Population-Based Incidence of Carbapenem-Resistant *Klebsiella pneumoniae* along the Continuum of Care, Los Angeles County

Author(s): Patricia Marquez, MPH; Dawn Terashita, MD, MPH; David Dassey, MD, MPH; Laurene Mascola, MD, MPH

Reviewed work(s):
Source: *Infection Control and Hospital Epidemiology*, Vol. 34, No. 2 (February 2013), pp. 144-150
Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America
Stable URL: http://www.jstor.org/stable/10.1086/669087
Accessed: 09/01/2013 11:33

ORIGINAL ARTICLE

# Population-Based Incidence of Carbapenem-Resistant *Klebsiella pneumoniae* along the Continuum of Care, Los Angeles County

**Patricia Marquez, MPH;[1] Dawn Terashita, MD, MPH;[1] David Dassey, MD, MPH;[1] Laurene Mascola, MD, MPH[1]**

OBJECTIVE. Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is an emerging multidrug-resistant pathogen associated with higher mortality, longer hospital stays, and increased costs. CRKP was thought to be sporadic in Los Angeles County (LAC); however, the actual incidence is unknown. To address this, LAC declared CRKP a laboratory-reportable disease on June 1, 2010.

DESIGN. Laboratory-based community-wide surveillance.

PATIENTS. Any individual who was identified as CRKP positive. CRKP was defined as a *K. pneumoniae* isolate resistant to all carbapenems by 2010 Clinical and Laboratory Standards Institute criteria.

METHODS. Laboratory directors of 102 LAC acute care hospitals (ACHs) and 5 reference laboratories were to submit susceptibility testing results for all CRKP-positive specimens. Positive specimens from the same patient within the same calendar month of previous culture were excluded.

RESULTS. A total of 814 reports were received from June 1, 2010, through May 31, 2011, from 69 laboratories; 675 (83%) met the case definition. Cases were reported from ACHs (387 [57%]), long-term ACHs (LTACs; 231 [34%]), and skilled nursing facilities (57 [8%]); an outbreak in 1 LTAC was identified. The pooled mean incidence rate in LAC ACHs and LTACs was 0.46 per 1,000 patient-days; the rate in LTACs (2.54 per 1,000 patient-days) was higher than that in ACHs (0.31 per 1,000 patient-days; $P < .001$). Sixty-five individuals had multiple incidences, accounting for 147 case reports.

CONCLUSION. CRKP is more present in LAC than suspected. Rates were consistently higher in LTACs than in ACHs. Heightened awareness of this problem is needed in all LAC healthcare facilities, as patients access services along the continuum of care.

*Infect Control Hosp Epidemiol* 2013;34(2):144-150

Carbapenem-resistant Enterobacteriaceae is an emerging bacterial pathogen that represents significant morbidity and mortality in acute care settings.[1-4] The most prevalent of these organisms, carbapenem-resistant *Klebsiella pneumoniae* (CRKP), has been found in healthcare settings around the world.[5-7] In the United States, it was identified first in New York City hospitals in 2002 and quickly spread to the surrounding New England area.[8] Outbreaks of CRKP have increasingly been reported from varying healthcare settings, including long-term acute care hospitals (LTACs).[9,10] A 2007 Centers for Disease Control and Prevention (CDC) analysis of hospital surveillance data suggests that 8% of all *Klebsiella* isolates are CRKP; recent studies have shown that it accounts for 5%–24% of *Klebsiella* isolates identified in hospitalized patients.[11-13]

Resistance to carbapenems in Enterobacteriaceae can be conferred through different mechanisms, most commonly through production of carbapenemases.[14] The most common plasmid-mediated *K. pneumoniae* carbapenemase (KPC) is a class A carbapenemase that can disseminate readily.[15,16] The high clonality of KPC seen in hospital outbreaks is worrisome, as the resistance plasmid can easily be transferred horizontally to carbapenem-susceptible strains.[17-19] This organism poses a threat to patients, hospitals, and doctors, as carbapenem antibiotics are often the last line of defense against gram-negative bacteria, and no new antimicrobials in this class are being developed.[20]

