

# Disease and Treatment Epidemiology of Initial *Clostridium difficile* Infection in a National Cohort



Tristan T Timbrook, PharmD, MBA, BCPS<sup>1,2</sup>, Haley J Morrill, PharmD<sup>1,2,3</sup>, Kerry L LaPlante, PharmD<sup>1,2,4</sup>, and Aisling R Caffrey, Ph.D., MS<sup>1,2,3</sup>

<sup>1</sup>Infectious Diseases Research Program, Providence Veterans Affairs Medical Center (VAMC), Providence, RI; <sup>2</sup>College of Pharmacy, URI, Kingston, RI;

<sup>3</sup>Veterans Affairs Medical Center, Center of Innovation in Long-Term Support Services, Providence, RI;

<sup>4</sup>Warren Alpert Medical School of Brown University, Providence, RI



## ABSTRACT

**Background:** *Clostridium difficile* infection (CDI) is a major public health threat with high mortality and recurrence. However, the epidemiology of initial CDI (iCDI) is not well described in Veterans

**Objectives:** To describe clinical characteristics, treatment patterns, and outcomes among Veterans with iCDI between 2011 and 2014.

**Methods:** This national, retrospective cohort study included patients with a positive stool sample for *C. diff* toxin(s) and at least 2 days of CDI therapy (PO or IV metronidazole [MTZ], PO or PR vancomycin [VAN] with or without MTZ IV, or fidaxomicin [FID]), with no CDI in the last year. Patients with CDI by lab test in the previous one year were excluded. Descriptive statistics were used to summarize the data

**Results:** iCDI was identified in 46,752 patients. The mean age of patients was 66.3±14 years, 93.5% (N=43,707) were male, and 74.3% (N=34,717) were white. Commonly observed comorbid conditions that are considered risk factors for recurrent CDI included COPD (7.6%, N=3,570), CKD (8.7%, N=4,075), diabetes (13.1%, N=6,129), and malignancies (8.3%, N=3,895). Most iCDI was diagnosed in the outpatient setting (68.2%, N=31,894). Utilization of MTZ monotherapy was high (81.5%, N=38,095), as compared with combination therapy of MTZ+VAN (10.3%, N=4,815) or VAN monotherapy (8.0%, N=3,752). FID was used in <1% of iCDI. The 30-day all-cause mortality was 10.3% (N=4,824).

**Conclusions:** A majority of Veterans had acid suppression therapy and/or antibiotics shortly before their iCDI. Most Veterans were treated outpatient, with MTZ, and for a duration of 7 days. We found that 30-day mortality was similar to those previously reported

Note: abstract updated 8/9/16

## BACKGROUND

- *Clostridium difficile* infection (CDI) is a major public health threat<sup>1</sup>
- CDI has been associated with 14,000 deaths annually and \$4.8 billion in increased costs for acute care facilities in the US<sup>2</sup>
- CDI recurrence rates are common and average 20% nationally while 30-day mortality has been estimated around 9%<sup>2</sup>
- Characteristics of iCDI in a large population with laboratory-confirmed CDI have not been previously described

## OBJECTIVES

- To describe clinical characteristics, treatment patterns, and outcomes among Veterans with iCDI, 2011-2014

## METHODS

- Data source: VA databases created from electronic medical records
- Population: national, retrospective cohort of patients ≥ 18 years of age, 2011-2014; inpatient (acute and long-term care) and outpatient settings
- iCDI definition: (1) positive stool sample for *C. difficile* toxin(s) by PCR or culture AND (2) at least 2 days of CDI therapy (metronidazole [MTZ] PO/IV, vancomycin [VAN] PO or PR with or without MTZ IV, or fidaxomicin PO [FID]), AND (3) no positive CDI test in the last year
- Comorbidities: ICD-9 diagnosis codes from index encounter and year prior
- Treatments: pharmacy records
- Outcomes: 30-day all-cause mortality, 30-day CDI recurrence, length of stay
- Analysis: descriptive statistics

