ORIGINAL ARTICLE

Outbreak of Carbapenem-Resistant Enterobacteriaceae at a Long-Term Acute Care Hospital: Sustained Reductions in Transmission through Active Surveillance and Targeted Interventions

Amit S. Chitnis, MD, MPH;[1,2] Pam S. Caruthers, RN;[3] Agam K. Rao, MD;[1,2] JoAnne Lamb, MPH;[4] Robert Lurvey, MD, JD;[1] Valery Beau De Rochars, MD, MPH;[2,5] Brandon Kitchel, MS;[1] Margarita Cancio, MD;[3] Thomas J. Török, MD, MPH;[5,6] Alice Y. Guh, MD, MPH;[1] Carolyn V. Gould, MD, MSCR;[1] Matthew E. Wise, PhD, MPH[1]

OBJECTIVE. To describe a *Klebsiella pneumoniae* carbapenemase (KPC)–producing carbapenem-resistant Enterobacteriaceae (CRE) outbreak and interventions to prevent transmission.

DESIGN, SETTING, AND PATIENTS. Epidemiologic investigation of a CRE outbreak among patients at a long-term acute care hospital (LTACH).

METHODS. Microbiology records at LTACH A from March 2009 through February 2011 were reviewed to identify CRE transmission cases and cases admitted with CRE. CRE bacteremia episodes were identified during March 2009–July 2011. Biweekly CRE prevalence surveys were conducted during July 2010–July 2011, and interventions to prevent transmission were implemented, including education and auditing of staff and isolation and cohorting of CRE patients with dedicated nursing staff and shared medical equipment. Trends were evaluated using weighted linear or Poisson regression. CRE transmission cases were included in a case-control study to evaluate risk factors for acquisition. A real-time polymerase chain reaction assay was used to detect the bla_{KPC} gene, and pulsed-field gel electrophoresis was performed to assess the genetic relatedness of isolates.

RESULTS. Ninety-nine CRE transmission cases, 16 admission cases (from 7 acute care hospitals), and 29 CRE bacteremia episodes were identified. Significant reductions were observed in CRE prevalence (49% vs 8%), percentage of patients screened with newly detected CRE (44% vs 0%), and CRE bacteremia episodes (2.5 vs 0.0 per 1,000 patient-days). Cases were more likely to have received β-lactams, have diabetes, and require mechanical ventilation. All tested isolates were KPC-producing *K. pneumoniae*, and nearly all isolates were genetically related.

CONCLUSION. CRE transmission can be reduced in LTACHs through surveillance testing and targeted interventions. Sustainable reductions within and across healthcare facilities may require a regional public health approach.

Infect Control Hosp Epidemiol 2012;33(10):984-992

Carbapenem-resistant Enterobacteriaceae (CRE) are important[1] because carbapenems are antimicrobials of last resort used to treat multidrug-resistant Enterobacteriaceae infections.[2] In addition, all-cause mortality among hospitalized patients with CRE infections is approximately 40%.[3,4] In the United States, carbapenem resistance is primarily associated with *Klebsiella pneumoniae* carbapenemase (KPC), a serine β-lactamase.[5] Over the past decade, numerous KPC-producing CRE outbreaks have been described in acute care hospitals[6-11] and in long-term acute care hospitals (LTACHs).[11-15] Recent outbreaks have had introduction and dissemination of CRE in acute care hospitals via transfer of patients with CRE from LTACHs.[11-14]

LTACHs provide post–acute care hospitalization for patients with complicated medical illnesses.[16] About two-thirds of LTACH patients are 65 years old or more and on Medicare, and most patients have lengths of stay of 25 days or more.[16] Patients in LTACHs have multiple risk factors for colonization with multidrug-resistant organisms (MDROs), including

Affiliations: 1. Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia; 2. Office of Workforce and Career Development, Epidemic Intelligence Service, CDC, Atlanta, Georgia; 3. Division of Infection Prevention, Kindred Hospital Bay Area–St. Petersburg, St. Petersburg, Florida; 4. Epidemiology Program, Disease Control Division, Pinellas County Health Department, St. Petersburg, Florida; 5. Division of Disease Control, Bureau of Epidemiology, Florida Department of Health, Tallahassee, Florida; 6. Career Epidemiology Field Office Program, Office of Public Health Preparedness and Response, CDC, Atlanta, Georgia.

Received April 11, 2012; accepted June 3, 2012; electronically published August 20, 2012.

 0899-823X/2012/3310-0004$15.00. DOI: 10.1086/667738

CRE.[17] However, interventions to prevent MDRO transmission in LTACHs are poorly understood.

In July 2010, the Florida Department of Health became aware of CRE detected in clinical cultures from LTACH A. As a result, the county and state health department and LTACH A developed an infection prevention plan to assess and reduce CRE transmission at the facility. Because of ongoing CRE detection among LTACH A patients, the state health department requested assistance from the Centers for Disease Control and Prevention (CDC) in February 2011. In this report, we describe the epidemiologic and laboratory investigation of a CRE outbreak conducted to determine the occurrence, clinical impact, and risk factors for transmission of CRE at LTACH A and to identify and implement measures to control the outbreak.

METHODS

Setting

LTACH A is a freestanding 82-bed facility consisting of an 8-bed intensive care unit (ICU) and 3 medical-surgical units. All LTACH A patients are assigned to single-patient rooms.

Active Surveillance Testing for CRE

Prior to January 2010, active surveillance testing for CRE was not conducted, and CRE was detected on the basis of clinical cultures. Per LTACH A policy beginning in January 2010, all patients were presumptively placed under contact precautions upon admission and had urine and sputum surveillance cultures collected within 3 days of admission to screen for MDROs, including CRE. Patients with a history of or who tested positive for an MDRO remained under contact precautions for their entire hospitalization. In July 2010, local and state health departments recommended that LTACH A screen all patients for CRE by means of rectal swabs[18] within 3 days of admission and conduct a hospital-wide CRE point-prevalence survey among all hospitalized patients. In September 2010, LTACH A initiated biweekly CRE point-prevalence surveys for all patients who had no previous cultures positive for CRE and who were not screened for CRE by rectal surveillance culture in the previous 7 days.

