Annual Surveillance Summary: Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections in the Military Health System (MHS), 2015

NMCPHC-EDC-TR-177-2017

By Jessica Spencer and Uzo Chukwuma
EpiData Center Department
Prepared March 2017

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188

PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ORGANIZATION.

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
March 2017	Technical Report	01 January 2015 - 31 December 2015

4. TITLE AND SUBTITLE
Annual Surveillance Summary: Methicillin-Resistant Staphylococcus aureus (MRSA) Infections in the Military Health System (MHS), 2015

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Jessica Spencer, Uzo Chukwuma

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
EpiData Center
Navy and Marine Corps Public Health Center
620 John Paul Jones Circle, Suite 1100
Portsmouth, VA 23708-2103

8. PERFORMING ORGANIZATION REPORT NUMBER
NMCPHC-EDC-TR-177-2017

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
EpiData Center
Navy and Marine Corps Public Health Center
620 John Paul Jones Circle, Suite 1100
Portsmouth, VA 23708-2103

10. SPONSOR/MONITOR'S ACRONYM(S)
EDC, NMCPHC

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
NMCPHC-EDC-TR-177-2017

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

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The EpiData Center (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) 2015. 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 DOD AD populations are decreasing. Inducible clindamycin resistance is slowly increasing in the MHS; no additional changes in antibiotic susceptibility emerged in 2015. 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.

15. SUBJECT TERMS
Health Level 7 (HL7), Microbiology, Surveillance, Methicillin-resistant Staphylococcus aureus (MRSA), inducible clindamycin resistance

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 MPH
U	U	U	UU	28	19b. TELEPHONE NUMBER (Include area code) 757-953-0970

Reset

Standard Form 298 (Rev. 8/98)
Prescribed by ANSI Std. Z39.18
Adobe Professional 7.0

Abstract

The EpiData Center (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) 2015.

Multiple data sources were linked to assess descriptive and clinical factors related to MRSA. Health Level 7 (HL7)-formatted microbiology data identified *S. aureus* infections resistant to oxacillin, cefoxitin, or methicillin. These infections were matched to HL7-formatted 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 2015. 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

Staphylococcus aureus is a common gram-positive bacterium. Methicillin-resistant *S. aureus* (MRSA) is a specific type of *Staphylococcus* bacteria that has developed resistance to β-lactam antibiotics such as methicillin, oxacillin, and penicillin,[1-5] thus complicating treatment of the infection. MRSA infections are a national concern for public health and hospital officials due to the opportunistic nature of the bacteria and the limited treatment options created by the emergence of antibiotic resistance. Surveillance of MRSA is important to ensure effective antibiotic stewardship and to monitor mutations that may alter treatment options.

MRSA is known for its ease in transmission and spreads readily from person to person through contaminated objects or casual contact. MRSA typically presents in three forms: colonization, non-invasive infection, or invasive infection. MRSA is a common colonizer of the nares, axillae, vagina, and pharynx. Colonization often serves as a reservoir from which bacteria can cause infection.[6,7] Non-invasive infections account for the majority of MRSA infections and generally manifest as skin or soft tissue infections (SSTIs) in locations where skin integrity is compromised (e.g., cuts, abrasions) or covered by hair.[8] Invasive infections, though less common, occur when MRSA bacteria invade the bloodstream, resulting in bacteremia that can lead to endocarditis, sepsis, or other invasive infections, which may be fatal.[9] Efforts to reduce the spread of MRSA in recent years focused on the screening and decolonization of select groups of hospitalized patients, such as intensive care unit (ICU) patients, using intranasal mupirocin and chlorahexidine bathing.[10]

MRSA strains commonly identified in healthcare facilities are different from those found in the community setting, and each of these settings has unique risk factors. Healthcare-associated (HA) MRSA infections occur when a patient has a history of hospitalization within the 12 months prior to the current admission, during which a MRSA infection was presumably contracted. Among HA MRSA infections, the common risk factors include advanced age, weakened immune system, hospitalization, residence in a long-term care facility, or use of an invasive medical device. MRSA is the leading cause of HA infections among antibiotic-resistant organisms,[11,12] and these infections lead to a significant burden on hospital resources. Recent estimates suggest that up to 65% of HA *S. aureus* infections are caused by methicillin-resistant strains.[13] Hospital-onset (HO) MRSA infections occur when a patient is admitted without a MRSA infection, but subsequently develops a MRSA infection three or more days after the admission date. HA and HO MRSA infections are typically more severe or potentially life threatening than community-associated (CA) MRSA; examples of HA or HO MRSA include bacteremia or infections occurring at the site of a surgical wound. Fortunately, invasive HA and HO MRSA infections appear to have declined in recent years.[13] In 2014, the Centers for Disease Control and Prevention (CDC) estimated the overall infection rate of invasive MRSA in the United States (US) to be approximately 22.7 cases per 100,000 persons in the general population, with a death rate of approximately 2.9 per 100,000 persons.[14] These rates reflect a 40% decrease in overall MRSA incidence since 2005, when the infection rate was estimated to be 35.5 cases per 100,000 persons in the general population, with a death rate of 6.8 per 100,000 persons.[15]

MRSA in the community setting was not a common occurrence until the late 1990's. Since then, CA MRSA infections have emerged among individuals with no recent healthcare contact or other apparent risk factors. [11] CA MRSA outbreaks have been reported in populations with intense physical activity and skin-to-skin contact, such as military recruits, prison inmates, and athletic teams.[16] The CDC has identified that between 12 – 14% of MRSA infections are CA.[17,18] CA MRSA is most often identified as an SSTI, and while rates of non-invasive MRSA infections are not available for comparison in a similar nationwide scale, a study of 11 emergency departments in the US found MRSA was the cause of 59% of SSTIs overall, making it a prominent cause of SSTIs in the community setting.[19]

Seasonal variations in *S. aureus* infections occur, with some studies reporting an increase in infections during the summer months of most climates and the fall months of temperate and tropical climatic regions.[20-24] However, some experts dispute reports on the seasonality of MRSA infections, as many of the reports focus primarily on SSTIs. Conducive environmental conditions (e.g., warm temperatures) that promote bacterial growth and spread of infection may contribute to the increased incidence of *S. aureus* during the warmer months.[24]

In January 2013, the Infectious Disease Society of America (IDSA) published updated clinical practice guidelines for the treatment of MRSA infections according to the treatment setting (inpatient or outpatient) and infection type (SSTI, bacteremia, pneumonia, and other invasive infections). General treatment for MRSA SSTIs may include oral antibiotics such as clindamycin, trimethoprim/sulfamethoxazole, doxycycline, or minocycline. For more complicated SSTIs, intravenous vancomycin or linezolid is recommended.[25,26] Vancomycin or daptomycin are recommended for uncomplicated MRSA bacteremia and other invasive infections. In instances of vancomycin resistance, high-dose intravenous daptomycin in combination with gentamicin, rifampin, or linezolid is suggested. For infections with less susceptibility to both vancomycin and daptomycin, therapeutic options include intravenous quinupristin-dalfopristin, intravenous trimethoprim-sulfamethoxazole, intravenous or oral linezolid, or intravenous telavancin.[26] Treatment options for CA MRSA infections may differ from HA MRSA infections, as CA MRSA infections often do not possess the same level of multidrug-resistance (MDR) as HA MRSA infections. Greater susceptibility of CA MRSA infections has led to the reappearance of older antibiotic classes for management of these infections, such as lincosamides and macrolides. CA MRSA infections are often susceptible to trimethoprim/sulfamethoxazole, clindamycin, doxycycline or minocycline, and fluoroquinolones; however, susceptibility patterns may vary by geographic region.[27]

The susceptibility of *S. aureus* to available antibiotics complicates the treatment of MRSA infections. Per the IDSA clinical practice guidelines, clindamycin is commonly used to treat MRSA and is more cost effective than newer antibiotic drugs such as linezolid and daptomycin.[27] Since the early 2000s, concerns have risen over the possibility for inducible clindamycin resistance, which occurs when organisms have the genetic potential to become resistant to clindamycin during the course of treatment, thereby causing treatment failures and enhancing the virulence of the MRSA pathogen.[27] Reports from several studies identify 18% to 52% of all *S. aureus* isolates have induced clindamycin resistance.[28,29] The expression of

induced clindamycin resistance is only detected through the use of agar disk diffusion (D-test) in accordance with recommendations from the Clinical and Laboratory Standards Institute (CLSI).[30] Additionally, vancomycin is generally restricted for use in severe MRSA infections as an antibiotic of last resort. The increased use and misuse of vancomycin to treat MRSA propagates the mechanism of resistance and allows for changes in virulence and resistance patterns of *S. aureus*, leading to vancomycin-resistant *S. aureus* (VRSA) infections. Although VRSA infections are quite rare and none have been identified in the US military, it is concerning that seven strains of VRSA have been isolated in the US since 2002.[31] Careful consideration and close monitoring of antibiotics used to treat MRSA is needed to ensure continued susceptibility of *S. aureus* to available antimicrobial therapies.

