

- 31  
32  
33 481 1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in  
34  
35 482 China. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2002032 [published Online First:  
36  
37 483 2020/02/29]  
38  
39  
40 484 2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia  
41  
42 485 in China, 2019. *N Engl J Med* 2020;382(8):727-33. doi:  
43  
44 486 10.1056/NEJMoa2001017 [published Online First: 2020/01/25]  
45  
46  
47 487 3. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at  
48  
49 488 Johns Hopkins University. Available online at: <https://coronavirus.jhu.edu/maphtml>  
50  
51 489 Accessed April 20, 2020  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 490 4. Centers for Disease Control Cases of Coronavirus Disease (COVID-19) in the US.  
4  
5 491 Available online at: [https://www.cdc.gov/coronavirus/2019-ncov/cases-  
7 updates/cases-in-us.html](https://www.cdc.gov/coronavirus/2019-ncov/cases-<br/>6 updates/cases-in-us.html). Accessed April 20, 2020.  
8 492  
9  
10 493 5. Michigan.gov. Coronavirus Resources - Confirmed cases by Jurisdiction. Available  
11  
12 494 online at: [https://www.michigan.gov/coronavirus/0,9753,7-406-98163-520743--  
14 .00.html](https://www.michigan.gov/coronavirus/0,9753,7-406-98163-520743--<br/>13 .00.html). Accessed April 20, 2020.  
15 495  
16  
17 496 6. Blue Cross Blue Shield Collaborative Quality Initiatives. Available online at:  
18  
19 497 [https://www.bcbsm.com/providers/value-partnerships/collaborative-quality-  
21 initiatives.html](https://www.bcbsm.com/providers/value-partnerships/collaborative-quality-<br/>20 initiatives.html). Accessed April 20, 2020.  
22 498  
23  
24 499 7. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical Characteristics of Covid-19 in New York  
25  
26 500 City. *N Engl J Med* 2020 doi: 10.1056/NEJMc2010419 [published Online First:  
27  
28 501 2020/04/18]  
29  
30  
31 502 8. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the  
32  
33 503 Seattle Region - Case Series. *N Engl J Med* 2020 doi: 10.1056/NEJMoa2004500  
34  
35 504 [published Online First: 2020/04/01]  
36  
37  
38 505 9. Myers LC, Parodi SM, Escobar GJ, et al. Characteristics of Hospitalized Adults With  
39  
40 506 COVID-19 in an Integrated Health Care System in California. *JAMA* 2020 doi:  
41  
42 507 10.1001/jama.2020.7202 [published Online First: 2020/04/25]  
43  
44  
45 508 10. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of  
46  
47 509 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy  
48  
49 510 Region, Italy. *JAMA* 2020 doi: 10.1001/jama.2020.5394 [published Online First:  
50  
51 511 2020/04/07]  
52  
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3 512 11. Xie J, Tong Z, Guan X, et al. Clinical Characteristics of Patients Who Died of  
4  
5 513 Coronavirus Disease 2019 in China. *JAMA Netw Open* 2020;3(4):e205619. doi:  
6  
7 514 10.1001/jamanetworkopen.2020.5619 [published Online First: 2020/04/11]  
8  
9  
10 515 12. Gold JAW, Wong KK, Szablewski CM, et al. Characteristics and Clinical Outcomes  
11  
12 516 of Adult Patients Hospitalized with COVID-19 - Georgia, March 2020. *MMWR*  
13  
14 517 *Morb Mortal Wkly Rep* 2020;69(18):545-50. doi: 10.15585/mmwr.mm6918e1  
15  
16 518 [published Online First: 2020/05/08]  
17  
18  
19 519 13. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases  
20  
21 520 and 1286 of their close contacts in Shenzhen, China: a retrospective cohort  
22  
23 521 study. *Lancet Infect Dis* 2020 doi: 10.1016/S1473-3099(20)30287-5 [published  
24  
25 522 Online First: 2020/05/01]  
26  
27  
28 523 14. Sharfstein JM, Becker SJ, Mello MM. Diagnostic Testing for the Novel Coronavirus.  
29  
30 524 *JAMA* 2020 doi: 10.1001/jama.2020.3864 [published Online First: 2020/03/10]  
31  
32  
33 525 15. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,  
34  
35 526 Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19  
36  
37 527 in the New York City Area. *JAMA* 2020 doi: 10.1001/jama.2020.6775 [published  
38  
39 528 Online First: 2020/04/23]  
40  
41  
42 529 16. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America  
43  
44 530 Guidelines on the Treatment and Management of Patients with COVID-19. *Clin*  
45  
46 531 *Infect Dis* 2020 doi: 10.1093/cid/ciaa478 [published Online First: 2020/04/28]  
47  
48  
49 532 17. Rice TW, Janz DR. In Defense of Evidence-Based Medicine for the Treatment of  
50  
51 533 COVID-19 ARDS. *Ann Am Thorac Soc* 2020 doi: 10.1513/AnnalsATS.202004-  
52  
53 534 325IP [published Online First: 2020/04/23]  
54  
55  
56  
57  
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60

