Annual Surveillance Summary: *Clostridium difficile* Infections in the Military Health System (MHS), 2017

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14. ABSTRACT
The EpiData Center conducts routine surveillance of Clostridium difficile infection (CDI) among all beneficiaries seeking care within the Military Health System. This report is a calendar year (CY) 2017 update. CDI incidence in the MHS population in both CY 2017 and CY 2016 showed normal variation when compared to the average annual incidence for CYs 2014-2016 and 2013-2015, respectively. Demographic and clinical characteristics in CY 2017 were similar to trends reported in CY 2016. 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
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Abstract

The EpiData Center (EDC) conducts routine surveillance of *Clostridium difficile* (CD) incidence among all beneficiaries seeking care within the Military Health System (MHS). This report is a calendar year (CY) 2017 update to the CY 2016 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 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 both CY 2017 and CY 2016 showed normal variation when compared to the average annual incidence for CYs 2014-2016 and 2013-2015, respectively. Demographic and clinical characteristics in CY 2017 were similar to trends reported in CY 2016. The burden of CDI continues to largely manifest in the community setting, among beneficiaries aged 45 years and older, and in patients with previous antibiotic and gastric-acid suppressant use. Patients with CDI and specific comorbidities, 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 worse health outcomes, such as recurrent CDI and increased risk of mortality, when compared to patients without those comorbidities. 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. 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 (MDROs).

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 *Clostridium difficile* infection (CDI) among Military Health System (MHS) beneficiaries.

This report presents analytical results and discussion of CY 2017 data for CDI in the MHS. The background, methods, and limitations relevant to this analysis have been discussed in previous reports (CY 2015 and 2016 annual reports for CDI[1,2]). No new methods or limitations were applied to this annual summary. Recent literature reviews did not present any relevant developments in CDI research since CY 2016 analyses.

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.[3,4]

Results

Section A – Descriptive Epidemiology

Incidence of *Clostridium difficile*

In 2017, a total of 1,939 *Clostridium difficile* (CD) incident episodes occurred among 1,841 MHS beneficiaries treated at a military treatment facility (MTF). The overall annual CDI incidence rate (IR) was 20.6 per 100,000 persons per year, a 1.8% relative decrease from the weighted historic IR (Table 1). The 2017 rate was within two standard deviations (SDs) of the weighted historic IR. The Air Force and Army service-specific rates increased from the weighted historic IR but remained within two standard deviations of the weighted historic IR. The Navy rate was below the weighted historic IR and was outside of the normal variation of two standard deviations from the weighted historic IR. The Marine Corps was below the weighted historic IR and was within two standard deviations of the weighted historic IR. In general, these results indicate that MHS, Army, Air Force, and Marine Corps CD incidence rates are within expected variation of the weighted historic rate. In contrast, the Navy CD rates are decreasing more than the expected variation from the weighted historic rate.