Epidemiologic Investigation

Occurrence of CRE in LTACH A was assessed by identifying CRE transmission in the facility and CRE present on admission. We also describe CRE bacteremia in LTACH A patients to focus on a subset of patients in whom CRE had a clear clinical impact.

Definitions. CRE transmission cases were classified as either probable or possible. A probable CRE transmission case was defined as CRE isolated from a surveillance or clinical culture in an LTACH A patient during March 2009–February 2011 whose initial 3 surveillance cultures (ie, urine, sputum, and rectal) and all clinical cultures collected within 3 calendar days of admission were negative for CRE. A possible CRE transmission case was defined as CRE isolated from a surveillance or clinical culture in an LTACH A patient who had initial surveillance cultures obtained from less than 3 body sites but for whom all surveillance and clinical cultures collected within 3 days of admission were negative for CRE.

A CRE present-on-admission case was defined as CRE isolated from surveillance or clinical cultures from an LTACH A patient within 3 days of admission during March 2009–February 2011.

Detection of CRE cases at LTACH A. LTACH A microbiology records were reviewed to identify cultures positive for any CRE during March 2009–July 2011 as part of the on-site investigation. Carbapenem resistance was detected using 2008 Clinical Laboratory Standards Institute (CLSI) guidelines for antimicrobial susceptibility testing.[19] Beginning in July 2009, a modified Hodge test was performed for all Enterobacteriaceae isolates that were not susceptible to ertapenem, imipenem, or meropenem using 2008 CLSI breakpoints.[19] Medical records were reviewed for all patients with a positive CRE culture to identify the date of admission of CRE cases and bacteremia episodes.

Newly detected CRE, CRE prevalence, and CRE bacteremia incidence at LTACH A. The prevalence of CRE on admission to LTACH A was calculated by dividing the number of CRE present-on-admission cases by the total number of monthly admissions.

Two estimates of CRE occurrence were calculated based on biweekly point-prevalence data collected by the infection preventionist at LTACH A as part of ongoing CRE prevention efforts during July 2010–July 2011. The proportion of screened patients with newly detected CRE was calculated by dividing the number of CRE patients who screened positive on the point-prevalence survey by the total number of patients screened. Overall CRE prevalence was calculated by dividing the total number of CRE patients (ie, patients previously known to have CRE and patients with newly detected CRE based on the point-prevalence survey) by the total number of LTACH A patients present on the date of the survey.

A CRE bacteremia episode was defined as CRE isolated in blood from an LTACH A patient during March 2009–July 2011 who had no prior blood cultures positive for the same CRE pathogen in the previous 14 days. Incidence of monthly CRE bacteremia episodes was calculated by dividing the number of CRE bacteremia episodes by the total number of LTACH A patient-days (reported as episodes per 1,000 patient-days).

Case-control study. Probable CRE transmission cases detected since July 2010, the period when rectal surveillance cultures were obtained at LTACH A, were included as cases in a case-control study. One control was selected for each probable CRE transmission case among LTACH A patients who had active surveillance cultures collected from 3 body sites on admission, had no cultures positive for CRE during the hospitalization, and were present in LTACH A at the same time the case had his or her first CRE-positive culture (index

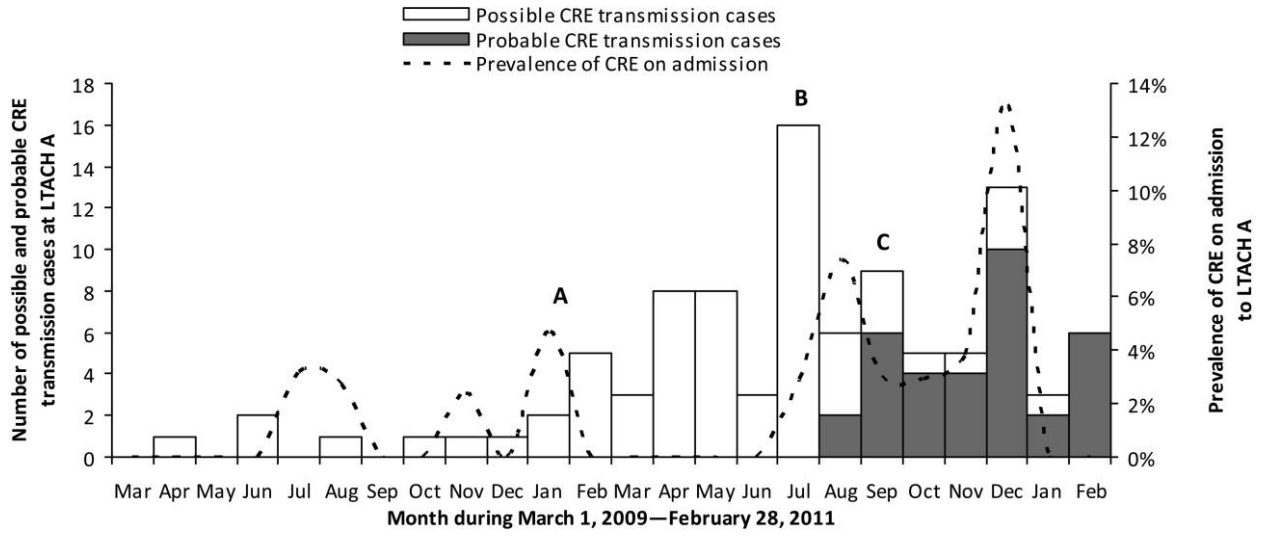

FIGURE 1. Carbapenem-resistant Enterobacteriaceae (CRE) transmission cases and prevalence of CRE on admission among patients admitted to long-term acute care hospital (LTACH) A, March 1, 2009, through February 28, 2011. A = Urine and sputum admission surveillance cultures started during January 2010. B = Rectal admission surveillance cultures for CRE started and one-time point-prevalence survey for CRE conducted during July 2010. C = Biweekly point prevalence surveys for CRE via rectal swabs started during September 2010.

date). Medical records were reviewed for data on demographics, comorbidities, hospital course, invasive device use and procedures, and antimicrobials, which were collected for up to 30 days prior to the index date.

