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

NMCPHC-EDC-TR-408-2018

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14. ABSTRACT
The EpiData Center Department conducts routine surveillance of Klebsiella species incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for infections in calendar year 2017. Overall, incidence rates of Klebsiella species infections in the MHS beneficiary and DOD active duty populations decreased in 2017. Klebsiella demonstrated low susceptibility to nitrofurans (46.6%), yet nitrofurans were one of the most frequently prescribed classes of drugs for Klebsiella infection in 2017 (34.2% of all prescriptions). Further investigation is warranted.

15. SUBJECT TERMS
Health Level 7 (HL7), microbiology, surveillance, Klebsiella species, Military Health System (MHS), antibiotic resistance, nitrofurans, nitrofurantoin

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Abstract

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

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

Overall, incidence rates (IRs) of *Klebsiella* species infections in the MHS beneficiary and DOD AD populations decreased in 2017. The annual *Klebsiella* species IR decreased by 4.9% compared to the weighted historic IR; this decrease was within expected variation of *Klebsiella* species infections in the MHS population. Fluoroquinolones present better treatment options compared to nitrofurans based on susceptibility analysis. Nitrofurans, despite being one of the most frequently prescribed classes of drugs (34.2% of all prescriptions) for *Klebsiella* infections, presented lowest efficacy (46.6%). Therefore, the current use of nitrofurantoin as a treatment option for *Klebsiella* species infections within the MHS population warrants further investigation. Current infection control practices appear effective and continued surveillance is recommended.

Contents

Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns for *Klebsiella* species infections among Military Health System (MHS) beneficiaries. This report presents analytical results and discussion of CY 2017 data for *Klebsiella* species infections in the MHS.

The background, methods, and limitations relevant to this analysis have been discussed in previous reports (CY 2015 and 2016 annual reports for *Klebsiella* species[1,2]). The CY 2017 report does not include an analysis of burden associated with deployment-related infections using Contingency Tracking System (CTS) data; all other methods and limitations are the same as in recent years. Recent literature reviews did not present any relevant developments in *Klebsiella* species research since CY 2016 analyses.

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

Results

Section A – Descriptive Epidemiology
Incidence of *Klebsiella* species

In 2017, the annual incidence rate (IR) for *Klebsiella* species infection among MHS beneficiaries treated at a military treatment facility (MTF) was 94.8 per 100,000 persons per year. This reflects a 4.9% change below the weighted historic IR. Similar decreases were demonstrated within the Air Force, Army, Marine Corps, and Navy beneficiary populations. The Air Force experienced an 8.8% decrease in *Klebsiella* species infections, which was more than two standard deviations below the weighted historic IR. However, the 2017 IRs are within two standard deviations of the weighted historic IRs of *Klebsiella* in the MHS beneficiary, Army, Navy, Marine Corps, and Department of Defense (DOD) active duty (AD) populations (Table 1).

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

Population	2017 IR	Weighted Historic[a] IR 2014 - 2016	Two Standard Deviations: Weighted Historic[a] IR	2017	
				Direction	Percent Change[b]
MHS Beneficiaries	94.8	99.7	8.2	↓	4.9%
Air Force	83.6	91.7	3.6	↓	8.8%
Army	98.1	100.6	10.5	↓	2.4%
Marine Corps	83.2	87.3	7.6	↓	4.8%
Navy	87.0	92.8	9.9	↓	6.2%
DOD Active Duty	89.4	92.7	8.3	↓	3.5%

Rates are presented as the rate per 100,000 persons per year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
[a] Historic IR reflects the weighted average of the three years prior to the analysis year.
[b] This reflects the percent change from the weighted historic IR to the IR of the current analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Demographic Distribution of *Klebsiella* species

In 2017, there were 8,908 incident *Klebsiella* species infections identified among all MHS beneficiaries treated at an MTF. The IR among females (149.9 per 100,000 persons) exceeded that of males (41.7 per 100,000 persons) by 3.5 times. By age, IRs were relatively evenly distributed across all groups with the exception of the age group 0 to 17, which represented the lowest incidence (27.2 per 100,000 persons). IRs for other age groups ranged from 97.2 per 100,000 (age group 25-34) to 120.5 per 100,000 (age group 65+). By beneficiary type, retirees demonstrated the lowest rates (58.0 per 100,000 persons) (Table 2).

