

National Prevalence of Multidrug-Resistance (MDR) in Enterobacteriaceae (ENT) in the Ambulatory and Acute Care Settings in the United States in 2015-2016

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Abstract

BACKGROUND: Infections caused by resistant Gram-negative bacteria are a serious global public health concern. The purpose of this study was to estimate the national prevalence of MDR ENT events in the acute care and ambulatory settings based on a large database from Becton Dickinson & Company.

METHODS: Susceptibility data from non-duplicate ENT organisms (*E. coli*, *K. pneumoniae*, *P. mirabilis*, *E. aerogenes*, *E. cloacae*, *S. marcescens*, *C. freundii*, & *M. morganii*) and were identified from 348 hospitals nationwide from July 2015 to June 2016. ENT isolates were characterized as MDR using NHSN definitions. Organisms were classified into ambulatory, admission, and hospital-onset (HO) periods based on collection time. All data were linked to Centers for Medicare and Medicaid Services (CMS) National Hospital Data Provider IDs. The raking method was applied across the CMS national hospital distribution by location, teaching status, urban/rural status, and bed size to project the national prevalence estimates.

RESULTS: Of 969,456 isolates tested, 43,812 were MDR ENT. The number of national projection of MDR ENT events was estimated to be 384,696 in the HO, ambulatory and acute care settings (table below). The MDR ENT rates were highest in the hospital-onset, followed by admission and ambulatory setting. National Projections for MDR ENT for each region were: ambulatory (3.1%, 3.2%, 4.3% & 3.4%), admission (5.7%, 5.9%, 5.9% & 6.2%) and HO (7.4%, 10.1%, 8.5% & 9.3%) for the Midwest, Northeast (NE), South, and West regions, respectively.

Period Tested	Observed Events (348 hospitals)			National Projection		
	Isolates tested	Confirmed MDR ENT	% MDR	Isolates tested	MDR ENT Events	% MDR ENT
Ambulatory	737,891	27,069	3.7%	6,826,222	246,211	3.6%
Admission	124,515	7,406	5.9%	1,035,030	60,866	5.9%
Hospital-onset	107,050	9,337	8.7%	902,519	77,619	8.6%
Total	969,456	43,812	4.5%	8,763,772	384,696	4.4%
Regions						
Midwest	266,999	9,837	3.7%	2,586,668	98,190	3.8%
NE	142,025	5,937	4.2%	1,266,480	55,222	4.4%
South	413,643	20,860	5.0%	3,315,998	164,266	5.0%
West	146,789	7,178	4.9%	1,594,625	67,018	4.2%
Total	969,456	43,812	4.5%	8,763,772	384,696	4.4%

CONCLUSION: Although the highest prevalence for MDR ENT events was in the hospital-onset setting, about 80% of MDR ENT events occurred in the ambulatory and admission settings. Overall prevalence of MDR ENT was highest in the South region, but the NE has the highest projected prevalence for the admission and hospital-onset periods.

Introduction

According to the Antibiotic Resistance Threats in the United States, 2013 report from the CDC, it is estimated that overall approximately 2 million people in the US become infected with antibiotic-resistant bacteria and at least 23,000 die annually¹. Among all of the bacterial resistance problems, Gram-negative pathogens are particularly worrisome because they are becoming resistant to nearly all drugs that could be considered for treatment. Approximately 20% of all healthcare-associated infections reported during 2009–2010 were caused by multidrug-resistant (MDR) pathogens and Enterobacteriaceae made up 25% of the overall reported pathogens with multi drug-resistance rates reported 2%². However, little has been reported on the prevalence of infections in non-hospital settings. The purpose of this study was to estimate the national prevalence of MDR ENT events in the acute care and ambulatory settings in the US in July 2015 to June 2016 based on a large database from Becton Dickinson & Company.

