Published in final edited form as:

Infect Control Hosp Epidemiol. 2017 December ; 38(12): 1464–1471. doi:10.1017/ice.2017.238.

Prevalence and factors associated with multidrug-resistant Gram-negative organisms in patients with spinal cord injury

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Abstract

Objective: Infections caused by multidrug-resistant Gram-negative organisms (MDRGNOs) have been increasing every year. The objective of this study was to describe the prevalence of MDRGNOs and factors associated with MDRGNOs in patients with spinal cord injury or disorder (SCI/D).

Design: Retrospective cohort study

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This work was presented in part at the Annual Paralyzed Veterans of America Summit 2016, Orlando, Florida, August 30-September 1, 2016 and IDWeek 2016, New Orleans, LA, October 26-30, 2016.

Methods: Department of Veterans Affairs (VA) electronic health record data from 142 VA facilities were evaluated for 19,642 patients with SCI/D. Multivariable cluster adjusted models were fit to identify factors associated with MDRGNO.

Results: A Gram-negative (GN) culture occurred in 44% of patients with SCI/D receiving care at VA facilities and 11,527 (41.3%) GN cultures had an MDRGNO. The most frequent GNs were *Escherichia coli* (28.5%), *Klebsiella pneumoniae* (17.0%), and *Pseudomonas aeruginosa* (16.0%). Two-thirds of GN cultures were from the outpatient setting, where MDRGNO prevalence was 37.6%. Significant geographic variation in prevalence of MDRGNOs was identified (South-44.7%, Northeast-44.3%, West-36.8%, Midwest-34.4%). Other factors associated with an MDRGNO were older age, injury characteristics, comorbidities, specimen type, healthcare setting, and healthcare exposure. Black (OR=1.58, 95% CI 1.39-1.78) and Hispanic race (OR=1.58, 95% CI 1.28-1.95), polymicrobial culture (OR=2.67, 95% CI 2.46-2.90), and antibiotic use in the previous 90 days (OR=1.62, 95% CI 1.50-1.76) were also associated with having an MDRGNO.

Conclusions: MDRGNOs were common in community and healthcare settings in Veterans with SCI/D, with significant geographic variation. Health care and antibiotic exposures were significant factors associated with MDRGNOs. Priority should be given to controlling the spread of MDRGNOs in this special population, including a focus on judicious use of antibiotics.

Introduction

Approximately 282,000 persons live with traumatic spinal cord injury or disorder (SCI/D) in the United States.¹ High healthcare utilization is expected during their lifetimes because of morbidity from secondary complications.² Individuals with SCI/D are at high risk for infections due to frequent health-care contact, antibiotics, and use of invasive medical devices.³⁻⁶ Although many of these infections are caused by antibiotic-resistant organisms, such as multidrug-resistant Gram-negative organisms (MDRGNOs), little data exist on the burden of MDRGNOs in persons with SCI/D.⁷⁻⁸

MDRGNOs account for an increasing rate of infections annually.⁹ The Centers for Disease Control and Prevention (CDC) have made controlling MDRGNOs a high priority because of their increasing burden on morbidity and mortality.¹⁰ CDC National Healthcare Safety Network (NHSN) data from 2009-2010 showed significant increases in resistance in all Gram-negative organisms across various infections.^{9,11} In addition, MDRGNOs have been associated with increased morbidity and mortality, longer length of stay in healthcare institutions, and increased healthcare costs.¹²⁻¹³