Table 2. Demographic Characteristics of *Klebsiella* species Infections in the MHS, CY 2017

	N = 8,908	
	Count	**Rate**
Gender		
Female	6,911	149.9
Male	1,997	41.7
Age Group (in Years)		
0-17	531	27.2
18-24	1,247	110.3
25-34	1,151	97.2
35-44	871	102.9
45-64	2,410	117.9
65+	2,698	120.5
Beneficiary Type		
Active Duty	1,215	89.4
Family Members	5,667	103.7
Retired	1,275	58.0
Other[a]	751	--

[a] Rate is not reported due to variation in population denominator.
Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
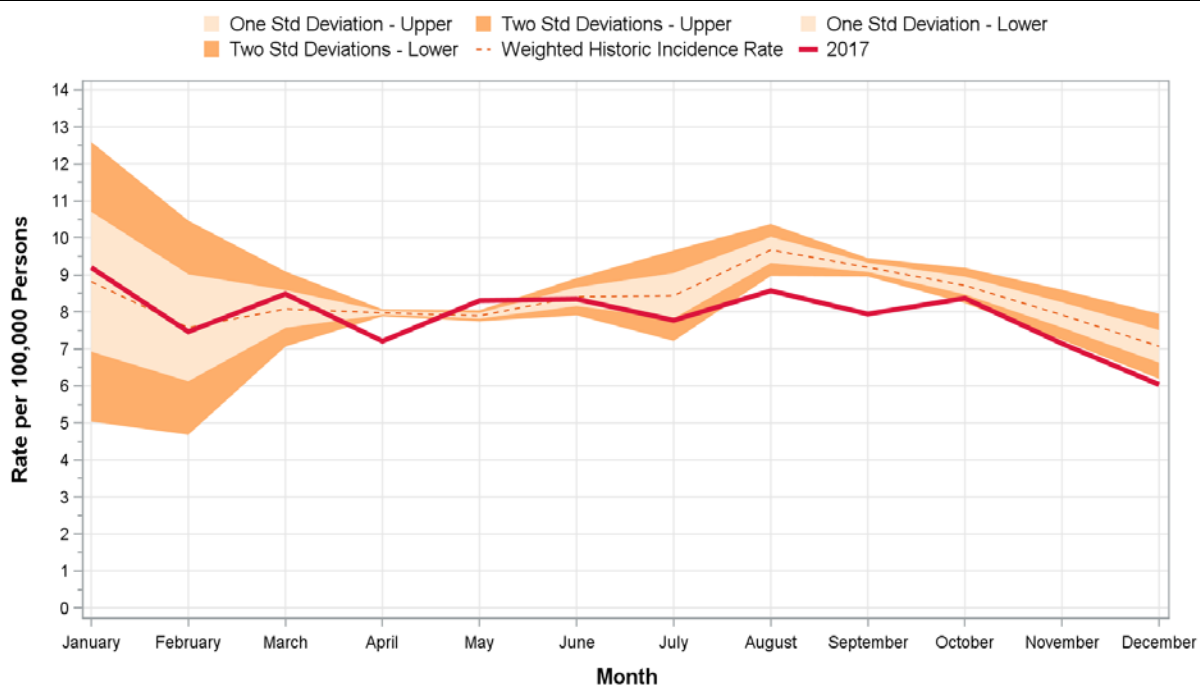Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Seasonality

Monthly IRs of *Klebsiella* species infections in 2017 were lower than the weighted historic IR for the majority of the calendar year. Most monthly rates were within two standard deviations of the weighted historic IR, except for the rates in April, August, and September, which were more than two standard deviations lower than the weighted historic IR, and the rate in May, which was more than two standard deviations higher than the weighted historic IR. The IRs in January and March were higher than, but within two standard deviations of, the weighted historic IR. Monthly IRs were consistently lower than weighted historical rates from July to December.

Figure 1. Monthly Incidence of *Klebsiella* species Infections and Weighted Historic Incidence Rate (IR) Comparisons in the MHS, CY 2017

Rates are presented as the rate per 100,000 persons per year.
Bands indicate one and two standard deviations above and below the weighted historic monthly IRs.
The weighted historic monthly IR is a weighted average of the three years prior to the analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Klebsiella species Clinical Characteristics

There were 9,981 prevalent *Klebsiella* species infections identified among all MHS beneficiaries treated at an MTF in 2017. The infection burden was higher in the outpatient setting (92.1%) and generally consisted of non-invasive infections (97.2%). Most specimens were collected from urine samples (87.1%), and collection sites from a skin or soft tissue infection (SSTI) or wound represented the second highest proportion (5.3%). The majority of prevalent infections were caused by *K. pneumoniae* (89.4%), followed by *K. oxytoca* (9.0%) (Table 3). Invasive infections were primarily collected from blood samples (n=177; 63.7%), followed by respiratory samples (n=62; 22.3%) (data not shown).

