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Epidemiology of extended-spectrum β-lactamase–producing Enterobacterales in five US sites participating in the Emerging Infections Program, 2017

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Abstract

Objective: The incidence of infections from extended-spectrum β-lactamase (ESBL)–producing Enterobacterales (ESBL-E) is increasing in the United States. We describe the epidemiology of ESBL-E at 5 Emerging Infections Program (EIP) sites.

Methods: During October–December 2017, we piloted active laboratory- and population-based (New York, New Mexico, Tennessee) or sentinel (Colorado, Georgia) ESBL-E surveillance. An incident case was the first isolation from normally sterile body sites or urine of *Escherichia coli* or

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Klebsiella pneumoniae/oxytoca resistant to ≥1 extended-spectrum cephalosporin and nonresistant to all carbapenems tested at a clinical laboratory from a surveillance area resident in a 30-day period. Demographic and clinical data were obtained from medical records. The Centers for Disease Control and Prevention (CDC) performed reference antimicrobial susceptibility testing and whole-genome sequencing on a convenience sample of case isolates.

Results: We identified 884 incident cases. The estimated annual incidence in sites conducting population-based surveillance was 199.7 per 100,000 population. Overall, 800 isolates (96%) were from urine, and 790 (89%) were *E. coli*. Also, 393 cases (47%) were community-associated. Among 136 isolates (15%) tested at the CDC, 122 (90%) met the surveillance definition phenotype; 114 (93%) of 122 were shown to be ESBL producers by clavulanate testing. In total, 111 (97%) of confirmed ESBL producers harbored a $bla_{\text{CTX-M}}$ gene. Among ESBL-producing *E. coli* isolates, 52 (54%) were ST131; 44% of these cases were community associated.

Conclusions: The burden of ESBL-E was high across surveillance sites, with nearly half of cases acquired in the community. EIP has implemented ongoing ESBL-E surveillance to inform prevention efforts, particularly in the community and to watch for the emergence of new ESBL-E strains.

Extended-spectrum β-lactamase (ESBL)–producing *Escherichia coli* and *Klebsiella* spp were highlighted in the most recent Centers for Disease Control and Prevention (CDC) Antibiotic Resistance Threats Report as a serious threat. They caused an estimated 197,400 infections and 9,100 deaths among hospitalized US patients in 2017.[1] In addition, ESBL-producing Enterobacterales (ESBL-E) are a global problem, with significant spread in Europe, Asia, Africa, the Middle East, Latin America, and North America.[2,3] ESBLs are a subset of enzymes that confer resistance to a broad range of β-lactam antibiotics including penicillins, third-generation cephalosporins, and monobactams. ESBLs are inhibited by β-lactamase inhibitors such as clavulanate, sulbactam, and tazobactam.[3] The most common ESBL producers are gram-negative organisms of the order Enterobacterales, and *E. coli* and *Klebsiella* spp account for most ESBL producers among the Enterobacterales.[4] ESBLs are highly heterogeneous, with >200 different ESBL enzymes, of which TEM, SHV, and CTX-M types are the most common.[2] Most of these enzymes are located on mobile genetic elements, which allows ESBL genes to be transferred among different organisms.[5] Because ESBL-producing organisms often display a multidrug-resistant phenotype, few reliable treatment options[6] are available other than carbapenems.[2]

The emergence of ESBL-producing organisms in the United States is largely driven by the dissemination of the CTX-M family of ESBL enzymes.[2,4,7] Previously published reports indicated that ESBL-E rates have been increasing in some areas[8]; however, the data on ESBL-E burden are mostly limited to regional studies or studies in hospitalized patients,[1,9,10] which highlights the need for acquiring population-based ESBL-E surveillance data across the United States.

We conducted a surveillance pilot program through the Emerging Infections Program Healthcare-Associated Infections-Community Interface (EIP HAIC) Multisite Gram-Negative Surveillance Initiative (MuGSI)[11] to describe the epidemiology of ESBL-E and to refine methods for ongoing surveillance.

