



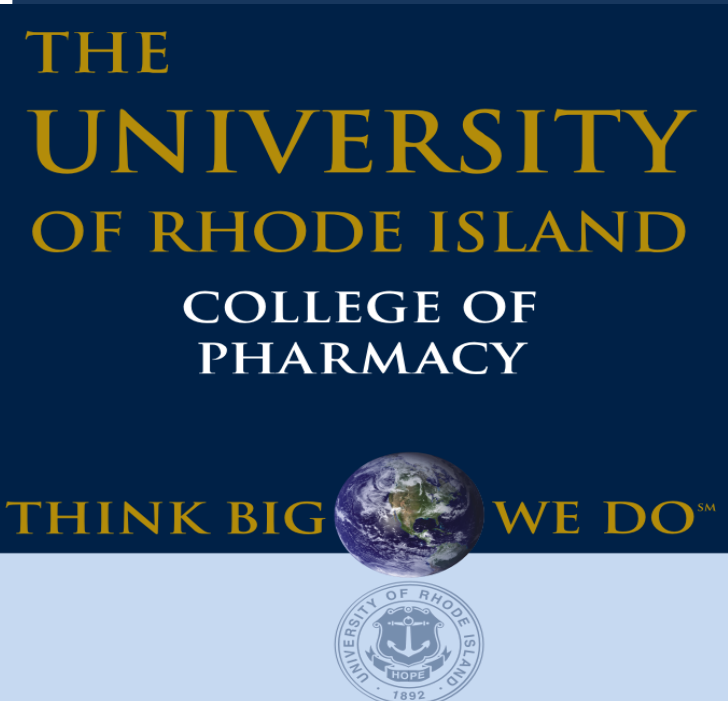
Differences in Characteristics and Outcomes among Veterans with *Clostridium difficile* infection (CDI) by Treatment

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ABSTRACT

Background: Clinical characteristics and outcomes by treatment among Veterans with first episode CDI are largely unknown.

Methods: This was a retrospective study in a national cohort of adult Veterans with a first CDI episode between 2011-2014, defined as a positive stool sample for *C. diff* toxin(s) and receipt of ≥2 days of CDI treatment (IV or PO MTZ, PO or PR VAN, or FID) and no CDI episodes in prior year. Recurrence was a CDI episode within 30 days of the end of treatment. Differences between patients treated with MTZ vs. VAN, MTZ+VAN, and FID alone or in combination with VAN +/- MTZ (FID/+) were assessed using Fisher's exact or χ^2 tests and Wilcoxon Rank Sum test.

Results: 46,752 episodes of iCDI were identified. The table below includes characteristics and crude outcomes by treatment. Data presented as n (%) or median (IQR) (*p<0.05).

	MTZ	VAN	MTZ+VAN	FID/+
Median Age (IQR)	65 (58-75)	68 (23-79)*	68 (62-80)*	68 (64-77)*
Gender, male	35,470 (93.1)	35,56 (94.8)*	4,593 (95.4)*	88 (97.8)
White Race	28,276 (74.2)	2,822 (75.2)*	3,553 (73.8)	66 (73.3)
Inpatient treatment	9,292 (24.4)	1,991 (53.1)*	3,510 (72.9)*	66 (72.2)
Comorbidities				
Solid Organ Cancer	2,213 (5.8)	417 (11.1)*	700 (14.5)*	12 (13.3)
COPD	2,350 (6.2)	445 (11.9)*	756 (15.7)*	19 (21.1)
CKD	2,578 (6.8)	636 (17.0)*	846 (17.6)*	15 (16.7)
DM	1,309 (3.4)	260 (6.9)*	312 (6.5)*	7 (7.8)
30-Day CDI Recurrence	1,721 (4.5)	271(7.2)*	360(7.5)	6 (6.7)
30-Day All-Cause Mortality	3,277(8.6)	453(12.1)*	1,078(22.4)*	16 (17.8)
30-Day Re/admission	6,774(17.8)	807(21.5)*	1,162(24.1)*	19 (21.1)

Conclusions: Patients that received VAN, MTZ+VAN, or FID/+ were sicker, older and had higher mortality rates compared to those that received MTZ. Higher recurrence rates were observed in those that received VAN and MTZ+VAN compared to MTZ.

BACKGROUND

- CDI has been associated with 14,000 deaths annually and 4.8 billion in increased costs for acute care facilities in the US¹
- Clinical characteristics and outcomes by treatment among Veterans with first episode CDI are largely unknown.

METHODS

- National retrospective cohort study of Veterans
- Inclusion: Patients age ≥ 18 years with a first positive stool for *C. diff* toxin(s) and ≥2 days of CDI therapy (metronidazole [MTZ] PO or IV, vancomycin [VAN] PO or PR +/- MTZ IV, or fidaxomicin [FID] PO) during the study period of 2011-2014
- Exclusion: CDI in the previous year
- Differences between patients treated with MTZ vs. VAN, MTZ+VAN, and FID alone or in combination with VAN +/- MTZ (FID/+) were assessed using Fisher's exact or χ^2 tests and Wilcoxon Rank Sum test.

