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Epidemiology of Carbapenem-Resistant Enterobacteriaceae in 7 US Communities, 2012-2013

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Abstract

IMPORTANCE—Carbapenem-resistant Enterobacteriaceae (CRE) are increasingly reported worldwide as a cause of infections with high-mortality rates. Assessment of the US epidemiology of CRE is needed to inform national prevention efforts.

OBJECTIVE—To determine the population-based CRE incidence and describe the characteristics and resistance mechanism associated with isolates from 7 US geographical areas.

DESIGN, SETTING, AND PARTICIPANTS—Population- and laboratory-based active surveillance of CRE conducted among individuals living in 1 of 7 US metropolitan areas in Colorado, Georgia, Maryland, Minnesota, New Mexico, New York, and Oregon. Cases of CRE were defined as carbapenem-nonsusceptible (excluding ertapenem) and extended-spectrum cephalosporin-resistant *Escherichia coli, Enterobacter aerogenes, Enterobacter cloacae* complex, *Klebsiella pneumoniae*, or *Klebsiella oxytoca* that were recovered from sterile-site or urine cultures during 2012-2013. Case records were reviewed and molecular typing for common carbapenemases was performed.

EXPOSURES—Demographics, comorbidities, health care exposures, and culture source and location.

MAIN OUTCOMES AND MEASURES—Population-based CRE incidence, site-specific standardized incidence ratios (adjusted for age and race), and clinical and microbiological characteristics.

RESULTS—Among 599 CRE cases in 481 individuals, 520 (86.8%; 95% CI, 84.1%-89.5%) were isolated from urine and 68 (11.4%; 95% CI, 8.8%-13.9%) from blood. The median age was 66 years (95% CI, 62.1-65.4 years) and 284 (59.0%; 95% CI, 54.6%-63.5%) were female. The overall annual CRE incidence rate per 100 000 population was 2.93 (95% CI, 2.65-3.23). The CRE standardized incidence ratio was significantly higher than predicted for the sites in Georgia (1.65 [95% CI, 1.20–2.25]; $P < .001$), Maryland (1.44 [95% CI, 1.06-1.96]; $P = .001$), and New York (1.42 [95% CI, 1.05-1.92]; $P = .048$), and significantly lower than predicted for the sites in Colorado (0.53 [95% CI, 0.39-0.71]; $P < .001$), New Mexico (0.41 [95% CI, 0.30-0.55]; $P = .01$), and Oregon (0.28 [95% CI, 0.21-0.38]; $P < .001$). Most cases occurred in individuals with prior hospitalizations (399/531 [75.1%; 95% CI, 71.4%-78.8%]) or indwelling devices (382/525 [72.8%; 95% CI, 68.9%-76.6%]); 180 of 322 (55.9%; 95% CI, 50.0%-60.8%) admitted cases resulted in a discharge to a long-term care setting. Death occurred in 51 (9.0%; 95% CI, 6.6%-11.4%) cases, including in 25 of 91 cases (27.5%; 95% CI, 18.1%-36.8%) with CRE isolated from normally sterile sites. Of 188 isolates tested, 90 (47.9%; 95% CI, 40.6%-55.1%) produced a carbapenemase.

CONCLUSIONS AND RELEVANCE—In this population- and laboratory-based active surveillance system in 7 states, the incidence of CRE was 2.93 per 100 000 population. Most CRE cases were isolated from a urine source, and were associated with high prevalence of prior hospitalizations or indwelling devices, and discharge to long-term care settings.

Carbapenem-resistant Enterobacteriaceae (CRE) are a worldwide clinical and public health problem. These multidrug-resistant organisms cause infections associated with high mortality and limited treatment options, and are increasingly recognized as an important cause of health care-associated infections.[1-5] In the United States, much of the initial dissemination of CRE can be attributed to organisms producing the *Klebsiella pneumoniae* carbapenemase, a type of β-lactamase enzyme that confers resistance to carbapenem antimicrobials.

Since the first case was reported in North Carolina in 2001, cases of *K pneumoniae* carbapenemase-producing CRE have been reported in almost every state and it remains the carbapenemase most commonly identified in isolates sent to the US Centers for Disease Control and Prevention (CDC).[6] To date, 23 states have required some form of CRE reporting; however, requirements and definitions vary by state. The current US reporting requirements are available online.[7]

To describe CRE epidemiology in the catchment areas and inform prevention efforts, the CDC formally initiated population-based surveillance in 2012 in select US geographical areas using the Emerging Infections Program (EIP). This surveillance system provides the most extensive US population-based evaluation of CRE to date, allowing for the monitoring of the burden of disease over time, identification of risk factors, and characterization of strains. We present the population-based incidence of CRE and describe the clinical characteristics and resistance mechanism associated with a subset of isolates from the 7 participating communities.