MRSA also poses a particular threat for the Military Health System (MHS) beneficiary population due to environmental and occupational exposures unique to military service. These exposures may facilitate transmission of infections and thereby compromise force health and operational readiness. Outbreaks have occasionally occurred among military trainees.[32] Although rates of HA MRSA infection among active duty (AD) personnel have declined in recent years, this population remains at significant risk for CA MRSA due to environmental and occupational exposures, such as combat-associated deployments.[33,34] Some studies have shown that during military training, approximately 5% of all individuals will experience an SSTI, with *S. aureus* isolated in 91% of these cases, and MRSA identified in 70% of the *Staphylococcus* infections.[34-36]

It is important, therefore, to monitor MRSA trends and changes in epidemiology on an ongoing basis. This analysis presents an annual update for calendar year (CY) 2015 of MRSA infection burden among MHS beneficiaries from previously reported retrospective data. This report describes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns for MRSA infections among MHS beneficiaries, Department of Defense (DOD) AD service members, and Department of the Navy (DON) AD service members with deployment-related infections.

Methods

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducted retrospective surveillance of MRSA infection in the MHS in CY 2015 (01 January 2015 to 31 December 2015). Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data was used to identify records with *S. aureus* growth in 2015. *S. aureus* infections resistant to oxacillin, cefoxitin, or methicillin were classified as MRSA. A unique MRSA infection was defined as the first positive MRSA laboratory result per person per 30 days. Incidence represented the first unique infection per person per calendar year and prevalence was defined as all unique MRSA infections.

Demographic Classification

Demographic information for each incident infection was described using data within the HL7-formatted CHCS microbiology record and infections were classified according to the patient's gender, age, sponsor service (Air Force, Army, Marine Corps, or Navy), duty status (Active Duty, Retired, Family Member, or Other), and region of the facility where the specimen was collected. The Active Duty category included both active duty and recruit personnel, defined by the beneficiary type codes of 11 and 13, respectively.

MRSA incidence rates and prevalence infections were aggregated into six spatial regions and visualized as maps created in ESRI ArcGIS software (version 10.2.2). Organisms identified in each region may act as a reservoir within that region and contribute to the burden of exposure. Geographic regions were assessed within the continental United States (CONUS) and outside the CONUS (OCONUS), with the spatial regions identified as follows:

- **Northeast**: Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, Pennsylvania, New Jersey.
- **Midwest**: Michigan, Wisconsin, Minnesota, Ohio, Indiana, Illinois, Iowa, Missouri, Kansas, Nebraska, North Dakota, South Dakota.
- **West**: California, Oregon, Washington, Idaho, Montana, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Alaska, Hawaii.
- **South**: Texas, Oklahoma, Arkansas, Louisiana, Mississippi, Alabama, Tennessee, Kentucky.
- **South Atlantic**: Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida.
- **OCONUS**: All US territories and non-US countries.[37]

Clinical Characteristics Classification

Clinical characteristics were described for prevalent infections using information within the HL7-formatted CHCS microbiology record. Specimens were classified as inpatient or outpatient based on the Medical Expense and Performance Reporting System (MEPRS) codes of the location where the specimen was collected. A MEPRS code of A indicated specimen collection in the inpatient setting. All other MEPRS codes were considered outpatient encounters.

Infections were classified into invasive and non-invasive categories using the specimen source or body site variables in the HL7-formatted CHCS microbiology record. The terms used to group the data into these categories are described in Table 1. In addition, infections were further categorized based on body collection sites specific to the organism of interest (e.g., urine, respiratory, bloodstream) to provide enhanced granularity to the source of infection. Clinical characteristics were presented as a proportion of all infections within the population meeting the definition criteria.

Table 1. Invasive and Non-Invasive Infection Classification for MRSA Infections Accessing the MHS

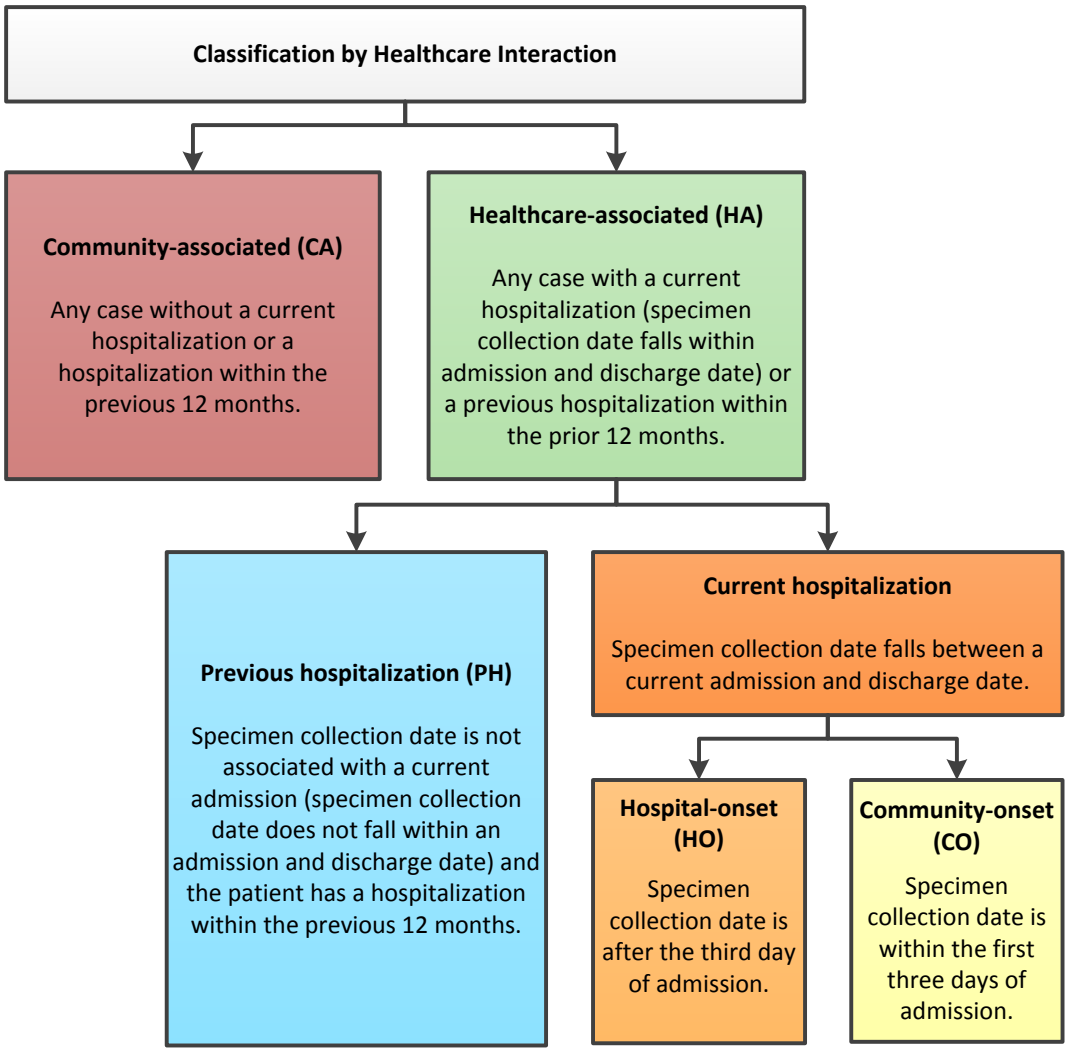
Infection Classification	If Body Site or Specimen Source Sample Taken From:
Invasive Infections	Blood, bone, cerebrospinal fluid, peritoneal fluid, pleural fluid, or synovial fluid
Other Non-Invasive Infections	Abscess, aspirate, body fluid, boil, bursa, carbuncle, cellulitis, cyst, discharge, drainage, exudate, eye, genital, lesion, pus, pustule, respiratory, skin, sputum, stool, swab, throat, tissue, urine, or wound