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2  
3 535 18. Waterer GW, Rello J, Wunderink RG. SARS-CoV-2: First Do No Harm. *Am J Respir*  
4  
5 536 *Crit Care Med* 2020 doi: 10.1164/rccm.202004-1153ED [published Online First:  
6  
7 537 2020/04/21]
- 8  
9  
10 538 19. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to  
11  
12 539 moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ*  
13  
14 540 2020;369:m1849. doi: 10.1136/bmj.m1849 [published Online First: 2020/05/16]
- 15  
16  
17 541 20. Mahevas M, Tran VT, Roumier M, et al. Clinical efficacy of hydroxychloroquine in  
18  
19 542 patients with covid-19 pneumonia who require oxygen: observational  
20  
21 543 comparative study using routine care data. *BMJ* 2020;369:m1844. doi:  
22  
23 544 10.1136/bmj.m1844 [published Online First: 2020/05/16]
- 24  
25  
26 545 21. Rosenberg ES, Dufort EM, Udo T, et al. Association of Treatment With  
27  
28 546 Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With  
29  
30 547 COVID-19 in New York State. *JAMA* 2020 doi: 10.1001/jama.2020.8630  
31  
32 548 [published Online First: 2020/05/12]
- 33  
34  
35 549 22. Bessiere F, Rocchia H, Deliniere A, et al. Assessment of QT Intervals in a Case  
36  
37 550 Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated  
38  
39 551 With Hydroxychloroquine Alone or in Combination With Azithromycin in an  
40  
41 552 Intensive Care Unit. *JAMA Cardiol* 2020 doi: 10.1001/jamacardio.2020.1787  
42  
43 553 [published Online First: 2020/05/02]
- 44  
45  
46  
47 554 23. Angus DC. Optimizing the Trade-off Between Learning and Doing in a Pandemic.  
48  
49 555 *JAMA* 2020 doi: 10.1001/jama.2020.4984 [published Online First: 2020/04/01]  
50  
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3 556 24. Wells K. Hospitals Vary Treatment for Coronavirus Patients. *National Public Radio*  
4  
5 557 2020; Available online at: <https://www.npr.org/2020/05/18/857727140/hospitals->  
6  
7 [vary-treatment-for-coronavirus-patients](https://www.npr.org/2020/05/18/857727140/hospitals-vary-treatment-for-coronavirus-patients). Accessed May 19, 2020.  
8 558  
9  
10 559 25. Imam Z, Odish F, Gill I, et al. Older age and comorbidity are independent mortality  
11  
12 560 predictors in a large cohort of 1305 COVID-19 patients in Michigan, United  
13  
14 561 States. *J Intern Med* 2020;288(4):469-76. doi: 10.1111/joim.13119 [published  
15  
16 Online First: 2020/06/05]  
17 562  
18  
19 563 26. Kim L, Garg S, O'Halloran A, et al. Risk Factors for Intensive Care Unit Admission  
20  
21 564 and In-hospital Mortality Among Hospitalized Adults Identified through the US  
22  
23 565 Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance  
24  
25 Network (COVID-NET). *Clin Infect Dis* 2021;72(9):e206-e14. doi:  
26 566  
27 10.1093/cid/ciaa1012 [published Online First: 2020/07/17]  
28 567  
29  
30 568 27. Ko JY, Danielson ML, Town M, et al. Risk Factors for Coronavirus Disease 2019  
31  
32 569 (COVID-19)-Associated Hospitalization: COVID-19-Associated Hospitalization  
33  
34 570 Surveillance Network and Behavioral Risk Factor Surveillance System. *Clin*  
35  
36 571 *Infect Dis* 2021;72(11):e695-e703. doi: 10.1093/cid/ciaa1419 [published Online  
37  
38 572 First: 2020/09/19]  
39  
40  
41 573 28. Price-Haywood EG, Burton J, Fort D, et al. Hospitalization and Mortality among  
42  
43 574 Black Patients and White Patients with Covid-19. *N Engl J Med*  
44  
45 575 2020;382(26):2534-43. doi: 10.1056/NEJMsa2011686 [published Online First:  
46  
47 576 2020/05/28]  
48  
49  
50 577 29. Donnelly JP, Wang XQ, Iwashyna TJ, et al. Readmission and Death After Initial  
51  
52 578 Hospital Discharge Among Patients With COVID-19 in a Large Multihospital  
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3 579 System. *JAMA* 2021;325(3):304-06. doi: 10.1001/jama.2020.21465 [published  
4  
5 580 Online First: 2020/12/15]  
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8 581 30. Mahase E. Covid-19: What do we know about "long covid"? *BMJ* 2020;370:m2815.  
9  
10 582 doi: 10.1136/bmj.m2815 [published Online First: 2020/07/16]  
11  
12 583 31. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,  
13  
14 584 Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19  
15  
16 585 in the New York City Area. *JAMA* 2020;323(20):2052-59. doi:  
17  
18 586 10.1001/jama.2020.6775 [published Online First: 2020/04/23]  
19  
20  
21 587 32. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in  
22  
23 588 the Seattle Region - Case Series. *N Engl J Med* 2020;382(21):2012-22. doi:  
24  
25 589 10.1056/NEJMoa2004500 [published Online First: 2020/04/01]  
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592 **Table 1. Demographic and Clinical Characteristics of COVID-19 Positive Patients**  
 593 **(n=1,024)**  
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Residence prior to hospitalization - no. (%)		
	Home	824 (80.5%)
	Congregated living facility <sup>1</sup>	165 (16.1%)
	Sub-acute rehabilitation facility	9 (0.9%)
	Unknown	18 (1.8%)
Admission location - no. (%)		
	Emergency department	951 (92.9%)
	Transfer from Another Hospital	60 (5.9%)
	Direct admission	7 (0.7%)
Median age (IQR) - yr		63.3 (50.9-74.4)
Male Sex - no. (%)		533 (52.1%)
Race - no. (%)		
	Black	526 (51.4%)
	White	390 (38.1%)
	Unknown	45 (4.4%)
	Asian	30 (2.9%)
	Other	26 (2.5%)
	Native	4 (0.4%)
	Islander	3 (0.3%)
Ethnicity - no. (%)		
	Non-Hispanic	873 (85.3%)
	Hispanic	30 (2.9%)
	Unknown	117 (11.4%)
Insurance – no. (%)		
	Medicare	497 (48.5%)
	Commercial	251 (24.5%)
	Medicaid	128 (12.5%)
	Self-pay	29 (2.8%)
	Other <sup>2</sup>	117 (11.4%)
BMI - median (IQR)		30.6 (25.9-37.1)
Smoking history - no. (%)		
	Never	615 (60.2%)
	Former	279 (27.3%)
	Current	61 (6.0%)
	Unknown	65 (6.4%)
Vaping history - no. (%)		
	Never	645 (63.2%)
	Former	366 (35.8%)
	Current	6 (0.6%)
	Unknown	3 (0.3%)
Coexisting disorder - no. (%)		
	Hypertension	670 (65.4%)
	Diabetes	377 (36.8%)
	Cardiovascular Disease	266 (26.0%)
	Moderate/ Severe Kidney Disease	239 (23.3%)
	Asthma	132 (12.9%)
	CHF/Cardiomyopathy	131 (12.8%)
	Dementia	123 (12.0%)
	Chronic Obstructive Pulmonary Disease	115 (11.2%)
	Cerebrovascular disease/ paraplegia	97 (9.5%)

