Emerging Infections Program (EIP) Network Report
Healthcare-Associated Infections Community Interface Activity
Multi-site Gram-negative Surveillance Initiative
Carbapenem-Resistant Enterobacterales (CRE) Surveillance, 2017

Case Definition:

A carbapenem-resistant Enterobacterales (CRE) case was defined as isolation of *Escherichia coli*, *Enterobacter aerogenes* (now *Klebsiella aerogenes*), *Enterobacter cloacae* complex, *Klebsiella pneumoniae,* or *Klebsiella oxytoca* with the following criteria:

- Carbapenem-resistant (doripenem, imipenem, meropenem, or ertapenem) using the current Clinical and Laboratory Standards Institute clinical breakpoints (1);
- Isolated from normally sterile body sites (e.g., blood, cerebrospinal fluid, pleural fluid, pericardial fluid, peritoneal fluid, joint/synovial fluid, bone, internal body sites, or muscle) or urine;
- Identified in residents of the surveillance area in 2017.

Surveillance Catchment Areas:

Colorado (5 county Denver area); Georgia (8 county Atlanta area); Maryland (4 county Baltimore area); Minnesota (2 county Minneapolis – St. Paul area); New Mexico (1 county Albuquerque area); New York (1 county Rochester area); Oregon (3 county Portland area); and Tennessee (8 county Nashville area). This report does not include data from California (3 county San Francisco area), which started surveillance for CRE in August 2017.

Population:

The surveillance area represents 15,543,478 persons.
Source: National Center for Health Statistics bridged-race vintage 2017 file.

Methods:

Case finding was active, laboratory-based, and population-based. Clinical laboratories that serve residents of the surveillance area were routinely contacted for case identification through a query of minimum inhibitory concentration (MIC) values from automated testing instruments. When possible, the MIC values obtained directly from the automated testing instruments were used to determine if an isolate met the phenotypic case definition. An incident CRE case was defined as the first CRE isolate meeting the case definition from a patient during a 30-day period.

A standardized case report form was completed for each incident case through review of medical records. Inpatient and outpatient medical records were reviewed for information on patient demographics, clinical syndrome, outcome of illness, and relevant healthcare exposures.

A convenience sample of CRE isolates (N=611) was collected from sites and submitted to CDC for additional testing including species confirmatory testing, antimicrobial susceptibility testing by reference broth microdilution with a metallo-β-lactamase (MBL) screen, screening for carbapenemase production using the Modified Carbapenem Inactivation Method (mCIM), real-time polymerase chain reaction (PCR) screening for carbapenemase-encoding genes, including bla_{KPC}, bla_{NDM}, and $bla_{\text{OXA-48-like}}$ genes, and PCR testing for other

carbapenemase genes (i.e., *bla*$_{VIM}$) if MBL screen positive and negative for *bla*$_{KPC}$, *bla*$_{NDM}$, and *bla*$_{OXA-48-like}$ genes.

Incidence rates for incident CRE cases were calculated using the 2017 US Census estimates of the surveillance area population as the denominator. Assessment of vital status in patients admitted to a hospital occurred at the time of discharge from the acute care hospital. For patients in a long-term care facility, long-term acute care facility, or in an outpatient dialysis center, vital status was assessed 30 days after culture collection. For all other patients, vital status was assessed using medical records from the healthcare facility encounter associated with the culture.

CRE surveillance data underwent regular data cleaning to ensure accuracy and completeness. Patients with complete case report form data as of 9/10/2021 were included in this analysis. Because data can be updated as needed, analyses of datasets generated on a different date may yield slightly different results.

