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Multidrug-Resistant Gram-Negative Bacterial and Carbapenem-Resistant Enterobacteriaceae Infections in the Department of the Navy: Annual Report 2013

NMCPHC-EDC-TR-139-2015

By Paul Meddaugh and Uzo Chukwuma
EpiData Center Department
March 2015

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
19-03-2015	Annual Report	1 January 2005 - 31 December 2013

4. TITLE AND SUBTITLE
Multidrug-Resistant Gram-Negative Bacterial and Carbapenem-Resistant Enterobacteriaceae Infections in the Department of the Navy: Annual Report 2013

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Paul Meddaugh, Uzo Chukwuma

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

8. PERFORMING ORGANIZATION REPORT NUMBER
NMCPHC-EDC-TR-139-2015

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

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

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
NMCPHC-EDC-TR-139-2015

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release. Distribution is not limited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Gram-negative bacterial infections are a growing global public health and clinical concern. Additionally, epidemics of multidrug-resistant (MDR) gram-negative bacteria have occurred worldwide in the last couple decades, including regions where United States (US) military forces are regularly deployed. In 2013, the incidence of MDR Escherichia coli, Enterobacter, Klebsiella, and Pseudomonas aeruginosa in Department of Defense (DOD) beneficiaries seeking care in the Military Health System (MHS) increased from 2012. MDR E. coli was the organism most frequently identified with an incidence 37-40 times higher than the next most frequent organism. A pronounced gender disparity was noted for all organisms except MDR P. aeruginosa. Overall, DOD female beneficiaries were impacted much more than their male counterparts. Furthermore, MDR E. coli, MDR Enterobacter, and MDR Klebsiella cases commonly manifested as urinary tract infections (UTIs), which is consistent with historic observations. In 2013, cases of MDR P. aeruginosa more commonly manifested as respiratory infections, which is also consistent with historic observations. MDR P. aeruginosa did not display any consistent high susceptibilities at the population level.

15. SUBJECT TERMS
Health Level 7 (HL7), Microbiology, Surveillance, Gram-negative bacteria, Multidrug-Resistant (MDR), Extensively Drug-Resistar

16. SECURITY CLASSIFICATION OF: U			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** Uzo Chukwuma
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**	UU	33	**19b. TELEPHONE NUMBER** *(include area code)*
U	U	U			757-953-0706

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

Abstract

Gram-negative bacterial infections are a growing global public health and clinical concern. Additionally, epidemics of multidrug-resistant (MDR) gram-negative bacteria have occurred worldwide in the last couple decades, including regions where United States (US) military forces are regularly deployed. In 2013, the incidence of MDR *Escherichia coli*, *Enterobacter*, *Klebsiella*, and *Pseudomonas aeruginosa* in Department of Defense (DOD) beneficiaries seeking care in the Military Health System (MHS) increased from 2012. MDR *E. coli* was the organism most frequently identified with an incidence 37-40 times higher than the next most frequent organism. A pronounced gender disparity was noted for all organisms except MDR *P. aeruginosa*. Overall, DOD female beneficiaries were impacted much more than their male counterparts. Furthermore, MDR *E. coli*, MDR *Enterobacter*, and MDR *Klebsiella* cases commonly manifested as urinary tract infections (UTIs), which is consistent with historic observations. In 2013, cases of MDR *P. aeruginosa* more commonly manifested as respiratory infections, which is also consistent with historic observations. MDR *P. aeruginosa* did not display any consistent high susceptibilities at the population level.

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Executive Summary

The EpiData Center Department (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) conducts routine surveillance of clinically significant organisms within the Department of the Navy (DON) and the Department of Defense (DOD). This report provides a summary of the incidence and prevalence of selected multidrug-resistant (MDR) gram-negative bacteria (*Escherichia coli*, *Enterobacter* species, *Klebsiella* species, and *Pseudomonas aeruginosa*) and carbapenem-resistant Enterobacteriaceae (CRE) *E. coli* and *Klebsiella* prevalence in calendar year (CY) 2013 among all DOD beneficiaries, active duty DON service members, DON service members deployed in support of United States (US) Central Command (CENTCOM) missions, and DON recruits. This report includes details on case demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns.

The linking of several data sources in this analysis allows for the assessment of a variety of unique descriptive and clinical factors related to MDR gram-negative bacteria within multiple populations. Health Level 7 (HL7) formatted microbiology data were used to identify specific MDR gram-negative and CRE organisms. These isolates were then matched to three databases. Microbiology records were matched to HL7 formatted pharmacy data to assess prescription practices associated with MDR gram-negative bacterial cases. Cases were also matched to the Standard Inpatient Data Record (SIDR) database to determine exposure associations within the Military Health System (MHS). Microbiology records were also matched to the Defense Manpower Data Center (DMDC) active duty roster to determine the burden of MDR gram-negative bacteria among active duty DON service members and recruits. The linking of these various data sources allows for the broadest view of MDR gram-negative bacteria among DOD beneficiaries seeking care within the MHS.

The findings of this analysis of MDR *E. coli*, MDR *Enterobacter*, MDR *Klebsiella*, and MDR *P. aeruginosa* within the MHS in CY 2013 follow previously observed trends of incidence and prevalence in the DON and DOD. The incidence of all four organisms increased from 2012 to 2013, and the increases for MDR *E. coli* and MDR *Enterobacter* were above the baselines established for those organisms. A marked gender disparity and high prevalence of urinary tract infections (UTIs) appeared for all organisms and populations except MDR *P. aeruginosa*. MDR *P. aeruginosa* was more commonly identified as a respiratory pathogen. Both of these observations are consistent with historical observations from 2005 to 2012. MDR *P. aeruginosa* did not display high antibiotic susceptibilities at the population level, which is also consistent with historic observations. At the individual level, however, isolates regularly had at least one antibiotic to which they displayed adequate susceptibility. Continued monitoring of the disease dynamics will help military healthcare providers predict the evolving resistance and burden of MDR gram-negative bacterial infections in the MHS and identify effective treatment, prevention, and control programs.

Introduction

Gram-negative bacterial infections are a growing problem in both the general global population and among United States (US) military service members. In most countries around the world, the medical community has observed recent epidemics of gram-negative bacterial infections that are resistant to many types of antimicrobial agents.[1] In the US, the most clinically significant organisms within this group of bacteria are *P. aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, *Berkholderia cepacia*, *E. coli*, *Klebsiella*, *Enterobacter*, *Salmonella*, and *Shigella* species.[2-4] In 2003, the prevalence of antibiotic-resistant gram-negative bacteria in the US increased by 20% from the previous four years, while the incidence remained relatively stable.[5] Through a variety of different resistance mechanisms, some gram-negative bacteria have displayed resistance to all available antibiotics.[2,3] The rising prevalence of multidrug-resistance among gram-negative bacteria in community and hospital settings is cause for concern.

Bacteria from the family Enterobacteriaceae (e.g., *Salmonella* species, *E. coli*, *Klebsiella* species, *Shigella* species, and *Enterobacter* species) are the most common pathogenic bacteria in humans and cause a variety of diseases including cystitis, pneumonia, and bacteremia.[6] In recent decades, carbapenems have been used with increasing frequency as the only effective treatment against gram-negative organisms.[6] In the early 2000s, resistance to carbapenems emerged among Enterobacteriaceae. CRE are unique among multidrug-resistant organisms (MDROs) because there are no reliable treatments to combat them, resulting in wide-ranging global public health implications. Further, bacterial genes conferring carbapenem-resistance typically confer other resistance factors and enhanced virulence factors as well, resulting in a wide range of resistance patterns including extensively drug-resistant (XDR) organisms, which are described below.[6]

The term resistance is difficult to define among gram-negative bacteria as no international consensus or standard definitions currently exist.[7] The terms multidrug and pandrug resistance (MDR and PDR, respectively) have been used to describe infections with a variety of different genotypic and phenotypic characteristics.[1] Within the last decade, standard categories of resistance were used with some consistency, though standard definitions are still lacking.[8] In 2011, a panel of international experts convened in an attempt to develop definitions for resistant organisms. Based on this panel of experts, MDR is defined as any antibiotic non-susceptible (resistant or intermediately susceptible) to at least one antibiotic in at least three different antimicrobial categories deemed pertinent to a given species. Extensively drug-resistant isolates are non-susceptible to at least one antibiotic in all but two or fewer antimicrobial categories deemed pertinent to a given species. PDR isolates are non-susceptible to all antimicrobial agents in all antimicrobial categories deemed pertinent for a given species.[9]

Throughout Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF), a large number of resistant gram-negative bacteria have been identified in US combat support hospitals. The USNS *Comfort* (T-AH 20) also reported infections at the beginning of OIF. In the early days of the conflicts, these infections were observed primarily in non-US patients.[10] Between

2002 and 2005, however, antibiotic-resistance in *P. aeruginosa* and *K. pneumoniae* among service members injured in OIF/OEF accounted for the majority of infections caused by those organisms, and antibiotic-resistance was seen in nearly all agents tested at one military medical treatment facility (MTF).[10,11] Elsewhere in the Middle East, studies performed in Egypt during several years of Operation Bright Star (OBS) found that MDR *E. coli* was extremely prevalent in the region and a frequent cause of travelers' diarrhea.[12]

In 2001, Jones et al. reported that nosocomial infections accounted for more than 77,000 deaths per year in the US, costing $5-$10 billion annually. While gram-positive organisms have typically been the most frequent cause of nosocomial infections and continue to be a concern, gram-negative organisms have been emerging with resistance at troubling rates.[13] In intensive care units, gram-negative bacteria have been identified, to varying degrees, as a frequent cause of the four most common types of healthcare-associated infections: nosocomial pneumonia, urinary tract infections (UTIs), surgical site infections (SSIs), and blood stream infections (BSIs).[14] Most antibiotic-resistant healthcare-associated infections (HAIs) are preventable. Endemic, rather than epidemic, problems represent the majority of HAIs. Therefore, routine surveillance is a necessary infection control tool to aid in the prevention of HAIs and containment of MDR pathogens. The Society for Healthcare Epidemiology of America and the Hospital Infection Control Practices Advisory Committee (SHEA/HICPAC) have developed several metrics recommended for the surveillance of HAIs. Exposure burden is an important metric for detecting importation of MDROs into the healthcare facility that potentially serves as a reservoir for HAIs.[15] metrics can be used to assess the overall organism-specific and device- or procedure-associated incidence. Both sets of metrics can be used to track changes over time and direct prevention efforts.

This report is an annual update of MDR gram-negative bacterial incidence and burden among DON and DOD beneficiaries. This update compares the 2013 incidence to historical trends established from 2005 – 2012 in the DON and DOD as a reference for assessing the current year's burden.

Methods

Study Design, Setting, and Population

This annual report is a retrospective surveillance summary for CY 2013, assessing the burden and trends of MDR gram-negative bacteria throughout the DON and DOD. The EDC assessed all outpatient and inpatient isolates as determined by the Medical Expense and Performance Reporting System (MEPRS) codes in microbiology data. For DON active duty service members and recruits, and DOD beneficiaries who sought care within the MHS, a MEPRS code beginning with 'A' indicated isolate collection in the inpatient setting. All other MEPRS codes were considered outpatient isolates.

Antibiotic susceptibility results from the microbiology record were used to establish the level of antibiotic resistance among cases. Isolates non-susceptible (resistant or intermediately susceptible) to at least one antibiotic in at least three different classes were considered MDR. The antibiotic classes involved in this classification include select penicillins, cephalosporins, fluoroquinolones, aminoglycosides, carbapenems, folate pathway inhibitors, glycylcyclines, monobactams, phenicols, phosphoric acids, penicillins and β-lactamase inhibitor combinations, polymyxins, and tetracyclines. Organisms non-susceptible to at least one antibiotic in all but one or two classes were considered XDR. Finally, PDR organisms were organisms that were non-susceptible to all antibiotics in all antibiotic classes identified.[9] Carbapenem resistance, defined as antibiotic resistance to at least one carbapenem and non-susceptibility to all third generation cephalosporins tested, was also evaluated.[16] Only *E. coli* and *Klebsiella* species were monitored for carbapenem resistance. For the remainder of this report, unless otherwise stated, resistant and resistance are defined as gram-negative bacterium displaying any level of antibiotic resistance, whether it be MDR, XDR, PDR, or CRE. See the Appendix (Tables A-1 and A-2) for resistance definitions and a list of antibiotics included in each antimicrobial category.

The first MDR gram-negative bacterial or CRE isolate per person, per organism, per month was kept as a unique case for analysis to estimate annual prevalence of individual MDR gram-negative bacterial or CRE species. The first MDR gram-negative bacterium per person, per organism, per year was used to identify the incidence of MDR gram-negative bacteria only and was used to calculate annual incidence rates. MDR and CRE isolates were considered separately, therefore isolates could have been counted under both classifications. Only the following organisms were monitored as part of this report: *E. coli*, *Enterobacter* species, *Klebsiella* species, and *P. aeruginosa*.

Data Collection, Processing, and Analysis

Health Level 7 (HL7) formatted microbiology data that originated from the Composite Health Care System (CHCS) at fixed MTFs were used to identify MDR gram-negative bacteria cases. The data contain information for DOD beneficiaries who sought care (both inpatient and outpatient) at fixed MTFs. Surveillance cultures, defined as specimens isolated from nares, axilla, groin, and rectal swab samples, were excluded from consideration in this analysis, as surveillance cultures are typically indicative of colonization and not true infection. The EDC utilized the World Health Organization's (WHO) BacLink and WHONET software applications to organize antibiotic susceptibilities within microbiology records. Microbiology data were used to identify beneficiary service (Air Force, Army, Marine Corps, or Navy), setting of specimen collection (inpatient or outpatient), gender, and beneficiary status (active duty, family member, retired, or other).

To determine active duty status for DON cases, the EDC matched the microbiology cases to the DMDC active duty roster for CY 2013 using a unique identifier. DON CENTCOM-related cases were identified where the microbiology specimen collection dates occurred between the start and end dates of deployment in the DMDC Contingency Tracking System (CTS) database.

DON recruits were also identified using the DMDC active duty roster when the start of federal service date occurred during CY 2013. This analysis estimates the end of recruit training for each service member by calculating the date for the end of the standard training period from the start of federal service date (9 weeks for Navy recruits and 13 weeks for Marine recruits). If a microbiology record was identified for a recruit between the start date of federal service and seven days after the estimated end date of basic training, then the service member was considered a recruit case.

To evaluate laboratory-confirmed MDR gram-negative bacteria cases for recent healthcare exposure, SIDR records were matched to microbiology records if the specimen collection date was linked to the hospital admission date in SIDR. Hospital-onset (HO) cases were defined as MDR gram-negative organisms identified after the third day of the current admission. Healthcare-associated (HA) cases were defined as patients who had a current admission with a gram-negative bacteria and a prior hospitalization within the previous year. Community-onset (CO) cases were defined as those MDR gram-negative cases collected within the first three days of the current admission, indicating the patient acquired the organism within the community and likely arrived at the treating facility with it.[14] These classifications were applied only to cases identified in the inpatient setting.

Established metrics were used to assess HAI exposure and infection burden for the MDR gram-negative organisms at DOD MTFs. HAI exposure burden metrics evaluate the admission and overall prevalence of MDROs within the healthcare facility. Admission prevalence measures the magnitude of importation of any of the four MDROs of interest into fixed MTFs, while overall prevalence measures the magnitude of a patient's exposure in the healthcare setting to other patients with the specific MDR organism. Though excluded from the general analysis, surveillance cultures were included in the overall and admission prevalence analysis, as they contribute to the colonization pressure and exposure burden for those not already colonized or infected. HAI infection burden metrics include HO bacteremia, HO UTIs, SSIs, central line-associated bloodstream infections (CLABSIs), and ventilator-associated pneumonia (VAP). All five metrics measure the burden of infections associated with and/or are as a direct result of hospitalization. Infection burden metrics include only the first HO MDR gram-negative isolate per patient per admission. Device- and procedure-associated metrics (CLABSI, VAP, SSI) require the use of International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes to identify the use of a device or performance of a procedure. These codes can be found in the SIDR. Table 1 presents the classification for each metric.