Methods

From October through December 2017, we conducted a pilot program of active, laboratory-based surveillance in selected counties at 5 EIP sites. Population-based surveillance was conducted in 2017 at 3 sites in selected counties with a total population of 1,578,127: New Mexico (Bernalillo County; population, 676,773), New York (Monroe County; population, 747,642), and Tennessee (Maury, Lewis, Wayne, and Marshall Counties; total population, 153,712). However, 2 sites did not enroll all clinical laboratories in their catchment areas because of limitations with feasibility for the pilot program; therefore, these sites conducted sentinel surveillance in selected laboratories in specific counties: Georgia (Clayton County), and Colorado (Boulder County).

An incident ESBL-E case was defined as the first isolation of *E. coli, K. pneumoniae*, or *K. oxytoca* resistant to at least 1 extended-spectrum cephalosporin (ceftazidime, cefotaxime or ceftriaxone) and nonresistant (ie, susceptible or intermediate) to all tested carbapenems from urine or a normally sterile body site in a resident of the surveillance catchment area during a 30-day period. Respiratory specimens were not included for this surveillance pilot.

To identify cases, site staff obtained lists of *E. coli, K. pneumoniae*, and *K. oxytoca* isolates that met the case definition phenotype from participating laboratories through queries of the Laboratory Information Systems (LIS) or the Automated Testing Instruments (ATIs) with preference for obtaining data from the ATI. Site staff reviewed medical records and completed case report forms (CRFs) for all incident ESBL-E cases including information on patient demographics, location of culture collection, healthcare exposures, types of infection associated with culture, underlying conditions, patient outcomes, and selected other risk factors. Site staff conducted queries of state vital records to determine mortality within 30 days of incident culture collection.

We categorized ESBL-E cases as healthcare-associated if the incident culture was collected either (1) >3 calendar days after admission to a hospital or (2) at an outpatient visit or during the first 3 days of a hospitalization from a patient with a history of hospitalization, surgery, residence in a long-term care facility (LTCF) or residence in long-term acute-care hospital (LTACH) in the year prior to culture, or from a patient on chronic dialysis or with an indwelling device or external urinary catheter in the 2 days prior to culture collection. If none of these risk factors was identified, we categorized the case as community-associated. Healthcare-associated cases were categorized as hospital onset (HO), LTCF onset, or LTACH onset if the patient was located in one of these facility types >3 calendar days before the date of incident culture. A case was considered healthcare-associated community-onset (HACO) if the patient was located at other facility types (eg, assisted living facility) or at a private residence and had 1 or more of the healthcare exposures listed above.

A convenience sample of isolates from incident cases was submitted to the CDC for confirmatory testing and molecular characterization. At the CDC, isolates underwent species identification using matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry using a Biotyper 3.1 system (Bruker Daltonics, Billerica, MA). Isolates also underwent reference antimicrobial susceptibility testing using broth microdilution and

phenotypic screening for ESBL production using ceftazidime and cefotaxime alone and in combination with clavulanate.[12] Whole-genome sequencing analysis of isolates was performed using Illumina MiSeq (Illumina, San Diego, CA). Sequences were screened for the presence of acquired β-lactamase genes (including ESBL genes) using ResFinder and ArgAnnot databases.[13,14] Sequence types (STs) were determined using multilocus sequence type (MLST) schemes available from pubMLST and Institute Pasteur.[15,16] We used the Achtmann multi-locus sequence type (MLST) scheme[17] from Enterobase[18] to identify *E. coli* sequence types (STs), and the Pasteur MLST scheme (http://bigsdb.pasteur.fr/)[16] for *Klebsiella* spp.

Surveillance data were collected and managed using Research Electronic Data Capture (REDCap)[19] hosted at the CDC. REDCap is a secure, web-based software platform designed to support data capture for research studies. The data were finalized in March 2019. We analyzed data using SAS version 9.4 software (SAS Institute, Cary, NC). Because surveillance was conducted during a 3-month period, we estimated the crude annual incidence rates per 100,000 population for the 3 EIP sites conducting population-based surveillance as the number of cases multiplied by 4 divided by population based on the 2017 US Census.[20] We performed descriptive analyses of cases with completed CRFs.

This activity was reviewed by the human subjects research advisors in the CDC National Center for Emerging and Zoonotic Infectious Diseases and was determined to constitute a nonresearch public health surveillance activity. Therefore, review by the CDC Institutional Review Board (IRB) was not required. The project also underwent review in each of the participating EIP sites and was either approved by the IRB with a waiver of informed consent or was considered a nonresearch public health activity.

