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ORIGINAL ARTICLE

Statewide Surveillance of Carbapenem-Resistant Enterobacteriaceae in Michigan

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BACKGROUND. Carbapenem-resistant Enterobacteriaceae (CRE) are clinically challenging, threaten patient safety, and represent an emerging public health issue. CRE reporting is not mandated in Michigan.

METHODS. The Michigan Department of Community Health–led CRE Surveillance and Prevention Initiative enrolled 21 facilities (17 acute care and 4 long-term acute care facilities) across the state. Baseline data collection began September 1, 2012, and ended February 28, 2013 (duration, 6 months). Enrolled facilities voluntarily reported cases of *Klebsiella pneumoniae* and *Escherichia coli* according to the surveillance algorithm. Patient demographic characteristics, laboratory testing, microbiology, clinical, and antimicrobial information were captured via standardized data collection forms. Facilities reported admissions and patient-days each month.

RESULTS. One-hundred two cases over 957,220 patient-days were reported, resulting in a crude incidence rate of 1.07 cases per 10,000 patient-days. Eighty-nine case patients had test results positive for *K. pneumoniae*, whereas 13 had results positive for *E. coli*. CRE case patients had a mean age of 63 years, and 51% were male. Urine cultures (61%) were the most frequently reported specimen source. Thirty-five percent of cases were hospital onset; sixty-five percent were community onset (CO), although 75% of CO case patients reported healthcare exposure within the previous 90 days. Cardiovascular disease, renal failure, and diabetes mellitus were the most frequently reported comorbid conditions. Common ris

k factors included surgery within the previous 90 days, recent infection or colonization with a multidrug-resistant organism, and recent exposures to antimicrobials, especially third- or fourth-generation cephalosporins.

CONCLUSIONS. CRE are found throughout Michigan healthcare facilities. Implementing a regional, coordinated surveillance and prevention initiative may prevent CRE from becoming hyperendemic in Michigan.

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In less than a decade, a transposon (Tn4401)–mediated outbreak of carbapenem-resistant Enterobacteriaceae (CRE) producing bla_{KPC} has disseminated worldwide. Although initially outbreaks were seen mainly in hospitals, the spread to non–acute care healthcare facilities rapidly followed.[1-14] CRE infections are associated with devastating outcomes,[15] because therapeutic options are scarce,[12] and effective therapy is often delayed or unavailable.[16,17] Reported mortality rates are over 70% for individuals with CRE bloodstream infection.[18] Initially, expansion of CRE, attributed to a single *Klebsiella pneumoniae* clone, sequence type (ST) 258 according to multilocus sequence typing (MLST), was predominant.[2,8] However, as time progressed, the epidemiology of CRE became more complex, with additional species becoming involved (eg, *Escherichia coli* and *Enterobacter* species),[13,19] and other non–bla_{KPC}-mediated carbapenem resistance mechanisms being identified.

Carbapenems are broad-spectrum β-lactam agents, often used as a last resort because of known efficacy for treating multidrug-resistant Enterobacteriaceae infections.[20-22] The emergence of resistance to carbapenems among such common human enteric bacteria prompted immediate action by

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TABLE 1. Characteristics of Facilities Participating in the Carbapenem-Resistant Enterobacteriaceae (CRE) Surveillance and Prevention Initiative

Facility	Acute care beds, median (range)	ICU beds, median (range)	Teaching facility, % of facilities
Acute care (n = 17)	410 (39–1052)	75 (0–226)	88
LTAC (n = 4)	49 (30–94)	3 (0–6)	25

NOTE. ICU, intensive care unit; LTAC, long-term acute care.

many institutions, regions, and even countries worldwide, who issued specific sets of preventive guidance in an attempt to contain the continued spread and evolution of CRE.[2,13,20] CRE are epidemiologically and clinically significant for individual patients as well as for general public health.[1-20]

The modern continuum of medical care consists of populations that transfer between multiple healthcare institutions with various levels of acuity.[23] Patients are frequently elderly, debilitated, cognitively impaired, require invasive foreign medical devices, and have substantial exposures to antimicrobials,[14,15,24] which puts them at particular risk for acquiring CRE. The frequent sharing of patients among institutions means that those who are asymptomatically colonized with CRE can unknowingly introduce CRE into new facilities.[11] Although healthcare facilities have enacted interventions to prevent CRE transmission within individual institutions,[2,13,25,26] it is evident that successful CRE prevention efforts require coordinated action between healthcare institutions in a region.[2,23,27]

Regions, states, and countries with coordinated plans aimed at CRE prevention have witnessed excellent results;[2,28-31] however, typically these efforts are established in response to large-scale outbreaks. Over the past 5 years, local studies have suggested that CRE has reached low levels of endemicity in Michigan.[10,11,16,24] Michigan chose to proactively engage healthcare and public health partners to address the increasing threat of CRE. These collaborations facilitate open communication pertaining to laboratory detection and infection prevention.