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Epidemiologic Infection Classification

To evaluate all laboratory-confirmed MRSA infections for recent contact with the healthcare system, MRSA prevalence infections were matched to the Standard Inpatient Data Record (SIDR) to determine epidemiologic infection classification. Records were categorized as either community-associated (CA) or healthcare-associated (HA). CA cases were defined as patients without a current hospitalization nor a hospitalization in the previous 12 months. HA cases were defined as patients who were hospitalized at the time of infection (currently hospitalized) or who had a hospitalization within the previous 12 months. Current hospitalizations were further categorized as a hospital-onset (HO) case or a community-onset (CO) case. HO cases were defined as patients with a MRSA organism identified after the third day of the current admission. CO cases were identified as patients with a specimen collected within the first three days of the current admission yielding a MRSA organism, indicating the patient likely acquired the organism within the community and arrived at the treating facility with it.[38] Figure 1 presents the definitions for epidemiologic infection classifications.

Figure 1. Epidemiologic Infection Classifications[a]



[a]Cohen A, Calfee D, Fridkin SK, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infect Cont Hosp Ep*. 2008;29(10):901-913.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Exposure Burden Metrics

Only the first unique multidrug-resistant organism (MDRO) infection per patient per admission was used to analyze exposure burden metrics in the MHS. Admission prevalence estimated the exposure of infection at the time of admission (importation of MDROs into the MHS), which included MDROs isolated 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. Overall prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, or samples that tested positive for infection in the prior calendar year.

Admitted patients with a history of colonization or infection were identified by searching prevalence infections from the prior calendar year to determine a history of infection. These beneficiaries were counted in both the admission and overall prevalence populations as they contributed to the colonization pressure and exposure burden for those not already colonized or infected in both populations.[38] The historical review of data is included to show a reservoir of antimicrobial resistance and pressure among MRSA infections. Regional rates of exposure burden were calculated as the rate of exposure (admission or overall prevalence) per 1,000 inpatient admissions per region per year.

Pharmacy Transactions

To analyze antimicrobial prescription practices in the MHS, the HL7-formatted microbiology MRSA prevalence infections were matched to pharmacy data to identify antibiotic prescriptions associated with MRSA infections in all pharmacy databases (outpatient oral (OP), inpatient oral (unit dose, or UD), and inpatient and outpatient intravenous (IV)). Prescriptions were considered to be associated with a MRSA infection if the transaction date in the pharmacy record occurred either seven days before or after the date the specimen was certified in the laboratory data. All pharmacy transactions, regardless of database source (UD, IV, OP), were evaluated as one data source. Cancelled prescriptions or those with zero or null filled prescriptions were removed prior to analysis. A unique antibiotic prescription was defined as the first dispensed prescription for an antibiotic per prevalence infection. Antimicrobials recommended for treatment of MRSA infections according to the Johns Hopkins Antibiotic Guide were retained for analysis.[39]

Antimicrobial Resistance Classification

To evaluate changes in antimicrobial susceptibility for MRSA infections, an antibiogram was created using antibiotic susceptibility results from the microbiology record according to the CLSI guidelines.[40] The antibiogram includes the first isolate per person per organism per year from 2010 to 2015. The Cochran-Armitage trend test was used to assess patterns in susceptibility across years. Trend direction for a single antibiotic over time was established using the two-tailed *P*-value; an increase in susceptibility was denoted by a green upward arrow and a decrease in susceptibility was denoted by a blue downward arrow. A statistically significant trend was established using a $P\text{-value} \leq .05$.

Additional analyses were conducted to assess trend, demographic, and clinical characteristics of specimens that exhibit inducible clindamycin resistance. Inducible clindamycin resistance (ICR) was determined only when the susceptibility results indicated both erythromycin and clindamycin resistance.

Special Populations

MRSA infections identified among DON AD personnel were matched to the Defense Manpower Data Center (DMDC) Contingency Tracking System (CTS) to explore deployment-related infections occurring on or between the start and end dates of the deployment plus 30 days. Thirty days post-end of deployment was used to ensure all MRSA infections related to the deployment were included. Records with no deployment end date (i.e., service member remains

deployed) were also included provided that the infection occurred in the analysis year (2015) and the start date of deployment was within 180 days of the specimen certification date.

Statistical Analysis

The MHS Data Mart (M2) was used to obtain counts of TRICARE eligible MHS beneficiaries for denominators. The annual incidence rate was defined as the count of all incident infections per year divided by the corresponding annual M2 eligible beneficiary count (represented by the count in July) per year. A weighted average of incidence rates by month for the three years prior to the current analysis year (weighted historic monthly baseline) was used to assess the seasonal component of MRSA infections in 2015. One and two standard deviations, both above and below the weighted historic monthly baseline, were used to indicate statistically significant changes in incidence rates of MRSA infections in the analysis year.

All incidence rates are presented as an estimated rate per 100,000 persons per year. Due to the transient nature of the military beneficiary population and an inability to account for the proportion of the beneficiary population that receives medical care outside of the MHS, estimated rates are used for comparison of rates from year to year. A historical baseline was created using the weighted average of the immediately preceding three years. The historical baseline of the incidence rate serves as a clinical reference for the 2015 incidence rate. Two standard deviations on either side of the baseline were calculated to assess variation in incidence rate in the three years prior to the current evaluation period. Two standard deviations provide the upper and lower bounds (approximately 95%) for assessing whether the observed occurrence was likely due to change, and for consideration of clinically significant trends.

Results

Section A – Descriptive Epidemiology

Incidence of MRSA

In 2015, the annual incidence rate (IR) for MRSA infection among MHS beneficiaries treated at a military treatment facility (MTF) was 61.1 per 100,000 persons per year. This reflects a 10.4% change below the weighted historic IR. Incidence rates across all services and the DOD AD population in 2015 were also below the weighted historic IRs. This reflects a greater than 10% change below the weighted historic IRs for the DOD AD population and all services, except the Air Force, which experienced a 4.6% change below the weighted historic IR. However, the 2015 IRs are within two standard deviations of the weighted historic IRs of MRSA in the MHS, service-specific, and the DOD AD populations (Table 2).

Table 2. Incidence Rate (IR) for MRSA Infections in the MHS, CY 2015

Population	2015 IR	Weighted Historic[a] IR 2012 - 2014	Two Standard Deviations: Weighted Historic[a] IR	2015	
				Direction	Percent Change[b]
MHS Beneficiaries	61.1	68.2	16.0	↓	10.4%
Air Force	36.8	38.6	8.7	↓	4.6%
Army	67.9	76.7	23.3	↓	11.4%
Marine Corps	102.9	116.8	30.7	↓	12.0%
Navy	54.4	61.0	8.9	↓	10.7%
DOD Active Duty	161.5	186.3	56.2	↓	13.3%

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 and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Demographic Distribution of MRSA

In 2015, there were 5,761 incident MRSA infections identified among all MHS beneficiaries treated at an MTF. The highest incidence rates among each demographic category occurred in 18-24 year olds, males, and active duty service members (Table 3).