Results

We identified 884 ESBL-E incident cases among 815 patients (Table 1). Of the 884 cases, 790 (89%) were *E. coli* bacteremia and 94 (11%) were *Klebsiella* spp bacteremia. The estimated annual incidence rate per 100,000 population was 199.7 overall in the 3 population-based sites. Site-specific incidence rates were 182.6 per 100,000 population in New Mexico, 173.9 per 100,000 population in New York, and 400.7 per 100,000 population in Tennessee. The estimated annual incidence rate among females (303.4 per 100,000 population) was 3.9 times the rate among males (78.6 per 100,000 population) (Table 2). The estimated annual incidence rate increased with age from 107.8 per 100,000 population among persons aged 19–49 years to 1,098.7 per 100,000 population among persons aged ≥80 years.

Characteristics of incident ESBL-E cases with complete CRFs (n = 837, 94%) are presented in Table 3. Almost all ESBL-E cases were identified from either urine (n = 800, 96%) or blood (n = 30, 4%). The most documented infection types or syndromes associated with incident cultures were urinary tract infection (UTI; n = 696, 83%) and bacteremia or sepsis (n = 55; 7%). Among ESBL-E cases, 393 (47%) were classified epidemiologically as community-associated, 282 (34%) were HACO, and 40 (5%) were HO. The most frequently reported healthcare exposures among HACO ESBL-E cases in the year before incident

culture were acute care hospitalization (n = 209, 74%), surgery (n = 111, 39%), and the presence of a urinary catheter in the 2 days before culture collection (n = 72, 26%). Also, 247 cases (30%) were hospitalized at the time of or within 30 days after initial culture collection. Within 30 days of positive culture collection, 22 cases (3%) died.

Clinical characteristics and risk factors are presented in Table 4. Most ESBL-E cases (76%) occurred in patients with underlying medical conditions. Antibiotic use within 30 days before culture was reported for 315 (38%) ESBL-E cases overall, including 102 (26%) of 393 community-associated cases. The most frequently used antibiotics were intravenous cephalosporins (n = 83, 10%), fluoroquinolones (n = 68, 8%), β-lactam combination agents (n = 64, 8%), trimethoprim-containing antibiotics (n = 51, 6%), and nitrofurantoin (n = 45, 5%).

Characteristics of ESBL-E isolates tested at CDC are presented in Table 5. By reference broth microdilution testing, 122 (90%) isolates met our surveillance definition phenotype of an ESBL producer using current CLSI breakpoints.[12] Among 104 *E. coli* isolates meeting the surveillance phenotype by reference testing, 97 (93%) were phenotypically ESBL-screen positive. Among ESBL-screen positive *E. coli*, CTX-M-type β-lactamases predominated (98%), with $bla_{\text{CTX-M-15}}$ being most common (56%). In total, 23 unique STs were detected among the 97 ESBL-screen positive *E. coli* isolates; ST131 was most common (54%) followed byST38(12%) and ST10 (5%). In addition to β-lactam resistance, *E. coli* isolates meeting the surveillance phenotype frequently displayed resistance to ciprofloxacin (75%), tetracycline (54%), trimethoprim-sulfamethoxazole (53%), and gentamicin (29%). Among 18 *Klebsiella* spp isolates meeting the surveillance phenotype, 17 were ESBL-screen positive and 16 carried an ESBL gene. All ESBL genes were of the CTX-M type ($bla_{\text{CTX-M-15}}$ and $bla_{\text{CTX-M-14}}$). In total, 11 unique STs were observed among *K. pneumoniae*. Among 2 K. oxytoca isolates meeting the surveillance definition, 1 harbored $bla_{\text{CTX-M-15}}$ and belonged to ST11.

The antimicrobial susceptibility results for ST131 and non-ST131 *E. coli* are presented in Table 6. ST131 isolates displayed lower levels of fluoroquinolone susceptibility (4%) than non-ST131 isolates (42%), but otherwise showed similar susceptibility profiles for other antimicrobial classes. Among 52 ST131 isolates tested, 23 (44%) were community-associated.