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3	Cancer <sup>3</sup>	77 (7.5%)
4	Peripheral Vascular Disorders	41 (4.0%)
5	Chronic Pulmonary Disease (non-asthma/COPD)	35 (3.4%)
6	Rheumatoid Arthritis	29 (2.8%)
7	Peptic Ulcer Disease	10 (1.0%)
8	HIV/AIDS	7 (0.7%)
9	Organ transplant	8 (0.8%)
10	Inflammatory Bowel Disease	8 (0.8%)
11	No reported comorbidities	152 (14.9%)
12	Home Medications	
13	ACE Inhibitors	180 (17.6%)
14	Steroids/immunosuppressive therapy	115 (11.3%)
15	ARBs	136 (13.3%)
16	NSAIDs	182 (17.8%)
17	Statins	378 (37.0%)
18	Beta Blockers	298 (29.2%)
19	Anticoagulants	149 (14.6%)
20	Oral Steroids <sup>4</sup>	62 (6.1%)
21	Inhaled steroids	43 (4.2%)
22	Inhaled long-acting beta-agonist	30 (2.9%)
23	Inhaled long-acting anti-cholinergic	5 (0.5%)
24	Home oxygen therapy	36 (3.5%)
25	Duration of symptoms before admission, days - median (IQR)	6 (3-9)
26	Respiratory symptoms - no. (%)	
27	Cough (New or Worsening)	751 (73.3%)
28	Fever - no. (%)	735 (71.8%)
29	Fever (99.0 - 100.4 [F])	151 (14.7%)
30	Fever ( >100.4 [F])	390 (38.1%)
31	Subjective fever	194 (18.9%)
32	Dyspnea / shortness of breath	739 (72.2%)
33	Nausea/vomiting or diarrhea	403 (39.4%)
34	Fatigue	361 (35.3%)
35	Myalgias	264 (25.8%)
36	Weakness	253 (24.7%)
37	Sputum production	146 (14.3%)
38	Altered Mental Status	144 (14.1%)
39	Non-pleuritic chest pain	100 (9.8%)
40	Generalized malaise	91 (8.9%)
41	Rhinorrhea	75 (7.3%)
42	Pleuritic chest pain	75 (7.3%)
43	No reported symptoms	14 (1.4%)
44	Sick contacts - no. (%)	381 (37.2%)
45	Known COVID-19 positive	244 (23.8%)
46	Unknown COVID-19 status	236 (23.0%)
47	Healthcare worker - no. (%)	72 (7.0%)
48	Service worker - no. (%) <sup>5</sup>	59 (5.8%)
49	Initial location of admission - no. (%)	
50	General Medical/Surgical ward	608 (59.5%)
51	ICU	138 (13.5%)
52	Step-down unit	160 (15.7%)
53	Observation unit	115 (11.3%)
54	Missing/Unknown	3 (0.3%)
55	Admitted to COVID-19 specific (i.e., cohorted) unit	419 (40.9%)
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<i>Advanced Directives on admission</i>		
	DNR/DNI	64 (6.3%)
	No CPR (intubation OK)	19 (1.9%)
	No intubation (CPR OK)	3 (0.3%)
<p>Abbreviations: COVID-19, coronavirus disease 2019; SE=standard error; IQR, inter-quartile range</p> <p><sup>1</sup> <i>Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.</i></p> <p><sup>2</sup> <i>Includes other payers, Michigan, out-of-state and government.</i></p> <p><sup>3</sup> <i>Includes leukemia, lymphoma, hematologic cancer and any malignancy.</i></p> <p><sup>4</sup> <i>Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.</i></p> <p><sup>5</sup> <i>Service workers include food service, transportation, postal/delivery and other related fields.</i></p>		