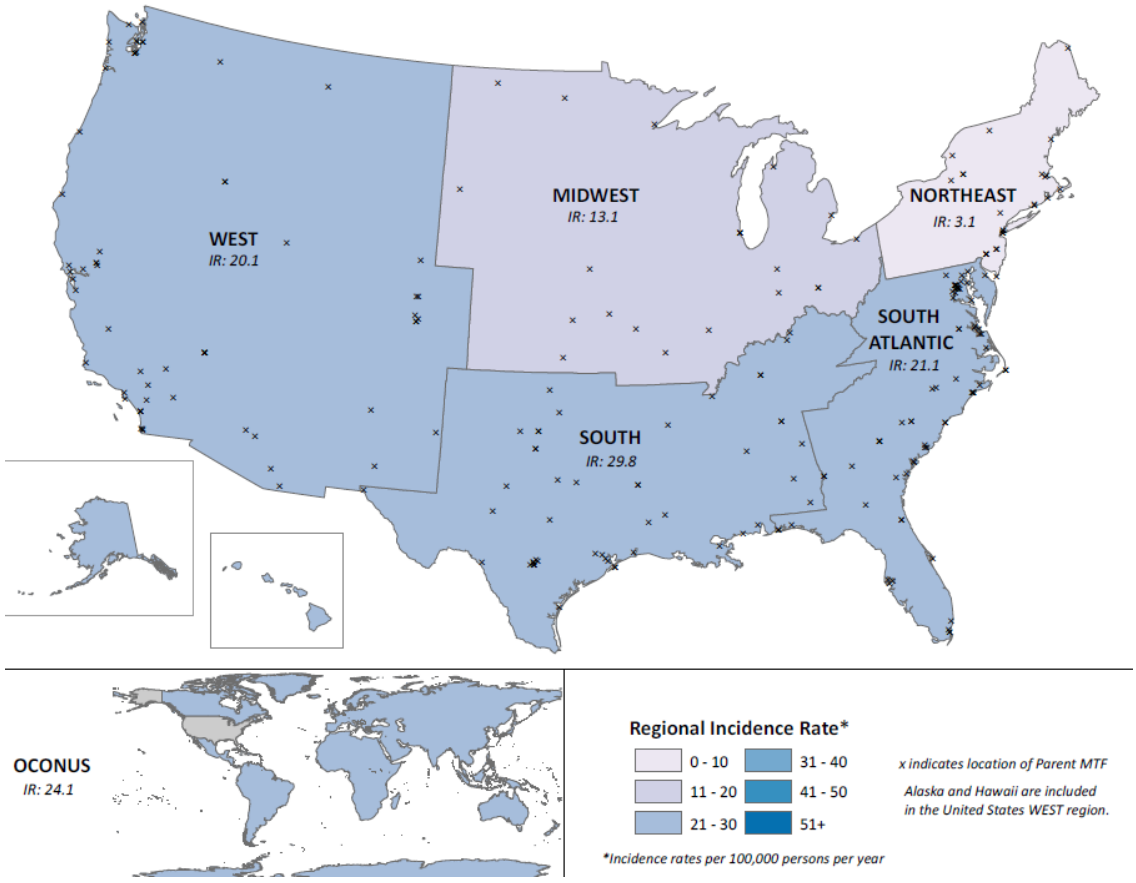
Table 1. Incidence Rate (IR) for *C. difficile* Infections in the MHS, CY 2017

Population	2017 IR	Weighted Historic[a] IR 2014 - 2016	Two Standard Deviations: Weighted Historic[a] IR	2017	
				Direction	Percent Change[b]
MHS	20.6	21.0	2.5	↓	1.8%
Air Force	20.9	20.8	2.1	↑	0.7%
Army	21.1	19.9	2.3	↑	6.1%
Marine Corps	13.9	17.0	6.6	↓	18.3%
Navy	15.0	18.3	1.9	↓	17.9%
Other	69.0	70.2	6.6	↓	1.7%
DOD Active Duty	25.8	24.2	2.2	↑	6.7%

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 2018.

Regionally, the IRs for the US South, US South Atlantic, and regions outside the continental US (OCONUS) were above the overall annual CDI MHS IR (20.6 per 100,000 persons per year), whereas the IRs in the US West, US Midwest, and US Northeast 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 2017



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 2018.

Demographic Distribution of *Clostridium difficile*

CDI was most likely to occur among family members (49.9%) and individuals aged 45 years and older (52.2%); 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. 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 2017

	N = 1,841	
	Count	**Percent**
Gender		
Female	895	48.6
Male	946	51.4
Age Group (in Years)		
0-17	240	13.0
18-24	175	9.5
25-34	270	14.7
35-44	195	10.6
45-64	453	24.6
65+	508	27.6
Beneficiary Type		
Active Duty	364	19.8
Family Members	918	49.9
Retired	354	19.2
Other	205	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 2018.

C. difficile Clinical Characteristics

Table 3 shows the most common comorbidities that are potential risk factors for CDI acquisition.[4] In 2017, 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 worse 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 CDI, CY 2017

	Count	Percent
Diabetes	262	14.2
Renal failure	198	10.8
Chronic obstrucutive pulmonary disease	185	10.0
Cancer	115	6.2
Congestive heart failure	133	7.2
Liver disease	94	5.1

[a] The percent of each selected comorbidity among distinct CD incident infections (n= 1,841).
[b] 4.1% 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 2018.

