BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044921
Article Type:	Original research
Date Submitted by the Author:	21-Sep-2020
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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

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Abstract Word Count: 256

Word Count: 3005

Conflicts of Interest: No relevant conflicts disclosed by coauthors.

Primary Funding Source: Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships program.

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Keywords:

Covid-19; Quality in Health care; Protocols and Guidelines

Additional Contributions & Acknowledgements:

The authors thank Qisu (Sue) Zhang, MPH, Tawny Czilok, RN, MHI, Liz Vasher, RN, Jessica Southwell, RN, MSN, Danny Nielsen, MS, and Jennifer Horowitz, MA for help with data analytics and project management.

We also thank all the BCBSM Collaborative Quality Initiatives (CQI's) that partnered together on data collection and offered project management/analytics support. Lastly, we are grateful to all of the hospitals who volunteered to be part of MiCOVID-19 including: Beaumont-Dearborn, Beaumont-Grosse Pointe, Beaumont- Farmington Hills, Beaumont- Royal Oak, Beaumont- Taylor, Beaumont- Trenton, Beaumont- Troy, Beaumont- Wayne, Bronson Battle Creek, Bronson Methodist, Detroit Medical Center-Detroit Receiving, Detroit Medical Center-Harper Hutzel, Detroit Medical Center-Detroit-Huron Valley Sinai, Henry Ford, Henry Ford Allegiance, Henry Ford Macomb, Henry Ford West Bloomfield, Henry Ford West Wyandotte, Holland Hospital, Hurley Medical Center, Lakeland Hospital, McLaren Flint, McLaren Greater Lansing, McLaren Port Huron, Mercy Health Muskegon, Mercy Health St. Mary's, Metro Health, Michigan Medicine, MidMichigan Alpena, MidMichigan Gratiot, MidMichigan Midland, Munson Medical Center, Oaklawn Hospital, Sinai Grace, Sparrow, St. Joseph Mercy Ann Arbor, St. Joseph Mercy Chelsea, St. Joseph Mercy Livingston, St. Joseph Mercy Oakland, St. Mary Mercy Livonia.

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.

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

LIMITATIONS

Rationales for management decisions could not be determined; findings may be biased by patients who remain hospitalized; implications of variability of clinical care on outcomes is unknown.

CONCLUSIONS

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

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,[1 2] over 4.5 million cases of COVID-19, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been reported.[3] 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.[4] 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.[5]

Michigan has a long history of collaborative quality improvement work that spans several disciplines including cardiovascular medicine, emergency medicine and hospital medicine, among others.[6] 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 ≥18 years of age that underwent testing for COVID-19 via reverse-transcriptase polymerase chain reaction, including both positive cases and

persons under investigation (PUI) who eventually had a negative test. Demographic data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was selected for detailed abstraction. Positive cases were sorted by day of admission (e.g., Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge) was used to select patients for detailed abstraction. Patients who were pregnant, transitioned to hospice within 3 hours of hospital admission, or discharged against medical advice were excluded. All data were entered into a registry (Mi-COVID19) using a structured data collection template.

Patient characteristics including comorbidities, home medications, presenting symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare worker) were collected. Clinical data during hospitalization including location of care (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body mass index (BMI), laboratory and radiology findings and therapeutics were abstracted. Organ supports such as mechanical ventilation and other respiratory support, vasopressor use, renal replacement therapy (continuous renal replacement therapy [CRRT] and intermittent hemodialysis [iHD]) were also collected.

The primary outcomes of interest included hospital mortality, receipt of cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric therapy for presumed thrombosis). In addition, we performed pre-specified exploratory analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine variation in patient characteristics, management and outcomes. Specifically, we

assessed variation in use of COVID-19 specific treatments (defined as hydroxychloroquine, combination hydroxychloroquine plus azithromycin, Vitamin C [oral or intravenous], IL-6 inhibitors or remdesivir), antibiotic therapy, use of organ support (e.g., use of vasopressors, mechanical ventilation and CPR), occurrence of venous thrombosis and in-hospital mortality.

Descriptive statistics (e.g., mean, median, proportion) with measures of dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize data. Data that were not documented in medical records (e.g., values of certain laboratory tests) were reported as missing. Pairwise comparisons were made using t-tests for continuous data and chi-square tests for categorical data, respectively. Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables. All statistical tests were two-sided with $p<0.05$ considered statistically significant. The study was reviewed by the Institutional Review Board and deemed “not regulated”. It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

DEMOGRAPHIC DATA

Demographic-only data from 1,593 COVID-19 positive and 1,259 PUI discharges from 32 Michigan hospitals were collected. PUIs had a median age of 64.4 years, 52.6% were male and 32.0% Black. COVID-19 positive patients had similar age and gender as PUIs (63.9 years, and 52.1% male, respectively), but were more commonly

Black (57.1% vs. 32.0%, p<0.01). In the demographic-only cohort, 398 (25.0%) COVID-19 positive patients died during hospitalization.

Detailed data were abstracted on 1,024 (64.3%) randomly-selected COVID-19 positive patients. The most prevalent comorbidities were hypertension (65.4%), diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%); 14.9% of patients had no comorbidities. Though 12.8% of patients had a diagnosis of asthma and 11.2% had a diagnosis of chronic obstructive pulmonary disease, pre-hospital use of inhaled steroids, long-acting beta-agonists and long-acting antimuscarinic agents was low at 4.2%, 2.9%, and 0.5%, respectively. Current smoking or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former vaping. 115 (11.3%) patients were on immunosuppressive medications prior to hospitalization, including 62 (6.1%) who were on oral steroids. Essential workers comprised 12.8% of the cohort, including healthcare workers (7.0%) and service workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of patients resided in congregated living facilities, including nursing homes and homeless shelters **(Table 1).**

CLINICAL PRESENTATION AND INITIAL EVALUATION

In the detailed abstraction cohort (n=1,024), median duration of symptoms prior to hospitalization was 6 days (IQR 3-9). The most common presenting symptoms were cough (73.3%), fever (71.8%), and shortness of breath (72.2%); only 8% of patients did not report one of these 3 complaints **(Table 1)**. Gastrointestinal symptoms including nausea, vomiting and diarrhea occurred in 39.4% of patients. Over a third of patients

(37.2%) reported sick contacts at the time of admission, and 23.8% reported contact with a patient known to have COVID-19. The location of diagnostic testing for COVID-19 varied: 67.5% of patients were tested in hospital laboratories, 23.2% in commercial laboratories, and 8.0% in the state laboratory. Patients were most commonly admitted to a general medical/surgical ward (59.5%), but 15.7% were admitted to intermediate care, 13.5% were admitted directly to ICU, and 11.3% were admitted to an observation unit **(Figure 1)**. A total of 419 (40.9%) of patients were admitted to a "cohorted" (COVID-19 only) unit. At admission, 6.3% of patients had do not resuscitate/do not intubate orders, which increased to 13.8% by discharge.

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% Fi02 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 (≥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

antibiotics, with use being more common in the ICU than general wards (91.8% vs 70.5%, p<0.001).

