

Medical Student Edition

Welcome to this quarter's issue of Value Added!

The Center for Value-Based Care Research (CVCR) conducts novel research on interventions that improve value in healthcare. With a mission of making quality healthcare possible for all Americans by conducting research to identify value in healthcare, CVCR seeks to deliver the right care, at the right time, to the right patients, at lower costs.

In this issue, we report on recent studies conducted by medical students from Cleveland Clinic Lerner College of Medicine.

In our first story, fifth year student **Sidra Speaker** describes how oral temperatures have changed over time and what standards may be appropriate for interpretation of oral temperature measurements in the future. Following this, 4th- year student **Megan Sheehan** highlights key details of her study, conducted together with recent CCLCM graduate **Dr. Radhika Rastogi**, regarding the potential harms of treating hypertension in hospitalized non-cardiac patients.

Continuing, recent-graduate **Dr. Kaitlin Keenan** discusses her work on opioid prescribing in the hospital and its association with long term use. Lastly, 5th-year student **Zheyi Han** shares his ongoing work concerning the impact of active *Clostridium difficile* infection on quality of life.

We hope you enjoy this quarter's updates!

Featured Publication

Social Behaviors Associated with a Positive COVID-19 Test Result

Sidra L. Speaker, Christine M. Doherty, Elizabeth Pfoh, Aaron Dunn, Bryan Hair, Lynn Daboul, Victoria Shaker, Michael Rothberg

February 1, 2021

Infection Control and Hospital Epidemiology

CVCR CELEBRATIONS

- **Residency match day success: Congratulations to CVCR's 2019-2020 medical student researchers:**

* **Daniel Moussa** **Detroit Medical Center/Wayne State University** **OB/GYN**

* **Zheyi Han** **University of Michigan** **Internal Medicine**

* **Sidra Speaker** **UC San Diego** **Emergency Medicine**

Congratulations to all the graduating CCLCM medical students. Best of luck to our new physician-scientists!

- **Dr. Matthew Pappas received the Society of Hospital Medicine's 2021 Junior Investigator Award. Each year, the award is given to a single outstanding junior/early-stage investigator, defined as a faculty within 5 years of first faculty appointment, to recognize outstanding research potential. Applicants are young investigators whose research interests focus on the care of hospitalized patients, the organization of hospitals or the practice of hospitalists. We hope this award contributes to a successful future in research for Dr. Pappas. Congratulations!**

Oral Temperature in Noninfected Nonsurgical Hospital Patients

Sidra Speaker

What problem were you interested in addressing?

We wanted to know what constitutes a normal temperature in the hospital. Although we frequently use temperature to screen patients for signs of infection or other causes of inflammation such as immune-mediated reactions, the "normal" range for temperature that we use in the hospital is based on data derived with different tools in a different patient population over 150 years ago. Furthermore, there is evidence that in outpatient populations, "normal" temperature is lower than the traditional 98.6°F, varies between individuals, and is affected by other factors such as time of day. We set out to establish the expected temperature for a noninfected hospitalized patient, and to explore how various demographic factors and disease conditions affect this temperature.

What are the most compelling aspects of your data/results so far? What additional questions, if any, have arisen since starting the work?

Temperature among noninfected hospitalized patients is lower (98.0°F) than commonly believed by most hospital caregivers, and varies less between patients inside the hospital than among outpatients. One important finding is that only 0.5% of noninfected inpatient temperatures are over 99.9°F, which suggests that patients with a temperature of 100°F or more should be carefully evaluated for causes of fever. One important question we are hoping to address is how temperature changes among patients who are bacteremic or who have other common infections. We are also hoping to examine how oral temperatures compare to core temperatures (such as rectal temperatures) regarding their sensitivity for multiple serious hospital infections.

How do you think this study will add to existing literature on the topic?

This work expands upon recent studies of temperature in healthy outpatients to encompass non-surgical hospital inpatients without infection, cancer or immune disorders.

In what ways could the results impact care of the affected population?

We hope our work will shed light on the nuanced role for temperature measurement in caring for hospital inpatients, and that it will encourage hospital providers to broaden their focus from the binary dogma that "100.4°F is a fever and temperatures below this are within normal limits".