Table 3. Clinical Characteristics of *Klebsiella* species Prevalent Infections in the MHS, CY 2017

	N = 9,981	
	Count	Percent
Specimen Collection Location		
Inpatient	789	7.9
Outpatient	9,192	92.1
Infection Type		
Invasive	278	2.8
Non-Invasive	9,703	97.2
Body Collection Site		
Blood	177	1.8
Respiratory	332	3.3
SSTI/Wound	531	5.3
Urine	8,692	87.1
Other	249	2.5
Organism Species		
Klebsiella oxytoca	902	9.0
Klebsiella ozaenae	61	0.6
Klebsiella pneumoniae	8,928	89.4
Klebsiella rhinoscleromatis	2	0.0
Klebsiella species	88	0.9

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

Exposure Burden Metrics

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

The admission MDRO prevalence rate measures the rate of *Klebsiella* species importation into the MHS and includes 1) hospitalized patients in 2017 that tested positive for infection within the first three days of admission and 2) all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016. The 2016 samples are included in the calculation of admission prevalence to estimate the reservoir of *Klebsiella* impacting the MHS. In 2017, the admission MDRO prevalence rate for *Klebsiella* species was 1.2 per 1,000 inpatient admissions. Within the MHS, locations outside the continental United States (OCONUS) had the highest rate of admission MDRO prevalence (1.7 per 1,000 inpatient admissions). The US Northeast region did not have any prevalent cases of inpatient admission *Klebsiella* species.

The overall MDRO prevalence rate measures the cumulative community reservoir and healthcare-associated exposure burden for *Klebsiella* species and includes 1) hospitalized patients in 2017 that tested positive for the infection at any time during admission and 2) all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016. The 2016 samples are included in the calculation of the overall prevalence rate to estimate the reservoir of *Klebsiella* species impacting the MHS. In 2017, the overall MDRO prevalence rate for *Klebsiella* species was 1.4 per 1,000 inpatient admissions. The OCONUS region had 1.9 overall MDRO prevalent admissions per 1,000 inpatient admissions; the US South, US South Atlantic, and US West had rates within 1.4 to 1.5 per 1,000 inpatient admissions.

By definition, admission MDRO prevalence infections are included in the calculation of the overall MDRO prevalence rate. In 2017, the admission prevalence rate comprised 86.8% of the overall prevalence rate of *Klebsiella* species in the MHS (1.2 of the 1.4 per 1,000 inpatient admissions). This suggests that the majority of *Klebsiella* species infections were imported into the MHS from the community reservoir.

Table 4. MDRO Community- and Healthcare-Associated Exposure Burden Metrics among *Klebsiella* species in the MHS, CY 2017

	Admission MDRO Prevalence[a]		Overall MDRO Prevalence[b]		Percentage[d] of Admission (Imported) Prevalent Infections among Overall Prevalent Infections
	Count	Rate[c]	Count	Rate[c]	
Region					
OCONUS	27	1.7	30	1.9	90
US Midwest	8	--	9	--	88.9
US Northeast	0	--	0	--	--
US South	62	1.2	74	1.4	83.8
US South Atlantic	95	1.2	107	1.4	88.8
US West	91	1.3	106	1.5	85.8
Total	283	1.2	326	1.4	86.8

[a] Admission MDRO prevalence included hospitalized patients in 2017 that tested positive for infection within the first three days of admission and all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016.
[b] Overall MDRO prevalence included hospitalized patients in 2017 that tested positive for the infection at any time during admission and all other hospitalized patients in 2017 that tested positive for the infection or colonization in 2016.
[c] Rates are presented as the rate per 1,000 inpatient admissions per year. Rates are not provided when the prevalence count is less than or equal to 10.
[d] Percentage reflects the proportion of MDRO infections that were imported into the healthcare system in the calendar year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and SIDR databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

