Annual Surveillance Summary: Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections in the Military Health System (MHS), 2016

NMCPHC-EDC-TR-368-2017

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14. ABSTRACT
The EpiData Center Department (EDC) conducts routine surveillance of methicillin-resistant Staphylococcus aureus (MRSA) 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 MRSA in calendar year (CY) 2016. Multiple data sources were linked to assess descriptive and clinical factors related to MRSA. Overall, incidence rates of MRSA in the general United States (US), MHS beneficiary, and Department of Defense (DOD) active duty (AD) populations are decreasing. Inducible clindamycin resistance is slowly increasing in the MHS; no additional changes in antibiotic susceptibility emerged in 2016. Clindamycin, trimethoprim/sulfamethoxazole, doxycycline, and vancomycin remain viable treatments for MRSA, although clindamycin should be used cautiously in the inpatient setting due to reduced efficacy. Current infection control practices appear effective and continued surveillance is recommended.

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Abstract

The EpiData Center Department (EDC) conducts routine surveillance of methicillin-resistant *Staphylococcus aureus* (MRSA) 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 MRSA in calendar year (CY) 2016.

Multiple data sources were linked to assess descriptive and clinical factors related to MRSA. Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data identified *S. aureus* infections resistant to oxacillin, cefoxitin, or methicillin. 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, Defense Manpower Data Center (DMDC) rosters to determine burden among Department of Defense (DOD) active duty (AD) service members, and the DMDC Contingency Tracking System (CTS) to determine Department of the Navy (DON) deployment-related infections.

Overall, incidence rates of MRSA in the general United States (US), MHS beneficiary, and DOD AD populations are decreasing. Inducible clindamycin resistance is slowly increasing in the MHS; no additional changes in antibiotic susceptibility emerged in 2016. Clindamycin, trimethoprim/sulfamethoxazole, doxycycline, and vancomycin remain viable treatments for MRSA, although clindamycin should be used cautiously in the inpatient setting due to reduced efficacy. Current infection control practices appear effective and continued surveillance is recommended.

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, prescription practices, and antibiotic susceptibility patterns for methicillin-resistant *Staphylococcus aureus* (MRSA) infections among Military Health System (MHS) beneficiaries.

Literature review did not provide any new developments or research for MRSA infections. Additionally, no new methods or limitations were applied to this annual summary. As such, this report presents analytical results and discussion of CY 2016 data for MRSA infections in the MHS. The background, methods, and limitations relevant to this analysis have been discussed in a previous report (CY 2015 annual report for MRSA[1]).

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.[2,3]

Results

Section A – Descriptive Epidemiology

Incidence of MRSA

In 2016, the annual incidence rate (IR) for MRSA infection among MHS beneficiaries treated at a military treatment facility (MTF) was 56.4 per 100,000 persons per year. This reflects an 11.2% change below the weighted historic IR. Incidence rates across all services and the Department of Defense (DOD) active duty (AD) population in 2016 were also below the weighted historic IRs. The DOD AD, Army, and Marine Corps populations reported a change of more than 10% below the weighted historic IRs. The 2016 IRs are within or below two standard deviations of the weighted historic IRs in the MHS, service-specific, and the DOD AD populations (Table 1).

Table 1. Incidence Rate (IR) for MRSA Infections in the MHS, CY 2016

Population	2016 IR	Weighted Historic[a] IR 2013 - 2015	Two Standard Deviations: Weighted Historic[a] IR	2016	
				Direction	Percent Change[b]
MHS Beneficiaries	56.4	63.5	4.7	↓	11.2%
Air Force	34.4	37.2	2.1	↓	7.6%
Army	60.2	70.6	5.4	↓	14.7%
Marine Corps	93.6	107.6	9.5	↓	13.0%
Navy	52.1	57.0	6.0	↓	8.6%
DOD Active Duty	147.7	169.4	18.3	↓	12.8%

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 and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Demographic Distribution of MRSA

In 2016, there were 5,306 incident MRSA infections identified among all MHS beneficiaries treated at an MTF. The highest incidence rates in each demographic category occurred among 18-24 year olds, males, and AD service members (Table 2).