Discussion

This 3-month pilot for ESBL-E is the first report of an active laboratory- and population-based surveillance initiative conducted in the United States. Our pilot program yielded several key findings. First, we confirmed a high burden of ESBL-E,[1,9] with an estimated annual incidence rate of 199.7 per 100,000 population in sites conducting population-based surveillance. Thus, the incidence of ESBL-E at surveillance sites appears to be much higher than previously published estimates for other resistant phenotypes such as carbapenem-resistant Enterobacterales (2.93 per 100,000 population per year).[21] In addition, only 30% of cases occurred in hospitalized patients. This finding is notable because it indicates that the high burden of ESBL-E in hospitalized patients recently described by CDC represents only

a fraction of the total infection burden.[1,9] Second, almost half were community-associated with no previous specified healthcare exposure. Finally, ESBL-producing *E. coli* isolates were predominantly ST131, and most ESBL isolates harbored $bla_{\text{CTX-M}}$ genes. These findings suggest that the large degree of transmission of ESBL-E that has occurred in the United States may be partly driven by a single strain that has successfully established itself in the community.

Along with previous single- or multicenter studies reporting on the changing epidemiology of ESBL-E,[22,23] the high proportion of community-associated cases in our data points to the presence of person-to-person transmission or other sources of ESBL-E in the community. Recent studies through modeling and molecular characterization of ESBL isolates from Europe have suggested that most transmission of ESBL-E organisms occurs person to person.[24–27] Currently, few community-based strategies to decrease ESBL-E incidence in the United States have proven effective. Improving antibiotic use in the outpatient setting, especially for the treatment of urinary tract infection where *E. coli* is the most common etiology, might help reduce selective pressure for ESBL-E. In our study, almost 40% of all cases and a quarter of community-associated cases received prior antibiotics, which might have been underestimated because we did not assess antibiotic use beyond the previous 30 days and because medical records for outpatients and hospitalized patients might lack data on prior antibiotic exposures.[28] In addition, Low et al[29] suggested that outpatient fluoroquinolone use increases the community risk for acquiring fluoroquinolone-resistant *E. coli* even for individuals who never received fluoroquinolone treatment. Thus, antibiotic stewardship could play a role in reducing the risk of resistance not only in the individual but also across the population. A possible future strategy under development is an effective vaccine for extraintestinal *E. coli* infections.[30] Initial studies have suggested an acceptable safety profile and immunogenicity[31] of a candidate *E. coli* vaccine, which, if successful in clinical trials of efficacy, might be a promising strategy for preventing infections from ESBL-producing *E. coli* in the community.

Better understanding of sources of and risk factors for acquisition in the community is necessary to inform public health measures that reduce the incidence of infections caused by ESBL-E. Some risk factors for acquisition of ESBL-E have been explored by other investigators.[28,32] Studies in both the United Kingdom and the United States suggest that the predominant ESBL strains causing disease in humans are rare in retail meat samples, other food, or animals,[26,33] and investigators in the Netherlands have described household hygiene behaviors[24] and international travel[27] as contributors to ESBL-E transmission. More work is needed to determine what factors are most important in the United States. This research could include investigation of sources for ESBL-E acquisition such as water sources,[34,35] travel to high-risk countries,[27] investigation of household transmission,[36] or screening for antimicrobial resistance genes or ESBL-E organisms in the environment.[35] Investigation of geographic variation could also contribute to better understanding of ESBL-E risk factors in the United States.

Although a large proportion of ESBL-E in our study were community-associated, slightly more than half of cases occurred in persons with prior healthcare exposures. A recent systematic review and meta-analysis by Vinks et al[37] identified a pooled acquisition

prevalence of 3.73% for ESBL-E in healthcare settings in Europe and North America, and they highlighted the contribution of LTCFs in sustaining national outbreaks. Thus, efforts to reduce transmission of ESBL-E and development of infections in colonized individuals in healthcare settings[38] are also an important public health strategy for EBSL-E prevention. For example, more than a quarter of HACO cases in our pilot program had a urinary catheter in place, so ensuring proper catheter care (including removal of unnecessary catheters) might help with ESBL-E prevention.

Multiple reports have indicated that certain strain types, such as ST131 and ST38, are playing an important role in the worldwide dissemination of ESBL-producing *E. coli*.[3,39] Similarly, in the convenience sample of E. coli isolates characterized in our pilot program, ST131 predominated and displayed higher levels of fluoroquinolone resistance than non-ST131 isolates. In addition, 52% of the ST131 isolates displayed resistance to trimethoprim-sulfamethoxazole, another drug commonly used to treat community urinary tract infections. Hence, the limited availability of oral antibiotics and continued spread of ST131 represents a challenge to manage community-associated UTIs.