Table 0-1. Classification of Healthcare-Associated Infection Metrics[14]

	Metric	Definition
Exposure Burden	Overall Prevalence	Any record where an MDR gram-negative bacterium[a] was isolated from specimen collected at least three days after admission.
	Admission Prevalence	Any record where an MDR gram-negative bacterium was isolated from specimen collected within the first three days of admission.
Infection Burden	HO Bacteremia	Any record with body site or specimen source of blood that was collected at least three days after admission.
	HO UTI	Any record with body site or specimen source of urine that was collected at least three days after admission.
	SSI	Any record following NHSN operative procedure groupings;[17] The procedure is within admission and discharge dates; AND Infection occurs within 30 days of the procedure.
	CLABSI	Any record with body site or specimen source of blood; Records with ICD-9-CM procedure codes: 38.91, 38.92, 38.93, or 38.97; AND Specimen was collected at least three days after admission.
	VAP	Any record with body site or specimen source of respiratory sample; Records with ICD-9-CM procedure codes: 96.7, 96.04, 96.71, or 96.72; AND Specimen was collected at least three days after admission.

[a]*Escherichia coli*, *Enterobacter* species, *Klebsiella* species, and *Pseudomonas aeruginosa*.
[15]Cohen A, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC position paper. *Infection Control and Hospital Epidemiology*. 2008;29(10):901-913.
[17]Centers for Disease Control and Prevention. Surgical site infections (SSI) event. CDC/NHSN Protocol and Instructions. http://www.cdc.gov/nhsn/PDFs/pscManual/9pscSSIcurrent.pdf?agree=yes&next=Accept. Published January 2013. Accessed January 2013.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 04 February 2014.

Demographic and clinical information for the specimen were described for each case using the information within the HL7 formatted microbiology record. Specimen sources of MDR gram-negative bacterial cases were categorized based on the specimen source and body site indicated in the microbiology record. Urinary tract and urine samples were classified as UTIs, blood and blood vessel samples were classified as blood stream infections (BSIs), and respiratory discharge and respiratory tract samples were grouped as respiratory infections; all remaining specimen sources and body sites were grouped as other.

The EDC created an antibiogram for each MDR gram-negative species identified in 2013 using antibiotic susceptibility testing results within the HL7 formatted microbiology record according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, which include a single isolate per person per year.[18] The EDC selected antibiotics for the antibiogram based on CLSI guidelines and frequency of testing in the MHS. Antibiotics were only reported if for each year of analysis the antibiotic was tested ≥30 times against the same MDR gram-negative organism.

Historical antibiotic susceptibility data were included in the antibiogram for each organism from 2005-2013. Trends in susceptibility of relevant antibiotics were calculated using the Cochrane-

Armitage trend test for linearity. Significance in antibiotic susceptibilities was determined at *P* = .05. Any antibiotic showing a *P*-value of less than or equal to .05 from 2005-2013 was considered to have significant changes in susceptibility.

HL7 formatted pharmacy records were used to identify antibiotic prescriptions associated with MDR gram-negative cases. HL7 formatted pharmacy data consist of three distinct databases depending on the patient setting where a provider prescribed the antibiotic and the route by which the antibiotic was to be administered: outpatient oral antibiotics (OP), inpatient oral antibiotics (unit dose – UD), or intravenous (IV) antibiotics. For this analysis, prescriptions associated with an MDR gram-negative bacterium were identified as those with a pharmacy transaction date up to seven days following the microbiology specimen collection date.

To provide a spatial context to MDR gram-negative bacterial cases in the DON and DOD in 2013, cases were identified by TRICARE service region. This was accomplished by using the Defense Medical Information System (DMIS) identification (ID) number of the facility requesting the microbiology test. Each facility is assigned a unique DMIS ID which is grouped by region. Using the requesting facility's DMIS ID allows for identification of the case as close to the point of exposure as possible using available electronic records.

Annual incidence and prevalence rates were calculated using MHS Data Mart (M2) beneficiary counts to obtain the number of TRICARE eligible beneficiaries by demographic category. Beneficiary counts were retrieved on a monthly basis for the monthly rate denominators. To provide context for 2013 annual incidence rates, the EDC calculated historic mean incidence rates from 2005-2012 for eligible DOD beneficiaries and DON active duty service members.

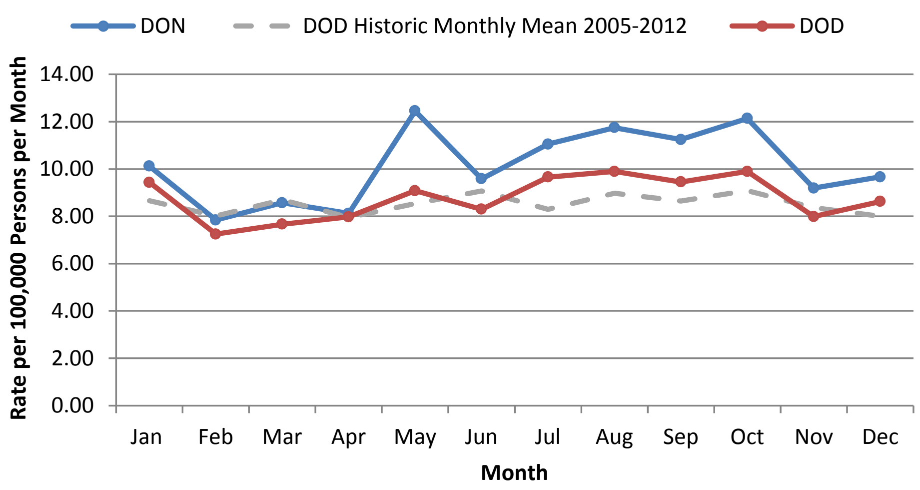
Results

MDR *E. coli*

DON/DOD

MDR *E. coli* incidence rates in the DON and DOD in 2013 generally followed a similar pattern to the mean rate established for the DOD from 2005-2012, though differed in magnitude. The DON however did exhibit rates between 5.5% and 47.1% higher than the historic mean from May to December (Figure 1).

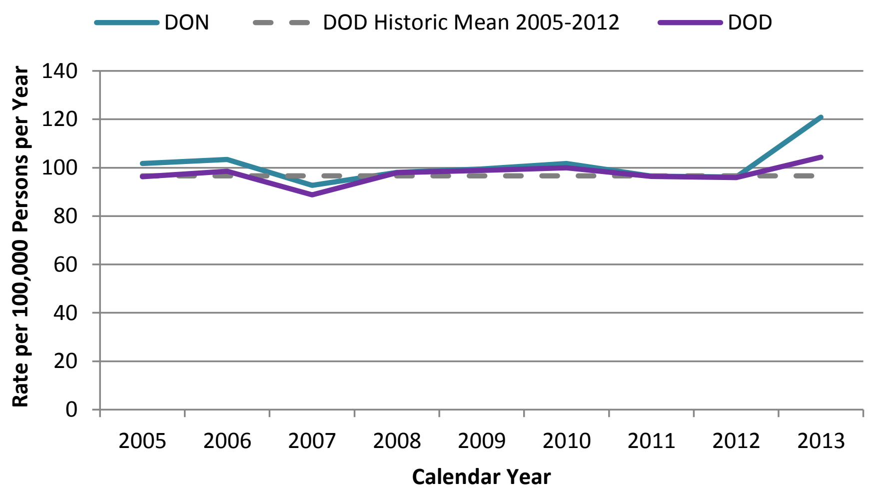
Figure 1. Multidrug-Resistant *Escherichia coli* Incidence Rate in DON and DOD Beneficiaries by Month, 2013



Mean rate calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 13 August 2014.

Figure 2 displays the DON and DOD annual incidence trends from 2005-2013. The overall incidence of MDR *E. coli* cases from 2005-2013 did not vary significantly across the years and showed a stable trend for both the DON and DOD. The 2013 annual incidence rates in the DON and DOD (120.9 and 104.4 per 100,000 persons per year, respectively) were above the 2012 annual incidence rate (96.2 and 95.9 per 100,000 persons per year, respectively) and the DOD historic mean (96.6 per 100,000 persons per year).

Figure 2. Multidrug-Resistant *Escherichia coli* Annual Incidence Rates among DON and DOD Beneficiaries with Annual Historic Mean, 2005-2013



Mean rate calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 13 August 2014.

Table 2 presents the demographics and prevalence rates for DON and DOD MDR *E. coli* cases. The EDC identified 3,419 MDR *E. coli* cases among 2,859 DON beneficiaries and 9,891 cases among 8,666 DOD beneficiaries. DON females, consistent with DOD, had a disproportionate burden, about 8 times that of male beneficiaries. Other demographic categories most impacted in both the DON and DOD were beneficiaries between the ages of 25 and 34 years old, Marine Corps beneficiaries, sponsor family members, and the OCONUS TRICARE service region.

Table 0-1. Demographics of MDR *Escherichia coli* Burden in the DON and DOD, CY 2013

DON			DOD		
N = 3,419	Count	Rate[a]	N = 9,891	Count	Rate[a]
Gender			**Gender**		
Female	3,065	302.4	Female	8,815	192.8
Male	354	33.8	Male	1,076	22.7
Age Group (in years)			**Age Group (in years)**		
0-17	317	55.6	0-17	912	66.4
18-24	765	176.3	18-24	1,893	158.5
25-34	715	199.9	25-34	2,120	179.1
35-44	384	150.6	35-44	1,205	147.8
45-64	683	108.9	45-64	2,005	95.9
65+	555	96.3	65+	1,756	84.9
Sponsor Service			**Sponsor Service**		
			Air Force	2,086	80.2
			Army	4,386	112.4
Marine Corps	930	123.7	Marine Corps	930	123.7
Navy	2,489	120.8	Navy	2,489	120.8
Beneficiary Type			**Beneficiary Type**		
Active Duty	690	132.6	Active Duty	1,797	128.3
Family Member	2,444	158.5	Family Member	7,090	143.6
Retired	241	38.6	Retired	798	38.3
Other	44	35.0	Other	206	23.0
TRICARE Region			**TRICARE Region**		
Alaska	1	*NR**	Alaska	88	108.1
North	987	132.0	North	2,530	88.6
OCONUS	210	312.6	OCONUS	808	217.0
South	605	110.9	South	2,748	90.3
West	1,567	235.3	West	3,358	120.8
Unknown[b]	49		Unknown[b]	359	

*Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
[a]Rates per 100,000 eligible beneficiaries per year.
[b]TRICARE service region cannot be identified from the microbiology record.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 13 August 2014.

Table 3 displays the clinical characteristics of MDR *E. coli* cases in the DON and DOD. Most cases were identified in the outpatient setting and were overwhelmingly from urinary tract samples. In the DON, 443 of the 2,859 beneficiaries had at least 2 MDR *E. coli* cases; likewise in the DOD, 966 of the 8,666 DOD beneficiaries had at least 2 cases (data not shown). No CRE *E. coli* cases were identified in the DON and four CREs were identified in the DOD, accounting for less than one percent of the overall burden. No XDR or PDR *E. coli* cases were identified in the DON or DOD in 2013.

In 2013, 131 DON and 409 DOD inpatient cases of MDR *E. coli* were identified. The majority of these cases in both the DON and DOD (58.8% and 67.2%, respectively) were CO. This indicates that organism acquisition was most frequently associated with exposures outside of the MHS.

Table 0-2. Clinical Description of MDR *Escherichia coli* and Carbapenem-Resistant Enterobacteriaceae Burden in the DON and DOD, CY 2013

DON			DOD		
N = 3,419	Count	Percent	N = 9,891	Count	Percent
Encounter Type			**Encounter Type**		
Inpatient	131	3.8	Inpatient	409	4.2
Outpatient	3,288	96.2	Outpatient	9,482	96.8
Healthcare Association[a]			**Healthcare Association**[a]		
Hospital-onset (HO)	9	6.9	Hospital-onset (HO)	29	7.1
Healthcare-associated (HA)	45	34.4	Healthcare-associated (HA)	105	25.7
Community-onset (CO)	77	58.8	Community-onset (CO)	275	67.2
Infection Type			**Infection Type**		
Urinary Tract	3,271	95.7	Urinary Tract	9,431	96.3
Blood Stream	26	0.8	Blood Stream	88	0.9
Respiratory	19	0.6	Respiratory	47	0.5
Wound	15	0.4	Wound	91	0.9
Other	88	2.6	Other	234	2.4
Carbapenem Resistant Enterobacteriaceae[b]			**Carbapenem Resistant Enterobacteriaceae**[b]		
Yes	0	--	Yes	4	0.04

[a]Healthcare association evaluated for inpatient cases.
[b]All CRE isolates also identified as MDR.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 13 August 2014.

In the DOD in 2013, MDR *E. coli* was most susceptible to carbapenems (meropenem [99.9%] and imipenem [99.7%]), followed by amikacin (99.5%) (Table 4). MDR *E. coli* was least susceptible to ampicillin (0.9%), followed by ampicillin/sulbactam (6.8%) and piperacillin (8.9%). MDR *E. coli* has shown statistically significant changes in susceptibility over time for many commonly tested antibiotics. The only antibiotics not showing any significant linear trend are cefazolin, meropenem, and trimethoprim/sulfamethoxazole. With only 3 of 27 antibiotics showing a non-linear trend, it is clear that the majority of antibiotics relevant to *E. coli* have undergone significant changes over time from 2005-2013. Of the antibiotics displaying a stable trend, only meropenem was highly effective.

