Annual Surveillance Summary: *Clostridioides* (*Clostridium*) *difficile* Infections in the Military Health System (MHS), 2018

NMCPHC-EDC-TR-535-2019

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Prepared 01 May 2019

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01/05/2019	Technical report, annual	01/01/2018 - 12/31/2018

4. TITLE AND SUBTITLE
Annual Surveillance Summary: Clostridium difficile Infections in the Military Health System (MHS), 2018

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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8. PERFORMING ORGANIZATION REPORT NUMBER
NMCPHC-EDC-TR-535-2018

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
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10. SPONSOR/MONITOR'S ACRONYM(S)
EDC, NMCPHC

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
NMCPHC-EDC-TR-535-2018

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The EpiData Center conducts routine surveillance of Clostridium difficile infection (CDI) among all beneficiaries seeking care within the Military Health System. CDI incidence in the MHS population in CY 2018 decreased slightly overall and was just below expected normal variation when compared to the weighted historic IR for CYs 2015-2017. Demographic and clinical characteristics in CY 2018 were similar to trends reported in CY 2017. Patients with CDI and specific comorbidities are especially vulnerable and may benefit from prompt CDI identification and treatment. Use of antibiotics and gastric acid inhibitors is regarded as a risk factor for CDI.

15. SUBJECT TERMS
Health Level 7 (HL7), microbiology, surveillance, Clostridium difficile, Military Health System (MHS), antibiotic resistance, gastric acid inhibitor

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Uzo Chukwuma
					19b. TELEPHONE NUMBER *(Include area code)*
U	U	U	UU	17	757-953-0970

Standard Form 298 (Rev. 8/98)
Prescribed by ANSI Std. Z39.18

Abstract

The EpiData Center (EDC) conducts routine surveillance of *Clostridioides* (formerly *Clostridium*) *difficile* (CD) incidence among all beneficiaries seeking care within the Military Health System (MHS). This report is a calendar year (CY) 2018 update to the CY 2017 annual report on *C. difficile* infection (CDI) among MHS beneficiaries.

Multiple data sources were linked to assess descriptive and clinical factors related to CD. Health Level 7 (HL7)-formatted microbiology and chemistry data identified CDI. These infections were matched to HL7-formatted CHCS pharmacy data to assess prescription practices and the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures.

CDI incidence in the MHS population in CY 2018 decreased slightly overall and was just below expected normal variation when compared to the weighted historic IR for CYs 2015-2017.[1-3] Demographic and clinical characteristics were similar to trends reported in CY 2017.[3 4] The most frequent first-line antibiotic treatment in 2018 was vancomycin, a change from metronidazole in previous year's annual reports. Oral vancomycin is the first-line therapy recommended in current guidelines.[4] There has not been a change in guidelines for first-line therapy in three decades. The burden of CDI continues to largely manifest in the community setting, among older age groups, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with specific comorbidities considered risk factors for CDI, such as diabetes, renal failure, chronic obstructive pulmonary disease (COPD), and cancer, represent a patient group within the MHS population that is especially vulnerable to poorer health outcomes, such as recurrent CDI and increased risk of mortality, when compared to patients without those comorbidities.[6] This group may especially benefit from prompt CDI identification and treatment.

Interventions that reduce antibiotic exposure are the primary measures recommended to reduce CDI incidence and recurrence. These measures include limiting the use of unnecessary antibiotics, prescribing antibiotics that are lower risk for contributing to CDI, and using antibiotics for the shortest reasonable duration.[7] The MHS population can benefit from these interventions to decrease both CDI incidence and antibiotic selective pressure that may influence the development of multidrug-resistant organisms.

Contents

Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, and prescription practices for *Clostridioides* (formerly *Clostridium*) *difficile* infection (CDI) among Military Health System (MHS) beneficiaries. The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.[5] This report presents analytical results and discussion of CY 2018 data for CDI in the MHS.