Methods

Surveillance Population

The Multi-site Gram-negative Surveillance Initiative is an ongoing, population-based (ie, based on the entire population of the included catchment areas), active, laboratory-based surveillance system. Surveillance of CRE was initiated in January 2012 at 3 EIP sites (metropolitan areas in Georgia, Minnesota, and Oregon) and expanded in 2013 to 4 additional sites (metropolitan areas in Colorado, Maryland, New Mexico, and New York).

The total population in the 7 participating areas under surveillance in 2013 was an estimated 13.2 million[8]; this includes Atlanta, Georgia (estimated population, 3 864 091), Denver, Colorado (estimated population, 2 583 519), Baltimore, Maryland (estimated population, 1 917 263), Minneapolis/St Paul, Minnesota (estimated population, 1725 492), Portland, Oregon (estimated population, 1 709 394), Rochester, New York (estimated population, 749 606), and Albuquerque, New Mexico (estimated population, 674 221).

The surveillance project was reviewed at the CDC by the National Center for Emerging and Zoonotic Diseases in accordance with institutional policy and was determined not to meet

the regulatory definition of research (under 45 CFR §46.102[d]), and therefore it was not subject to institutional review board requirements. Similarly, the project was reviewed at each of the participating EIP sites in accordance with institutional policies. In places where institutional review board approval was sought, a formal waiver of informed consent was obtained.

Race and ethnicity were collected from the medical record and could have been defined by the case-patient or the facility. These variables were included to evaluate the need for and to allow for rate adjustment between sites.

Case Definitions and Ascertainment

A CRE case was defined as a carbapenem-nonsusceptible and extended-spectrum cephalosporin-resistant (ceftriaxone, ceftazidime, ceftizoxime, and cefotaxime) *Escherichia coli, Enterobacter aerogenes, Enterobacter cloacae* complex, *K pneumoniae*, or *Klebsiella oxytoca* isolate recovered from a body site that is normally sterile (eg, bloodstream) or urine from individuals residing in the surveillance area during January 2012-December 2013. Because the minimum inhibitory concentration for ertapenem against Enterobacteriaceae is lower than for the other carbapenems, ertapenem was excluded from this CRE definition to increase specificity for carbapenemase-producing CRE. Isolates were identified by local laboratories through a query of automated testing instruments based on the protocols of the laboratories[9] and using the 2012 Clinical and Laboratory Standards Institute break points.[10]

An incident CRE case was defined as the first CRE isolate from a patient during a 30-day period that met the surveillance definition. All incident CRE cases underwent medical record review using a standardized abstraction form. Both inpatient and outpatient medical records were reviewed for patient demographics, underlying clinical comorbidities, location of culture collection, specimen source, associated infectious syndromes, relevant health care exposures (exposure to long-term acute care hospital was collected starting in 2013), and patient outcomes.

Information could not be identified for all variables because of the limitations of medical record review, therefore, denominators often varied for each of the variables. All-cause mortality was determined based on documentation in the medical record at the time of outpatient evaluation for outpatients, at discharge if hospitalized, or at the end of a 30-day period for individuals undergoing outpatient dialysis or residing in a long-term care facility or a long-term acute care hospital.

Isolate Collection and Evaluation

Laboratories serving the catchment areas were requested to submit CRE isolates to the CDC meeting the case definition for carbapenem-resistance mechanism testing. Isolates, particularly those from urinary sources, were difficult to acquire because they are often not saved. Due to this common practice limitation, an isolate was submitted for only the minority of cases. Polymerase chain reaction was performed by the CDC on submitted isolates for genes encoding *K pneumoniae* carbapenemase, New Delhi metallo-β-lactamase,[11] and OXA-48-type enzymes.[12]

Isolates were evaluated for metallo-β-lactamase production using a broth microdilution screening method consisting of serial dilutions of imipenem with and without chelators at fixed concentrations. A decrease in the minimum inhibitory concentration of the drug by 2 or more doubling dilutions in the presence of chelators was considered a positive metallo-β-lactamase screening.[11] Any isolate positive for metallo-β-lactamase but negative for New Delhi metallo-β-lactamase was further tested by polymerase chain reaction for genes encoding Verona integron-encoded metallo-β-lactamase and Imipenemase metallo-β-lactamase. The modified Hodge test was performed on all submitted isolates using both ertapenem and meropenem; a positive result for either carbapenem was considered indicative of carbapenemase production.

