Assessing the Real-World Inpatient Treatment Paradigm for Recurrent Clostridium Difficile

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Background and Objective

- Clostridium difficile infection (CDI) results or occurs in over 200,000 hospitalizations in the United States annually[1]
- Treatment with antibiotics is often successful but 20-30% of patients experience a recurrence; among those with a second recurrence, 40-60% suffer from additional episodes[2]
- Treatment recommendations for recurrent CDI (rCDI) exist but are weak and typically based on low-quality evidence[3,4]
- This analysis of real-world hospital data aimed to characterize the treatment regimens for inpatients experiencing rCDI, including both hospital- and community-acquired recurrence, and to compare these regimens to current treatment guidelines

Methods

Data Source

- Hospitalization discharge records were sourced from the Premier Hospital Database, which is the largest acute care database in the US

Cohort Selection

- Hospital discharges between October 2017 and December 2018 reporting rCDI (ICD-10-CM diagnosis code A04.71, which was introduced in October 2017)
- Discharges were required to have indicated the use of at least one antibiotic commonly used to treat rCDI – vancomycin, metronidazole, fidaxomicin, or rifaximin. Identification of antibiotic use was conducted through the review of discharge billing records

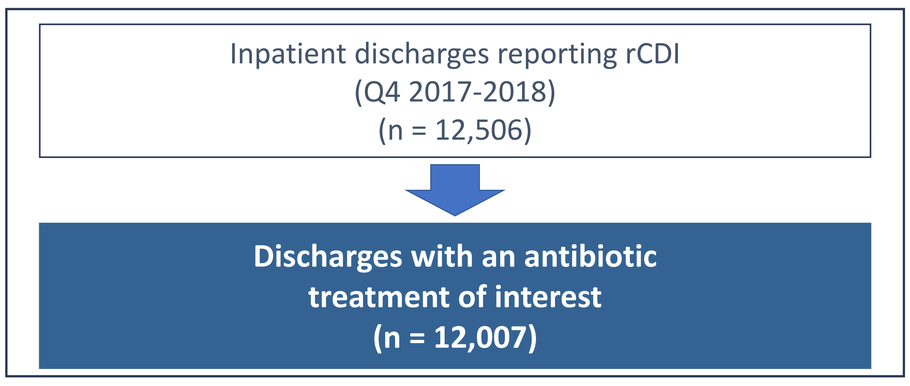
Analysis

- Summary measures were calculated for patient demographics, antibiotic treatments (including type and whether used as a monotherapy or combination therapy), and length of stay (LOS)

Results

- 12,007 hospitalizations reporting rCDI across 9,824 patients were identified

Figure 1. Patient Identification



- On average, patients were 66.1 years old, more likely to be female (62%), and receiving Medicare coverage (71%)

Table 1. Patient Characteristics

	N	% of Total
Patients	9,824	100%
Age (Mean, 95% Confidence Interval)	66.1	(65.8, 66.4)
Age Group		
≤ 10	58	1%
11-17	37	0%
18-34	518	5%
35-44	532	5%
45-54	1,023	10%
55-64	1,707	17%
65-74	2,364	24%
≥ 75	3,585	36%
Gender		
Female	6,107	62%
Male	3,717	38%
Race		
White	8,086	82%
Black	927	9%
Other	715	7%
Unknown	96	1%
Payer		
Medicare	7,023	71%
Commercial	1,368	14%
Medicaid	1,047	11%
Other	386	4%

- Vancomycin was used in 94% of hospitalizations; metronidazole and fidaxomicin were reported in 51% and 14% of cases, respectively
- Of rCDI discharges where vancomycin was used, 44% featured vancomycin only, while the other 56% featured vancomycin and at least one other antibiotic
- Of rCDI discharges where metronidazole was used, 6% featured metronidazole only, while the other 94% featured metronidazole and at least one other antibiotic
- Of rCDI discharges where fidaxomicin was used, 16% featured fidaxomicin only, while the other 84% featured fidaxomicin and at least one other antibiotic