Table 0-3. Cumulative Annual Antibiogram of Percent Susceptibility for MDR *Escherichia coli* in the DOD with Trend Over Time, 2005-2013

	Year									
Antibiotic	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	***P*-value[b]**
Amikacin	99.0%	99.0%	98.8%	99.3%	99.5%	99.2%	99.4%	99.4%	99.5%	<.001
Amoxacillin/Clavulanic Acid	51.6%	50.2%	52.9%	49.4%	48.8%	51.2%	54.7%	54.8%	52.9%	<.001
Ampicillin	1.5%	1.2%	1.0%	1.0%	0.9%	2.4%	1.6%	1.1%	0.9%	<.001
Ampicillin/Sulbactam	6.7%	6.6%	7.0%	6.3%	8.0%	8.4%	8.9%	9.0%	6.8%	<.001
Aztreonam	88.1%	92.4%	93.3%	92.7%	91.3%	83.4%	84.2%	84.8%	84.7%	<.001
Cefazolin	63.5%	63.4%	63.4%	64.1%	62.9%	61.0%	61.1%	64.7%	62.6%	.08
Cefepime	96.4%	96.0%	94.9%	94.3%	93.5%	92.3%	90.6%	91.5%	90.7%	<.001
Cefotaxime	94.9%	93.9%	93.8%	93.5%	93.4%	93.6%	92.6%	93.1%	92.7%	.003
Cefotetan	97.5%	97.0%	97.6%	98.2%	97.2%	95.2%	95.4%	97.3%	95.2%	.005
Cefoxitin	89.9%	85.9%	86.8%	82.7%	80.5%	80.6%	83.2%	77.8%	80.1%	<.001
Ceftazidime	93.0%	94.3%	93.3%	92.9%	92.6%	91.2%	90.5%	90.1%	89.2%	<.001
Ceftriaxone	94.6%	94.2%	93.4%	91.0%	90.5%	87.0%	87.3%	88.1%	86.9%	<.001
Cefuroxime	83.4%	82.3%	81.4%	84.1%	83.5%	81.7%	81.0%	81.8%	79.6%	<.001
Cephalothin	23.9%	19.9%	97.6%	21.0%	16.7%	22.4%	20.0%	18.0%	14.3%	<.001
Ciprofloxacin	75.8%	72.8%	68.4%	66.0%	64.6%	63.4%	62.7%	63.7%	62.6%	<.001
Gentamicin	80.0%	78.5%	76.6%	74.9%	73.4%	73.4%	73.8%	73.7%	74.4%	<.001
Imipenem	99.5%	99.4%	99.5%	99.6%	99.5%	99.3%	99.6%	99.7%	99.7%	.04
Levofloxacin	77.0%	73.7%	69.6%	68.5%	67.2%	67.1%	66.9%	67.1%	63.7%	<.001
Mereopenem	100.0%	99.6%	99.8%	99.6%	99.6%	99.5%	99.7%	99.8%	99.9%	.66
Nitrofurantoin	95.8%	95.0%	95.0%	94.7%	94.6%	93.9%	94.0%	92.4%	93.8%	<.001
Norfloxacin	83.7%	79.4%	73.9%	76.8%	70.2%	68.4%	76.6%	74.5%	77.4%	<.001
Piperacillin	12.0%	12.8%	18.6%	24.0%	21.4%	14.8%	8.4%	7.8%	8.9%	<.001
Piperacillin/Tazobactam	89.5%	94.6%	95.9%	95.2%	91.6%	88.4%	92.0%	93.0%	90.4%	<.001
Tetracycline	35.5%	37.0%	37.4%	36.1%	39.6%	43.3%	42.9%	43.2%	42.1%	<.001
Ticarcillin/ Clavulanic Acid	59.2%	56.4%	65.6%	65.5%	62.0%	67.6%	72.4%	69.7%	64.1%	<.001
Tobramycin	84.1%	81.9%	81.1%	79.5%	78.9%	76.3%	76.3%	77.7%	76.5%	<.001
Trim/ Sulfa[a]	33.0%	33.4%	33.5%	33.5%	34.6%	35.0%	33.6%	32.7%	34.5%	.17

[a]Trimethoprim/Sulfamethoxazole.
[b]*P*-values were established for a single antibiotic over time using a two-tailed Cochrane-Armitage trend test for linearity.
Data Source: NMCPHC HL7 formatted microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 19 August 2014.

In 2013, fluoroquinolones (ciprofloxacin and moxifloxacin) were the most common class of antibiotic used to treat MDR *E. coli* in the DON regardless of the route of administration, followed by nitrofurans (nitrofurantoin) and sulfonamides (trimethoprim/sulfamethoxazole). Table 5 presents antibiotic prescriptions by class for the DON. The most commonly administered oral antibiotic was nitrofurantoin followed by ciprofloxacin and trimethoprim/sulfamethoxazole. Ceftriaxone was the most commonly prescribed IV antibiotic (data not shown).

Table 0-4. Antibiotic Prescriptions, by Class, for MDR *Escherichia coli* in the DON, CY 2013

Class	Oral (N = 2,362)		Intravenous (N = 251)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	6	0.3	22	8.8	Gentamicin
Cephalosporins	279	11.8	83	33.1	Ceftriaxone
Carbapenems	9	0.4	28	11.2	Meropenem
Glycylcyclines	1	0.0	1	0.4	Tigecycline*
Fluoroquinolones	711	30.1	48	19.1	Ciprofloxacin
Lincosamides	17	0.7	4	1.6	Clindamycin*
Macrolides	33	1.4	5	2.0	Azithromycin
Monobactams	0	0.0	3	1.2	Aztreonam*
Nitroimidazoles	16	0.7	5	2.0	Metronidazole*
Nitrofurans	697	29.5	0	0.0	Nitrofurantoin*
Penicillins	30	1.3	8	3.2	Amoxicillin
Penicillins & Inhibitors	88	3.7	38	15.1	Piperacillin/Tazobactam
Polymyxins	5	0.2	1	0.4	Polymyxin B
Sulfonamides	433	18.3	2	0.8	Trimethoprim/Sulphmethoxazole*
Tetracyclines	37	1.6	3	1.2	Doxycycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 14 August 2014.

The DOD showed the same pattern of overall prescription practices for MDR *E. coli* as the DON did in 2013. Overall, the most commonly prescribed class of antibiotics were fluoroquinolones (ciprofloxacin and moxifloxacin), followed by nitrofurans (nitrofurantoin) and sulfonamides (trimethoprim/sulfamethoxazole). Table 6 presents antibiotic prescriptions by class for the DOD. The most frequently prescribed oral antibiotic was nitrofurantoin followed by ciprofloxacin and trimethoprim/sulfamethoxazole. Similar to the DON, ceftriaxone was also the most commonly prescribed IV antibiotic for the DOD followed by piperacillin/tazobactam and levofloxacin (data not shown).

Table 0-5. Antibiotic Prescriptions, by Class, for MDR *Escherichia coli* in the DOD, CY 2013

Class	Oral (N = 6,900)		Intravenous (N = 971)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	12	0.2	67	6.9	Gentamicin
Cephalosporins	703	10.2	295	30.4	Ceftriaxone
Carbapenems	28	0.4	125	12.9	Ertapenem
Glycylcyclines	1	0.0	3	0.3	Tigecycline*
Fluoroquinolones	2,155	31.2	217	22.3	Ciprofloxacin
Lincosamides	58	0.8	14	1.4	Clindamycin*
Macrolides	86	1.2	14	1.4	Azithromycin
Monobactams	0	0.0	13	1.3	Aztreonam*
Nitroimidazoles	45	0.7	33	3.4	Metronidazole*
Nitrofurans	2,020	29.3	0	0.0	Nitrofurantoin*
Penicillins	81	1.2	22	2.3	Amoxicillin
Penicillins & Inhibitors	284	4.1	152	15.7	Amoxicillin/Clavulanate
Polymyxins	11	0.2	1	0.1	Polymyxin B
Sulfonamides	1,316	19.1	5	0.5	Trimethoprim/Sulphmethoxazole*
Tetracyclines	100	1.4	10	1.0	Doxycycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 14 August 2014.

Table 7 presents the healthcare-associated infection metric rates for MDR *E. coli*. The rate of importation of MDR *E. coli* into DOD MTFs, as displayed by the admission prevalence metric, was 3.0 per 1,000 admissions in 2013, a negligible decrease from an admission prevalence rate of 3.1 per 1,000 admissions in 2012. However, the overall prevalence of MDR *E. coli* was 3.2 per 1,000 admissions, or 1.7 times higher than the rate from 2012. The majority of infection burden rates were similar to those observed from 2012 except for SSIs. In 2013, beneficiaries were seven times less likely to experience an MDR *E. coli* SSI than they were in 2012.

Table 0-6. Healthcare-Associated Infection Metrics for MDR *Escherichia coli* Cases among DOD Beneficiaries, 2013

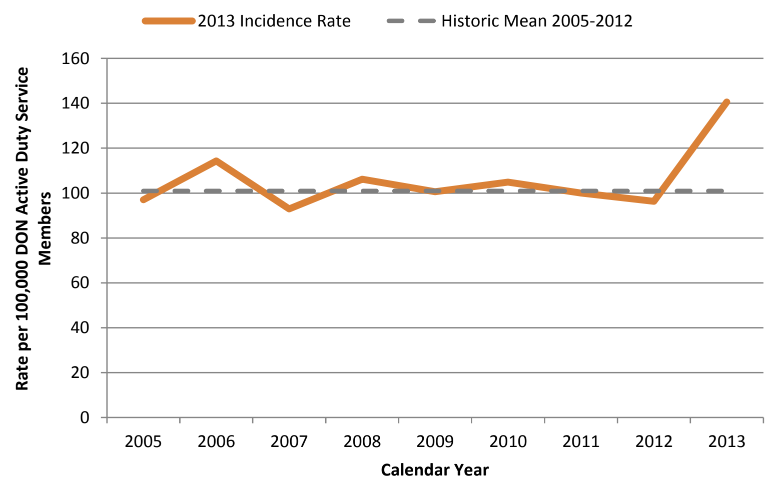
Metric	Rate/Density-Rate	
Exposure Burden		
Admission Prevalence	3.0	per 1,000 Admissions
Overall Prevalence	3.2	per 1,000 Admissions
Infection Burden		
HO Bacteremia	0.003	per 1,000 Patient-Days
HO UTI	0.03	per 1,000 Patient-Days
Device Associated		
CLABSI	0.02	per 1,000 Central-Line Days
VAP	0.1	per 1,000 Vent-Days
Procedure Associated		
SSI	0.2	Per 100 Procedures

Data Sources: SIDR and NMCPHC HL7 formatted microbiology databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 14 August 2014.

DON Active Duty

In 2013, there were 732 MDR *E. coli* cases identified among 700 DON active duty service members for an overall incidence rate of 140.6 per 100,000 DON active duty service members per year. Overall, from 2005-2013, MDR *E. coli* incidence rates among DON active duty service members remained relatively stable, except for the recent increase in 2013 (Figure 3). In 2013, the rate was 39.3% higher than the historic baseline and 45.9% higher than the 2012 incidence rate.

Figure 3. Multidrug-Resistant *Escherichia coli* Incidence in DON Active Duty Service Members with Historic Mean Rate, CY 2005-2013



Historic mean rate calculated as the rate of DON active duty service member case counts per total number of DON active duty service members from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

MDR *E. coli* occurred with much more frequency among female active duty service members than males, with males accounting for less than 10.0% of all MDR *E. coli* cases in 2013. Among other demographic categories, MDR *E. coli* most often occurred among 17 to 24 year olds, Navy service members, and the West TRICARE service region (Table 8).

Table 0-7. Demographics of Multidrug-Resistant *Escherichia coli* Burden among DON Active Duty Service Members, CY 2013

N = 732	Count	Percent
Gender		
Female	680	92.9
Male	52	7.1
Age Group (in years)		
17-24	349	47.7
25-34	245	33.5
35-44	105	14.3
45-64	32	4.4
65+	1	0.1
Sponsor Service		
Marine Corps	259	35.4
Navy	473	64.6
TRICARE Region		
Alaska	0	--
North	233	31.8
OCONUS	61	8.3
South	126	17.2
West	299	40.8
Unknown[a]	13	1.8

[a]TRICARE service region cannot be identified from the microbiology record.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 9 displays the clinical characteristics of DON active duty MDR *E. coli* cases. The majority of the cases were identified in the outpatient setting (94.4%) and predominantly manifested as UTIs (94.3%). Thirty-four DON service members with MDR *E. coli* were hospitalized in 2013. More than half of hospitalized cases (55.9%) were HA, indicating that organism acquisition could be attributed to exposure in the MHS within the previous year. No CRE *E. coli* cases were identified.

Table 0-8. Clinical Description of Multidrug-Resistant *Escherichia coli* Burden among DON Active Duty Service Members, CY 2013

N = 732	Count	Percent
Encounter Type		
Inpatient	34	4.6
Outpatient	698	95.4
Healthcare Association[a]		
Hospital-onset (HO)	2	5.9
Healthcare-associated (HA)	19	55.9
Community-onset (CO)	13	38.2
Infection Type		
Urinary Tract	690	94.3
Blood Stream	5	0.7
Respiratory	1	0.1
Wound	7	1.0
Other	29	4.0
Carbapenem Resistant Enterobacteriaceae		
Yes	0	--

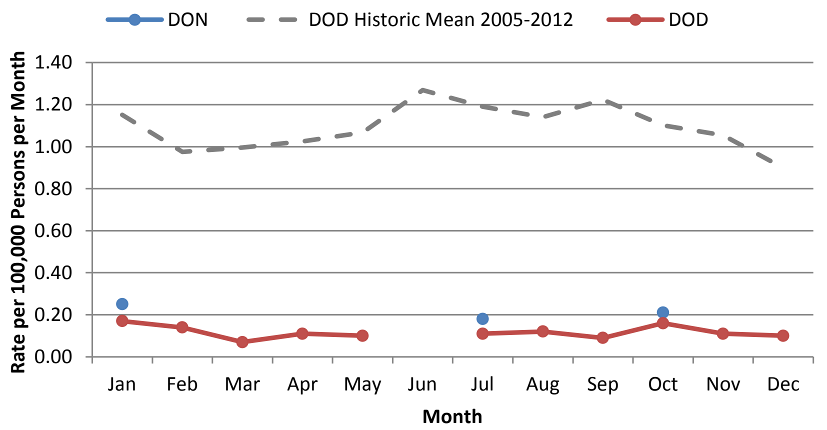
[a]Healthcare association evaluated for inpatient cases.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

MDR *Enterobacter* Species

DON/DOD

In 2013, MDR *Enterobacter* species incidence rates in both the DON and DOD were well below the DOD mean rate for 2005-2012 (Figure 4). The DON consistently showed low case counts (N < 5) throughout 2013, making the majority of monthly incidence rates not reportable. The DOD had higher case counts, but a low case count for the month of June, which was not reportable.

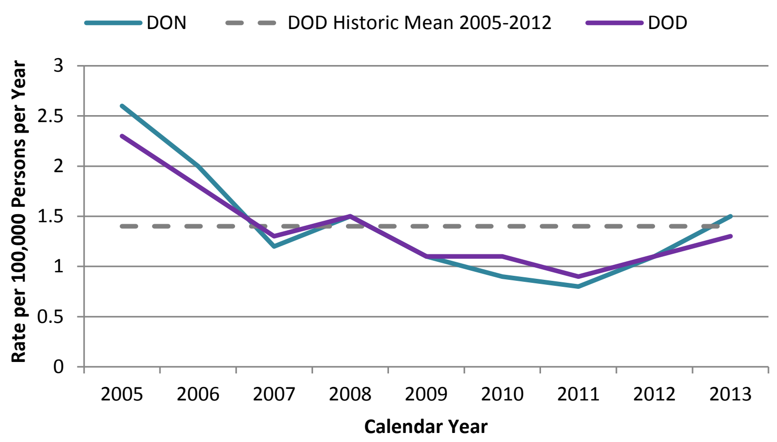
Figure 4. Multidrug-Resistant *Enterobacter* Species Monthly Incidence Rates in DON and DOD Beneficiaries, 2013



Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
Mean rate calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Figure 5 displays MDR *Enterobacter* annual incidence in the DON and DOD from 2005-2013; similar patterns were observed for both populations. Overall, trends decreased by 42.3% and 43.5% for the DON and DOD, respectively. Though annual rates have increased since 2011, they remain below the highest rates seen in 2005, with DOD rates since 2011 still below the historic mean. The 2013 annual incidence rate for the DON (1.5 per 100,000 persons per year) was slightly above the DOD historic mean (1.4 per 100,000 persons per year), while the DOD annual incidence rate for 2013 (1.3 per 100,000 persons per year) was slightly below.

Figure 5. Multidrug-Resistant *Enterobacter* Species Annual Incidence Rates among DON and DOD Beneficiaries with Annual Historic Mean, 2005-2013



Mean calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 10 presents the demographics and prevalence rates for cases of MDR *Enterobacter* the DON and DOD. The EDC identified 41 MDR *Enterobacter* cases among 34 unique DON beneficiaries and 122 MDR *Enterobacter* cases among 104 unique DOD beneficiaries. For both the DON and the DOD, the most highly impacted groups were active duty service members and beneficiaries between the ages of 18 and 24. Contrary to the DOD, in the DON, cases of MDR *Enterobacter* were more often seen among males than females. The West TRICARE service region had the highest prevalence for DON beneficiaries while DOD was most impacted in the North TRICARE service region. The highest prevalence occurred among the Marine Corps beneficiaries.