Unlike many states, most healthcare-associated infections are not mandated to be reported in Michigan. Although an initial case of CRE in a facility or laboratory is reportable as an "unusual occurrence," and all outbreaks or epidemics are reportable (per the Communicable Disease Rules R 325.171-3 and 333.5111), subsequent cases are not required by law to be reported. Thus, the statewide burden of CRE in Michigan was unknown. In September 2011, the Michigan Department of Community Health (MDCH) began a CRE surveillance and prevention initiative.

In March 2012, the CRE Collaborative, a multidisciplinary group comprising infection preventionists, microbiologists, infectious disease physicians, pharmacists, and long-term acute care (LTAC) quality management and public health representatives, met to determine the future direction of CRE surveillance and prevention in Michigan. In this report, we describe a statewide effort to estimate the incidence and burden of CRE in Michigan and characterize patient factors through a nonmandated public health surveillance and prevention initiative.

METHODS

Enrollment and Participation

In July 2012, healthcare facilities across Michigan that indicated interest in CRE surveillance and prevention were invited to join the CRE Surveillance and Prevention Initiative. Thirty acute care and LTAC facilities were approached regarding participation; 21 (70%) ultimately enrolled (17 acute care and 4 LTACs; Table 1). At the time of this report, there were 110 acute care and 19 LTAC facilities in Michigan indicating participation rates of 15% and 21%, respectively. Facilities were distributed across the state, with the greatest concentration in eastern and western Michigan. Facilities agreed to report CRE cases monthly and committed to implementing CRE prevention measures. The CRE Surveillance and Prevention Initiative spans 24 months, including a 6-month baseline period (September 1, 2012, through February 28, 2013), the results of which are described here, and a subsequent 18-

TABLE 2. Incidence Rates of Carbapenem-Resistant Enterobacteriaceae (CRE) by Facility Type

Facility	No. of cases	Total no. of patient-days	Crude incidence rate (95% CI)[a]
Acute care	94	929,939	1.01 (0.82–1.24)
LTAC	8	27,281	2.93 (1.26–5.78)
Overall	102	957,220	1.07 (0.87–1.29)

NOTE. For the acute care rate compared with the LTAC rate, P = .018. CI, confidence interval; LTAC, long-term acute care.

[a] Rates are not adjusted for patient acuity or facility-level characteristics. Rates are cases per 10,000 patient-days.

TABLE 3. Incidence Rates of Carbapenem-Resistant Enterobacteriaceae (CRE) by Region in Michigan

Variable	No. of facilities	Total no. of patient-days	No. (%) of cases	Crude incidence rate (95% CI)[a]	P[b]
East	11	654,635	81 (79)	1.24 (0.98–1.54)	Ref
West	4	194,029	10 (10)	0.52 (0.25–0.95)	.006
Mid-North	2	83,118	3 (3)	0.36 (0.07–1.06)	.023
LTAC facilities	4	27,281	8 (8)	2.93 (1.26–5.78)	

NOTE. CI, confidence interval; LTAC, long-term acute care.
[a] Rates are not adjusted for patient acuity or facility-level characteristics. Rates are cases per 10,000 patient-days.
[b] Test of significance is using the East region as the comparison group.

month intervention period (March 1, 201, through August 31, 2014).

Surveillance Definition

Participating facilities were asked to report cases of infection or colonization due to *K. pneumoniae* and *E. coli* strains that were nonsusceptible (intermediate or resistant) to any carbapenem. Facilities were asked to closely examine the antibiograms for all *K. pneumoniae* and *E. coli* isolates and to adjust for new but not-yet-implemented 2012 recommendations for interpreting carbapenem minimum inhibitory concentration (MIC) values.[32] If the isolate had an MIC to imipenem of 2–4 μg/mL, an MIC to meropenem of 2–4 μg/mL, or an MIC to ertapenem of 2 μg/mL and a positive or unknown modified Hodge test (MHT) result, the case was reported as nonsusceptible. If the isolate did not meet the MIC criteria and/or was negative according to MHT, the case did not meet criteria.