Table 2. Demographic Characteristics of MRSA Infections in the MHS, CY 2016

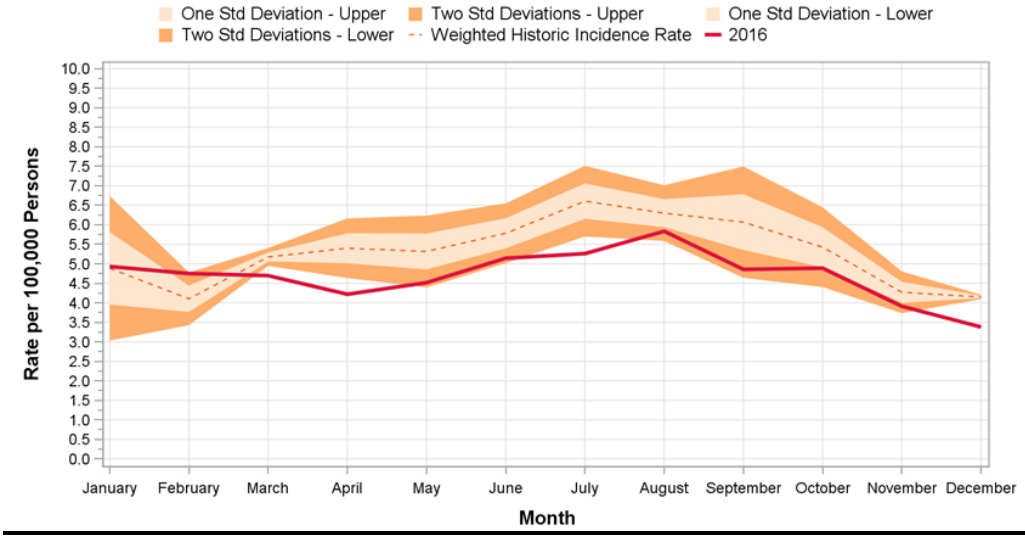
	N = 5,306	
	Count	**Rate**
Gender		
Female	1,896	41.1
Male	3,410	71.1
Age Group (in Years)		
0-17	936	47.8
18-24	1,513	132.2
25-34	894	74.4
35-44	481	57.6
45-64	817	39.8
65+	665	30.0
Beneficiary Type		
Active Duty	2,017	147.7
Family Members	2,004	36.6
Retired	654	29.9
Other[a]	631	--

[a] Rate is not reported due to variation in population denominator.
Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Seasonality

Monthly incidence rates of MRSA infections were equal to or higher than the monthly weighted historic IR in January and February 2016; however, any increase in monthly incidence rates remained within two standard deviations of the weighted historic IR and was therefore consistent with previously observed rates. All other monthly incidence rates (March – December) for MRSA infections were below the weighted historic monthly IR and often more than two standard deviations below the weighted historic IR (Figure 1). A seasonal component to MRSA infections was observed in 2016, with an increase in infections in May, a peak in monthly incidence in August, and descending rates throughout the remainder of the year.

Figure 1. Monthly Incidence of MRSA Infections and Weighted Historic Incidence Rate (IR) Comparisons in the MHS, CY 2016



Rates are presented as the rate per 100,000 persons per year.
Bands indicate one and two standard deviations above and below the weighted historic monthly incidence rates (IR).
The weighted historic monthly IR is a weighted average of the three years prior to the analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

MRSA Clinical Characteristics

There were 5,712 prevalent MRSA infections identified among all MHS beneficiaries treated at an MTF in 2016. The infection burden was higher in the outpatient setting (88.9%) and patients generally presented with non-invasive infections (94.7%) (Table 3). Seventy-two percent of MRSA infections were from sources indicative of a skin or soft tissue infection (SSTI) or wound.