Table 0-9. Demographics of MDR *Enterobacter* Species Burden in the DON and DOD, CY 2013

DON			DOD		
N = 41	Count	Rate[a]	N = 122	Count	Rate[a]
Gender			**Gender**		
Female	16	1.6	Female	62	1.4
Male	25	2.4	Male	60	1.3
Age Group (in years)			**Age Group (in years)**		
0-17	7	1.2	0-17	12	0.9
18-24	12	2.8	18-24	20	1.7
25-34	6	1.7	25-34	16	1.4
35-44	0	--	35-44	11	1.3
45-64	6	1.0	45-64	29	1.4
65+	10	1.7	65+	34	1.6
Sponsor Service			**Sponsor Service**		
			Air Force	17	0.7
			Army	64	1.6
Marine Corps	13	1.7	Marine Corps	13	1.7
Navy	28	1.4	Navy	28	1.4
Beneficiary Type			**Beneficiary Type**		
Active duty	14	2.7	Active duty	24	1.7
Family Member	19	1.2	Family Member	64	1.3
Retired	7	1.1	Retired	32	1.5
Other	1	*NR**	Other	2	*NR**
TRICARE Region			**TRICARE Region**		
Alaska	0	--	Alaska	0	--
North	16	2.1	North	54	1.9
OCONUS	1	*NR**	OCONUS	3	*NR**
South	2	*NR**	South	19	0.6
West	22	3.3	West	40	1.4
Unknown[b]	0		Unknown[b]	6	

*Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
[a]Rates per 100,000 eligible beneficiaries per year.
[b]TRICARE service region cannot be identified from the microbiology record.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 11 displays the clinical characteristics of MDR *Enterobacter* cases in the DON and DOD. Most cases were identified in the outpatient setting and from urinary tract samples. Five of the 34 DON beneficiaries had at least 2 cases of MDR *Enterobacter*; likewise in the DOD, 15 of the 104 DOD beneficiaries had at least 2 cases of MDR *Enterobacter* (data not shown). No XDR or PDR *Enterobacter* cases were identified in either the DON or DOD in CY 2013.

The majority of inpatient cases in both the DON and DOD (76.9% and 82.5%, respectively) were CO. This indicates that organism acquisition was most frequently associated with exposures outside of the MHS.

Table 0-10. Clinical Description of MDR *Enterobacter* Species Burden in the DON and DOD, CY 2013

DON			DOD		
N = 41	**Count**	**Percent**	**N = 122**	**Count**	**Percent**
Encounter Type			**Encounter Type**		
Inpatient	13	31.7	Inpatient	40	32.8
Outpatient	28	68.3	Outpatient	82	67.2
Healthcare Association[a]			**Healthcare Association**[a]		
Hospital-onset (HO)	1	7.7	Hospital-onset (HO)	3	7.5
Healthcare-associated (HA)	2	15.4	Healthcare-associated (HA)	4	10.0
Community-onset (CO)	10	76.9	Community-onset (CO)	33	82.5
Infection Type			**Infection Type**		
Urinary Tract	16	39.0	Urinary Tract	73	59.8
Blood Stream	1	2.4	Blood Stream	2	1.6
Respiratory	9	22.0	Respiratory	16	13.1
Wound	0	0.0	Wound	5	4.1
Other	15	36.6	Other	26	21.3

[a]Healthcare association evaluated for inpatient cases.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In the DOD in 2013, MDR *Enterobacter* was most susceptible to amikacin and imipenem at 93.1% and 92.4%, respectively; least susceptible to cefazolin (0.0%) and ampicillin (2.4%) (Table 12). From 2005-2013, MDR *Enterobacter* showed statistically significant changes in susceptibility over time for several antibiotics: amikacin, cefepime, cefuroxime, ciprofloxacin, gentamicin, imipenem, levofloxacin, nitrofurantoin, tobramycin, and trimethoprim/sulfamethoxazole. The remaining antibiotics listed below did not show significant changes in susceptibility over time, thus demonstrating a stable trend.

Table 0-11. Cumulative Annual Antibiogram of Percent Susceptibility for MDR *Enterobacter* Species in the DOD with Trend Over Time, 2005-2013

	Year									
Antibiotic	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	***P*-value[b]**
Amikacin	77.3%	84.8%	84.5%	97.4%	95.6%	98.4%	96.2%	100.0%	93.1%	<.001
Amoxacillin/ Clavulanic Acid	7.1%	1.7%	2.0%	4.3%	0.0%	6.5%	8.3%	1.4%	3.1%	.68
Ampicillin	0.5%	0.7%	1.1%	0.0%	0.0%	1.6%	0.0%	1.3%	2.4%	.20
Ampicillin/ Sulbactam	4.5%	2.6%	3.2%	6.5%	6.0%	6.1%	7.0%	9.5%	3.7%	.23
Aztreonam	14.9%	26.8%	21.1%	25.0%	15.3%	16.3%	27.7%	34.0%	20.6%	.29
Cefazolin	2.8%	0.7%	0.0%	0.8%	0.0%	2.3%	1.4%	2.4%	0.0%	.47
Cefepime	67.9%	68.9%	71.4%	83.7%	81.2%	87.1%	91.0%	87.7%	75.4%	<.001
Ceftazidime	24.4%	18.1%	19.5%	28.4%	21.1%	20.9%	33.3%	33.8%	23.9%	.12
Ceftriaxone	28.7%	26.6%	25.9%	36.1%	23.9%	27.5%	21.1%	36.1%	22.3%	.87
Cefuroxime	17.6%	15.4%	9.3%	16.7%	2.9%	12.9%	7.1%	8.3%	6.7%	.03
Ciprofloxacin	67.6%	64.0%	57.3%	60.4%	68.7%	62.0%	66.3%	83.0%	81.3%	.001
Gentamicin	50.7%	49.7%	56.8%	67.9%	75.7%	78.6%	76.1%	76.0%	83.3%	<.001
Imipenem	95.9%	97.9%	97.5%	98.9%	100.0%	95.3%	94.3%	93.7%	92.4%	.04
Levofloxacin	74.5%	67.9%	73.6%	76.4%	75.4%	82.4%	86.0%	91.3%	88.2%	<.001
Nitrofurantoin	50.0%	38.3%	33.3%	40.0%	27.9%	25.9%	36.2%	32.0%	30.8%	.02
Piperacillin/ Tazobactam	30.0%	40.2%	40.3%	56.2%	29.7%	30.3%	28.1%	39.3%	27.9%	.14
Tetracycline	63.9%	73.3%	75.9%	68.8%	77.4%	71.0%	71.9%	82.1%	82.9%	.09
Tobramycin	39.9%	41.1%	52.4%	57.3%	67.6%	74.0%	76.9%	71.2%	74.6%	<.001
Trim/ Sulfa[a]	45.8%	44.2%	50.0%	59.7%	59.2%	56.7%	54.5%	63.6%	81.0%	<.001

[a]Trimethoprim/Sulfamethoxazole.
[b]*P*-values were established for a single antibiotic over time using a two-tailed Cochrane-Armitage trend test for linearity.
Data Source: NMCPHC HL7 formatted microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 22 October 2013.

In 2013, fluoroquinolones (ciprofloxacin and levofloxacin) were the most common class of antibiotic used to treat MDR *Enterobacter* cases in the DON, regardless of the route of administration, followed by carbapenems (ertapenem and meropenem) and penicillin/inhibitor combinations (amoxicillin/clavulanate, ampicillin/sulbactam, piperacillin/tazobactam, and ticarcillin/clavulanate). Table 13 presents antibiotic prescriptions by class for the DON. The most commonly administered oral antibiotic was ciprofloxacin, followed by trimethoprim/sulfamethoxazole. Meropenem was the most commonly prescribed IV antibiotic (data not shown).

Table 0-12. Antibiotic Prescriptions, by Class, for MDR *Enterobacter* Species in the DON, CY 2013

Class	Oral (N = 28)		Intravenous (N = 15)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	0	0.0	2	13.3	Gentamicin*
Cephalosporins	1	3.6	4	26.7	Ceftriaxone
Carbapenems	2	7.1	5	33.3	Meropenem
Fluoroquinolones	10	35.7	0	0.0	Ciprofloxacin
Lincosamides	1	3.6	2	13.3	Clindamycin*
Macrolides	3	10.7	0	0.0	Erythromycin
Nitroimidazoles	1	3.6	0	0.0	Metronidazole*
Nitrofurans	1	3.6	0	0.0	Nitrofurantoin*
Penicillins & Inhibitors	4	14.3	2	13.3	Piperacillin/Tazobactam
Sulfonamides	4	14.3	0	0.0	Trimethoprim/Sulphmethoxazole*
Tetracyclines	1	3.6	0	0.0	Doxycycline*

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In 2013, fluoroquinolones (ciprofloxacin, levofloxacin, and moxifloxacin) were the most commonly used class of antibiotic for treatment of MDR *Enterobacter* cases in the DOD, regardless of the route of administration, followed by penicillin/inhibitor combinations (amoxicillin/clavulanate, ampicillin/sulbactam, piperacillin/tazobactam, and ticarcillin/clavulanate). Table 14 presents antibiotic prescriptions by class for the DOD. The most commonly administered oral antibiotic was ciprofloxacin, followed by levofloxacin and trimethoprim/sulfamethoxazole. Piperacillin/tazobactam was the most commonly prescribed IV antibiotic (data not shown).

Table 0-13. Antibiotic Prescriptions, by Class, for MDR *Enterobacter* Species in the DOD, CY 2013

Class	Oral (N = 84)		Intravenous (N = 52)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	0	0.0	6	11.5	Gentamicin
Cephalosporins	8	9.5	11	21.2	Ceftriaxone
Carbapenems	6	7.1	11	21.2	Meropenem
Fluoroquinolones	28	33.3	7	13.5	Ciprofloxacin
Lincosamides	3	3.6	3	5.8	Clindamycin*
Macrolides	5	6.0	1	1.9	Azithromycin & Erythromycin
Nitroimidazoles	3	3.6	2	3.8	Metronidazole*
Nitrofurans	7	8.3	0	0.0	Nitrofurantoin*
Penicillins & Inhibitors	11	13.1	10	19.2	Piperacillin/Tazobactam
Sulfonamides	10	11.9	1	1.9	Trimethoprim/Sulphmethoxazole*
Tetracyclines	3	3.6	0	0.0	Doxycycline*

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 15 presents the healthcare-associated infection metric rates for MDR *Enterobacter* occurring at DOD MTFs. The rate of importation of MDR *Enterobacter* into DOD MTFs, as indicated by the admission prevalence metric, was 0.10 per 1,000 admissions in 2013, a decrease from the 2012 rate of 0.49 per 1,000 admissions. The overall prevalence of MDR *Enterobacter* was 0.11 per 1,000 admissions, which is also a decrease from 2012 where the overall prevalence was 0.54 per 1,000 admissions. In 2013, MDR *Enterobacter* was not the cause of HO bacteremia or CLABSIs in DOD MTFs; metrics for HO UTI, VAP, and SSI were all very low. Although the infection burden metrics were low in 2013, they displayed increases from 2012 with the exception of SSI. In 2012, MDR *Enterobacter* was not identified for UTI or VAP metrics, whereas in 2013, the rate of SSIs was two times less than it was in 2012.

Table 0-14. Healthcare-Associated Infection Metrics for MDR *Enterobacter* Cases among DOD Beneficiaries, 2013

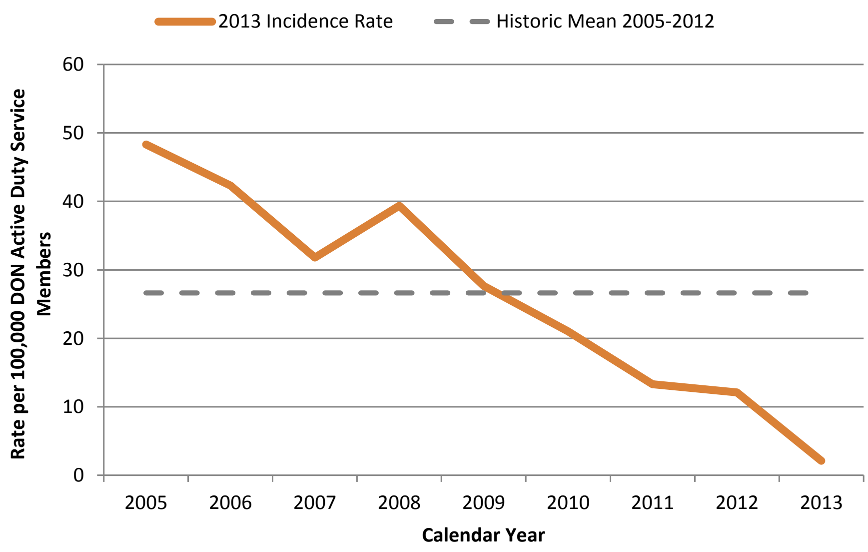
Metric	Rate/Density-Rate	
Exposure Burden		
Admission Prevalence	0.10	per 1,000 Admissions
Overall Prevalence	0.11	per 1,000 Admissions
Infection Burden		
HO Bacteremia	--	per 1,000 Patient-Days
HO UTI	0.002	per 1,000 Patient-Days
Device Associated		
CLABSI	--	per 1,000 Central-Line Days
VAP	0.03	per 1,000 Vent-Days
Procedure Associated		
SSI	0.01	Per 100 Procedures

Data Sources: SIDR and HL7 formatted microbiology databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 09 October 2014.

DON Active Duty

In 2013, there were 11 MDR *Enterobacter* cases among 6 DON active duty service members with an incidence rate of 2.1 per 100,000 DON active duty service members per year. Since 2010 the incidence of MDR *Enterobacter* has been below the historic mean rate (26.6 per 100,000 active duty service members), a trend continued in 2013. It was also the lowest rate observed since enterprise-wide surveillance began in 2005 with a 95.7% decrease from 2005.

Figure 6. Multidrug-Resistant MDR *Enterobacter* Species Incidence in the DON Active Duty Service Members with Historic Mean Rate, CY 2005-2013



Historic mean rate calculated as the rate of DON active duty service member case counts per total number of DON active duty service members from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 17 presents the demographics of active duty MDR *Enterobacter* cases in the DON in 2013. Cases most frequently occurred among males, 17-24 year olds, Sailors, and the North TRICARE service region.

Table 0-15. Demographics of Multidrug-Resistant *Enterobacter* Species Burden among DON Active Duty Service Members, CY 2013

N = 11	Count	Percent
Gender		
Female	2	18.2
Male	9	81.8
Age Group (in years)		
17-24	5	45.5
25-34	4	36.4
35-44	0	--
45-64	1	9.1
65+	1	9.1
Sponsor Service		
Marine Corps	5	45.5
Navy	6	54.5
TRICARE Region		
Alaska	0	--
North	7	63.6
OCONUS	0	--
South	0	--
West	4	36.4
Unknown	0	

Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 18 displays the clinical characteristics of DON active duty MDR *Enterobacter* cases. Cases were mostly identified in the inpatient setting (63.6%) and from body sites other than the urinary tract, blood stream, respiratory system, and wounds (54.5%). In 2013, six of the inpatient cases (85.7%) were CO, indicating that organism acquisition was most frequently associated with exposures outside of the MHS. No XDR or PDR *Enterobacter* cases were identified in DON active duty service members.

