

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Variation in COVID-19 Characteristics, Treatment, and Outcomes in Michigan: An Observational Study in 32 Hospitals
AUTHORS	Chopra, Vineet; Flanders, Scott A.; Vaughn, Valerie; Petty, Lindsay; Gandhi, Tejal; McSparron, Jakob; Malani, Anurag; O'Malley, Megan; Kim, Tae; McLaughlin, Elizabeth; Prescott, Hallie

VERSION 1 – REVIEW

REVIEWER	Campioli, Cristina Mayo Clinic
REVIEW RETURNED	22-Oct-2020

GENERAL COMMENTS	<p>Chopra Vineet et al. report a retrospective cohort study on the variation in COVID-19 among different Michigan hospitals.</p> <ol style="list-style-type: none">1. The study raised the right questions and observations, and while it is essential to understand the type of patient population in the specific community, my major reservation is that it was reported what we already know about COVID-19. The study's major limitation is the retrospective and descriptive aspect of it, prematurely in the pandemic.2. It is important to acknowledge that the study illustrated and highlighted a diverse patient population, presentation, and hospital treatment. This reflects the lack of clear and research-based guidance, especially at the beginning of the pandemic. The study provides insights into how studies can influence the medical community without suitable scientific bases and peer-review which are delivered to vulnerable patients. The majority of those COVID-19 specific therapies were later disproven.3. The findings should serve as criticism for how we treat patients in a time of crisis. I believe the study could focus on this primarily.4. The difference among hospitals in terms of the treatment, admission unit, and transfers may be due to the resources available in each one. They reported higher mortality and higher black population as a form of racial disparity among COVID-19 infected patients, which is considered a hot topic.5. Of note, it is not mentioned the type of diagnostic test and sample utilized for the COVID-19 diagnosis. Along with the multicenter aspect of it, the laboratories were not the same, adding variations in the diagnosis.
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REVIEWER	Qiu, Haibo Southeast University Zhongda Hospital
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REVIEW RETURNED	18-Jan-2021
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GENERAL COMMENTS	<p>Dr. Vineet and co-workers retrospectively analyze the characteristics, treatment and outcomes of COVID-19 patients in Michigan. However, there were numerous studies about the characteristics, treatment and outcome in patients with COVID-19 previously. Few new information was given by this study.</p> <p>Major Questions:</p> <ol style="list-style-type: none"> 1. The study referred the incidence of different race with COVID-19, but the results did not clarify the relationship of COVID-19 and different race. 2. The study only lists the characteristics and treatments of the patients, did not explain whether the characteristics and treatments could influence the outcomes. 3. Does the duration of viral shedding relate with characteristics and treatments? 4. There were several variations of demographics, illness severity, care process, treatments, and outcomes of COVID-19 as the study referred across different hospital, however, what is the important parameters leads to the variations?
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VERSION 1 – AUTHOR RESPONSE

Comments from the Reviewers:

Reviewer: 1

Dr. Cristina Campioli, Mayo Clinic

Comments to the Author:

Chopra Vineet et al. report a retrospective cohort study on the variation in COVID-19 among different Michigan hospitals.

1. The study raised the right questions and observations, and while it is essential to understand the type of patient population in the specific community, my major reservation is that it was reported what we already know about COVID-19. The study's major limitation is the retrospective and descriptive aspect of it, prematurely in the pandemic.

>>> **Response:** Thank you for your comment. We would like to clarify that in addition to an in-depth understanding of the COVID-19 population, ours is the first multi-hospital study among COVID-19 patients in Michigan. Because we included multiple sites, our study is unique in that it provides an understanding of variation in clinical care and outcomes across a heterogeneous sample of hospitals. We believe that these data are important to provide insights for potential future clinical and policy interventions.

2. It is important to acknowledge that the study illustrated and highlighted a diverse patient population, presentation, and hospital treatment. This reflects the lack of clear and research-based guidance, especially at the beginning of the pandemic. The study provides insights into how studies can influence the medical community without suitable scientific bases and peer-review which are delivered to vulnerable patients. The majority of those COVID-19 specific therapies were later disproven.

>>> **Response:** Thank you for your summary and input. The substantial variation in patient population, presentation, hospital treatment, and clinical outcomes in the COVID-19 patients not only

provides evidence of the scarcity of treatment guidelines, but also shows how hospitals implemented various treatment approaches many of which were based on anecdote.

3. The findings should serve as criticism for how we treat patients in a time of crisis. I believe the study could focus on this primarily.

>>> **Response:** We agree that early treatments of COVID-19 were later questioned and proved to be of limited or no benefit. We specifically highlight this in the Discussion section and provide additional input as follows: *“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”*.

4. The difference among hospitals in terms of the treatment, admission unit, and transfers may be due to the resources available in each one. They reported higher mortality and higher black population as a form of racial disparity among COVID-19 infected patients, which is considered a hot topic.