Risk factors for colonization and infection with CRKP are similar to those associated with other multidrug-resistant organisms.[21] Increased lengths of hospitalization, prior extended-spectrum cephalosporin and fluoroquinolone use, and invasive procedures are associated with an increased risk of acquisition of CRKP.[22-24] In addition, higher mortality rates are associated with CRKP infection versus carbapenem-susceptible *K. pneumoniae*, with some hospital surveillance reports showing mortality between 47% and 57%.[2,25,26] Active surveillance in hospital intensive care units has been recommended to establish the presence of the organism, as asymptomatic colonization with the organism is common in this patient population.[27,28] Colonized patients, both identified and unidentified, may then transmit CRKP in other healthcare facilities to which they are transferred.[29]

In the fall of 2009, the CDC contacted the Los Angeles

Affiliation: 1. Acute Communicable Disease Control Program, Los Angeles County Department of Public Health, Los Angeles, California.
Received June 29, 2012; accepted September 6, 2012; electronically published December 19, 2012.
 0899-823X/2013/3402-0007$15.00. DOI: 10.1086/669087

TABLE 1. Carbapenem-Resistant *Klebsiella pneumoniae* Case Characteristics

| | Value |
|---|---|
| Total no. confirmed | 675 |
| Female sex | 379 (56) |
| Age, mean (range), years | 73 (1–103) |
| Reported from | |
| Acute care hospital | 387 (57) |
| Long-term acute care hospital | 231 (34) |
| Skilled nursing facility | 57 (8) |
| Specimens with admit date | 598 (89) |
| Hospital onset | 363 (61) |
| Community onset | 235 (39) |
| From skilled nursing facility | 154 (66) |
| Collected on admission | 141 (60) |

NOTE. Data are no. (%), unless otherwise indicated.

County Department of Public Health (LAC DPH) regarding 2 patients identified with panresistant *K. pneumoniae* from 2 distinct hospitals. Previously, the CDC agreed to test select isolates from LAC hospitals for confirmatory testing of the KPC enzyme and identified these patients as having identical isolates that stood out due to high resistance to colistin and tigecycline. In the course of our investigation of these 2 cases, we identified several patients positive for CRKP in one of the facilities where a case was hospitalized. Because of the lack of knowledge regarding the presence of CRKP in LAC, the DPH initiated a surveillance system to detect the incidence of this emerging multidrug-resistant organism. This report describes our laboratory surveillance of the LAC healthcare community as a whole and identifies areas of high risk for infection that are the target of further study.

## METHODS

### Surveillance

The LAC DPH declared CRKP a laboratory-reportable disease on June 1, 2010. CRKP was defined as any specimen positive for *K. pneumoniae* showing resistance to carbapenems by the 2010 revised M100-S20 Clinical and Laboratory Standards Institute (CLSI) guidelines for carbapenems and Enterobacteriaceae.[30] All laboratories were required to submit a final laboratory report with culture and sensitivity, including minimum inhibitory concentrations (MICs), as well as the DPH confidential morbidity report (CMR) form with basic patient demographic information. Laboratory reports that did not include results of carbapenem testing did not meet the case definition and were excluded from the analysis.

### Case Demographics

Basic demographic information collected from the CMR form included name, date of birth, address at time of reporting, sex, and date of admission to facility if hospitalized. Addresses on the form were cross-referenced with a database of skilled nursing facilities (SNFs) in LAC to determine whether the case was a resident of a SNF. Attempts were made to obtain missing information from forms submitted; this included contacting the infection preventionist (IP) at the reporting facility as well as contacting laboratories directly.