Case Onset Determination

CRE cases were categorized as community onset (CO) or healthcare onset (HO) on the basis of facility admission and specimen collection dates. Categorization followed the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) LabID event definitions.[36] Cases in which the positive specimen was collected from an outpatient or an inpatient 3 days or less after admission to the facility are CO. Cases in which the positive specimen was collected more than 3 days after admission to the facility are HO. Cases previously submitted within the previous 30 days from a facility with the same organism (from any body site) were considered duplicates and excluded from the analysis.

Data Collection and Submission

Facilities completed a standard data collection form, designed by the collaborative, that was submitted securely to MDCH. Data collection forms for all facilities captured information on patient demographic characteristics, laboratory testing, microbiology information, antimicrobial susceptibilities for carbapenems, date of admission, initiation date of contact precautions, and previous healthcare facility exposures. Additionally, acute care facility data collection forms captured information on antimicrobial susceptibilities for aminoglycosides, tigecycline, and colistin; clinical information; infections and colonizations with other multidrug-resistant organism (MDROs); indwelling devices; comorbidities; and antimicrobial therapy information. All facilities reported monthly denominator data (number of admissions and patient-days). Attempts were made to obtain all missing or unknown information from submitted forms.

Statistical Analysis

All information submitted on case report forms was entered into a Microsoft Access database. Monthly denominator data for admissions and patient-days was entered into Microsoft Excel. Data were analyzed using Excel and SAS, version 9.3 (SAS Institute). Confidence intervals were constructed using Taylor Series; *P* values were determined using Fisher exact test.

RESULTS

During the 6-month baseline data collection period, 21 initiative facilities reported 102 cases of CRE over 957,220 patient-days for a crude incidence rate of 1.07 cases per 10,000 patient-days (95% confidence interval [CI], 0.87–1.29; Table 2). The 17 acute care hospitals had a CRE rate of 1.01 cases per 10,000 patient-days (95% CI, 0.82–1.24). Among the acute care facilities, the CRE incidence rate was highest in Michigan's eastern region (1.24 cases per 10,000 patient-days [95% CI, 0.98–1.54]) compared with the western region (0.52 cases per 10,000 patient-days [95% CI, 0.25–0.95]) and the mid-northern region (0.36 cases per 10,000 patient-days [95% CI, 0.07–1.06]; Table 3). The CRE incidence rate in the LTACs, 2.93 cases per 10,000 patient-days (95% CI, 1.26–5.78), was significantly higher than the acute care rate.

Fifty-two (51%) of the reported case patients were male (Table 4). The mean age was 63 years. Eighty-nine (87%) of the reported cases involved *K. pneumoniae*, whereas 13 (13%) involved *E. coli*. Ninety-nine specimens (97%) were from

TABLE 4. Patient Characteristics for 102 Cases of Carbapenem-Resistant Enterobacteriaceae (CRE) Reported September 1, 2012, through February 28, 2013

Characteristic	Cases
Demographic characteristic	
Patient age, years, median (range)	63 (20–95)
Male sex	52 (51)
White race[a]	58 (57)
Organism	
Klebsiella pneumoniae	89 (87)
Escherichia coli	13 (13)
Specimen source	
Blood	10 (10)
Respiratory/sputum specimen	16 (15)
Urine	62 (61)
Wound, skin, or soft tissue	8 (8)
Rectal/perianal	2 (2)
Other	4 (4)
Patient type	
Inpatient	
ICU	39 (38)
Non-ICU	50 (49)
Outpatient	11 (11)
Referral patient	2 (2)
Location from which patient was admitted[b]	
Home	27 (36)
Outside acute care hospital	11 (15)
Long-term acute care facility	4 (5)
Long-term care/skilled nursing	27 (36)
Other	6 (8)
Indwelling devices[c]	
At least 1 indwelling device	56 (63)
No indwelling device	33 (37)
Central venous line	35 (43)
Urinary catheter	38 (48)
Mechanical ventilation	22 (29)
Comorbidities[c]	
At least 1 comorbidity	76 (87)
No comorbidity	11 (13)
Renal failure	34 (39)
Cardiovascular disease	44 (51)
Malignancy	12 (14)
Diabetes mellitus	32 (37)
Chronic lung disease	28 (32)
Para-/hemi-/quadri-plegia	6 (7)

NOTE. Data are no. (%) of cases, unless otherwise indicated. ICU, intensive care unit.