COVID-19 SPECIFIC THERAPIES

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

CLINICAL OUTCOMES

The in-hospital mortality rate for the full cohort of COVID-19 positive patients (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age, ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years **(Figure 2).** Among 219 decedents with detailed abstraction, 134 (61.5%) died following ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were transitioned to comfort care prior to death. The most common causes of death were

refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both DVT and PE.

Among the 805 patients that survived to hospital discharge, 86% were discharged home and 8% were discharged to a skilled nursing facility or rehabilitation center. Only 1 patient (0.1%) was discharged to the Detroit field hospital **(Table 3).**

VARIATION ACROSS HOSPITALS

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

72.9% of patients received at least one COVID-19 specific therapy (e.g., hydroxychloroquine, hydroxychloroquine plus azithromycin, interleukin-6 inhibitor, antiviral therapy), but use varied from 32% to 96.3% across sites. Similarly, 65% of

patients received concurrent antibiotics and COVID-19 specific treatment during hospitalization, with frequency varying from 50% to 100% in ICU patients vs. 17% to 95% in general care patients.

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

DISCUSSION

While reports of COVID-19 patients from New York, Washington, and California exist,[7-9] this is the first multi-center study to examine epidemiology, treatment and outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients treated at a diverse set of 32 academic and community hospitals.

The demographics of our cohort differ from other cohorts. First, patients with confirmed COVID-19 in Michigan are disproportionally Black (over half of our cohort). This is in contrast to 32% of PUIs—indicating that the predominance of black patients with COVID-19 is not a reflection of local demographics, but rather disproportionate impact of COVID-19 on black patients. Second, in contrast to prior studies,[1 7 10] our cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this difference are unclear.

Consistent with prior reports, the main presenting symptoms were cough, dyspnea and fever. Similar to other studies,[11] a substantial proportion of patients had multiple comorbidities; but notably, 15% of our cohort had no known medical

problems.[12] We found that a substantial proportion of patients reported contact with a known COVID-19 positive patient prior to developing symptoms. These findings mirror those of a study from Shenzen, China, where contacts of those with disease experienced a significantly higher rate of infection than the general public.[13] Additionally, patients underwent COVID-19 testing through a number of venues including hospital, commercial and state-run laboratories, illustrating the myriad ways in which diagnosis was obtained early in the outbreak when testing was limited.[14] Although only 14% of the sample was admitted directly to an ICU, an additional 9% were transferred to an ICU later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%, but increased with age, consistent with prior studies.[15]

A key finding of our study is that a majority of patients hospitalized for COVID-19 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the body's immune response. More than half of patients were treated with hydroxychloroquine, and an additional 6% were treated with antivirals or immune modulating agents. Experts have increasingly questioned the use of unproven COVID-19 therapies outside of a clinical trial,[16] and have argued that supportive care and trial enrollment are the best options until data regarding efficacy of therapies acrrues.[17 18] Accumulating observational and trial data now suggest no benefit from hydroxychloroquine,[19-21] and concerns regarding harm from empiric use remain.[22] Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of experimental COVID-19 therapies outside empiric studies represents a lost opportunity for learning. It is also emblematic of the strong desire—particularly early in the pandemic—to use therapies with a theoretical potential to target the virus even though

improved survival from critical illness is largely attributed to improvements in supportive care.[23] Notably, we still do not have targeted therapies for sepsis or acute respiratory distress syndrome, which are the major mechanisms by which patients die from COVID-19 infection.

Another strength of our study is the variation in clinical presentation and outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals. While we are unable to ascertain reasons for such variation, we anecdotally observed that practice evolved across hospitals over time. For example, at some Michigan hospitals, routine use of hydroxychloroquine was common in the first few weeks of the pandemic but curbed as trial data became available. In contrast, use of hydroxychloroquine continues to be encouraged at other hospitals even today.[24] While it is unclear if these practice changes influenced outcomes, future studies exploring the rationale and impact of these changes on patients will be valuable.

Our study has limitations. First, given the observational nature of the study, rationales for treatment or management decisions cannot be determined. Second, 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. Third, while variation in care was observed, the implications of such variability on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are

scarce and not without risks, reducing variation may improve patient safety and resource use. Fourth, our study depends on available documentation, so symptoms, comorbidities, or treatments not documented in the medical record may be omitted. For example, it is possible that the low use of prone positioning observed in our cohort may be due to incomplete documentation of this practice. Finally, we did not collect patient identifiers, so inter-hospital transfers could be reported as two separate hospitalizations. However, we did collect admission and discharge locations, and only 6% of the cohort was transferred from another hospital.

Our study also has strengths. 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. Second, 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. Third, 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. Finally, data collection for this effort remains ongoing, including longitudinal monitoring of patients after discharge. These data will help shed new light on the post hospital sequelae of COVID-19.

Michigan remains one of the regions most affected by COVID-19. This multi-center study provides granular clinical data regarding patients, care practices and clinical outcomes in the state. The wide variation in observed practices and outcomes

suggests caution when interpreting findings from single center studies. Our study also demonstrates the value of hospital collaboratives to help inform best practices.

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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[1]	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[2]	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%)

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

Advanced Directives on admission	
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

[1] *Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.*

[2] *Includes other payers, Michigan, out-of-state and government.*

[3] *Includes leukemia, lymphoma, hematologic cancer and any malignancy.*

[4] *Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.*

[5] *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*
Vital signs on day of hospital admission, no. (%)			
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
Day 1 laboratory measures, median (IQR)			
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[1]	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
Imaging findings - no. (%)			
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

Respiratory support on day of admission - no. (%)			
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%fio2)	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
Treatments during hospitalization - no. (%)			
Covid-19 Specific treatment(s)			
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
Corticosteroids[2]	79 (34.1%)	143 (18.1%)	<.0001
Antibiotics	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[3]	123 (53.0%)	115 (14.5%)	<.0001
Antivirals[4]	1 (0.4%)	13 (1.6%)	0.1626
Enrolled in clinical trial	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%)
*Respiratory support ever received, no.(%)**			
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_2)	159 (15.5%)	76 (9.4%)	83 (37.9%)
*Maximum respiratory support received, no. (%)***			
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_2)	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%)
Max FIO_2 received, no.(%)			
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%)
Non-respiratory organ support received, no. (%)			
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; Fi02=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							
	Min	10th Pctl	25th Pctl	Median	75th Pctl	90th Pctl	Max	*p*[1]
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[2]	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[3]	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[4]	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

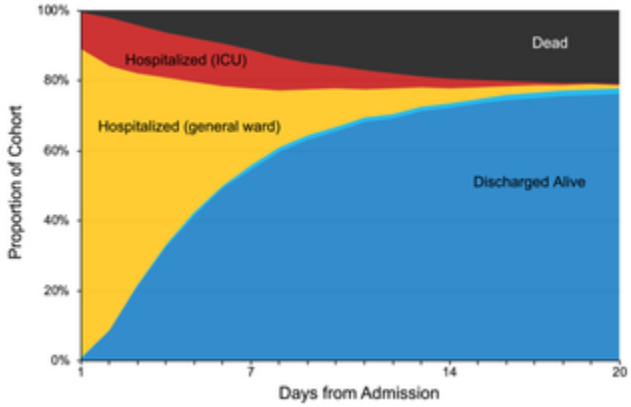
[1] Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.
[2] Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.
[3] For patients ever on mechanical ventilation
[4] 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

Figure Legend 1

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.