### Case Reporting

Most forms and laboratory reports were submitted to the DPH via fax and entered by staff into the reportable diseases surveillance system. The DPH applied for and received a CRKP Systematized Nomenclature of Medicine—Clinical Terms code. This code allowed hospital laboratories with electronic laboratory reporting to code their data appropriately and transmit them electronically as well as upload laboratory records to the DPH. All reported cases were designated as confirmed if they met our case definition; otherwise, they were designated as false and excluded from further analysis.

### Case Onset Definitions

Nosocomial cases were defined using the CDC National Healthcare Safety Network (NHSN) LabID component criteria. Individuals with specimens collected on or before the third day after admission were considered community onset; those with specimens collected on or after the fourth day after admission were considered healthcare facility onset. Per LabID criteria, positive specimens for cases that had already been reported in the same calendar month, from either the same or a different reporting facility, were classified as duplicates and excluded from the analysis.

### Statistical Analysis

All information from the CMR form was extracted from the surveillance system, and corresponding laboratory susceptibility testing was entered into an Access database for analysis. For laboratory data, all carbapenem MICs, when available, were entered. Other antimicrobials in the laboratory report were indicated to be susceptible, intermediate, or resistant, as determined by the reporting laboratory, in data entry. Average daily census for reporting LAC acute care hospitals (ACHs) and LTAC facilities, which are licensed in California as ACHs and for the purpose of this analysis were considered a subset of ACHs, was obtained via personal communication with IPs by the DPH. This daily census was used to estimate patient-days for each ACH and LTAC for each reporting month. Incidence rates were calculated and demographic variables were analyzed using SAS, version 9.2 (SAS Institute).

## RESULTS

From June 1, 2010, through May 31, 2011, a total of 814 laboratory reports were submitted to the DPH. Of these, 675 (83%) were confirmed as CRKP cases (Table 1). The remaining 139 (17%) reports did not meet the case definition and are not included in this analysis. Reasons for exclusion include lack of carbapenem testing in the laboratory report as well as isolates being extended-spectrum $\beta$-lactamase (ESBL) positive but carbapenem susceptible. Of the 102 ACHs in LAC, 65 (64%) reported at least 1 case; this includes the

subset of 8 LTACs and the 4 LAC public ACHs. Additional reporting sources included 2 out-of-county ACHs, 1 outpatient medical center, and 1 large regional laboratory that serves the SNF population.

Women (379 [56%]) accounted for a slightly larger proportion of cases reported than men. The mean age of CRKP cases was 73 years, with a range of 1–102 years. Race/ethnicity was available for only 175 (26%) cases; the breakdown was not representative of LAC, with white (54 [31%]), African American (53 [30%]), Latino (40 [23%]), and Asian (28 [16%]) cases accounting for nearly equal proportions. The 1-year-old was positive for New Delhi metallo-$\beta$-lactamase, the first such case reported in LAC. Although detection of KPC enzymes was not a reporting requirement, the IP at the reporting facility was alarmed to have identified this organism and promptly called the DPH. This individual had recently traveled to Pakistan and received medical care there prior to hospitalization in the LAC facility.

Incidence rates were calculated for all 65 LAC ACHs reporting at least 1 case. The overall pooled mean incidence rate for the 12 months of data in LAC ACHs, including LTACs, was 0.46 per 1,000 patient-days; for LTACs the pooled mean was 2.54 per 1,000 patient-days, and for ACHs the pooled mean was 0.31 per 1,000 patient-days. Rates in LTACs were consistently higher than rates in ACHs each month during the surveillance period ($P < .001$). This trend was seen in every month, with rates in LTACs reaching as much as 8 times the rates in ACHs and consistently 2–5 times higher (Figure 1). Rates were not calculated for SNFs or out-of-county ACHs because of lack of census data.