Statistical Analyses

Annual incidence rates for CRE cases and case-patients were calculated using the 2012 and 2013 US census estimates of the surveillance area population as the denominator. Standardized incidence ratio, which is an indirect standardization, was calculated to compare incident CRE rates among EIP sites. Standardized incidence ratio was used for this analysis because the relatively small number of CRE cases produced stratum-specific estimates (by age and race) that were too low to allow accurate direct standardization for disease rate comparison.[13] Missing values for race were imputed based on the distribution of known race by age, sex, and surveillance site.

The standardized incidence ratio was calculated by dividing the number of observed cases by the number of predicted cases. The number of predicted cases was estimated from a multivariable negative binomial regression predicting CRE infection incidence, adjusted by age (0-18 years, 19-49 years, 50-64 years, and ≥65 years) and race (white and nonwhite), and constructed from CRE surveillance data during 2012-2013 using surveillance site US census data as the denominator.[13]

The CRE incidence estimates aggregated across all participating sites during this same period represent the population used to standardize CRE incidence (standard population). The 95% confidence intervals for the standardized incidence ratios were constructed using the site-specific predicted case counts from each EIP site. A standardized incidence ratio of less than 1.0 indicates fewer observed CRE cases than predicted compared with the standard population, whereas a ratio greater than 1.0 indicates more observed CRE cases than predicted compared with the standard population.

Descriptive analyses were performed to summarize specimen information, health care exposures, outcomes, and microbiological results of incident CRE cases; χ^2 tests were used to compare groups when applicable. Demographic information, underlying comorbidities, and travel history of unique CRE case-patients were described for first incident CRE episode for the entire surveillance period. Charlson comorbidity index scores were calculated.

All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc). A 2-sided *P* value of <.05 was considered statistically significant.

Results

During 2012-2013, 599 incident CRE cases were identified in 481 individuals across the 7 EIP sites. Of the 599 cases, 351 (58.6%; 95% CI, 54.6%-62.6%) were *K pneumoniae*; 89 (14.9%; 95% CI, 12.0%-17.7%), *E coli*; 79 (13.2%; 95% CI, 9.8%-15.2%), *E cloacae*; 75 (12.5%; 95% CI, 9.8%-15.2%), *E aerogenes*; and 5 (0.8%; 95% CI, 0.1%-1.6%), *K oxytoca* (Table 1). Most of the CRE cases were *K pneumoniae* in Georgia (235/356 [66.0%; 95% CI, 61.1%-71.0%]), Maryland (69/92 [75.0%; 95% CI, 66.0%-84.0%]), and New York (17/27 [63.0%; 95% CI, 43.5%-82.4%]), whereas most of the cases were *E coli* in New Mexico (3/6 [50.0%; 95% CI, 0%-100%]) and *E aerogenes* in Minnesota (29/79 [40.8%; 95% CI, 29.1%-52.6%]).

Of the 481 unique individuals with CRE, 409 (85.0%) had 1 incident CRE-positive culture and 72 (15.0%) had 2 or more incident cultures during the 2-year surveillance period (range, 2-6 episodes). Of the 72 individuals with more than 1 incident culture, 13 (18.1%) had more than 1 species reported.

Incidence Rates and Standardized Incidence Ratios

The overall crude annual CRE incidence across the EIP sites during the 2-year period was 2.93 (95% CI, 2.65-3.23) per 100 000 population. Site-specific crude incidence rates in 2012 ranged from 0.35 (95% CI, 0.14-0.74) per 100 000 population in Oregon to 4.58 (95% CI, 3.94-5.30) per 100 000 population in Georgia (Table 2). The site-specific crude incidence rates in 2013 ranged from 0.82 (95% CI, 0.47-1.34) per 100 000 population in Oregon to 4.80 (95% CI, 3.89-5.85) per 100 000 population in Maryland.

Significantly higher than predicted CRE standardized incidence ratios adjusted for age and race, which were independently associated with increased risk of CRE, for the 2-year period were observed for Georgia ($P < .001$), Maryland ($P = .001$), and New York ($P = .048$). Significantly lower than predicted standardized incidence ratios were observed for Colorado ($P < .001$), New Mexico ($P = .01$), and Oregon ($P < .001$).

Specimen Information and Prior Health Care Exposures of Incident CRE Cases

Data on the health care location of specimen collection (eg, outpatient, short-stay acute care), specimen source, and type of infection appear in Table 3. Although medical record review identified lower urinary tract infection (UTI) as the most commonly associated infection, only 102 of the 392 reported cases of UTI (26.0%; 95% CI, 21.7%-30.4%) met the revised McGeer criteria and the CDC National Healthcare Safety Network long-term care facility surveillance definition.[14,15]

Prior health care exposures were reported for individuals in 531 of 575 cases (92.3%; 95% CI, 90.2%-94.5%). Hospitalization during the prior year was the most common health care exposure overall and among both cases with a carbapenemase-producing CRE and those cases not linked to a carbapenemase-producing CRE.