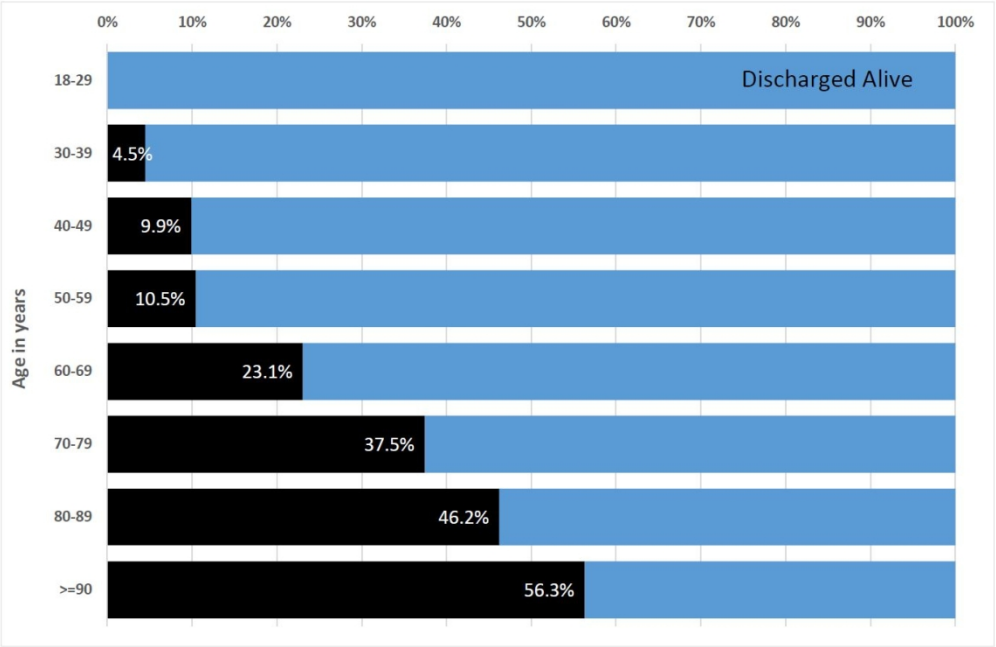
Figure Legend 2

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.



Caption : 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 (300 x 300 DPI)



Caption : 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.

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	
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
Methods			
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*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
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) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—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	
Discussion			
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	
Other Information			
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.

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044921.R1
Article Type:	Original research
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
Primary Subject Heading:	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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Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals

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Abstract Word Count: 299

Word Count: 3109

Conflicts of Interest: No relevant conflicts disclosed by coauthors.

Primary Funding Source: Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships program.

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Keywords:

Covid-19; Quality in Health care; Protocols and Guidelines

Additional Contributions & Acknowledgements:

The authors thank Qisu (Sue) Zhang, MPH, Tawny Czilok, RN, MHI, Liz Vasher, RN, Jessica Southwell, RN, MSN, Danny Nielsen, MS, and Jennifer Horowitz, MA for help with data analytics and project management.

We also thank all the BCBSM Collaborative Quality Initiatives (CQI's) that partnered together on data collection and offered project management/analytics support. Lastly, we are grateful to all of the hospitals who volunteered to be part of MiCOVID-19 including: Beaumont-Dearborn, Beaumont-Grosse Pointe, Beaumont- Farmington Hills, Beaumont- Royal Oak, Beaumont- Taylor, Beaumont- Trenton, Beaumont- Troy, Beaumont- Wayne, Bronson Battle Creek, Bronson Methodist, Detroit Medical Center-Detroit Receiving, Detroit Medical Center-Harper Hutzel, Detroit Medical Center-Detroit-Huron Valley Sinai, Henry Ford, Henry Ford Allegiance, Henry Ford Macomb, Henry Ford West Bloomfield, Henry Ford West Wyandotte, Holland Hospital, Hurley Medical Center, Lakeland Hospital, McLaren Flint, McLaren Greater Lansing, McLaren Port Huron, Mercy Health Muskegon, Mercy Health St. Mary's, Metro Health, Michigan Medicine, MidMichigan Alpena, MidMichigan Gratiot, MidMichigan Midland, Munson Medical Center, Oaklawn Hospital, Sinai Grace, Sparrow, St. Joseph Mercy Ann Arbor, St. Joseph Mercy Chelsea, St. Joseph Mercy Livingston, St. Joseph Mercy Oakland, St. Mary Mercy Livonia.

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

median age was 63 years, median BMI was 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.

During hospitalization, 232 (22.7%) patients were treated in an ICU, 558 (54.9%) in a "cohorted" unit, 161 (15.7%) received mechanical ventilation, and 90 (8.8%) received high-flow nasal cannula. ICU patients more often received hydroxychloroquine (66% vs. 46%), corticosteroids (34% vs 18%), and antibiotic therapy (92% vs 71%) than general ward patients ($p<0.05$ for all). Overall, 219 (21.4%) patients died, with in-hospital mortality ranging from 7.9% to 45.7% across hospitals. 73% received at least one COVID-19-specific treatment, ranging from 32% to 96% across sites.
Across 14 hospitals, the proportion of patients admitted directly to an ICU ranged from 0% to 43.8%; mechanical ventilation on admission from 0% to 12.8%; mortality from 7.9% to 45.7%. Use of at least one COVID-19 specific therapy varied from 32% to 96.3% across sites.

CONCLUSIONS

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

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,[1 2] over 4.5 million cases of COVID-19, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been reported.[3] 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.[4] 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.[5]

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.[6] 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.

Using a well-established data collection strategy, we examined variations in clinical care processes, treatment approaches, and clinical outcomes across Michigan hospitals.

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 ≥18 years of age that underwent testing for COVID-19 via reverse-transcriptase polymerase chain reaction, including both positive cases and persons under investigation (PUI) who eventually had a negative test. Demographic data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was selected for detailed abstraction. Positive cases were sorted by day of admission (e.g., Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge) was used to select patients for detailed abstraction. Patients who were pregnant, transitioned to hospice within 3 hours of hospital admission, or discharged against medical advice were excluded. All data were entered into a registry (Mi-COVID19) using a structured data collection template.

Patient characteristics including comorbidities, home medications, presenting symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare worker) were collected. Clinical data during hospitalization including location of care (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body

mass index (BMI), laboratory and radiology findings and therapeutics were abstracted. Organ supports such as mechanical ventilation and other respiratory support, vasopressor use, renal replacement therapy (continuous renal replacement therapy [CRRT] and intermittent hemodialysis [iHD]) were also collected.