Paired dates of admission and specimen collection were available for 587 (87%) cases. The mean length of hospitalization from admission to first CRKP-positive culture was 18 days, with a range of 0–247 days. Cases with a longer length of hospitalization were generally reported from LTAC facilities, with a mean length of hospitalization of 30 days, compared with 11 days for ACHs. A large proportion of cases (355 [60%]) had their positive specimen collected 4 or more days after admission and are considered healthcare onset by NHSN definitions. The remaining 232 (40%) cases with specimens collected within the first 3 days after admission are considered community onset. Of these community-onset cases, 141 (61%) had their positive specimen collected on the day of admission. A large proportion of the community-onset cases (147 [63%]) were admitted from SNFs; we were unable to assess prior healthcare exposure in the remaining 37% of community-onset cases, as it was not possible through laboratory data alone. Twelve cases were reported CRKP positive more than 100 days after admission. These were reported from LTACs or from hospitals that have sub–acute care units.

Early in our surveillance, an outbreak was identified in a 177-bed LTAC. Twenty-four CRKP-positive cases were identified over a 2-month period and were positive in various specimen sources, the majority in sputum (11 [46%]). All cases had a central line in place (24 [100%]), several had an indwelling urinary catheter (19 [79%]), and some had an endotracheal tube and were ventilator dependent (13 [54%]). Although these 24 had the most common risk factors for acquisition of CRKP, many cases were not patients in the intensive care unit but rather were in the main subacute

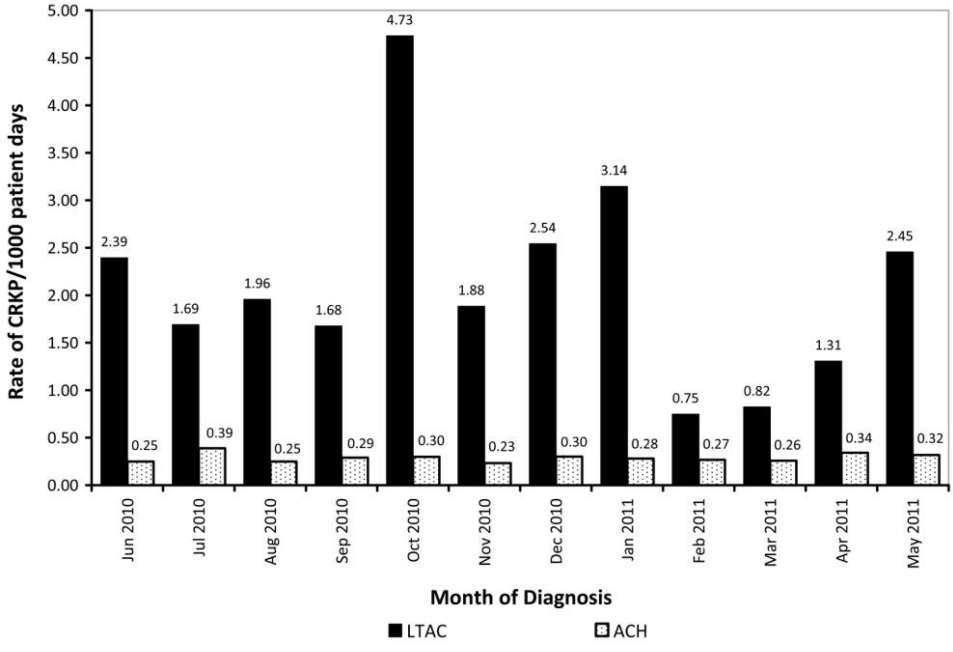


FIGURE 1. Monthly carbapenem-resistant *Klebsiella pneumoniae* (CRKP) pooled mean rate of infection by facility type for long-term acute care hospitals (LTACs; $n = 8$) and acute care hospitals (ACHs; $n = 57$) in Los Angeles County (excluding skilled nursing facilities and out-of-county reporting facilities).