Results:

Table 1. Specimen Sources for CRE Cases by Organism, 2017 (N=1173)

Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood[a] %	Other Sterile Sites No.	Other Sterile Sites, %
Enterobacter cloacae complex	416	382	91.8	20	4.8	14	3.4
Escherichia coli	321	295	91.9	16	5.0	10	3.1
Klebsiella pneumoniae	339	296	87.3	32	9.4	11	3.2
Klebsiella aerogenes	75	70	93.3	3	4.0	2	2.7
Klebsiella oxytoca	22	16	72.7	2	9.1	4	18.2
Total	**1173**	**1059**	**90.3**	**73**	**6.2**	**41**	**3.5**

[a] Category includes cases with both a positive blood and urine specimen collected

Table 2 Incidence Rates of CRE Cases by Sex, Race and Age, 2017 (N=1173)

Sex	No. of Cases	%	Incidence Rate[a]
Female	747	63.7	9.39
Male	426	36.3	5.62

Race	No. of Cases	%	Incidence Rate[a]
White	662	56.4	6.12
Black or African American	321	27.4	9.25
Other[b]	45	3.8	3.56
Unknown	145	12.4	-

Age groups, years	No. of Cases	%	Incidence Rate[a]
0–18	21	1.8	0.56
19–49	206	17.6	3.02
50–64	236	20.1	8.06
65–79	406	34.6	25.77
≥80	304	25.9	65.22
Invasive cases[c]	121	10.3	0.78
All cases	1173	100.0	7.55

[a] Cases per 100,000 population for EIP areas (crude rates)

[b] Other race includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported

[c] Invasive cases include cases with a sterile incident specimen source or an incident urine specimen with a subsequent non-incident sterile specimen collected on the date of incident specimen collection or in the 29 days after

Table 3. CRE Cases by Race and Ethnicity, 2017 (N=1173)

Race/Ethnicity	No. of Cases	%
Hispanic, any race	82	7.0
Not known to be Hispanic[a] – White[b]	615	52.4
Not known to be Hispanic[a] – Black or African American[c]	320	27.3
Not known to be Hispanic[a] – Asian[d]	34	2.9
Not known to be Hispanic – Other or multiple races[e]	11	0.9
Not known to be Hispanic[a,f]– Unknown race	111	9.5

[a] Records either indicated ethnicity was non-Hispanic, or ethnicity was not known

[b] 100 CRE cases with unknown ethnicity

[c] 54 CRE cases with unknown ethnicity

[d] 6 CRE cases with unknown ethnicity

[e] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 2 CRE cases with unknown ethnicity

[f] Of cases with unknown race, 95 CRE cases had unknown ethnicity

Table 4. Selected Characteristics of CRE Cases, 2017 (N=1173)

Location of patient on the 3rd calendar day before incident specimen collection	No. of Cases	%
Private residence	683	58.2
Long-term care facility	238	20.3
Acute-care hospital (inpatient)	180	15.3
Long-term acute care hospital	23	2.0
Homeless/incarcerated/other	7	0.6
Unknown	42	3.6

Location of incident specimen collection	No. of Cases	%
Outpatient setting or emergency department	691	58.9
Acute care hospital	271	23.1
Long-term care facility	184	15.7
Long-term acute care hospital	25	2.1
Unknown	2	0.2

Infection types[a]	No. of Cases	%
Urinary tract infection	805	68.6
Bacteremia[b]	98	8.4
Septic shock	26	2.2
Other	59	5.0
None[c]	160	13.6
Unknown	90	7.7

[a] Patients could have more than one type of infection reported

[b] Bacteremia includes cases with a positive blood specimen (incident or non-incident) or a documented diagnosis of sepsis, septicemia, bacteremia, or blood stream infection

[c] No infection types reported

Table 5. Selected Clinical Characteristics of CRE Cases, 2017[a] (N=1173)

Charlson comorbidity index	No. of Cases	%
0	260	22.2
1	241	20.5
≥2	625	53.3
Unknown	47	4.0
Median (IQR)	2	1–3

