Increased carbapenemase testing following implementation of national VA guidelines for carbapenem-resistant *Enterobacteriaceae* (CRE)

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Background

- Carbapenem-resistant *Enterobacteriaceae* (CRE) are difficult to treat multidrug-resistant organisms (MDROs) with potential for rapid spread.[1,2]
- Carbapenemase-producing CRE (CP-CRE) contain mobile genetic elements that facilitate transmission of resistance to other Gram-negative bacteria and are associated with high morbidity and mortality.[3]
- All four major carbapenemase enzymes have been identified in the U.S.: *Klebsiella pneumoniae* carbapenemase (KPC), New Dehli metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), Imipenemase (IMP), and Oxacillinase-48-like (OXA-48).
- Different enzymes are associated with unique epidemiologic risks and antibiotic susceptibilities.
- The VA has been a leader in developing guidelines for the management and prevention of CRE, publishing national CRE guidelines in both 2015 and 2017, with the latter recommending PCR to confirm CP-CRE.[4]
- In this study, we:
  1. Analyzed trends in carbapenemase testing and detection in VA hospitals following publication of VA CRE guidelines
  2. Described testing for and detection of specific carbapenemase enzymes
  3. Identified culture and facility-level characteristics associated with carbapenemase testing

Methods

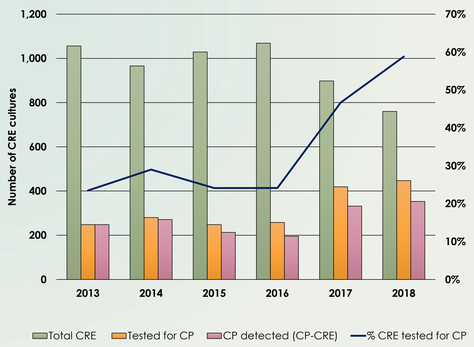
- Retrospective cohort study of adult patients at VA medical centers (VAMCs) between Jan 1, 2013 and Dec 31, 2018 with bacterial cultures that grew *Escherichia coli*, *Klebsiella* spp. or *Enterobacter* spp. and met either the 2015 or 2017 VA CRE definition.
  - The 2015 definition includes *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. that are: 1.) non-susceptible to imipenem, meropenem and/or doripenem; 2.) resistant to ertapenem; and, 3.) resistant to any tested 3rd generation cephalosporin.
  - The 2017 CRE definition includes *E. coli*, *Klebsiella pneumoniae, K. oxytoca*, and *Enterobacter* spp. and simplifies the antibiotic susceptibility criteria to resistant to imipenem, meropenem and/or doripenem and recommends PCR-based tests to identify carbapenemases.

Methods

- Data extracted from the VA Corporate Data Warehouse (CDW) included:
  - Microbiologic and laboratory data (carbapenemase testing and detection was extracted from text in Microbiology culture and Laboratory reports)
  - Characteristics of VAMC facilities with CRE cultures, including U.S. Census Bureau geographic region, complexity level, urban vs. rural location, and presence of specialty care units or services
- Descriptive statistics were used to summarize culture sources, care settings, bacterial species, and carbapenemase testing for unique CRE cultures and facility characteristics for unique VAMCs where CRE cultures were obtained. Bivariate statistics with Chi-square and Fisher's Exact test were used to associate culture and facility level variables with carbapenemase testing. P-value < 0.05 was considered statistically significant.

