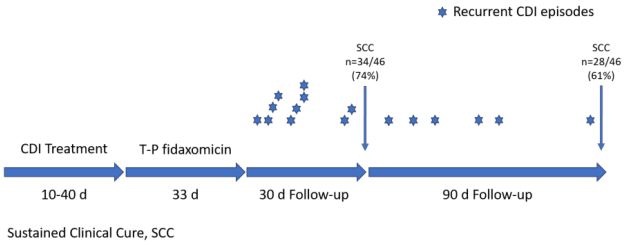
and 90 days, respectively. Among the 44 patients that successfully completed the T-P fidaxomicin regimen, recurrence developed in 10 (22.7%) and 16 (36.4%) of patients at 30 and 90 days, respectively, with a median (min-max) time to recurrence of 20 (3-87) days (Figure 1). Four patients with recurrence had received subsequent systemic antibiotics.

Figure 1. Course of CDI therapy and follow-up



Conclusion: A tapered-pulsed fidaxomicin strategy may be effective in patients with multiply rCDI who are refractory to other treatments, including a vancomycin tapered and pulsed regimen.

Disclosures: Larry H. Danziger, PharmD, Merck (Speaker's Bureau)

798. Metronidazole Exposure Prior to *Clostridiodes difficile* Infection (CDI) is a Risk Factor for Severe *C. difficile* Disease in Cancer Patients

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Session: P-32. HAI: C. difficile

Background: Antibiotic use is a risk factor for CDI. Few studies have correlated use of prior antibiotics with CDI severity in cancer patients. This study identified clinical and microbiology risk factors associated with severe CDI in patients with cancer. We hypothesized that previous antibiotic exposure and microbiome composition at time of CDI presentation, are risk factors for severe disease in cancer patients.

Methods: This non-interventional, prospective, single-center cohort study examined patients with cancer who had their first episode or first recurrence of CDI between Oct 27, 2016 and Jul 1, 2019. *C. difficile* was identified using nucleic acid amplification testing. Multivariate analysis was used to determine significant clinical risk factors for severe CDI as defined in the 2018 IDSA/SHEA guidelines. Alpha, and beta diversities were calculated to measure the average species diversity and the overall microbial composition. Differential abundance analysis and progressive permutation analysis were used to single out the significant microbial features that differed across CDI severity levels.

Results: Patient (n=200) demographics show mean age of 60 yrs., 53% female, majority White (76%) and non-Hispanic (85%). Prior 90 day metronidazole use (Odds Ratio OR 4.68 [1.47-14.91] p0.009) was a significant risk factor for severe CDI. Other factors included Horn's Index > 2 (OR 7.75 [1.05-57.35] p0.045), Leukocytosis (OR 1.29 [1.16-1.43] p< 0.001), Neutropenia (OR 6.01 [1.34-26.89] p0.019) and Serum Creatinine >0.95 mg/dL (OR 25.30 [8.08-79.17] p< 0.001). Overall, there were no significant differences in alpha and beta diversity between severity levels. However, when identifying individual microbial features, the high presence of *Bacteroides uniformis, Ruminococceae, Citrobacter koseri* and *Salmonella* were associated with protection from severe CDI (p< 0.05).

Table 1 - Results of multivariate logistic regression analysis of factors associated with severe CDI

Table 1: Results of multivariate logistic regression analysis of factors associated with severe CDI