Demographics and Clinical Information

Of 481 unique individuals with CRE, 284 were women (59.0%; 95% CI, 54.6%-63.5%); the median age was 66 years (range, <1-100 years; Table 4). Clinical characteristics were available for 454 unique individuals. Of these 454 individuals, 415 (91.4%; 95% CI, 88.8%-94.0%) had at least 1 underlying comorbid condition with a median Charlson comorbidity index of 2 (range, 0-12) and 39 (8.6%; 95% CI, 6.0%-11.2%) had no documented underlying condition. The most commonly reported conditions included diabetes (201 [44.3%; 95% CI, 39.7%-48.9%]) and neurological disorders (185; 40.7% [95% CI, 36.2%-45.3%]). Of the 185 individuals with neurological disorders, 107 (57.8%; 95% CI, 50.7%-65.0%) had an indwelling urinary catheter within 2 days prior to their initial positive culture. Two individuals were hospitalized outside the United States (India and Italy) during the 2 months prior to their positive culture.

Outcome of CRE Cases

Among 569 CRE cases with data available, 371 (65.2%; 95% CI, 61.3%-69.1%) were in individuals who were hospitalized at the time of or within 30 days after having a positive culture (Table 5), including at least 171 (46.1%; 95% CI, 41.5%-51.7%) whose cultures were initially collected outside a short-stay acute care setting. Among 322 cases in hospitalized individuals with data available, 180 (55.9%; 95% CI, 50.0%-60.8%) were discharged directly to either a long-term care facility (153; 47.5% [95% CI, 42.0%-53.0%]) or a long-term acute care hospital (27; 8.4% [95% CI, 5.3%-11.4%]). Of 566 cases, death occurred in 51 (9.0%; 95% CI, 6.6%-11.4%); this included 25 (27.5%; 95% CI, 18.1%-36.8%) of 91 with sterile-site positive cultures compared with 26 (5.5%; 95% CI, 3.4%-7.5%) of 475 with only urine cultures ($P < .001$). Of the 25 individuals with a sterile-site positive culture who died, 20 (80.0%) had positive blood cultures.

Microbiological Results

Among cases with antimicrobial susceptibility results available from local clinical laboratories, 262 (88.8%; 95% CI, 85.2%-92.4%) were susceptible to tigecycline, 470 (81.7%; 95% CI, 78.6%-84.9%) to at least 1 aminoglycoside, 136 (25.3%; 95% CI, 21.7%-29.2%) to at least 1 fluoroquinolone, 68 (13.2%; 95% CI, 10.2%-16.1%) to piperacillin and tazobactam, and 19 (4.5%; 95% CI, 2.5%-6.5%) to aztreonam (Table 6).

Of the 188 CRE isolates submitted from the 6 EIP sites for carbapenemase testing (Table 1), *K pneumoniae* carbapenemase was the only one identified (90 [47.9%; 95% CI, 40.6%-55.1%]). It was most commonly found in *K pneumoniae* (69/87 [79.3%; 95% CI, 70.6%-88.0%]) and less commonly seen in other species (12/32 [37.5%; 95% CI, 19.8%-55.2%] in *E cloacae* complex; 7/32 [21.9%; 95% CI, 6.7%-37.0%] in *E coli*; and 2/37 [5.4%; 95% CI, 0%-13.0%] in *E aerogenes*).

Antimicrobial susceptibility results for carbapenemase-producing and non-carbapenemase-producing isolates and for sterile and nonsterile isolates appear in Table 6. A carbapenemase was detected in 15 of 25 (60.0%; 95% CI, 39.4%-80.6%) sterile-site isolates and 75 of 163 (46.0%; 95% CI, 38.3%-53.7%) urine isolates ($P = .19$). All 90 isolates for which a carbapenemase was detected were found to be positive using the modified Hodge test. There

were 24 of 98 (24.5%; 95% CI, 15.8%-33.2%) non-carbapenemase-producing isolates found to be positive using the modified Hodge test.

Discussion

During this 2-year surveillance period, 599 incident CRE cases were reported across 7 EIP sites, resulting in an overall crude incidence of 2.93 per 100 000 population. This estimate is substantially lower than the incidence of infections due to other pathogens traditionally associated with health care exposures, including methicillin-resistant *Staphylococcus aureus* (25.1 per 100 000 population),[16] invasive candidiasis (13.3-26.2 per 100 000),[17] and *Clostridium difficile* (147.2 per 100 000).[18] We found variation by site for the distribution of species, annual incidence, and the percentage of isolates that produced carbapenemase. Ninety-one percent of CRE cases were in individuals with preceding health care exposures and underlying comorbidities.