Laboratory Investigation

All available CRE isolates from cultures collected during February–March 2011 were sent to the CDC for detection of the bla_{KPC} gene using a real-time polymerase chain reaction assay[20] and for pulsed-field gel electrophoresis (PFGE) to determine genetic relatedness using the CHEF mapper electrophoresis system (Bio-Rad) and a procedure that has been described elsewhere.[21] PFGE patterns were compared using the Dice coefficient and clustering by the unweighted pair group method using average linkages (Bionumerics 5.10; Applied Maths). In addition, PFGE patterns for isolates collected during the investigation were compared with an archived picture of PFGE patterns for another set of available CRE isolates obtained from LTACH A patients in September 2010, which were previously analyzed at the state health department.

Infection Prevention Observations

As part of the on-site epidemiologic investigation conducted in March 2011, more than 40 hours of infection prevention observations of healthcare personnel (HCP) were conducted. This included audits of hand hygiene and glove and gown use and observations of HCP using invasive devices, performing procedures, and conducting daily patient assessments.

Interventions to Reduce CRE Transmission

A stepwise process of implementing infection prevention measures was initiated on the basis of results of biweekly CRE point-prevalence surveys and observations. Beginning in July 2010, LTACH A staff, in consultation with local and state health departments, implemented the following measures: addition of audits of glove and gown use to ongoing weekly hand hygiene audits, monthly educational sessions on proper hand hygiene and isolation precautions for all HCP, and weekly reminders on appropriate cleaning practices for high-touch surfaces to environmental services staff. Starting in December 2010, CRE patients were cohorted and spatially separated from non-CRE patients into one section of a medical-surgical unit with dedicated nursing staff. Daily staff meetings were conducted to increase facility communication about CRE prevention efforts.

In March 2011, LTACH A implemented additional recommendations from the on-site investigation, including daily audits of hand hygiene and PPE use, observations of insertion and maintenance practices for invasive devices, and daily assessments of the need for invasive devices, especially urinary catheters. Biweekly conference calls with LTACH A, local and state health departments, and the CDC were initiated in April 2011 to discuss results of ongoing point-prevalence surveys, to optimize infection prevention efforts at the facility, and to discuss regional CRE prevention efforts in healthcare facilities. Additional measures implemented included dedicating shared medical equipment (ie, hoyer lifts, scales, and blood pressure machines) to CRE patients and assigning dedicated nursing staff to CRE patients in the ICU. The facility also began a campaign to reduce unnecessary urinary catheter use concurrently with CRE-specific measures.

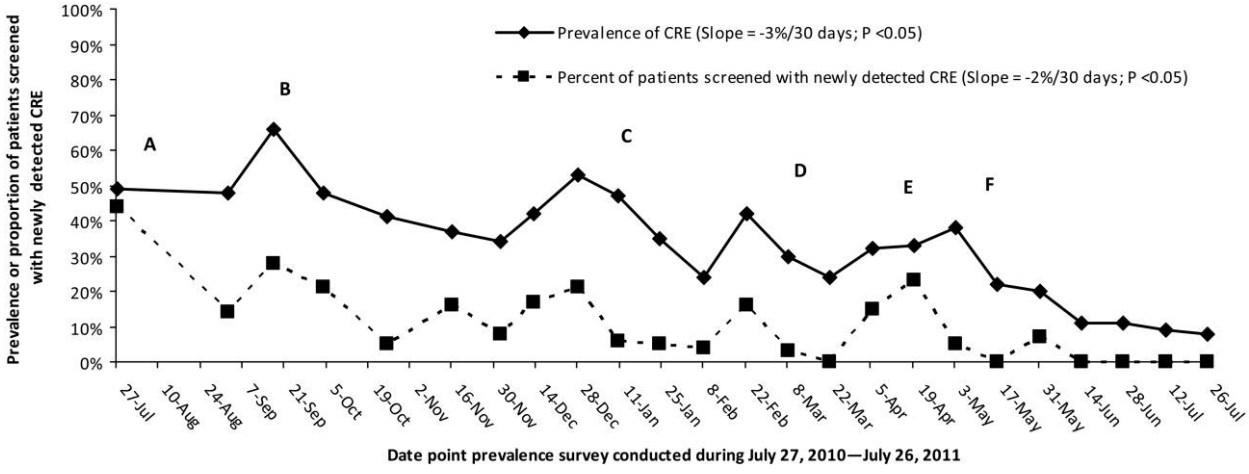

FIGURE 2. Prevalence of carbapenem-resistant Enterobacteriaceae (CRE), percentage of screened patients with newly detected CRE on the date a point-prevalence survey was conducted, and infection prevention interventions implemented to reduce CRE transmission at long-term acute care hospital (LTACH) A, July 27, 2010, through July 26, 2011. A = Audits of hand hygiene and personal protective equipment use initiated. B = Biweekly point-prevalence surveys initiated. C = CRE patients cohorted and spatially separated from non-CRE patients in one wing of a medical-surgical unit; nursing staff in this wing were cohorted to care for CRE patients. D = Daily audits and assessment of use and need for invasive devices conducted. E = Biweekly conference calls initiated with the Centers for Disease Control and Prevention, LTACH A, and state and local health departments. F = Dedicated nurses assigned to CRE patients in intensive care unit (ICU). Shared medical equipment (ie, hoyer lifts, scales, and blood pressure machines) dedicated to CRE patients on non-ICU floors. As a result of an ongoing intervention to decrease use of urinary catheters, LTACH A noted a 50% reduction in utilization of urinary catheters compared with that in previous months.