The primary outcomes of interest included hospital mortality, receipt of cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric therapy for presumed thrombosis). In addition, we performed pre-specified exploratory analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine variation in patient characteristics, management and outcomes. Specifically, we assessed variation in use of COVID-19 specific treatments (defined as hydroxychloroquine, combination hydroxychloroquine plus azithromycin, Vitamin C [oral or intravenous], IL-6 inhibitors or remdesivir), antibiotic therapy, use of organ support (e.g., use of vasopressors, mechanical ventilation and CPR), occurrence of venous thrombosis and in-hospital mortality.

Descriptive statistics (e.g., mean, median, proportion) with measures of dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize data. Data that were not documented in medical records (e.g., values of certain laboratory tests) were reported as missing. Pairwise comparisons were made using t-tests for continuous data and chi-square tests for categorical data, respectively. Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables. All statistical tests were two-sided with $p<0.05$ considered statistically significant. The study was reviewed by the

Institutional Review Board of the University of Michigan and deemed “not regulated”. It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

DEMOGRAPHIC DATA

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

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

workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of patients resided in congregated living facilities, including nursing homes and homeless shelters **(Table 1).**

CLINICAL PRESENTATION AND INITIAL EVALUATION

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

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% Fi02 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 (≥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 antibiotics, with use being more common in the ICU than general wards (91.8% vs 70.5%, p<0.001).

COVID-19 SPECIFIC THERAPIES

A total of 747 (72.9%) patients were treated with therapies targeting COVID-19, or the body's response to COVID-19, most commonly hydroxychloroquine (51%), hydroxychloroquine plus azithromycin (36%), and Vitamin C (10%). Treatment with IL-6 inhibitors and remdesivir was infrequent (27 and 17 patients, respectively). Use of COVID-19 treatments was more common in ICU than general care patients (88% vs. 69%, p<0.001). No patients in our sample received convalescent plasma. The proportion of patients treated with COVID-19 specific therapies decreased over time from 78.1% of patients admitted during March 8 to March 31 to 65.0% of patients

admitted during April 1 to May 11 (p<0.001). Only 21 (2.0%) patients were enrolled into a clinical trial **(Table 2).**

CLINICAL OUTCOMES

The in-hospital mortality rate for the full cohort of COVID-19 positive patients (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age, ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years **(Figure 2).** Among 219 decedents with detailed abstraction, 134 (61.5%) died following ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were transitioned to comfort care prior to death. The most common causes of death were refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both DVT and PE**.**

Among the 805 patients that survived to hospital discharge, 86% were discharged home and 8% were discharged to a skilled nursing facility or rehabilitation center. Only 1 patient (0.1%) was discharged to the Detroit field hospital **(Table 3).**

VARIATION ACROSS HOSPITALS

Among 14 hospitals with at least 25 detailed abstractions, substantial variation in demographics, illness severity, care processes, treatments, and outcomes of COVID-19 positive patients were observed **(Table 4).** The proportion of patients over 65 years of

age ranged from 30.2% to 65.5%, while the proportion of Black patients ranged from 0% to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from 0% to 43.8%, while the proportion of patients who were transferred to an ICU after admission ranged from 0% to 24.1%. Treatment in "cohorted" units ranged from 0% to 100%. Mechanical ventilation on admission ranged from 0% to 12.8% while use of vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness on presentation (defined as admission to an ICU with receipt of vasopressors or mechanical ventilation on admission) varied from 0% to 7.7%.

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

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

DISCUSSION

While reports of COVID-19 patients from New York, Washington, and California exist,[7-9] this is the first multi-center study to examine epidemiology, treatment and outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-

hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients treated at a diverse set of 32 academic and community hospitals.

The demographics of our cohort differ from other cohorts. First, patients with confirmed COVID-19 in Michigan are disproportionally Black (over half of our cohort). This is in contrast to 32% of PUIs—indicating that the predominance of black patients with COVID-19 is not a reflection of local demographics, but rather disproportionate impact of COVID-19 on black patients. Second, in contrast to prior studies,[1 7 10] our cohort was nearly 50:50 male:female, rather than male dominant. The reasons for this difference are unclear.

Consistent with prior reports, the main presenting symptoms were cough, dyspnea and fever. Similar to other studies,[11] a substantial proportion of patients had multiple comorbidities; but notably, 15% of our cohort had no known medical problems.[12] We found that a substantial proportion of patients reported contact with a known COVID-19 positive patient prior to developing symptoms. These findings mirror those of a study from Shenzen, China, where contacts of those with disease experienced a significantly higher rate of infection than the general public.[13] Additionally, patients underwent COVID-19 testing through a number of venues including hospital, commercial and state-run laboratories, illustrating the myriad ways in which diagnosis was obtained early in the outbreak when testing was limited.[14] Although only 14% of the sample was admitted directly to an ICU, an additional 9% were transferred to an ICU later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%, but increased with age, consistent with prior studies.[15]

A key finding of our study is that a majority of patients hospitalized for COVID-19 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the body's immune response. More than half of patients were treated with hydroxychloroquine, and an additional 6% were treated with antivirals or immune modulating agents. Experts have increasingly questioned the use of unproven COVID-19 therapies outside of a clinical trial,[16] and have argued that supportive care and trial enrollment are the best options until data regarding efficacy of therapies acrrues.[17 18] Accumulating observational and trial data now suggest no benefit from hydroxychloroquine,[19-21] and concerns regarding harm from empiric use remain.[22] Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of experimental COVID-19 therapies outside empiric studies represents a lost opportunity for learning. It is also emblematic of the strong desire—particularly early in the pandemic—to use therapies with a theoretical potential to target the virus even though improved survival from critical illness is largely attributed to improvements in supportive care.[23] Notably, we still do not have targeted therapies for sepsis or acute respiratory distress syndrome, which are the major mechanisms by which patients die from COVID-19 infection.

Another strength of our study is the variation in clinical presentation and outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals. While we are unable to ascertain reasons for such variation, we anecdotally observed that practice evolved across hospitals over time. For example, at some Michigan hospitals, routine use of hydroxychloroquine was common in the first few weeks of the

pandemic but curbed as trial data became available. In contrast, use of hydroxychloroquine continues to be encouraged at other hospitals even today.[24] While it is unclear if these practice changes influenced outcomes, future studies exploring the rationale and impact of these changes on patients will be valuable.

Our study has limitations. First, given the observational nature of the study, rationales for treatment or management decisions cannot be determined. Second, 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. Third, while variation in care was observed, the implications of such variability on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are scarce and not without risks, reducing variation may improve patient safety and resource use. Fourth, our study depends on available documentation, so symptoms, comorbidities, or treatments not documented in the medical record may be omitted. For example, it is possible that the low use of prone positioning observed in our cohort may be due to incomplete documentation of this practice. Finally, we did not collect patient identifiers, so inter-hospital transfers could be reported as two separate hospitalizations. However, we did collect admission and discharge locations, and only 6% of the cohort was transferred from another hospital.

Our study also has strengths. 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. Second, 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. Third, 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. Finally, data collection for this effort remains ongoing, including longitudinal monitoring of patients after discharge. These data will help shed new light on the post hospital sequelae of COVID-19.