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**Table 2 – Clinical and Laboratory Data in COVID-19 Positive Patients by ICU-status (n=1,024)**

	Ever ICU (n = 232)	General Ward (n = 792)	p
<b>Vital signs on day of hospital admission, no. (%)</b>			
Fever (>100.4 [F])	95 (40.9%)	295 (37.2%)	0.3073
Hypoxia / new or escalated O2 requirement	142 (61.2%)	257 (32.4%)	<.0001
Supplemental oxygen use	96 (41.4%)	145 (18.3%)	<.0001
Respiratory rate > 20	139 (59.9%)	306 (38.6%)	<.0001
Heart rate > 100 per minute	99 (42.7%)	321 (40.5%)	0.5596
Systolic blood pressure < 100 mmHg	27 (11.6%)	45 (5.7%)	0.0018
<b>Day 1 laboratory measures, median (IQR)</b>			
Hemoglobin	13.2 (11.4-14.7)	13.2 (12.0-14.6)	0.4573
White blood cell count, K/uL	7.3 (5.5-9.7)	6.5 (4.8-8.4)	<.0001
Absolute lymphocyte count, K/uL	0.80 (0.60-1.20)	1.00 (0.70-1.30)	0.3440
Platelet count, K/uL	197 (149-256)	204 (159-268)	0.4875
ALT, IU/L	32.0 (20.0-60.0)	27.0 (18.0-41.0)	0.2228
Lactate, mmol/L	1.6 (1.2-2.5)	1.4 (1.0-1.8)	0.0010
Troponin pg/mL	9 (0-38)	0 (0-12)	0.5872
Brain Natriuretic Peptide (BNP), pg/mL	79 (34-236)	49 (18-157)	0.0088
Procalcitonin, ng/mL	0.30 (0.17-0.94)	0.12 (0.06-0.29)	0.5054
D-dimer, mg/L	2.88 (1.19-35.00)	1.65 (0.59-368.00)	0.8240
Ferritin, ng/mL	872 (379-1531)	559 (237-1019)	0.1074
CRP, mg/dL	24.3 (12.0-107.1)	13.8 (5.8-66.2)	0.0031
LDH, IU/L	476 (337-668)	346 (254-455)	<.0001
Creatinine, mg/dL	1.3 (1.0-2.0)	1.1 (0.8-1.5)	0.5736
Total Bilirubin, mg/dL	0.6 (0.4-0.9)	0.5 (0.4-0.8)	0.7147
Respiratory viral panel positive for non-COVID-19 respiratory virus	2 (0.9%)	7 (0.9%)	0.9443
Positive blood culture within 1 day of admission	7 (3.0%)	9 (1.1%)	0.0422
Positive respiratory culture within 1 day of admission	4 (1.7%)	4 (0.5%)	0.0636
Any Chest imaging <sup>1</sup>	139 (59.9%)	389 (49.1%)	0.0038
Chest X-ray	118 (50.9%)	322 (40.7%)	0.0058
Chest Computed Tomography	34 (14.7%)	106 (13.4%)	0.6201
<b>Imaging findings - no. (%)</b>			
Pneumonia	61 (26.3%)	100 (12.6%)	<.0001
Non-specified opacities/air-space disease	84 (36.2%)	161 (20.3%)	<.0001
Pleural effusion	32 (13.8%)	37 (4.7%)	<.0001
Normal/no abnormalities	5 (2.2%)	30 (3.8%)	0.2287
Pulmonary Edema	25 (10.8%)	29 (3.7%)	<.0001
CT with Ground Glass Infiltrates	14 (6.0%)	58 (7.3%)	0.4995