>>> **Response:** Thank you for this comment. We believe a key strength of our study is how it highlights differences and potential disparities in care and outcomes among patients with COVID-19. We believe that this is the strength of our study and studies examining reasons for these disparities are urgently needed.

5. Of note, it is not mentioned the type of diagnostic test and sample utilized for the COVID-19 diagnosis. Along with the multicenter aspect of it, the laboratories were not the same, adding variations in the diagnosis.

>>> **Response:** Thank you for this comment. We agree that variation in testing could have led to differences in rates of diagnosis and detection of COVID-19.

Reviewer: 2

Dr. Haibo Qiu, Southeast University Zhongda Hospital

Comments to the Author:

Dr. Vineet and coworkers' retrospect the characteristics, treatment and outcomes of COVID-19 patients in Michigan. However, there were numerous studies about the characteristics, treatment and outcome in patients with COVID-19 previously. Few new information was given by this study.

>>> **Response:** Thank you for your comment. As noted in the previous answers and in the Discussion section, ours is the first multi-center study to examine epidemiology, treatment and outcomes of COVID-19 hospitalizations in Michigan – a state hit hard by the pandemic early in the evolution of this disease. It is important to understand the trajectory of COVID-19 clinical care and treatment in this hard hit population, and the variation across a diverse set of 32 academic and community hospitals. Moreover, we believe that these data also provide insights for potential future studies to examine disparities in healthcare use and outcomes in the state of Michigan and the US.

Major Questions:

1. The study referred the incidence of different race with COVID-19, but the results did not clarify the relationship of COVID-19 and different race.

>>> **Response:** COVID-19 is considered to have a disproportionate impact on historically disadvantaged populations, such as Black, Latinx, and Native Americans, in the US.ⁱ This study provided a descriptive view of the racial variation in the state of Michigan. As mentioned above, future studies in social determinants of health are warranted to further understand the issue.

2. The study only lists the characteristics and treatments of the patients, did not explain whether the characteristics and treatments could influence the outcomes.

>>> **Response:** As mentioned in the Discussion section, “*given the observational nature of the study, rationales for treatment or management decisions cannot be determined.*” The goal of the study was to delineate the patient characteristics, symptoms, patterns of care and outcomes for COVID-19 patients in Michigan. Future studies examining the associations between certain patient characteristics, treatment, and clinical outcomes may be considered but given the observational approach used, should be interpreted with caution. The main purpose of our study was to describe the epidemiology of the patients, hospitals, care processes and outcomes.

3. Does the duration of viral shedding relate with characteristics and treatments?

>>> **Response:** Given the nature of the data, only duration of symptoms before admission is available, which is reported in Table 1 with a median of 6 days. No hospitals quantitatively measured viral shedding or quantified viral load. This would be out of scope of the present study.

4. There were several variations of demographics, illness severity, care process, treatments, and outcomes of COVID-19 as the study referred across different hospital, however, what is the important parameters leads to the variations?

>>> **Response:** As stated in the manuscript, the precise driver for these variations in care cannot be discerned by the design of our study. However, it is important to note that there were substantial differences to approaches for clinical care – some of which could have benefited vs. harmed patients. We also highlight that mortality and adverse outcomes disproportionately affected minorities and African American patients, suggesting the need for a dedicated research agenda to examine whether differences in pre, intra vs. post-hospital care may explain these outcomes.

References

ⁱ Thakur N, Lovinsky-Desir S, Bime C, et al. The Structural and Social Determinants of the Racial/Ethnic Disparities in the US COVID-19 Pandemic. What’s Our Role? *Am J Respir Crit Care Med.* 2020;202(7), 943-949.

VERSION 2 – REVIEW

REVIEWER	Campoli, Cristina Mayo Clinic
REVIEW RETURNED	09-Feb-2021

GENERAL COMMENTS	The authors have incorporated the changes recommended throughout the manuscript. My major reservation continues to be that it reports what we already know about COVID-19 prematurely in the pandemic. Nevertheless, I recognize that this is the first multi-hospital study among COVID-19 patients in Michigan, providing an understanding of clinical care variation and outcomes across a heterogeneous sample of hospitals.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Cristina Campioli, Mayo Clinic

Comments to the Author:

The authors have incorporated the changes recommended throughout the manuscript. My major reservation continues to be that it reports what we already know about COVID-19 prematurely in the pandemic.

Nevertheless, I recognize that this is the first multi-hospital study among COVID-19 patients in Michigan, providing an understanding of clinical care variation and outcomes across a heterogeneous sample of hospitals.

AU Reply: Thank you for this thought. We agree that the novelty of this data is limited given the lengthy review process. We have attempted to put this information into context and added more clarity on some of the methodological issues as requested by the editor. We note that, to date, there are no multi-center studies from Michigan that examine patterns of care, clinical outcomes and variation across sites the way we have done here. Therefore, we still continue to believe our work is relevant and important to readers as the history of COVID begins to be written. The variation we find – and the consequences from it – are cautionary tales for how we manage future threats.