Most studies of MDRGNOs have focused on the incidence and spread of these organisms in acute care, however, data show a considerable burden in long-term care facilities and in specialty outpatient settings such as dialysis clinics.¹⁰ We speculate that due to multiple risk factors, such as antibiotic exposure, patients with SCI/D may have a higher burden of MDRGNOs.⁴ Most of the literature from SCI/D or acute rehabilitation units is from 20-30 years ago and were single site studies showing a range of 22-34% of Gram-negatives being MDR (using older MDR definitions of resistant to 2 classes).^{8,14,15} More recent data demonstrated that 60% of Gram-negative bacteria were MDR, defined as intermediate or resistant to 3 antimicrobial classes.¹⁶ Thus, current literature in persons with SCI/D

does not reflect the changing and increasing prevalence of resistance in these organisms, nor does it define the burden across a national sample of patients with chronic SCI/D. The Department of Veterans Affairs (VA) is the largest provider of SCI/D care in the U.S.; making this system an excellent resource for assessing the burden of MDRGNOs in SCI/D. Therefore, the goal of this study was to describe the epidemiology of MDRGNOs, including burden, geographic variability, and factors associated with resistance in a cohort of Veterans with SCI/D.

Methods

Study Design, Setting, and Patients

This was a retrospective cohort study of national VA medical encounter, pharmacy, and microbiology data from adult patients with SCI/D treated at 142 VA facilities. Microbiology culture data and antibiotic sensitivities were evaluated for the study time period January 1, 2012–December 31, 2013, while data from January 1, 2011–December 31, 2011 was utilized to determine exposures.

Data collection

Several national VA data sources were used for this study. The VA Spinal Cord Dysfunction (SCD) Registry and Spinal Cord Injury and Disorders Outcomes (SCIDO) databases are derived from clinical patient registries maintained at individual VA facilities. These data sources were used to obtain spinal cord characteristics including injury date (for duration of injury), level (paraplegia vs. tetraplegia), and completeness (complete vs. incomplete) of injury.

The VA Corporate Data Warehouse (CDW) is a national repository including clinical and administrative data and was used to obtain demographics (age, gender, race/ethnicity); clinical setting at the time of culture (outpatient clinic/emergency, inpatient, long term care (LTC), home care), comorbidity diagnoses in the past year (used to develop Charlson score), previous healthcare exposure (i.e. intensive care unit (ICU) stay, LTC), facility characteristics (i.e. SCI Center, geographic region based on U.S. Census Bureau regions¹⁷), microbiology data (i.e. date/time of culture, specimen type, organisms, and susceptibilities), and antibiotic exposures. For clinical setting, if a patient had a culture obtained during an outpatient visit but was subsequently admitted, the culture was categorized as an outpatient culture. Facility characteristics were evaluated based on whether care was provided at a VA with a specialty SCI Center (24 facilities) versus non-SCI center (118 facilities). All relevant exposure or independent variables (i.e. antibiotic exposure) were evaluated 90 days prior to culture date, unless otherwise noted.

Outcomes

The primary outcome was prevalence of MDRGNOs; where MDR was defined as any Gram-negative organism that was resistant or had intermediate susceptibility to one or more antibiotics in three or more antimicrobial classes. These definitions varied by organism but were defined by criteria established by a panel of experts from the European and US CDC and other partners.¹⁸ All Gram-negative isolates were defined as MDR or non-MDR based

on these definitions which accounted for intrinsic resistance. Any Gram-negative culture that had at least one MDR isolate was defined as an MDRGNO culture. The sample was limited to those cultures with antibiotic sensitivities; removing multiple cultures from the same patient within 30 days, and removing cultures that did not grow at least one Gram-negative organism.

Statistical analyses

The prevalence of MDRGNOs at the culture-level was described by patient demographic, medical, and facility-level characteristics using univariate and bivariate statistics. For the bivariate analyses, continuous variables were compared using the Students t-test or Wilcoxon two-sample test dependent on the distribution of the variables. Categorical variables were compared using Chi-square tests and unadjusted odds ratios (ORs) and 95% confidence intervals (CIs). A multivariable random effect logistic regression model, accounting for multiple cultures within the same patient during the study timeframe, was used to identify independent factors associated with having a MDRGNO versus non-MDRGNO culture. A multilevel random effect model was also fit nesting cultures, within patients, within facilities. However, this model was not significantly different from the model clustering on patients and thus the final model reported adjusts for multiple cultures per patient. The most parsimonious model was used, only including covariates that were significant at the 0.01 level due to multiple comparisons, and presented with adjusted ORs and 95% CIs. Descriptive and bivariate analyses were conducted using SAS software, version 9.3 and regression models were fit using STATA software 14.1.