Table 3. Demographic Characteristics of MRSA Infections in the MHS, CY 2015

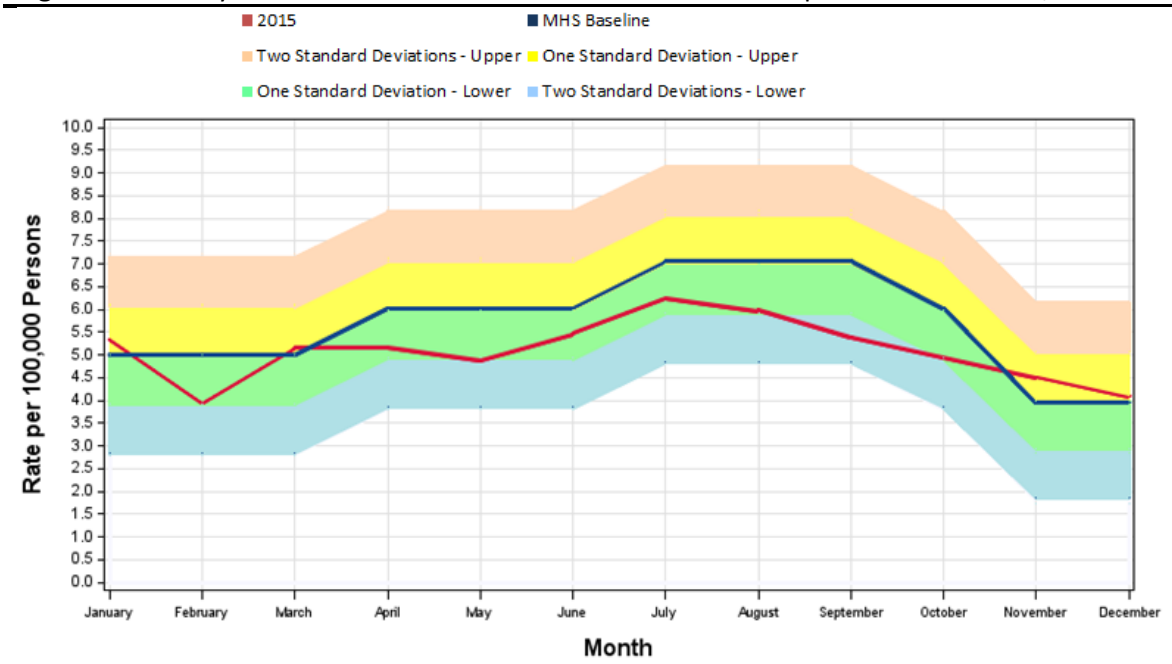
	N = 5,761	
	Count	**Rate**
Gender		
Female	2,138	46.1
Male	3,623	75.6
Age Group (in Years)		
0-17	998	50.8
18-24	1,670	144.4
25-34	1,073	89.4
35-44	500	60.0
45-64	857	41.1
65+	663	30.3
Beneficiary Type		
Active Duty	2,222	161.5
Family Members	2,184	39.6
Retired	703	32.4
Other[a]	652	--

[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 database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Seasonality

Monthly incidence rates of MRSA infections in 2015 were at times higher than the monthly baseline (January, March, November, and December); however, any increase in monthly incidence rates remained within one standard deviation of the weighted historic baseline and was therefore within historical observation. Other monthly incidence rates (February, April – October) for MRSA infections were below the weighted historic monthly baseline and within one to two standard deviations (Figure 2). A seasonal component to MRSA infections was observed in 2015, with an increase in infections in March, a peak in monthly incidence in July, and then descending rates throughout the remainder of the year.

Figure 2. Monthly Incidence of MRSA Infections and Baseline Comparisons in the MHS, CY 2015



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 baseline.
The monthly baseline 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 28 February 2017.

MRSA Clinical Characteristics

There were 6,258 prevalent MRSA infections identified among all MHS beneficiaries treated at an MTF in 2015. The infection burden was higher in the outpatient setting (89.5%) and generally presented as non-invasive infections (94.3%) (Table 4). Seventy-five percent of MRSA infections were from sources indicative of an SSTI or wound. Of all invasive MRSA infection types, blood infections accounted for 38% of the specimens (data not shown).

Table 4. Clinical Characteristics of MRSA Prevalent Infections in the MHS, CY 2015

	N = 6,258	
	Count	**Percentage**
Specimen Collection Location		
Inpatient	654	10.5
Outpatient	5,604	89.5
Infection Type		
Invasive	354	5.7
Other Non-Invasive	5,904	94.3
Body Collection Site		
Blood	136	2.2
Respiratory	425	6.8
SSTI/Wound	4,696	75.0
Urine	331	5.3
Other	670	10.7

Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Exposure Burden Metrics

Table 5 presents two different metrics defining MDRO infection rates for healthcare-associated exposures. In 2015, there were 252,751 direct care inpatient admissions across all MHS MTFs. The overall MDRO prevalence rate for MRSA was 6.2 per 1,000 inpatient admissions; this measures the exposure of infection at any point during the admission or one year prior. Within the US, the West region had the highest overall MDRO prevalence rate (6.6 per 1,000 inpatient admissions) and the Midwest region had the lowest rate (5.7 per 1,000 inpatient admissions). The admission MDRO prevalence rate for MRSA was 5.8 per 1,000 inpatient admissions; this measures the magnitude of 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 (6.1 per 1,000 inpatient admissions) and the Midwest region had the lowest rate (5.6 per 1,000 inpatient admissions). OCONUS locations had the lowest overall and admission MDRO prevalence rates across all regions in 2015 (4.6 and 4.4 per 1,000 inpatient admissions, respectively) (Table 5). Among MRSA infections, the overall MDRO prevalence rate was higher than the admission MDRO prevalence rate (6.2 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 5. MDRO Healthcare-Associated Exposure Burden Metrics among MRSA in the MHS, CY 2015

	Overall MDRO Prevalence[a]		Admission MDRO Prevalence[b]	
	Count	Rate[c]	Count	Rate[c]
Region				
OCONUS	81	4.6	76	4.4
US Midwest	58	5.7	57	5.6
US Northeast	1	--	1	--
US South	362	6.2	342	5.8
US South Atlantic	536	6.4	505	6.0
US West	537	6.6	494	6.1
Total	1,575	6.2	1,475	5.8

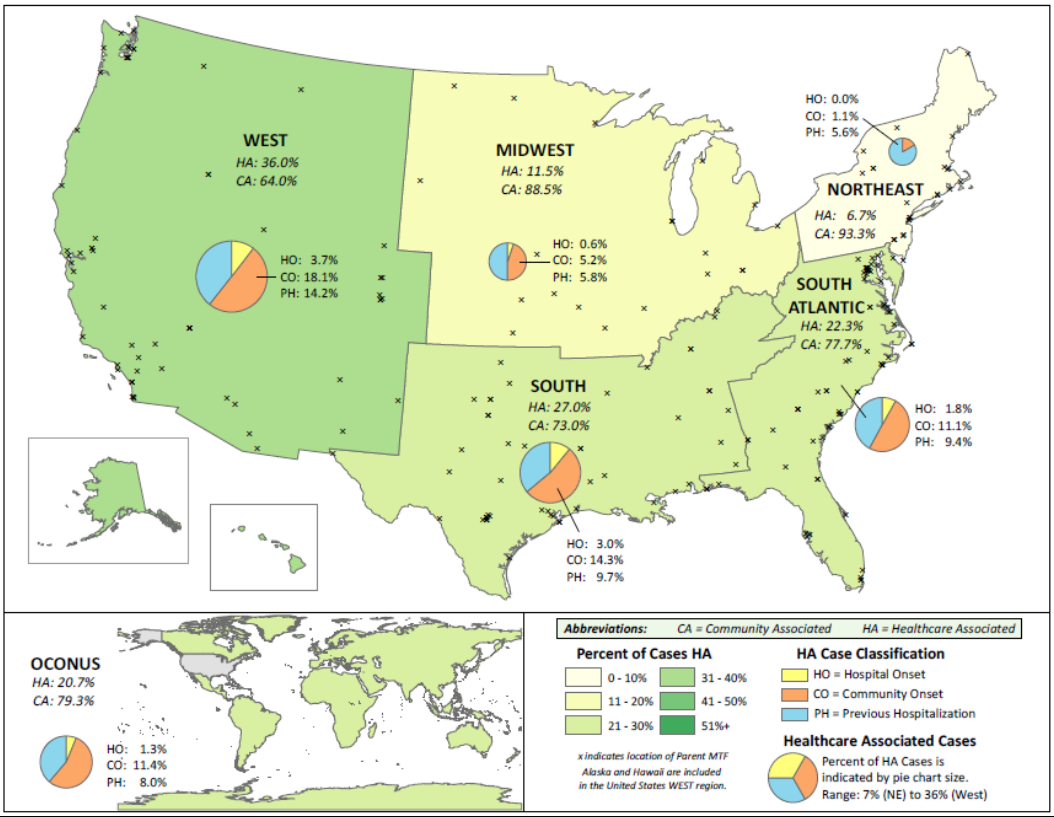
[a] Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.
[b] Admission MDRO prevalence included all individuals with an MDRO infection 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. Rates are not provided when the prevalence count is less than or equal to 5.
Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Regional Epidemiologic Infection Classifications