Although most cases were from cultures collected outside a short-stay acute care hospital, almost half were among individuals hospitalized within 30 days after their initial culture. The majority of hospitalized cases resulted in a discharge directly to a long-term care facility or long-term acute care hospital. Urine was the most common source of CRE, which likely accounted for the low overall mortality observed.

The variability in CRE incidence and the frequency with which different species are represented in EIP sites might reflect the degree to which carbapenemase-producing strains have emerged within and across regions of the United States. Carbapenemase-producing CRE carry antimicrobial resistance genes on mobile plasmids that can move between organisms, potentially facilitating a wider and more rapid spread, adding to the background of non-carbapenemase-producing CRE. Failure to address the spread of carbapenemase-producing CRE could lead to further increases in CRE incidence in areas in which they are already present and wider spread of CRE to areas that have not seen these organisms regularly.

Recommended control measures (eg, contact precautions) should be generally implemented to prevent further spread of all CRE, with more aggressive interventions used for carbapenemase-producing CRE (eg, surveillance cultures of hospitalized roommates).[3,19] Regionwide control measures also have been recommended to achieve maximal benefit.[19] Only half of all submitted CRE isolates meeting the case definition were found to possess a carbapenemase gene. The epidemiological significance of these cases of non-carbapenemase-producing CRE is less clear because they do not appear to have spread as rapidly during the last 15 years as cases of carbapenemase-producing CRE have. Continued multisite, population-based surveillance beyond the time frame provided in this report will be needed to better understand the relative contributions of carbapenemase-producing and non-carbapenemase-producing CRE to the spread of these organisms in the United States.

Although the majority of cases included in this report were identified from cultures collected in an outpatient setting (65.5%), more were actually collected in a short-stay acute care hospital (33.9%) than in a long-term care facility (26.9%) or a long-term acute care hospital

(7.5%). The most common preceding health care exposure among cases was a prior short-stay acute care hospitalization (75.1%). Although previous studies have found a substantially higher incidence of CRE in certain postacute care settings, particularly in long-term acute care hospitals compared with short-stay acute care hospitals,[20-22] and have demonstrated the vital role of long-term acute care hospitals in the regional dissemination of CRE,[23,24] our data suggest that short-stay acute care hospitals also have an important role in the regional epidemiology of CRE.

Approximately 8% of the cases were in individuals who did not have any documented relevant health care exposures prior to their positive CRE culture; however, the extent to which these cases represent community-associated CRE compared with undocumented health care exposures is not clear. The possible spread of CRE from health care settings into the community, as has been recognized with other resistant gramnegative bacilli,[25-28] is a concerning prospect requiring further evaluation.

Hospitalization around the time of the positive CRE culture was common among cases, with the majority among surviving individuals (55.9%), resulting in discharge directly to a long-term care facility or a long-term acute care hospital. This likely reflects the high prevalence of underlying comorbidities and older age among these individuals. The frequent movement of these individuals across the continuum of care underscores their important role in the interfacility spread of CRE,[23,24,29] especially if CRE status is not communicated to accepting facilities as part of the transfer process.

This investigation had several limitations. First, because the definition for carbapenem nonsusceptibility did not include ertapenem, organisms that were nonsusceptible to only ertapenem were not captured.

Second, the case definition relied on susceptibility test-ing performed locally; it is possible that methods varied across laboratories. Results from the local laboratory rather than results from confirmatory susceptibility testing were used to determine inclusion in this project to allow for a more inclusive description of CRE epidemiology from the perspective of health care facilities and laboratories.

Third, because not all commercial laboratories serving the catchment areas participated, these results may underestimate the CRE burden. However, these laboratories frequently serve postacute care and outpatient settings. Therefore, cases identified by these commercial laboratories are often captured later by cultures from acute care hospitalizations performed at other participating laboratories in the catchment area.

Fourth, surveillance definitions are limited in their ability to differentiate urinary isolates that represent true infections from those that do not. Because many of the case-patients were elderly and had isolates collected outside short-stay acute care settings, we applied a recognized long-term care facility UTI surveillance definition to determine if the reported UTIs might be true infections.

Fifth, although a broad set of catchment areas are included in this surveillance system, it is not designed to be representative of the United States. In addition, isolates from only one-

third of all cases were available for molecular characterization. Although attempts were made to systematically collect isolates, a nonrepresentative sample might have been selected at some sites.