<b>Respiratory support on day of admission - no. (%)</b>				
	Invasive mechanical ventilation	46 (19.8%)	2 (0.3%)	<.0001
	Non-invasive positive pressure	5 (2.2%)	2 (0.3%)	0.0020
	HHFNC	5 (2.2%)	5 (2.2%)	0.1905
	Oxygen mask (>40% <i>fio</i> <sub>2</sub> )	17 (7.3%)	20 (2.6%)	0.0006
	Nasal cannula oxygen, 1-6L	76 (32.8%)	261 (33.0%)	0.9555
	No supplemental oxygen	83 (8.1%)	502 (49.0%)	<.0001
<b>Treatments during hospitalization - no. (%)</b>				
<i>Covid-19 Specific treatment(s)</i>				
	Hydroxychloroquine	154 (66.4%)	364 (46.0%)	<.0001
	Hydroxychloroquine + Azithromycin	112 (48.3%)	260 (32.8%)	<.0001
	Vitamin C (PO or IV)	35 (15.1%)	68 (8.6%)	0.0038
	Remdesivir	7 (3.0%)	10 (1.3%)	0.0658
	IL-6 receptor inhibitor	27 (11.6%)	. (.%)	<.0001
	<i>Corticosteroids</i> <sup>2</sup>	79 (34.1%)	143 (18.1%)	<.0001
	<i>Antibiotics</i>	213 (91.8%)	558 (70.5%)	<.0001
	Azithromycin	149 (64.2%)	415 (52.4%)	0.0014
	Ceftriaxone	124 (53.4%)	345 (43.6%)	0.0079
	Cefepime	90 (38.8%)	79 (10.0%)	<.0001
	Doxycycline	37 (15.9%)	111 (14.0%)	0.4615
	Vancomycin	115 (49.6%)	106 (13.4%)	<.0001
	Linezolid	12 (5.2%)	8 (1.0%)	<.0001
	Anti-pseudomonals <sup>3</sup>	123 (53.0%)	115 (14.5%)	<.0001
	<i>Antivirals</i> <sup>4</sup>	1 (0.4%)	13 (1.6%)	0.1626
	<i>Enrolled in clinical trial</i>	10 (4.3%)	12 (1.5%)	0.0098
Abbreviations: COVID-19=coronavirus disease 2019; HHFNC=heated high flow nasal cannula; SE=standard error.				
<sup>1</sup> Includes chest imaging results 7 days before hospital encounter <sup>2</sup> Hydrocortisone, Methylprednisolone, prednisolone or prednisone <sup>3</sup> Cefepime, gentamicin, imipenem, meropenem, piperacillin-tazobactam, ceftazadime, aztreonam or tobramycin <sup>4</sup> Non-remdesivir antivirals including Oseltamivir, Lopinavir/Ritonavir, Ribavirin, others				

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**Table 3. Organ support for COVID-19 Positive Patients by Discharge Status (n=1,024)**

	All patients (n =1,024)	Discharged Alive n = 805	Died in Hospital n = 219
Treated in an ICU	232 (22.7%)	101 (12.5%)	131 (59.8%)
<i>Respiratory support ever received, no. (%)*</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure ventilation	27 (2.6%)	10 (1.2%)	17 (7.8%)
HHFNC	90 (8.8%)	57 (7.1%)	33 (15.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	159 (15.5%)	76 (9.4%)	83 (37.9%)
<i>Maximum respiratory support received, no. (%)**</i>			
Invasive mechanical ventilation	161 (15.7%)	47 (5.8%)	114 (52.1%)
Non-invasive positive pressure	15 (1.5%)	6 (0.7%)	9 (4.1%)
HHFNC	60 (5.9%)	40 (5.0%)	20 (9.1%)
Oxygen mask (>40%FIO <sub>2</sub> )	88 (8.6%)	48 (6.0%)	40 (18.3%)
Nasal canula oxygen, 1-6L/min	441 (43.1%)	415 (51.6%)	26 (11.9%)
No respiratory support	259 (25.3%)	249 (30.9%)	10 (4.6%)
<i>Max FIO<sub>2</sub> received, no. (%)</i>			
91-100%	126 (12.3%)	34 (4.2%)	92 (42%)
81-90%	30 (2.9%)	13 (1.6%)	17 (7.8%)
71-80%	86 (8.4%)	42 (5.2%)	44 (20.1%)
61-70%	16 (1.6%)	9 (1.1%)	7 (3.2%)
51-60%	26 (2.5%)	14 (1.7%)	12 (5.5%)
41-50%	24 (2.3%)	20 (2.5%)	4 (1.8%)
31-40%	170 (16.6%)	144 (17.9%)	26 (11.9%)
21-30%	287 (28%)	280 (34.8%)	7 (3.2%)
<i>Non-respiratory organ support received, no. (%)</i>			
Vasopressor	141 (13.8%)	35 (4.3%)	106 (48.4%)
Any dialysis***	53 (5.2%)	17 (2.1%)	36 (16.4%)
CRRT only	17 (1.7%)	1 (0.1%)	16 (7.3%)
iHD only	28 (2.7%)	15 (1.9%)	13 (5.9%)
CPR	41 (4.0%)	1 (0.1%)	40 (18.3%)
Abbreviations: SE=standard error; ECMO=extra-corporeal membrane oxygenation; HHFNC=heated high flow nasal cannula; FiO <sub>2</sub> =fraction of inspired oxygen; L= liters/min; ICU=intensive care unit; PE=pulmonary embolism; DVT=deep vein thrombosis; CPR=cardiopulmonary resuscitation; CRRT=continuous renal replacement therapy; iHD=intermittent hemodialysis;			
* Represents any use of respiratory support. Numbers are greater than 100% as one patient may have received multiple treatments.			
** Represents the highest level of respiratory support a patient received during hospitalization.			
*** Includes Intermittent Hemodialysis (iHD), dialysis and ultrafiltration			