Among all MRSA prevalent infections identified in the MHS, 75% were CA cases and 25% were HA cases. Regionally, the US West region reported the highest proportion of HA MRSA cases (36%), followed by the US South (27%), US South Atlantic (22.3%), and OCONUS locations (20.7%).

HA cases were further categorized into HO, CO, or previous hospitalization (PH) groupings. Of all HA MRSA cases regardless of regional location, 12.8% were CO cases, indicating that the infection most likely originated from the community. Only 2.3% of all HA MRSA cases were HO, indicating that the infection was most likely contracted during the current hospitalization. Regionally, in the 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 3). However, in the US Midwest and Northeast regions, PH cases comprised the largest proportion of HA MRSA cases (5.8% and 5.6%, respectively), 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 3. Proportion of Healthcare- and Community-Associated Cases among MRSA Infections in the MHS by Region, CY 2015



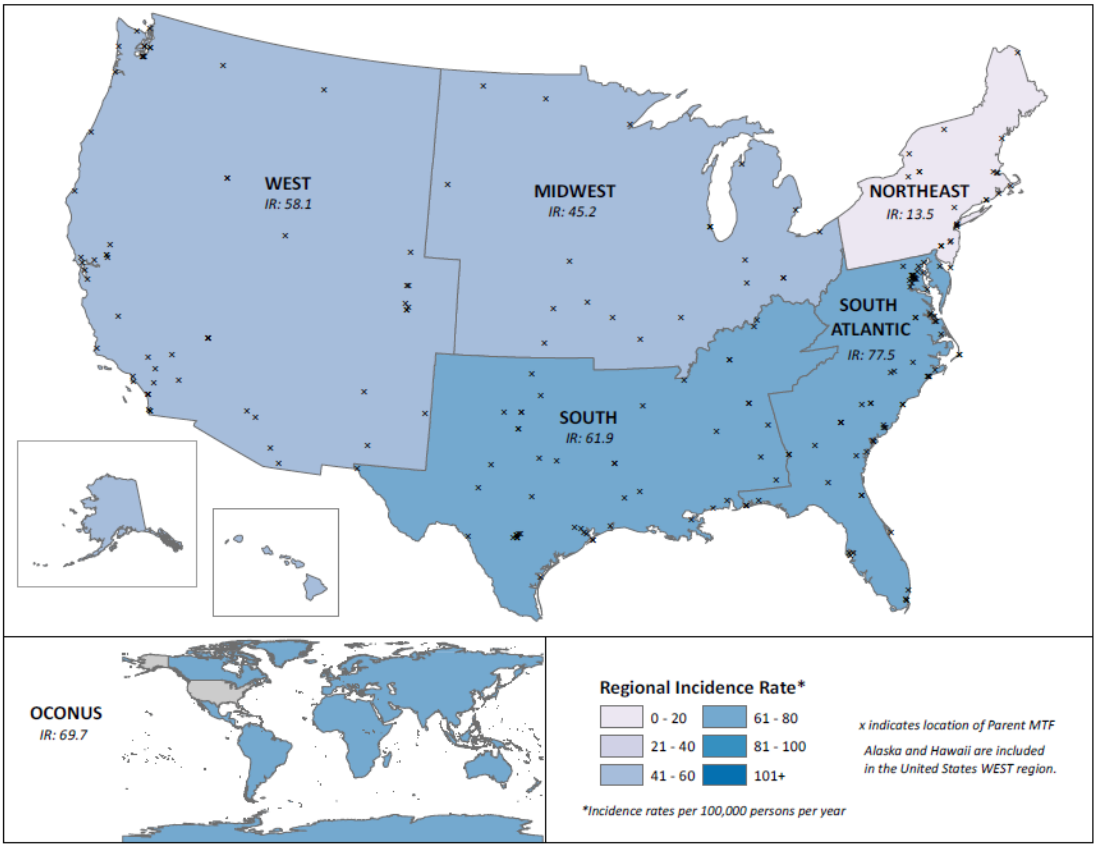
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Section B – Antimicrobial Resistance and Use

Regional Multidrug Resistance

The 2015 annual incidence rate of MRSA among all MHS beneficiaries was 61.1 per 100,000 persons per year. Regionally, the highest incidence rates occurred in the US South Atlantic region (77.5 per 100,000 persons per year), followed by OCONUS locations (69.7), and the US South region (61.9) (Figure 4). The lowest incidence rate was observed in the US Northeast region at 13.5 per 100,000 persons per year.

Figure 4. Annual Incidence Rate (IR) of MRSA Infections in the MHS by Region, CY 2015



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 28 February 2017.

Emerging Resistance Patterns

In 2015, 15.2% of all MRSA prevalent infections in the MHS were resistant to both erythromycin and clindamycin (ICR). This reflects an 8.2% change above the weighted historic ICR among MRSA infections in the MHS (Table 6). The 2015 percentage of ICR in the MHS was more than two standard deviations above the weighted historic ICR and thus higher than the historical observations. All services, except for the Marine Corps, had a 2015 ICR percentage above the weighted historic ICR. However, the percentage ICR is within two standard deviations of the weighted historic ICR for all services except the Navy, which indicates that an expected level of variation for ICR existed in the Army, Air Force, and Marine Corps populations. The Navy ICR percentage (16.6%) was more than two standard deviations above the weighted historic ICR (13.9%) and had the highest percent change (19.7%); this is higher than historical observations of ICR. The percentage of ICR among DOD AD service members was 8.5% in 2015. This reflects a 3.3% change above the weighted historic ICR among MRSA infections in this population. However, the percentage ICR is within two standard deviations of the weighted historic ICR for the DOD AD population and thus reflects normal variation.

Table 6. Percentage of MRSA Infections with ICR[a] in the MHS, CY 2015

Population	2015 ICR Percentage	Weighted Historic[b] ICR 2012 - 2014	Two Standard Deviations: Weighted Historic[b] ICR	2015	
				Direction	Percent Change[c]
MHS Beneficiaries	15.2	14.0	1.0	↑	8.2%
Air Force	17.9	15.2	3.0	↑	17.6%
Army	13.3	12.6	2.2	↑	6.1%
Marine Corps	9.0	9.2	4.4	↓	2.7%
Navy	16.6	13.9	0.8	↑	19.7%
DOD Active Duty	8.5	8.2	0.4	↑	3.3%

[a] Specimen must be resistant to both erythromycin and clindamycin to meet criteria for inducible clindamycin resistance.
[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 28 February 2017.

Antibiogram

Table 7 displays an antibiogram of MRSA incident infections for all MHS beneficiaries from 2010 – 2015. In 2015, MRSA infections were most susceptible to daptomycin (100%), vancomycin (99.8%), linezolid (99.6%), and quinupristin/dalfopristin (99.4%). Infections were least susceptible to erythromycin (17.2%) and clindamycin (84.1%). Statistically significant trends in susceptibility were observed for clindamycin, erythromycin, minocycline, tetracycline, doxycycline, rifampin, and trimethoprim/sulfamethoxazole; all of these antibiotics displayed a decrease in susceptibility, except for erythromycin.