Statistical Analysis

Trends in overall CRE prevalence and proportion of screened patients with newly detected CRE at LTACH A were assessed using linear regression models weighted for the number of patients in LTACH A and the number of patients screened at the time of the point-prevalence surveys, respectively. Monthly trends in CRE bacteremia incidence were evaluated using Poisson regression.

For the case-control study, bivariate analysis was conducted using the χ^2 or Fisher exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Variables that had a P value less than .05 in bivariate analysis or that were known risk factors for CRE were included as candidate variables in a forward-selection multivariable logistic regression model (entry criterion, $P < .10$). Goodness of fit was assessed using the Hosmer-Lemeshow test. All reported P values are 2-sided, and a P value less than .05 was considered statistically significant. All analyses were conducted using SAS 9.2 (SAS Institute).

RESULTS

Epidemiologic Investigation

Detection of CRE cases at LTACH A. Ninety-nine CRE transmission cases (34 probable, 65 possible) were detected from March 1, 2009, through February 28, 2011. The median number of monthly CRE transmission cases increased from 1 (range, 0–2) during March 2009–January 2010 to 6 (range, 3–16) during February 2010–February 2011. Of the 99 CRE transmission cases, 90 (91%) had *K. pneumoniae*, 4 (4%) had *Enterobacter aerogenes*, and 1 (1%) had *Enterobacter* species recovered from cultures during their LTACH A hospitalization; both *K. pneumoniae* and *Enterobacter* species were recovered for 4 (4%) CRE transmission cases. Twenty-one (21%) CRE transmission cases developed CRE bacteremia.

Sixteen present-on-admission CRE cases were detected from March 1, 2009, through February 28, 2011; these cases were transferred to LTACH A from 7 different acute care hospitals in the surrounding region, with 1 acute care hospital accounting for 44% ($n = 7$) of cases. During this period, this acute care hospital accounted for the second highest number of admissions to LTACH A. Carbapenem-resistant *K. pneumoniae* was recovered from 15 (94%) of 16 present-on-admission cases; *Escherichia coli* was detected in 1 patient. One present-on-admission case developed CRE bacteremia.

During March–December 2009, when active surveillance testing for CRE was not performed, the median monthly CRE prevalence on admission was 0% (range, 0%–3%; Figure 1). During January–June 2010, when active surveillance testing for CRE was performed using urine and sputum cultures, the median monthly CRE prevalence on admission was 0% (range, 0%–5%). During July 2010–February 2011, when active surveillance testing included rectal cultures, the median CRE prevalence on admission was 3% (range, 0%–13%; Figure 1).

Newly detected CRE, CRE prevalence, and CRE bacteremia

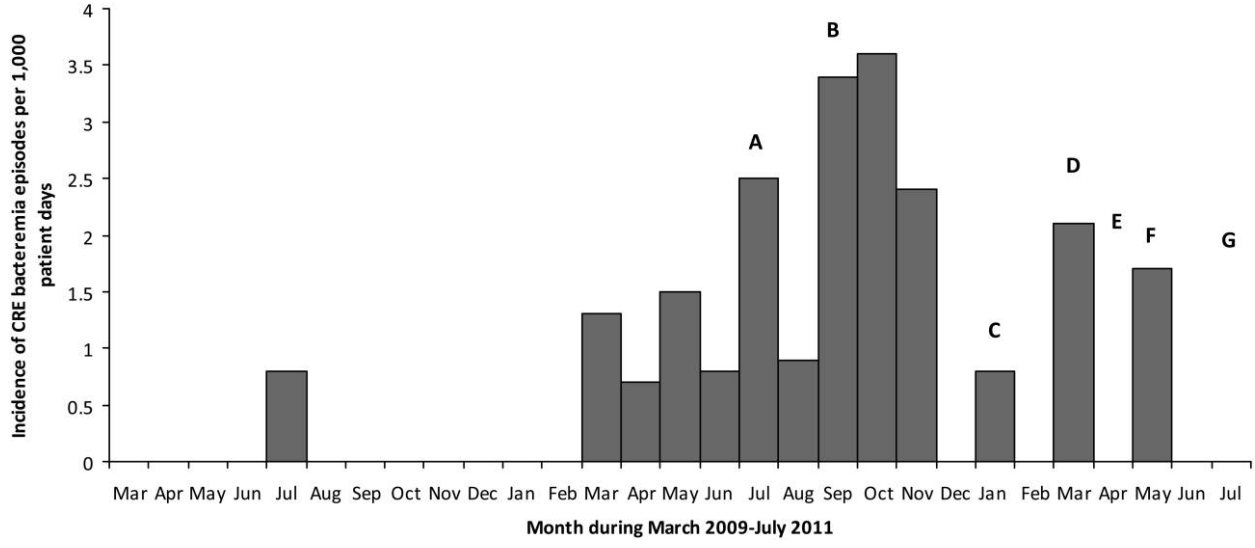

FIGURE 3. Incidence of carbapenem-resistant Enterobacteriaceae (CRE) bacteremia episodes per 1,000 patient-days at long-term acute care hospital (LTACH) A, March 1, 2009, through July 31, 2011. A = Audits of hand hygiene and personal protective equipment use initiated. B = Biweekly point-prevalence surveys initiated. C = CRE patients cohorted and spatially separated from non-CRE patients in one wing of a medical-surgical unit; nursing staff in this wing were cohorted to care for CRE patients. D = Daily audits and assessment of use and need for invasive devices conducted. E = Biweekly conference calls initiated with the Centers for Disease Control and Prevention, LTACH A, and state and local health departments. F = Dedicated nurses assigned to CRE patients in an intensive care unit (ICU). Shared medical equipment (ie, hoyer lifts, scales, and blood pressure machines) dedicated to CRE patients on non-ICU floors. As a result of an ongoing intervention to decrease use of urinary catheters, LTACH A noted a 50% reduction in utilization of urinary catheters compared with that in previous months. G = During June 2011–April 2012, no CRE bacteremia episodes were detected among LTACH A patients.