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**Table 4. Variation in Clinical Care and Outcomes in COVID-19 Positive Patients Across Hospitals**

	Range across Hospitals							<i>p</i> <sup>†</sup>
	Min	10 <sup>th</sup> Pctl	25 <sup>th</sup> Pctl	Median	75 <sup>th</sup> Pctl	90 <sup>th</sup> Pctl	Max	
Patient characteristics								
Age >65, %	30.2	35.3	39.6	51.3	56.8	64.4	65.5	<.0001
Black, %	0.0	17.7	29.7	46.2	76.4	93.7	94.6	<.0001
Male, %	39.2	45.6	47.1	53.0	56.8	72.4	73.8	0.07
Charlson comorbidity index, median	0.0	1.0	1.0	1.0	1.0	2.0	2.0	0.01
BMI, median	24.3	28.4	29.5	31.1	33.3	36.5	36.9	0.09
Age, median in years	39.0	46.5	60.8	62.4	66.4	73.5	76.0	<.0001
Admission information, %								
Hospital-to-hospital transfer	0.0	0.0	0.0	0.00	2.8	10.7	20.9	<.0001
Admitted directly to ICU	0.0	0.0	2.9	6.15	14.8	20.5	43.8	<.0001
Transferred from floor to ICU	0.0	0.0	0.0	8.4	17.6	18.8	24.1	0.09
Admitted to a Cohorted unit	0.0	2.1	18.6	67.9	85.71	96.3	97.1	<.0001
Severe illness on presentation <sup>2</sup>	0.0	0.00	0.00	0.0	3.7	7.1	7.7	0.09
Vasopressor use on day 1	0.0	0.00	0.00	2.1	6.4	10.3	14.8	0.04
Mechanical ventilation on day 1	0.0	0.00	0.00	2.51	8.6	11.1	12.8	0.03
Treatment, %								
Treated in a Cohorted Unit	0.0	0.00	6.3	57.1	90.9	100.0	100.0	<.0001
Treated in an ICU	4.2	5.4	14.0	19.1	31.0	38.5	62.5	<.0001
COVID-19 Specific treatment	32.4	57.1	69.2	76.4	81.4	90.2	96.3	<.0001
Concurrent antibiotic and COVID-19 specific treatment(s)	24.3	42.9	59.4	69.8	76.7	84.3	96.3	<.0001
Hydroxychloroquine	13.5	31.4	42.3	59.7	65.5	81.5	82.4	<.0001
Mechanical ventilation	2.1	2.7	6.4	10.9	31.0	38.5	40.6	<.0001
Vasopressors	2.2	2.9	7.0	12.1	25.0	32.1	32.5	<.0001
CPR before death	0.0	0.0	8.3	14.3	33.3	40.0	66.7	0.0102
Outcomes, %								
Days of mechanical ventilation, median <sup>3</sup>	1.0	1.0	1.0	5.0	8.0	8.0	9.0	0.01
Length of stay, median	2.0	3.0	3.0	4.5	6.0	8.0	8.5	<.0001
ICU length of stay, median <sup>4</sup>	1.0	2.0	3.5	5.0	6.5	7.5	9.5	0.01
DVT	0.0	0.0	0.0	0.0	2.1	3.5	7.1	0.05
VTE	0.0	0.0	0.0	2.9	5.2	6.3	10.7	0.20
PE	0.0	0.0	0.0	1.8	3.9	6.3	7.1	0.72
Discharge status, %								
Death	7.9	8.3	14.6	21.3	31.0	41.4	45.7	<.0001
Transferred to another hospital	0.0	0.0	0.0	0.0	1.6	2.7	5.1	0.07

Discharged home	42.3	48.2	62.1	67.5	72.9	80.0	82.5	<.0001
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<sup>1</sup> Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.

<sup>2</sup> Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.

<sup>3</sup> For patients ever on mechanical ventilation

<sup>4</sup> For patients ever in ICU

\* Variables marked with asterisk represent variation from the demographic cohort

Abbreviations: BMI=body mass index; ICU=intensive care unit; CPR=cardiopulmonary resuscitation; DVT=deep vein thrombosis; VTE=venous thromboembolism; PE=pulmonary embolism