Determining an appropriate surveillance definition for ESBL-E is challenging. ESBL-E should test intermediate or resistant to extended-spectrum cephalosporins when using current clinical antimicrobial susceptibility testing break points.[12] However, resistance to cephalosporins[40] may also result from other mechanisms, such as AmpC-type β-lactamases. Guidelines from the Clinical and Laboratory Standards Institute (CLSI) recommend ESBL confirmatory testing of *K. pneumoniae, K. oxytoca, E. coli,* and *P. mirabilis* only when laboratories have not implemented current breakpoints or for infection control purposes.[12] A high proportion of isolates tested at CDC (90%) met the pilot surveillance case definition phenotype. Thus, the definition appears to have a good positive predictive value for identifying ESBL-producing isolates. In addition, the definition was easy to use. More than 80% of cases identified from urine had a UTI diagnosis by a medical provider or had symptoms associated with a UTI documented in the medical record, suggesting that the majority were considered to represent clinical infection by the treating provider although over-diagnosis could occur. However, the use of our case definition might underestimate true ESBL-E incidence. We did not include respiratory specimens, wound cultures, or skin cultures in the definition because of added complexities with assessing clinical significance of Enterobacterales isolates from these sources. We also did not include isolates resistant to or nonsusceptible to carbapenems.

Our pilot program had several limitations as well as important strengths. First, the ESBL-E pilot data were collected for only 3 months; and therefore, we did not account for the effect of seasonality on incidence. Given that it is not known whether ESBL-E incidence has seasonal variation in the United States, our reported incidence might have been under- or overestimated, and the generalizability of incidence might be limited. Second, surveillance was population based at only 3 of the 5 EIP sites. The other 2 sites conducted sentinel surveillance because of feasibility limitations. Third, available data on prior antibiotic use in some patients may have reflected empiric treatment of the ESBL-E infection rather than use that predated and potentially increased the risk of ESBL-E infection. In addition, we may have missed data on outpatient healthcare exposures if it was not documented in the

record. Finally, we had only a limited subset of *E. coli* and *Klebsiella* spp isolates for testing, and we did not evaluate susceptibility to some oral antibiotics such as nitrofurantoin. The strengths of this study included a description of ESBL-E cases in entire counties regardless of healthcare setting, diversity of geographic regions, and confirmation of ESBL gene presence.

In conclusion, ESBL-E causes a high burden of infections in the community and in healthcare, and additional data are needed to further characterize risk factors and sources of acquisition to focus prevention efforts. Our results support those of other published literature,[2,4,7,22] suggesting that the CTX-M β-lactamase is the predominant mechanism among ESBL-E in the United States. Based on our findings, the EIP implemented ongoing active population-based ESBL-E surveillance at 6 US sites in July 2019 to describe ESBL-E burden in additional areas and to assess the effect of efforts to combat antimicrobial resistance among Enterobacterales over time.

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Data availability.

Raw sequences have been deposited in the NCBI BioProject (ID no. PRJNA288601).

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Table 1.

Number of Incident Extended-Spectrum β-Lactamase–Producing Enterobacterales Cases and Estimated Annual Incidence Rate per 100,000 Population, by Organism, 5 Emerging Infections Program sites, United States, 2017 (N=884)

	Incident Cases, No. (%)			Estimated Annual Incidence per 100,000 Population		
EIP Site	***E. coli*, No. (%)**	***Klebsiella*[a] spp, No. (%)**	**Total**	***E. coli***	***Klebsiella*[a] spp**	**Total**
Colorado[b]	58 (90.6)	6 (9.4)	64	...	...	...
Georgia[b]	26 (81.3)	6 (18.8)	32	...	...	...
New Mexico	270 (87.4)	39 (12.6)	309	159.6	23.1	182.6
New York	294 (90.5)	31 (9.5)	325	157.3	16.6	173.9
Tennessee	142 (92.2)	12 (7.8)	154	369.5	31.2	400.7
Total	790 (89.4)	94 (10.6)	884	178.9	20.8	199.7

Note. EIP, CDC Emerging Infections Program.

[a]Klebsiella pneumoniae, Klebsiella oxytoca.