incidence at LTACH A. From July 27, 2010, through July 26, 2011, there was a significant decrease in CRE prevalence (49% to 8%) and in the percentage of screened patients with newly detected CRE (44% to 0%; Figure 2). To determine whether the percentage of newly detected CRE patients on July 27, 2010, influenced the trend analyses, we restricted data to the period from September 2, 2010, through July 26, 2011; these analyses were also statistically significant.

During March 2009–July 2011, 29 CRE bacteremia episodes were detected among 25 LTACH A patients; 28 (96%) of these episodes were detected after January 2010. Beginning in February 2010, the median number of CRE bacteremia episodes detected per month was 1 (range, 0–5); the incidence peaked at 3.6 episodes per 1,000 patient-days in October 2010 and decreased to 0 episodes per 1,000 patient-days by June 2011 (Figure 3). No statistically significant trend in incidence was detected during March 2009–July 2011 ($P = .48$). However, when limiting the analysis to July 2010–July 2011, the period when interventions were implemented, a statistically significant decrease ($P = .01$) in incidence was detected.

Case-control study. Compared with controls, probable transmission cases were more likely to be female, have had a greater number of total parenteral nutrition–days, have received β-lactam antimicrobials, and have diabetes (Table 1). In multivariable analysis, CRE acquisition was significantly associated with having had a greater number of ventilator-days, receiving β-lactam antimicrobials, and having diabetes (Table 2). A Hosmer-Lemeshow test did not indicate poor model fit ($P = .18$).

Laboratory Investigation

Nineteen CRE isolates were sent to the CDC for identification and characterization. All isolates were *K. pneumoniae* with the bla_{KPC} gene present.

There were 2 PFGE patterns among *K. pneumoniae* isolates tested (Figure 4). PFGE pattern A was detected in 17 isolates (from 8 probable transmission and 2 present-on-admission cases) and was more than 83% similar to the PFGE pattern for 4 *K. pneumoniae* isolates (from 3 probable and 1 possible transmission case) tested at the state health department in September 2010. PFGE pattern B was detected in 2 isolates (from 2 probable transmission cases) and shared 70% similarity with PFGE pattern A.

Infection Prevention Observations

During March 2011, hand hygiene was successfully performed at 30 (31%) of 96 opportunities. Gloves were worn during 78 (77%) of 102 opportunities, and gowns were worn during 78 (89%) of 88 opportunities. Suboptimal maintenance practices for invasive devices were noted, including inconsistent performance of hand hygiene prior to accessing central venous catheters. In addition, HCP did not adequately clean and disinfect some shared portable medical equipment (eg,

TABLE 1. Comparison of Demographic Characteristics, Clinical Characteristics, and Outcomes among Carbapenem-Resistant Enterobacteriaceae (CRE) Cases and Controls at Long-Term Acute Care Hospital (LTACH) A, July 1, 2010, through February 28, 2011

Variable	Cases (n = 34)	Controls (n = 34)	P[a]
Demographic characteristic			
Age	75 (43–88)	68 (43–98)	.19
Male	13 (38)	22 (65)	.03
White	22 (64)	26 (76)	.29
Clinical characteristics			
Hospitalization			
Admitted to LTACH A for management of respiratory failure	30 (88)	29 (76)	.72
Previous admissions to LTACH A	5 (15)	5 (15)	1.0
LOS prior to index date	23 (6–71)	18 (5–69)	.07
Transfers to healthcare facilities prior to index date	3 (9)	2 (6)	1.0
Admitted to ICU at LTACH A prior to index date	20 (59)	18 (53)	.63
Devices[b]			
Ventilator-days, median (IQR)	18 (6–26)	13 (0–19)	.06
Central line–days, median (IQR)	15 (7–23)	14 (6–18)	.70
Urinary catheter–days, median (IQR)	18 (9–22)	13 (5–19)	.20
Wound vacuum	2 (6)	2 (6)	1.0
Rectal tube	2 (6)	1 (3)	1.0
Procedures and treatments[b]			
Hemodialysis	3 (9)	2 (6)	1.0
TPN-days	0 (0–24)	0 (0–2)	.04
Invasive procedures,[c] median (IQR)	1 (0–2)	0 (0–1)	.05
Patient-specific risk factors for CRE			
Charlson score,[d] median (IQR)	2 (2–4)	2 (1–3)	.08
Diabetes	15 (44)	7 (21)	.03
Wound[e]	20 (59)	17 (50)	.47
Stool incontinence	33 (97)	30 (88)	.36
Contact precautions[f]	23 (68)	15 (44)	.05
Class of antimicrobials[b]			
β-Lactams	15 (44)	5 (15)	<.001
Cephalosporins	16 (47)	12 (35)	.32
Carbapenems	15 (44)	13 (38)	.62
Fluoroquinolones	11 (32)	9 (26)	.59
Outcomes[g]			
Died	16 (47)	10 (29)	.13
Died within 30 days of index date	5 (15)	8 (24)	.35

NOTE. Categorical variables are no. (%) of cases or controls; continuous variables are median (range), unless otherwise noted. ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; TPN, total parenteral nutrition.