Table 3. Clinical Characteristics of MRSA Prevalent Infections in the MHS, CY 2016

	N = 5,712	
	Count	**Percentage**
Specimen Collection Location		
Inpatient	636	11.1
Outpatient	5,076	88.9
Infection Type		
Invasive	304	5.3
Non-Invasive	5,408	94.7
Body Collection Site		
Blood	125	2.2
Respiratory	422	7.4
SSTI/Wound	4,113	72.0
Urine	324	5.7
Other	728	12.7

Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Exposure Burden Metrics

Table 4 presents two different metrics describing the burden of MDRO infection rates for healthcare-associated exposures. In 2016, there were 239,946 direct care inpatient admissions across all MHS MTFs. The overall MDRO prevalence rate for MRSA was 6.3 per 1,000 inpatient admissions; this metric measures the amount of exposure to colonization or infection at any point during the admission or one year prior. Within the United States (US), the West region had the highest overall MDRO prevalence rate (6.9 per 1,000 inpatient admissions) and the Northeast region had the lowest rate (4.4 per 1,000 inpatient admissions). The admission MDRO prevalence rate for MRSA was 5.8 per 1,000 inpatient admissions; this metric measures the magnitude of importation of MRSA infection at the time of admission (importation of MDRO into the healthcare system) or one year prior. As with overall MDRO prevalence, within the US, the West region had the highest admission MDRO prevalence rate (6.3 per 1,000 inpatient admissions) and the Northeast region had the lowest rate (4.4 per 1,000 inpatient admissions). Locations outside of the continental US (OCONUS), as a group, had the lowest overall and admission MDRO prevalence rates across all regions in 2016 (3.4 and 3.2 per 1,000 inpatient admissions, respectively) (Table 4). Among MRSA infections, the overall MDRO prevalence rate was higher than the admission MDRO prevalence rate (6.3 vs. 5.8 per 1,000 inpatient admissions); this observation suggests that the majority of MRSA infections were imported into the hospital setting from the community, adding to the burden of MRSA.

Table 4. MDRO Healthcare-Associated Exposure Burden Metrics among MRSA in the MHS, CY 2016

	Overall MDRO Prevalence[a]		Admission MDRO Prevalence[b]	
	Count	Rate[c]	Count	Rate[c]
Region				
OCONUS	60	3.4	55	3.2
US Midwest	47	4.8	46	4.7
US Northeast	7	4.4	7	4.4
US South	359	6.4	325	5.8
US South Atlantic	519	6.5	482	6.0
US West	510	6.9	469	6.3
Total	1,502	6.3	1,384	5.8

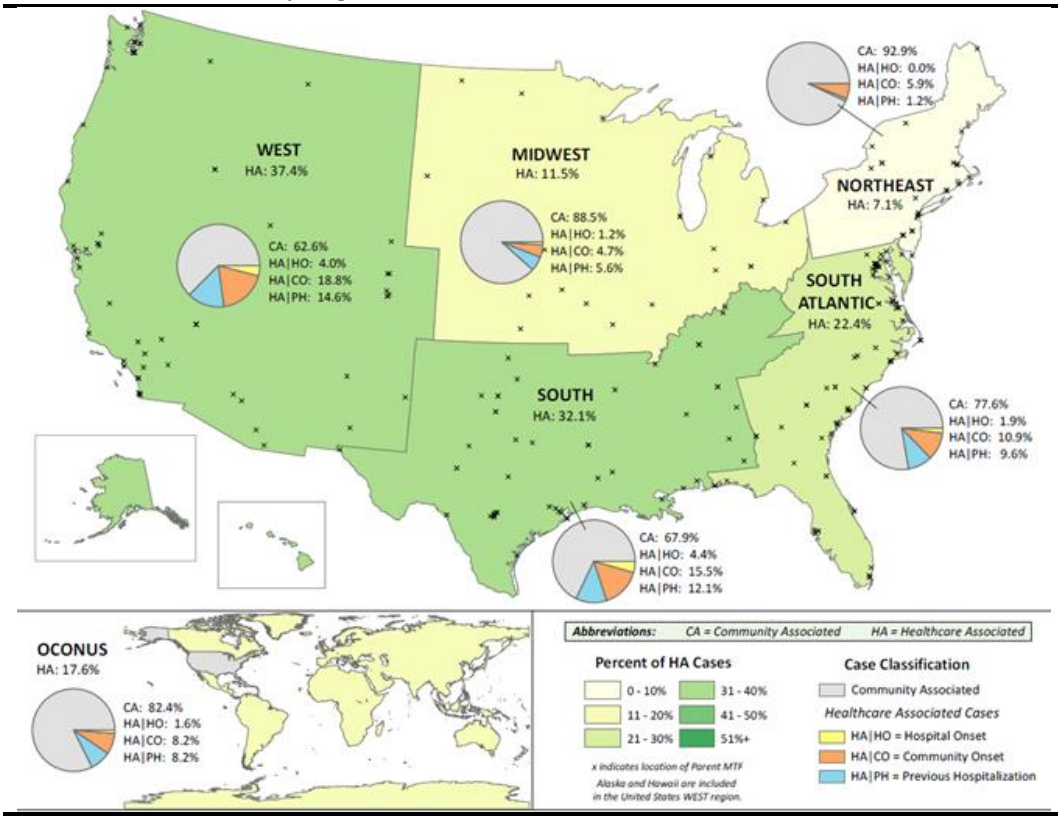
[a] Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.
[b] Admission MDRO prevalence included all individuals with an MDRO infection identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.
[c] Rates are presented as the rate per 1,000 inpatient admissions per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Regional Epidemiologic Infection Classifications