[b]Because surveillance in Colorado and Georgia was not population based, incidence is not provided.

Table 2.

Number of Incident Extended-Spectrum β-Lactamase–Producing Enterobacterales Cases and Crude Incidence Rate per 100,000 Population, by Demographic Characteristics, 3 Emerging Infections Program sites, United States, 2017 (N=788)

Characteristic	Incident Cases, No. (%)	Estimated Annual Incidence per 100,000 Population[a]
Sex		
Female	614 (77.9)	303.4
Male	151 (19.2)	78.6
Unknown	23 (2.9)	...
Race		
White	553 (70.2)	170.0
Black	51 (6.5)	119.0
Other[b]	34 (4.3)	129.0
Unknown	150 (19.0)	...
Ethnicity		
Hispanic	149 (18.9)	144.5
Not Hispanic	544 (69.0)	186.7
Unknown	95 (12.1)	...
Age		
0–18 y	33 (4.2)	36.4
19–49 y	173 (22.0)	107.8
50–64 y	154 (19.5)	194.8
65–79 y	254 (32.2)	525.4
≥80 y	174 (22.1)	1,098.7

[a]Incidence estimate for sites conducting population-based surveillance (New Mexico, New York, Tennessee). Because surveillance in Colorado and Georgia was not population based, incidence is not provided.

[b]Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander.

Table 3.

Characteristics of Incident Extended-Spectrum β-Lactamase–Producing Enterobacterales Cases With Complete Case Report Forms by Species, 5 Emerging Infections Program sites, United States, 2017 (N=837)

		Organism	
Characteristic	**Total (n=837), No. (%)**	***E. coli* (n=747), No. (%)**	***Klebsiella* spp[a] (n=90), No. (%)**
Culture source			
Urine	800 (95.6)	719 (96.3)	81 (90.0)
Blood	30 (3.6)	23 (3.1)	7 (7.8)
Other sterile[b]	7 (0.8)	5 (0.7)	2 (2.2)
Location of culture collection			
Outpatient clinic[c]	467 (55.8)	429 (57.4)	38 (42.2)
Emergency room	217 (25.9)	188 (25.2)	29 (32.2)
Acute care hospital	92 (11.0)	72 (9.7)	20 (22.2)
LTCF	59 (7.1)	56 (7.5)	3 (3.3)
LTACH	2 (0.2)	2 (0.3)	0
Infection types			
Urinary tract infection/Pyelonephritis	696 (83.2)	628 (84.1)	68 (75.6)
Bacteremia/Sepsis	55 (6.6)	46 (6.2)	9 (10.0)
Internal abscess	9 (1.1)	7 (0.9)	2 (2.2)
Pneumonia	8 (1.0)	7 (0.9)	1 (1.1)
Other [d]	18 (2.2)	14 (1.9)	4 (4.4)
None	95 (11.4)	84 (11.2)	11 (12.2)
Unknown	18 (2.2)	16 (2.1)	2 (2.2)
Epidemiologic classification			
Community associated	393 (47.0)	363 (48.6)	30 (33.3)
Healthcare associated	439 (52.6)	379 (50.8)	60 (66.7)
HACO	282 (33.7)	242 (32.4)	40 (44.4)
LTCF onset	116 (13.9)	106 (14.9)	10 (11.1)