Results

Figure 1. Carbapenemase testing and detection



Results

Variable	Value	Overall CRE cultures n=5,778[a]	Tested for CP n=1,905 (33.0%)	Not tested for CP n=3,873 (67.0%)	p-value
Culture Variables					
Organism	E.coli	591 (10.2)	147 (24.9)	444 (75.1)	<0.001
	Klebsiella spp.	3,932 (68.1)	1,372 (34.9)	2,560 (65.1)	
	Enterobacter spp.	1,255 (21.7)	386 (30.8)	869 (69.2)	
Care setting of CRE culture	Inpatient	2719 (47.1)	935 (34.4)	1,784 (64.6)	<0.001
	Outpatient	2283 (39.5)	660 (28.9)	1,623 (71.1)	
	Long-term care	776 (13.4)	310 (39.9)	466 (60.1)	
Source	Blood	481 (8.3)	189 (39.3)	292 (60.7)	0.009
	Urine	3573 (61.8)	1163 (32.5)	2,410 (67.5)	
	Respiratory	771 (13.3)	235 (30.5)	536 (69.5)	
	Rectal	67 (1.2)	28 (41.8)	39 (58.2)	
	Other	886 (15.3)	290 (32.7)	596 (67.3)	
Facility variables					
Geographic region	Midwest	688 (11.9)	207 (30.1)	481 (69.9)	<0.001
	West	621 (10.8)	213 (34.3)	408 (65.7)	
	South	1,708 (29.6)	659 (34.7)	1,049 (61.4)	
	Outside continental U.S.	1,601 (27.7)	394 (24.6)	1,207 (75.4)	
Rurality	Rural	275 (4.8)	74 (26.9)	201 (73.1)	0.03
	Urban	5,503 (95.2)	1,831 (33.3)	3,672 (66.7)	
Specialty care services or units					
Blind rehab	No	3,673 (63.6)	1,327 (36.1)	2,346 (63.9)	<0.001
	Yes	3,183 (55.1)	956 (30.0)	2,227 (70.0)	
Spinal cord injury	No	2,595 (44.9)	949 (36.6)	1,646 (63.4)	<0.001
	Yes	3,292 (57.0)	953 (28.9)	2,339 (71.1)	
Polytrauma	No	2,486 (43.0)	952 (38.3)	1,534 (61.7)	<0.001
	Yes	3,292 (57.0)	953 (28.9)	2,339 (71.1)	
Advanced surgical and/or procedural care services					
Int. Cardiology	No	1,048 (18.1)	256 (24.4)	792 (75.6)	<0.001
	Yes	4,730 (81.9)	1,649 (34.9)	3,081 (65.1)	
Transplant surgery	No	4,997 (86.5)	1,695 (33.9)	3,302 (66.1)	<0.001
	1-2 in-house or 3 sharing programs	707 (12.2)	173 (24.5)	534 (75.5)	
	3+ in-house programs	74 (1.3)	37 (50.0)	37 (50.0)	

Results

Figure 2. Carbapenemase mechanism testing

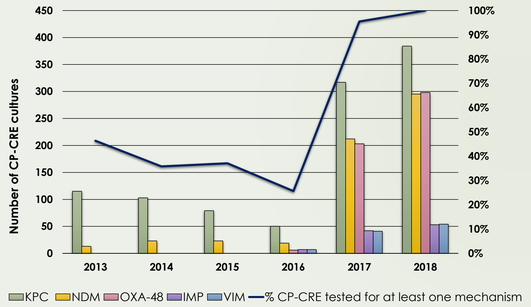
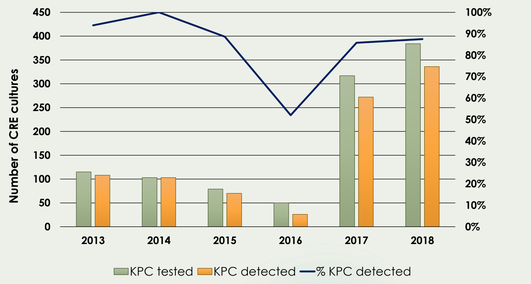


Figure 3. KPC testing and detection



Conclusions

- Following publication of initial CRE guidelines in 2015, carbapenemase testing and detection increased in the VA.
- Testing for and detection of non-KPC carbapenemases was infrequent; surveillance of non-KPC carbapenemases is important due to global dissemination and enhanced antibiotic resistance.
- Testing CRE for carbapenemases was more likely in inpatient or long-term care settings than outpatient. Urban location, higher complexity, and presence of specialty care services and advanced surgical/procedural services were also associated with a greater likelihood of VAMCs testing for carbapenemases.
- Efforts to expand and support laboratory and staff resources, particularly in low complexity, rural facilities, could further increase carbapenemase testing per VA CRE guidelines recommendations.

References

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