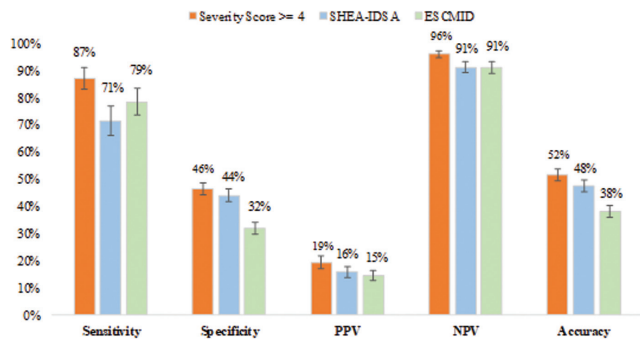significantly higher among patients who died during admission than those who survived (median 6 vs. 4). A score of ≥4 was defined as severe. The performance of severity score was better than that of SHEA-IDSA or ESCMID definition (see figure).

Predictive Performance for In-Hospital Death

PPV = positive predictive value; NPV = negative predictive value.

Conclusion. Current guidelines use WBC, sCr increase, sCr, or albumin to define the severity of CDI. Our severity scoring system improved the predictive performance by adding novel indicators of comorbidities, BUN, BUN/sCr, and anti-diarrhea medications use.

Disclosures. All authors: No reported disclosures.

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485. On- and Post-Antibiotic Effects on the Risk of Hospital-Acquired *Clostridium difficile* Infection (CDI)

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Background. *Clostridium difficile* infection (CDI) is one of the most common nosocomial infections worldwide. While exposure to antimicrobials is the most important risk factor for CDI, the magnitude of the risk from different antimicrobials has not been well quantified through big data analysis of large healthcare systems.

Methods. We conducted a retrospective cohort study of all inpatients with no recent history of CDI in the US Department of Veterans Affairs Health Care System admitted between January 1, 2008 and December 31, 2013. For patients with multiple hospitalizations, only the first hospitalization during the study period was considered. Patients were followed until the development of hospital-acquired CDI (HA-CDI), death, or discharge, whichever came first. HA-CDI was defined as a laboratory test indicating the presence of toxin or toxin genes from a stool sample collected on hospital day 4 or later. Antimicrobial exposures were assessed daily for current ("on") or recent ("post") exposures by class. The impact of time-varying antimicrobial exposure on the risk of HA-CDI was assessed using multivariable Cox proportional hazards regression models with robust covariance estimation. Patient factors, such as age and comorbidity, were included as adjustors. Only patient-days at risk for HA-CDI (i.e., day 4 or later) were included.

Results. Approximately 2.8 million patient-days from 476,679 patients were included in the analysis. Table 1 shows the impact of on- and post-antibiotic exposures by class on the risk of HA-CDI after accounting for patient factors, including concomitant antimicrobial exposures.

Conclusion. We observed risks of HA-CDI associated with cephalosporins and fluoroquinolones lower than previously reported. Tetracycline exposure appears to be protective. This big data analysis from the nationwide VA healthcare system helps to better quantify the risk of CDI during and after receiving different categories of antimicrobials. This work could better guide antimicrobial selection and antimicrobial stewardship efforts, potentially reducing the risk of CDI among patients

Class	On-Antibiotic aHR (95% CI)	Post-Antibiotic aHR (95% CI)
Carbapenems	2.0 (1.8 - 2.2)	0.77 (0.62 - 0.96)
Penicillins	1.7 (1.6 - 1.8)	1.4 (1.2 - 1.5)
Tetracyclines	0.61 (0.49 - 0.76)	0.56 (0.41 - 0.78)
1st + 2nd Gen Cephalosporins	0.51 (0.44 - 0.59)	1.0 (0.94 - 1.1)
3rd + 4th Gen Cephalosporins	1.8 (1.6 - 1.9)	1.5 (1.3 - 1.6)
Fluoroquinolones	1.1 (1.0 - 1.1)	1.3 (1.2 - 1.4)
Clindamycin	0.63 (0.52 - 0.77)	0.91 (0.76 - 1.1)

Disclosures. All authors: No reported disclosures.