In summary, the results of this investigation further inform local efforts to prevent CRE transmission. The low CRE incidence in the catchment areas, compared with other more established resistant organisms, highlights that CRE are emerging and suggests that control interventions implemented now could have a substantial effect.

The fact that heterogeneity exists (with respect to the incidence and the types of CRE found in these different surveillance areas) further highlights the need to understand the local epidemiology to tailor prevention efforts in individual regions of the United States. The frequency with which individuals with CRE are transferred between facilities emphasizes the need for regional control efforts in all the facilities. In addition, the finding that many CRE do not produce a carbapenemase suggests the potential need for a tiered response to these organisms as well as the need for more rapid and readily available laboratory tests to differentiate these strains.

Conclusions

In this population- and laboratory-based active surveillance system in 7 states, the incidence of CRE was 2.93 per 100 000 population. Most CRE cases were isolated from a urine source, and were associated with high prevalence of prior hospitalizations or indwelling devices, and discharge to long-term care settings.

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Table 1.

Carbapenem-Resistant Enterobacteriaceae (CRE) Organisms and Carbapenemase-Producing Isolates by Emerging Infections Program Site, 2012-2013

Emerging Infections Program Site	Total No.	CRE Organism or Isolate, No. (%)					Isolates Submitted for Carbapenemase Testing	No. of Carbapenemase-Producing Isolates/Total No. of Isolates Submitted for Testing (%)[a]
		Enterobacter aerogenes	*Enterobacter cloacae Complex*	*Escherichia coli*	*Klebsiella pneumoniae*	*Klebsiella oxytoca*		
Colorado[b]	27	7 (25.9)	10 (37.0)	3 (11.1)	7 (25.9)	0	16 (59.3)	5/16 (31.3)
Georgia	356	22 (6.2)	38 (10.7)	56 (15.7)	235 (66.0)	5 (1.4)	75 (21.1)	48/75 (64.0)
Maryland[b]	92	8 (8.7)	6 (6.5)	9 (9.8)	69 (75.0)	0	17 (18.5)	13/17 (76.5)
Minnesota	71	29 (40.8)	16 (22.5)	10 (14.1)	16 (22.5)	0	58 (81.7)	17/58 (29.3)
New Mexico[b]	6	2 (33.3)	0	3 (50.0)	1 (16.7)	0	*c*	*c*
New York[b]	27	3 (11.1)	2 (7.4)	5 (18.5)	17 (63.0)	0	9 (33.3)	5/9 (55.6)
Oregon	20	4 (20.0)	7 (35.0)	3 (15.0)	6 (30.0)	0	13 (65.0)	2/13 (15.4)
Total	599	75 (12.5)	79 (13.2)	89 (14.9)	351 (58.6)	5 (0.8)	188 (31.4)	90/188 (47.9)

[a] *Only K pneumoniae* carbapenemase was detected among the submitted CRE isolates.

[b] Only 2013 data are available.

[c] New Mexico did not submit any CRE isolates during 2012-2013 for molecular characterization.

Table 2.

Carbapenem-Resistant Enterobacteriaceae (CRE) Cases and Individuals With CRE, Annual Crude Incidence, and Standardized Incidence Ratio by Emerging Infections Program Site, 2012-2013

Emerging Infections Program Site	Incident CRE Cases[a]					Individuals With CRE			
	No. of Cases		Crude Annual Incidence Rate/100 000 Population		Standardized Incidence Ratio (95% CI)[c]	No. of Case-Patients[d]		Crude Annual Incidence Rate/100 000 Population	
	2012[b]	2013	2012[b]	2013		2012[b]	2013	2012[b]	2013
Colorado		27		1.05	0.53 (0.39-0.71)		26		1.01
Georgia	175	181	4.58	4.68	1.65 (1.20-2.25)	136	154	3.56	3.99
Maryland		92		4.80	1.44 (1.06-1.96)		74		3.86
Minnesota	31	40	1.82	2.32	0.94 (0.69-1.27)	29	35	1.70	2.03
New Mexico		6		0.89	0.41 (0.30-0.55)		6		0.89
New York		27		3.60	1.42 (1.05-1.92)		18		2.40
Oregon	6	14	0.35	0.82	0.28 (0.21-0.38)	6	14	0.35	0.82
Total	212	387	2.94	2.93		171	327	2.37	2.47

[a] Defined as the first carbapenem-nonsusceptible and extended-spectrum cephalosporin-resistant (ceftriaxone, ceftazidime, ceftizoxime, and cefotaxime) *Escherichia coli, Enterobacter aerogenes, Enterobacter cloacae* complex, *Klebsiella pneumoniae*, or *Klebsiella oxytoca* isolate recovered every 30 days from a body site that is normally sterile (eg, bloodstream) or urine from individuals residing in the surveillance area during January 2012-December 2013.

