

Annual Surveillance Summary: Vancomycin-Resistant Enterococci (VRE) Infections in the Military Health System (MHS), 2017

NMCPHC-EDC-TR-381-2018

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Abstract

The EpiData Center (EDC) conducts routine surveillance of vancomycin-resistant enterococci (VRE) incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for VRE infections in the calendar year (CY) 2017.

Multiple data sources were linked to assess descriptive and clinical factors related to VRE. Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data identified *Enterococcus* species infections resistant to vancomycin. These infections were matched to HL7-formatted CHCS pharmacy data to assess prescription practices, the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures, and the Defense Manpower Data Center (DMDC) rosters to determine burden among Department of Defense (DOD) active duty (AD) service members.

Overall, incidence rates (IRs) of VRE infections declined among MHS beneficiaries to 1.22 per 100,000 persons per year. A slight increase in incidence was observed among Navy beneficiaries; however, the IR was within the expected variance with only a 3.7% increase in incident infections. The United States (US) West and South Atlantic regions had the highest IRs, and healthcare-associated (HA) cases comprised the largest proportion of all infections identified (82.3%). While the largest proportion of all prevalent infections were classified as community-onset (CO) (35.4%), a substantial proportion was also identified as hospital-onset (HO) (28.5%). Treatment for VRE infections among DOD beneficiaries primarily included daptomycin and linezolid, which remained effective through 2017. Current infection control practices appear effective, and continued surveillance is recommended.



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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, prescription practices, and antibiotic susceptibility patterns for vancomycinresistant enterococci (VRE) infections among Military Health System (MHS) beneficiaries. This report presents analytical results and discussion of CY 2017 data for VRE infections 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 VRE^{1,2}). The CY 2017 report does not include an analysis of burden associated with deployment-related infections using Contingency Tracking System (CTS) data; all other methods and limitations are the same as in recent years. Recent literature reviews did not present any relevant developments in VRE 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 VRE

In 2017, the annual incidence rate (IR) for VRE infection among MHS beneficiaries treated at a military treatment facility (MTF) was 1.22 per 100,000 persons per year. This reflects a 16.4% change below the weighted historic IR and is more than two standard deviations below the weighted historic IR. Decreases also occurred in the Air Force and Army beneficiary populations; however, the Navy beneficiary population exhibited a 3.7% increase from the weighted historic IRs are within two standard deviations of the weighted historic IRs of VRE in the MHS (Table 1).

Table 1. Incidence Rate (IR) for VRE Infections in the MHS, CY 2017							
		Weighted	Two Standard	2017			
Population	2017 IR	Historic ^a IR 2014 - 2016	Deviations: Weighted Historic ^a IR	Direction	Percent Change ^b		
MHS Beneficiaries	1.22	1.46	0.20	4	16.4%		
Air Force	0.82	1.26	0.45	4	35.2%		
Army	0.89	0.91	0.13	↓	1.8%		
Marine Corps							
Navy	1.49	1.44	0.47	1	3.7%		
DOD Active Duty							

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.

Rates are not provided when the incidence count is less than or equal to 10.

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.



Demographic Distribution of VRE

In 2017, there were 115 incident VRE infections identified among all MHS beneficiaries. Male and female IRs were almost equal, with the male rate (1.23 per 100,000 persons) slightly exceeding that of females (1.21 per 100,000 persons). Beneficiaries aged 65+ years (3.80 per 100,000 persons) and 45-64 years (1.03 per 100,000 persons) demonstrated the highest rates, as well as retirees (1.64 per 100,000 persons) (Table 2).

	N = 115					
	Count	Rate				
Gender						
Female	56	1.21				
Male	59	1.23				
Age Group (in Years))	_				
0-17	0					
18-24	2					
25-34	4					
35-44	3					
45-64	21	1.03				
65+	85	3.80				
Beneficiary Type		_				
Active Duty	3					
Family Members	50	0.92				
Retired	36	1.64				
Other ^a	26					
tate is not reported due opulation denominator. Ites are presented as the proons per year.						

Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.

Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.



Seasonality

Throughout 2017, VRE monthly incidence rates were variable, trending above and below the weighted historic IR; however, these highly variable trends may be explained by the overall low frequency of infections identified during the year (n=115), thus translating to even lower monthly frequencies (range: n=2 to 15 incident infections per month; median: n=9 incident infections in 2017). The highest monthly IR occurred in June (n=15; 0.16 per 100,000 persons per year), and the lowest monthly IR occurred in November (n=2; 0.02 per 100,000 persons per year). The monthly incident rate for VRE infections did not exceed 0.16 per 100,000 throughout the entire year (data not shown).



VRE Clinical Characteristics

There were 130 prevalent VRE infections identified among all MHS beneficiaries in 2017. The infection burden was slightly higher in the outpatient setting (50.8%), and the majority consisted of non-invasive infections (83.8%). Sixty-three percent of VRE infections were collected from urine samples; collection from a skin or soft tissue infection (SSTI) or wound represented the second highest proportion of collection sites (15.4%). The majority of prevalent infections was caused by *E. faecium* (43.8%), followed by unspecified *Enterococcus* species (40.0%) (Table 3).

Table 3. Clinical Characteristics of VRE PrevalentInfections in the MHS, CY 2017							
	N = 130						
	Count	Percent					
Specimen Collection Lo	ocation						
Inpatient	64	49.2					
Outpatient	66	50.8					
Infection Type							
Invasive	21	16.2					
Non-Invasive	109	83.8					
Body Collection Site							
Blood	13	10.0					
Respiratory	3	2.3					
SSTI/Wound	20	15.4					
Urine	83	63.8					
Other	11	8.5					
Organism Species							
Enterococcus faecalis	21	16.2					
Enterococcus faecium	57	43.8					
Enterococcus species	52	40.0					
Data Source: NMCPHC HI	Data Source: NMCPHC HI 7-formatted CHCS						

Data Source: NMCPHC HL7-formatted CHCS microbiology database. 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 VRE infection metrics related to community and healthcare exposures.

The admission MDRO prevalence rate measures the rate of VRE 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 VRE impacting the MHS. In 2017, the admission MDRO prevalence rate for VRE infection was 0.43 per 1,000 inpatient admissions. Within the MHS, the US West region had the highest admission MDRO prevalence rate (0.70 per 1,000 inpatient admissions).

The overall MDRO prevalence rate measures the cumulative community reservoir and healthcareassociated exposure burden for VRE 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 VRE impacting the MHS. In 2017, the overall MDRO prevalence rate for VRE infection was 0.59 per 1,000 inpatient admissions. The US West region had the highest overall MDRO prevalence rate (0.99 per 1,000 inpatient admissions).

By definition, admission MDRO prevalence infections are included in the calculation of the overall MDRO prevalence rate. In 2017, the admission prevalence rate comprised 73.13% of the overall prevalence rate of VRE in the MHS (0.43 of the 0.59 per 1,000 inpatient admissions). This suggests that the majority of VRE infections were imported into the MHS from the community reservoir.



a	among VRE in the MHS, CY 2017							
		Admission MDRO Prevalence ^a		Overall Preva		Percentage ^d of Admission (Imported) Prevalent Infections		
		Count Rate ^c Count Rate ^c		among Overall Prevalent Infections				
	Region							
	OCONUS	1		1				
	US Midwest	3		3				
	US Northeast	0		0				
	US South	18	0.34	24	0.45	75.00		
	US South Atlantic	27	0.35	37	0.48	72.97		
	US West	49	0.70	69	0.99	71.01		
	Total	98	0.43	134	0.59	73.13		
а	a Administry NADRO providence included becautelized actions in 2017 that tested							

 Table 4. MDRO Community- and Healthcare-Associated Exposure Burden Metrics

 among
 VRE in the MHS, CY 2017

^a Admission MDRO 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 MDRO 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 MDRO infection 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.