	Univariate analysis		Multivariate analysis [a]	
Variable	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Episode		0.19		-
First episode	3.99 (0.51, 31.22)			
Recurrent episode	Reference			
Symptoms				
Abdominal pain	1.59 (0.80, 3.18)	0.19		-
Bloating	2.23 (0.77, 6.43)	0.14		-
Mucus in stools	3.90 (0.53, 28.55)	0.18		-
Antimicrobial Exposure				
Cephalosporin	1.90 (0.95, 3.79)	0.07		-
Metronidazole	2.77 (1.15, 6.68)	0.02	4.68 (1.47, 14.91)	0.009
Use of GABA mimetics –Other Benzodiazepines	0.57 (0.24, 1.38)	0.21		-
Charlson co-morbidity score	1.13 (0.99, 1.28)	0.07		-
Horn's Index		0.17		0.045
1 - Medical management	Reference		Reference	
2,3,4 - ICU stay or critically ill	2.96 (0.64, 13.78)		7.75 (1.05, 57.35)	
Laboratory Parameters				
WBC	1.14 (1.07, 1.22)	< .0001	1.29 (1.16, 1.43)	< .0001
Neutropenia	0.54 (0.22, 1.32)	0.18	6.01 (1.34, 26.89)	0.019
Leukopenic	0.51 (0.25, 1.04)	0.07		-
Serum albumin	0.67 (0.39, 1.15)	0.14		-
Serum Creatinine > 0.95 mg/dL	8.60 (3.95, 18,71)	< .0001	25.30 (8.08, 79.17)	< .0001
Co-pathogen present -Sapovirus [b]	*	0.12		#

Abbreviations: OR = Odds ratio; 95% CI = 95% confidence interval.

[a] Elimination procedure (p> 0.05 in multivariate analysis).

[b] Patient with sapovirus had non-severe CDI.

Figure 1. Microbiome features identified by progressive permutation analysis as seen in a volcano plot.

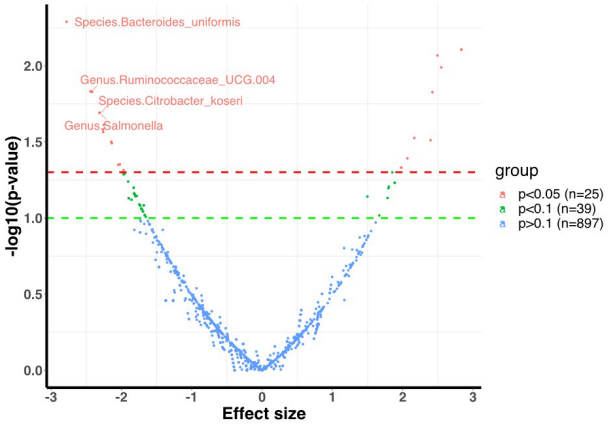

Figure 1. Microbiome features identified by progressive permutation analysis as seen in a volcano plot. *Bacteroides uniformis, Citrobacter koseri* at the species level and *Salmonella* and *Ruminococcaceae* at the genus level, were associated with protection from severe CDI. This was confirmed by differential abundance analysis when compared to non-severe CDI cases.

Conclusion: A number of risk factors for severe CDI were identified among this population, including prior 90 day metronidazole use. Also, increased relative abundance of *Bacteroides uniformis, Ruminococceae, Citrobacter koseri* and *Salmonella* were linked to protection from severe CDI. Reducing metronidazole use in patients with cancer may help prevent subsequent severe CDI.

Disclosures: **Adilene Olvera, MPH MLS (ASCP)**, **MERK** (Grant/Research Support, Scientific Research Study Investigator) **Kevin W. Garey, PharmD, MS, FASHP**, **Merck & Co.** (Grant/Research Support, Scientific Research Study Investigator) **Ryan J. Dillon, MSc**, **Merck & Co., Inc.,** (Employee) **Engels N. Obi, PhD**, **Merck & Co.** (Employee)

799. Mini Root Cause Analysis Reveals Opportunities for Reducing *Clostridioides difficile* Infection Rates

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Session: P-32. HAI: C. difficile

Background: *C. difficile* remains the single most common pathogen among healthcare-associated infections. We conducted a multi-center, prospective study using on-site, near real-time root cause analyses to identify opportunities for reducing hospital-onset *C. difficile* infection rates (HO-CID).