Methods

■ Non-duplicate isolates (first isolate of a species per 30 day period) collected from 348 nationwide hospitals (Table 1) from respiratory, blood, urine, skin, intra-abdominal, and other sources were identified as MDR per National Healthcare Safety Network (NHSN) definitions²:

- *E. coli*, *K. pneumoniae*, *P. mirabilis*, *Enterobacter species* (*E. aerogenes* + *E. cloacae*), *S. marcescens*, *C. freundii*, *M. morganii* were identified as multidrug-resistant (MDR) per the following NHSN definitions: tested as intermediate or resistant to at least 1 drug in 3 of the 5 following classes: extended-spectrum cephalosporins (ceftazidime, cefepime, ceftriaxone, or cefotaxime), fluoroquinolones, aminoglycosides, carbapenems, and piperacillin or piperacillin/tazobactam.

■ Isolates were categorized into three settings by the specimen collection time totals:

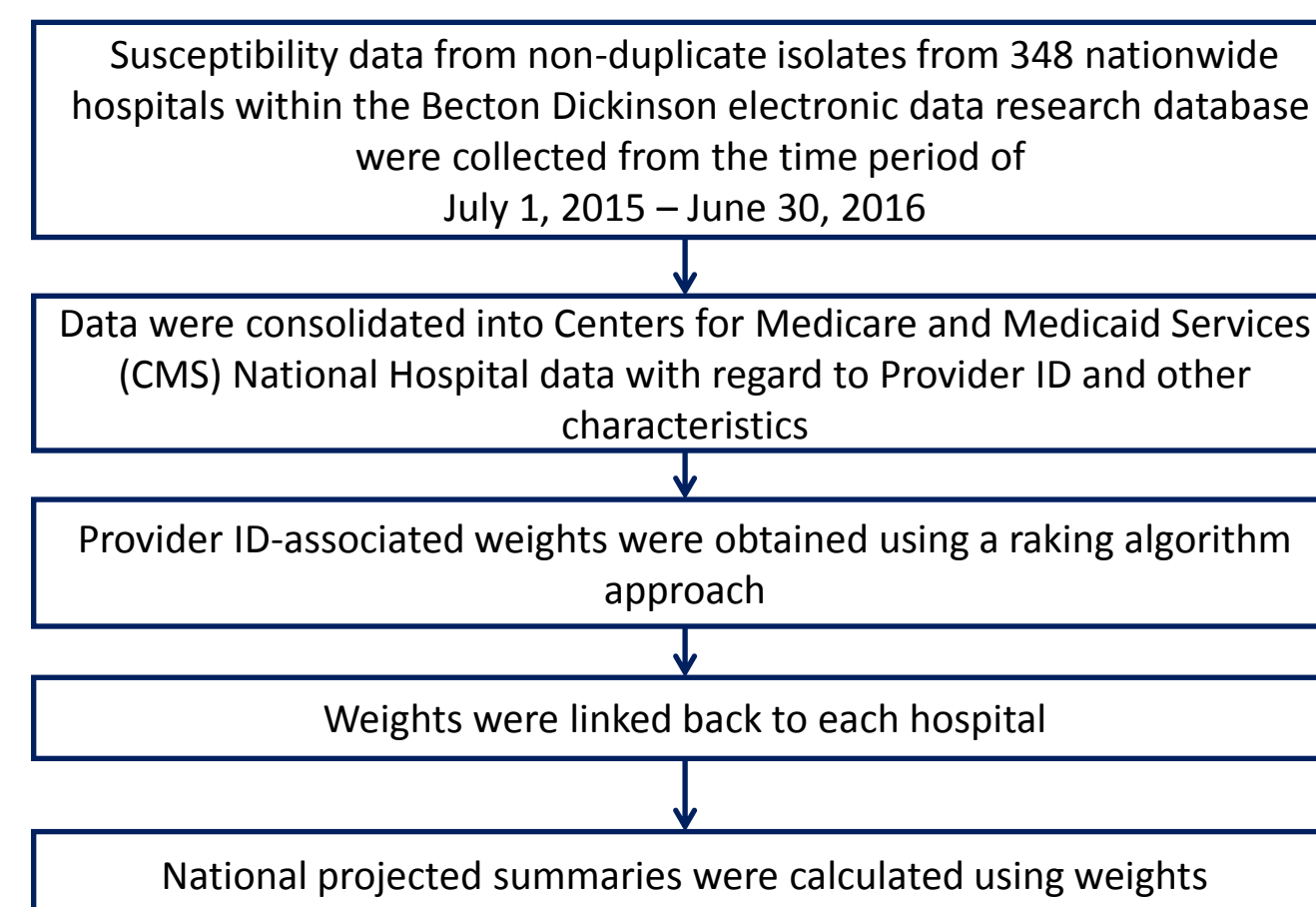
- **Admission:** Within 3 days of an inpatient admission and no previous admission within 14 days
- **Hospital-onset:** 3 days or more post-admission or within 14 days of discharge
- **Ambulatory:** Neither a or b.