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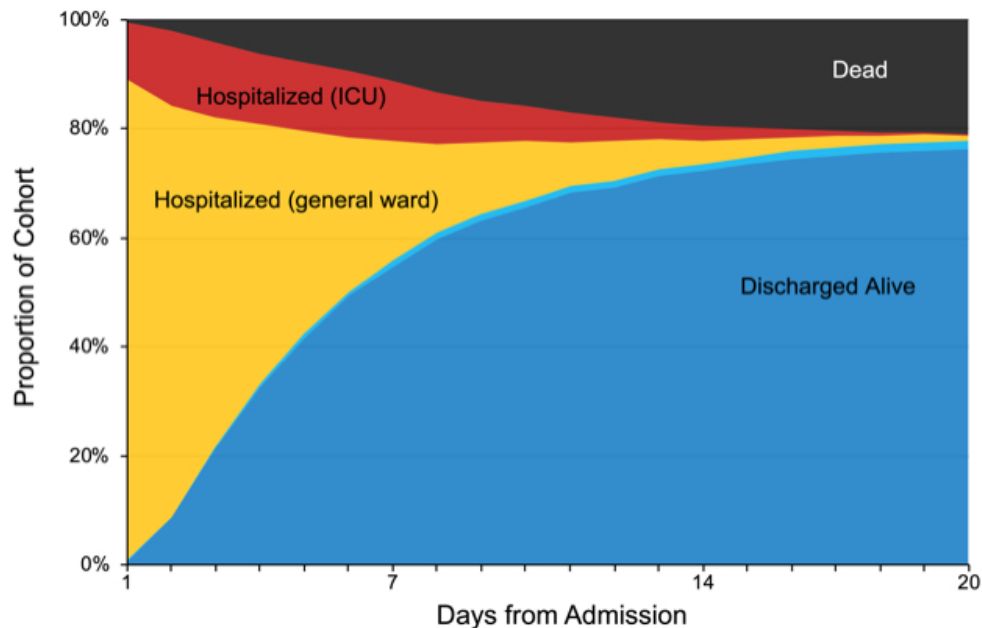
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3 **683 Figure Legend 1**

4 684  
5 685 *Legend. Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on*  
6 686 *general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a*  
7 687 *new hospital (light blue) and deceased over time to day 20 of hospital admission.*  
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10 **689 Figure Legend 2**

11 690  
12 691 *Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital*  
13 692 *by decade of age. Black shading indicates death whereas blue shading indicates discharge*  
14 693 *alive.*  
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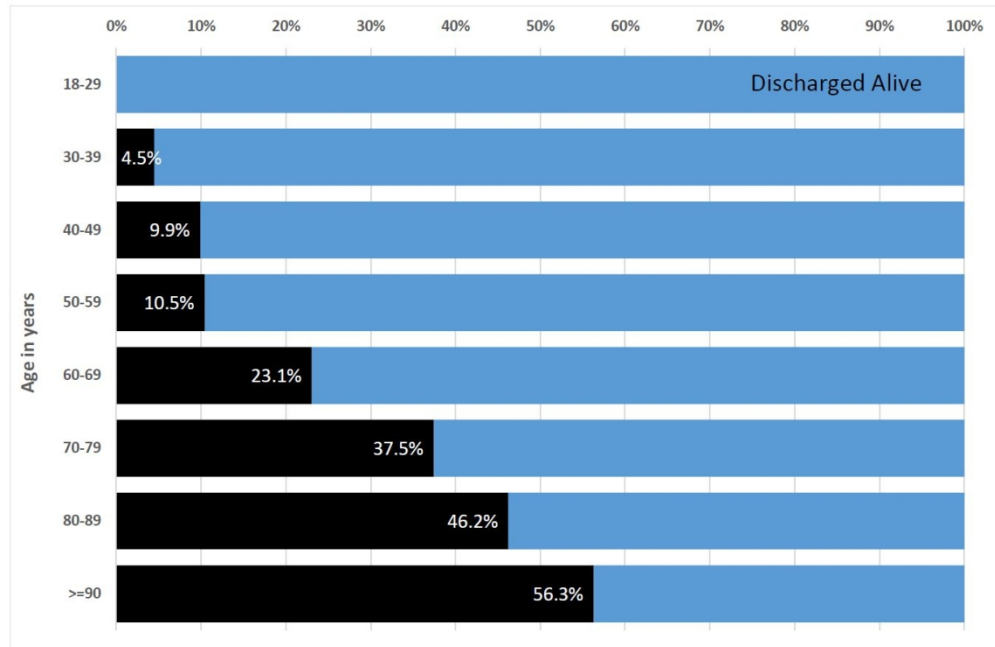
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Caption : Figure 1. Proportion of COVID-19 Positive Patients in hospital, ICU, dead, and discharged over time (n=1,024). Legend. Figure depicts the proportion of the N=1024 patient cohort who are hospitalized on general care/ward (yellow), hospitalized in ICU (red), discharged alive (blue), transferred to a new hospital (light blue) and deceased over time to day 20 of hospital admission.

27x17mm (600 x 600 DPI)





Caption : Figure 2. Mortality rate for COVID-19 positive patients by decade of age (demographic data cohort, n=1,593) Legend. Graph depicts the proportion of the demographic cohort (n=1593) who died in hospital by decade of age. Black shading indicates death whereas blue shading indicates discharge alive.