TABLE 2. Carbapenem-Resistant *Klebsiella pneumoniae*–Positive Specimen Characteristics

| | No. (%) |
|---|---|
| Specimen type | |
| Urine | 315 (47) |
| Sputum | 177 (26) |
| Wound | 77 (11) |
| Blood | 53 (8) |
| Other | 50 (7) |
| Modified Hodge test positive | 106 (16) |
| ESBL positive | 53 (8) |
| Coinfections | 294 (44) |
| *Pseudomonas aeruginosa* | 82 (28) |
| *Acinetobacter baumanii* | 58 (20) |
| *Proteus mirabilis* | 57 (19) |
| VRE | 31 (10) |
| MRSA | 19 (6) |
| ESBL-positive *Escherichia coli* | 13 (4) |

NOTE. ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

medical/surgical unit. Thirteen of these cases were transferred to various ACHs nearby for further treatment of their infections.

Positive specimen sources included urine, sputum, wounds, and blood; positive urine specimens were most frequently reported (263 [43%]; Table 2). Two hundred forty-nine cases were positive for at least 1 other organism in the CRKP-positive specimen. The most frequently identified coinfections were *Pseudomonas aeruginosa* (82 [33%]) and *Acinetobacter baumanii* (58 [23%]). Laboratory reports were not evaluated to differentiate between infection and colonization in specimens positive for CRKP. For facilities that included these test results, 106 (16%) were modified Hodge test positive. Fifty-three (8%) CRKP isolates also tested ESBL positive.

The antimicrobial imipenem was the most frequently reported carbapenem tested for susceptibility (640 [94%]; Table 3). Ertapenem was often used to confirm carbapenem resistance in *K. pneumoniae* isolates and was included in approximately half (314 [47%]) of laboratory reports received; doripenem was rarely reported in susceptibility testing and was not analyzed. Availability of MICs in laboratory reports varied among the reporting facilities, as many hospitals indicated that their standard practice is to remove carbapenem MICs in final laboratory reports so doctors do not prescribe these antimicrobials. The mean MIC for all carbapenems was well above the new CLSI breakpoints.

Other antimicrobials used for susceptibility testing varied by facility; all included at least 1 quinolone, aminoglycoside, cephalosporin, penicillin, and sulfonamide. Susceptibility data were available for 20 antimicrobials, with isolates showing 100% resistance to nearly all cephalosporins and greater than 97% resistance to quinolones (Table 4). Forty-five (65%) facilities performed susceptibility testing for tigecycline; 30 (43%) facilities tested for colistin. Although interpretation of results were facility specific due to lack of CLSI interpretation guidelines for these drugs against Enterobacteriaceae, isolates showed susceptibility to colistin but intermediate susceptibility to tigecycline.

By NHSN LabID component definitions, 65 (9%) individuals had CKRP isolated on multiple occasions and accounted for 147 laboratory reports. The majority of these (44 [68%]) were reported from a combination of healthcare facilities, including various ACHs (14 [32%]) as well as ACHs and LTACs (16 [36%]). Two cases were reported from an ACH, LTAC, and SNF during the surveillance period; 1 of these was reported 5 different times over a 9-month period.

## DISCUSSION

This is the first report describing community-wide laboratory surveillance for CRKP. Implementation of a county-wide laboratory surveillance system allowed us to obtain a comprehensive understanding of the incidence and transmission of CRKP in LAC that could not be done through surveillance by individual healthcare facilities.[31] In 12 months, this surveillance system identified more cases of CRKP than expected. Previous case-specific CDC laboratory results from LAC hospitals indicated that CRKP was identified sporadically in the area, and its prevalence in our healthcare community was unknown.

In our study, the 675 confirmed cases from 814 laboratory reports submitted identified CRKP as a significant problem due to the high risk of transmission in the LAC healthcare system. CRKP was previously found mainly in traditional ACH settings; however, this surveillance system found it circulating throughout the healthcare community as a whole. The identification of 147 incidents in 65 patients as they accessed healthcare services along the continuum of care highlights the interconnectedness of healthcare facilities. Hospitals more than ever are likely to see drug-resistant organisms introduced by patients who may have had non–acute care facility exposure. Although length of colonization is not well understood, studies have shown repeated positive cultures up to 6 weeks after the initial positive result.[12,32] This reinforces the need for a strong antibiotic stewardship program in all healthcare facilities for the judicious use of antibiotics in their patient populations.