[a] Reported if known.

[b] Data from inpatients only ($n = 75$).

[c] Acute care cases only if data were available; cases could report more than 1 comorbid condition or indwelling device.

clinical cultures. Urine cultures were the most common source (61%), followed by respiratory and sputum samples (15%) and blood specimens (10%). Antimicrobial susceptibilities and MIC ranges are displayed separately in Table 5.

The average time from patient admission to specimen collection was 7.6 days. Fifty (49%) of the patients were non–intensive care unit (ICU) inpatients at the time of specimen collection, and 39 (38%) were ICU patients (Table 4). The remaining 13 patients (13%) were either outpatients or referral patients, where the initiative facility acted as a reference laboratory and tested and reported a CRE case from an outside facility. For inpatient cases for which data were available ($n = 75$), 27 (36%) involved patients who were admitted from home, and 48 (64%) involved patients who were admitted from another healthcare facility (acute care hospital, LTAC facility, skilled nursing facility, or assisted living facility). Sixty-six (65%) of cases met criteria for CO infection, whereas the remaining 36 (35%) were determined to be HO (Table 6). Of the CO cases for which recent healthcare history was available, 33 (75%) of 44 reported exposure to a skilled nursing facility, LTAC facility, or acute care hospital within the previous 90 days. Similarly, of 16 HO cases with available recent healthcare exposure data, 14 (88%) involved a recent exposure to a skilled nursing facility, acute care hospital, or LTAC facility.

In addition to recent healthcare exposure, reported cases shared many risk factors. Where data were available, 34 (43%) of the patients were infected or colonized with an MDRO within the 90 days before CRE isolation, including 23 (29%) who had a history of previous CRE infection or colonization (Table 4). Indwelling devices were also common, with 56 (63%) of the cases reported in patients who had at least 1 indwelling device. Thirty-five cases (43%) were in patients who had a central venous catheter, 38 (48%) were in patients who had a urinary catheter, and 22 (29%) were in patients who were receiving mechanical ventilation at the time of specimen collection. Thirty-six (43%) of the patients had undergone a surgical procedure within the 90 days before specimen collection. Comorbid conditions were present in 76 cases (87%). The most common comorbid conditions were cardiovascular disease (51%), renal failure (39%), diabetes mellitus (37%), chronic lung disease (32%), and malignancy (14%).

Antimicrobial therapy within the previous 90 days was also common. Forty-three patients (46%) received at least 1 antimicrobial within the 90 days before specimen collection, with third- and fourth-generation cephalosporins (22%), fluoroquinolones (15%), aminogylcosides (14%), and carbapenems (14%) being the most frequently reported.

Paired dates of antimicrobial susceptibility results and initiation of contact precautions were available for 67 acute care cases. Sixty-five (97%) of the cases were in patients who were placed under contact precautions within 24 hours after the test result was reported (range, 0–11 days; mean time to contact precautions, 6 hours). It is important to note that some patients were under contact precautions for other MDROs before the CRE culture result; time from antimi-

TABLE 5. Antimicrobial Susceptibility Testing Results for Cases of Carbapenem-Resistant Enterobacteriaceae

Antimicrobial	Nonsusceptible isolates[a]/no. of isolates tested (%)	MIC range for susceptible isolates, μg/mL	MIC range for nonsusceptible isolates, μg/mL
Imipenem[b]	32/37 (86)	≤1 to ≤4	0.15 to >16
Meropenem[b]	52/56 (93)	≤0.25 to <4	<1 to ≥16
Doripenem[b]	33/34 (97)	≤0.5	≥2
Ertapenem[b]	58/59 (98)	≤1	≤0.5 to >32
Amikacin[c]	6/37 (16)	≤2 to ≤16	32 to ≥64
Tobramycin[c]	62/92 (67)	≤1 to ≤4	≥8 to >16
Gentamicin[c]	44/92 (48)	≤1 to ≤8	8 to ≥16
Tigecycline[c]	8/64 (13)	≤0.5 to ≤2	3 to ≥8
Colistin[c]	34[d]	0.12–0.5[e]	...