Table 7. Antibiogram of MRSA Infections Identified in the MHS, CY 2010-2015

Antibiotics	2010	2011	2012	2013	2014	2015	Susceptibility Trend	Comment[a]
Clindamycin	87.7	87.4	85.9	84.9	84.9	84.1	90 80	↓
Erythromycin	12.0	14.5	14.5	16.3	17.0	17.2	20 10	↑
Minocycline	99.3	98.0	97.4	98.0	96.7	96.2	100 90	↓
Tetracycline	95.9	96.1	96.0	95.6	95.7	94.3	100 90	↓
Doxycycline	97.8	97.9	99.4	95.5	95.3	95.8	100 90	↓
Quinupristin/ Dalfopristin	99.2	99.1	99.5	99.4	99.8	99.4	100 90	
Rifampin	99.3	99.4	99.3	99.0	98.8	98.6	100 90	↓
Trimethoprim/ Sulfamethoxazole	99.0	98.8	98.5	98.2	98.0	97.2	100 90	↓
Vancomycin	99.8	99.7	99.9	99.9	99.9	99.8	100 90	
Linezolid	99.3	99.7	99.8	99.4	99.8	99.6	100 90	
Daptomycin	100.0	100.0	99.8	100.0	100.0	100.0	100 90	
Telavancin	--	--	--	--	--	--		
Ceftaroline	--	--	--	--	--	--		

'--' 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.

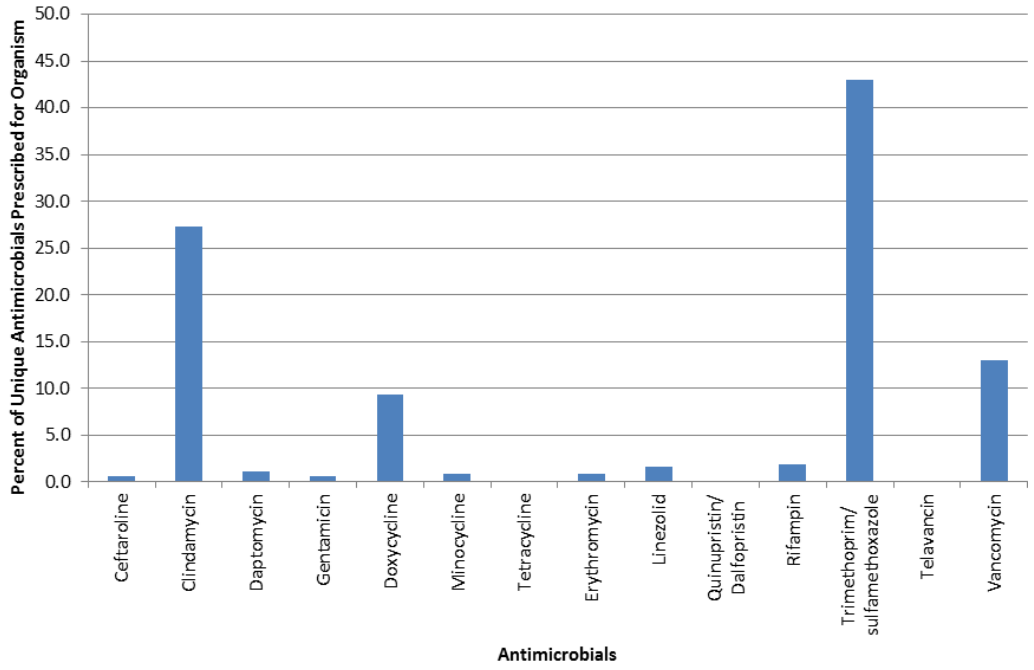
Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotics associated with MRSA infections in 2015 were trimethoprim/sulfamethoxazole (43%), clindamycin (27%), and vancomycin (13%) (Figure 5). Doxycycline was also commonly prescribed (9%). The remaining antibiotics were prescribed for less than 2% of infections in 2015.

Figure 5. MRSA Infection and Prescription Practices in the MHS, CY 2015



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 Department, Navy and Marine Corps Public Health Center, on 28 February 2017.

Section C – Special Populations

Of the 6,258 prevalent MRSA infections in 2015, 0.2% (N = 11) occurred among DON AD deployed personnel. Of these deployment-related MRSA infections, 91% were male and 91% were Navy service members. All DON AD deployment-related infections occurred among service members aged 18-44, with 45% occurring among those aged 25-34.

Discussion

MRSA incidence rates in the general US population have been declining in recent years; this decrease continued in 2015.[14] Overall, the MRSA incidence rates in the MHS surveillance population were lower in 2015 compared to the 2012 – 2014 weighted historic incidence rate. Beneficiaries from all services (Army, Air Force, Marine Corps, and Navy) and the DOD AD population experienced a decline in incidence rates in 2015 compared to the 2012 – 2014 weighted historic incidence rates. 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.

Although overall MRSA incidence rates are declining, it is important to remain vigilant due to the bacteria's changing epidemiology.[16,41] Historically, MRSA was most often seen in the hospital setting, predominately affecting those with established risk factors (i.e., hospitalized, elderly, or immunocompromised individuals). However, recent literature shows that CA MRSA has disproportionately affected groups without typical risk factors, such as children or young adults.[11,17,18] Within the MHS, the burden of MRSA infections in 2015 were CA (75%). Further analysis revealed that approximately three-fourths of these CA MRSA cases represented individuals under the age of 34, a shift from the typical age group impacted (65 and older). Overall, CA MRSA cases within the MHS follow typical patterns generally observed in the US for CA MRSA. The explanation for the shift to predominately CA MRSA infections is likely multi-faceted, but the change may be to some extent attributed to the misuse of antibiotics and the absence of infection control interventions in the community.[16,41] 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 this 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.

Seasonality is another important factor in the spread of MRSA infection and research has demonstrated that seasonal variations exist.[20,23,24] Also, regional differences in MRSA infections exist due to climatic conditions; geographic locations with warmer temperatures generally report higher rates of MRSA. Infections tend to peak during the summer and fall months in climatic regions that are temperate or tropical.[20] Within the MHS, the highest incidence rates occurred between the months of March and September and within the US South and South Atlantic regions. Generally, these elevated rates aligned with the normal variability of typical geographical and seasonal patterns.

Susceptibility patterns of MRSA infections dictate effective treatment options. In the 2015 surveillance period, susceptibility of MRSA remained stable in the MHS with over 95% susceptibility reported for minocycline, doxycycline, quinupristin/dalfopristin, rifampin, trimethoprim/sulfamethoxazole, vancomycin, linezolid, and daptomycin. These findings suggest that there have been limited changes to the resistance patterns seen among MRSA within the

MHS and that, in general, the antibiotics recommended by Johns Hopkins and IDSA for treatment of MRSA remain as viable treatment options for this population.[26,39]

MRSA infections in the MHS were less than 85% susceptible to clindamycin and erythromycin in 2015. Since 2010, MRSA susceptibility to clindamycin has displayed a statistically significant descending trend and MRSA susceptibility to erythromycin has displayed a statistically significant ascending trend. Since the early 2000s, experts have been concerned about the emergence of ICR. This type of resistance occurs when *S. aureus* organisms have the genetic potential to become resistant to clindamycin during the course of treatment, thereby causing treatment failures and enhancing the virulence of the MRSA pathogen.[29] Within the MHS in 2015, the burden of inducible resistance to clindamycin among MRSA infections was among the highest seen since surveillance began 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%).[27,29,42,43] However, analysis of ICR by branch of DOD service identified that select services, namely the Air Force and Navy, are nearing the lower end of the threshold of ICR seen among the general US population, as well as being nearly 20% above the weighted historic ICR in 2015. Continued monitoring of clindamycin susceptibility is necessary to ensure optimal disease prevention and treatment measures. Additional analyses may be warranted among the DOD services to determine if enhanced prevention measures are needed.