Underlying conditions	No. of Cases	%
Neurologic condition, any	419	35.7
Diabetes mellitus	369	31.5
Cardiovascular disease[b]	355	30.3
Urinary tract problems/abnormalities	311	26.5
Chronic pulmonary disease[c]	292	24.9
Skin condition	213	18.2
Malignancy (hematologic or solid organ)	188	16.0
Chronic renal disease	129	11.0
Gastrointestinal disease[d]	68	5.8
Transplant (solid organ)	20	1.7
Unknown	47	4.0

[a] Patients could have more than one underlying condition reported

[b] Defined as myocardial infarction, congestive heart failure, congenital heart disease, stroke, transient ischemic attack, or peripheral vascular disease

[c] Defined as cystic fibrosis or any chronic respiratory condition resulting in symptomatic dyspnea

[d] Defined as peptic ulcer disease or liver disease

Table 6. Selected Healthcare Exposures or Risk Factors of CRE Cases, 2017[a] (N=1173)

Healthcare facility stay in the year before the date of incident specimen collection	No. of Cases	%
Acute care hospitalization	661	56.4
Long-term care facility residence	365	31.1
Long-term acute care hospitalization	58	4.9

Exposure	No. of Cases	%
Surgery in the year before the date of incident specimen collection	291	24.8
Specimen collected ≥3 days after hospital admission	165	14.1
Chronic dialysis	43	3.7

Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection	No. of Cases	%
Urinary catheter	404	34.4
Central venous catheter	186	15.9
Other[b]	242	20.6
None of the above healthcare exposures[c]	270	23.0
Healthcare exposures are unknown	27	2.3
International travel in the 2 months prior to date of incident specimen	8	0.7

[a] Patients could have more than one prior healthcare risk factor reported
[b] Other medical devices include endotracheal or nasotracheal tube, tracheostomy, gastrostomy tube, nephrostomy tube, nasogastric tube
[c] Defined as having no healthcare exposures in the year before specimen collection, no selected medical devices in place in the 2 days before specimen collection, and specimen collected before calendar day 3 after hospital admission if hospitalized

Table 7. Outcomes of Incident CRE Cases, 2017 (N=1173)

Outcomes	**No. of Cases**	**%**
Hospitalized on the day of or in the 29 days after the date of incident specimen collection	555	47.3
ICU admission in the 6 days after the date of incident specimen collection	87	7.4

Discharge location among hospitalized	**No. of Cases**	**%**
Private residence	274/555	49.4
Long-term care facility	197/555	35.5
Long-term acute care hospital	20/555	3.6
Died during hospitalization	54/555	9.7
Other	9/555	1.6
Unknown	1/555	0.2
Died within 30 days of incident specimen collection date	48	4.1
Cases with an incident sterile site specimen	20/114	17.5
Cases with an incident urine specimen[a]	28/1059	2.6

[a] One incident CRE case had a subsequent non-incident blood specimen collected on the date of incident specimen collection or in the 29 days after

Laboratory Characterization:

Table 8a. Antimicrobial Susceptibility and Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC, 2017 (N=611)

Organism	Isolates Submitted to CDC	Carbapenemase-producing [a,b,c], No.	%
Enterobacter cloacae complex	248	14	5.6
Escherichia coli	134	19	14.2
Klebsiella pneumoniae	186	110	59.1
Klebsiella aerogenes	34	0	0.0
Klebsiella oxytoca	9	2	22.2
Total	**611**	**145**	**23.7**

Table 8b. Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC, 2017 by Carbapenemase Gene (N=611)

Organism	*bla*$_{KPC}$, No.	*bla*$_{KPC}$ %	*bla*$_{NDM}$, No.	*bla*$_{NDM}$ %	*bla*$_{OXA-48-like}$, No.	*bla*$_{OXA-48-like}$ %
Enterobacter cloacae complex	14	5.6	0	0.0	0	0.0
Escherichia coli	10	7.5	3	2.2	6	4.5
Klebsiella pneumoniae	106	57.0	3	1.6	2	1.1
Klebsiella aerogenes	0	0.0	0	0.0	0	0.0
Klebsiella oxytoca	2	22.2	0	0.0	0	0.0
Total	**132**	**21.6**	**6**	**1.0**	**8**	**1.3**