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486. Endemic Corridors: A Useful Tool for the Approach of *Clostridium difficile*: A 5-Year Epidemiologic Surveillance Program in a Teaching Hospital of a Middle-Income Country

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Background. *Clostridium difficile* infection (CDI) is a healthcare-associated infection causing morbidity, mortality, and increase in the economic burden of health. Accurate and accesible methods to predict the epidemiologic trends of CDI are scarce. The systematic collection of data contributes to the development of an endemic corridor which estimates the expected cases in a period of time, facilitating the identification of outbreaks. In Guatemala, no obligatory report is required and no national surveillance programs for CDI exist. Therefore, understanding local epidemiologic trends of CDI is important in order to make future predictions.

Methods. All consecutive primary CDI eopisodes (January 2012–December 2017) obtained from active surveillance in the surgery department were included. CDI was defined as diarrhoea and a positive stool PCR test for *C. difficile* toxin A and/or B. An endemic corridor was developed to describe trends. The geometric mean and a 95% confidence interval were used to calculate upper and lower limits of weekly incidence. Demographics, clinical characteristics, antimicrobial treatment, and outcome of CDI were analyzed.

Results. A total of 208 CDI episodes were included in the study (9 healthcare workers). The incidence of CDI cases increased from 12.85/1,000 discharges (2016) to 18.53/1,000 discharges (2017). CDI was higher among male (54.8%) adults (18–64 years; 72.23%). NAP1 strain was identified in 38% of all cases, with a constant increase from 2012 to 2017. All cases were treated according to guidelines. No recurrences or deaths occurred during the studied time period. The highest incidence of CDI was observed between epidemiologic weeks 7, 8, and 42. Eleven outbreaks were identified in the studied time period, the first and major outbreak occurred in 2013; 2015 had the most outbreaks with 4. Both 2016 and 2017 had threeoutbreaks each.

Conclusion. Owing to the active and systematic surveillance of CDI, an endemic corridor was created. This will be a useful tool to develop interventions according to the epidemiologic trends of local CDI. Prompt identification of cases and strict adherence to patient isolation and treatment guidelines resulted in null mortality rates despite the alarming increase in NAP1 strains.

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487. Severity and Clinical Outcomes of *Clostridium difficile* Infection Based on Toxin B Assay Results

Jorge Jo Kamimoto, MD[1]; Sandra Susanibar, MD[1]; Meera Mohan, MD[2]; Piroon Jenjaroenpun, PhD[3]; Krishnan Gayathri, MD[4]; Juan Carlos Rico, MD[5]; Mary J Burgess, MD[5]; Ruslana Tytarenko, MS[1]; Nicole Emery, BS M(ASCP)[6]; Eric Rosenbaum, MD, MPH[6]; Brian Walker, PhD[1]; Intawat Nookaew, PhD[3] and Atul Kothari, MD[5]; [1]Myeloma Institute, University of Arkansas for Medical Sciences, Little Rock, Arkansas, [2]Division of Hematology Oncology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, [3]Department of Biomedical Informatics, University of Arkansas for Medical Sciences, Little Rock, Arkansas, [4]Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, [5]Division of Infectious Diseases, UAMS, Little Rock, Arkansas, [6]Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

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Background. *Clostridium difficile* infection (CDI) remains a major health problem in the United States. The IDSA guidelines recommend using stool toxin assay as part of a multistep algorithm rather than nucleic acid amplification test (NAAT) alone. However, the clinical significance of toxin negative tests remains a subject of debate. We performed a prospective study in our institution to describe clinical outcomes of CDI based on the results of the stool toxin assay.

Methods. Our laboratory utilizes a 2-step algorithm, using glutamate dehydrogenase plus detection of toxin B by enzyme immunoassay (EIA) arbitrated by NAAT for testing stool samples submitted for *C. difficile* testing. The study was conducted between January and December 2017. Patients diagnosed with CDI based on laboratory results were divided into two groups based on toxin B assay results. Shotgun metagenomics was performed directly on stool specimens using Illumina NextSeq in a subset of patients. Chart reviews were performed to assess clinical outcomes. Our primary outcome was incidence of severe CDI and 30-day mortality.