Among all prevalent MRSA infections identified in the MHS in 2016, 73.4% were community-associated (CA) cases and 26.6% were healthcare-associated (HA) cases. Regionally, the US West region had the highest proportion of HA MRSA cases (37.4%), followed by the US South (32.1%), US South Atlantic (22.4%), and OCONUS locations (17.6%).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Of all prevalent MRSA infections, regardless of HA or CA classification or regional location, 13.0% were CO cases, indicating that the infection most likely originated from the community. Only 2.8% of all prevalent MRSA infections were HO, indicating that the infection was most likely acquired during the current hospitalization. Regionally, in the US Northeast, US West, US South, US South Atlantic, and OCONUS locations, the same overall pattern was observed, with CO cases accounting for the majority of HA MRSA cases (Figure 2). However, in the US Midwest region, PH cases comprised the largest proportion of MRSA infections (5.6%), which indicates that the specimens were not associated with a current admission but that the patient had a prior hospitalization in the previous 12 months.

Figure 2. Proportion of Healthcare- and Community-Associated Cases among MRSA Infection in the MHS by Region, CY 2016



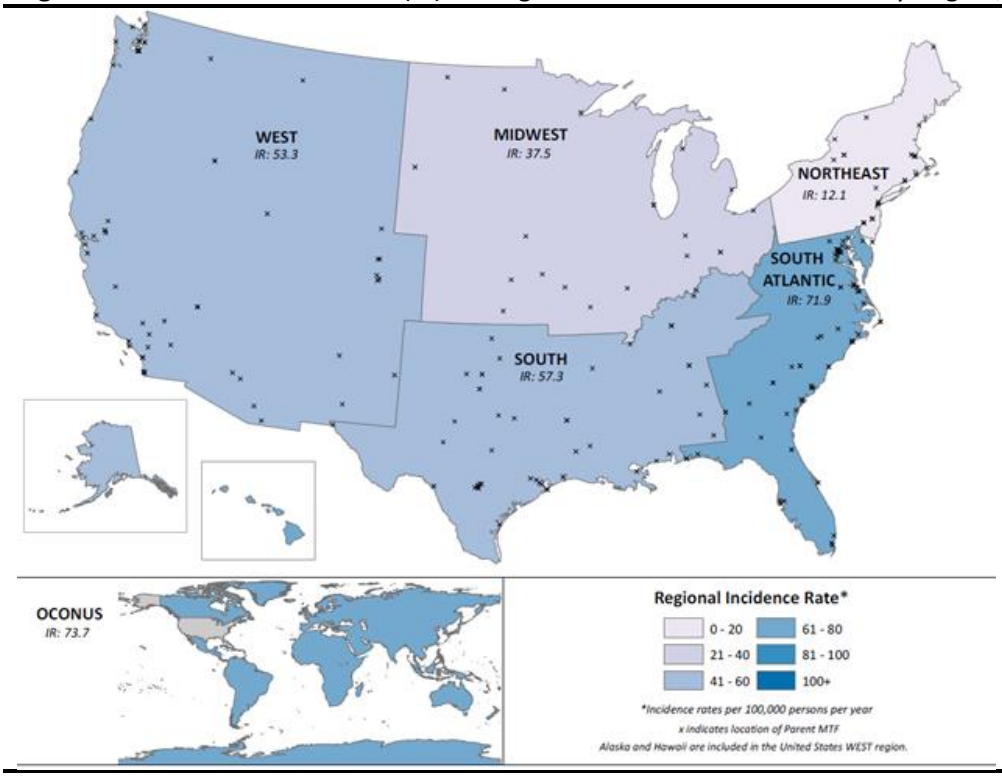
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section B – Antimicrobial Resistance and Use