Michigan remains one of the regions most affected by COVID-19. This multi-center study provides granular clinical data regarding patients, care practices and clinical outcomes in the state. The wide variation in observed practices and outcomes suggests caution when interpreting findings from single center studies. Our study also demonstrates the value of hospital collaboratives to help inform best practices.

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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[1]	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[2]	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%)

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

Advanced Directives on admission	
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

[1] *Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.*

[2] *Includes other payers, Michigan, out-of-state and government.*

[3] *Includes leukemia, lymphoma, hematologic cancer and any malignancy.*

[4] *Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.*

[5] *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*
Vital signs on day of hospital admission, no. (%)			
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
Day 1 laboratory measures, median (IQR)			
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[1]	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
Imaging findings - no. (%)			
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

Respiratory support on day of admission - no. (%)			
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%fio2)	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
Treatments during hospitalization - no. (%)			
Covid-19 Specific treatment(s)			
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
Corticosteroids[2]	79 (34.1%)	143 (18.1%)	<.0001
Antibiotics	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[3]	123 (53.0%)	115 (14.5%)	<.0001
Antivirals[4]	1 (0.4%)	13 (1.6%)	0.1626
Enrolled in clinical trial	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%)
*Respiratory support ever received, no.(%)**			
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_2)	159 (15.5%)	76 (9.4%)	83 (37.9%)
*Maximum respiratory support received, no. (%)***			
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_2)	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%)
Max FIO_2 received, no.(%)			
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%)
Non-respiratory organ support received, no. (%)			
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; Fi02=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							
	Min	10th Pctl	25th Pctl	Median	75th Pctl	90th Pctl	Max	*p*[1]
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[2]	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[3]	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[4]	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

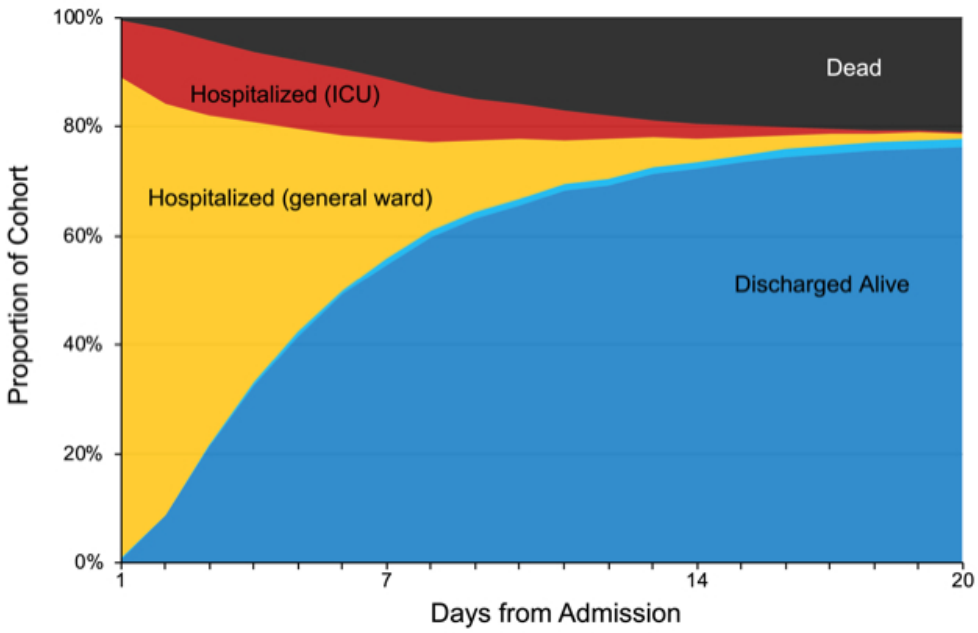
[1] Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.
[2] Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.
[3] For patients ever on mechanical ventilation
[4] 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

Figure Legend 1

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.

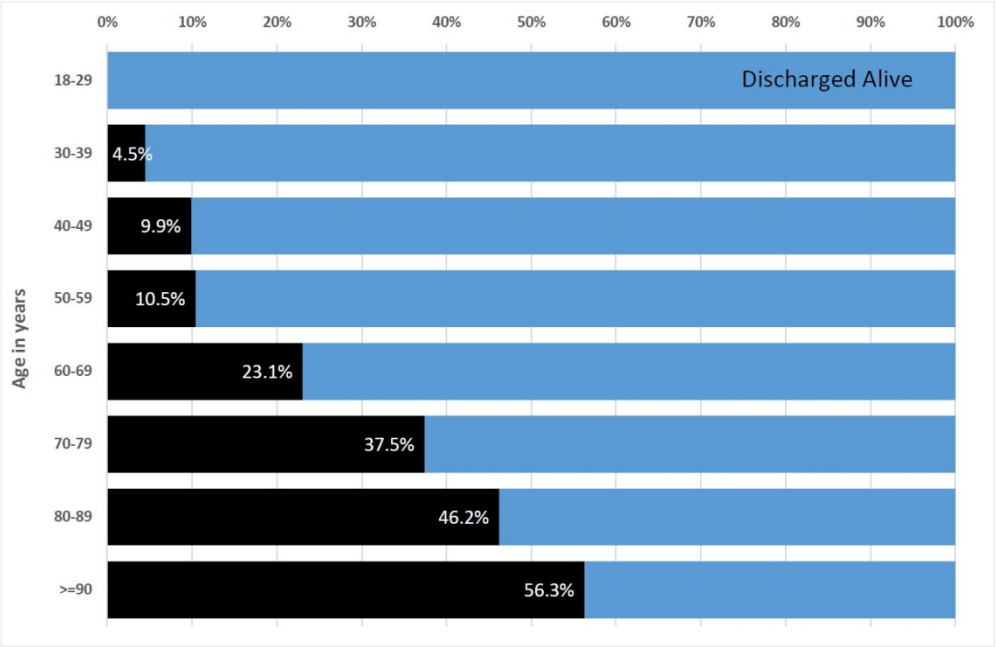
Figure Legend 2

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.



Caption : 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 : 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.

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	
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
Methods			
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*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
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) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—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	
Discussion			
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	
Other Information			
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.

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BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-044921.R2
Article Type:	Original research
Date Submitted by the Author:	25-Jun-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
Primary Subject Heading:	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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Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals

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Abstract Word Count: 299

Word Count: 3407

Conflicts of Interest: No relevant conflicts disclosed by coauthors.

Primary Funding Source: Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships program.

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Keywords:

Covid-19; Quality in Health care; Protocols and Guidelines

Additional Contributions & Acknowledgements:

The authors thank Qisu (Sue) Zhang, MPH, Tawny Czilok, RN, MHI, Liz Vasher, RN, Jessica Southwell, RN, MSN, Danny Nielsen, MS, and Jennifer Horowitz, MA for help with data analytics and project management.