The background, methods, and limitations relevant to this analysis have been discussed in previous reports (CY 2015, 2016, 2017 annual reports for CDI[1-3]). The CY 2018 report does not include an analysis of burden associated with deployment-related infections using Contingency Tracking System (CTS) data. In addition, select large facilities in the MHS transitioned in CY 2018 from the Composite Health Care System (CHCS) to the GENESIS electronic health record system. These facilities include Naval Hospital Bremerton, 92nd Medical Group at Fairchild Air Force Base, Naval Health Clinic Oak Harbor, and Madigan Army Medical Center. The EDC does not receive GENESIS data, and records from these facilities are not included in this analysis. All other methods and limitations are the same as in recent years.

In 2018, the Clinical and Laboratory Standards Institute (CLSI) and the Centers for Disease Control and Prevention (CDC) adopted the new name *Clostridioides* (formerly *Clostridium*) *difficile* for guidelines and reports. *C. diff* remains a commonly used abbreviation. In 2018, the Infectious Disease Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) released updated CDI guidelines changing first-line treatment from metronidazole to vancomycin or fidaxomicin.[4] Recent literature reviews did not present any other relevant developments in CDI research since CY 2017 analyses.

Results

Section A – Descriptive Epidemiology

Incidence of *C. difficile*

In 2018, a total of 1,875 *Clostridioides difficile* (CD) incident episodes occurred among 1,789 MHS beneficiaries treated at a military treatment facility (MTF). The overall MHS annual CDI incidence rate (IR) was 19.8 per 100,000 persons per year, a 6.4% relative decrease from the weighted historic IR (Table 1). The 2018 rate was just below the two standard deviation (SD) lower limit of the weighted historic IR. The Air Force, Army, and Navy service-specific rates also decreased from the respective weighted historic IRs. The Air Force rate was below the two SD lower limit of the weighted historic IR. The Army and Navy remained within two SDs of the weighted historic IR. The overall Department of Defense (DOD) active duty and the Marine Corps service-specific IRs were above the respective weighted historic IRs but within normal variation of two SDs from the weighted historic IR. In general, these results indicate that Army, Navy, and Marine Corps CD incidence rates are within expected variation of the weighted historic rates. In contrast, the overall MHS and the Air Force CD rates decreased slightly more than the expected variation from the weighted historic rate.

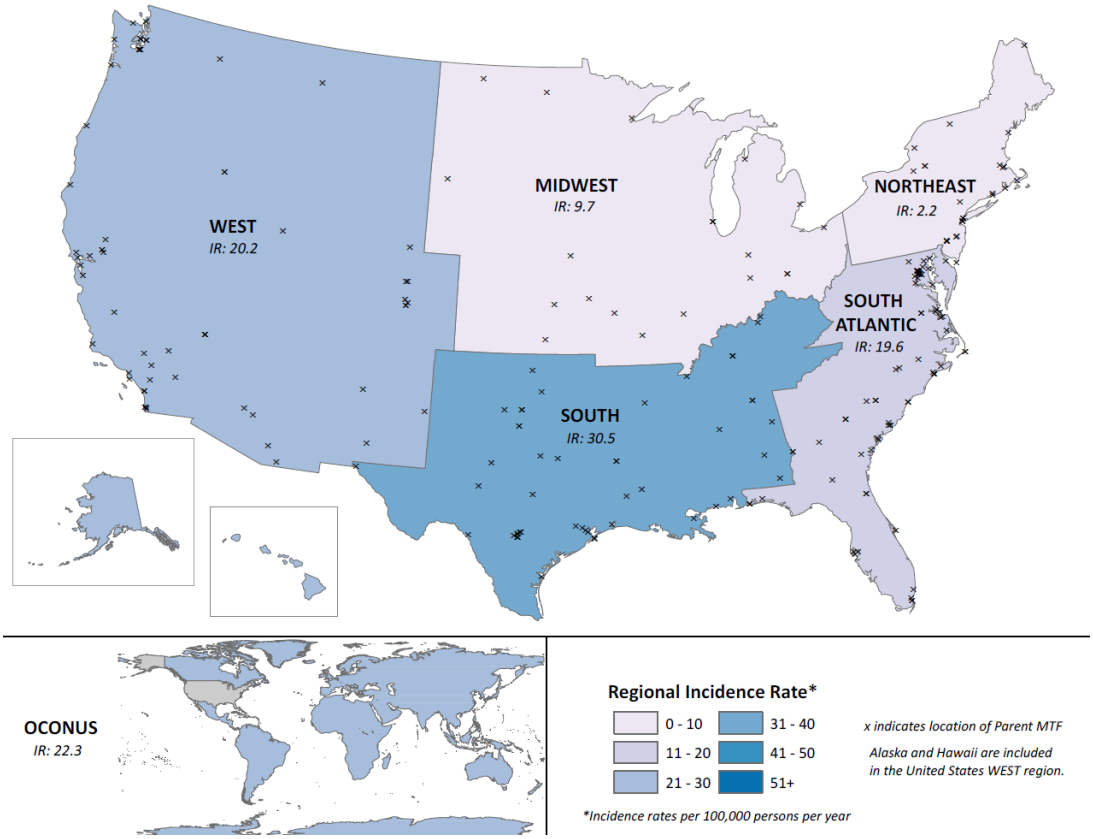
Table 1. Incidence Rate (IR) for *C. difficile* Infections in the MHS, CY 2018