Clindamycin is one of the most frequently recommended antibiotics for MRSA treatment per the IDSA guidelines.[40] Studies show that susceptibility patterns differ between the inpatient and outpatient settings and sites of infection,[44] thus treatment practices for MRSA may vary slightly depending on these factors. Additional analysis of the data showed that MRSA susceptibility to clindamycin differed drastically between healthcare settings, with lower susceptibility (average 62.4%) in the inpatient setting and higher susceptibility (average 88.1%) in the outpatient setting from 2005 – 2015 (data not shown). Additionally, for both the inpatient and outpatient settings, the majority of infections were from sites indicative of SSTIs (primarily wounds or abscesses). Findings suggest that clindamycin alone may not be the most viable treatment option for MRSA SSTIs in the inpatient setting for DOD beneficiaries. It is important to monitor clindamycin prescription practices and changes in susceptibility that would affect treatment choices.

This annual report summarized MRSA incidence and prevalence in the MHS beneficiary population in 2015 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 identify any changes in burden, susceptibility, and treatment options and to guide targeted prevention efforts.

Limitations

HL7-formatted data are generated within the CHCS at fixed MTFs; therefore, this analysis does not include microbiology records from purchased care providers, shipboard facilities, battalion aid stations, or in-theater facilities.

Microbiology data are useful for identifying laboratory-confirmed infections. However, infections that were treated presumptively without laboratory confirmation do not exist in the microbiology data. Clinical practice with regards to culturing varies between providers and facilities. Examples of situations where cultures may not be performed include confirmatory tests for patients with influenza-like illness (ILI) symptoms, or patients with superficial infections who are treated presumptively. Therefore, infections identified here may be an underestimate of the actual burden of MRSA in the MHS.

The data restructuring process for the analysis of clinical characteristics and antimicrobial resistance does not capture non-standard CHCS records. These non-standard records may include those containing the results of tests performed at reference laboratories or novel organism antibiotic combinations. The use of microbiology data for analysis of antibiotic resistance is also limited by the practice of cascade reporting, in which antibiotic sensitivity results are conditionally reported in CHCS to guide antimicrobial selection and treatment decisions. Cascade reporting is practiced to varying degrees at MHS MTFs. Because the EDC uses interpreted values for resistant, intermediate, and susceptible classifications, this report may over- or under-report MRSA. Specific information on the type of testing conducted is not necessarily available and it is assumed that records identified with erythromycin and clindamycin resistance (ICR) were tested appropriately using the D-test to confirm genetic mutations specific to this type of resistance that causes clindamycin treatment failure for MRSA.

The EDC data feed does not include records on medical encounters conducted outside the MHS (e.g., purchased care in the community) and it cannot be determined if an individual truly had no healthcare contact or other risk factors for MRSA infection, or if the individual had a risk factor that was not visible in the available data. Data on other factors commonly used to define HA cases were not available (e.g., presence of an invasive device, history of dialysis or surgery, a long-term care facility stay in the 12 months preceding the culture). Therefore, there may be HA cases currently miscategorized as CA cases. Without the ability to identify these HA cases, a more accurate estimate of CA cases could not be determined. Given the relatively healthy military population, however, any misclassification bias is likely minimal.

The pharmacy databases consist of outpatient non-intravenous prescriptions (outpatient), inpatient non-intravenous prescriptions (unit dose), and intravenous prescriptions (intravenous). Though treatment compliance in the inpatient setting can be assumed, outpatient pharmacy records indicate that a patient received a prescription and subsequent compliance is unknown. Due to near real-time data feeds, analysts are able to determine if a prescription was edited or canceled; however, the time difference between these events may allow for a short period of treatment not considered in this analysis. During ongoing surveillance efforts, patient treatment status may change as edited or canceled prescription records are received.

It is possible that not all antibiotic prescriptions were dispensed in response to a MRSA infection. Antibiotics that were prescribed within the appropriate timeframe to be associated with a MRSA specimen collection date may have actually been provided for reasons other than the documented infection, such as a different infection occurring after MRSA was isolated. However, most antibiotics identified as being associated with a MRSA infection were antibiotics that are typically used to treat MRSA, so it is likely that the majority of prescriptions in this analysis were truly in response to the MRSA infection.

DMDC provides monthly snapshots of each active duty, reserve, and deployed Navy and Marine Corps service member's personnel record. Data are provided to DMDC by the service and analyses are dependent on the quality and completeness of these data. Any changes in service member status after the monthly data are extracted will not be captured until the following month. Active duty and reserve personnel records are maintained in separate databases, but activated reservists may be captured in the active duty DMDC file rather than the reserve DMDC file. Unit Identification Codes (UICs) reported for Marine Corps service members represent Reporting Unit Codes (RUCs), rather than UICs.

Personnel records for deployed service members are provided via CTS. The purpose of DMDC CTS is to capture personnel information for Central Command (CENTCOM) deployments. Additionally, deployment start and end dates are derived from the following systems and may not reflect the actual dates of deployment: Defense Finance Accounting System (DFAS), the Deployed Theater Accountability System (DTAS), the Secure Personnel Accountability System (SPA), historical PERSTEMPO files, and the Individual Personnel TEMPO Program. A country location of ZZ may represent shipboard or an unknown deployment location.

Infections may not be uniformly distributed within a spatial region; no distinctions were made with regard to the heterogeneity of incidence rates or prevalence among subunits (e.g., states, non-US countries). The choropleth maps represent an annual snapshot of infections and do not reflect the geographic movement of service members within the course of a year. Infections were georeferenced according to the locations of the MTFs where they were encountered, not according to the deployment locations or home locations of the service members. Map area does not equate to population size; parent MTF locations are displayed within US regions to convey the density of military medical facilities within each region.

POINT OF CONTACT

Navy and Marine Corps Public Health Center
Hospital Associated Infections and Patient Safety Division
EpiData Center Department **757.953.0970**
WWW.NMCPHC.MED.NAVY.MIL/
usn.hampton-roads.navmcpublhlthcenpors.list.nmpch-epi@mail.mil

References

1. Crum NF, Lee RU, Thornton SA, et al. Fifteen-year study of the changing epidemiology of methicillin-resistant *Staphylococcus aureus*. *Am J Med.* 2006;119:943-951.

2. Diekema DJ, Pfaller MA, Schnitz FJ, et al. Survey of infections due to *Staphylococcus* species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe and the Western Pacific Region for the SENTRY Antimicrobial Surveillance Program, 1997-1999. *Clin Infect Dis.* 2001;32(Suppl 2):S114-S132.

3. Kallen AJ, Mu Y, Bulens S, et al. Health care-associated invasive MRSA infections, 2005-2008. *JAMA.* 2010;304(6):641-648.

4. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA.* 2007;298(15):1763-1771.

5. Styers D, Sheehan DJ, Hogan P, Sahm DF. Laboratory-based surveillance of current antimicrobial resistance patterns and trends among *Staphylococcus aureus* strains. *Clin Infect Dis.* 2008;46:S360-S367.

6. Zeller JL, Burke AE, Glass RM. MRSA infections. *JAMA.* 2007;298(15):1826.

7. Ellis MW, Hospenthal DR, Dooley DP, et al. Natural history of community-acquired methicillin-resistant *Staphylococcus aureus* colonization and infection in soldiers. *Clin Infect Dis.* 2004;39:971-979.

8. General Information about MRSA in the Community. Centers for Disease Control and Prevention web site. http://www.cdc.gov/mrsa/community/index.html. Published September 2013. Updated September 2013. Accessed August 2015.

9. Lowy FD. *Staphylococcus aureus* infections. *N Engl J Med.* 1998;339(8):520-532.

10. Huang SS, Septimus E, Kleinman K, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med.* 2013. Downloaded from nejm.org at USUHS LRLC UNIFORMED SVCS UNIV on June 6, 2013.

11. Gordon RJ, Lowy FD. Pathogenesis of methicillin-resistant *Staphylococcus aureus* infection. *Clin Infect Dis.* 2008;46:S350-S359.