This study was accepted for publication in the Journal of the American Medical Association (JAMA). Sidra Speaker is anticipated to graduate from CCLCM and begin residency Summer 2021.

Treatment and Outcomes of Inpatient Hypertension Among Adults With Noncardiac Admissions

Co-First Authors: Radhika Rastogi, MD and Megan Sheehan

What was the purpose of this study?

This study investigated elevated blood pressure in patients who are hospitalized and examined the impact of treatment on inpatient outcomes. Elevated blood pressure in the hospital is common, but these acute vital sign changes are often not representative of chronic disease. We were interested in learning more about the frequency of treatment and outcomes associated with treatment.

How did you use this data?

In this study, we used data from hospitalizations that took place at CCF during 2017. We looked at patients with elevated blood pressure in the hospital, and compared those who were treated with a new class of medication in response to elevated blood pressure with those who were not treated to examine outcomes associated with treatment.

What did you find?

Elevated blood pressure was very common in the hospital – 78% of patients had at least one elevated blood pressure reading during their hospitalization. However, treatment was not as frequent – about a third of patients were treated with an anti-hypertensive medication. We also found that treatment of elevated blood pressure in the hospital was associated with higher rates of acute kidney injury, myocardial infarction, and stroke. This relationship was seen with both oral and intravenous treatment, and occurred at all blood pressure levels.

How is this meaningful and how do you feel it could impact decision-making in the hospital?

This study provides evidence that aggressive treatment of elevated blood pressures in the hospital is not associated with better outcomes, and is even associated with harm. With this in mind, if a patient has elevated blood pressure in the hospital without signs of end organ damage, physicians should think twice before treating with additional medications to lower blood pressure acutely. There are no guidelines for management of elevated blood pressure during hospitalization, and hopefully this work will contribute to formation of guidelines to help decision-making.

Since publication of this paper, Radhika Rastogi has graduated from Cleveland Clinic Lerner College of Medicine and is currently working as a resident.

Opioid Receipt During Medical Hospitalization and Association with Long Term Use

Kaitlyn Keenan, MD

What prompted your study of risk of long-term opioid use following a medical hospitalization?

Given the scope of the opioid epidemic, there is understandable concern that exposure to opioids through the healthcare system could lead to long-term opioid use. Prior studies have shown that receipt of opioids following surgery or in the emergency department are associated with an increased risk of long-term use. However, risk of long-term use following opioid receipt during a medical hospitalization has received less attention. A recent study found a small but significant association between receipt of an opioid during a medical hospitalization and long-term use; however, this study did not account for patient pain. Because patients who are not in pain are unlikely to get opioids in the hospital or to need them later, this was an important limitation. Because we had access to pain scores during the admission, we sought to examine this association, controlling for patient-reported pain level during the hospitalization.

Were there any findings that surprised you?

Among 2,971 opioid-naïve patients, 64% received an opioid, which was a much higher percentage than we expected. Because we wanted to understand why patients received opioids during their hospitalization, we also did a chart review of 100 patients who received opioids. Almost no charts contained any documentation for why the patient was prescribed an opioid, and a quarter of them didn't even document that an opioid was given.

Are patients who receive opioids during a medical hospitalization more likely to use them long-term?

We looked at inpatient opioid exposure with two questions in mind. First, we asked if the patient received an opioid during their hospital stay, and second, if they received opioids both during their stay and at discharge. For patients that only received opioids during their stay but not at discharge, there was no increased risk of opioid use at six to twelve months. Patients who received opioids at discharge did have a statistically significantly higher risk of long-term use, but this only applied to 3% of patients, which, in real world terms, is a very small number of people.

What did you find regarding the role of patient pain in the association between inpatient opioid receipt and long-term use?