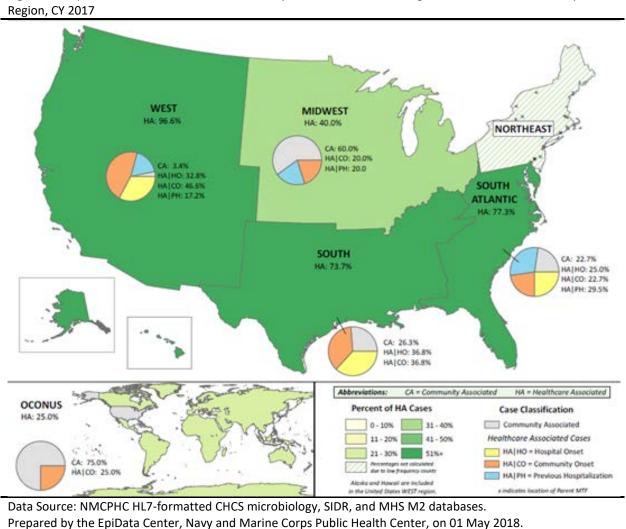
Regional Epidemiologic Infection Classifications

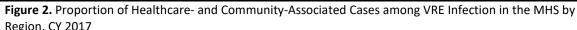
Among all prevalent VRE infections identified in the MHS in 2017, 82.3% were healthcareassociated (HA) cases and 17.7% were community-associated (CA) cases. Except the US Midwest and regions outside the continental United States (OCONUS), all regions demonstrated a substantially larger proportion of HA cases than CA cases, with the US West region experiencing 96.6% of cases as HA. In the US Midwest, the percentage of CA cases was 60%, while 75% of the OCONUS cases were CA. There were no VRE infections identified in the US Northeast in 2017 (Figure 2).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Among all prevalent VRE infections (regardless of HA or CA classification or region), the greatest proportion was classified as CO cases (35.4%), indicating that the infection was most likely acquired in the community (i.e., specimens were collected within the first three days of hospital admission). The second largest proportion of prevalent infections were HO (28.5%) demonstrating that the infection was likely a result of the current hospitalization.

The distribution of HA case classifications varied by region. Of all regions, the US South Atlantic had the most similar proportions between PH (29.5%), HO (25.0%), and CO (22.7%). OCONUS locations, as a group, demonstrated the largest difference between HO cases and CO cases (0.0% vs. 25.0%).









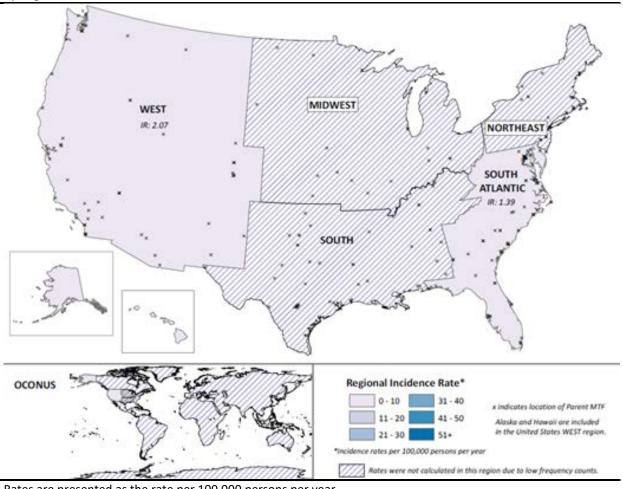
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Section B – Antimicrobial Resistance and Use Regional Multidrug Resistance

In 2017, the IR of VRE infection among all MHS beneficiaries was 1.22 infections per 100,000 persons per year. Regionally, the highest IRs occurred in the US West (2.07 per 100,000 persons) and US South Atlantic (1.39 per 100,000 persons). Low frequencies of infections occurred in the US Midwest (n=5), US Northeast (n=0), US South (n=18), and OCONUS regions (n=4); rates were not calculated for these regions (Figure 2).

