Emerging Infections Program (EIP) Network Report
Healthcare-Associated Infections Community Interface Activity
Multi-site Gram-negative Surveillance Initiative
Carbapenem-Resistant Enterobacterales (CRE) Surveillance, 2022

Case Definition:

A carbapenem-resistant Enterobacterales (CRE) case was defined as isolation of *Escherichia coli*, *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 a normally sterile specimen (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 2022.

Surveillance Catchment Areas:

California (3 county San Francisco area), Colorado (5 county Denver area); Connecticut (statewide); 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).

Population:

The surveillance area represents 23,141,988 persons.
Source: U.S. Census Bureau, Population Division, Vintage 2022 Special Tabulation.

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.

Standardized case report forms were completed for incident cases 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=772) was collected from EIP 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 $bla_{OXA\text{-}48\text{-}like}$ genes, and PCR testing for other carbapenemase genes (i.e., $bla_{VIM,}$ bla_{imp}) if MBL screen positive and negative for bla_{KPC}, bla_{NDM}, and $bla_{OXA\text{-}48\text{-}like}$ genes.

Incidence rates for CRE cases were calculated using the 2022 U.S. 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 8/15/2024 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, 2022 (N=1479)

Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood[a] %	Other sterile specimens No.	Other sterile specimens %
Enterobacter cloacae complex	630	540	85.7	63	10.0	27	4.3
Klebsiella pneumoniae	393	339	86.3	41	10.4	13	3.3
Escherichia coli	348	308	88.5	28	8.0	12	3.4
Klebsiella aerogenes	77	63	81.8	9	11.7	5	6.5
Klebsiella oxytoca	31	22	71.0	7	22.6	2	6.5
Total	**1479**	**1272**	**86.0**	**148**	**10.0**	**59**	**4.0**

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

Table 2. Incidence Rates of CRE Cases by Sex, Race and Age, 2022 (N=1479)

Sex	No. of Cases	%	Incidence Rate[a]
Female	858	58.0	7.3
Male	618	41.8	5.4
Unknown	3	0.2	-

Race	No. of Cases	%	Incidence Rate[a]
White	893	60.4	5.8
Black or African American	351	23.7	8.1
Asian	71	4.8	3.0
American Indian, Alaska Native	10	0.7	4.2
Another race[b] or unknown	154	10.4	-

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

[b] Data for Native Hawaiian, and Pacific Islander case-patients were included in the another race category for privacy

Age groups, years	No. of Cases	%	Incidence Rate[a]
0–18	33	2.2	0.6
19–49	207	14.0	2.1
50–64	275	18.6	6.3
65–79	556	37.6	19.6
≥80	408	27.6	50.1
Invasive cases[b]	214	14.5	0.9
All cases	1479	100.0	6.4

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

[b] 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, 2022 (N=1479)

Race/Ethnicity	No. of Cases	%
Hispanic or Latino, any race	138	9.3
Not known to be Hispanic or Latino[a] – White[b]	832	56.3
Not known to be Hispanic or Latino[a] – Black or African American[c]	339	22.9
Not known to be Hispanic or Latino[a] – Asian[d]	70	4.7
Not known to be Hispanic or Latino[a] – Another race or multiracial[e]	15	1.0
Not known to be Hispanic or Latino[a]– Unknown race[f]	85	5.7

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

[b] 18 CRE cases with unknown ethnicity

[c] 9 CRE cases with unknown ethnicity

[d] 1 CRE case with unknown ethnicity

[e] American Indian or Alaska Native, Native Hawaiian or Pacific Islander, or ≥2 races reported; no CRE cases with unknown ethnicity

[f] 69 CRE cases had unknown ethnicity

Table 4. Selected Characteristics of CRE Cases, 2022 (N=1479)

Location of patient on the 3rd calendar day before incident specimen collection	No. of Cases	%
Private residence or other location	921	62.3
Acute-care hospital (inpatient)	275	18.6
Long-term care facility	214	14.5
Long-term acute care hospital	27	1.8
Homeless[a]	7	0.5
Unknown	35	2.4

[a] Includes patients documented as experiencing homelessness at the time of positive culture. A patient experiencing homelessness is defined as an individual who lacks permanent housing