We also thank all the BCBSM Collaborative Quality Initiatives (CQI's) that partnered together on data collection and offered project management/analytics support. Lastly, we are grateful to all of the hospitals who volunteered to be part of MiCOVID-19 including: Beaumont-Dearborn, Beaumont-Grosse Pointe, Beaumont- Farmington Hills, Beaumont- Royal Oak, Beaumont- Taylor, Beaumont- Trenton, Beaumont- Troy, Beaumont- Wayne, Bronson Battle Creek, Bronson Methodist, Detroit Medical Center-Detroit Receiving, Detroit Medical Center-Harper Hutzel, Detroit Medical Center-Detroit-Huron Valley Sinai, Henry Ford, Henry Ford Allegiance, Henry Ford Macomb, Henry Ford West Bloomfield, Henry Ford West Wyandotte, Holland Hospital, Hurley Medical Center, Lakeland Hospital, McLaren Flint, McLaren Greater Lansing, McLaren Port Huron, Mercy Health Muskegon, Mercy Health St. Mary's, Metro Health, Michigan Medicine, MidMichigan Alpena, MidMichigan Gratiot, MidMichigan Midland, Munson Medical Center, Oaklawn Hospital, Sinai Grace, Sparrow, St. Joseph Mercy Ann Arbor, St. Joseph Mercy Chelsea, St. Joseph Mercy Livingston, St. Joseph Mercy Oakland, St. Mary Mercy Livonia.

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Lindsay A. Petty MD – manuscript planning; manuscript drafting/revisions; final approval to be published

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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

median age was 63 years, median BMI was 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.

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

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

CONCLUSIONS

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

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,[1 2] over 4.5 million cases of COVID-19, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been reported.[3] 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.[4] 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.[5]

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.[6] 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.

Using a well-established data collection strategy, we examined variations in clinical care processes, treatment approaches, and clinical outcomes across Michigan hospitals.

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 ≥18 years of age that underwent testing for COVID-19 via reverse-transcriptase polymerase chain reaction, including both positive cases and persons under investigation (PUI) who eventually had a negative test. Abstractors were asked to abstract as many eligible cases as possible for their hospital. Demographic data (age, gender, race, ethnicity, payor) and in-hospital mortality were collected for all confirmed and PUI cases. A sample of COVID-19 positive cases from each hospital was selected for detailed abstraction. Positive cases were sorted by day of admission (e.g., Mon-Sun) and, for each day, a pseudo-random number (minute of hospital discharge) was used to select patients for detailed abstraction. Patients who were pregnant, transitioned to hospice within 3 hours of hospital admission, or discharged against medical advice were excluded. All data were entered into a registry (Mi-COVID19) using a structured data collection template. Of the 92 noncritical access, nonfederal hospitals in Michigan, data from 32 hospitals (34.8%) was included in the sample. Included

hospitals are diverse in terms of size, teaching status, and ownership structure (Appendix 1).

Patient characteristics including comorbidities, home medications, presenting symptoms and risk factors for COVID-19 (e.g., exposure to sick contacts, healthcare worker) were collected. Clinical data during hospitalization including location of care (ward vs. intensive care unit [ICU], a “cohorted” COVID-19 only unit), vital signs, body mass index (BMI), laboratory and radiology findings and therapeutics were abstracted. Organ supports such as mechanical ventilation and other respiratory support, vasopressor use, renal replacement therapy (continuous renal replacement therapy [CRRT] and intermittent hemodialysis [iHD]) were also collected.

The primary outcomes of interest included hospital mortality, receipt of cardiopulmonary resuscitation (CPR), and occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE) (based on positive imaging findings or initiation of empiric therapy for presumed thrombosis). In addition, we performed pre-specified exploratory analyses in hospitals with at least 25 detailed abstractions (n=14 hospitals) to examine variation in patient characteristics, management and outcomes. Specifically, we assessed variation in use of COVID-19 specific treatments (defined as hydroxychloroquine, combination hydroxychloroquine plus azithromycin, Vitamin C [oral or intravenous], IL-6 inhibitors or remdesivir), antibiotic therapy, use of organ support (e.g., use of vasopressors, mechanical ventilation and CPR), occurrence of venous thrombosis and in-hospital mortality.

Descriptive statistics (e.g., mean, median, proportion) with measures of dispersion (e.g., standard error, inter-quartile range [IQR]) were used to summarize data. Data that were not documented in medical records (e.g., values of certain laboratory tests) were reported as missing. Pairwise comparisons were made using t-tests for continuous data and chi-square tests for categorical data, respectively. Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables. All statistical tests were two-sided with $p<0.05$ considered statistically significant. The study was reviewed by the Institutional Review Board of the University of Michigan and deemed “not regulated”. It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Patient and Public Involvement

No patient involved.

Data Availability

All data relevant to the study are included in the article or uploaded as supplementary information.

RESULTS

DEMOGRAPHIC DATA

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

Detailed data were abstracted on 1,024 (64.3%) randomly-selected COVID-19 positive patients. The most prevalent comorbidities were hypertension (65.4%), diabetes (36.8%), cardiovascular disease (26.0%) and chronic kidney disease (23.3%); 14.9% of patients had no comorbidities. Though 12.8% of patients had a diagnosis of asthma and 11.2% had a diagnosis of chronic obstructive pulmonary disease, pre-hospital use of inhaled steroids, long-acting beta-agonists and long-acting antimuscarinic agents was low at 4.2%, 2.9%, and 0.5%, respectively. Current smoking or vaping was uncommon, but 27.3% were former smokers, and 35.8% reported former vaping. 115 (11.3%) patients were on immunosuppressive medications prior to hospitalization, including 62 (6.1%) who were on oral steroids. Essential workers comprised 12.8% of the cohort, including healthcare workers (7.0%) and service workers (5.8%, e.g., postal, food service, transportation). Prior to admission, 16.1% of patients resided in congregated living facilities, including nursing homes and homeless shelters **(Table 1).**

CLINICAL PRESENTATION AND INITIAL EVALUATION

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

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 2). 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% Fi02 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 (≥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 antibiotics, with use being more common in the ICU than general wards (91.8% vs 70.5%, p<0.001).

COVID-19 SPECIFIC THERAPIES

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

CLINICAL OUTCOMES

The in-hospital mortality rate for the full cohort of COVID-19 positive patients (demographic plus detailed abstractions) was 25.0%. Mortality varied by decade of age,

ranging from 4.5% among patients aged 30-39 to 37.5% in patients aged 70-79 years **(Figure 2).** Among 219 decedents with detailed abstraction, 134 (61.5%) died following ICU treatment and 114 (52.1%) died after receiving mechanical ventilation. 40 of 219 decedents (18.3%) received cardiopulmonary resuscitation, and 91 (41.6%) were transitioned to comfort care prior to death. The most common causes of death were refractory hypoxemia (29.4%), cardiac arrhythmia (15.9%) and refractory shock (10.7%). Venous thromboembolism occurred in 32 (3.1%) of patients, of which 9 experienced proximal lower-extremity DVT, 21 experienced PE, and 2 experienced both DVT and PE**.**

Among the 805 patients that survived to hospital discharge, 86% were discharged home and 8% were discharged to a skilled nursing facility or rehabilitation center. Only 1 patient (0.1%) was discharged to the Detroit field hospital **(Table 3).**

VARIATION ACROSS HOSPITALS

Among 14 hospitals with at least 25 detailed abstractions, substantial variation in demographics, illness severity, care processes, treatments, and outcomes of COVID-19 positive patients were observed **(Table 4).** The proportion of patients over 65 years of age ranged from 30.2% to 65.5%, while the proportion of Black patients ranged from 0% to 94.6%. Similarly, the proportion of patients admitted directly to an ICU ranged from 0% to 43.8%, while the proportion of patients who were transferred to an ICU after admission ranged from 0% to 24.1%. Treatment in “cohorted” units ranged from 0% to 100%. Mechanical ventilation on admission ranged from 0% to 12.8% while use of vasopressors on admission ranged from 0% to 14.8% across hospitals. Critical illness

on presentation (defined as admission to an ICU with receipt of vasopressors or mechanical ventilation on admission) varied from 0% to 7.7%.