Population	2018 IR	Weighted Historic[a] IR 2015 - 2017	Two Standard Deviations: Weighted Historic[a] IR	2018	
				Direction	Percent Change[b]
MHS Beneficiaries	19.8	21.1	1.3	↓	6.4%
Air Force	19.5	21.1	0.4	↓	7.5%
Army	19.7	20.8	1.3	↓	5.2%
Marine Corps	19.8	16.2	5.3	↑	22.2%
Navy	14.7	16.9	3.7	↓	13.1%
DOD Active Duty	27.0	25.2	2.1	↑	7.3%

Rates are presented as the rate per 100,000 persons per year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
[a] Historic IR reflects the weighted average of the three years prior to the analysis year.
[b] This reflects the percent change from the weighted historic IR to the IR of the current analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Regionally, the IRs for the US South, US West, and locations outside the continental US (OCONUS) were above the overall annual CDI MHS IR (19.8 per 100,000 persons per year), whereas the IRs in the US Midwest, US Northeast, and US South Atlantic regions were lower than the overall annual rate (Figure 1).

Figure 1. Annual Incidence Rate (IR) for *C. difficile* Infections in the MHS by Region, CY 2018



Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, SIDR, and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Demographic Distribution of *C. difficile*

CDI was most likely to occur among family members (50.6%) and individuals aged 45 years and older (50.3%); CDI occurred almost equally in males and females (Table 2). Approximately 8.4% (n = 163) of patients experiencing an incident CDI episode also experienced a recurrent CDI episode (data not shown). The demographic distribution of patients with recurrent CDI was similar to patients who experienced an incident episode (data not shown).

Table 2. Demographic Characteristics of *C. difficile* Infections in the MHS, CY 2018

	N = 1,789	
	Count	**Percent**
Gender		
Female	879	49.1
Male	910	50.9
Age Group (in Years)		
0-17	255	14.3
18-24	200	11.2
25-34	244	13.6
35-44	190	10.6
45-64	444	24.8
65+	456	25.5
Beneficiary Type		
Active Duty	365	20.4
Family Members	905	50.6
Retired	320	17.9
Other	199	11.1

The frequency is based on the demographic value of the index incident episode.
Data Source: NMCPHC HL7-formatted CHCS microbiology and chemistry databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

C. difficile Clinical Characteristics

Table 3 shows the most common comorbidities that are potential risk factors for CDI acquisition.[4] In 2018, diabetes, renal failure, and chronic obstructive pulmonary disease (COPD) were the three most frequently identified comorbidities of interest among MHS CDI patients. Patients with these comorbidities represent a group within the MHS beneficiary population that may be especially vulnerable to poorer health outcomes, such as recurrent CDI and increased risk of mortality, when compared to patients without these comorbidities.