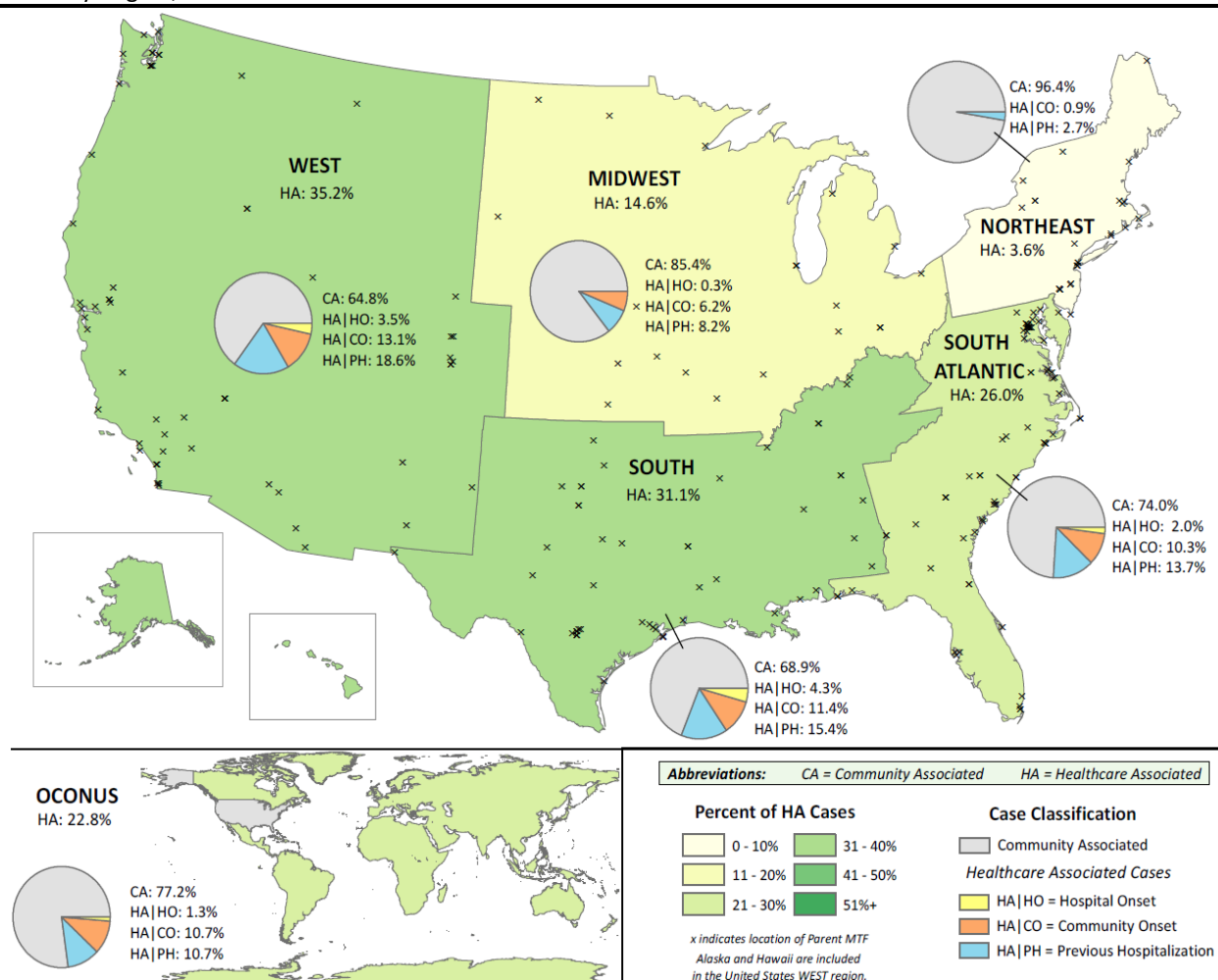## Regional Epidemiologic Infection Classifications

Among all prevalent *Klebsiella* species infections identified in the MHS in 2017, 71.4% were community-associated (CA) cases and 28.6% were healthcare-associated (HA) cases. Regionally, the US West reported the highest proportion of HA *Klebsiella* species cases (35.2%), followed by the US South (31.1%), US South Atlantic (26.0%), OCONUS (22.8%), US Midwest (14.6%), and the US Northeast (3.6%) (Figure 2).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Among all prevalent *Klebsiella* species infections (regardless of HA or CA classification or region), the highest proportion were classified as PH cases (14.8%). Although PH cases comprised 14.8% of all prevalent *Klebsiella* species infections, the PH category accounted for 51.8% of HA cases, indicating that slightly more than half the proportion of all HA *Klebsiella* species infections were associated with a prior hospitalization in the previous 12 months. The second largest proportion of all prevalent infections were CO cases (11.0%), indicating that the specimens were collected within the first three days of hospital admission and therefore the infections most likely originated from the community; CO cases comprised 38.4% of HA cases. Only 2.8% of prevalent *Klebsiella* species infections were HO, indicating that the infection was identified after the third day of admission and likely contracted during the current hospitalization (data not shown). HO cases comprised 9.7% of the HA cases.

A similar distribution of HA case classifications were observed by region, where PH cases accounted for the largest proportion, followed by CO cases and HO cases (Figure 2). By region, PH cases represented approximately half of all HA cases in the West, Midwest, South, South Atlantic, and OCONUS regions. In the Northeast region, previous hospitalizations accounted for three-fourths of all HA cases (Figure 2).

Figure 2. Proportion of Healthcare- and Community-Associated Cases among *Klebsiella* species Infection in the MHS by Region, CY 2017

Abbreviations: CA = Community Associated   HA = Healthcare Associated

Percent of HA Cases

0 - 10%	31 - 40%	
11 - 20%	41 - 50%	
21 - 30%	51%+	

x indicates location of Parent MTF
Alaska and Hawaii are included
in the United States WEST region.