Regional Multidrug Resistance

The 2016 annual incidence rate of MRSA among all MHS beneficiaries was 56.4 per 100,000 persons per year. Regionally, the highest incidence rates occurred in OCONUS locations (73.7 per 100,000 persons per year), followed by the US South Atlantic region (71.9), and the US South region (57.3) (Figure 3). The lowest incidence rate was observed in the US Northeast region at 12.1 per 100,000 persons per year.

Figure 3. Annual Incidence Rate (IR) among MRSA Infections in the MHS by Region, CY 2016



Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Emerging Resistance Patterns

In 2016, 16.7% of all prevalent MRSA infections in the MHS were resistant to both erythromycin and clindamycin, also known as inducible clindamycin resistance (ICR). This reflects a 13.8% change above the weighted historic ICR percentage among MRSA infections in the MHS (Table 5). The 2016 percentage of ICR in the MHS was more than two standard deviations above the weighted historic ICR. All services had a 2016 ICR percentage above the weighted historic ICR. The percentage ICR is within two standard deviations of the weighted historic ICR for the Air Force, Marine Corps, and Navy, which indicates that ICR in these populations generally aligned with historical observations. However, the overall MHS, Army, and DOD AD ICR percentages (16.7%, 14.2%, and 9.4%, respectively) were more than two standard deviations above the weighted historic ICR (14.7%, 13.1%, and 8.3%, respectively). The Navy had the highest percent change (18.3%). DOD AD service members had a 12.9% change above the weighted historic ICR among MRSA infections in this population.

Table 5. Percentage of MRSA Infections with ICR[a] in the MHS, CY 2016

Population	2016 ICR Percentage	Weighted Historic[b] ICR 2013 - 2015	Two Standard Deviations: Weighted Historic[b] ICR	2016	
				Direction	Percent Change[c]
MHS Beneficiaries	16.7	14.7	1.0	↑	13.8%
Air Force	18.7	16.7	2.7	↑	11.4%
Army	14.2	13.1	0.7	↑	8.3%
Marine Corps	10.1	8.7	1.5	↑	15.8%
Navy	18.1	15.3	2.7	↑	18.3%
DOD Active Duty	9.4	8.3	0.3	↑	12.9%

[a] Specimen must be resistant to both erythromycin and clindamycin to meet criteria for inducible clindamycin resistance (ICR).
[b] Historic ICR reflects the weighted average of the three years prior to the current analysis year's data.
[c] This reflects the percent change from the weighted historic ICR to the ICR of the current analysis year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Antibiogram

Table 6 displays an antibiogram of MRSA incident infections for all MHS beneficiaries from 2011-2016. In 2016, MRSA infections were most susceptible to vancomycin (100.0%), linezolid (99.8%), quinupristin/dalfopristin (99.8%), and daptomycin (99.5%). Infections were least susceptible to erythromycin (17.7%) and clindamycin (82.5%). Statistically significant trends in susceptibility were observed for clindamycin, doxycycline, erythromycin, rifampin, tetracycline, and trimethoprim/sulfamethoxazole; all of these antibiotics displayed a decrease in efficacy, except for erythromycin.