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

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

DISCUSSION

While reports of COVID-19 patients from New York, Washington, and California exist,[7-9] this is the first multi-center study to examine epidemiology, treatment and outcomes of COVID-19 hospitalizations in Michigan. Also, in contrast to prior multi-hospital US cohorts, the Mi-COVID19 registry includes a large sample of patients treated at a diverse set of 32 academic and community hospitals.

The demographics of our cohort differ from other cohorts. First, patients with confirmed COVID-19 in Michigan are disproportionally Black (over half of our cohort). This is in contrast to 32% of PUIs—indicating that the predominance of black patients with COVID-19 is not a reflection of local demographics, but rather disproportionate impact of COVID-19 on black patients. Second, in contrast to prior studies,[1 7 10] our

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

Consistent with prior reports, the main presenting symptoms were cough, dyspnea and fever. Similar to other studies,[11] a substantial proportion of patients had multiple comorbidities; but notably, 15% of our cohort had no known medical problems.[12] We found that a substantial proportion of patients reported contact with a known COVID-19 positive patient prior to developing symptoms. These findings mirror those of a study from Shenzen, China, where contacts of those with disease experienced a significantly higher rate of infection than the general public.[13] Additionally, patients underwent COVID-19 testing through a number of venues including hospital, commercial and state-run laboratories, illustrating the myriad ways in which diagnosis was obtained early in the outbreak when testing was limited.[14] Although only 14% of the sample was admitted directly to an ICU, an additional 9% were transferred to an ICU later in hospitalization. Hospital mortality in cases with detailed abstractions was 21%, but increased with age, consistent with prior studies.[15]

A key finding of our study is that a majority of patients hospitalized for COVID-19 were treated with therapies intended to mitigate SARS-CoV-2 viral replication or the body's immune response. More than half of patients were treated with hydroxychloroquine, and an additional 6% were treated with antivirals or immune modulating agents. Experts have increasingly questioned the use of unproven COVID-19 therapies outside of a clinical trial,[16] and have argued that supportive care and trial enrollment are the best options until data regarding efficacy of therapies acrrues.[17 18] Accumulating observational and trial data now suggest no benefit from

hydroxychloroquine,[19-21] and concerns regarding harm from empiric use remain.[22] Unfortunately, only 2% of our sample was enrolled in clinical trials. The high rate of experimental COVID-19 therapies outside empiric studies represents a lost opportunity for learning. It is also emblematic of the strong desire—particularly early in the pandemic—to use therapies with a theoretical potential to target the virus even though improved survival from critical illness is largely attributed to improvements in supportive care.[23] Notably, we still do not have targeted therapies for sepsis or acute respiratory distress syndrome, which are the major mechanisms by which patients die from COVID-19 infection.

Another strength of our study is the variation in clinical presentation and outcomes we observed across a heterogeneous sample of hospitals. Use of COVID-19 specific treatments, corticosteroids, and antibiotics varied markedly across hospitals. While we are unable to ascertain reasons for such variation, we anecdotally observed that practice evolved across hospitals over time. For example, at some Michigan hospitals, routine use of hydroxychloroquine was common in the first few weeks of the pandemic but curbed as trial data became available. In contrast, use of hydroxychloroquine continues to be encouraged at other hospitals even today.[24] While it is unclear if these practice changes influenced outcomes, future studies exploring the rationale and impact of these changes on patients will be valuable.

Our finding provides corroboratory information regarding the first COVID wave within Michigan. For example, in a single center retrospective study, Imam and colleagues found that advanced age and increasing number of comorbidities were independent predictors of in-hospital mortality in hospitalized Michigan patients, just as

we did in our cohort.[25] Similarly, in two national population-level studies led by the Centers for Disease Prevention and Control, individuals over 65 years of age and those with ≥3 comorbidities experienced greater risk of hospitalization and adverse outcomes, again consistent with our findings.[26 27] Our findings are also similar to others regarding disparities in COVID care and outcomes, especially among minority populations.[28] Despite these findings, our study also differ from other national studies in important ways. For example, we observed a low rate of readmissions in our cohort. In contrast, Donnely et al. using Veterans Health Affairs (VHA) data reported a readmission rate of 19.9% at 60-days.[29] While the reasons for this discrepancy are unclear, it is possible that practice pattern differences including variation in threshold for readmission and differences in patient characteristics may account for these discrepancies. As we begin to understand and manage the chronic sequelae of acute COVID,[30] studies understanding reasons for these pattern differences would be important. Another important difference lies in the use of therapeutics targeting COVID-19. For example, reports from New York City and Seattle show greater rates of use of remdesivir, and IL-6 inhibitors.[31 32] Whether these differences were due to practice variation (which occurred widely in the early US waves of COVID-19), vs. lack of access to therapeutics which was also reported is unclear.

Our study has limitations. First, given the observational nature of the study, rationales for treatment or management decisions cannot be determined. Second, 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. Third, while variation in care was observed, the implications of such variability on clinical outcomes is unknown. Nevertheless, given that therapeutic modalities are scarce and not without risks, reducing variation may improve patient safety and resource use. Fourth, our study depends on available documentation, so symptoms, comorbidities, or treatments not documented in the medical record may be omitted. For example, it is possible that the low use of prone positioning observed in our cohort may be due to incomplete documentation of this practice. Finally, we did not collect patient identifiers, so inter-hospital transfers could be reported as two separate hospitalizations. However, we did collect admission and discharge locations, and only 6% of the cohort was transferred from another hospital.

Our study also has strengths. 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. Second, 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. Third, 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. Finally, data collection for this effort

remains ongoing, including longitudinal monitoring of patients after discharge. These data will help shed new light on the post hospital sequelae of COVID-19.

Michigan remains one of the regions most affected by COVID-19. This multi-center study provides granular clinical data regarding patients, care practices and clinical outcomes in the state. The wide variation in observed practices and outcomes suggests caution when interpreting findings from single center studies. Our study also demonstrates the value of hospital collaboratives to help inform best practices.

Ethics Statement

The study was deemed “not regulated” by the University of Michigan IRB (HUM 00179611).