12. Multi-drug resistant organism & *Clostridium difficile*-associated disease (MDRO/CDAD) module. Centers for Disease Control and Prevention web site. http://www.cdc.gov/nhsn/PDFs/pscManual/12pscMDRO_CDADcurrent.pdf. Published January 2015. Modified April 2015. Accessed April 2015.

13. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections. Centers for Disease Control and Prevention web site.

http://www.cdc.gov/hai/pdfs/toolkits/MRSA_toolkit_white_020910_v2.pdf. Accessed February 2017.

14. Centers for Disease Control and Prevention. 2014. Active bacterial core surveillance report, Emerging Infections Program Network, methicillin-resistant *Staphylococcus aureus*, 2014. Centers for Disease Control and Prevention web site. http://www.cdc.gov/abcs/reports-findings/survreports/mrsa14.html. Updated 06 April 2016. Accessed February 2017.

15. Active bacterial core surveillance report, Emerging Infections Program Network, methicillin-resistant *Staphylococcus aureus*, 2005. Centers for Disease Control and Prevention web site. http://www.cdc.gov/abcs/reports-findings/survreports/mrsa05.html. Updated 30 January 2012. Accessed January 2013.

16. Boucher HW, Corey GR. Epidemiology of methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis.* 2008;46:S344-S349.

17. General information about MRSA in the community. Centers for Disease Control and Prevention web site. http://www.cdc.gov/mrsa/community/index.html#q2. Updated 10 September 2013. Accessed September 2014.

18. Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA.* 2003;290(22):2976-84.

19. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med.* 2006;355(7):666-674.

20. Mermel LA, Machan JT, Parenteau S. Seasonality of MRSA infections. *PLoS One*. 2011;6(3):e17925.

21. Van De Griend P, Herwaldt LA, Alvis B, et al. Community-associated methicillin-resistant *Staphylococcus aureus*, Iowa, USA. *Emerg Infect Dis.* 2009;15:1582-1589.

22. Szczesiul JM, Shermock KM, Murtaza UI, Siberry GK. No decrease in clindamycin susceptibility despite increased use of clindamycin for pediatric community-associated methicillin-resistant *Staphylococcus aureus* skin infections. *Pediatr Infect Dis J.* 2007;26:852-854.

23. Loffeld A, Davies P, Lewist A, Moss C. Seasonal occurrence of impetigo: a retrospective 8-year review (1996-2003). *Clin Exp Dermatol*. 2005;30:512-514.

24. Perencevich EN, McGregor JC, Shardell M, et al. Summer peaks in the incidences of gram-negative bacterial infection – among hospitalized patients. *Infect Control Hosp Epidemiol*. 2008;29:1124 -1131.

25. New clinical guidelines for MRSA treatment. Centers for Disease Control and Prevention web site. http://blogs.cdc.gov/safehealthcare/new-clinical-guidelines-for-mrsa-treatment/. Posted 18 March 2011. Updated 18 November 2016. Accessed February 2017.

26. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infectious in adults and children. *Clin Infect Dis.* 2011;52:1-38.

27. Lewis JS II, Jorgensen JH. Inducible clindamycin resistance in Staphylococci: should clinicians and microbiologists be concerned? *Clin Infect Dis.* 2005;40:280-5.

28. Mallick SK, Basak S, Bose S. Inducible clindamycin resistance in *Staphylococcus aureus*-a therapeutic challenge. *Journal of Clinical and Diagnostic Research.* 2009;3:1513-1518.

29. Patel M, Waites KB, Moser SA, et al. Prevalence of inducible clindamycin resistance among community- and hospital-associated *Staphylococcus aureus* isolates. *J Clin Microbiol.* 2006;44(7):2481.

30. National Committee for Clinical Laboratory Standards (NCCLS). *Performance Standards for Antimicrobial Susceptibility Testing; Fourteenth Informational Supplement*. CNNLS document M100-S14. Wayne, PA: NCCLS; 2004.

31. Appelbaum PC. Microbiology of antibiotic resistance in *Staphylococcus aureus*. *Clin Infect Dis.* 2007;45(Supplement 3):S165-S170.

32. Zinderman CE, Conner B, Malakooti MA, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* among military recruits. *Emerg Infect Dis.* 2004;10(5):941-944.

33. Leamer NK, Clemmons NS, Jordan NN, Pacha LA. Update: Community-acquired methicillin-resistant *Staphylococcus aureus* skin and soft tissue infection surveillance among active duty military personnel at Fort Benning GA, 2008-2010. *Mil Med.* 2013;178(8):914-20.

34. Landrum MI, Neumann C, Cook C, et al. Epidemiology of *Staphylococcus aureus* blood and skin and soft tissue infections in the US military health system, 2005-2010. *JAMA.* 2012;308(1):50-59.

35. Ellis MW, Griffith ME, Dooley DP, et al. Targeted intranasal mupirocin to prevent colonization and infection by community associated methicillin resistant *Staphylococcus aureus* strains in soldiers: a cluster randomized controlled trial. *Antimicrob Agents Chemother.* 2007;51(10):3591-3598.

36. Whitman TJ, Herlihy RK, Schlett CD, et al. Chlorhexidine-impregnated cloths to prevent skin and soft tissue infection in Marine recruits: a cluster-randomized, double-blind, controlled effectiveness trial. *Infect Control Hosp Epidemiol.* 2010;31(12):1207-1215.

37. O'Hara FP, Amrine-Madsen H, Mera RM, et al. Molecular characterization of *Staphylococcus aureus* in the United States 2004-2008 reveals the rapid expansion of USA300 among inpatients and outpatients. *Microb Drug Resist.* 2012;18(6):555-561.

38. Cohen A, Calfee D, Fridkin SK, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infect Control Hosp Epidemiol*. 2008;29(10):901-913.

39. Spacek LA. *Staphylococcus aureus*. Johns Hopkins Antibiotic (ABX) Guide. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540214/all/Staphylococcus_species. Updated 28 November 2014. Accessed 31 January 2017.

40. Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth Informational Supplement.* CLSI document M100-S25. Wayne, PA: CLSI; 2015.

41. Boyce JM. Are the epidemiology and microbiology of methicillin-resistant *Staphylococcus aureus* changing? *JAMA.* 1998;279(8):623-624.

42. O'Sullivan MVN, Yongwei C, Fanrong K, et al. Influence of disk separation distance on accuracy of the disk approximation test for detection of inducible clindamycin resistance in *Staphylococcus* spp. *J Clin Microbiol.* 2006;44(1):4072.

43. Woods CR. Macrolide-inducible resistance to clindamycin and the D-test. *Pediatr Infect Dis J.* 2009;28(12):1115-1118.

44. Huang H, Flynn NM, King JH, et al. Comparisons of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and hospital-associated MRSA infections in Sacramento, California. *J Clin Microbiol.* 2006;44(7):2423-2427.

Appendix A: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
CA	community-associated
CDC	Centers for Disease Control and Prevention
CENTCOM	Central Command
CHCS	Composite Health Care System
CLSI	Clinical and Laboratory Standards Institute
CO	community-onset
CONUS	continental United States
CTS	Contingency Tracking System
CY	calendar year
DFAS	Defense Finance Accounting System
DMDC	Defense Manpower Data Center
DOD	Department of Defense
DON	Department of the Navy
DTAS	Deployed Theater Accountability System
EDC	EpiData Center Department
HA	healthcare-associated
HL7	Health Level 7 format
HO	hospital-onset
ICR	inducible clindamycin resistance
ICU	intensive care unit
IDSA	Infectious Disease Society of America
ILI	influenza-like illness
IV	intravenous
M2	Military Health System (MHS) Management Analysis and Reporting Tool
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MEPRS	Medical Expense and Performance Reporting System
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
OP	outpatient oral
RUC	reporting unit code
SHEA	Society for Healthcare Epidemiology of America
SIDR	Standard Inpatient Data Record
SPA	Secure Personnel Accountability System
SSTI	skin and soft tissue infection
UD	unit dose
UIC	unit identification code
US	United States
UTI	urinary tract infection
VRSA	vancomycin-resistant *Staphylococcus aureus*