Table 8c. Confirmatory Antimicrobial Susceptibility Results of CRE Isolates Submitted to CDC

Organism	Carbapenem-resistant, No.	Carbapenem-resistant - %	Difficult to treat[e], No.	Difficult to treat[e] - %
Enterobacter cloacae complex	85	34.3	11	4.4
Escherichia coli	45	33.6	8	6.0
Klebsiella pneumoniae	126	67.7	93	50.0
Klebsiella aerogenes	13	38.2	0	0.0
Klebsiella oxytoca	5	55.6	0	0.0
Total	**274**	**44.8**	**112**	**18.3**

[a] Testing was performed by PCR

[b] Carbapenemase-producing isolates were collected from urine (n=125/145; 86.2%), blood (n=17/145; 11.7%), and other normally sterile site (n=3/145; 2.1%)

[c] All isolates that were mCIM positive were also PCR positive, except for four isolates that were mCIM positive and PCR negative

[d] One isolate had *bla*$_{NDM}$ and *bla*$_{OXA-48-like}$ gene and one isolate had *bla*$_{KPC}$ and *bla*$_{VIM}$

[e] Difficult to treat (2) is defined as non-susceptibility to all first-line agents tested (i.e., carbapenems, extended-spectrum cephalosporins, fluoroquinolones, piperacillin-tazobactam, and aztreonam)

Summary:

Surveillance data from 2017 represent the sixth full year of population-based surveillance for CRE through the Emerging Infections Program. The overall crude incidence rate of CRE in 2017 was 7.55 cases per 100,000 persons. The incidence rate increased with age and was higher in women than in men and higher in persons of Black or African American race than in persons of other races. More CRE were isolated from a urine source than from normally sterile body sites. Underlying conditions were commonly reported, with more than half of CRE cases having a Charlson comorbidity index of ≥2. Prior healthcare exposures were reported for most cases, with hospitalization in the prior year, presence of indwelling medical devices, and prior long-term care facility residency being the most common exposures. Approximately half of the CRE cases required hospitalization, and overall crude 30-day mortality was 4.1%, with a higher 30-day mortality observed in cases with a sterile-site specimen source compared to those with a urine specimen source.

Among the 611 CRE isolates submitted to CDC, 23.7% were carbapenemase-producing. KPC was detected in 21.6% of the isolates, NDM in 1.0% of isolates, and OXA-48-like in 1.3% of isolates.

References:

1. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100 (ISBN 1-56238-804-5 [Print]; ISBN 1-56238-805-3 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2017.

2. Kadri SS, Adjemian J, Lai YL, Spaulding AB, Ricotta E, Prevots DR, et al. Difficult-to-Treat Resistance in Gram-negative Bacteremia at 173 US Hospitals: Retrospective Cohort Analysis of Prevalence, Predictors, and Outcome of Resistance to All First-line Agents. Clin Infect Dis. 2018 Nov 28;67(12):1803-14.

Citation:

Centers for Disease Control and Prevention. 2023. Emerging Infections Program, Healthcare-Associated Infections – Community Interface Surveillance Report, Multi-site Gram-negative Surveillance Initiative (MuGSI), Carbapenem-Resistant Enterobacterales Surveillance, 2017. Available at: https://www.cdc.gov/hai/eip/pdf/mugsi/2017-CRE-Report-508.pdf

For more information, visit our web sites:

- Multi-site Gram-negative Surveillance Initiative (MuGSI) (https://www.cdc.gov/hai/eip/mugsi.html)
- Healthcare-Associated Infections - Community Interface Data Visualization (HAICViz) (https://www.cdc.gov/hai/eip/haicviz.html)