Results

Between January 1, 2012 and December 31, 2013, 19,657 patients with SCI/D received care in VA facilities. Of these, 13,940 patients had 125,394 microbiology cultures. After exclusions, the final sample included 8,681 patients with 34,760 Gram-negative isolates in 27,904 Gram-negative cultures (mean=3.1 Gram-negative cultures/patient).

Of all the cultures with a Gram-negative organism isolate, 11,527 (41.3%) had an MDRGNO. Among Gram-negative isolates, 12,567 (36.2%) were MDR. The most frequent Gram-negative isolates were *Escherichia coli* (28.5%), *Klebsiella pneumoniae* (17.0%), and *Pseudomonas aeruginosa* (16.0%). Multidrug resistance among these isolates was 54.1%, 31.1%, and 20.7% respectively (Table 1).

Overall, the 8,681 patients included had a mean age of 62.1±13.2 years, duration of injury of 19.4±15.5 years, and a mean Charlson score of 2.3±2.0. Most cultures were from the outpatient setting (62.8%), followed by the inpatient setting (30.6%), LTC (4.3%) and home care (2.3%). Most specimens were from urine (86.6%). Over one-fourth (27.7%) of cultures were obtained from patients who had a healthcare exposure in the previous 90 days and 67.3% were obtained from patients with an antibiotic exposure in the previous 90 days.

Unadjusted associations between demographic, medical, and facility characteristics and having an MDRGNO culture were identified (Table 2). Older age, Black or Hispanic race/ethnicity, and complete injury had higher odds of a MDRGNO, while paraplegia

(vs tetraplegia) had a lower odds. MDRGNO cultures were also associated with culture location where a higher odds was found in the inpatient, LTC, and home care settings compared to the outpatient setting. Having a polymicrobial culture, pressure ulcer, higher Charlson comorbidity score, and other healthcare exposures in the previous 90 days were associated with having an MDRGNO. Antibiotic exposure in the previous 90 days was also associated with an MDRGNO culture, with carbapenems and colistin having the highest odds. Facilities with a SCI Center had a higher prevalence of MDRGNO cultures (compared to non-SCI centers). There was also significant regional variation (Table 2). The Figure shows the geographic distribution of MDRGNO cultures and patients in VA facilities across the U.S., where 3.1% to 53.1% of SCI/D patients cared for in a particular facility had at least one MDRGNO (Interquartile range (IQR) 9.6%, median 15.9%). For SCI Centers, SCI/D patients with MDRGNOs was 13.4% to 53.1%, IQR=13.6%, median=30.2%, while those facilities without SCI Centers showed a range of 3.1% to 44.8%, IQR=8.2%, median=13.9%.

Overall, in the final model, we found that older age, Black and Hispanic race, and having a complete injury were still associated with a higher odds of MDRGNO cultures (Table 3). However, unlike the unadjusted analyses, the multilevel random effect model found that duration of injury for 21 or more years demonstrated a lower odds of MDRGNO culture as compared to those injured for 10 or less years. Being at an SCI Center was no longer significant, but significant regional variation was still apparent. The South and Northeast had similar odds of having an MDRGNO culture, but the Midwest and West had lower odds. Cultures collected from inpatient and LTC settings remained associated with higher odds of MDRGNO cultures. Cultures obtained from blood and other specimen types (vs urine cultures) were less likely to have MDRGNOs. Higher Charlson score, polymicrobial culture, and healthcare and antibiotic exposure in the previous 90 days were also associated with a MDRGNO culture. When individual antibiotic classes were included in the model, fluoroquinolones had the highest odds of being associated with MDRGNO cultures, followed by sulfonamides. Carbapenems, extended spectrum penicillins (piperacillin, piperacillin/tazobactam and ticarcillin/clavulanate), and tetracyclines were also associated with MDRGNO cultures. No other antibiotic classes were associated with MDR.