Table 6. Antibiogram of MRSA Infections Identified in the MHS, CY 2011-2016

Antibiotics	2011	2012	2013	2014	2015	2016	Susceptibility Trend	Comment[a]
Ceftaroline	--	--	--	--	--	--		
Clindamycin	87.4	85.9	84.9	84.9	84.1	82.5	90 80	↓
Daptomycin	100.0	99.8	100.0	100.0	100.0	99.5	100 90	
Doxycycline	97.9	99.4	95.5	95.3	95.8	96.5	100 90	↓
Erythromycin	14.5	14.5	16.3	17.0	17.2	17.7	20 10	↑
Linezolid	99.7	99.8	99.4	99.8	99.6	99.8	100 90	
Minocycline	98.0	97.4	98.0	96.7	96.2	97.6	100 90	
Quinupristin/ Dalfopristin	99.1	99.5	99.4	99.8	99.4	99.8	100 90	
Rifampin	99.4	99.3	99.0	98.8	98.6	99.1	100 90	↓
Telavancin	--	--	--	--	--	--		
Tetracycline	96.1	96.0	95.6	95.7	94.3	94.8	100 90	↓
Trimethoprim/ Sulfamethoxazole	98.8	98.5	98.2	98.0	97.2	96.6	100 90	↓
Vancomycin	100.0	100.0	100.0	100.0	100.0	100.0	100 90	

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

[a] Arrow indicates the antibiotics with a significant change in direction of trend for significant two-tailed Cochrane-Armitage tests for trend established for a single antibiotic over time. A significant increase in susceptibility is denoted by a green upward arrow and a significant decrease in susceptibility is denoted by a blue downward arrow.

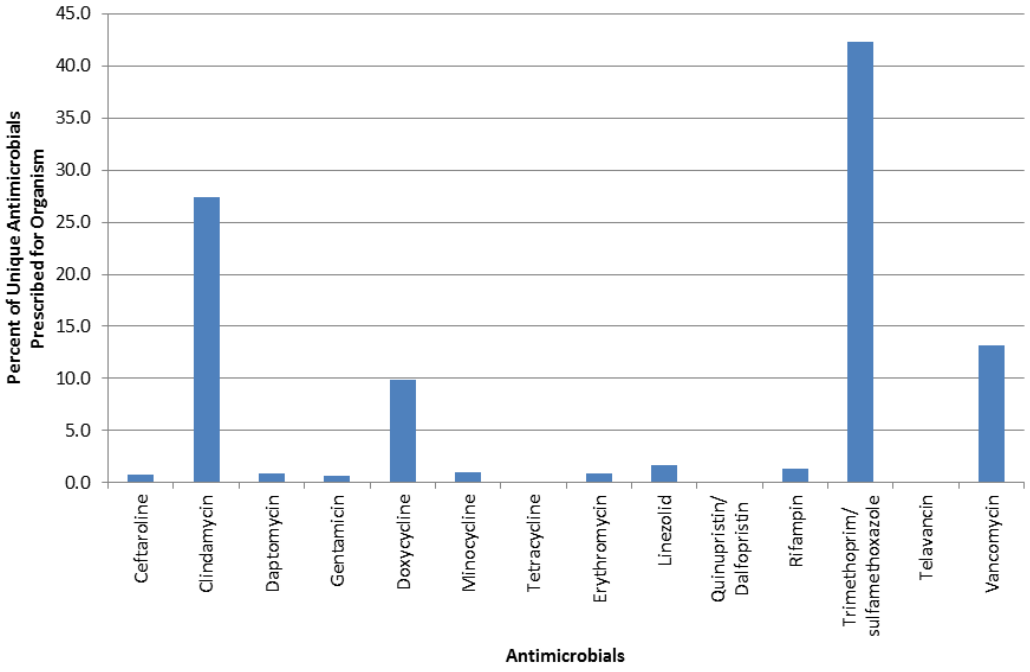
Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotics associated with MRSA infections in 2016 were trimethoprim/sulfamethoxazole (42.3%), clindamycin (27.4%), and vancomycin (13.2%) (Figure 4).

Figure 4. MRSA Infection and Prescription Practices in the MHS, CY 2016



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 pharmacy databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section C – Special Populations

Of the 5,712 prevalent MRSA infections in the MHS in 2016, 0.2% (N = 10) occurred among Department of the Navy (DON) AD deployed personnel. Of these deployment-related MRSA infections, 91% (N = 7) were male. All DON AD deployment-related infections occurred among service members aged 18-44, with 45% (N = 5) occurring among those aged 25-34.