## RESULTS

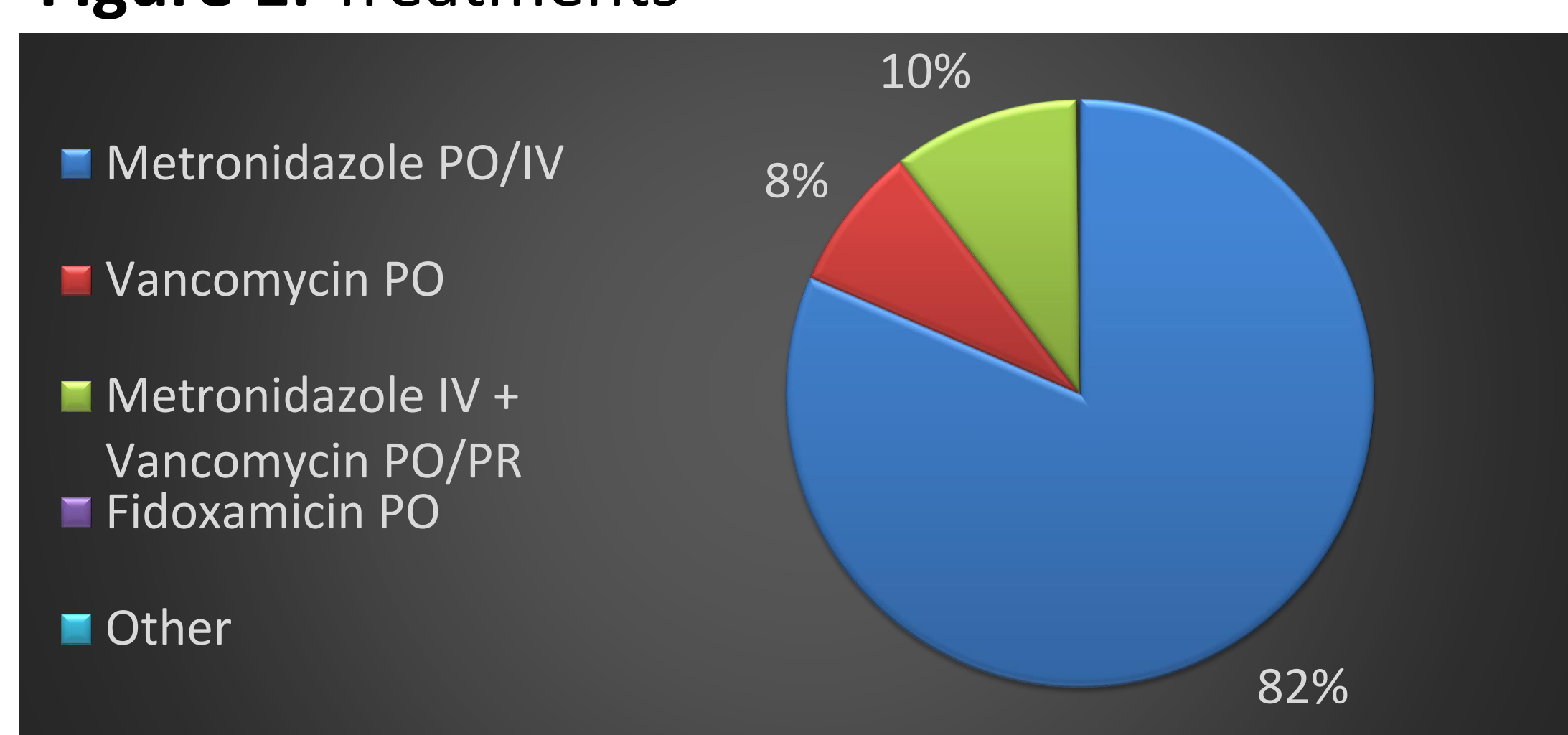
- iCDI was identified in 46,752 patients
- The mean age of patients was 66.3±14.0 years, 93.5% (N=43,707) were male, 68.2% (N=31,894) were outpatient
- MTZ monotherapy was utilized in 81.5% (N=38,095) of patients
- The 30-day all-cause mortality was 10.3% (N=4,824)

**Table 1.** Characteristics of Adults with iCDI

Demographics	No.	%
Age (years), mean (SD)	66.3	(±14)
Male Gender	43,707	(93.5)
BMI*, median (IQR)	28	(24.8-31.0)
<b>Race</b>		
Black	7,405	(15.8)
White	34,717	(74.3)
Other	4,630	(9.9)
<b>Common Comorbid Risk Factors for CDI Present at Treatment</b>		
Diabetes	6,129	(13.1)
Chronic Kidney Disease	4,075	(8.7)
Other Gastrointestinal disorders	4,057	(8.7)
Malignancies	3,895	(8.3)
Congestive Obstructive Pulmonary Disorder	3,570	(7.6)
Urinary Tract Infections	3,556	(7.6)

IQR = interquartile range, SD = standard deviation; BMI = body mass

**Figure 1.** Treatments



**Table 2.** Patient Clinical Presentation

Diagnosis Setting	No.	%
Outpatient	31,894	68.2
<b>Laboratory Values</b>	<b>Median</b>	<b>IQR</b>
Albumin (g/dL)*	3	(2.5-3.7)
Blood Urea Nitrogen (mg/dL)*	18	(12-29)
Serum Creatinine (mg/dL)*	1	(0.8-1.5)
White Blood Cell (K/uL)*	10	(6.8-14.2)
<b>Healthcare CDI Risks</b>	<b>No.</b>	<b>%</b>
Non-CDI antibiotics given 30d before treat start	28,973	(62.0)
Non-CDI antibiotics given during treat	30,976	(66.3)
PPI or H2RA given 90d before treat start	30,157	(64.5)
Immunosuppressant given 90d before treat start	7,891	(16.9)
Surgery within 90d before admission/current	8,242	(17.6)

Note. IQR = interquartile range; CDI = *Clostridium difficile* infection; IQR = interquartile range; PPI = proton pump inhibitor; H2RA = histamine receptor 2 antagonist; d = day; \*when available (>70% of cases)

**Table 3.** Clinical Outcomes

Outcomes	No.	%
30-day Mortality	4,824/46,752	(10.3)
Inpatient	2,265/14,858	(15.2)
Outpatient	2,559/31,894	(8.0)
CDI 30-day recurrence	2,358/14,858	(5.0)
Inpatient	1,089/14,858	(7.3)
Outpatient	1,269/31,894	(4.0)
Colectomy during treatment or within 30 days after treatment	261	(<1)
Length of Stay (d)*, median (IQR)	9	(4-20)

IQR = interquartile range; \*For inpatients; \*\*For outpatients and long term care facility patients

## CONCLUSIONS

- Risk factors associated with the occurrence of CDI, such as antibiotic therapy, were observed in the majority of Veterans in 30-90 days before iCDI
- iCDI cases occurred mostly outpatient, were treated with oral MTZ, and duration of therapy was around 7 days typically
- The 30-day mortality observed in this study approximated those reported nationally. In contrast, our initial recurrences were lower.

**References 1.** Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013.

<http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>. Accessed September 1, 2015. **2.** Lessa FC, Mu Y, Bamberg WM, et al. Burden of *Clostridium difficile* Infection in the United States. *N Engl J Med*. 2015;372(9):825-834.

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