Case Classification

Community Associated

Healthcare Associated Cases

HA|HO = Hospital Onset
HA|CO = Community Onset
HA|PH = Previous Hospitalization

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

Section B – Antimicrobial Resistance and Use
### Regional Multidrug Resistance

In 2017, the IR of *Klebsiella* species infection was 94.8 infections per 100,000 persons per year; the IR of drug-resistant *Klebsiella* species infection (i.e., resistant to antibiotics in at least three classes) was 7.2 infections per 100,000 persons per year. Regionally, the US South (115.0 per 100,000 persons), US South Atlantic (107.0 per 100,000 persons), and US West (104.4 per 100,000 persons) had the highest total IRs. OCONUS locations had a total IR of 94.6 per 100,000 persons. The US Midwest and US Northeast regions accounted for the lowest total *Klebsiella* species IRs by region (52.9 per 100,000 persons and 16.7 per 100,000 persons, respectively) (Figure 3).

Prevalent drug-resistant *Klebsiella* species infections are further categorized by drug-resistance type; among the 796 drug-resistant prevalent infections identified during 2017, 55.5% (n=442) were classified as MDR and 44.5% as possible extensively drug-resistant (PXDR) (n=354) (data not shown). These two drug-resistant *Klebsiella* classifications are described as a proportion of all prevalent infections by region in Figure 3. OCONUS locations, as a group, account for the largest proportion of prevalent infections classified as PXDR (5.4%), followed by the US West (5.2%), US South (3.5%), US South Atlantic (2.5%), and US Midwest (1.8%) regions. The US Northeast region did not have any prevalent infections classified as PXDR (Figure 3).

Prevalent *Klebsiella* species infections were also assessed for carbapenem resistance. Of the 9,981 prevalent infections identified among MHS beneficiaries in 2017, 0.30% (n=30) were classified as carbapenem-resistant (CR). The majority of CR *Klebsiella* species infections during 2017 occurred among beneficiaries in the US South (n=12), followed by those in the US South Atlantic (n=9) and US Midwest and OCONUS (n=4, each). One infection was identified in the US West region; there were no CR *Klebsiella* species infections in the US Northeast.

Figure 3. Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among *Klebsiella* species Infections in the MHS by Region, CY 2017
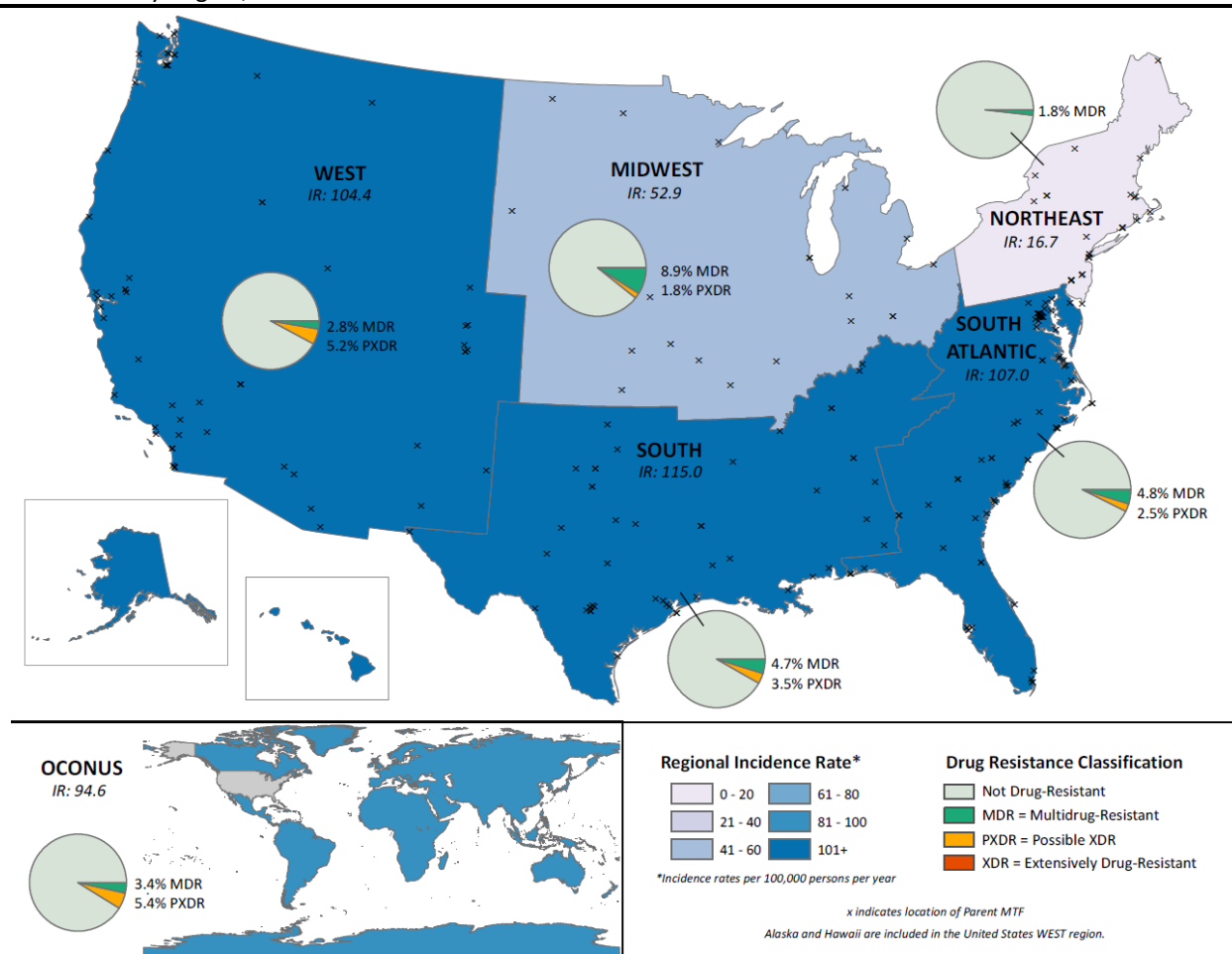
Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Antibiogram