Methods: This prospective cohort study enrolled inpatients with HO-CDI admitted to one of 20 participating hospitals in the southeastern United States from July 2019 to June 2020. For each HO-CDI case, mini root cause analyses were conducted by on-site physicians, infection preventionists, or stewardship pharmacists to assess appropriateness of *C. difficile* testing and inpatient antibiotic use from the 30 days preceding HO-CDI diagnosis.

Results: The cohort captured 554 total HO-CDI cases and 956 antibiotic use events. 147 (26.5%) of HO-CDI cases were adjudicated as likely inappropriate and a further 51 (9.2%) as potentially inappropriate. Among inappropriately tested cases, 103 (52.0%) had received either laxatives or tube feeds in the preceding 48 hours. 132 (13.8%) of antibiotic use events were identified as potentially inappropriate. Among potentially inappropriate antibiotic use events, 40 (30.3%) received unnecessarily broad-spectrum antibiotics, 20 (15.2%) lacked a confirmed infectious diagnosis, and 4 (3.0%) received a longer than guideline-recommended duration. Risk of inappropriate antibiotic use varied by infection type, with treatment of urinary tract infection being associated with the highest risk of inappropriate antibiotic use (table 1).

Table 1: Relative Risk of Inappropriate Antibiotic Use by Indication

Infection Type	RR for inappropriate antibiotic use (95% CI)
Bacteremia	0.22 (0.08-0.58)
Intra-abdominal	0.42 (0.19-0.92)
Skin/soft tissue	0.65 (0.17-2.47)
Pneumonia	1.11 (0.72-1.71)
Urinary tract	1.52 (1.02-2.26)

Conclusion: Mini root cause analyses may be a helpful tool for identifying -specific opportunities to reduce HO-CDI rates. We found a high rate of inappropriate testing, usually related to alternative causes for diarrhea such as laxative receipt or tube feeds. While rates of inappropriate antibiotic use were lower than has been reported elsewhere, the majority of opportunities for improvement related to overly broad-spectrum coverage. Urinary tract infections were most strongly associated with inappropriate antibiotic use preceding HO-CDI.

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800. Oral Vancomycin Prophylaxis Against Clostridioides difficile in Patients Admitted to a Tertiary Academic Medical Center

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Session: P-32. HAI: C. difficile

Background: In an effort to more accurately diagnose *Clostridioides difficile* infection (CDI), many hospitals have switched to two-step testing algorithms that rely on nucleic acid amplification testing with reflex enzyme immunoassay for toxin. Additionally, oral vancomycin prophylaxis (OVP) against CDI is increasingly being used; initial studies focused on preventing recurrence in patients with a prior history of CDI, but OVP is also being studied in primary prevention. We hypothesized that following the implementation of two-step testing, clinicians may use OVP for prevention of a patient's first episode of CDI based on knowledge of prior PCR+/Toxin- testing.

Methods: We performed a single-center, retrospective cohort study of patients admitted to Beth Israel Deaconess Medical Center. We identified patients who received oral vancomycin once daily or BID for the prevention of CDI following implementation of two-step testing. Patients who received oral vancomycin as part of a taper following acute infection were excluded. We categorized rationale for prophylaxis based on clinical documentation and collected details of patients' CDI history, antibiotic exposure, and subsequent CDI testing during hospitalization.

Results: In the 12 months following implementation of two-step testing, there were 80 patients who received OVP during hospitalization (2 daily and 78 BID). The vast majority (73, 91.3%) had a history of CDI and received OVP for secondary prevention while receiving systemic antibiotics. There were only 3 patients (3.8%) without known clinical history of CDI whose clinicians documented prophylaxis based on previous PCR+/Toxin- testing. Patients on OVP received a mean of 4.1 systemic antibiotics during hospitalization. When continuing OVP for a finite period after discontinuation of systemic antibiotics, this was most commonly done for 2-7 days (16 of 26, 61.5%). 22 patients underwent stool testing for CDI while receiving OVP in the hospital and all resulted PCR-negative.

OVP Indication