Table 0-16. Clinical Description of Multidrug-Resistant *Enterobacter* Species Burden among DON Active Duty Service Members, CY 2013

N = 11	Count	Percent
Encounter Type		
Inpatient	7	63.6
Outpatient	4	36.4
Healthcare Association[a]		
Hospital-onset (HO)	0	0.0
Healthcare-associated (HA)	1	14.3
Community-onset (CO)	6	85.7
Infection Type		
Urinary Tract	4	36.4
Blood Stream	0	0.0
Respiratory	1	9.1
Wound	0	0.0
Other	6	54.5

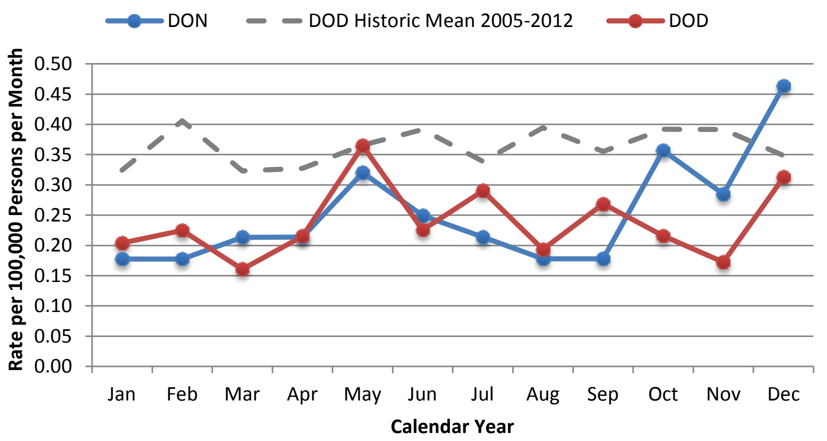
[a]Healthcare association evaluated for inpatient cases.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

MDR *Klebsiella* Species

DON/DOD

In 2013, MDR *Klebsiella* species monthly incidence rates in both the DON and DOD were typically at or below the DOD mean rates established for 2005-2012. Incidence increased near the end of the year, and the DON rate in December was 31.4% higher than the historic mean rate (Figure 7).

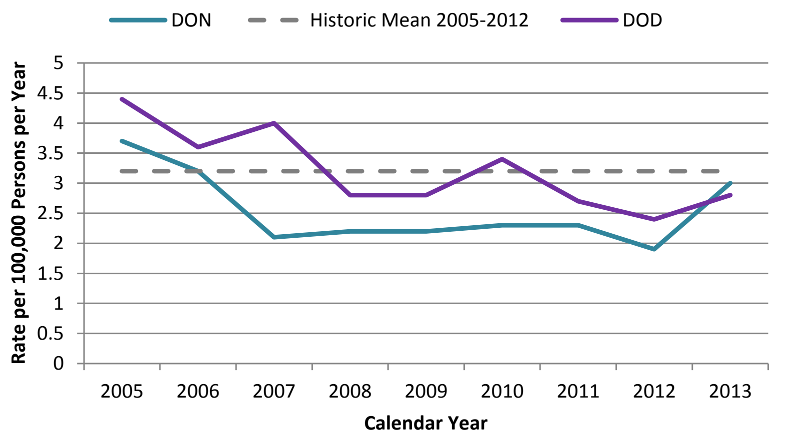
Figure 7. Multidrug-Resistant *Klebsiella* Species Incidence Rates in DON and DOD Beneficiaries by Month, 2013



Mean rate calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Figure 8 displays the DON and DOD annual incidence trends from 2005-2013. The overall incidence of MDR *Klebsiella* cases from 2005-2013 showed a generally descending trend for both the DON and DOD with an overall decrease from 2005 of 18.9% and 57.1%, respectively. The 2013 annual incidence rates in the DON and DOD (3.0 and 2.8 per 100,000 persons per year, respectively) were above the 2012 annual incidence rates (1.9 and 2.4 per 100,000 persons per year, respectively) but remained below the DOD historic mean (3.2 per 100,000 persons per year).

Figure 8. Multidrug-Resistant *Klebsiella* Species Incidence Rates in DON and DOD Beneficiaries with Annual Mean, 2005-2013



Historic mean calculated for all DOD incident cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 18 presents the demographic prevalence rates for DON and DOD MDR *Klebsiella* cases. The EDC identified 85 MDR *Klebsiella* cases among 65 DON beneficiaries and 265 cases among 222 DOD beneficiaries. In the DON, females were disproportionately affected and had approximately three times the prevalence rate of males; a similar pattern existed in the DOD where females had approximately two times the prevalence rate of males. DON and DOD cases most frequently occurred in beneficiaries older than 65 years, family members, and the OCONUS TRICARE service region. The sponsor service with the highest prevalence rate was the Army, whose beneficiary rates were between one and two times higher than the rates of other sponsor services.

Table 0-17. Demographics of MDR *Klebsiella* Species Burden in the DON and DOD, CY 2013

DON			DOD		
N = 85	Count	Rate[a]	N = 265	Count	Rate[a]
Gender			**Gender**		
Female	63	4.7	Female	180	3.9
Male	22	1.5	Male	85	1.8
Age Group (in years)			**Age Group (in years)**		
0-17	10	1.8	0-17	25	1.3
18-24	5	1.2	18-24	25	2.1
25-34	10	2.8	25-34	35	3.0
35-44	10	4.1	35-44	23	2.8
45-64	23	3.7	45-64	66	3.2
65+	27	4.7	65+	91	4.4
Sponsor Service			**Sponsor Service**		
			Air Force	51	2.0
			Army	129	3.3
Marine Corps	19	2.5	Marine Corps	19	2.5
Navy	66	3.2	Navy	66	3.2
Beneficiary Type			**Beneficiary Type**		
Active duty	7	1.3	Active duty	27	1.9
Family Member	61	4.0	Family Member	169	3.4
Retired	17	2.7	Retired	62	3.0
Other	0	--	Other	7	0.8
TRICARE Region			**TRICARE Region**		
Alaska	0	--	Alaska	0	--
North	31	3.0	North	88	3.1
OCONUS	8	8.0	OCONUS	20	5.4
South	9	1.3	South	65	2.1
West	36	3.9	West	85	3.1
Unknown[b]	1		Unknown[b]	7	

[a]Rates per 100,000 persons per year.
[b]TRICARE service region cannot be identified from the microbiology record.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 19 displays the clinical characteristics of MDR *Klebsiella* cases in the DON and DOD. Most cases were identified in the outpatient setting and were predominantly from urinary tract specimens. Fourteen of the 65 DON beneficiaries had at least 2 cases of MDR *Klebsiella*; likewise in the DOD, 33 of the 222 beneficiaries had at least 2 cases of MDR *Klebsiella* (data not shown). Four CRE *Klebsiella* cases were identified in the DON and eight more were identified in the DOD, accounting for 4.7% and 4.5% of the MDR *Klebsiella* burden, respectively; all CRE *Klebsiella* cases were also identified as MDR. No XDR or PDR *Klebsiella* cases were identified in the DON or DOD in 2013.

The majority of the inpatient MDR *Klebsiella* cases in both the DON and DOD (47.1% and 79.7%, respectively) were CO. This indicates that organism acquisition was most frequently associated with exposures outside of the MHS.

Table 0-18. Clinical Description of MDR *Klebsiella* Species and Carbapenem-Resistant Enterobacteriaceae Burden in the DON and DOD, CY 2013

DON			DOD		
N = 85	Count	Percent	N = 265	Count	Percent
Encounter Type			**Encounter Type**		
Inpatient	13	15.3	Inpatient	59	22.3
Outpatient	72	84.7	Outpatient	206	77.7
Healthcare Association[a]			**Healthcare Association[a]**		
Hospital-onset (HO)	1	5.9	Hospital-onset (HO)	8	13.6
Healthcare-associated (HA)	4	23.5	Healthcare-associated (HA)	4	6.8
Community-onset (CO)	8	47.1	Community-onset (CO)	47	79.7
Infection Type			**Infection Type**		
Urinary Tract	67	78.8	Urinary Tract	205	77.4
Blood Stream	2	2.4	Blood Stream	13	4.9
Respiratory	7	8.2	Respiratory	24	9.1
Wound	0	0.0	Wound	6	2.3
Other	9	11.1	Other	17	6.4
Carbapenem-Resistant Enterobacteriaceae[b]			**Carbapenem-Resistant Enterobacteriaceae[b]**		
Klebsiella species	4	4.7	*Klebsiella* species	12	4.5

[a]Healthcare association evaluated for inpatient cases.
[b]All carbapenem-resistant Enterobacteriaceae (CRE) isolates also identified as MDR.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In the DOD in 2013, MDR *Klebsiella* was most susceptible to carbapenems (meropenem [96.9%] and imipenem [93.6%]), followed by amikacin (94.3%) (Table 20); the lowest susceptibility was to ampicillin/sulbactam (9.4%), followed by tetracycline (21.8%). MDR *Klebsiella* has shown statistically significant changes in susceptibility over time for the majority of commonly tested antibiotics, however no significant linear trend from 2005-2013 was observed for the following antibiotics, indicating that susceptibilities of MDR *Klebsiella* to these antibiotics have remained stable: amoxicillin/clavulanate, ampicillin/sulbactam, cefoxitin, meropenem, and piperacillin/tazobactam. Of the antibiotics displaying a stable trend, only meropenem was highly susceptible, indicating that it has been, and remains, a viable treatment for MDR *Klebsiella* infections in the MHS. Conversely, ampicillin/sulbactam had consistently low susceptibilities over time, indicating that they have consistently been a poor choice for treating MDR *Klebsiella* in the MHS. The majority of remaining antibiotics relevant to *Klebsiella* showed significant changes in susceptibility over time.

Table 0-19. Cumulative Annual Antibiogram of MDR *Klebsiella* Species in the DOD with Trend Over Time, 2005-2013

	Year									
Antibiotic	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	***P*-value[b]**
Amikacin	87.6%	78.5%	85.9%	92.2%	91.3%	94.4%	96.0%	94.5%	94.3%	<.001
Amoxacillin/ Clavulanic Acid	52.6%	48.0%	36.8%	25.4%	32.7%	54.2%	34.0%	45.3%	52.5%	.50
Ampicillin/ Sulbactam	7.0%	6.2%	7.5%	5.3%	9.4%	6.3%	5.5%	7.4%	9.4%	.52
Aztreonam	35.6%	25.2%	30.6%	42.6%	50.0%	41.2%	51.4%	60.2%	63.3%	<.001
Cefazolin	20.5%	18.1%	21.7%	22.9%	29.4%	28.0%	26.3%	34.7%	28.0%	<.001
Cefepime	40.0%	35.8%	48.4%	54.5%	68.4%	67.3%	62.4%	64.3%	66.0%	<.001
Cefotaxime	36.0%	32.8%	37.9%	51.0%	66.1%	86.0%	91.4%	83.9%	80.0%	<.001
Cefoxitin	47.7%	52.3%	56.3%	41.7%	43.5%	69.9%	62.7%	59.6%	40.9%	.35
Ceftazidime	35.9%	38.0%	39.6%	51.9%	66.1%	73.5%	54.3%	69.0%	69.2%	<.001
Ceftriaxone	44.4%	34.5%	41.1%	43.9%	55.9%	54.0%	49.1%	61.1%	60.4%	<.001
Cefuroxime	30.3%	25.5%	27.8%	42.3%	38.5%	60.9%	50.0%	44.0%	44.6%	<.001
Cephalothin	10.4%	9.3%	10.3%	8.7%	19.4%	55.2%	21.2%	20.0%	29.6%	<.001
Ciprofloxacin	44.8%	44.4%	46.0%	45.0%	46.7%	57.4%	45.4%	53.6%	57.0%	<.001
Gentamicin	40.9%	42.2%	44.4%	63.9%	64.9%	66.7%	68.9%	70.7%	69.9%	<.001
Imipenem	98.4%	97.9%	96.9%	97.0%	96.4%	96.0%	94.1%	97.2%	93.6%	.01
Levofloxacin	49.2%	48.2%	54.8%	52.6%	62.3%	68.8%	63.3%	70.9%	66.7%	<.001
Mereopenem	98.4%	95.5%	97.5%	100.0%	91.9%	96.8%	92.6%	88.5%	96.9%	.11
Nitrofurantoin	35.7%	37.0%	34.7%	32.6%	26.2%	29.2%	27.8%	22.7%	26.1%	<.001
Piperacillin/ Tazobactam	43.2%	56.6%	63.0%	54.1%	56.2%	47.3%	58.6%	61.5%	53.6%	.15
Tetracycline	22.3%	15.3%	18.5%	16.5%	30.3%	44.5%	31.2%	19.5%	21.8%	.049
Tobramycin	37.5%	34.9%	43.2%	61.6%	65.6%	62.4%	57.5%	63.1%	66.9%	<.001
Trim/ Sulfa[a]	23.6%	25.6%	26.5%	28.7%	34.3%	41.2%	34.5%	37.9%	37.4%	<.001

[a]Trimethoprim/Sulfamethoxazole.
[b]*P*-values were established for a single antibiotic over time using a two-tailed Cochrane-Armitage trend test for linearity.
Data Source: NMCPHC HL7 formatted microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In 2013, cephalosporins (cefazolin, cefdinir, cefixime, cefpodoxime, ceftriaxone, and cephalexin) were the most common class of antibiotic used to treat MDR *Klebsiella* cases in the DON regardless of the route of administration, followed by fluoroquinolones (ciprofloxacin and levofloxacin), penicillin and inhibitor combinations (amoxicillin/clavulanate, ampicillin/sulbactam, and piperacillin/tazobactam), and sulfonamides (trimethoprim/sulfamethoxazole). Table 21 presents antibiotic prescriptions by class for the DON. The most commonly administered oral antibiotic was ciprofloxacin, followed by trimethoprim/sulfamethoxazole and levofloxacin. Piperacillin/tazobactam was the most commonly prescribed IV antibiotic (data not shown).

Table 0-20. Antibiotic Prescriptions, by Class, for MDR *Klebsiella* Species in the DON, CY 2013

Class	Oral (N = 65)		Intravenous (N = 24)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	1	1.5	3	12.5	Gentamicin*
Cephalosporins	18	27.7	6	25.0	Ceftriaxone
Carbapenems	0	0.0	4	16.7	Doripenem, Ertapenem, Meropenem
Glycylcyclines	0	0.0	1	4.2	Tigecycline*
Fluoroquinolones	19	29.2	1	4.2	Ciprofloxacin
Macrolides	2	3.1	0	0.0	Azithromycin*
Monobactams	0	0.0	1	4.2	Aztreonam*
Nitroimidazoles	3	4.6	0	0.0	Metronidazole*
Nitrofurans	5	7.7	0	0.0	Nitrofurantoin*
Penicillins	1	1.5	0	0.0	Amoxicillin*
Penicillins & Inhibitors	6	9.2	5	20.8	Piperacillin/Tazobactam
Sulfonamides	7	10.8	1	4.2	Trimethoprim/Sulphmethoxazole*
Tetracyclines	3	4.6	2	8.3	Doxycycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In 2013, fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin) were the most common class of antibiotic used to treat MDR *Klebsiella* cases in the DOD, regardless of the route of administration, followed by cephalosporins (cefazolin, cefdinir, cefepime, cefixime, cefotaxime, cefpodoxime, ceftazidime, ceftriaxone, and cephalexin) and nitrofurans (nitrofurantoin). Table 22 presents antibiotic prescriptions by class for the DOD. The most commonly administered oral antibiotic was ciprofloxacin, followed by levofloxacin and trimethoprim/sulfamethoxazole. Piperacillin/tazobactam was the most commonly prescribed IV antibiotic (data not shown).