RESULTS

- 46,752 episodes of iCDI were identified between 2011 and 2014 within VA
- Most iCDI was diagnosed in the outpatient setting (68.2%, N=32,894)
- MTZ PO/IV monotherapy used in 81.5% (N=38,095), VAN PO/PR monotherapy in 8.0% (N=3,752), MTZ PO/IV and VAN PO/PR combination in 10.3% (N=4,815), and FID alone or in combination with VAN +/- MTZ (FID/+) <1% (N=90)
- Median duration (interquartile range [IQR] of treatment was 7 days (3-11)

Table 1. Characteristics of Adults with iCDI by Treatment

	MTZ N=38,095	VAN N=3,752	MTZ+VAN N=4,815	FID/+ N=90
Median Age (IQR)	65 (58-75)	68 (23-79)*	68 (62-80)*	68 (64-77)*
Gender, male	35,470 (93.1)	35,56 (94.8)*	4,593 (95.4)*	88 (97.8)
White Race	28,276 (74.2)	2,822 (75.2)	3,553 (73.8)	66 (73.3)
Inpatient tx	9,292 (24.4)	1,991 (53.1)*	3,510 (72.9)*	66 (72.2)*
Comorbidities				
Solid Organ Cancer	2,213 (5.8)	417 (11.1)*	700 (14.5)*	12 (13.3)*
COPD	2,350 (6.2)	445 (11.9)*	756 (15.7)*	19 (21.1)*
CKD	2,578 (6.8)	636 (17.0)*	846 (17.6)*	15 (16.7)*
DM	1,309 (3.4)	260 (6.9)*	312 (6.5)*	7 (7.8)*
Lab Values				
Albumin, median (IQR)	3(2.6-3.8)	3(2.3-3.4)*	3(2.2-3.2)*	3(2.2-3.2)*
BUN, median (IQR)	17(11-27)	21(13-35)*	22(14-39)*	26(13.1-40.5)*
SCr, median (IQR)	1(0.8-1.5)	1(0.8-1.8)*	1(0.8-2.0)*	1(0.8-1.8)
WBC, median (IQR)	9 (6.7-13.5)	10 (7-15.8)*	13 (8.2-19.3)*	11 (7.1-18.1)*

RESULTS

Table 1. Characteristics of Adults with iCDI (Cont.)

	MTZ	VAN	MTZ+VAN	FID/+
Antibiotics given 30d before tx start	23,176 (60.8)	2,335(62.2)	3,413(70.9)*	49 (54.4)
Antibiotics given during tx	25,131 (66.0)	2,034(54.2)*	3,752(77.9)*	59 (65.6)
PPI or H2RA given 30d before tx start	19,633 (51.5)	2,077(55.4)*	3,061(63.6)*	55 (61.1)
Immunosuppressant 30d before tx start	4,809 (12.6)	628 (16.7)*	949 (19.7)*	20 (22.2)*
Surgery w/in 90d before event	6,557 (17.2)	608 (16.2)	1065 (22.1)*	12 (13.3)

Data presented as no. (%) unless otherwise specified; BUN = blood urea nitrogen; COPD = congestive obstructive pulmonary disorder; GI = gastrointestinal; FID= fidaxomicin; ICD-9 = International Classification of Diseases Ninth Revision; IQR = interquartile range, MTZ= metronidazole; SCr = serum creatinine; VAN= vancomycin; Tx= Treatment; WBC = white blood cell; W/in= within; *p<0.05

Table 2. Clinical Outcomes of Adults with iCDI

	MTZ	VAN	MTZ+VAN	FID/+
30-day mortality	3,277(8.6)	453(12.1)*	1,078(22.4)*	16 (17.8)*
30-day re/admission	6,774(17.8)	807(21.5)*	1,162(24.1)*	19 (21.1)
30-day CDI recurrence	1,721 (4.5)	271(7.2)*	360(7.5)*	6 (6.7)
Colectomy during treatment	115(<1)	<5 (<1)*	26 (<1)*	<5 (<1)
Length of Stay, median (IQR)	8 (4-18)	12 (5-30)*	11 (5-21)*	17 (7-42)*
Tx Duration, median (IQR)	6 (3-11)	8 (4-14)*	8 (4-14)*	12 (6-20)*

Data presented as no. (%) unless otherwise specified; FID= fidaxomicin; IQR = interquartile range, MTZ= metronidazole; VAN= vancomycin; Tx= Treatment; *p<0.05

CONCLUSIONS

- Patients that received VAN, MTZ+VAN, or FID/+ had higher mortality rates vs. MTZ. Higher recurrence rates were observed in those that received VAN and MTZ+VAN vs. MTZ. Comparative effectiveness studies are needed to identify optimal CDI treatment.

References 1. 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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