Results. A total of 2,823 samples were submitted to the laboratory for testing for suspected CDI. Three hundred thirty-eight samples in 290 discrete patients were considered positive using the two step algorithm. Whole genome sequencing was performed on samples from 57 patients (Figure 1). Clinical outcome data were available for 53 patients. Thirty percent were on active chemotherapy. Thirty-four were toxin B positive (group 1), 19 were toxin B negative (group 2) by EIA. Hospital onset disease was seen in 10 (27%) of patients in group 1 vs. 7 (37%) in group 2 (P = 0.57). Thirty-day mortality was 3% in toxin positive vs. 5% in toxin negative groups (P = 0.67). Severe CDI was seen in 14 (41%) in group 1 vs. 8 (42%) in group 2 (P = 0.94). NAP 1 strain was detected in 10.5% of patients in group 2. Percentage of *C. difficile* reads on sequencing in fecal samples in group 1 (0.17%) was not significantly different from group 2 (0.24%) (P = 0.70, Figure 2).

Conclusion. In our cohort, detection of *C. difficile* toxin in stool samples was not associated with increased severity of disease. Our cohort has a higher prevalence of patients on active chemotherapy than previously studied cohorts.

Bioburden of *C. difficile* was not significantly different in toxin positive and negative disease.
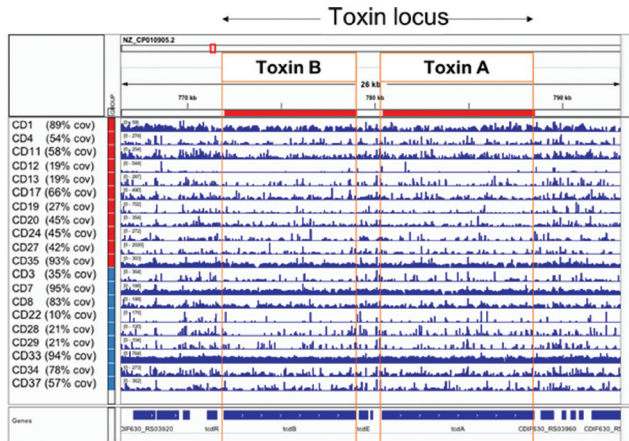

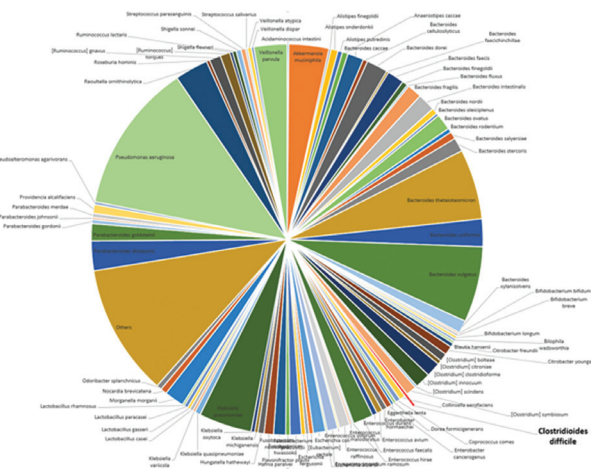Figure 1. Mapping of tcdB and tcdA reads using shotgun metagenomics in fecal samples

Fig 2: Microbiome in Patients with Active CDI

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488. Oral Vancomycin Plus Intravenous Metronidazole for Severe *Clostridium difficile* Infection in Critically Ill Patients

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Background. There remains a paucity of data regarding optimal treatment of patients with severe *Clostridium difficile* infection (CDI) in the intensive care unit (ICU). Based on expert opinion, the 2018 SHEA-IDSA CDI Clinical Practice Guidelines recommend combination therapy (oral vancomycin [PO VAN] plus intravenous metronidazole [IV MDZ]) in fulminant CDI only. A 2015 study suggested a mortality benefit with combination therapy of PO VAN plus IV MDZ for ICU patients regardless of severity. The objective of this study was to determine the impact of combination therapy on clinical outcomes in ICU patients with severe CDI, compared with PO VAN monotherapy.

