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.

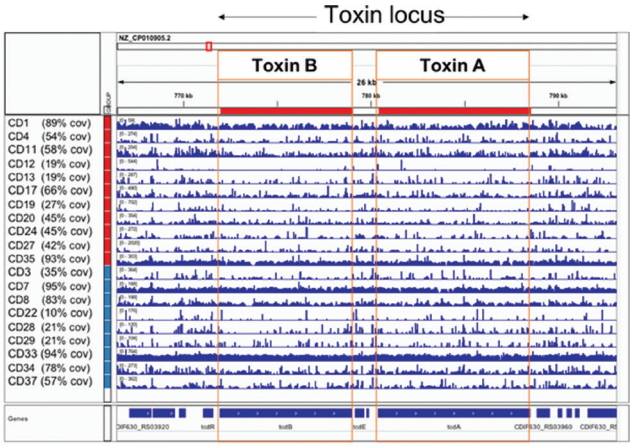

Figure 1. Mapping of tcdB and tcdA reads using shotgun metagenomics in fecal samples

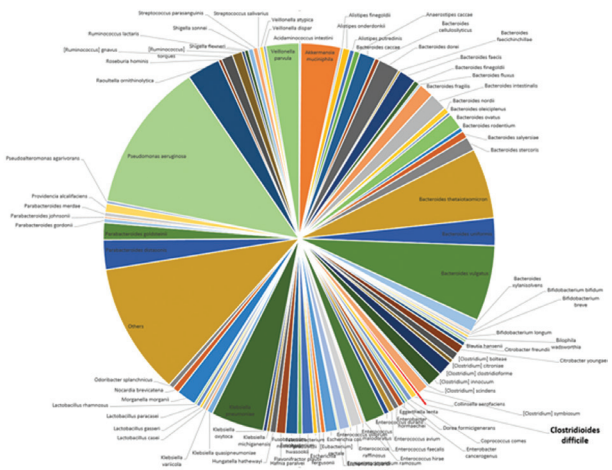

Fig 2: Microbiome in Patients with Active CDI

Disclosures. **All authors:** No reported disclosures.

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.

Disclosures. **E. Heil**, ALK-Abelló: Grant Investigator, Research grant. **K. Claeys**, Nabriva: Scientific Advisor, Consulting fee. Melinta: Scientific Advisor, Consulting fee.

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

Disclosures. **All authors:** No reported disclosures.

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

than toxin EIAs to detect colonization rather than true disease. Limited data indicate patients positive by toxin EIA (toxin+) have worse outcomes than those positive by NAAT (NAAT+) only, suggesting toxin EIA detects true infection more often than NAAT. We used multisite CDI surveillance data from the Centers for Disease Control and Prevention's Emerging Infections Program to compare clinical course and outcomes between toxin+ and NAAT+ only patients.

Methods. A case was defined as a positive *C. difficile* test in a person ≥1 year old with no positive tests in the prior 8 weeks. Cases detected during 2014–2015 by a testing algorithm using toxin EIA and NAAT were classified as toxin+ or NAAT+ only. Medical charts were reviewed. Death data were obtained from state death registries. Multivariable logistic regression models were used to compare CDI recurrence and 90-day mortality between the two groups, adjusting for age, sex, race, Charlson comorbidity index, and receipt of oral vancomycin. For the outcome of recurrence, we also adjusted for history of CDI in the prior 6 months.

Results. Of 4,878 cases, 2160 (44%) were toxin+ and 2,718 (56%) were NAAT+ only. Toxin+ cases were more likely than NAAT+ only cases to be ≥65 years old (48% vs. 38%; $P < 0.0001$), have white blood cells ≥15,000/μL (483/1,539 [31%] vs. 423/1,978 [21%]; $P < 0.0001$), and have received oral vancomycin ≤3 days of diagnosis (32% vs. 29%; $P = 0.03$). Comparing toxin+ to NAAT+ only cases, 21% vs. 11% had a recurrence ($P < 0.0001$), of which 71% vs. 33% had a toxin+ recurrence ($P < 0.0001$), and 10% vs. 9% died ≤90 days of diagnosis ($P = 0.12$). In multivariable analysis, a toxin+ result was associated with recurrence (adjusted odds ratio [aOR]: 1.89, 95% CI: 1.61–2.22) but not with 90-day mortality (aOR: 0.99; 95% CI: 0.81–1.22).

Conclusion. Toxin+ CDI is more severe by some markers and more likely to recur as toxin+. However, there was no difference in adjusted mortality, which may reflect an effect on mortality in NAAT+ only cases from mild CDI, receipt of unnecessary CDI treatment, or other factors.

Disclosures. **G. Dumyati**, Seres: Scientific Advisor, Consulting fee.

491. Clinical Manifestations and Outcomes of *Clostridium difficile* Infection in Long-Term Care Patients: An 8-Year Retrospective Cohort Study

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Background. Residents of long-term care facilities (LTCF) have high risk of *Clostridium difficile* infection (CDI) and its associated adverse outcomes. We describe the clinical characteristics and outcomes of CDI in LTCF patients admitted to an acute care (AC) hospital.