[a] The χ^2 or Fisher exact test was used to compare categorical variables; the Wilcoxon rank-sum test was used to compare continuous variables.

[b] Data were abstracted for a period of 30 days prior to the index date.

[c] Central or peripherally inserted central catheter, bronchoscopy, tracheostomy, thoracentesis, esophagogastroduodenoscopy and percutaneous endoscopic gastrostomy tube placement, or debridement of a sacral wound; all invasive procedures were performed at LTACH A.

[d] Non-age-adjusted Charlson comorbidity index.

[e] Documentation of an arterial, venous, surgical, diabetic, or necrotic wound in the medical chart.

[f] Placed under contact precautions 30 days prior to the index date for infection or colonization with a multidrug-resistant organism aside from CRE.

[g] Deaths attributed to CRE could not be determined using medical and vital records data.

X-ray and ultrasound machines) used for both CRE and non-CRE patients; high-touch surfaces, including medication cabinets in patient rooms, were also not cleaned and disinfected during observations.

DISCUSSION

A large CRE outbreak began in February 2010 at LTACH A. CRE bacteremia was identified in 25 patients, 21 of whom

TABLE 2. Multivariable Analysis of Risk Factors for Carbapenem-Resistant Enterobacteriaceae among Cases and Controls at Long-Term Acute Care Hospital A, July 1, 2010, through February 28, 2011

Variable	Multivariate analysis, adjusted[a] OR (95% CI)	*P*
Ventilator-days[b]	1.4 (1.0–1.8)	.03
TPN-days[b]	10.1 (0.5–215.1)	.14
Diabetes	4.3 (1.2–15.0)	.02
β-Lactams	5.7 (1.4–22.0)	.01

NOTE. CI, confidence interval; OR, odds ratio; TPN, total parenteral nutrition.

[a] Logistic regression model using a forward selection strategy with a significance level for entering the model equal to .10.

[b] Variables were scaled to 5-day increments (ie, variable was divided by 5) to reflect a clinically meaningful value for use of a ventilator or TPN.

likely acquired CRE in the facility (probable and possible CRE transmission cases). Suboptimal infection prevention practices and transfers of CRE patients from acute care hospitals to LTACH A facilitated ongoing CRE transmission. A stepwise approach to implementation of multiple infection prevention interventions at LTACH A over a 1-year period decreased CRE prevalence 6-fold and drastically reduced CRE transmission and bacteremia episodes.

Major interventions implemented at LTACH A temporally coincided with reductions in CRE transmission. These included biweekly point prevalence surveys, cohorting and spatial separation of CRE patients from other patients, and dedication of nursing staff and certain high-touch medical equipment to CRE patients. Dedication of nursing staff in the ICU (where spatial separation was challenging) and dedication of shared medical equipment to CRE patients in non-ICU areas were implemented immediately preceding sustained reductions in CRE transmission. A successful effort to decrease urinary catheter utilization among LTACH A patients was another intervention that may have contributed to reductions in CRE transmission. Since outbreaks of multidrug-resistant gram-negative urinary tract infections have been associated with use of urinary catheters,[22,23] decreasing urinary catheter utilization may have reduced opportunities for CRE transmission via HCP who manipulate these devices.

Interventions implemented at LTACH A included many components of a bundled intervention used in a previous investigation[15] of carbapenem-resistant *K. pneumoniae* transmission at an LTACH. One notable difference was that daily chlorhexidine bathing of patients was not implemented at LTACH A. Prevention of CRE transmission in LTACH A may have been facilitated by the presence of single-patient rooms, and additional strategies (eg, chlorhexidine bathing) may be needed to prevent CRE transmission in other LTACHs that do not have dedicated single-patient rooms. Another important component of the success in preventing CRE transmission at LTACH A was ongoing biweekly communication between the facility, state, and county health departments and CDC staff after the on-site investigation, which allowed for refinement of infection prevention efforts in response to evidence of ongoing transmission.

Dedication of shared medical equipment with high potential for skin contact was another component of this investigation that may have been effective, suggesting that transient environmental contamination of high-touch shared medical items may play a role in CRE transmission. Although other pathogens, such as *Acinetobacter baumannii* and vancomycin-resistant enterococci, are known to survive in the environment for long periods of time and are frequently found on environmental surfaces during outbreaks,[24] the extent to which environmental contamination contributes to CRE transmission has not been well described.

Detection of present-on-admission CRE cases from multiple acute care hospitals in the surrounding region highlights the challenge of regional spread of CRE between healthcare facilities. As part of ongoing regional CRE prevention efforts, local and state health departments worked with acute care hospitals to ensure that these facilities were aware of CDC guidance regarding CRE prevention;[25] in addition, LTACH A collaborated with facilities to ensure that interfacility transfer forms, which include information on CRE colonization or infection status, are completed for all patients transferred to LTACH A. Although the CRE outbreak at LTACH A was successfully controlled, continued influx of CRE patients from surrounding facilities may hamper long-term control efforts and necessitate continued use of active surveillance testing upon admission to the LTACH. Furthermore, although LTACHs were implicated as epicenters for amplification and regional dissemination of CRE in a previous study,[14] control of CRE transmission at an LTACH in this published study did not prevent ongoing CRE spread within the region. This indicates that attributing spread of CRE and other MDROs solely to LTACHs and other long-term care facilities may not be justified, as successful control of CRE may require coordinated infection prevention efforts across settings with involvement of local and state health departments. Such a strategy has been successfully implemented in Israel, where CRE prevention efforts were coordinated at a national level and effectively decreased CRE occurrence and spread.[26]

The case-control study may be the first study to detect an association between diabetes and CRE. LTACH A patients with diabetes may be at increased risk for CRE acquisition because of suppression of the immune system, more frequent interactions with HCP compared with that for patients without diabetes, or other unmeasured risk factors for CRE acquisition. Similar to other case-control studies, use of β-lactam antimicrobials[27,28] and mechanical ventilation[3] were identified as independent risk factors for CRE.