■ All data were linked with publicly available CMS (Centers for Medicare and Medicaid Services) National Hospital Data using Provider IDs.

■ The raking method was applied per CMS national hospital distribution by location, teaching status, urban/rural status, and bed size to project the national prevalence estimates. Raking has been borrowed from survey research methods. Raking uses an iterative proportional fitting algorithm to force estimates to match known underlying distribution totals.

■ Figure 1 demonstrates the projection methodology for determining national prevalence estimates.

Figure 1. Projection Methodology for determining national prevalence estimates



Results

■ For the 348 facilities 969,456 non-duplicate ENT isolates were identified and tested for susceptibility in 826,323 patients

- 43,812 (4.5%) of the isolates were determined to be MDR ENT (Table 2) in 30,676 patients
- The percentage of observed MDR ENT events was highest in the hospital onset period (8.7%), followed by admission (5.9%) and ambulatory (3.7%) settings (Table 2)
- Of the 43,812 MDR ENT non-duplicate isolates in 30,676 patients, 89.3% were *E. coli*, *K. pneumoniae* and *P. mirabilis* (Figure 3)

■ The top three sources identified as MDR ENT isolates were: urine (76.3% of isolates), skin (9.2% of isolates), and blood (6.3% of isolates) (Figure 2)

■ The national projected number of MDR ENT events was 384,696 (4.4%) (Table 2, Figure 4-5) in 265,025 patients

■ National projections for MDR ENT for each region were: ambulatory (3.1%, 3.2%, 4.3%, & 3.4%), admission (5.7%, 5.9%, 5.9% & 6.2%) and hospital-onset (7.4%, 10.1%, 8.5% & 9.3%) for the Midwest, Northeast, South & West regions, respectively (Table 3)

Table 1. Hospital Characteristics

Hospital Characteristics	BD Database N=348 Hospitals	CMS Database N=4,650 Hospitals
Teaching Status		
Major	12.9%	9.6%
Limited	19.3%	13.2%
Graduate	4.6%	2.8%
No Affiliation	63.2%	74.5%
Bed Size		
<100 beds	22.8%	50.8%
100-300 beds	41.3%	30.3%
≥300 beds	35.8%	19.0%
Urban/Rural Status		
Urban	75.9%	57.8%
Rural	24.1%	42.2%
Region		
Northeast	9.5%	8.9%
South	47.7%	41.1%
Midwest	27.0%	30.1%
West	15.8%	19.9%

BD= Becton Dickinson; CMS= Centers for Medicare and Medicaid Services

Figure 2: Source distribution for MDR Enterobacteriaceae (N=43,812 episodes) from 348 facilities