A striking finding was the high incidence of CRKP in LTACs. All 8 LTAC facilities in LAC reported at least 1 case, accounting for 34% of confirmed cases during the surveillance period. Each of the 8 facilities has an average daily

TABLE 3. Minimum Inhibitory Concentrations (MICs) for Carbapenems, Tigecycline, and Colistin

| Antimicrobial | No. tested | MIC, mean (range), μg |
|---|---|---|
| Imipenem | 640 | 12 (4–32) |
| Meropenem | 191 | 9 (4–16) |
| Ertapenem | 314 | 6 (4–10) |
| Tigecycline | 315 | 3 (0.5–16) |
| Colistin | 223 | 2 (0.5–16) |

TABLE 4. Antibiogram for Carbapenem-Resistant *Klebsiella pneumoniae* Cases Reported

| Antimicrobial | No. resistant/no. tested (%) |
|---|---|
| Amikacin | 321/605 (53) |
| Ampicillin | 643/644 (100) |
| Ampicillin-sulbactam | 367/375 (98) |
| Aztreonam | 209/210 (100) |
| Cefazolin | 595/596 (100) |
| Cefipime | 535/551 (97) |
| Cefotaxime | 224/239 (94) |
| Cefoxitin | 216/216 (100) |
| Cefuroxime | 147/147 (100) |
| Ceftazidime | 507/508 (100) |
| Ceftriaxone | 565/577 (98) |
| Ciprofloxacin | 390/397 (98) |
| Gentamicin | 244/665 (37) |
| Levofloxacin | 562/570 (99) |
| Moxifloxacin | 32/33 (97) |
| Nitrofurantoin | 287/299 (96) |
| Piperacillin-tazobactam | 498/518 (96) |
| Tetracycline | 32/75 (43) |
| Tobramycin | 542/564 (96) |
| Trimethoprim-sulfamethoxazole | 380/641 (59) |

census of 80 beds or fewer, much smaller than the majority of LAC hospitals. While it is alarming that so many cases were identified in these small facilities, the patient population they serve has many of the known risk factors for infection and colonization with CKRP.[33] As part of our routine surveillance, an outbreak was identified in an LTAC that would otherwise not have been reported. These patients underwent many of the invasive procedures traditionally associated with risk for acquisition of CRKP and had accessed services along the continuum of care prior to their admission.

Case demographics in our population were similar to what has been reported in the literature, with more female cases and older patients reported. However, the surveillance encompassed cases from LTACs and SNFs and was not limited to ACHs only. The large proportion of cases identified as community onset in this surveillance system, especially the large number of community-onset cases admitted from a SNF, may also point to an overall problem in the healthcare community. Increased attention to infection control procedures and surveillance is needed in these facilities to prevent the spread of MDROs. As patients receive treatment along the continuum of care, more individuals will be transferring back and forth between acute care, long-term acute care, and subacute care, bringing with them the organisms they acquired from the previous healthcare facility.[9,34,35] Proper disclosure of MDRO infection or colonization status to the admitting facility when patients are transferred would allow for implementation of appropriate infection control procedures, such as contact precautions for colonized or infected patients, as well as initiation of unit-based active surveillance if an outbreak is suspected.