Discussion

In this study, over one-third of Gram-negative isolates and two of five Gram-negative cultures had an MDRGNO. Earlier studies in SCI/D demonstrated the prevalence of MDRGNO to be between 22-33%.^{8,14} Our results suggest that MDRGNOs are common in this population and the burden is higher than older reports. Particularly since these studies used a definition that was less conservative for defining multi-drug resistance (resistant to 2 classes), while our definition required being resistant to 3 antibiotic classes and accounted for intrinsic resistance. Our data show the percentage of patients with MDRGNOs across facilities ranged from 3.1%- 53.1%. Significant variability across facilities was even more apparent when stratified by presence of an SCI Center (median=30.2%) as compared to non-SCI Centers (median=13.9%).

The most frequent Gram-negatives identified in this study were *E. coli* and *K. pneumoniae*, with *E. coli* and *P. mirabilis* having the highest prevalence of MDR (54.1% and 43.6%, respectively). The prevalence of MDR *E. coli* and *K. pneumoniae* in this study were both significantly higher than that observed in HAIs in general acute care, long-term acute care, and inpatient rehabilitation reported to the CDC's NHSN (54.1% vs. 11.1% for *E. coli*; 31.1% vs. 20.9% for *K. pneumoniae*).¹⁹ In fact, the prevalence of MDRGNOs from the outpatient setting in this study was higher (37.6%) than reported from NHSN in acute care, demonstrating the high risk of SCI outpatients for having MDRGNOs.¹⁹ MDR *Enterobacteriaceae* and *P. aeruginosa* are highlighted as urgent or serious threats by the CDC.¹² Therefore, this increased prevalence highlights the need for increased surveillance and prevention strategies targeted to patients with SCI/D.

Factors associated with MDRGNOs in this study included older age, having a complete injury, higher Charlson score, and previous healthcare exposure. These factors are not surprising, as previous articles demonstrated an association with specific MDRGNOs (e.g., carbapenem-resistant *Enterobacteriaceae*).²⁰⁻²³ Rarely reported is racial/ethnicity differences in risk for MDRGNOs, where we found Blacks and Hispanics had a higher prevalence of MDRGNOs. One study found increased fluoroquinolone resistance in GNO causing healthcare-acquired UTIs in African-Americans compared to Whites.²⁴ In a study of outpatients with SCI, MDRGNOs were more common in African-Americans than Whites, but this difference was non-significant.⁶ Other studies have shown variation in methicillin-resistant *Staphylococcus aureus* (MRSA) by race/ethnicity.²⁵⁻²⁷ Differential risk for MDROs by race/ethnicity, may be due to lower socio-economic status and overcrowding in urban areas. These factors have been cited as reasons for the emergence of community-associated MRSA in urban areas.²⁸ In addition, despite controlling for these factors, differences in healthcare exposures (e.g., antibiotics) may vary by race/ethnicity and geographic area. Complete injuries were more common in ESBL- and non-ESBL-producing *Enterobacteriaceae* than controls in a national case-case-control study of veterans with SCI.²⁹ A study of nursing home residents found that colonized cases of MDR *A. baumannii* occurred in persons who were more functionally disabled than controls.³⁰ We also found that those injured for a longer time had a lower prevalence of MDRGNOs, which was surprising, especially since older age was associated. This may be secondary to increased immunity over time against bacterial invasion due to repeated infections.^{3,31-32} This finding warrants further exploration. Polymicrobial cultures were also associated with MDRGNOs, independent of urine cultures, which are often polymicrobial.^{8,33} Polymicrobial cultures have been shown to be a risk factor for inadequate antibiotic treatment,¹⁵ which may provide an opportunity for Gram-negatives to spread drug resistance. This emphasizes the need for continued and focused infection control. The increased association of MDRGNOs with LTC and hospitalization further emphasizes this point. The complex environments involved in caring for SCI/D (ie. physical therapy, shared equipment) could pose additional barriers to optimal infection control. Finally, antibiotic exposure had the second highest odds of association with MDRGNOs. The high prevalence of exposure to antibiotics (67.3%) in this population highlights the need for stewardship. Estimates suggest an opportunity for a 30% reduction in unnecessary antibiotic prescribing in community and acute care settings.³⁴⁻³⁵ In addition, broad spectrum antibiotics, which can increase resistance, are

frequently selected over first-line narrower spectrum agents.³⁶⁻³⁹ Our findings demonstrate sulfonamides and broad spectrum agents, such as fluoroquinolones, were associated with MDRGNOs. Tetracyclines are commonly used to treat osteomyelitis. These patients have prolonged hospitalizations and courses of parenteral antibiotics. Thus, a high rate of MDRGNOs would be expected.