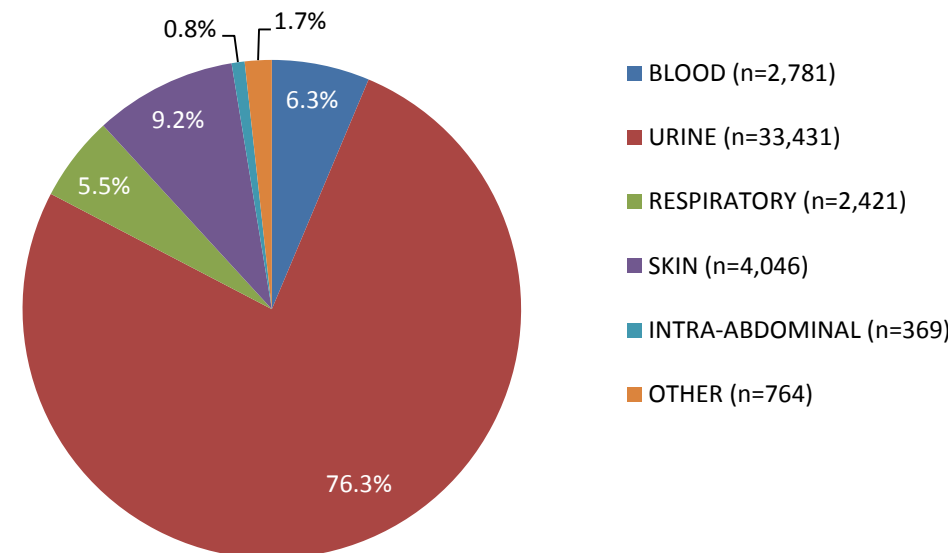


Figure 3: Pathogen distribution for MDR Enterobacteriaceae (N=30,676 patients) from 348 facilities. First patient isolate (43,812 episodes in 30,676 patients)

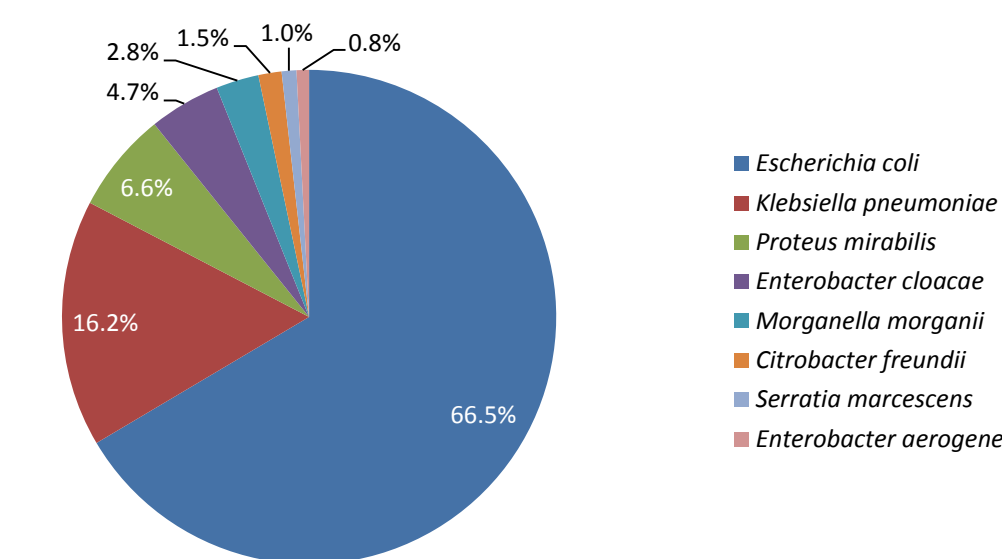


Figure 4: Source distribution of MDR Enterobacteriaceae for projections of national prevalence by setting type