[b] Only 3 Emerging Infections Program sites participated in 2012.

[c] Data are for 2012 and 2013 combined when data for both years were available.

[d] Individuals could be included in both 2012 and 2013 so the total for these 2 columns is 498. This total exceeds that reported in the text (n = 481) because individuals were only counted once in the text for the 2-year period.

Table 3.

Isolate Collection Location, Culture Source, Infection Type, and Prior Health Care Exposures Among Incident Carbapenem-Resistant Enterobacteriaceae Cases, 2012-2013

	No./Total (%)		
	All Cases	**Case Linked to Carbapenemase-Producing Isolate**	**Case Linked to Non-Carbapenemase-Producing Isolate**
Collection Location			
Short-stay acute care hospital	198/584 (33.9)	40/90 (44.4)	19/98 (19.3)
Outside acute care hospital	386/584 (66.1)	49/90 (54.4)	78/98 (79.6)
Outpatient setting or emergency department	253/386 (65.5)	29/49 (59.2)	51/78 (65.4)
Long-term care facility	104/386 (26.9)	17/49 (34.7)	23/78 (29.5)
Long-term acute care facility	29/386 (7.5)	3/49 (6.1)	4/78 (5.1)
Culture Source			
Urine	520/599 (86.8)	76/90 (84.4)	88/98 (89.8)
Blood[a]	68/599 (11.4)	12/90 (13.3)	6/98 (6.1)
Peritoneal fluid	8/599 (1.3)	1/90 (1.1)	1/98 (1.0)
Pleural fluid	3/599 (0.5)	0/90	1/98 (1.0)
Other normally sterile sites	7/599 (1.2)	2/90 (2.2)	2/98 (2.0)
Infection Types			
Lower urinary tract infection	392/559 (70.0)	61/86 (70.9)	66/92 (71.7)
Bacteremia	68/559 (12.2)	12/86 (14.0)	6/92 (6.5)
Septic shock	17/559 (3.0)	2/86 (2.3)	0/92
Pneumonia	16/559 (2.9)	3/86 (3.5)	2/92 (2.2)
Other infection types[b]	47/559 (8.4)	6/86 (7.0)	8/92 (8.7)
Health Care Exposures During Prior Year			
Acute care hospitalization	399/531 (75.1)	68/87 (78.2)	54/76 (71.1)
Resident of a long-term care facility	259/531 (48.8)	53/87 (60.9)	35/76 (46.1)
Admission to a long-term acute care hosptial[c]	42/318 (13.2)	5/54 (9.3)	5/55 (9.1)
Inpatient or outpatient surgery	194/531 (36.5)	30/87 (34.5)	32/76 (42.1)
Current maintenance dialysis	60/531 (11.3)	13/87 (15.0)	7/76 (9.2)

	No./Total (%)		
	All Cases	Case Linked to Carbapenemase-Producing Isolate	Case Linked to Non-Carbapenemase-Producing Isolate
Indwelling device (2 calendar days prior to culture)	382/525 (72.8)	70/87 (80.5)	42/75 (56.0)
Urinary catheter	285/382 (74.6)	54/70 (77.1)	29/42 (69.1)
Central venous catheter	163/382 (42.7)	24/70 (34.3)	18/42 (42.9)
Gastrostomy or jejunostomy tube	151/382 (39.2)	30/70 (42.9)	16/42 (38.1)
Trachoestomy	120/382 (31.4)	21/70 (30.0)	12/42 (28.6)
Other device	81/382 (21.2)	15/70 (21.4)	7/42 (16.7)

[a] Category includes 7 cases with both a positive blood and urine culture.

[b] Includes pyelonephritis, surgical site infections, decubitus ulcers, and chronic wounds.

[c] Data collected in 2013 only.

Table 4.