Table 3. Selected Comorbid Medical Conditions[a,b] among MHS Beneficiaries with *C. difficile* Infections, CY 2018

Selected Comorbid Medical Condition[c]		
	Count	Percent
Diabetes	260	14.5
Renal failure	202	11.3
Chronic pulmonary disease	176	9.8
Cancer	107	6.0
Congestive heart failure	124	6.9
Liver disease	70	3.9

[a] The percent of each selected comorbidity among distinct CD incident infections (n= 1,789).
[b] 3.1% of CDI patients had no MHS encounter data to evaluate comorbidity.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and SIDR databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Exposure Burden Metrics

In 2018, there were 209,478 direct care inpatient admissions across all MHS MTFs. Table 4 details two different CD infection metrics related to community and healthcare exposures.

The admission CDI prevalence rate measures the rate of CD importation into the MHS and includes 1) hospitalized patients in 2018 that tested positive for the infection within the first three days of admission and 2) all other hospitalized patients in 2018 that tested positive for the infection or colonization in 2017. The 2017 samples are included in the calculation of the admission prevalence rate to estimate the reservoir of CD impacting the MHS. In 2018, the admission CDI prevalence rate was 4.1 per 1,000 inpatient admissions. Within the MHS, the US South region had the highest admission CDI prevalence rate (5.9 per 1,000 inpatient admissions), and OCONUS locations, as a group, had the lowest rate (1.1 per 1,000 inpatient admissions).

The overall CDI prevalence rate measures the cumulative community reservoir and healthcare-associated exposure burden for CDI and includes 1) hospitalized patients in 2018 that tested positive for the infection at any time during admission and 2) all other hospitalized patients in 2018 that tested positive for the infection or colonization in 2017. The 2017 samples are included in the calculation of the overall prevalence rate to estimate the reservoir of CDI impacting the MHS. In 2018, the overall prevalence rate for CDI was 3.4 per 1,000 inpatient admissions. The overall CDI prevalence rate varied by region (ranging from 1.5 per 1,000 inpatient admissions OCONUS to 4.6 per 1,000 inpatient admissions in the US South).

By definition, admission CD prevalence infections are included in the calculation of the overall CDI prevalence rate. In 2018, the admission prevalence rate comprised 84.8% of the overall prevalence rate of CDI in the MHS (3.4 of the 4.1 per 1,000 inpatient admissions). This suggests that the majority of CD infections were imported into the MHS from the community reservoir.

Table 4. *C. difficile* Community- and Healthcare-Associated Exposure Burden Metrics in the MHS, CY 2018

	Admission CDI Prevalence[a]		Overall CDI Prevalence[b]		Percentage[d] of Admission (Imported) Prevalent Infections among Overall Prevalent Infections
	Count	Rate[c]	Count	Rate[c]	
Region					
OCONUS	17	--	18	--	94.4
US Midwest	12	--	13	--	--
US Northeast	2	--	2	--	--
US South	264	5.9	313	4.6	84.3
US South Atlantic	234	3.6	270	3.1	86.7
US West	195	4.3	238	3.6	81.9
Total	724	4.1	854	3.4	84.8