Characteristic	Total (n=837), No. (%)	Organism	
		E. coli (n=747), No. (%)	*Klebsiella* spp[a] (n=90), No. (%)
Hospital onset	40 (4.8)	30 (4.0)	10 (11.1)
LTACH onset	2 (0.2)	2 (0.3)	0 (0.0)
Unknown	5 (0.6)	5 (0.7)	0 (0.0)
Healthcare exposures among HACO cases			
Total	282	242	40
Acute-care hospitalization in the year before culture	209 (74.1)	179 (74.0)	30 (75.0)
Surgery in the year before culture	111 (39.4)	98 (40.5)	13 (32.5)
Urinary catheter in place in 2 d before culture	72 (25.5)	52 (21.5)	20 (50.0)
Residence in LTCF	36 (12.8)	30 (12.4)	6 (15.0)
Central venous catheter in place in 2 d before culture	23 (8.1)	20 (8.3)	3 (7.5)
Other indwelling device in place in 2 d before culture	19 (6.8)	15 (6.2)	4 (10.0)
Chronic dialysis	15 (5.3)	12 (5.0)	3 (7.5)
Admitted to LTACH in the year before culture	0	0	0
Outcomes			
Hospitalized at the time of or within 30 d after initial culture	247 (29.5)	208 (27.8)	39 (43.3)
Admitted to intensive care unit at time of or 7 d after initial culture	41 (4.9)	30 (4.0)	11 (12.2)
Discharge location among hospitalized patients who survived			
Total	234	199	35
Private residence	135 (57.7)	115 (57.8)	20 (57.1)
LTCF	85 (35.7)	71 (35.7)	14 (40.0)
LTACH	4 (1.7)	4 (2.0)	0 (0.0)
Unknown or other[e]	10 (4.1)	9 (4.5)	1 (2.9)
Died within 30 d of positive culture collection			
Total	22/837 (2.6)	18/747 (2.4)	4/90 (4.4)
Cases with positive blood or other sterile body site culture (N=37)	5/37 (13.5)	5/28 (17.9)	0/9 (0.0)
Cases with positive urine culture source (N=800)	17/800 (2.1)	13/719 (1.8)	4/81 (4.9)

Note. LTCF, long-term care facility; LTACH, long-term acute care hospital; HACO, healthcare-associated community-onset.

[a]Klebsiella pneumoniae, Klebsiella oxytoca.

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[b] Peritoneal fluid, bone, deep tissue, vitreous humor.

[c] Clinic/doctors' office, surgery, dialysis center, other outpatient clinics.

[d] Surgical site infection, decubitus/pressure ulcer, peritonitis, appendicitis, atrioventricular fistula/graft infection, cholangitis, chronic ulcer/wound, osteomyelitis, prostatitis.

[e] Homeless, left against medical advice, living in a shelter.

Table 4.

Clinical Characteristics, and Risk Factors Among Incident Extended-Spectrum β-Lactamase–Producing Enterobacterales Cases With Complete Case Report Forms, 5 Emerging Infections Program Sites, by Epidemiologic Class, United States, 2017 (N=837)

Characteristic[a]	Total (n=837), No. (%)	Community Associated (n=393), No. (%)	Healthcare Associated (n=439), No. (%)
Charlson comorbidity index, median (IQR)	1.0 (0–3)	0.0 (0–1)	2.0 (0–3)
Underlying conditions			
Diabetes	266 (31.8)	98 (25.0)	168 (38.3)
Urinary tract problems/abnormalities	224 (26.8)	76 (19.4)	147 (33.4)
Neurological problems	166 (19.8)	35 (8.9)	131 (29.8)
Chronic pulmonary disease	162 (19.4)	61 (15.6)	101 (23.0)
Congestive heart failure	94 (11.2)	18 (4.6)	75 (17.1)
Cerebrovascular accident/stroke	90 (10.8)	21 (5.4)	69 (15.7)
Dementia	80 (9.6)	16 (4.1)	64 (14.6)
Chronic renal insufficiency	76 (9.1)	14 (3.6)	62 (14.1)
Solid tumor	76 (9.1)	27 (6.9)	49 (11.1)
Decubitus/pressure ulcer	52 (6.2)	1 (0.3)	51 (11.6)
Previous myocardial infarct	44 (5.3)	14 (3.6)	30 (6.8)
Peripheral vascular disease	38 (4.6)	12 (3.1)	26 (5.9)
Connective tissue disease	38 (4.6)	14 (3.6)	24 (5.5)
Hemiplegia/paraplegia	35 (4.1)	2 (0.5)	33 (7.5)
Other underlying conditions[b]	112 (13.4)	22 (5.6)	89 (20.2)
Unknown condition	3 (0.4)	1 (0.3)	0
None	199 (23.8)	156 (40.0)	43 (9.8)
Risk factors			
Antibiotic use in 30 d prior to culture	315 (37.6)	102 (26.0)	213 (48.5)
International travel in the 2 mo prior to culture	17 (2.0)	12 (3.1)	5 (1.1)

Note. IQR, interquartile ratio.

[a]Epidemiologic classification of 5 cases is unknown; these are included only in the total column.