This investigation has several limitations. We may have underestimated the clinical impact of CRE among LTACH A patients, as we could not determine retrospectively whether sputum or urine cultures positive for CRE represented true infections. Nevertheless, we identified 25 LTACH A patients who had CRE bacteremia. Since rectal surveillance cultures

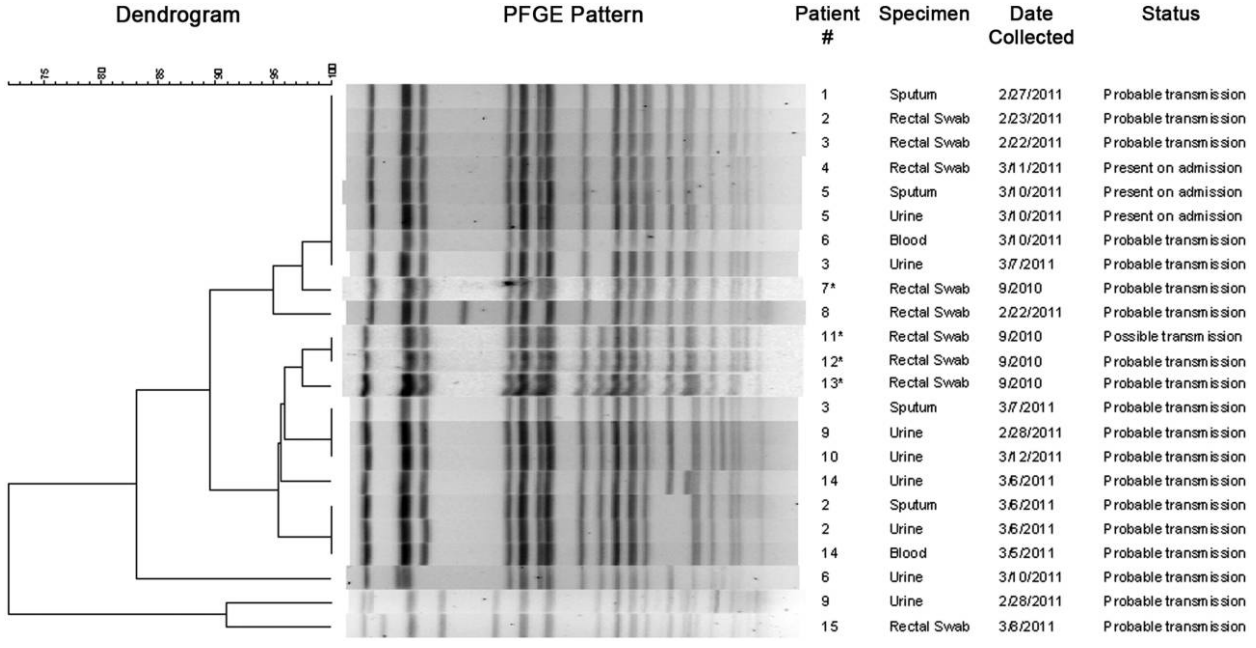

FIGURE 4. Pulsed-field gel electrophoresis (PFGE) patterns for carbapenem-resistant *Klebsiella pneumoniae* isolates from long-term acute care hospital (LTACH) A patients, September 1, 2010, through, March 31, 2011. An image of the PFGE patterns for previously analyzed CRE isolates (September 2010) was compared with the PFGE patterns for isolates collected during the investigation (February–March 2011) using Bionumerics software. Isolates obtained from LTACH A patients in September 2010, indicated by asterisks, were analyzed at the state health department.

(which are more sensitive for Enterobacteriaceae than cultures collected from noninguinal or nonrectal anatomic sites[29]) were not used at LTACH A to detect CRE before July 2010, we could not accurately assess the number of CRE transmission cases and CRE prevalence on admission prior to implementation of this screening test. The implementation of multiple interventions over a short period of time precluded us from determining the effectiveness of each intervention. Finally, the limited regional epidemiologic information and number of CRE isolates collected during this investigation did not allow for a complete understanding of CRE transmission among healthcare facilities within the region.

This investigation demonstrates that CRE incidence and prevalence can be reduced in LTACHs through implementation of targeted infection prevention interventions, even when CRE prevalence exceeds 50%. However, involvement of state and local public health agencies in regional coordination of broader CRE infection prevention activities among healthcare facilities will be needed to ensure sustainable reductions in healthcare-associated CRE transmission.

ACKNOWLEDGMENTS

Financial support. All funding and material support for this work was provided by the US Department of Health and Human Services, Pinellas County Health Department, and the Florida Department of Health. No commercial entity had any role in this work.

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Amit S. Chitnis, MD, MPH, 1600 Clifton Road, MS A-24, Atlanta, GA 30333 (amit.chitnis@cdph.ca.gov).