Table 0-21. Antibiotic Prescriptions, by Class, for MDR *Klebsiella* Species in the DOD, CY 2013

Class	Oral (N = 191)		Intravenous (N = 111)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	6	3.1	9	8.1	Tobramycin
Cephalosporins	33	17.3	25	22.5	Ceftriaxone
Carbapenems	5	2.6	23	20.7	Meropenem
Glycylcyclines	0	0.0	2	1.8	Tigecycline*
Fluoroquinolones	57	29.8	13	11.7	Levofloxacin
Lincosamides	3	1.6	2	1.8	Clindamycin*
Macrolides	2	1.0	3	2.7	Azithromycin
Monobactams	0	0.0	2	1.8	Aztreonam*
Nitroimidazoles	5	2.6	3	2.7	Metronidazole*
Nitrofurans	20	10.5	0	0.0	Nitrofurantoin*
Penicillins	4	2.1	1	0.9	Amoxicillin
Penicillins & Inhibitors	25	13.1	20	18.0	Piperacillin/Tazobactam
Sulfonamides	22	11.5	4	3.6	Trimethoprim/Sulphmethoxazole*
Tetracyclines	9	4.7	4	3.6	Doxycycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 23 presents healthcare-associated infection metric rates for MDR *Klebsiella*. The rate of importation of MDR *Klebsiella* into DOD MTFs, as indicated by admission prevalence, was 0.24 per 1,000 admissions in 2013, the same as it was in 2012. However, the overall prevalence of MDR *Klebsiella* was 0.28 per 1,000 admissions, a negligible increase from 0.26 per 1,000 admissions in 2012. In 2013, MDR *Klebsiella* was not the cause of CLABSIs or VAP in DOD MTFs; rates for HO bacteremia, HO UTI, and SSI were low. Although HO bacteremia, HO UTI, and SSI rates were low in 2013, they increased from 2012, when MDR *Klebsiella* was not identified in any HAI infection burden metrics except SSI. In 2013, SSIs caused by MDR *Klebsiella* were 4.5 times more common than in 2012.

Table 0-22. Healthcare-Associated Infection Metrics for MDR *Klebsiella* Cases among DOD Beneficiaries, 2013

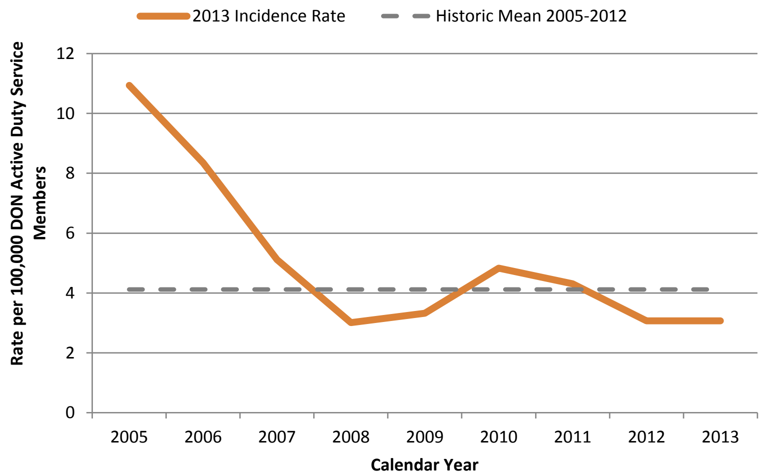
Metric	Rate/Density-Rate	
Exposure Burden		
Admission Prevalence	0.24	per 1,000 Admissions
Overall Prevalence	0.28	per 1,000 Admissions
Infection Burden		
HO Bacteremia	0.002	per 1,000 Patient-Days
HO UTI	0.008	per 1,000 Patient-Days
Device Associated		
CLABSI	--	per 1,000 Central-Line Days
VAP	--	per 1,000 Vent-Days
Procedure Associated		
SSI	0.01	Per 100 Procedures

Data Sources: SIDR and HL7 formatted microbiology databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 09 October 2014.

DON Active Duty

In 2013, there were 16 MDR *Klebsiella* cases identified among DON active duty service members, giving an overall incidence rate of 3.1 per 100,000 DON active duty service members per year. All 16 cases were incident cases. The 2013 rate was below the historic mean rate as it has been since 2012, and showed a generally descending trend with a 71.6% decrease since 2005 (Figure 9).

Figure 9. Historical Trend of Multidrug-Resistant *Klebsiella* Species Incidence in DON Active Duty Service Members with Historic Mean Rate, CY 2005-2013



Mean rate calculated as the rate of DON active duty service member incident counts per total number of DON active duty service members from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 24 presents the demographics of active duty MDR *Klebsiella* cases in the DON in 2013. Cases most often occurred in females, 17 to 24 and 25 to 34 year olds, Navy beneficiaries, and the West TRICARE service region.

Table 0-23. Demographics of Multidrug-Resistant *Klebsiella* Species Burden among DON Active Duty Service Members, CY 2013

N = 16	Count	Percent
Gender		
Female	14	87.5
Male	2	12.5
Age Group (in years)		
17-24	6	37.5
25-34	6	37.5
35-44	3	18.8
45-64	1	6.3
65+	0	--
Sponsor Service		
Marine Corps	4	25.0
Navy	12	75.0
TRICARE Region		
Alaska	0	--
North	4	25.0
OCONUS	4	25.0
South	1	6.3
West	6	37.5
Unknown	1	6.3

Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 25 displays the clinical characteristics of DON active duty MDR *Klebsiella* cases. Cases were mostly identified in the outpatient setting (81.3%) and from urinary tract specimens (68.8%). The majority of the inpatient DON active duty cases were CO. This indicates that organism acquisition for these cases was most commonly associated with exposures outside of the MHS. Two CRE *Klebsiella* cases were identified in DON active duty service members in 2013; both CRE cases were also identified as MDR cases

Table 0-24. Clinical Description of Multidrug-Resistant and Carbapenem-Resistant *Klebsiella* Species Burden among DON Active Duty Service Members, CY 2013

N = 16	Count	Percent
Encounter Type		
Inpatient	3	18.8
Outpatient	13	81.3
Healthcare Association[a]		
Hospital-onset (HO)	0	--
Healthcare-associated (HA)	1	33.3
Community-onset (CO)	2	66.7
Infection Type		
Urinary Tract	11	68.8
Blood Stream	1	6.3
Respiratory	1	6.3
Wound	0	0.0
Other	3	18.8
Carbapenem Resistant Enterobacteriaceae		
Yes	2	12.5

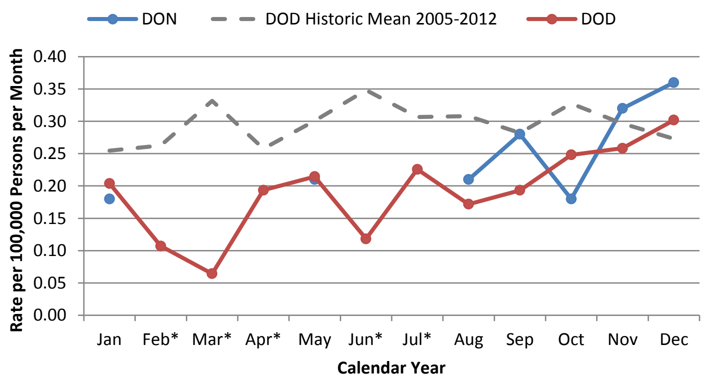
[a]Healthcare association evaluated for inpatient cases.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

MDR *Pseudomonas aeruginosa*

DON/DOD

In 2013, MDR *P. aeruginosa* monthly incidence rates in the DON and DOD differed from the mean rate established for the DOD from 2005-2012 (Figure 10). The DON had low case counts (N < 5) in several months of 2013, making the incidence rates for these months not reportable. Generally, of the reportable monthly rates, most were at or below the historic mean with increases in incidence near the end of the year. Incidence was above the mean in November for the DON and above the mean in December for both the DON and DOD.

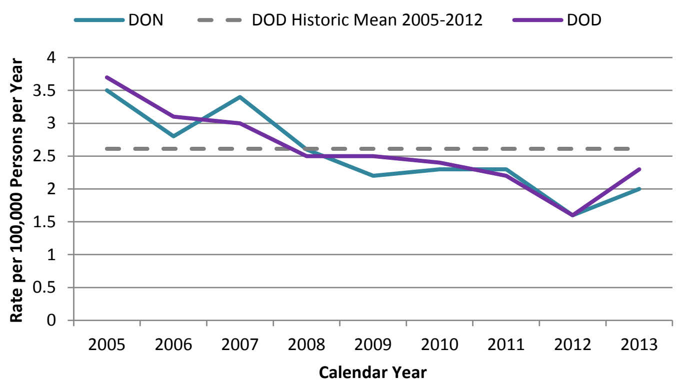
Figure 10. Multidrug-Resistant *Pseudomonas aeruginosa* Incidence Rates in DON and DOD Beneficiaries by Month with DOD Historic Monthly Mean, 2013



*Monthly rate is not reportable (NR) for the DON as case counts are <5.
Historic mean calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Figure 11 displays the DON and DOD annual historical trends from 2005-2013. The overall incidence of MDR *P. aeruginosa* from 2005-2013 demonstrated a general descending trend with a 42.5% and 37.8% decrease for the DON and DOD, respectively. The DON and DOD rates for 2013 (2.0 and 2.3 per 100,000 persons per year, respectively) were both above the 2012 incidence rates (both 1.6 per 100,000 persons per year) but remained below the historic DOD mean rate (2.6 per 100,000 persons per year).

Figure 11. Multidrug-Resistant *Pseudomonas aeruginosa* Incidence Rates among DON and DOD Beneficiaries with Annual Historic Mean, 2005-2013



Historic mean calculated for all DOD cases per eligible beneficiaries from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 26 presents the demographics and incidence rates for DON and DOD MDR *P. aeruginosa* cases. The EDC identified 57 MDR *P. aeruginosa* cases among 39 DON beneficiaries and 214 cases among 157 DOD beneficiaries. Females were impacted with a rate slightly higher than males in both the DON and DOD. Beneficiaries between the ages of 18 and 24 were mainly impacted in the DON; in the DOD, 25 to 34 year olds were principally impacted. In both the DON and DOD, cases were most often seen in the North TRICARE service region. The sponsor service with the highest prevalence among DON and DOD beneficiaries was the Marine Corps and the Air Force, respectively.

Table 0-25. Demographics of MDR *Pseudomonas aeruginosa* Burden in the DON and DOD, CY 2013

DON			DOD		
N = 57	Count	Rate[a]	N = 214	Count	Rate[a]
Gender			**Gender**		
Female	36	2.7	Female	113	2.5
Male	21	1.4	Male	101	2.1
Age Group (in years)			**Age Group (in years)**		
0-17	12	2.1	0-17	21	1.1
18-24	13	3.0	18-24	41	3.4
25-34	10	2.8	25-34	44	3.7
35-44	3	--	35-44	11	1.3
45-64	6	1.0	45-64	30	1.4
65+	13	2.3	65+	67	3.2
Sponsor Service			**Sponsor Service**		
			Air Force	71	2.7
			Army	86	2.2
Marine Corps	18	2.4	Marine Corps	18	2.4
Navy	39	1.9	Navy	39	1.9
Beneficiary Type			**Beneficiary Type**		
Active duty	7	1.3	Active duty	20	1.4
Family Member	38	2.5	Family Member	137	2.8
Retired	12	1.9	Retired	56	2.7
Other	0	--	Other	1	*NR**
TRICARE Region			**TRICARE Region**		
Alaska	0	--	Alaska	0	--
North	33	3.2	North	82	2.9
OCONUS	0	--	OCONUS	2	*NR**
South	3	*NR**	South	76	2.5
West	21	2.3	West	54	1.9
Unknown[b]	0		Unknown[b]	0	

*Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
[a]Rates per 100,000 persons per year.
[b]TRICARE service region cannot be identified from the microbiology record.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 27 displays the clinical characteristics of MDR *P. aeruginosa* cases in the DON and DOD. Most cases were identified in the outpatient setting and from respiratory samples. Twelve of the 39 DON beneficiaries had at least 2 MDR *P. aeruginosa* cases; likewise in the DOD, 36 of the 157 beneficiaries had at least 2 MDR *P. aeruginosa* cases (data not shown). No XDR cases were identified in the DON, however 18 XDR cases were identified in the DOD (data not shown). The EDC identified no PDR *P. aeruginosa* cases in either the DON or DOD in 2013.

The majority of the inpatient MDR *P. aeruginosa* cases in both the DON and DOD (100.0% and 75.6%, respectively) were CO. This indicates that organism acquisition was most frequently associated with exposures outside of the MHS.

Table 0-26. Clinical Description of Multidrug-Resistant *Pseudomonas aeruginosa* Burden in the DON and DOD, CY 2013

DON			DOD		
N = 57	**Count**	**Percent**	**N = 214**	**Count**	**Percent**
Encounter Type			**Encounter Type**		
Inpatient	16	28.1	Inpatient	78	36.4
Outpatient	41	71.9	Outpatient	136	63.6
Healthcare Association[a]			**Healthcare Association[a]**		
Hospital-onset (HO)	0	0.0	Hospital-onset (HO)	7	9.0
Healthcare-associated (HA)	0	0.0	Healthcare-associated (HA)	4	5.1
Community-onset (CO)	16	100.0	Community-onset (CO)	59	75.6
Infection Type			**Infection Type**		
Urinary Tract	13	22.8	Urinary Tract	59	27.6
Blood Stream	0	--	Blood Stream	1	0.5
Respiratory	32	56.1	Respiratory	100	46.7
Wound	1	1.8	Wound	10	4.7
Other	11	11.1	Other	26	12.1

[a]Healthcare association evaluated for inpatient cases.
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In the DOD in CY 2013, MDR *P. aeruginosa* was most susceptible to tobramycin (71.3%) and amikacin (67.7%) (Table 28). MDR *P. aeruginosa* was least susceptible to levofloxacin (16.1%) and ciprofloxacin (26.0%). Little variability in susceptibilities occurred from 2005-2013 with most antibiotics showing stable trends. Only aztreonam, ceftazidime, and tobramycin showed significant linear trends over time.

Table 0-27. Cumulative Annual Antibiogram of Percent Susceptibility for MDR *Pseudomonas aeruginosa* in the DOD, 2005-2013

	Year									
Antibiotic[a]	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	***P*-value[b]**
Amikacin	69.8%	61.0%	66.5%	62.8%	66.2%	65.4%	68.2%	70.5%	67.7%	.46
Aztreonam	12.2%	12.8%	15.3%	13.7%	16.4%	9.9%	21.2%	19.7%	33.8%	.03
Cefepime	18.4%	18.2%	24.4%	31.8%	31.8%	28.2%	26.7%	22.4%	35.8%	.82
Ceftazidime	28.3%	36.6%	39.3%	38.4%	38.4%	36.0%	56.8%	53.6%	61.5%	<.001
Ciprofloxacin	19.4%	21.6%	25.8%	26.7%	26.7%	31.9%	20.8%	19.6%	26.0%	.93
Gentamicin	29.4%	28.7%	29.2%	37.9%	37.9%	40.2%	34.1%	38.1%	31.8%	.14
Imipenem	42.2%	40.7%	42.7%	31.9%	31.9%	46.9%	38.7%	37.7%	37.5%	.12
Levofloxacin	22.5%	21.4%	15.7%	15.0%	15.0%	21.0%	14.8%	21.8%	16.1%	.96
Mereopenem	60.3%	38.5%	55.3%	46.9%	46.9%	46.2%	54.2%	48.8%	62.0%	.46
Piperacillin/Tazobactam	46.4%	45.6%	55.1%	57.9%	57.9%	43.2%	66.4%	58.1%	55.4%	.10
Tobramycin	55.9%	50.7%	56.1%	60.9%	60.9%	68.0%	66.7%	67.9%	71.3%	.01

[a]Antibiotics represent only those relevant antibiotics against which ≥30 isolates were tested.
[b]*P*-values were established for a single antibiotic over time using a two-tailed Cochrane-Armitage trend test for linearity.
Data Source: NMCPHC HL7 formatted microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In 2013, carbapenems (ertapenem and meropenem) were the most common class of antibiotic used to treat MDR *P. aeruginosa* cases in the DON, regardless of the route of administration, followed by fluoroquinolones (ciprofloxacin, levofloxacin, and ofloxacin) and penicillin/β-lactamase inhibitor combinations (amoxicillin/clavulanate and piperacillin/tazobactam). Table 29 presents antibiotic prescriptions by class for the DON. The most commonly administered oral antibiotic was azithromycin, followed by piperacillin/tazobactam and ciprofloxacin. Meropenem was the most commonly prescribed IV antibiotic (data not shown).