Figure 3. Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among VRE Infections in the MHS by Region, CY 2017



Rates are presented as the rate per 100,000 persons per year. Regional rates are not provided when the incidence count is less than or equal to 20. 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.



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Antibiogram

Table 5 displays an antibiogram of VRE incident infections for all MHS beneficiaries from 2012-2017. In 2017, VRE infections were most susceptible to daptomycin (100.0%), linezolid (89.7%), and gentamicin high level (78.6%). Ciprofloxacin (11.6%), tetracycline (14.7%), and penicillin (17.4%) demonstrated the lowest efficacies in 2017. No statistically significant trends in susceptibility were observed in 2017 for VRE infections.

Antibiotics	2012	2013	2014	2015	2016	2017	Susceptibility
							Trend ^a
Ampicillin	18.3	24.7	29.3	21.2	20.6	25.3	30 10
Ciprofloxacin	2.0	13.6	8.3	15.8	13.0	11.6	20]
Daptomycin			92.7	98.0	97.2	100.0	100] 🦟
Doxycycline							100 90
Erythromycin							20 I
Gentamicin High Level	73.0	84.5	82.5	86.6	81.3	78.6	90]
Levofloxacin	3.4		8.3	20.0			100 90]
Linezolid	92.9	97.4	87.5	95.2	91.7	89.7	100 80]
Nitrofurantoin	35.2	50.9	50.0	36.8	45.9	44.4	60 30]
Penicillin	9.2	28.8	24.0	16.7	20.7	17.4	30]
Quinupristin/							
Dalfopristin		75.0					
Rifampin							
Streptomycin High Level	69.5	77.8	69.4	68.2	69.6	73.6	80]
Tetracycline	14.1	16.0	18.3	8.2	20.9	14.7	40]

'--' indicates that fewer than 30 isolates were tested.

^a Susceptibility trends are displayed only for antibiotics with susceptibility data for at least five consecutive years.

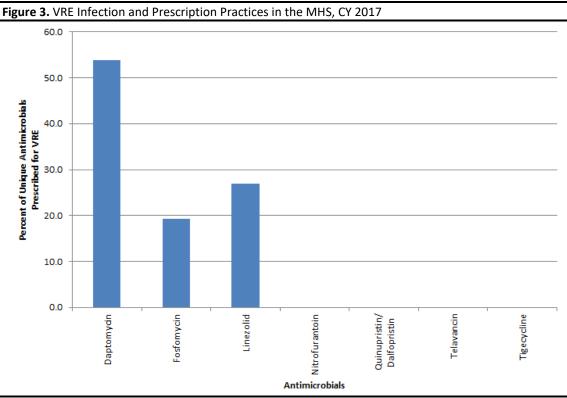
Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.



Antimicrobial Consumption/Prescription Practices

Figure 3 displays the percentage of unique antimicrobials associated with prevalent VRE infections during 2017, including seven antibiotic classes recommended for VRE treatment according to the Johns Hopkins Antibiotic Guide.⁵ Among all MHS beneficiaries, the most commonly prescribed antibiotic class associated with VRE infections in 2017 were daptomycin (53.8%) and linezolid (26.9%) (Figure 3). Fosfomycin was also prescribed (19.2%). No prescriptions for telavancin, quinupristin/dalfopristin, or nitrofurantoin were identified.



Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.

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



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Discussion

This analysis found a decrease in VRE infection rates from the weighted historic IR of 1.46 infections per 100,000 persons to 1.22 infections per 100,000 persons in 2017. This marks the second consecutive year of declining incidence in VRE infection rates within the MHS. Recent studies indicate VRE infections are rising in general populations. One US study reported hospitalizations due to VRE infections increased from 3.2 per 10,000 hospitalizations to 6.5 per 10,000 total hospitalizations from 2003-2006.⁶ An additional meta-analysis reviewing VRE incidence rates in the US between 2000 and 2015 found pooled national data did not increase, but studies from Atlanta and Detroit demonstrated increasing VRE infection rates.⁷ The results from this assessment indicate that changes in national VRE infection rates among MHS beneficiaries are also driven by regional trends. In the US South Atlantic region, VRE IR increased from 2016 to 2017 (from 1.15 infections to 1.39 infections per 100,000); in the US West region, rates decreased from 2016 to 2017 (from 2.18 infections to 2.07 infections per 100,000).