Discussion

MRSA incidence rates in the general US population and the MHS have been declining in recent years; this decrease continued in 2016.[1,4] Overall, the MRSA incidence rate in the MHS surveillance population remained low in 2016 compared to the weighted historic IR, with an overall decreasing percent change observed among incident MRSA infections. Additionally, compared to the weighted historic IRs, all services (Army, Air Force, Marine Corps, and Navy) and the DOD AD population experienced a decline in incidence rates in 2016. These trends, along with other indicators in this report, suggest that increased awareness, greater adherence to infection control and prevention strategies, and improved antimicrobial stewardship practices are proving effective in both the civilian and military healthcare communities.

Though overall MRSA incidence rates are declining, vigilance is warranted due to the bacteria's changing epidemiology.[5,6] Recent literature shows that CA MRSA has disproportionately affected groups without typical risk factors, such as children or young adults.[7-9] Within the MHS, the majority of prevalent MRSA infections in 2016 were classified as CA cases (73.4%) and followed typical patterns generally observed in the US for CA MRSA. The shift to predominately CA MRSA infections is likely multi-faceted, but it may be attributed to the trends toward shorter hospital stays, inappropriate antibiotic use, and the difficulty in implementing community-based infection control interventions.[5,6] However, this shift is not likely due to surveillance screening programs in use within the MHS, as these types of surveillance samples have been excluded from analysis. Interventions that support antimicrobial stewardship and infection control are more easily implemented and enforced in the healthcare setting than the community setting, which could potentially contribute to a reservoir of MRSA in the community.

MRSA infections in the MHS in 2016 were less susceptible to clindamycin and erythromycin than other antibiotics tested. Trends of clindamycin susceptibility since 2011 displays a statistically significant descending trend (from 87.4% in 2011 to 82.5% in 2016); erythromycin susceptibility displays a statistically significant ascending trend (from 14.5% in 2011 to 17.7% in 2016), but despite increases in effectiveness, this antimicrobial is not a viable treatment within the MHS. Since the early 2000s, experts have been concerned about ICR, a type of resistance among *S. aureus* organisms that has been documented in recent literature,[1,10] and defined in this analysis as MRSA isolates resistant to both erythromycin and clindamycin. Within the MHS in 2016, prevalent MRSA infections identified with inducible resistance to clindamycin were among the highest proportions seen since surveillance began in 2005, with ICR identified among 16.7% of MRSA infections in the MHS. Although the percentage of ICR in the MHS has increased each year since 2005, the proportion remains below that seen in the general US population (range 18 – 52%).[10-13] However, analysis of ICR by branch of DOD service identified that select services, namely the Air Force and Navy, are now within the lower end of the threshold of ICR seen among the general US population, as well as reporting an average 15% increase in ICR infections each year. Close monitoring of clindamycin susceptibility patterns of MRSA is needed to ensure optimal disease prevention and treatment measures. It is also recommended that military laboratories routinely utilize the D-test (agar disk diffusion) in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines in order to clearly identify isolates susceptible to clindamycin despite erythromycin resistance.[14,15] Additional

analyses may also be warranted of ICR infections observed among the different DOD services to determine if enhanced prevention measures are needed among select services.

This annual report summarized MRSA incidence and prevalence in the MHS beneficiary population in 2016 and reported changes from previously identified trends. Given the possible change in MRSA's epidemiology, the shifting viability of treatment options, and increasing proportions of ICR among select DOD services, it is important to monitor and manage the risk to the MHS population at large. Continued surveillance is warranted to monitor any changes in burden, susceptibility, and treatment options and to guide targeted prevention efforts.

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Appendix A: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
CA	community-associated
CHCS	Composite Health Care System
CO	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 Department
HA	healthcare-associated
HO	hospital-onset
HL7	Health Level 7
ICR	Inducible clindamycin resistance
IR	incidence rate
M2	MHS Data Mart
MDRO	multidrug-resistant organism
MHS	Military Health System
MRSA	methicillin-resistant *Staphylococcus aureus*
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
SSTI	skin and soft tissue infection
US	United States