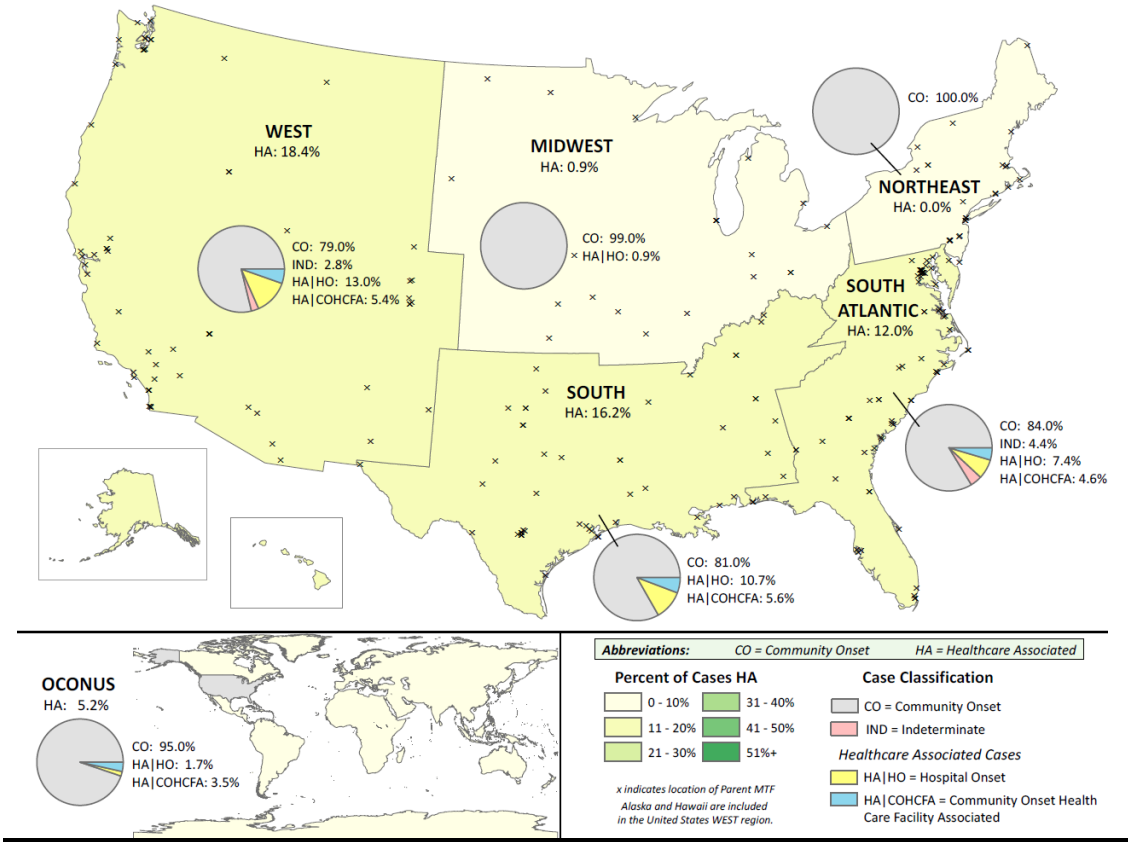
[a] Admission CDI prevalence included hospitalized patients in 2018 that tested positive for the infection within the first three days of admission and all other hospitalized patients in 2018 that tested positive for the infection or colonization in 2017.
[b] Overall CDI prevalence included hospitalized patients in 2018 that tested positive for the infection at any time during admission and all other hospitalized patients in 2018 that tested positive for the infection or colonization in 2017.
[c] Rates are presented as the rate per 1,000 inpatient admissions per year. Rates are not provided when the prevalence count is less than or equal to 20.
[d] Percentage reflects the proportion of CD infections that were imported into the healthcare system in the calendar year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Regional Epidemiologic Infection Classifications

Among the 1,875 CDI incident episodes identified among MHS beneficiaries in CY 2018, 83.3% were community onset (CO) cases and 13.7% were healthcare-associated (HA) cases. The indeterminate category (IND) represents CDI that do not meet any exposure setting criteria (3.0%) (data not shown). HA cases were further categorized into hospital onset (HO) or community onset-healthcare facility associated (CO-HCFA) groupings. Among the total number of incident CDI, 4.7% were CO-HCFA cases, indicating that the infection was not associated with the current admission, but that the patient had a prior hospitalization in the previous 12 months (data not shown). HO cases comprised 9.0% of all incident cases, indicating that the specimens were collected after the third day of hospital admission and the infections were likely contracted during the current hospitalization (data not shown).

Regionally, CO CDI was also the majority of incident episodes compared to HA CDI cases (Figure 2).