Some limitations of this study included the lack of information on prescribing, medical encounters, or cultures that occurred outside the VA system, limited availability of data on medical devices, culture rationale or quality (ie. surface swab vs tissue biopsy), a broad, but standardized definition for MDR¹⁸, and the inability of our methodology to distinguish between colonization and infection. Colonization is common in this patient population, with little clinical relevance for treating positive urine cultures in asymptomatic non-pregnant patients. In addition, antibiotic use in asymptomatic bacteriuria has been associated with increased risk for resistance.⁴⁰ Clinicians should carefully consider the clinical significance of positive urine cultures in SCI patients where symptoms may not be as apparent. Since, this is the largest national study to describe MDRGNOs in a high risk patient population, using data such as this provides the opportunity to benchmark current prevalence of MDRGNOs and direct infection control and stewardship interventions.

Clinicians treating patients with SCI/D should remain cognizant of the frequency of MDRGNOs. The risk for HAIs appears elevated in SCI/D compared to the general population. The rate of MDRGNO in the outpatient setting is substantial, with 37.6% of Gram-negative organisms demonstrating MDR. Healthcare and antibiotic exposure in the past 90 days are risk factors for MDRGNOs, and the choice of empiric antibiotics in outpatients needs to account for these factors. In addition, it is important to implement stewardship strategies to improve antibiotic susceptibilities in this population.

Acknowledgments

This work was supported by funding from the Veterans Health Administration, Office of Research and Development, Rehabilitation Research and Development Service SPIRE Award (B-1583-P), Health Services Research and Development Service Presidential Early Career Award for Scientists and Engineers [USA 12-564], Post-Doctoral Fellowship Award (TPR 42-005). Dr. Nasia Safdar is additionally supported by a VA-funded Patient Safety Center of Inquiry. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the U.S. government. All authors report no conflicts of interest relevant to this article.

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Figure.

Percentage of patients with spinal cord injury/disorder (SCI/D) with at least one multi-drug resistant Gram-negative organism (MDRGNO) at VA facilities, 2012-2013

*Alaska (11.3%) not shown

Table 1.

Frequency of Gram-negative isolates and prevalence of multi-drug resistance in clinical cultures (n=34,760)

Organism	Total (%) ^a	Number of Isolates that are MDR (%) ^b
Total	34,760	12,567 (36.2%)
All <i>Enterobacteriaceae</i>	27,483 (79.1%)	10,920 (39.7%)
<i>Escherichia coli</i>	9,901 (28.5%)	5,360 (54.1%)
<i>Klebsiella pneumoniae</i>	5,918 (17.0%)	1,843 (31.1%)
<i>Proteus mirabilis</i>	4,608 (13.3%)	2,007 (43.6%)
Other <i>Enterobacteriaceae</i>	7,056 (20.3%)	1,710 (24.2%)
<i>Pseudomonas aeruginosa</i>	5,555 (16.0%)	1,152 (20.7%)
<i>Pseudomonas</i> , non- <i>aeruginosa</i>	156 (0.4%)	29 (18.6%)
<i>Acinetobacter</i>	776 (2.2%)	457 (58.9%)
Other Gram-negative organisms ^c	790 (2.3%)	9 (1.1%)