Exposure Burden Metrics

In 2017, there were 226,808 direct care inpatient admissions across all MHS MTFs. Table 4 details two CD infection metrics related to community and healthcare exposures.

The admission MDRO prevalence rate measures the rate of CD importation into the MHS and includes 1) hospitalized patients in 2017 that tested positive for the infection within the first three days of admission and 2) all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016. The 2016 samples are included in the calculation of the admission prevalence rate to estimate the reservoir of CD impacting the MHS. In 2017, the admission CDI prevalence rate for CDI was 3.7 per 1,000 inpatient admissions. Within the MHS, the US West region had the highest admission CDI prevalence rate (4.6 per 1,000 inpatient admissions), and OCONUS regions, as a group, had the lowest rate (1.0 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 2017 that tested positive for the infection at any time during admission and 2) all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016. The 2016 samples are included in the calculation of the overall prevalence rate to estimate the reservoir of CDI impacting the MHS. In 2017, the overall prevalence rate for CD infection was 4.5 per 1,000 inpatient admissions. The overall CD prevalence rate varied by region (1.1 per 1000 inpatient admissions to 5.7 per 1,000 inpatient admissions).

By definition, admission CD prevalence infections are included in the calculation of the overall CD prevalence rate. In 2017, the admission prevalence rate comprised 83.8% of the overall prevalence rate of CDI in the MHS (3.7 of the 4.5 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 2017

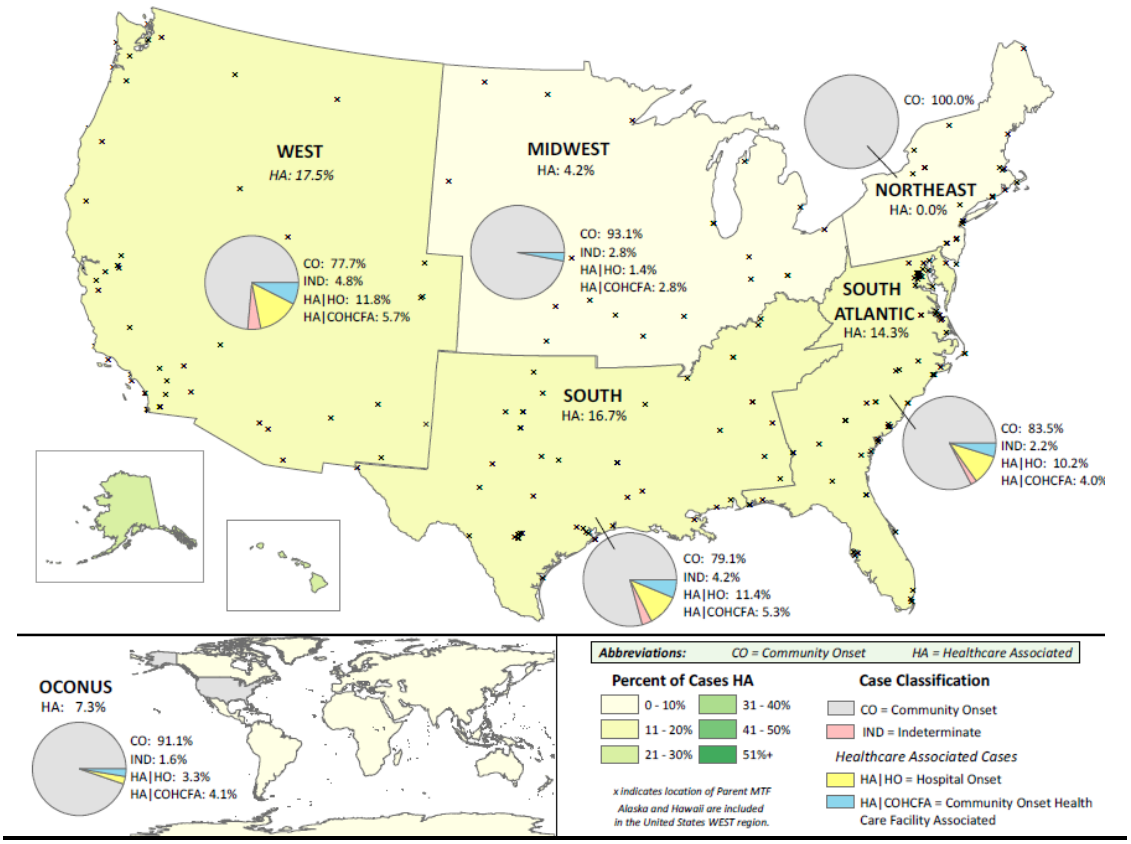
	Admission CDI Prevalence[a]		Overall CDI Prevalence[b]		Percentage[d] of Admission (Imported) Prevalent Infections among Overall Prevalent Infections
	Count	Rate[c]	Count	Rate[c]	
Region					
OCONUS	24	1.0	27	1.1	88.9
US Midwest	18	2.6	19	2.6	94.7
US Northeast	1	––	1	––	––
US South	241	4.3	296	5.3	81.4
US South Atlantic	243	3.2	296	3.8	82.1
US West	253	4.6	292	5.7	86.6
Total	780	3.7	931	4.5	83.8