116x75mm (300 x 300 DPI)

## MI-COVID19 Sites

Hospital	Bed Size <sup>1</sup>	Total Patient Discharges <sup>2</sup>	Teaching Hospital Status	Ownership Status <sup>3</sup>	Location <sup>4</sup>
Hospital 1	632	30354	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 2	330	13159	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 3	250	12186	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 4	1070	61758	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 5	189	6142	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 6	193	9816	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 7	458	34863	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 8	215	7797	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 9	179	7254	No	Proprietary	Metropolitan
Hospital 10	434	26705	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 11	273	10815	Yes	Proprietary	Metropolitan
Hospital 12	584	19882	Yes	Proprietary	Metropolitan
Hospital 13	189	8639	No	Voluntary non-profit - Private	Metropolitan
Hospital 14	443	17240	Yes	Voluntary non-profit - Other	Metropolitan
Hospital 15	158	7704	Yes	Proprietary	Metropolitan
Hospital 16	317	15093	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 17	378	17969	Yes	Voluntary non-profit - Private	Metropolitan

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Hospital	Bed Size <sup>1</sup>	Total Patient Discharges <sup>2</sup>	Teaching Hospital Status	Ownership Status <sup>3</sup>	Location <sup>4</sup>
Hospital 18	196	9307	No	Voluntary non-profit - Private	Metropolitan
Hospital 19	283	15855	Yes	Voluntary non-profit - Church	Metropolitan
Hospital 20	208	10476	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 21	1059	44920	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 22	139	4362	No	Proprietary	Micropolitan
Hospital 23	79	3349	Yes	Voluntary non-profit - Private	Micropolitan
Hospital 24	328	15767	Yes	Voluntary non-profit - Other	Metropolitan
Hospital 25	391	21759	Yes	Voluntary non-profit - Other	Micropolitan
Hospital 26	537	30614	Yes	Voluntary non-profit - Church	Metropolitan
Hospital 27	133	3763	No	Voluntary non-profit - Private	Metropolitan
Hospital 28	136	2767	Yes	Voluntary non-profit - Other	Metropolitan
Hospital 29	443	19102	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 30	304	15804	Yes	Voluntary non-profit - Private	Metropolitan
Hospital 31	404	18345	Yes	Proprietary	Metropolitan
Hospital 32	109	32636	Yes	Voluntary non-profit - Other	Metropolitan

<sup>1</sup>Data obtained from 2015 Michigan Certificate of Need Annual Survey, Basic Total Licensed Beds Utilization Statistics. Retrieved 3/21/2017 from [http://www.michigan.gov/documents/mdhhs/Report\\_011 - Licensed Beds in Hospitals by County 538170 7.pdf](http://www.michigan.gov/documents/mdhhs/Report_011_-_Licensed_Beds_in_Hospitals_by_County_538170_7.pdf)

<sup>2</sup>Data obtained from American Hospital Directory, Inc.'s *Individual Hospital Statistics for Michigan*. Retrieved 6/1/2020 from [https://www.ahd.com/states/hospital MI.html](https://www.ahd.com/states/hospital_MI.html)

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3 <sup>3</sup>Data obtained from data.medicare.gov; Hospital General Information. Retrieved from 06/03/2020 from [https://data.cms.gov/provider-](https://data.cms.gov/provider-data/dataset/xubh-q36u)  
4 [data/dataset/xubh-q36u](https://data.cms.gov/provider-data/dataset/xubh-q36u)

5 <sup>4</sup>Data obtained from [https://www2.census.gov/geo/maps/metroarea/stcbsa\\_pg/Feb2013/cbsa2013\\_MI.pdf](https://www2.census.gov/geo/maps/metroarea/stcbsa_pg/Feb2013/cbsa2013_MI.pdf)  
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8 \* The American Hospital Directory reports data for Ascension Providence Hospital, Novi Campus and Ascension Providence  
9 Hospital, Southfield Campus together, so individual discharge numbers and teaching status for these two sites was not available.  
10 The data presented in this table represents numbers for both of these sites combined.  
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**Appendix: Availability of Laboratory Tests**

Variable	N	% missing
Hemoglobin (Hgb)	959	6.3%
WBC *	959	6.3%
Absolute Lymphocyte Count *	776	24.2%
Platelet	957	6.5%
ALT *	803	21.6%
Lactate	586	42.8%
Troponin	588	42.6%
Brain Natriuretic Peptide (BNP)	282	72.5%
Procalcitonin	434	57.6%
D-dimer	333	67.5%
Ferritin *	419	59.1%
CRP *	460	55.1%
Lactic Acid Dehydrogenase (LDH)	392	61.7%
pH* (imputed)	326	68.2%
Creatinine *	956	6.6%
Total Bilirubin	777	24.1%

## STROBE (Strengthening The Reporting of OBServational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	
<b>Introduction</b>			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
<b>Methods</b>			
Study Design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed  <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study Size	10	Explain how the study size was arrived at	
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical Methods	12	(a) Describe all statistical methods, including those used to control for confounding	
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed  <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed  <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	

Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
<b>Discussion</b>			
Key Results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
<b>Other Information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.**