Methods. This is a descriptive retrospective study of CDI patients admitted to Detroit Medical Center (DMC) from LTCF from January 2009 to December 2017. Patients identified through chart review as having CDI on admission or within 48 hours of admission and without recent AC hospitalization in the prior 4 weeks were included. CDI and CDI severity were defined based on 2017 clinical consensus guidelines. Definitions: CDI-Either presence of diarrhea or evidence of ileus or megacolon and either presence of *C. difficile* toxin in stool or evidence of pseudomembranous colitis. Severe CDI-Presence of white blood counts ≥15,000 and serum creatinine >1.5 mg/dL. Complicated CDI-Presence of either toxic megacolon, sepsis, systemic inflammatory response syndrome, colonic perforation, or requiring ICU admission. Demographics, medical conditions, laboratory results, prior 60-day antibiotic use, CDI treatment, and outcomes were collected. Patients' follow-up extended 90 days; however, data were limited to hospital charts from index admission or readmission to the same hospital.

Results. Among the 85 patients who met the inclusion criteria, 45 (53%) were female, the mean age was 76 (SD: 16), and the median Charlson index score was 6 (range: 4–8). The common source of prior 60-day antimicrobial exposure was β-lactam/β-lactamase inhibitors (39%), Flagyl (15%), vancomycin (18%). The majority of patients were treated with flagyl (71%), 41% with vancomycin and 17% with concurrent or sequential flagyl and vancomycin. Majority of CDI patients (56%) experienced severe CDI with 25% experiencing complicated CDI. During the 90-day follow-up period, 32% of patients required readmission (within 30 days of discharge) for recurrent CDI and 15% of patients died in the hospital.

Conclusion. CDI patients admitted to DMC from LTCF experience considerable clinical burden. Further research is warranted toward understanding the burden of CDI among LTCF patients admitted to AC facilities.

Disclosures. **S. Chandramohan**, Pfizer Inc.: Collaborator, Research grant. **P. Zhang**, Pfizer Inc.: Employee, Salary. **K. Heinrich**, Pfizer Inc.: Employee, Salary. **E. Gonzalez**, Pfizer Inc.: Employee, Salary. **T. Chopra**, Pfizer Inc.: Collaborator, Research grant.

492. Long-Term Outcomes of *Clostridium difficile* Infection Among Medicare Beneficiaries

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Background. *Clostridium difficile* infection (CDI) is a common healthcare-associated infection, particularly among older adults. We used laboratory-confirmed CDI surveillance data from 8 states participating in the Centers for Disease Control and Prevention's Emerging Infections Program linked to claims data for Centers for Medicare and Medicaid Services (CMS) beneficiaries to measure variation in 1-year outcomes associated with CDI.

Methods. A CDI case was defined as a positive *C. difficile* stool test in 2014 in a person without a positive test in the prior 8 weeks. Cases aged ≥65 years were linked to their CMS beneficiary ID using unique combinations of date of birth, sex, and zip code. Each case was matched to five control beneficiaries who did not link to any case and were residents of the same catchment area. Inclusion criteria were continuous fee-for-service Medicare for the entire study period (1 year before and after event date), and no hospitalization or skilled nursing facility stay with an ICD-9-CM code for CDI in the year prior to their match date. Multivariable logistic regression models were used to compare mortality and hospitalization for 1 year following the event date between beneficiaries with and without CDI, adjusting for age, sex, race, catchment area, chronic conditions, number of hospitalizations in the prior year, and hospitalization status at the time of and 7 days preceding the event date.

Results. Of 5,097 cases aged ≥65, 3,082 (60%) were linked to a CMS ID, and 1,832 (59%) met inclusion criteria. In crude analysis, 34% of beneficiaries with CDI died within 1 year, compared with 5% of beneficiaries without CDI. Beneficiaries with CDI were also more likely to be hospitalized in the subsequent year (54% vs. 17%). Beneficiaries with CDI had a higher adjusted odds of death (adjusted OR 3.01, 95% CI: 2.46, 3.69) and hospitalization within 1 year (adjusted OR 1.93, 95% CI: 1.65, 2.25) than those without CDI.

Conclusion. Older adults with CDI were three times more likely to die in the year following infection and nearly two times more likely to be hospitalized compared with those without CDI, revealing independent long-term risk of poor outcomes. This excess morbidity and mortality supports the need to develop novel CDI prevention strategies for this population.

Disclosures. **All authors:** No reported disclosures.

493. Development of a Simple *Clostridium difficile* Infection Clinical Risk Prediction Tool for Medical Inpatients

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Background. Prevention of *Clostridium difficile* infection (CDI) remains a significant healthcare challenge. Risk prediction tools can potentially identify high-risk patients and allow for early prophylactic interventions. Various tools have been studied but none have been widely adopted. Our objective was to develop a simple risk prediction tool to identify medicine inpatients at high risk for developing primary CDI.

Methods. We conducted a retrospective, single-centre case–control study including patients admitted to the internal medicine service at our institution with a positive *C. difficile* polymerase chain reaction assay in loose stool. Controls were randomly selected from the same population. Risk factors for CDI were identified using univariate and multivariate logistic regression analyses. A model was created using variables that minimized Akaike Information Criterion and yielded higher area under the curve values.

Results. A total of 314 patients were included (157 with CDI and 157 controls). Variables included in the final 5-point, 3-variable risk prediction tool were age, modified Horn's index and antibiotic use within 3 months. The tool demonstrated good discrimination with a C statistic of 0.79 and model optimism of 0.04 based on a bootstrap sample of 2,000 replicates.

Conclusion. Our simple 3-variable risk prediction tool based on age, disease severity and recent antibiotic use facilitates rapid bedside assessment by clinicians to