NOTE. MIC, minimum inhibitory concentration.

[a] Nonsusceptible (intermediate and resistant) isolates as reported by the facility.

[b] All 102 cases reported susceptibility results for at least 1 carbapenem.

[c] Only 94 (acute care facilities only) of the 102 cases could report susceptibility results for amikacin, tobramycin, gentamicin, tigecycline, and colistin, if known.

[d] No. of isolates tested.

[e] There are no standardized criteria for interpretation of MIC values for colistin resistance.

crobial susceptibility result to initiation of contact precautions was zero hours for those cases.

DISCUSSION

This report highlights baseline findings of a voluntary, statewide initiative for CRE surveillance and prevention. Michigan has a well-documented history of antimicrobial resistance[33-35] and continues to be proactive in conducting surveillance and leading prevention efforts for healthcare-associated infections. The CRE Surveillance and Prevention Initiative enabled healthcare facilities across the continuum of care to unite with public health to implement regional CRE surveillance and prevention efforts. Because CRE is not mandated to be reported in Michigan, its incidence in our region had been previously unknown.

Over the baseline collection period, 102 cases were reported in participating acute and LTAC facilities within 957,220 patient-days, which resulted in an incidence rate of 1.07 cases per 10,000 patient-days. Incidence ratios reported for this period are unadjusted for facility- and patient-level characteristics. Overall, the pooled mean rate is lower than recently reported laboratory-based community-wide surveillance studies from other regions.[28] This is not surprising given a likely publication bias attributable to regions with "hyperendemic" CRE being more likely to publish rates. The fact that Michigan rates are lower than other published rates indicates an opportunity to prevent CRE from becoming hyperendemic in Michigan.

Additionally, our crude incidence rates for acute care and LTAC facilities were lower than those reported in other regional surveillance studies.[28] Rates in participating Michigan LTAC facilities were significantly higher than the rates in acute care facilities during the baseline period. This observed difference is not necessarily surprising given that our reported incidence rates were not adjusted for patient acuity, length of stay, and other reported CRE risk factors (eg, indwelling devices and exposure to antimicrobials), which may be disproportionately present in patients at LTAC facilities. This lack of adjustment may at least partially explain the elevated incidence rate observed among the small number of LTAC facilities recruited in this initiative. Although the crude incidence rate was higher among LTAC facilities, patients at LTAC facilities only contributed 8% of all of the CRE cases reported.

Facilities enrolled in the CRE Surveillance and Prevention Initiative were invited to participate and voluntarily reported CRE data. The number of participating facilities per region is representative of the population and number of healthcare facilities from each Michigan region. The acute care facility incidence rate in the eastern region was significantly higher than those for the western and mid-northern regions ($P < .05$). Although geographical differences in CRE were observed, it is important to recognize that CRE were reported in each Michigan region.

The epidemiology of CRE infections and associated patient factors detailed in this report, including previous antimicrobial exposure, previous healthcare exposure, MDRO history, presence of indwelling devices, and comorbid conditions, are consistent with previously reported CRE studies.[14,15,19] A potential new finding that requires additional investigation is the proportion of cases in this study that were not in the ICU. Previous studies indicated that CRE is found almost exclusively in patients in ICUs.[1,14,15] Forty-nine percent of our cases were positive for CRE while on a general care ward. This may depict a shift in CRE epidemiology, which suggests that CRE is no longer exclusive to the ICU setting and is now emerging in general care patients. This further highlights the importance of a coordinated regional effort.

Our data reflect a predominance of CO cases (66% or 65%; Table 6). We would insist, however, that these infections were

TABLE 6. Cases of Carbapenem-Resistant Enterobacteriaceae Stratified by Centers for Disease Control and Prevention LabID Onset Type

Variable	Proportion (%) of cases
Overall	
Healthcare onset	36/102 (35)
Community onset	66/102 (65)
Previous healthcare exposure	
Healthcare onset[a]	14/16 (88)
Community onset[b]	33/44 (75)

NOTE. Healthcare exposure may include any acute, long-term acute, long-term care, or skilled nursing facility within the last 90 days.