Demographic and Clinical Characteristics of Unique Individuals With Carbapenem-Resistant Enterobacteriaceae

	No./Total (%)[a]
Demographics	
Female sex	284/481 (59.0)
Age, median (range), y	66 (<1-100)
Age group, y	
0-18	3/481 (0.6)
19-49	92/481 (19.1)
50-64	132/481 (27.4)
65-79	149/481 (31.0)
≥80	105/481 (21.8)
White	199/430 (46.3)
Hispanic	17/253 (6.7)
Clinical Characteristics	
Charlson Comorbidity Index, median (range)[b]	2 (0-12)
Underlying conditions	
None	39/454 (8.6)
Cirrhosis	10/454 (2.2)
Chronic pulmonary disease	103/454 (22.7)
Chronic renal insufficiency	116/454 (25.6)
Congestive heart failure	98/454 (21.6)
Connective tissue disease	20/454 (4.4)
Decubitus or pressure ulcer	122/454 (26.9)
Diabetes	201/454 (44.3)
Liver failure	3/454 (0.7)
Myocardial infarction	28/454 (6.2)
Neurological disorder	185/454 (40.7)
Transplant recipient	18/454 (4.0)
Urinary tract problems or abnormalities	93/454 (20.5)
Any malignancy	44/454 (9.7)

[a] Unless otherwise indicated.

[b] Score range is 0 to 37; the higher the number, the more serious the constellation of coexisting comorbidities.

Table 5.

Outcome of Carbapenem-Resistant Enterobacteriaceae Cases

	No./Total (%)		
	All Cases	**Case Linked to Carbapenemase-Producing Isolate**	**Case Linked to Non-Carbapenemase-Producing Isolate**
Required hospitalization at the time of or within 30 d after initial positive culture	371/569 (65.2)	65/88 (73.9)	46/92 (50.0)
Required intensive care unit stay in the 7 d after positive culture	128/368 (34.8)	19/65 (29.2)	11/46 (23.9)
Discharge disposition			
Home (private residence)	141/322 (43.8)	24/60 (40.0)	21/40 (52.5)
Other setting			
Long-term acute care facility or long-term acute care hospital	180/322 (55.9)	36/60 (60.0)	19/40 (47.5)
Inpatient hospice	1/322 (0.3)	0	0
Died during hospitalization or at the end of the 30-d evaluation	51/566 (9.0)	6/88 (6.8)	5/92 (5.4)
Among any sterile-site positive culture	25/91 (27.5)	1/15 (6.7)	3/10 (30.0)
Among non-sterile-site positive culture only (ie, urine specimen)	26/475 (5.5)	5/73 (6.8)	2/84 (2.4)

Table 6.

Antimicrobial Susceptibility of Carbapenem-Resistant Enterobacteriaceae Isolates Based on Testing by Local Clinical Laboratories

Antimicrobial Agent[a]	Total No. of Susceptible Isolates/Total No. Tested (%)	No. of Susceptible Isolates/No. Tested (%)			
		From Sterile Site	From Nonsterile Site[b]	Linked to Carbapenemase-Producing Isolate[c]	Linked to Non-Carbapenemase-Producing Isolate
Any aminoglycoside	470/575 (81.7)	78/92 (84.8)	392/483 (81.2)	68/90 (75.6)	85/96 (88.5)
Amikacin	294/499 (58.9)	38/80 (47.5)	256/419 (61.1)	37/83 (44.6)	68/82 (82.9)
Gentamicin	367/575 (63.8)	57/92 (62.0)	310/483 (64.2)	44/90 (48.9)	72/96 (75.0)
Tobramycin	181/536 (33.8)	14/87 (16.1)	167/449 (37.2)	12/86 (14.0)	58/92 (63.0)
Any fluoroquinolone	136/537 (25.3)	15/84 (17.9)	121/453 (26.7)	6/89 (6.7)	48/95 (50.5)
Ciprofloxacin	124/537 (23.1)	13/84 (15.5)	111/453 (24.5)	6/89 (6.7)	47/95 (49.5)
Levofloxacin	111/499 (22.2)	13/79 (16.5)	98/420 (23.3)	4/71 (5.6)	41/88 (46.6)
Moxifloxacin	10/35 (28.6)	3/14 (21.4)	7/21 (33.3)	2/10 (20.0)	1/5 (20.0)
Other antibiotics					
Aztreonam	19/423 (4.5)	2/67 (3.0)	17/356 (4.8)	1/62 (1.6)	4/60 (6.7)
Colistin[d]	9/12 (75.0)	2/2 (100.0)	7/10 (70.0)	1/2 (50.0)	1/2 (50.0)
Piperacillin and tazobactam	68/517 (13.2)	8/86 (9.3)	60/431 (13.9)	1/80 (1.3)	21/86 (24.4)
Tigecycline	262/295 (88.8)	51/57 (89.5)	211/238 (88.7)	48/53 (90.6)	35/36 (97.2)

[a] None of the isolates were tested against polymyxin B.

[b] Only from urine.

[c] All were *Klebsiella pneumoniae* carbapenemase-positive isolates.

[d] The break points were based on 2 μg/mL or less of colstin for *Pseudomonas aeruginosa* because there are no Clinical and Laboratory Standards Institute break points for Enterobacteriaceae.