In addition, CRKP identification is not standardized among laboratories and is not easily identified through the automated testing systems used in many hospitals.[36,37] Many hospital laboratory reports did not conform to the new CLSI guidelines for carbapenem breakpoints, indicating intermediate susceptibility to carbapenems with a MIC of 8. When contacted, several of these hospitals stated that their laboratory testing mechanism followed Food and Drug Administration breakpoints and could not be calibrated to the new lower CLSI MICs. This problem in many of the automated testing systems in use allows many isolates of CRKP to go undetected, expediting their spread in facilities.[38] Although hundreds of CRKP-positive patients were identified through this surveillance system, this is most likely a gross underestimation of the true incidence in LAC. Improving knowledge of CLSI criteria for carbapenem-resistant Enterobacteriaceae and use of a standardized definition in laboratories, especially those that serve the long-term care community, is one way to enhance surveillance and obtain a more precise estimate of the incidence and prevalence of CRKP in LAC. The combined use of automated systems and modified Hodge test can be a more precise method to identify CRKP in facilities that are not able to manually lower the MIC breakpoints for carbapenems and Enterobacteriaceae.

There are several limitations to our surveillance. First, this is a passive surveillance system relying solely on IPs and laboratories to report CRKP-positive specimens using the reporting criteria. Many cases are missed due to use of old carbapenem breakpoints for Enterobacteriaceae and a general underreporting in passive surveillance systems. In addition, different hospitals use different antimicrobials for their susceptibility testing. While this lack of consistency was not ideal, the data were useful and generated a community-wide CRKP antibiogram. In addition, complete demographic information was not available for all cases, and date of admission was missing for 64 cases. Surveillance did not include any patient-specific variables, so additional information, such as infection versus colonization, underlying risk factors, morbidity, and mortality, were unavailable.

This community-wide laboratory surveillance in LAC, with minimum data elements collected from individual cases, was an effective method to approximate the incidence of an emerging MDRO in the LAC healthcare community. Improved disclosure of a patient's medical history between the transferring and receiving facility as they move along the continuum of care can be facilitated by use of a standardized transfer form, much like the CDC's interfacility infection control transfer form.[39] In addition, understanding the rates of CRKP among these varied types of healthcare settings will allow public health to improve prevention and control strategies with ACHs, LTACs, and SNFs to decrease the spread of CRKP in LAC.

## ACKNOWLEDGMENTS

We thank all the infection preventionists and laboratories for their diligent reporting to the Department of Public Health.

*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 Patricia Marquez, MPH, 313 North Figueroa Street, Room 212, Los Angeles, CA 90012 (pmarquez@ph.lacounty.gov).

Presented in part: 2011 Society for Healthcare Epidemiology of America Annual Scientific Meeting; Dallas, Texas.