Table 0-28. Antibiotic Prescriptions for MDR *Pseudomonas aeruginosa* in the DON, CY 2013

Class	Oral (N = 38)		Intravenous (N = 28)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	0	0.0	5	17.9	Tobramycin
Cephalosporins	3	7.9	6	21.4	Cefepime
Carbapenems	4	10.5	8	28.6	Meropenem
Glycylcyclines	0	0.0	1	3.6	Tigecycline*
Fluoroquinolones	9	23.7	2	7.1	Ciprofloxacin & Levofloxacin
Lincosamides	0	0.0	1	3.6	Clindamycin*
Macrolides	7	18.4	0	0.0	Azithromycin*
Monbactams	0	0.0	2	7.1	Aztreonam*
Nitroimidazoles	0	0.0	1	3.6	Metronidazole*
Nitrofurans	1	2.6	0	0.0	Nitrofurantoin*
Penicillins & Inhibitors	8	21.1	2	7.1	Piperacillin/Tazobactam
Polymyxins	3	7.9	0	0.0	Colistin*
Sulfonamides	0	0.0	0	0.0	Trimethoprim/Sulphmethoxazole*
Tetracyclines	3	7.9	0	0.0	Minocycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
[a]Cumulative count by class of antibiotic.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

In 2013, fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin) were the class of antibiotic most commonly used to treat MDR *P. aeruginosa* cases in the DOD regardless of the route of administration, followed by cephalosporins (cefazolin, cefepime, cefoxitin, cefpodoxime, ceftaroline, ceftazidime, ceftriaxone, and cefuroxime) and penicillins/β-lactamase inhibitor combinations (amoxicillin/clavulanate, ampicillin/sulbactam, and piperacillin/tazobactam). Table 30 presents antibiotic prescriptions by class for the DOD. The most commonly administered oral antibiotic was ciprofloxacin, followed by azithromycin and levofloxacin. Piperacillin/tazobactam was the most commonly prescribed IV antibiotic (data not shown).

Table 0-29. Antibiotic Prescriptions for MDR *Pseudomonas aeruginosa* in the DOD, CY 2013

Class	Oral (N = 191)		Intravenous (N = 111)		Antibiotic most frequently prescribed in class (overall)
	Count	Percent	Count	Percent	
Aminoglycosides	6	3.1	9	8.1	Tobramycin
Cephalosporins	33	17.3	25	22.5	Ceftriaxone
Carbapenems	5	2.6	23	20.7	Meropenem
Glycylcyclines	0	0.0	2	1.8	Tigecycline*
Fluoroquinolones	57	29.8	13	11.7	Levofloxacin
Lincosamides	3	1.6	2	1.8	Clindamycin*
Macrolides	2	1.0	3	2.7	Azithromycin
Monobactams	0	0.0	2	1.8	Aztreonam*
Nitroimidazoles	5	2.6	3	2.7	Metronidazole*
Nitrofurans	20	10.5	0	0.0	Nitrofurantoin*
Penicillins	4	2.1	1	0.9	Amoxicillin
Penicillins & Inhibitors	25	13.1	20	18.0	Piperacillin/Tazobactam
Sulfonamides	22	11.5	4	3.6	Trimethoprim/Sulphmethoxazole*
Tetracyclines	9	4.7	4	3.6	Doxycycline

N = Total number of antibiotics prescribed of that type (oral or intravenous).
*Only antibiotic in class prescribed.
[a]Cumulative count by class of antibiotic.
Data Source: NMCPHC HL7 formatted pharmacy database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 31 presents healthcare-associated infection metric rates for MDR *P. aeruginosa*. The rate of importation of MDR *P. aeruginosa* into DOD MTFs, as indicated by the admission prevalence rate, was 0.23 per 1,000 admissions, an increase from 0.18 per 1,000 admissions in 2012. The overall prevalence of MDR *P. aeruginosa* was 0.28 per 1,000 admissions, also an increase from 0.21 per 1,000 admissions in 2012. Infection burden rates were low in 2013 yet the HO bacteremia, HO UTI, and device-associated rates all increased from 2012, when MDR *P. aeruginosa* did not cause any of these types of infections. In 2013, the number of SSIs caused by MDR *P. aeruginosa* was 5 times that seen in 2012.

Table 0-30. Healthcare-Associated Infection Metrics for MDR *Pseudomonas aeruginosa* Cases among DOD Beneficiaries, 2013

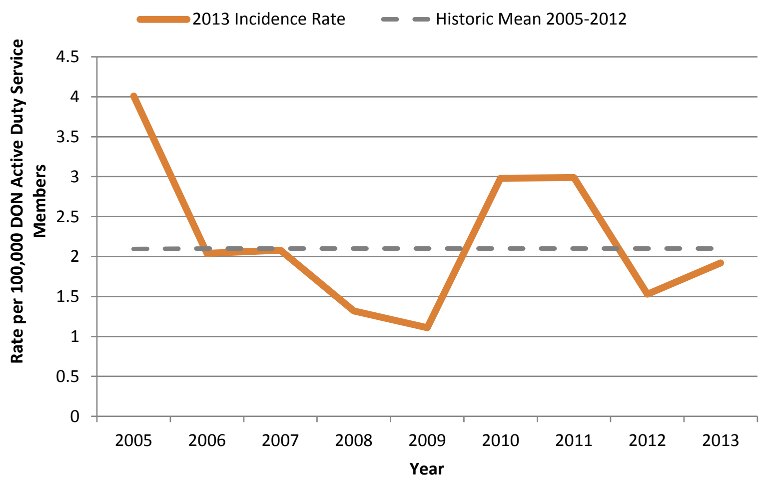
Metric	Rate/Density-Rate	
Exposure Burden		
Admission Prevalence	0.23	per 1,000 Admissions
Overall Prevalence	0.28	per 1,000 Admissions
Infection Burden		
HO Bacteremia	0.002	per 1,000 Patient-Days
HO UTI	0.003	per 1,000 Patient-Days
Device Associated		
CLABSI	0.02	per 1,000 Central-Line Days
VAP	0.03	per 1,000 Vent-Days
Procedure Associated		
SSI	0.01	Per 100 Procedures

Data Sources: SIDR and HL7 formatted microbiology databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 09 October 2014.

DON Active Duty

For 2013, there were 10 MDR *P. aeruginosa* cases identified among DON active duty service members, giving an overall incidence rate of 1.9 per 100,000 DON active duty service members per year. The 2013 rate was below the historic mean rate but was a 20.3% increase from 2012 (Figure 12).

Figure 12. Historical Trend of Multidrug-Resistant *Pseudomonas aeruginosa* Incidence in DON Active Duty Service Members with Mean Rate, CY 2005-2013



Historic mean rate calculated as the rate of DON active duty service member case counts per total number of DON active duty service members from 2005-2012.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 32 presents the demographics of active duty MDR *P. aeruginosa* cases in the DON in 2013. Cases most often occurred in females, 17 to 24 year olds, Marine Corps beneficiaries, and the North TRICARE service region.

Table 0-31. Demographics of Multidrug-Resistant *Pseudomonas aeruginosa* Burden among DON Active Duty Service Members, CY 2013

N = 10	Count	Percent
Gender		
Female	8	80.0
Male	2	20.0
Age Group (in years)		
17-24	5	50.0
25-34	3	30.0
35-44	2	20.0
45-64	0	--
65+	0	--
Sponsor Service		
Marine Corps	6	60.0
Navy	4	40.0
TRICARE Region		
Alaska	0	--
North	7	70.0
OCONUS	0	--
South	0	--
West	3	30.0
Unknown	0	--

Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 33 describes the clinical characteristics of MDR *P. aeruginosa* cases among DON active duty service members in 2013. Cases were mostly identified in the outpatient setting (60.0%) and from respiratory samples (60.0%). All of the inpatient DON active duty cases were CO. This indicates that organism acquisition for these cases was most commonly associated with exposure outside of the MHS.

Table 0-32. Clinical Description of Multidrug-Resistant *Pseudomonas aeruginosa* Burden among DON Active Duty Service Members, CY 2013

N = 10	Count	Percent
Encounter Type		
Inpatient	4	40.0
Outpatient	6	60.0
Healthcare Association[a]		
Hospital-onset (HO)	0	--
Healthcare-associated (HA)	0	0.0
Community-onset (CO)	4	100.0
Infection Type		
Urinary Tract	1	10.0
Blood Stream	0	--
Respiratory	6	60.0
Wound	0	--
Other	3	30.0
Level of Antibiotic Resistance		
Multidrug-Resistance (MDR)	10	100.0
Extensive drug-resistance (XDR)	0	--

[a]Percents calculated per number of inpatient encounters (N = 4).
Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

CENTCOM Related Deployments

DON service members deployed to the CENTCOM area of responsibility (AOR) had an MDR gram-negative bacterial incidence rate of 23.1 per 100,000 CENTCOM-deployed DON service members in 2013. Table 34 presents the demographics of DON CENTCOM deployment-related cases. The demographic groups with the highest prevalence rates were females, members between the ages of 17 and 24, Sailors, and members deployed to ships or unknown locations. MDR *E. coli* was the only MDR gram-negative bacteria identified among CENTCOM-related active duty service members in 2013, a slight change from 2012 where 12.9% of CENTCOM-related cases were MDR *Enterobacter* (data not shown).

Table 0-33. Demographics of Select Multidrug-Resistant Gram-Negative Bacteria[a] Burden among DON Active Duty Service Members Deployed in Support of CENTCOM Missions, CY 2013

N = 62	Count	Rate[b]
Gender		
Female	42	15.6
Male	20	7.4
Age Group		
17-24 years	42	15.6
25-34 years	11	4.1
≥35 years	9	3.4
Sponsor Service		
Marine Corps	11	4.1
Navy	51	19.0
Deployment Location[c]		
Afghanistan	6	2.2
Bahrain	5	1.9
Djibouti	1	*NR**
United Arab Emirates	1	*NR**
Kyrgyzstan	5	1.9
Afloat/Unknown	44	16.4

*Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
[a]Only MDR *E. coli* was identified in CY 2013 CENTCOM-deployed DON service members.
[b]Rates per 100,000 DON CENTCOM-related deployments.
[c]All deployments were in support of CENTCOM missions and reflect the country where the service member was located at the time of organism identification.
Data Sources: NMCPHC HL7 formatted microbiology and CTS databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 35 displays the clinical characteristics of MDR gram-negative bacterial cases among DON service members deployed in support of CENTCOM-related missions. Cases were primarily identified in the outpatient setting and from urinary tract samples. MDR *E. coli* was the primary organism identified. No XDR, PDR, or CRE cases were identified among CENTCOM-related deployments.

Table 0-34. Clinical Description of Select Multidrug-Resistant Gram-Negative Bacterial Infections among DON Active Duty Service Members Deployed in Support of CENTCOM Missions, CY 2013

N = 62	Count	Percent
Encounter Type		
Inpatient	4	6.5
Outpatient	58	93.5
Infection Type		
Urinary Tract	42	67.7
Blood Stream	4	6.5
Respiratory	0	--
Wound	0	--
Other	16	25.8
Species		
MDR *E. coli*	62	100.0
MDR *Klebsiella* species	0	--
MDR *Enterobacter* species	0	--
MDR *P. aeruginosa*	0	--
Carbapenem Resistant Enterobacteriaceae		
E. coli	0	--
Klebsiella species	0	--

Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

DON Recruits

DON recruits had an overall incidence rate of 102.8 per 100,000 DON recruits per year for all MDR gram-negative bacterial cases surveyed in 2013. Table 36 presents the demographics of DON recruit cases in 2013. Demographics with the highest prevalence rates were females, recruits between the ages of 17 and 24, and Navy recruits.

Table 0-35. Demographics of Multidrug-Resistant Gram-Negative Bacteria Burden among DON Recruits, CY 2013

N = 79	Count	Rate[a]
Gender		
Female	71	554.5
Male	8	12.5
Age Group		
17-24 years	71	98.6
25-34 years	8	10.4
≥35 years	0	*NR**
Sponsor Service		
Marine Corps	27	77.2
Navy	52	124.2

*Rates for counts of <5 are not statistically relevant and therefore not reportable (NR).
[a]Rates per 100,000 recruits per year.
Data Sources: NMCPHC HL7 formatted microbiology and M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table 37 displays the clinical characteristics of DON recruit MDR gram-negative bacteria cases. Cases predominantly occurred in the outpatient setting and predominantly from urinary tract samples. No XDR, PDR, or CRE cases were identified among DON recruits. MDR *E. coli* was the most commonly identified organism, followed by MDR *Enterobacter* species; in 2012 there were recruit cases of MDR *Klebsiella*. The organism with the highest incidence rate was MDR *E. coli* (73.5 per 100,000 DON recruits) (data not shown).

Table 0-36. Clinical Description of Multidrug-Resistant Gram-Negative Bacteria Burden among DON Recruits, CY 2013

N = 79	Count	Percent
Encounter Type		
Inpatient	1	1.3
Outpatient	78	98.7
Infection Type		
Urinary Tract	78	98.7
Blood Stream	0	--
Respiratory	0	--
Wound	0	--
Other	1	1.3
Species		
MDR *E. coli*	76	96.2
MDR *Klebsiella* species	0	--
MDR *Enterobacter* species	3	3.8
MDR *P. aeruginosa*	0	--
Carbapenem Resistant Enterobacteriaceae		
E. coli	0	--
Klebsiella species	0	--

Data Sources: NMCPHC HL7 formatted microbiology and SIDR databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Discussion

Among all MDR gram-negative bacteria cases evaluated for this report, incidence increased from 2012 to 2013. For MDR *E. coli* and MDR *Enterobacter*, these increases were above the organisms' established baselines. Conversely, MDR *Klebsiella* and MDR *P. aeruginosa* had incidence rates below their established baselines. Of the four organisms analyzed here, MDR *E. coli* had the highest incidence in both the DON and DOD. The incidence rates for MDR *E. coli* in the DON and DOD were 40.3 and 37.3 times higher, respectively, than the MDR gram-negative organism with the next highest incidence rates, MDR *Klebsiella*. Additionally, the 2013 incidence rates for MDR *Klebsiella*, MDR *Enterobacter*, and MDR *P. aeruginosa* in both the DON and DOD displayed analogous incidence rates and similar overall downward directionality of trends from 2005-2013. These observations are consistent with historical trends.

The incidence trends for DON active duty service members showed some similarities and some differences to the trends in the general DON and DOD beneficiary populations. DON active duty MDR *E. coli* incidence was quite similar to incidence in the general DON and DOD beneficiary populations from 2005-2013; rates for MDR *E. coli* in DON beneficiaries and DON active duty service members from 2012 to 2013 increased and were both above the established baseline for the respective populations. MDR *Enterobacter*, among DON active duty service members, decreased from 2005-2013 at 52.4% overall. The incidence of MDR *Klebsiella* in 2013 among DON active duty service members did increase since 2012, however the 2013 rate remained below the baseline and demonstrated an overall descending trend from 2005-2013. MDR *P. aeruginosa* did not demonstrate any consistent pattern during the surveillance period, with several fluctuations observed throughout 2005-2013 for DON active duty service members. For this organism, DON active duty service members showed an increase in incidence from 2012 to 2013, but incidence rates remained below the baseline.