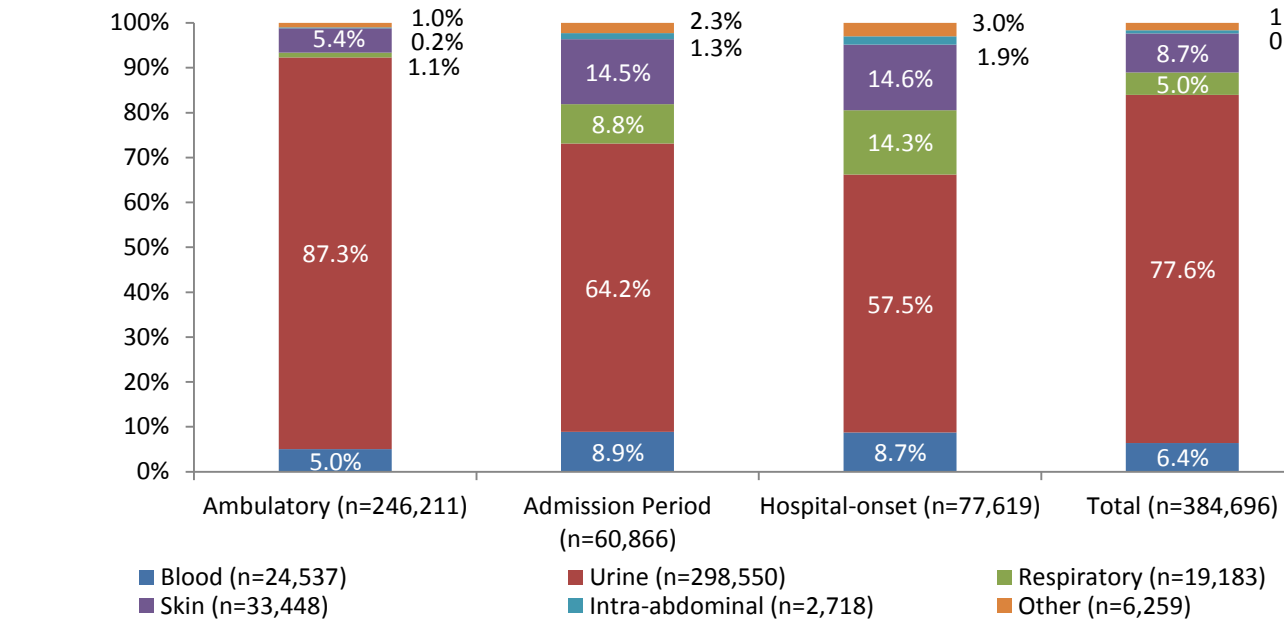


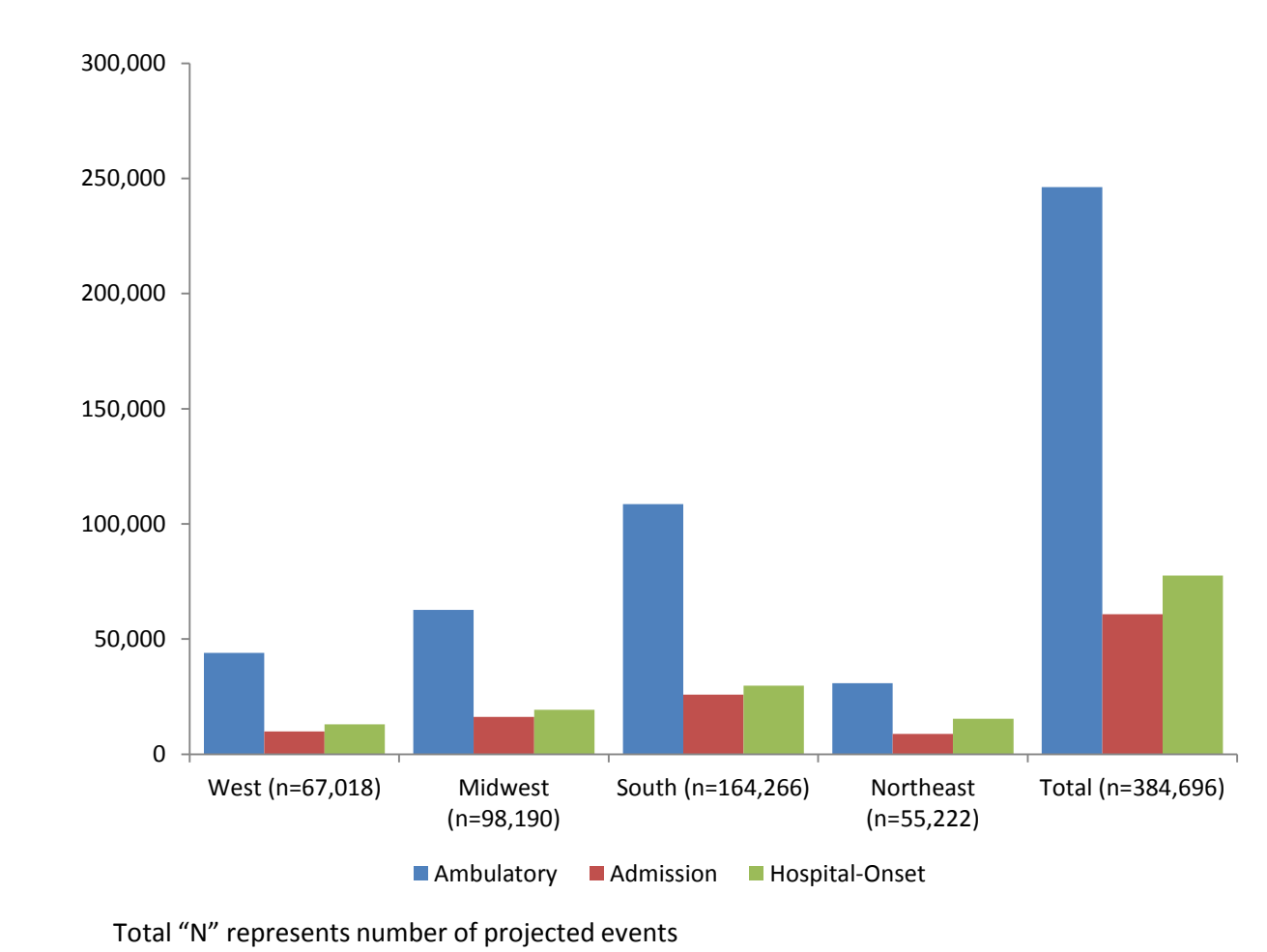
Table 2. National projection of MDR Enterobacteriaceae events estimated from observed events from the 348 hospitals in the BD database