Figure 2. Proportion of Healthcare-Associated and Community-Onset *C. difficile* Infections in the MHS by Region, CY 2018



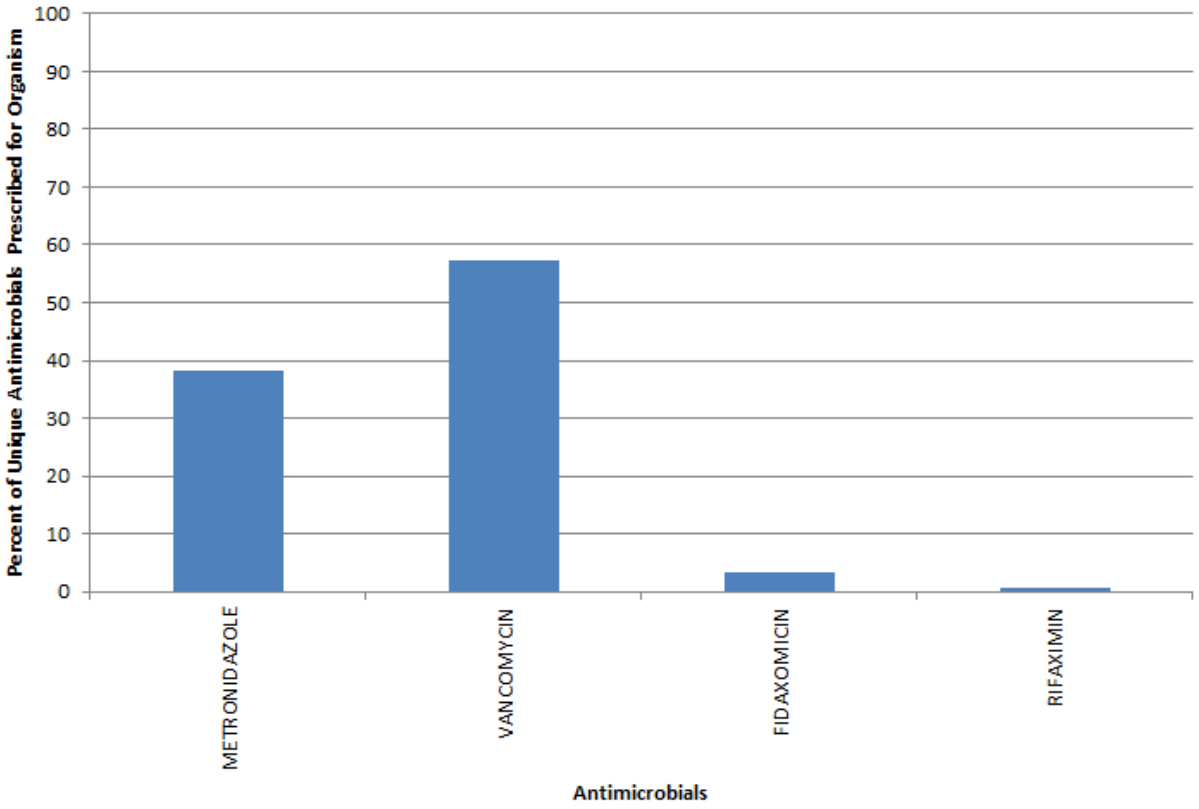
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Section B – Antimicrobial Use

Antimicrobial Consumption/Prescription Practices

Vancomycin was the most frequently prescribed medication for an initial CDI episode, representing 57.4% of CDI antibiotic treatment (Table 5). The IDSA and SHEA released updated guidelines in 2018 for CDI changing first-line treatment from metronidazole to vancomycin or fidaxomicin.[4]

Table 5. *C. difficile* Infection Prescription Practices in the MHS, CY 2018



The first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and pharmacy databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2019.