This analysis found that the MHS regions with the highest overall VRE rates, including the US West and US South Atlantic regions, also demonstrated the largest proportions of HA cases. In the US, surveillance for VRE primarily originates within hospital settings, and few studies suggest that transmission among healthy adults occurs at a significant extent in the community.⁸ However, as colonized patients leave the hospital environment, the possibility for transmission into the community cannot be disregarded. Research demonstrates that patients can remain colonized for weeks to months and are often still colonized at the time of readmission to the hospital.⁹ In this report, healthcare-associated exposure burden metrics implicate importation of VRE from the community to MHS healthcare settings. The admissions prevalence rate during 2017 (0.43 per 1,000 inpatient admissions) accounted for approximately three-fourths of the overall prevalence metric (0.59 per 1,000 inpatient admissions). This demonstrates that the majority of VRE burden was identified within the first three days of inpatient admission and thus more likely imported from the community rather than pre-existing in the hospital setting. These results underscore the need for drug-resistance surveillance outside of hospital settings due to the continued potential for community transmission.

Treatment for infections due to VRE, particularly *E. faecium*, may pose serious challenges due to resistance against multiple antibiotics; however, VRE infections continue to exhibit susceptibility to some antibiotics.^{5,8} Daptomycin and linezolid were the most commonly prescribed antimicrobials for VRE infections in the MHS during 2017, which is consistent with current treatment recommendations and MHS microbiology results confirming susceptibilities above 85% for these two antibiotics.⁵ Daptomycin remains the only antibiotic with in vitro bactericidal activity against VRE that is approved by the US Food and Drug Administration (FDA). Researchers caution clinicians to be aware of the potential emergence of daptomycin non-susceptible enterococci strains, particularly with the treatment of bloodstream infections, as data for this susceptibility remains limited.^{5,10,11} The Johns Hopkins Antibiotic Guide recommends evaluating the susceptibility of isolates to monitor minimum inhibitory concentrations of sequential isolates recovered during treatment.⁵ Close monitoring of daptomycin through antibiotic stewardship programs in MHS populations is warranted to ensure efficacy remains high and system practices do not encourage adaptations to resistance patterns.



In summary, descending trends in VRE infection rates among beneficiaries seeking care within the MHS contrast other literature supporting more recent rises in VRE infections. The US West and US South Atlantic regions had the highest incidence of VRE in 2017, with cases overwhelming characterized as HA. While the majority of VRE surveillance within the US originates from hospital settings, our results indicate a need to evaluate the potential for community transmission of VRE. This is demonstrated by the substantial percentage of HA cases classified as CO, as well as elevated MDRO admission metrics, which indicate a higher magnitude of VRE imported into the healthcare system as opposed to an existing reservoir of infection in the healthcare setting. Finally, our results indicate viable treatment options are available for VRE infections, and prescribing practices within MHS are supported by susceptibility testing trends. Continued surveillance for VRE is warranted to monitor any changes in burden, susceptibility, and treatment options and to guide targeted prevention efforts.

POINT OF CONTACT

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Appendix A: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
СА	community-associated
CHCS	Composite Health Care System
СО	community-onset
CTS	Contingency Tracking System
CY	calendar year
DMDC	Defense Manpower Data Center
DOD	Department of Defense
DON	Department of the Navy
EDC	EpiData Center
FDA	Food and Drug Administration
НА	healthcare-associated
HL7	Health Level 7 format
НО	hospital-onset
IR	incidence rate
MDRO	multidrug-resistant organism
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	outside the continental United States
PH	previous hospitalization
SIDR	Standard Inpatient Data Record
US	United States
VRE	vancomycin-resistant enterococci