^a percent = (organism isolates/total Gram-negative isolates)x100

^b percent = (MDR organism isolates/total organism isolates)x100

^c Other Gram-negative organisms include *Achromobacter*, *Aeromonas*, *Agrobacterium*, *Alcaligenes*, Anaerobes, *Bacteroides*, *Bordetella bronchiseptica*, *Burkholderia cepacia*, *Chryseobacterium*, *Comamonas testosteroni*, *Cupriavidus*, *Delftia acidovorans*, *Elizabethkingia*, *Fusobacterium*, Gram-negative, *Haemophilus*, *Moraxella*, *Myroides*, *Pantoea*, *Pasteurella*, *Porphyromonas*, *Prevotella*, *Rahnella*, *Ralstonia*, *Raoultella*, *Sphingomonas*, *Stenotrophomonas maltophilia*

Table 2.

Prevalence of multi-drug resistant Gram-negative organism (MDRGNO) cultures and unadjusted association between patient, medical and facility characteristics (n=27,904)

Characteristics	Prevalence of MDRGNO cultures N=27,904	MDRGNO cultures N=11,527	Non-MDRGNO cultures N=16,377	Unadjusted OR (95% CI)
Male Gender	41.4%	11,174 (96.9%)	15,827 (96.6%)	1.10 (0.76-0.91)
Age in years				
18-49	36.7%	1,650 (14.3%)	2,849 (17.4%)	Reference
50-64	43.0%	4,978 (43.2%)	6,590 (40.2%)	1.30 (1.21-1.40)
65+	41.4%	4,899 (42.5%)	6,938 (42.4%)	1.22 (1.14-1.31)
Race/Ethnicity				
White	38.0%	6,459 (56.0%)	10,537 (64.3%)	Reference
Black	48.5%	3,445 (29.9%)	3,657 (22.3%)	1.54 (1.45-1.63)
Hispanic	45.7%	826 (7.2%)	980 (6.0%)	1.38 (1.25-1.52)
Other	39.9%	797 (6.9%)	1,203 (7.4%)	1.08 (0.98-1.19)
Paraplegia Injury (vs tetraplegia/missing)	40.0%	5,009 (43.5%)	7,503 (45.8%)	0.91 (0.87-0.95)
Complete Injury (vs incomplete)	43.4%	5,313 (46.1%)	6,926 (42.3%)	1.17 (1.11-1.22)
Duration of injury in year				
<=10 years	42.0%	5,580 (48.4%)	7,714 (47.1%)	Reference
11-20	40.3%	1,782 (15.5%)	2,639 (16.1%)	0.93 (0.87-1.00)
21+	40.9%	4,165 (36.1%)	6,024 (36.8%)	0.96 (0.91-1.01)
Medical Characteristics				
Care setting				
Outpatient	37.6%	6,591 (57.2%)	10,924 (66.7%)	Reference
Inpatient	47.8%	4,078 (35.4%)	4,455 (27.2%)	1.52 (1.44-1.60)
Long-term care	48.7%	589 (5.1%)	621 (3.8%)	1.57 (1.40-1.77)
Home care	41.6%	269 (2.3%)	377 (2.3%)	1.18 (1.01-1.39)
Specimen type				
Urine	41.2%	9,955 (86.4%)	14,215 (86.8%)	Reference
Blood	42.0%	224 (1.9%)	309 (1.9%)	1.04 (0.87-1.23)
Other	42.1%	1,348 (11.7%)	1,853 (11.3%)	1.04 (0.96-1.12)
Polymicrobial culture	55.4%	3,301 (28.6%)	2,658 (16.2%)	2.07 (1.95-2.19)
Pressure ulcer in past year	49.8%	3,796 (32.9%)	3,823 (23.3%)	1.61 (1.53-1.70)
Mean Charlson score (SD)		2.0 (1.8)	1.7 (1.8)	<0.0001 *
Healthcare Exposures in the past 90 days				
Any healthcare	48.5%	3,756 (32.6%)	3,984 (24.3%)	1.50 (1.43-1.59)
Long-term care facility stay	50.6%	360 (3.1%)	352 (2.1%)	1.47 (1.26-1.70)
ICU stay	53.0%	1,076 (9.3%)	953 (5.8%)	1.67 (1.52-1.82)