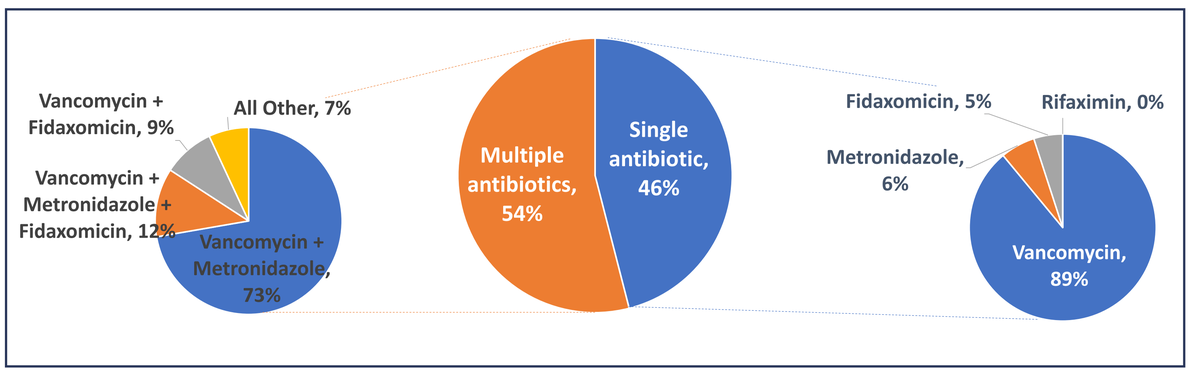
Results

Table 2. rCDI Treatments Reported Throughout Hospitalization

Treatment	Discharge Count	% of Total
Vancomycin	4,926	41%
Vancomycin + Metronidazole	4,727	39%
Vancomycin + Metronidazole + Fidaxomicin	747	6%
Vancomycin + Fidaxomicin	556	5%
Metronidazole	344	3%
Fidaxomicin	272	2%
All Other	435	4%

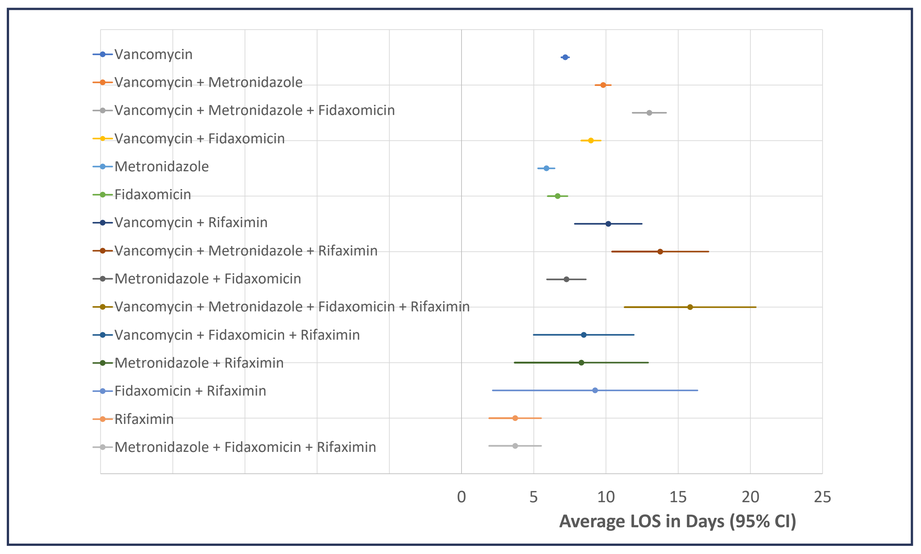
- The most common combination of antibiotics was vancomycin and metronidazole, which comprised 73% of all discharges where multiple antibiotics were used (39% of all rCDI hospitalizations). All other combinations accounted for less than 15% of all rCDI hospitalizations.

Figure 2. Proportion of Discharges Involving Multiple Antibiotics



- Patients receiving monotherapy had a shorter LOS than those receiving combination therapy (7.1 versus 10.2 days, respectively, $p < 0.001$)

Figure 3. Length of Stay by Treatment



Conclusions and Implications

- The real-world treatment of inpatients experiencing rCDI aligned only moderately with published guidelines, with higher use of metronidazole and lower use of fidaxomicin than might be expected per these recommendations

Table 3. Clinical Practice Guidelines for Treating rCDI in Adults[4]

Clinical Definition	Treatment used for Initial CDI Episode	Recommended Treatment	Strength of Recommendation / Quality of Evidence
First recurrence	Metronidazole	VAN for 10 days	Weak / Low
	Vancomycin	• VAN in tapered / pulsed regimen, OR	Weak / Low
		• FDX for 10 days	Weak / Moderate
Second or subsequent recurrence		• VAN in tapered / pulsed regimen, OR	Weak / Low
		• VAN for 10 days followed by RFX for 20 days, OR	Weak / Low
		• FDX for 10 days, OR	Weak / Low
		• Fecal microbiota transplantation	Strong / Moderate

Abbreviations: VAN - vancomycin; FDX - fidaxomicin; RFX - rifaximin

- The shorter lengths of stay observed among monotherapy patients may be explained by the severity of patients receiving the therapy, i.e., less severe patients may have received a single type of antibiotic. Further analyses exploring the treatment patterns at a deeper level and controlling for patient and other treatment factors will be needed to fully assess the association
- These findings raise questions about the clinical rationale driving use decisions and how these treatment regimens relate to patient characteristics and outcomes
- While current approaches to treatment rely heavily on the effectiveness of vancomycin, the rate of rCDI is increasing, suggesting the need for a more effective alternative and stronger evidence to define the optimal treatment regimen[5]

References

1. https://www.cdc.gov/drugresistance/pdf/threats-report/clostridioides-difficile-508.pdf
2. Cornely OA, et al. Clin Infect Dis. 2012 Aug;55 Suppl 2:S154-61.
3. Gupta A, et al. JAMA. 2018 Sep 11;320(10):1031-1032.
4. McDonald LC, et al. Clin Infect Dis. 2018 Mar 19;66(7):987-994.
5. Burke KE, Lamont JT. Gut Liver. 2014 Jan;8(1):1-6.