Use of antibiotics and gastric acid inhibitors is regarded as a risk factor for CDI. Table 6 shows that 59.3% of patients were prescribed an antibiotic within the 90 days before a CDI incident episode. The three antibiotics prescribed most frequently were cephalosporins (generations 1-4), fluoroquinolones, and penicillin/penicillin beta-lactam inhibitors. Overall 39.3% of CDI incident episodes had a gastric acid inhibitor prescribed 90 days before the incident event (proton pump inhibitors or PPIs (28.6%) and histamine 2 or H2 receptor blockers (10.7%)).

Table 6. Selected Medication Use 90 Days Prior to CDI , MHS Beneficiaries, CY 2018

	Count	Percent
Any Antibiotic Class Prescribed		
	1,111	59.3
Selected Antibiotic Classes [b]		
Aminoglycosides	29	1.5
Carbapenems	85	4.5
Cephalosporins (generations 1-4)		
first generation	161	8.6
second generation	20	1.1
third generation	231	12.3
fourth generation	98	5.2
Clindamycin	197	10.5
Fluoroquinolones	367	19.6
Glycopeptides	199	10.6
Macrolides	114	6.1
Metronidazole	173	9.2
Penicillins/penicillin beta-lactam inhibitors	326	17.4
Sulfonamides and/or trimethoprim	107	5.7
Nitrofuratoin	64	3.4
Tetracycline	51	2.7
Other	31	1.7
Range	1-7	
Mean ± SD	2.2 ± 1.5	
Other Selected Medication Classes[c]		
Proton Pump Inhibitor	536	28.6
H2 Receptor Blocker	201	10.7

[a] The percent of antibiotics prescribed per class per CD incident episode (n = 1,875) in the previous 90 days.
[b] The percent of each antibiotic class prescribed among CDI patients prescribed an antibiotic (n = 1,875) in the previous 90 days.
[c] The percent of each gastric acid suppressant class prescribed per CD incident episode (n = 1,875) in the previous 90 days.
Data Source: NMCPHC HL7-formatted CHCS microbiology, chemistry, and pharmacy databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Discussion

This report is a CY 2018 update to the CY 2017 *C. difficile* infection annual report for the MHS beneficiary population.[3] CDI incidence in the MHS population in CY 2018 showed a very slight decrease overall and was just below expected normal variation when compared to the average annual incidence for CYs 2015-2017.[1-3] Demographic and clinical characteristics were similar to trends reported in CY 2017.[3] The observed change in the most frequently prescribed first-line treatment from metronidiazole in previous years to oral vancomycin in 2018 is consistent with the recommendations in current treatment guidelines.[4] The burden of CDI continues to largely manifest in the community setting, among older age groups, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with specific comorbidities considered risk factors for CDI, such as diabetes, renal failure, COPD, and cancer, represent a patient group within the MHS population that is especially vulnerable to poorer health outcomes, such as recurrent CDI and increased risk of mortality, when compared to patients without those comorbidities.[6] This group may especially benefit from prompt CDI identification and treatment.

Interventions that reduce antibiotic exposure are the primary measures recommended to reduce CDI incidence and recurrence. These measures include limiting the use of unnecessary antibiotics, prescribing antibiotics that are lower risk for contributing to CDI, and using antibiotics for the shortest reasonable duration.[7] The MHS population can benefit from these interventions to decrease both CDI incidence and antibiotic selective pressure that may influence the development of multidrug-resistant organisms.

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Appendix A: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
CHCS	Composite Health Care System
CO	community-onset
CD	*Clostridioides difficile*
CDI	*Clostridioides difficile* infection
CO-HCFA	community-onset, healthcare facility associated
COPD	chronic obstructive pulmonary disease
CY	calendar year
EDC	EpiData Center
HA	healthcare-associated
HL7	Health Level 7
H2	histamine 2
HO	hospital-onset
IND	indeterminate
IDSA	Infectious Disease Society of America
IR	incidence rate
M2	MHS Data Mart
MDRO	multidrug-resistant organism
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	outside of the continental United States
PPI	proton pump inhibitor
SHEA	Society for Healthcare Epidemiology
SD	standard deviation
SIDR	Standard Inpatient Data Record
US	United States