[b] Chronic skin breakdown, chronic liver disease, alcohol abuse, peptic ulcer disease, metastatic solid tumor, hematologic malignancy, transplant recipient, spina bifida, injection drug use, liver failure, human immunodeficiency virus, premature birth.

Table 5.

Characteristics of Extended-Spectrum β-Lactamase–Producing Enterobacterales Isolates Tested at CDC, 5 Emerging Infections Program Sites, United States, 2017 (N=136)

Characteristic	Isolates, No. (%)
Isolates tested at CDC	
Total	136
E. coli	117 (86.0)
Klebsiella spp[a]	19 (14.0)
Isolates meeting pilot surveillance case definition phenotype[a]	
Total	122/136 (89.7)
E. coli	104 (85.2)
K. pneumoniae	16 (13.1)
K. oxytoca	2 (1.6)
Isolates determined to be phenotypically ESBL-screen positive	
Total	114/122 (93.4)
E. coli	97/104 (93.3)
K. pneumoniae	16/16 (100.0)
K. oxytoca	1/2 (50.0)
Acquired ESBL genes among ESBL-screen positive isolates	
Total	112/114 (98.2)
E. coli	
Total	97
$bla_{\text{CTX-M-15}}$	54 (55.7)
$bla_{\text{CTX-M-27}}$	14 (14.4)
$bla_{\text{CTX-M-14}}$	13 (13.4)
$bla_{\text{CTX-M-55}}$	9 (9.3)
$bla_{\text{CTX-M-1}}$	2 (2.1)
$bla_{\text{CTX-M-24}}$	1 (1.0)
$bla_{\text{CTX-M-65}}$	1 (1.0)
$bla_{\text{CTX-M-15}}$ and $bla_{\text{CTX-M-14}}$	1 (1.0)
$bla_{\text{SHV-12}}$	1 (1.0)
K. pneumoniae	
Total	16
$bla_{\text{CTX-M-15}}$	13 (81.3)
$bla_{\text{CTX-M-14}}$	2 (12.5)
K. oxytoca	
Total	1
$bla_{\text{CTX-M-15}}$	1 (100.0)

Characteristic	Isolates, No. (%)
E. coli ST	
Total	97
ST131	52 (53.6)
ST38	12 (12.4)
ST10	5 (5.2)
Other[b]	28 (28.9)
K. pneumoniae ST	
Total	16
ST45	5 (31.3)
ST307	2 (12.5)
Other[c]	9 (56.3)

Note. CDC, Centers for Disease Control and Prevention; ESBL, extended-spectrum β-lactamase; ST, sequence type.

[a]Klebsiella pneumoniae, Klebsiella oxytoca.

[b]Other *E. coli* ST types included 20 unique STs.

[c]Other *K. pneumoniae* ST types included 9 unique STs: ST17, ST37, ST323, ST462, ST869, ST896, ST1207, ST2004, ST2133.

Table 6.

Reference Antimicrobial Susceptibility Testing Results for *E. coli* ST131 and Non-ST131 Isolates Meeting the Surveillance Phenotype, 5 Emerging Infections Program Sites, United States, 2017 (N=104)[a]

		Susceptible Isolates, No. (%)	
Antimicrobial Class	**Antimicrobial Agent**	**ST131 (n=52)**	**Non-ST131 (n=52)**
β-lactam combination agents	Piperacillin-tazobactam	50 (96.2)	52 (100)
Aminoglycosides	Amikacin	51 (98.1)	52 (100)
	Gentamicin	36 (69.2)	36 (69.2)
	Tobramycin	28 (53.8)	41 (78.8)
Monobactams	Aztreonam	1 (1.9)	5 (9.6)
Cephalosporins/ cephamycins	Cefotaxime	0	0
	Ceftazidime	9 (17.3)	18 (34.6)
	Ceftriaxone	0	0
	Cefepime[b]	10 (19.2)	20 (38.5)
Fluoroquinolones	Ciprofloxacin	2 (3.8)	22 (42.3)
Tetracyclines	Tetracycline	23 (44.2)	19 (36.5)
Folate pathway antagonists	Trimethoprim-sulfamethoxazole	25 (48.1)	25 (48.1)

Note. ST, sequence type.

[a]Reference antimicrobial susceptibility testing was performed and interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines (M100 2020, 30th edition).

[b]% susceptible isolates include susceptible (S) and susceptible dose-dependent (SDD).