Methods. Single-center, retrospective, cohort of adult patients admitted to an ICU between April 2016 and April 2018 with a positive *C. difficile* nucleic acid amplification test and an order for PO VAN were screened for inclusion. Patients were excluded if they had life-threatening intra-abdominal complications, including toxic megacolon/emergent colectomy. The primary outcome was 30-day in-hospital all-cause mortality. In a subgroup analysis, patients were matched using Acute Physiology and Chronic Health Evaluation (APACHE) II scores. Logistic regression was conducted to identify clinical variables associated with mortality.

Results. One hundred one patients were included; 47 received combination therapy with IV MDZ. Baseline characteristics were similar across groups, except patients in the IV MDZ group had a higher median white blood cell (WBC) count at diagnosis (18.4 vs. 13.9, $P = 0.023$) and were more likely to receive a higher dose (500 mg) of PO VAN (36.2% vs. 7.4%, $P < 0.0001$). Thirty-day mortality was 14.9% in the combination group vs. 7.4% in the monotherapy group, ($P = 0.338$). APACHE II Score was the only variable independently associated with 30-day mortality (OR = 1.13, 95% CI 1.03 – 1.24). There was no difference in probability of receiving IV MDZ based on APACHE II score. In a subgroup of patients matched by APACHE II score ($n = 76$), mortality remained nonsignificantly different (15.8% vs. 9.7%, $P = 0.480$).

Conclusion. Our data question the utility of IV MDZ in addition to PO VAN for ICU patients with severe CDI. There remains a possibility for confounding by indication in this retrospective analysis.

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489. Validation of the SHEA/IDSA Severity Criteria to Predict Poor Outcomes Among Inpatients and Outpatients With *Clostridium difficile* Infection

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Background. The SHEA/IDSA clinical practice guidelines suggest using leukocytosis (WBC ≥15,000 cells/μl) and serum creatinine (SCr) to identify severe cases of *Clostridium difficile* infection (CDI). It is unclear whether these criteria adequately predict poor outcomes among patients with CDI in the inpatient and outpatient settings

Methods. Retrospective cohort study of patients with CDI in the Veterans Affairs Health System from January 1, 2006 to December 31, 2016. Patients were included the first time they had a positive laboratory test indicating toxin or toxin genes from a stool sample and were followed for poor outcomes - defined as hospital or intensive care unit admission within 7 days of diagnosis, colectomy within 14 days of diagnosis, or 30-day all-cause mortality. Severity was defined according to the 2010 and 2018 versions of the criteria. For the 2010 criteria, patients with leukocytosis or a serum creatinine 1.5 times or more than the baseline were classified as severe. For the 2018 criteria, patients with leukocytosis or a SCr value ≥1.5 mg/dL were classified as severe. Maximum WBC and SCr values were assessed within 3 days prior to diagnosis. Baseline SCr was calculated as the average of SCr levels from 4 to 90 days prior to diagnosis. Poor outcome was modeled as a function of the 2010 and 2018 severity criteria separately using logistic regression. Criteria were assessed using the sensitivity (Sn), false negative (FN) rate, positive predictive value (PPV), and the area under the curve (AUC)

Results. We analyzed data from 86,112 episodes of CDI. According to the 2010 and 2018 criteria, 29.9% and 44.0% of episodes would be classified as severe. Severity could not be determined due to missing data in 16.3% and 15.0% of episodes, respectively. Seventy-five% of unclassified episodes were among outpatients. The 2018 severity criteria had a higher Sn (65.2% vs. 48.4%) but lower PPV (28.5% vs. 30.7%) than the 2010 criteria. The FN rate was lower for the 2018 criteria (34.8% vs. 51.6%), and AUCs were poor and similar (.587 vs. .582)

Conclusion. Although the 2018 CDI severity criteria would allow for classification of more cases and result in fewer false negatives, the performance remains poor. More work is needed to develop criteria to reliably and prospectively identify patients at risk of poor outcomes

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490. Comparison of *Clostridium difficile* Infection Outcomes by Diagnostic Testing Method

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Background. US laboratories are increasingly using nucleic acid amplification tests (NAAT) to diagnose *Clostridium difficile* infection (CDI) due to their increased sensitivity over toxin enzyme immunoassays (EIA), but NAATs may be more likely