[a] Data available for 16 of 36 cases.

[b] Data available for 44 of 66 cases.

not truly acquired in the community, especially because 75% of CO cases involved some form of healthcare exposure in the 90 days before the specimen collection date. This suggests that the majority of CO cases may be a product of repeated healthcare exposures and not representative of a legitimately community-acquired condition. Furthermore, we propose that current CDC LabID onset classifications may not be sufficient for categorizing the onset of CRE infections. CDC CRE LabID definitions may therefore benefit from a community-onset healthcare-facility associated event classification similar to that used for *Clostridium difficile* surveillance.[36] Regardless of the true origination of CO CRE, the presence of a CRE reservoir in nonhospital settings is concerning and further supports the need for coordinated regional approaches to CRE prevention.

Data collection was not limited to carbapenemase producers; we requested reporting of any carbapenem-resistant isolate, regardless of the resistance mechanism. The data in Table 5 illustrate that characterization of CRE isolates on the basis of the MIC value is problematic. There is significant overlap between susceptible and nonsusceptible MIC ranges for imipenem, meropenem, and ertapenem. Only doripenem and other select antimicrobials provided a clear distinction between susceptible and nonsusceptible MIC values.

Five isolates reported as resistant had MIC values in the susceptible interpretive category (eg, imipenem MIC less than or equal to 1). This is a correct interpretation in laboratories that are using unmodified US Food and Drug Administration–cleared commercial test systems when (1) additional phenotypic testing (eg, MHT, double-disk EDTA test) indicates the isolate produces a carbapenemase or (2) MIC values for other carbapenems tested are in the resistant interpretive category. Conversely, only 5 isolates reported as susceptible would have been interpreted as nonsusceptible using newer recommended MIC breakpoints, which are lower than previous breakpoints. It appears that at least a few laboratories may be aware of the new (2012) Clinical and Laboratory Standards Institute–recommended lower MIC breakpoint interpretive values for carbapenems and performed repeat or supplemental testing (ie, MHT) on isolates with MICs near the new cutoffs.

Forty-six percent of reported case patients received at least 1 antimicrobial in the 90 days before their positive CRE result. Antimicrobial stewardship campaigns have demonstrated that reductions in antimicrobial use coincide with reductions in MDRO rates.[24,37-39] Additionally, it is crucial to place patients with an MDRO, especially CRE, under contact precautions as soon as possible. On average, cases in acute care facilities were placed under contact precautions 6 hours after antimicrobial susceptibility results were reported, and 97% were placed under contact precautions within 24 hours. These data show that intrafacility communication between laboratories, infection control departments, and clinicians aligns with current recommended guidelines and has resulted in rapid initiation of contact precautions for patients testing positive for CRE.[13] However, given the high frequency of CO CRE cases and the large number of hospital and nonhospital institutions caring for persons with CRE, interfacility communication is of incredible importance to help prevent the spread of CRE among institutions.

There are several limitations to our surveillance. This is a public health surveillance and prevention initiative, not a research-based study. We relied on voluntary, active reporting by a relatively small number of facilities interested in participating. Selection bias is a potential factor because of the limited number of facilities that participated. The time period for baseline data collection of 6 months was relatively short. Data collection form completeness relied on the availability of data within case charts. Patient identifiers were not collected, so patients could not be tracked across facilities, and therefore patient outcome data were not analyzed. Additionally, incidence rates reported in this study are unadjusted and did not take into account differences in patient- or facility-level factors that could have influenced CRE rates (eg, patient acuity).

This statewide surveillance demonstrates that CRE is established in varying levels around the state, indicating an overall low level of CRE endemicity. By coordinating with acute and long-term acute care facilities and uniting with public health to create a voluntary reporting system and commitment to implement CRE prevention measures, Michigan partners are creating awareness and actively preventing CRE from becoming hyperendemic in the state. On March 1, 2013, all enrolled facilities implemented facility-specific CRE prevention measures that will be monitored and documented. Given the unique and diverse epidemiology of CRE detailed in this report, it will be important to evaluate the different approaches implemented to prevent CRE transmission in hospital and nonhospital settings, identify the most effective strategies, and develop effective methods for interfacility communications pertaining to transfer and management of persons with CRE.

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