[a] Admission CDI prevalence included hospitalized patients in 2017 that tested positive for the infection within the first three days of admission and all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016.
[b] Overall CDI prevalence included hospitalized patients in 2017 that tested positive for the infection at any time during admission and all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016.
[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 5.
[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 2018.

Regional Epidemiologic Infection Classifications

Overall, the majority of the 1,939 CDI incident episodes identified among MHS beneficiaries in CY 2017 were community onset (CO) cases at 82.2% compared to the healthcare-associated (HA) cases at 14.4%. HA cases included hospital onset (HO) and community onset-healthcare facility associated (CO-HCFA) categories. Most HA CDI cases were HO CDI (9.7%) cases versus CO-HCFA CDI (4.6%) cases indicating that CD exposure most likely originated within the current hospitalization. The indeterminate category (IND) represents CDI that do not meet any exposure setting criteria (3.4%). Regionally, CO CDI reflected the overall CDI trend whereas the distribution of HA (HO and CO-HCFA) CDI varied by region (Figure 2).

Figure 2. Proportion of Healthcare- and Community-Associated *C. difficile* Infections in the MHS by Region, CY 2017



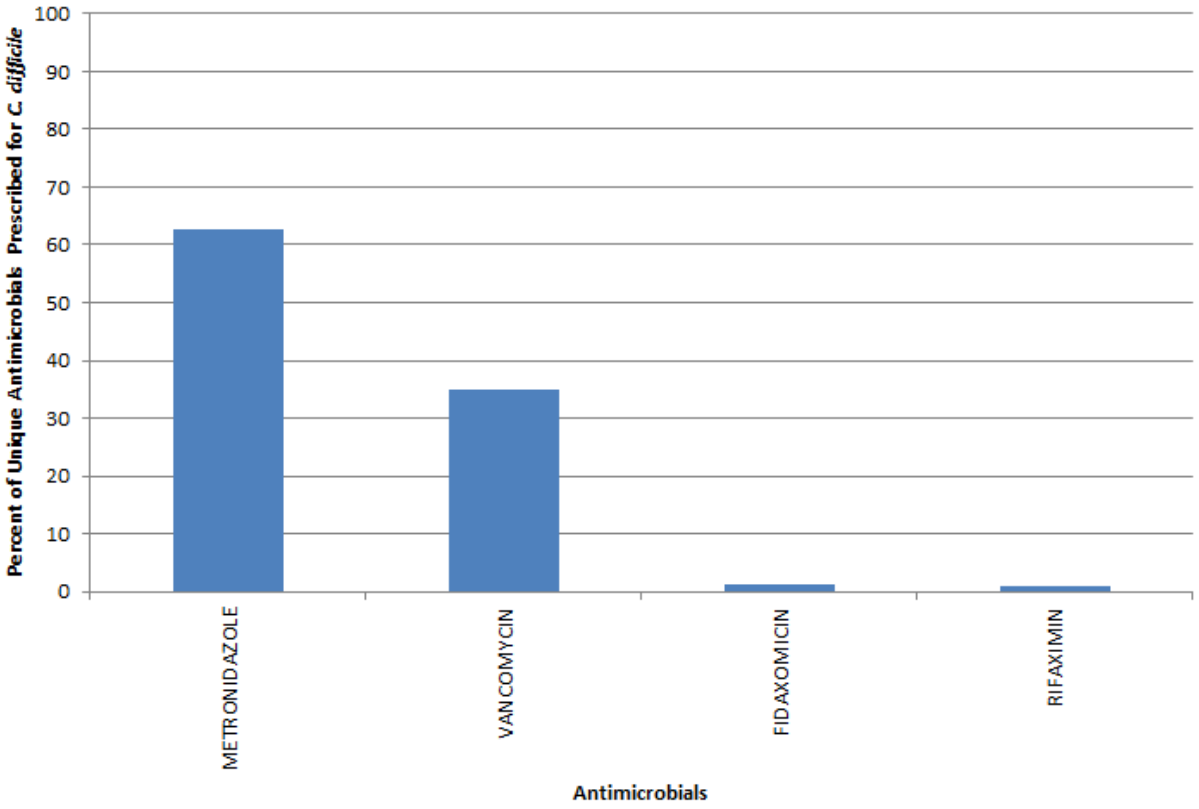
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Section B – Antimicrobial Use