Period	348 Facilities Observed			NATIONAL PROJECTIONS		
	Total Tested, N	MDR, N	% MDR	Projected Org Tested, N	Projected MDR, N	Projected % MDR
Ambulatory	737,891	27,069	3.7%	6,826,222	246,211	3.6%
Admission	124,515	7,406	5.9%	1,035,030	60,866	5.9%
Hospital-Onset	107,050	9,337	8.7%	902,519	77,619	8.6%
Grand Total	969,456	43,812	4.5%	8,763,772	384,696	4.4%

Table 3. National projection of MDR Enterobacteriaceae events by region and setting

Region	Setting	MDR % (n)
West	Ambulatory	3.4% (44,082/1,293,850)
	Admission	6.2% (9,896/160,150)
	Hospital-Onset	9.3% (13,040/140,625)
Subtotal	4.2% (67,018/1,594,625)	
Midwest	Ambulatory	3.1% (62,624/2,040,710)
	Admission	5.7% (16,192/285,816)
	Hospital-Onset	7.4% (19,374/260,142)
Subtotal	3.8% (98,190/2,586,668)	
South	Ambulatory	4.3% (108,583/2,529,112)
	Admission	5.9% (25,901/438,385)
	Hospital-Onset	8.5% (29,783/348,500)
Subtotal	5.0% (164,266/3,315,998)	
Northeast	Ambulatory	3.2% (30,923/962,550)
	Admission	5.9% (8,877/150,679)
	Hospital-Onset	10.1% (15,422/153,252)
Subtotal	4.4% (55,222/1,266,480)	

Figure 5. National projections of MDR Enterobacteriaceae events (n) by period tested and region.



Conclusions

- Although the highest rate for MDR ENT events was in the hospital-onset setting, approximately 80% of MDR ENT events occurred in the ambulatory and admission settings
- Overall rate and projected prevalence of MDR ENT was highest in the South region
- The limitations to this study include that many methodologies are available to determine projections, and projections beyond the underlying data sample always have underlying assumptions and carry some risk

References

- Centers for Disease Control: Antibiotic Resistance Threats in the United States, 2013. <http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>. Accessed July 25, 2016.
- Sievert DM, Ricks P, Edwards JR, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. *Infect Control Hosp Epidemiol.* 2013;34(1):1-14

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Author Disclosure Information

V. Gupta: D. Employee; Self; BD; M Olesky: D. Employee; Self; Tetraphase Pharmaceuticals; J Mohr: D. Employee; Self; Medical Affairs Strategic Solutions, LLC; H Patel: D. D. Former Employee; Self; Tetraphase Pharmaceuticals; YP Tabak: D. Employee; Self; BD.; H Hoffman-Roberts: D. Employee; Self; Theravance Biopharma; RS Johannes: D. Employee; Self; BD.