Table 5 displays an antibiogram of *Klebsiella* species incident infections for all MHS beneficiaries from 2012-2017. In 2017, *Klebsiella* species infections were susceptible to a wide range of antibiotics, with susceptibility above 99% for doripenem (100.0%), ertapenem (99.7%), meropenem (99.5%), amikacin (99.4%), and imipenem (99.3%). Infections were least susceptible to ampicillin/sulbactam (85%) and nitrofurantoin (46.6%). Statistically significant decreases in efficacy were observed for ampicillin/sulbactam, aztreonam, cefepime, cefotaxime, ceftazidime, ceftriaxone, gentamicin, imipenem, piperacillin/tazobactam, and tobramycin; significant increasing trends in efficacy were observed in nitrofurantoin (Table 5).

Table 5. Antibiogram of *Klebsiella* species Infections Identified in the MHS, CY 2012-2017

Antibiotics	2011	2012	2013	2014	2015	2016	2017	Susceptibility Trend[a]	Comment[b]
Amikacin	99.5	99.4	99.5	99.7	99.3	99.2	99.4		
Amoxicillin/ Clavulanate	95.9	96.0	96.4	96.0	96.5	95.8	96.0		
Ampicillin/ Sulbactam	87.6	88.1	86.7	85.8	85.8	85.5	85.0		↓
Aztreonam	95.8	95.2	95.6	97.3	96.8	97.2	96.9		↓
Cefepime	98.1	98.5	98.6	98.1	97.8	97.7	97.6		↓
Cefotaxime	98.8	98.2	98.4	97.7	98.0	97.6	96.7		↓
Cefpodoxime	99.3	95.9	98.3	97.1	--	--	--		
Ceftazidime	97.9	98.4	98.4	98.3	98.3	97.9	97.3		↓
Ceftriaxone	97.5	98.2	98.1	97.7	97.6	97.3	97.1		↓
Cefuroxime	95.2	94.0	94.4	94.4	95.0	94.2	93.4		
Ciprofloxacin	96.9	97.4	97.5	97.7	97.5	97.3	97.1		
Doripenem	--	--	100.0	100.0	100.0	100.0	100.0		
Ertapenem	99.8	99.9	99.4	99.8	99.6	99.7	99.7		
Fosfomycin	--	--	--	--	--	--	--		
Gentamicin	98.6	98.8	98.6	98.5	98.4	98.2	97.8		↓
Imipenem	99.5	99.7	99.4	99.7	99.4	99.2	99.3		↓
Levofloxacin	98.2	98.3	98.0	98.4	98.2	97.9	97.9		
Meropenem	99.7	99.4	99.9	99.8	99.4	99.7	99.5		
Nitrofurantoin	42.4	38.7	37.9	38.0	41.5	46.4	46.6		↑
Piperacillin/ Tazobactam	96.9	96.8	96.9	96.3	96.1	95.9	95.6		↓
Tobramycin	97.7	98.1	98.2	97.6	97.7	97.3	97.1		↓