Characteristics	Prevalence of MDRGNO cultures N=27,904	MDRGNO cultures N=11,527	Non-MDRGNO cultures N=16,377	Unadjusted OR (95% CI)
Previous hospitalization	48.5%	3,612 (31.3%)	3,829 (23.4%)	1.50 (1.42-1.58)
Mechanical ventilation	52.2%	584 (5.1%)	535 (3.3%)	1.58 (1.40-1.78)
Antibiotic Exposures in the past 90 days				
Any antibiotics	45.3%	8,503 (73.8%)	10,271 (62.7%)	1.67 (1.59-1.76)
Sulfonamides	48.1%	2,037 (17.7%)	2,196 (13.4%)	1.39 (1.30-1.48)
Nitrofurantoin	45.9%	1,330 (11.5%)	1,571 (9.6%)	1.23 (1.14-1.33)
Fluoroquinolones	51.4%	3,727 (32.3%)	3,525 (21.5%)	1.74 (1.65-1.84)
3 rd & 4 th Gen Cephalosporins	52.4%	2,269 (19.7%)	2,058 (12.6%)	1.71 (1.60-1.82)
Carbapenems	62.6%	1,561 (13.5%)	934 (5.7%)	2.59 (2.38-2.82)
Colistin	72.6%	106 (0.9%)	40 (0.2%)	3.79 (2.63-5.46)
Facility Characteristics				
SCI Center	42.7%	7,511 (65.2%)	10,072 (61.5%)	1.17 (1.11-1.23)
U.S. region				
South **	44.7%	6,678 (57.9%)	8,260 (50.4%)	Reference
Northeast	44.3%	1,172 (10.2%)	1,474 (9.0%)	0.98 (0.90-1.07)
Midwest	34.4%	1,766 (15.3%)	3,362 (20.5%)	0.65 (0.61-0.69)
West	36.8%	1,911 (16.6%)	3,281 (20.0%)	0.72 (0.68-0.77)

* t-test p-value

** South: Includes Puerto Rico due to small sample size

Table 3.

Multivariable random effect logistic regression analysis assessing the association between patient, medical and facility characteristics and having a multi-drug resistant Gram-negative organism in culture (n=27,904).

Characteristics	Adjusted OR (95% CI)
Age in years	
<50	Reference
50-64	1.40 (1.21-1.63)
65+	1.41 (1.21-1.64)
Race/Ethnicity	
White	Reference
Black	1.58 (1.39-1.78)
Hispanic	1.58 (1.28-1.95)
Other/Missing	1.21 (1.00-1.46)
Complete Injury (vs incomplete/missing)	1.40 (1.26-1.57)
Duration of injury in year	
<=10 years (missing)	Reference
11-20	0.87 (0.76-1.00)
21+	0.85 (0.75-0.95)
U.S. region	
South	Reference
Northeast	1.04 (0.87-1.23)
Midwest	0.60 (0.53-0.69)
West	0.78 (0.68-0.89)
Care Setting	
Outpatient	Reference
Inpatient	1.18 (1.08-1.29)
Long-term care	1.36 (1.11-1.66)
Home care	1.23 (0.97-1.57)
Specimen type	
Urine	Reference
Blood	0.75 (0.59-0.94)
Other	0.71 (0.64-0.79)
Polymicrobial culture	2.67 (2.46-2.90)
Mean Charlson score	1.05 (1.03-1.08)
Any healthcare in past 90 days	1.21 (1.12-1.32)
Any antibiotics in past 90 days	1.62 (1.50-1.76)
Model with individual antibiotics included	
Fluoroquinolones	1.97 (1.82-2.13)
Sulfonamides	1.48 (1.34-1.63)
Carbapenems	1.35 (1.18-1.53)

Characteristics	Adjusted OR (95% CI)
Extended spectrum penicillins *	1.22 (1.10-3.37)
Tetracyclines	1.37 (1.19-1.58)

* Includes piperacillin, piperacillin/tazobactam, and ticarcillin/clavulanate