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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[1]	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[2]	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%)

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

Advanced Directives on admission	
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

[1] *Includes assisted living, group home, skilled nursing facility, and homeless shelters, correctional facilities, community living and inpatient psychiatric facilities.*

[2] *Includes other payers, Michigan, out-of-state and government.*

[3] *Includes leukemia, lymphoma, hematologic cancer and any malignancy.*

[4] *Includes oral prednisone, prednisolone, hydrocortisone and dexamethasone.*

[5] *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*
Vital signs on day of hospital admission, no. (%)			
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
Day 1 laboratory measures, median (IQR)			
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[1]	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
Imaging findings - no. (%)			
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

Respiratory support on day of admission - no. (%)			
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%fio2)	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
Treatments during hospitalization - no. (%)			
Covid-19 Specific treatment(s)			
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
Corticosteroids[2]	79 (34.1%)	143 (18.1%)	<.0001
Antibiotics	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[3]	123 (53.0%)	115 (14.5%)	<.0001
Antivirals[4]	1 (0.4%)	13 (1.6%)	0.1626
Enrolled in clinical trial	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%)
*Respiratory support ever received, no.(%)**			
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_2)	159 (15.5%)	76 (9.4%)	83 (37.9%)
*Maximum respiratory support received, no. (%)***			
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_2)	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%)
Max FIO_2 received, no.(%)			
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%)
Non-respiratory organ support received, no. (%)			
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; Fi02=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							
	Min	10th Pctl	25th Pctl	Median	75th Pctl	90th Pctl	Max	*p*[1]
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[2]	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[3]	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[4]	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

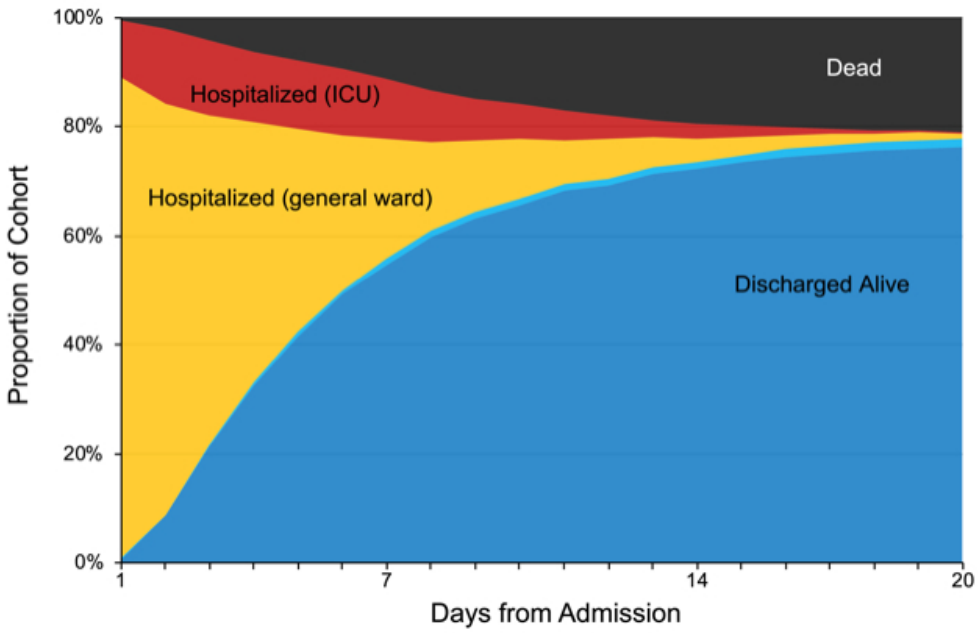
[1] Differences across hospitals were tested using the Kruskal–Wallis test for continuous variables and Pearson chi-square test for categorical variables.
[2] Defined as admission to ICU on day 1 of hospitalization and treatment with both mechanical ventilation and vasopressors.
[3] For patients ever on mechanical ventilation
[4] 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

Figure Legend 1

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.

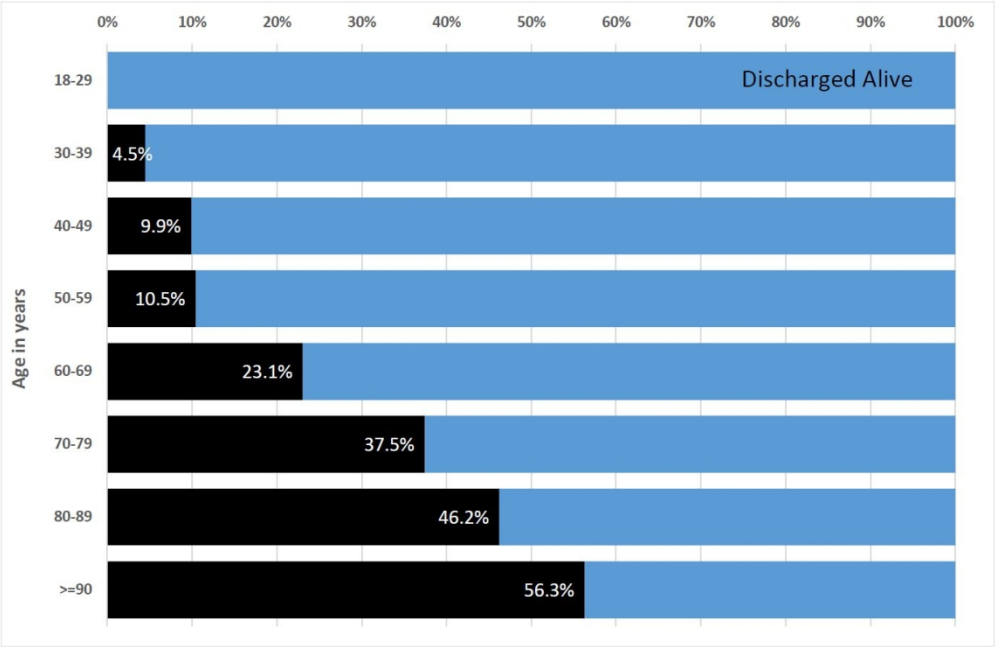
Figure Legend 2

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.



Caption : 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 : 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[1]	Total Patient Discharges[2]	Teaching Hospital Status	Ownership Status[3]	Location[4]
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

Hospital	Bed Size[1]	Total Patient Discharges[2]	Teaching Hospital Status	Ownership Status[3]	Location[4]
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

[1]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
[2]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

[3]Data obtained from data.medicare.gov; Hospital General Information. Retrieved from 06/03/2020 from https://data.cms.gov/provider-data/dataset/xubh-q36u
[4]Data obtained from https://www2.census.gov/geo/maps/metroarea/stcbsa_pg/Feb2013/cbsa2013_MI.pdf

* The American Hospital Directory reports data for Ascension Providence Hospital, Novi Campus and Ascension Providence Hospital, Southfield Campus together, so individual discharge numbers and teaching status for these two sites was not available. The data presented in this table represents numbers for both of these sites combined.

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.

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	
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	
Methods			
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*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—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 *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—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*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
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) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—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	
Discussion			
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	
Other Information			
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.