Antimicrobial Consumption/Prescription Practices

Metronidazole was the most frequently prescribed medication for an initial CDI episode, representing 62.5% of CDI antibiotic treatment (Table 5).

Table 5. *C. difficile* Infection Prescription Practices in the MHS, CY 2017



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 2018.

Use of antibiotics and gastric acid inhibitors is regarded as a risk factor for CDI. Table 6 shows that 60.6% 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. Approximately 42.4% of CDI incident episodes had a gastric acid inhibitor prescribed 90 days before the incident event (protein pump inhibitors, or PPIs, at 31.6% and histamine 2, or H2, receptor blockers at 10.9%).

Table 6. Selected Medication Use 90 Days Prior to CDI, MHS Beneficiaries, CY 2017

	Count	Percent
Any Antibiotic Class Prescribed[a]		
	1175	60.6
Selected Antibiotic Classes[b]		
Aminoglycosides	32	1.7
Carbapenems	101	5.2
Cephalosporins (generations 1-4)		
first generation	145	7.5
second generation	23	1.2
third generation	192	9.9
fourth generation	83	4.3
Clindamycin	216	11.1
Fluoroquinolones	449	23.2
Glycopeptides	188	9.7
Macrolides	115	5.9
Metronidazole	240	12.4
Penicillins/penicillin beta-lactam inhibitors	553	28.5
Sulfonamides and/or trimethoprim	112	5.8
Nitrofuratoin	50	2.6
Tetracycline	61	3.1
Other	33	1.7
Range	1-7	
Mean ± SD	2.2 ± 1.5	
Other Selected Medication Classes[c]		
Proton Pump Inhibitor	613	31.6
H2 Receptor Blocker	211	10.9

[a] The percent of antibiotics prescribed per class per CD incident episode (n = 1939) in the previous 90 days.
[b] The percent of each antibiotic class prescribed among CDI patients prescribed an antibiotic (n = 1939) in the previous 90 days.
[c] The percent of each gastric acid suppressant class prescribed per CD incident episode (n = 1939) 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 2017 update to the CY 2016 *C. difficile* infection annual report for the MHS beneficiary population.[2] CDI incidence in the MHS population in both CY 2017 and CY 2016 showed normal variation when compared to the average annual incidence for CYs 2014-2016 and 2013-2015, respectively. Demographic and clinical characteristics were similar to trends reported in CY 2016. 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 worse health outcomes, such as recurrent CDI and increased risk of mortality, when compared to patients without those comorbidities. This group may especially benefit from prompt CDI identification and treatment.[5]

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.[6] 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	*Clostridium difficile*
CDI	*Clostridium difficile* infection
CO-HCFA	community-onset, healthcare facility associated
COPD	chronic obstructive pulmonary disease
CY	calendar year
EDC	EpiData Center clostridium difficile incidence
HA	healthcare-associated
HL7	Health Level 7
H2	histamine 2
HO	hospital-onset
IND	indeterminate
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
SD	standard deviation
SIDR	Standard Inpatient Data Record
US	United States