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. Richet HM, Mohammeed J, McDonald LC, Jarvis WR. Building communications networks: international network for the study and prevention of emerging antimicrobial resistance. *Emerg Infect Dis* 2001;7:319–322.
2. Pitout JD, Laupland KB. Extended spectrum β-lactamase-producing Enterobacteriaceae: an emerging public health concern. *Lancet Infect Dis* 2008;8:159–166.
3. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. *Infect Control Hosp Epidemiol* 2008;29:1099–1106.
4. Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, Schwartz D, Leavitt A, Carmeli Y. Predictors of carbapenem-resistant *Klebsiella pneumoniae* acquisition among hospitalized patients and effect of acquisition on mortality. *Antimicrob Agents Chemother* 2008;52:1028–1033.
5. Queenan AM, Bush K. Carbapenemases: the versatile β-lactamases. *Clin Microbiol Rev* 2007;20:440–458.
6. Woodford N, Tierno PM Jr, Young K, et al. Outbreak of *Klebsiella pneumoniae* producing a new carbapenem-hydrolyzing class A

β-latctamase, KPC-3, in a New York medical center. *Antimicrob Agents Chemother* 2004;48:4793–4799.
7. Bratu S, Landman D, Haag R, et al. Rapid spread of carbapenem-resistant *Klebsiella pneumoniae* in New York City: a new threat to our antibiotics armamentarium. *Arch Intern Med* 2005;165: 1430–1435.
8. Nadkarni AS, Schliep T, Khan L, Zeana CB. Cluster of bloodstream infections caused by KPC-2 carbapenemase-producing *Klebsiella pneumoniae* in Manhattan. *Am J Infect Control* 2009; 37:121–126.
9. Munoz-Price LS, De La Cuesta C, Adams S, et al. Successful eradication of a monocolonal strain of *Klebsiella pneumonia* during a *K. pneumoniae* carbapenemase–producing *K. pneumoniae* outbreak in a surgical intensive care unit in Miami, Florida. *Infect Control Hosp Epidemiol* 2010;31:1074–1077.
10. Kontopoulou K, Protonotariou E, Vasilakos K, et al. Hospital outbreak caused by *Klebsiella pneumoniae* producing KPC-2 β-lactamase resistant to colistin. *J Hosp Infect* 2010;76:70–73.
11. Marchaim D, Chopra T, Pogue JM, et al. Outbreak of colistin-resistant, carbapenem-resistant *Klebsiella pneumoniae* in metropolitan Detroit, Michigan. *Antimicrob Agents Chemother* 2011; 54:5099–5104.
12. Endimiani A, Depasquale JM, Forero S, et al. Emergence of bla_{KPC}-containing *Klebsiella pneumoniae* in a long-term acute care hospital: a new challenge to our healthcare system. *J Antimicrob Chemother* 2009;64:1102–1110.
13. Perez F, Endimiani A, Ray AJ, et al. Carbapenem-resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* across a hospital system: impact of post–acute care facilities on dissemination. *J Antimicrob Chemother* 2010;65:1807–1818.
14. Won SY, Munoz-Price LS, Lolans K, et al. Emergence and rapid regional spread of *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae. *Clin Infect Dis* 2011;53:532–540.
15. Munoz-Price LS, Hayden MK, Lolans K, et al. Successful control of an outbreak of *Klebsiella pneumoniae* carbapenemase–producing *K. pneumoniae* in a long-term acute care hospital. *Infect Control Hosp Epidemiol* 2010;31:341–347.
16. Medicare Payment Advisory Commission. *Report to the Congress: Medicare Payment Policy.* http://www.medpac.gov/documents /mar11_entirereport.pdf. Published 2011. Accessed April 11, 2012.
17. Munoz-Price LS. Long-term acute care hospitals. *Clin Infect Dis* 2009;49:438–443.
18. Centers for Disease Control and Prevention. *Laboratory Protocol for Detection of Carbapenem-Resistant or Carbapenemase-Producing,* Klebsiella *Spp. and* E. coli *for Rectal Swabs.* http:// www.cdc.gov/HAI/pdfs/labSettings/Klebsiella_or_Ecoli.pdf. Accessed April 11, 2012.
19. Clinical and Laboratory and Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing: 18th Informational Supplement.* CLSI document M100-S18. Wayne, PA: CLSI, 2008.
20. Centers for Disease Control and Prevention. *Multiplex Real-Time PCR Detection of* Klebsiella pneumoniae *Carbapenemase (KPC) and New Delhi Metallo-β-lactamase (NDM-1).* http:// www.cdc.gov/HAI/pdfs/labSettings/KPC-NDM-protocol-2011 .pdf. Accessed April 11, 2012.
21. Ribot EM, Fair MA, Gautom R, et al. Standardization of pulsed-field gel electrophoresis protocols for the subtyping of *Escherichia coli* O157:H7, *Salmonella*, and *Shigella* for PulseNet. *Foodborne Pathog Dis* 2006;3:59–67.
22. Schaberg DR, Weinstein RA, Stamm WE. Epidemics of nosocomial urinary tract infection caused by multiply resistant gram-negative bacilli: epidemiology and control. *J Infect Dis* 1976;133: 363–366.
23. Yoon HJ, Choi JY, Park YS, et al. Outbreak of *Serratia marcescens* bacteriuria in a neurosurgical intensive care unit of a tertiary care teaching hospital: a clinical, epidemiologic, and laboratory perspective. *Am J Infect Control* 2005;33:595–601.
24. Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens. *Infect Control Hosp Epidemiol* 2011;32:687–699.
25. Centers for Disease Control and Prevention. Guidance for control of infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* in acute care facilities. *MMWR Morb Mortal Wkly Rep* 2009;58:256–260.
26. Schwaber MJ, Lev B, Israeli A, et al. Containment of a country-wide outbreak of carbapenem-resistant *Klebsiella pneumonia* in Israeli hospitals via a nationally implemented intervention. *Clin Infect Dis* 2011;52:848–852.
27. Falgas ME, Rafailidis PI, Kofteridis D, et al. Risk factors of carbapenem-resistant *Klebsiella pneumoniae* infections: a matched case-control study. *J Antimicrob Chemother* 2007;60:1124–1130.
28. Patel N, Harrington S, Dihmess A, et al. Clinical epidemiology of carbapenem-intermediate or -resistant *Enterobacteriaceae. J Antimicrob Chemother* 2011;66:1600–1608.
29. Weintrob AC, Roediger MP, Barber M, et al. Natural history of colonization with gram-negative multidrug-resistant organisms among hospitalized patients. *Infect Control Hosp Epidemiol* 2010; 31:330–337.