Location of incident specimen collection	No. of Cases	%
Outpatient setting or emergency department	916	61.9
Acute care hospital	402	27.2
Long-term care facility	107	7.2
Long-term acute care hospital	30	2.0
Unknown	24	1.6

Infection types[a]	No. of Cases	%
Urinary tract infection	1021	69.0
Bacteremia[b]	200	13.5
Septic shock	68	4.6
Other	135	9.1
None[c]	158	10.7
Unknown	88	5.9

[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, bacteremia, or blood stream infection

[c] No infection types reported

Table 5. Selected Clinical Characteristics of CRE Cases, 2022 (N=1479)

Charlson comorbidity index	No. of Cases	%
0	279	18.9
1	259	17.5
≥2	906	61.3
Unknown	35	2.4
Median (interquartile range)	2	1–4

Underlying conditions [a]	No. of Cases	%
Urinary tract problems/abnormalities	634	42.9
Neurologic condition, any	634	42.9
Cardiovascular disease[b]	561	37.9
Diabetes mellitus	560	37.9
Chronic renal disease	462	31.2
Skin condition	385	26.0
Chronic pulmonary disease[c]	345	23.3
Malignancy (hematologic or solid organ)	293	19.8
Gastrointestinal disease[d]	250	16.9
Transplant (hematopoietic stem cell or solid organ)	52	3.5
Unknown	35	2.4

SARS-CoV-2 testing	No. of Cases	%
Positive test for SARS-CoV-2 during hospitalization and on or before the date of incident specimen collection[e]	70/692	10.1

[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 diverticular disease, inflammatory bowel disease, peptic ulcer disease, short gut syndrome, or liver disease

[e] Among patients in the hospital on the date of incident specimen collection. Excludes patients who were admitted to the hospital after the date of incident specimen collection. A positive SARS-CoV-2 test was defined as any positive viral test for SARS-CoV-2, including antigen and nucleic acid amplification tests. Serologic tests were excluded

Table 6. Selected Healthcare Exposures or Risk Factors of CRE Cases, 2022[a] (N=1479)

Exposure	No. of Cases	%
Healthcare facility stay in the year before the date of incident specimen collection – any healthcare facility stay	946	64.0
Healthcare facility stay in the year before the date of incident specimen collection – acute care hospitalization	895	60.5
Healthcare facility stay in the year before the date of incident specimen collection – long-term care facility residence	362	24.5
Healthcare facility stay in the year before the date of incident specimen collection – long-term acute care hospitalization	55	3.7
Surgery in the year before the date of incident specimen collection	435	29.4
Specimen collected ≥3 days after hospital admission	248	16.8
Chronic dialysis	65	4.4
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – urinary catheter	523	35.4
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – central venous catheter	215	14.5
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – other [b]	311	21.0
None of the above healthcare exposures [c]	302	20.4
Healthcare exposures are unknown	41	2.8
International travel in the 12 months prior to date of incident specimen	44	3.0

[a] Patients could have more than one prior healthcare or exposure risk factor reported

[b] Other medical devices: 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, 2022 (N=1479)

Outcomes	No. of Cases	%
Outcome– hospitalized on the day of or in the 29 days after the date of incident specimen collection[a,b]	818	55.3
Outcome– ICU admission in the 6 days after the date of incident specimen collection[a]	110	7.4
Discharge location among hospitalized patients – private residence or other location	441/818	53.9
Hospitalized patient discharged to – long-term care facility	252/818	30.8
Hospitalized patient discharged to – died during hospitalization	92/818	11.2
Hospitalized patient discharged to – long-term acute care hospital	17/818	2.1
Hospitalized patient discharged to – other	9/818	1.1
Hospitalized patient discharged to – unknown	7/818	0.9
Died within 30 days of incident specimen collection date	83	5.6
Cases with an incident sterile site specimen	38/207	18.4
Cases with an incident urine specimen[c]	45/1272	3.5

[a] Patients could have more than one outcome

[b] Data include 275 cases considered to be hospital-onset

[c] No incident CRE cases had a subsequent non-incident blood specimen collected on the date of incident specimen collection or in the 29 days after

Laboratory Characterization:

8.a. Antimicrobial Susceptibility and Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC, 2022 (N=772)

Organism	Isolates Submitted to CDC	Carbapenemase-producing, [a,b,c] - N	%
Enterobacter cloacae complex	373	34	9.1
Klebsiella pneumoniae[d]	183	93	50.8
Escherichia coli	161	52	32.3
Klebsiella aerogenes	44	0	0
Klebsiella oxytoca	11	8	72.7
Total	**772**	**187**	**24.2**

Table 8.b. Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC, by Carbapenemase Gene[e], 2022 (N=772)

Organism	*bla*$_{KPC}$ - N	*bla*$_{KPC}$ - %	*bla*$_{NDM}$ - N	*bla*$_{NDM}$ - %	*bla*$_{OXA-48-like}$ - N	*bla*$_{OXA-48-like}$ - %	*bla*$_{vim}$ - N	*bla*$_{vim}$- %	*bla*$_{imp}$ - N	*bla*$_{imp}$ - %
Enterobacter cloacae complex	18	4.8	12	3.2	1	0.3	3	0.8	0	0
Klebsiella pneumoniae[d]	63	34.4	22	12.0	12	6.6	0	0	0	0
Escherichia coli	16	9.9	28	17.4	8	5.0	0	0	0	0
Klebsiella aerogenes	0	0	0	0	0	0	0	0	0	0
Klebsiella oxytoca	7	63.6	1	9.1	0	0	0	0	0	0
Total	**104**	**13.5**	**63**	**8.2**	**21**	**2.7**	**3**	**0.4**	**0**	**0**

Table 8.c. Confirmatory Antimicrobial Susceptibility Results of CRE Isolates Submitted to CDC, 2022 (N=772)

Organism	Carbapenem-resistant - N	Carbapenem-resistant - %
Enterobacter cloacae complex	199	53.4
Klebsiella pneumoniae[d]	140	76.5
Escherichia coli	90	55.9
Klebsiella aerogenes	21	47.7
Klebsiella oxytoca	9	81.8
Total	**459**	**59.5**

[a] Testing was performed by PCR

[b] Carbapenemase-producing isolates were collected from urine (n=144/187; 77.0%), blood (n=30/187; 16%), and other normally sterile specimens (n=13/187; 7.0%)

[c] All isolates that were PCR positive were also mCIM positive. Seven isolates were mCIM positive and PCR negative.

[d] Includes *Klebsiella pneumoniae* and *Klebsiella variicola*

[e] Four carbapenemase-producing isolates were not carbapenem-resistant (two isolates with *bla*$_{KPC}$, one isolate with *bla*$_{OXA-48,}$ and one isolate with *bla*$_{vim}$). Four isolates carried both *bla*$_{OXA-48}$ and *bla*$_{NDM}$ genes.

Summary:

Surveillance data from 2022 represent the eleventh full year of population-based surveillance for CRE (2011 was a pilot year) through the Emerging Infections Program. The overall crude incidence rate of CRE in 2022 was 6.4 cases per 100,000 persons. This is a 4.9% increase in the crude CRE incidence rate reported in 2021 (2). The incidence rate increased with increasing age, was higher in females than in males, and higher in persons of Black or African American race than in persons of other races. More cases of 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 an admission to a healthcare setting in the prior year, presence of indwelling medical devices, and surgery in the prior year being the most common exposures. Approximately half of the CRE cases were hospitalized, and overall crude 30-day mortality was 5.6%, with a higher 30-day mortality observed in cases with a sterile-site specimen source compared to those with a urine specimen source. Ten percent of patients in the hospital on the date of incident specimen collection had a positive viral test for SARS-CoV-2 during their hospitalization and on or before the date of incident specimen collection.

Among the 772 CRE isolates submitted to CDC, 24.2% were carbapenemase-producing. KPC was detected in 13.5% of the isolates, NDM in 8.2% of the isolates, OXA-48-like in 2.7% of the isolates, VIM in 0.4% of the isolates, and IMP in 0% of the isolates.

References:

1. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 32nd ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2022.

2. 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, 2021. Available at: https://www.cdc.gov/healthcare-associated-infections/media/pdfs/2021-CRE-Report-508.pdf

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For more information, visit our web sites:

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