While generalizations about the incidence of MDR gram-negative bacteria can be deduced for the general DON populations due to the existence of common patterns, the same cannot be said of MDR gram-negative bacteria among DON active duty service members. In the general DON and DOD beneficiary populations, incidence rates for each of the four organisms were relatively stable or contained normal fluctuations. In comparison, the DON active duty service member population demonstrated different trends for each organism. From 2005-2013, MDR *E. coli* displayed an increasing trend in incidence, MDR *Enterobacter* showed a large decrease, MDR *Klebsiella* showed a drop followed by stabilization, and MDR *P. aeruginosa* showed numerous fluctuations. These organisms must therefore be monitored and evaluated individually to provide accurate descriptions for each within the active duty population.

For each population and organism in this report, except for MDR *P. aeruginosa*, UTIs were the most common infection type and females were the most heavily impacted demographic group. Gram-negative bacteria, most notably *E. coli*, are common causes of UTIs among females of reproductive age.[19-21] This holds true for female beneficiaries seeking care in the MHS. Additionally, it is becoming more common for *E. coli* UTIs to be caused by MDR *E. coli*.[21] In the DON and DOD, except for MDR *Enterobacter* in the DON, females were consistently the most impacted demographic with prevalence rates far above their male counterparts. For MDR *E. coli*, the rate among females in the DON was 88.4% higher than DON males; for MDR *Klebsiella*, females had a prevalence rate 78.7% higher than males. In the DOD, the prevalence among females for MDR *E. coli* was 87.8% higher than males, 14.3% higher than males for MDR *Enterobacter*, and 53.8% higher than males for MDR *Klebsiella*. In the CENTCOM-related deployment population, the prevalence rate for MDR *E. coli* among female DON service members was 52.6% higher than males. Finally, among DON recruits, female prevalence of MDR gram-negative bacteria, of which only *E. coli* was identified, was 97.7% higher than males.

Further analysis of female UTIs related to the gram-negative organisms in this report showed that virtually all were among females of reproductive age. Given these findings, it can be concluded that the gender disparity that exists for MDR gram-negative bacteria (*E. coli*, *Enterobacter*, and *Klebsiella*) incidence and prevalence in the DON and DOD is not of major concern due to the demographics of the people affected. This gender disparity is not surprising and follows patterns similar to those identified in the general US population. While this indicates that there is not great cause for concern, it does not mean that this should be ignored. As previously stated, resistant infections pose serious challenges to clinical treatment.[6,19-21] To ensure that viable treatments remain available for UTIs and to prevent organisms causing UTIs from increasing in resistance and/or passing resistant determinants to other organisms, strict antimicrobial stewardship, treatment using individual organism resistance patterns as well as local antibiograms, and patient education are advised to prevent the propagation of these organisms and their progression to higher levels of resistance. Though MDR *P. aeruginosa* may cause UTIs, the low prevalence among these cases was expected for this organism as it is more commonly identified as a respiratory pathogen,[22] which is consistent with the findings reported here.

Antibiotic susceptibilities were relatively consistent for most of the MDR gram-negative organisms discussed in this report. Most isolates displayed high susceptibilities to several tested antibiotics, making population-level generalizations about susceptibility patterns possible for MDR *E. coli*, MDR *Enterobacter*, and MDR *Klebsiella*. MDR *P. aeruginosa*, however, posed a challenge in this regard. Isolates of MDR *P. aeruginosa* did not show susceptibilities over 72.0% to any antibiotics at the population level. Further stratification of antibiotic susceptibilities for MDR *P. aeruginosa* by geographic region did not provide any conclusive evidence of a particular region that was impacting the overall susceptibility patterns; all regions displayed a consistent low susceptibility to all antibiotics tested. Carbapenems, are a class of antibiotics typically reserved as a treatment of last resort[23], yet MDR *P. aeruginosa* had susceptibilities of 37.5% to imipenem and 62.0% to meropenem. Even these antibiotics of last resort display very low susceptibilities to MDR *P. aeruginosa* at the population level. However, at the individual level, isolates regularly had at least one antibiotic that it was susceptible to. Of note is that among all MDR *P. aeruginosa* cases, 6.2% (N = 13) of isolates were non-susceptible to all antimicrobials tested; of those, 10 isolates were resistant to all antimicrobials tested. This indicates that recommendations for the treatment of MDR *P. aeruginosa* cannot be made at the population level and should therefore be based on individual susceptibility patterns. Likewise, empirical treatment should be guided by facility-specific antibiograms prior to receipt of individual susceptibilities for the best results. Further, routine review of local empirical treatment guidance for MDR *P. aeruginosa* should be undertaken and updated as appropriate given any changes identified in local susceptibility patterns.

P. aeruginosa is an extremely common cause of HAIs, so common that it occurs with predictable frequency in healthcare facilities.[24] Additionally, the finding that all *P. aeruginosa* cases reported here had very limited antibiotic treatment options is cause for concern because the low susceptibilities reported indicates that certain strains present in healthcare facilities have no viable antibiotic treatment options. *P. aeruginosa* has multiple intrinsic mechanisms for antibiotic resistance.[25] If resistance spreads among isolates of *P. aeruginosa* as well as to other gram-negative bacteria with the ability to acquire resistance determinants, or if the level of resistance increases, there will be even greater numbers of untreatable *P. aeruginosa* infections. This may lead to a group of complicated infections with few or no options for treatment, by creating endemic conditions of an incurable bacterial infection that could be disastrous in the hospital environment. *P. aeruginosa* is primarily a nosocomial pathogen and rarely causes disease in healthy individuals,[24] suggesting that those presenting with *P. aeruginosa* likely had some underlying or comorbid condition (e.g. cystic fibrosis, which accounts for 6.2% of MDR *P. aeruginosa* cases in this report). The current analysis did not account for the presence or severity of underlying or comorbid conditions for individuals identified with MDR *P. aeruginosa*, yet it can be assumed, based on the available evidence, that *P. aeruginosa* does not typically infect those with healthy immune systems and is primarily a nosocomial pathogen, and that each of these individuals likely had some underlying or comorbid condition that allowed MDR *P. aeruginosa* to cause a secondary infection or exacerbate an existing one. While MDR *P. aeruginosa* is, for the moment, primarily confined to the healthcare setting, providers must be judicious in controlling the proliferation of this organism.

This annual report summarized MDR *E. coli*, MDR *Enterobacter*, MDR *Klebsiella*, and *MDR P. aeruginosa* rates and characteristics in the DON and DOD beneficiary populations in 2013 and reported changes from previously identified trends. Given the association of gram-negative bacteria, particularly *E. coli*, with common types of infection, namely female UTIs, and the recent increase in common infections caused by resistant bacteria, it is important to monitor and manage the significant risk presented by MDR organisms, which have the ability to confer resistance to other bacteria within and outside their respective genus to control the proliferation of resistance to other infection types. Continued surveillance of these organisms is recommended.

Limitations

HL7 formatted data are generated within the CHCS at fixed MTFs. Microbiology testing results only list the organism(s) that were identified, not the intended tests (e.g., if a physician suspects an organism different from the one that was identified, the record will not show the organism that the physician suspected). Microbiology data are used to identify laboratory-confirmed cases of illness. However, the microbiology data does not capture cases in which a physician chose to treat presumptively without laboratory confirmation. Clinical practices also vary among providers and facilities. For example, some clinicians may not perform cultures for confirmatory tests for patients with influenza-like illness symptoms or for patients with superficial infections who are treated presumptively. Therefore, the isolate counts here are likely an underestimate of the actual burden of the various MDR gram-negative bacteria in the DOD.

The use of microbiology data for analysis of antibiotic resistance is limited by the practice of cascade reporting, where antibiotic sensitivity results are conditionally reported to CHCS to guide treatment decisions. DOD MTFs practice cascade reporting to varying degrees. Furthermore, not all laboratories in the DOD operate under the same version of CLSI guidelines. As a result, certain facilities use guidelines with outdated antibiotic susceptibility breakpoints and may incorrectly report some susceptibilities. Thus, the EDC cannot project a complete picture of the susceptibility patterns for these MDR gram-negative organisms and the presumption of reduced susceptibility is applied to all antibiotics in a class if an isolate is shown to be resistant to that class. The may have led to some misclassifications of the level of resistance. This report therefore may be an underestimate of true MDR and/or XDR burden in the DOD.

A SIDR is created at discharge or transfer from an inpatient MTF for all TRICARE beneficiaries. For active duty personnel, this occurs for non-military medical treatment facility discharges as well. Data for medical surveillance are considered provisional and medical case counts may change if the discharge record is edited after the patient is discharged from the MTF. As this report presents an annual summary and several months were allotted in the new year to account for possible data lag and record corrections, it can be presumed with relative certainty that the records identified are the final and complete records for an inpatient encounter; however, the possibility does exist that records still may be modified, thereby altering the case counts. SIDR data are also limited in that it is difficult to associate a specific microbiology record with an anatomical location of an injury, particularly when a patient has multiple injuries identified in the record. This makes it difficult to definitively link an injury to a specific infection difficult. Ambulatory records are created at the close out of an outpatient medical encounter at DOD MTFs for all TRICARE beneficiaries.

DMDC stores data on service members using multiple rosters. The active duty roster lists all active duty service members and should include activated reservists. However, anecdotal analyses conducted by the EDC suggest that not all activated reservists are included on the active duty roster. Additionally, DMDC records are created only once a month. If a reservist was activated after his or her record was created, the record would not reflect the change in status until the following month. While this is the exception and not the standard for DMDC records, identification of active duty service members is incomplete as a result.

Providers may not have prescribed the antibiotics in response to the MDR gram-negative bacteria identified in this report. It is possible that antibiotics dispensed around the same timeframe as the positive gram-negative culture reflect treatment for other reasons. Additionally, cases where a physician chose to treat presumptively were not captured because HL7 formatted microbiology records were used to define cases.

All the above mentioned databases are limited in that they do not include data from purchased care providers, shipboard facilities, battalion aid stations, or in-theater facilities. Therefore, these results are only an estimate of the true MDR gram-negative bacterial burden in the DON and DOD. In addition, the proportion of cases imported from outside the treating MTF's geographic area is unknown.

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Appendix

Table A-1. Antibiotic Resistance Definitions and Antibiotic Classes[a] Used to Classify Them for Gram-Negative Bacteria in the DOD, CY 2013

	Aminoglycosides	Anti-MRSA cephalosporins	Antipseudomonal carbapenems	Antipseudomonal cephalosporins	Antipseudomonal fluroquinolones	Antipseudomonal penicillins+inhibitors	Carbapenems	Cephamycins	Extended Specturm cephalosporins	Fluorquinolones	Folate Pathway Inhibitors	Glycylcyclines	Monobactams	Non-extended spectrum cephalosporins	Penicillins	Penicillins+inhibitors	Phosphoric acids	Polymyxins	Tetracyclines
Enterobacter species[b]	x					x	x	x	x	x	x	x	x	x	x	x	x	x	x
Escherichia coli[b]	x	x				x	x	x	x	x	x	x	x	x	x	x	x	x	x
Klebsiella species[b,c]	x	x				x	x	x	x	x	x	x	x	x		x	x	x	x
Pseudomonas aeruginosa[b]	x		x	x	x	x							x				x	x	
Carbapenem-Resistant Enterobacteriaceae[d]	Non-susceptbile[e] to a carbapenem and resistant to all 3rd generation cephalosporins tested																		

[a]See Table A-2 for a list of antibiotics used in each class.
[b]MDR: Non-susceptible to ≥1 antibiotic in ≥3 of the marked classes.
XDR: Non-susceptible to ≥1 antibiotic in all but ≤2 of the marked classes.
PDR: Non-susceptible to ≥1 antibiotic in all the marked classes.
[c]Anti-MRSA cephalosporins used only for *K. pneumoniae* and *K. oxytoca*.
[d]Used for *E. coli* and *Klebsiella* species only.
[e]Non-susceptible: resistant or intermediately susceptible to a given antibiotic.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Table A-2. Antibiotics Included in the Resistance Definitions for Gram-Negative Bacteria in the DOD, CY 2013

Antibiotic Class	Antibiotics Inlcuded in Class
Aminoglycosides	Amikacin
	Gentamicin
	Netilmicin
	Tobramycin
Anti-MRSA cephalosporins[a]	Ceftaroline
Antipseudomonal penicillins & β-lactamase inhibitors	Piperacillin/Tazobactam
	Ticarcillin/Clavulanic Acid
Carbapenems	Doripenem
	Ertapenem[b]
	Imipenem
	Meropenem
1st & 2nd Generation Cephalosporins (non-extended specturm cephalosporins)	Cefazolin
	Cefuroxime
3rd & 4th Gneration Cephalosporins (Extended spectrum cephalosporins)	Cefotaxime or ceftriaxone
	Ceftazidime
	Cefepime
Cephamycins	Cefoxitin
	Cefotetan
Fluoroquinolones	Ciprofloxacin
	Levofloxacin[c]
Folate pathway inhibitors	Trimethoprim/Sulfamethoxazole
Glycylcyclines	Tigecycline
Monobactam	Aztreonam
Penicillins	Ampicillin
Penicillins & β-lactamase inhibitors	Amoxicillin/Clavulanic Acid
	Ampicillin/Sulbactam
Phenicols	Chloramphenicol
Phosphoric Acid	Fosfomycin
Polymyxins	Colistin
	Polymyxin B[c]
Tetracyclines	Doxycycline
	Minocycline
	Tetracycline

[a]Included only for *Escherichia coli*, *Klebsiella pneumoniae*, and *K. oxytoca*.
[b]Antibiotic excluded for *Pseudomonas aeruginosa*.
[c]Antibiotic included only for *P. aeruginosa*.
Source: Magiorakos et al., 2012[9].
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 02 October 2014.

Acronym/Abbreviation List

Acronym/Abbreviation	Definition
AOR	Area of Responsibility
BSI	Blood stream infection
CAUTI	Catheter-associated urinary tract infection
CENTCOM	United States Central Command
CHCS	Composite Health Care System
CLABSI	Central-line associated blood stream infection
CLSI	Clinical and Laboratory Standards Institute
CO	Community-onset
CRE	Carbapenem-Resistant Enterobacteriaceae
CTS	Contingency Tracking System
CY	Calendar year
DHSS	Defense Health Surveillance System
DMDC	Defense Manpower Data Center
DMIS ID	Defense Medical information System Identification Number
DOD	Department of Defense
DON	Department of the Navy
EDC	EpiData Center
HA	Healthcare-associated
HAI	Healthcare-associated infection
HL7	Health Level 7
HICPAC	Hospital Infection Control Practices Advisory Committee
HO	Hospital-onset
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
IV	Intravenous
M2	MHS Mart
MDR	Multidrug-resistant
MDRO	Multidrug-Resistant Organism
MEPRS	Medical Expense and Performance Reporting System
MHS	Military Health System
MTF	Military Treatment Facility
NHSN	National Healthcare Safety Network
OBS	Operation Bright Star
OCONUS	Outside of the continental United States
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OP	Outpatient
PDR	Pandrug-resistant
SHEA	The Society for Healthcare Epidemiology of America
SIDR	Standard Inpatient Data Record
SSI	Surgical site infection
UD	Unit dose
US	United States
USNS	United States Naval Ship
UTI	Urinary tract infection
VAP	Ventilator-associated pneumonia
WHO	World Health Organization
XDR	Extensively drug-resistant

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