One limitation of prior studies is that they didn't account for patient pain, and included patients who were not in pain and therefore not at risk of receiving an opioid. This makes it harder to detect an association between opioid receipt during a hospitalization and long-term use, if one exists. We limited our study to patients who reported pain during their hospitalization. Patients who report high levels of pain in the hospital should have their pain appropriately managed, which often requires use of opioids. Indeed, we found that patient-reported pain was highly associated with opioid receipt during the hospitalization and opioid use six to twelve months later. Accounting for necessary pain in studies of healthcare-associated opioid exposure and long-term use is therefore necessary. Studies that fail to do so will likely overstate the danger of using opioids to treat pain in medical inpatients.

How do you feel the findings of this work could affect physician decision-making regarding opioid prescription in the hospital?

There is, understandably, a lot of concern about this, but our findings suggest physicians don't need to worry that managing pain with opioids during a medical hospitalization is going to lead to long-term use. Additionally, while not the primary aim of our study, we found significant differences in opioid receipt based on non-clinical patient characteristics including race and age. This suggests physicians need to consider the factors contributing to their decision-making, and to closely examine which biases may be influencing them.

This study is in-press in Southern Medical Journal. Since completion of the study, Kaitlyn Keenan has graduated from Cleveland Clinic Lerner College of Medicine with her MD and is currently working as a resident.

Clostridioides difficile and the Impact on Quality of Life

Zheyi Han

What problem were you interested in addressing?

Clostridioides difficile continues to be a leading cause of hospital acquired infections with significant disease burden. *C. difficile* can cause a wide range of symptoms in patients, and many patients have reported persistent effects from infection that pervade their mental health and social life. Despite these effects, quantitative data on the impact of *C. difficile* infections on patient quality of life is limited.

What were the most compelling aspects of your results? What additional questions, if any, arose after starting the work?

We administered both disease-specific (Cdiff32) and generic quality of life questionnaires (PROMIS-GH) to patients hospitalized with active *C. difficile* infections. We found that these patients reported significantly lower physical and mental health scores compared with the general population. We identified recurrent infection, severe infection, and increased number of stools to be significantly associated with worse quality of life, as represented by decreased scores on the disease-specific questionnaire. We were also able to further validate the Cdiff32 questionnaire for use in the target populations of patients with both primary and recurrent *C. difficile* infection.

How do you feel this work added to the existing literature on the topic?

Previous studies have examined the quality of life in *C. difficile* patients through qualitative methods and through use of generic quality of life questionnaires such as the SF-36 and the EQ-5D. To our knowledge, ours was one of the first studies to examine the quality of life of hospitalized patients with active *C. difficile* infection using a disease-specific questionnaire. We were able to demonstrate quantitatively that patients with *C. difficile* infections experience decreased quality of life with respect to their physical, mental and social health. Additionally, we were able to provide additional data to support the use of the Cdiff32 questionnaire in patients with active infection.

In what ways do you hope your research will impact clinical work after publication?

One important takeaway for clinicians is that *C. difficile* infections impact quality of life beyond just physical health, with many patients reporting declines to their mental health and social life as well. We hope that future studies of *C. difficile* therapeutics will incorporate measures of patient quality of life using disease-specific questionnaires such as the Cdiff32.

This study was presented virtually at the Society for Medical Decision Making in October 2020. Zheyi is anticipated to graduate from CCLCM and begin residency Summer 2021.

RECENT PUBLICATIONS

Anjewierden S, Han Z, Brown AM, Donskey CJ, Deshpande A. Risk factors for Clostridioides difficile colonization among hospitalized adults: A meta-analysis and systematic review. Infect Control Hosp Epidemiol. 2020 Oct 29;:1-8. doi: 10.1017/ice.2020.1236. [Epub ahead of print].

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Durham SH, Le P, Cassano AT. Navigating changes in Clostridioides difficile prevention and treatment. J Manag Care Spec Pharm. 2020 December; 26(12-a Suppl):S3-S23. doi: 10.18553/jmcp.2020.26.12-a.s3

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Allgaierm, J, Lagu, T, Haessler, S, Imrey, PB, Deshpande, A, Guo, N, Rothberg, MB. Risk Factors, Management, and Outcomes of Legionella Pneumonia in a Large, Nationally Representative Sample. Chest. 2020. Dec 19;doi: 10.1016/j.chest.2020.12.013.

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