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

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

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

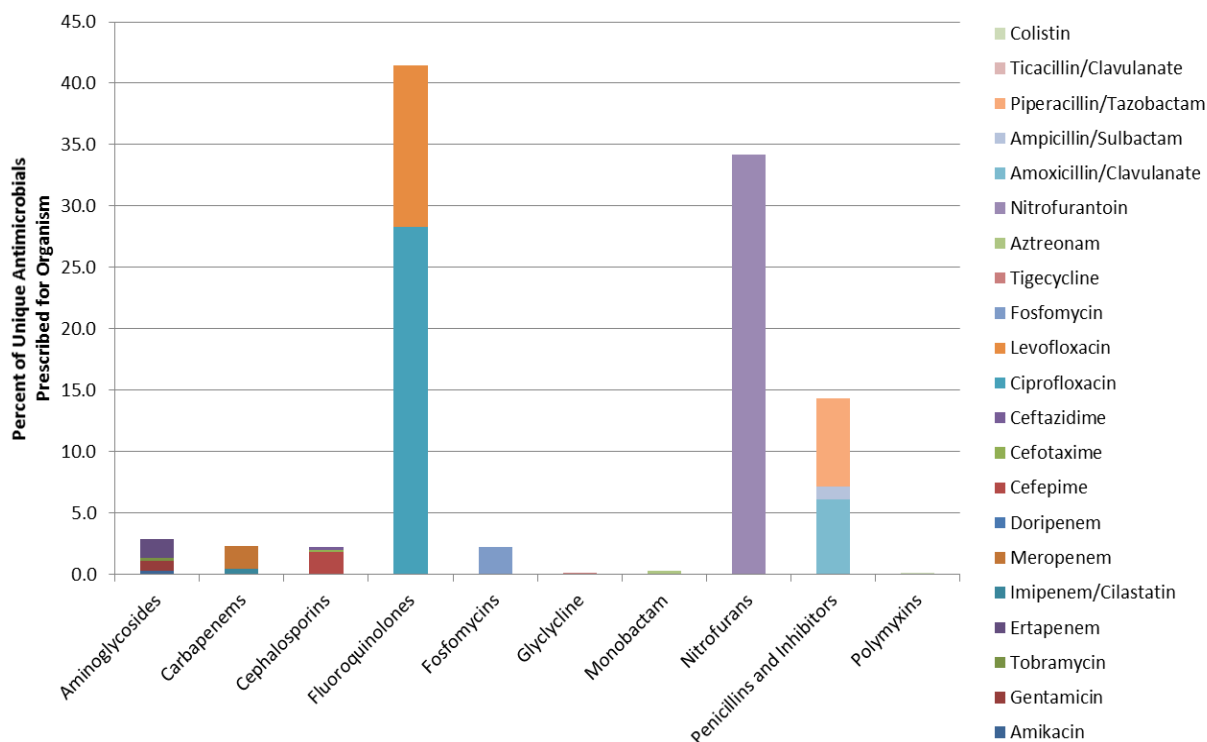Data Source: NMCPHC HL7-formatted CHCS microbiology database.

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

Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries in 2017, the most commonly prescribed antibiotic classes associated with *Klebsiella* species infections were fluoroquinolones (41.5%), nitrofurans (34.2%), and penicillins and inhibitors (14.3%) (Figure 4). Within the fluoroquinolone class, ciprofloxacin (28.3%) and levofloxacin (13.2%) were prescribed. Among penicillins and inhibitors, piperacillin/tazobactam (7.2%), amoxicillin/clavulanate (6.0%), and ampicillin/sulbactam (1.1%) were prescribed. Other classes of antibiotics prescribed for *Klebsiella* species infections in 2017 included carbapenems (3.7%), cephalosporins (2.3%), fosfomycins (2.2%), aminoglycosides (1.41%), and monobactam (0.3%).

Figure 4. *Klebsiella* species Infection and Prescription Practices in the MHS, CY 2017

Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.
Data Source: NMCPHC HL7-formatted CHCS microbiology and HL7-formatted pharmacy databases.
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Discussion

This report describes a decrease in *Klebsiella* species infection rates by 4.9 per 100,000 persons in 2017 from the weighted historic IR. When the current IRs were compared to the weighted historic IRs, percent decreases in the IRs of *Klebsiella* species infections were observed among beneficiaries from all service branches.

Assessment of clinical and demographic characteristics found that urinary tract infections (UTIs) were the most common manifestation of *Klebsiella* species infections, and rates were highest among women. These results are consistent with other literature citing *Klebsiella* species as the agent for 6-15% of all inpatient and outpatient UTIs, and women are significantly more likely to experience a UTI than men.[5] The IRs of *Klebsiella* species infections were distributed relatively evenly throughout all age groups; however, beneficiaries less than 17 years of age accounted for the lowest rate of *Klebsiella* species infections. The presence of infection in the 0-17 age category is not without consideration. UTIs in children can cause long-term medical sequelae, requiring prompt diagnosis and management to prevent subsequent complications.[6]

Klebsiella species infections classified as either MDR or PXDR occurred far less frequently than other *Klebsiella* species infections, where the multidrug-resistant organisms represented approximately 8% of the total *Klebsiella* species prevalence. The US South, OCONUS, US West, and US South Atlantic regions accounted for the top regional incidence rates of all MDR infections; however, in terms of prevalence, the US Midwest had the highest proportion of multidrug-resistance among prevalent *Klebsiella* species infections (10.8%) followed by OCONUS (8.8%) and US South (8.2%).

Analyses defining MDRO healthcare-associated exposure burden metrics implicate community acquisition of drug-resistant *Klebsiella* species across each region. A large proportion of MDR *Klebsiella* species infections were imported into the healthcare system; the admissions prevalence rate during 2017 (1.3 per 1,000 inpatient admissions) accounted for approximately 87% of the overall prevalence rate (1.5 per 1,000 inpatient admissions). With the exception of the US Northeast, elevated MDRO prevalence admissions rates were observed across all regions of the MHS. These results underscore the need for drug-resistance surveillance outside of traditional hospital settings as well as the diligent use of infection control practices, including the implementation of contact precautions, the promotion of hand hygiene adherence, and continued active surveillance within the healthcare setting.[7]

Klebsiella species isolates retained high susceptibilities to many tested antibiotics, indicating a range of viable treatment options for infections. Except for two antimicrobials (ampicillin/sulbactam and nitrofurantoin), *Klebsiella* species isolates displayed susceptibilities greater than 93% to all tested antibiotics. Although nitrofurantoin was the only antimicrobial that significantly increased in susceptibility over the surveillance period, it also maintained the lowest susceptibility in 2017. These results are noteworthy, as analysis also identified a large proportion of nitrofurantoin prescriptions during 2017 for treatment. Further assessments may be warranted to describe the occurrence of nitrofurantoin treatment followed by another recommended regimen for *Klebsiella* species infections, as some physicians could be empirically treating for UTIs thought

to be caused by *Escherichia coli*, which accounts for roughly 80% of CA UTIs.[8,9] Ciprofloxacin and levofloxacin represent two additional antimicrobials most commonly prescribed for *Klebsiella* species infections in this assessment, which are also recommended as oral medications by the Johns Hopkins Antibiotic Guide for mild to moderate, community-acquired infection of uncomplicated UTIs, or as intravenous regimens for severe, nosocomial infections without the risk of methicillin-resistant *Staphylococcus aureus*.[10]

In summary, this report documents a decrease in the rate of *Klebsiella* species infections in the MHS beneficiary population after a three year increase from 2014 to 2016. The characteristics of these infections during 2017 are concurrent with existing literature, which reports a higher burden among females and predominant clinical presentation as UTIs. Almost three-quarters of infections were classified as CA cases, underscoring the need for research and surveillance assessing *Klebsiella* species as a community-acquired infection. Furthermore, the elevated MDRO admission metrics indicate a higher magnitude of MDR *Klebsiella* species imported into the MHS, as opposed to an existing reservoir of infection in the healthcare setting. Finally, these results indicate viable treatment options are still present for *Klebsiella* species infections; however, the frequent use of nitrofurantoin in the MHS warrants further investigation, as approximately 60% of tested *Klebsiella* isolates did not demonstrate susceptibility to the drug.

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Appendix A: Antibiotics Used to Identify Resistance among *Klebsiella* species Infections in the MHS, CY 2017

Table A1. Antibiotics Included in the Resistance Definitions for *Klebsiella* in the DOD, CY 2017

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

[a] Included only for *Klebsiella pneumoniae* and *K. oxytoca*.
Source: Magiorakos et al., 2012.[11]
Prepared by the EpiData Center, Navy and Marine Corps Public Health Center, on 01 May 2018.

Appendix B: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
CA	community-associated
CHCS	Composite Health Care System
CO	community-onset
CONUS	continental United States
CR	carbapenem-resistant
CTS	Contingency Tracking System
CY	calendar year
DMDC	Defense Manpower Data Center
DOD	Department of Defense
DON	Department of the Navy
EDC	EpiData Center Department
HA	healthcare-associated
HL7	Health Level 7 format
HO	hospital-onset
M2	Military Health System (MHS) Management Analysis and Reporting Tool
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	outside the continental United States
PXDR	possible extensively drug-resistant
PH	previous hospitalization
SIDR	Standard Inpatient Data Record
US	United States
UTI	urinary tract infection