## REFERENCES

1. Ben-David D, Kordevani R, Keller N, et al. Outcome of carbapenem resistant *Klebsiella pneumoniae* bloodstream infections. *Clin Microbiol Infect* 2011;18(1):54–60.
2. Borer A, Saidel-Odes L, Riesenberg K, et al. Attributable mortality rate for carbapenem-resistant *Klebsiella pneumoniae* bacteremia. *Infect Control Hosp Epidemiol* 2009;30(10):972–976.
3. Schwaber M, Carmeli Y. Carbapenem-resistant Enterobacteriaceae: a potential threat. *JAMA* 2008;300(24):2911–2913.
4. Schwaber M, Klarfeld-Lidji S, Navon-Venezia S, et al. Predictors of carbapenem-resistant *Klebsiella pneumoniae* acquisition among hospitalized adults and effect of acquisition on mortality. *Antimicrob Agents Chemother* 2008;52(3):1028–1033.
5. Yan J, Ko W, Tsai S, et al. Outbreak of infection with multidrug-resistant *Klebsiella pneumoniae* carrying $bla_{\text{IMP-8}}$ in a university medical center in Taiwan. *J Clin Microbiol* 2001;39(12):4433–4439.
6. Quale J, Landman D, Bradford P, et al. Molecular epidemiology of a citywide outbreak of extended-spectrum $\beta$-lactamase–producing *Klebsiella pneumoniae* infection. *Clin Infect Dis* 2002;35(7):834–841.
7. Gupta N, Limbago B, Patel J, et al. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis* 2011;53(1):60–67.
8. Bratu S, Landman D, Haag R, et al. Rapid spread of carbapenem-resistant *Klebsiella pneumoniae* in New York City. *Arch Intern Med* 2005;165(12):1430–1435.
9. Won S, Munoz-Price L, Lolans K, et al. Emergence and rapid regional spread of *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae. *Clin Infect Dis* 2011;53(6):532–540.
10. Gregory CJ, Llata E, Stine N, et al. Outbreak of carbapenem-resistant *Klebsiella pneumoniae* in Puerto Rico associated with a novel carbapenemase variant. *Infect Control Hosp Epidemiol* 2010;31(5):476–484.
11. 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(10):256–260.
12. Weiner-Well Y, Rudensky B, Yinnon A, et al. Carriage rate of carbapenem-resistant *Klebsiella pneumoniae* in hospitalised patients during a national outbreak. *J Hosp Infect* 2010;74(4):344–349.
13. Bratu S, Mooty M, Nichani S, et al. Emergence of KPC-possessing *Klebsiella pneumoniae* in Brooklyn, New York: epidemiology and recommendations for detection. *Antimicrob Agents Chemother* 2005;49(7):3018–3020.
14. Srinivasan A, Patel JB. *Klebsiella pneumoniae* carbapenemase–producing organisms: an ounce of prevention really is worth a pound of cure. *Infect Control Hosp Epidemiol* 2008;29(12):1107–1109.
15. Nordmann P, Cuzon G, Naas T. The real threat of *Klebsiella pneumoniae* carbapenemase–producing bacteria. *Lancet Infect Dis* 2009;9(4):228–236.
16. Mathers AJ, Cox HL, Kitchel B, et al. Molecular dissection of an outbreak of carbapenem-resistant Enterobacteriaceae reveals intergenus KPC carbapenemase transmission through a promiscuous plasmid. *mBio* 2011;2(6):e00204-11.
17. Samra Z, Ofir O, Lishtzinsky Y, et al. Outbreak of carbapenem-resistant *Klebsiella pneumoniae* producing KPC-3 in a tertiary medical centre in Israel. *Int J Antimicrob Agents* 2007;30(6):525–529.
18. Ikonomidis A, Tokatlidou D, Kristo I, et al. Outbreaks in distinct regions due to a single *Klebsiella pneumoniae* clone carrying a $bla_{\text{VIM-1}}$ metallo-$\beta$-lactamase gene. *J Clin Microbiol* 2005;43(10):5344–5347.
19. Navon-Venezia S, Leavitt A, Schwaber M, et al. First report on a hyperepidemic clone of KPC-3-producing *Klebsiella pneumoniae* in Israel genetically related to a strain causing outbreaks in the United States. *Antimicrob Agents Chemother* 2009;53(2):818–820.
20. Elemam A, Rahimian J, Mandell W. Infection with panresistant *Klebsiella pneumoniae*: a report of 2 cases and a brief review of the literature. *Clin Infect Dis* 2009;49(2):271–274.
21. Hussein K, Sprecher H, Maschiach T, Oren I, Kassis I, Finkelstein R. Carbapenem resistance among *Klebsiella pneumoniae* isolates: risk factors, molecular characteristics, and susceptibility patterns. *Infect Control Hosp Epidemiol* 2009;30(7):666–671.
22. Gasink LB, Edelstein PH, Lautenbach E, Synnestvedt M, Fishman NO. Risk factors and clinical impact of *Klebsiella pneumoniae* carbapenemase–producing *K. pneumoniae. Infect Control Hosp Epidemiol* 2009;30(12):1180–1185.
23. Patel G, Huprikar S, Factor S, 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(12):1099–1106.
24. Falgas M, Rafailidis P, Kofteridis D, et al. Risk factors of carbapenem-resistant *Klebsiella pneumoniae* infections: a matched case–control study. *J Antimicrob Chemother* 2007;60(5):1124–1130.
25. Woodford N, Tierno P, Young K, et al. Outbreak of *Klebsiella pneumoniae* producing a new carbapenem-hydrolyzing class A $\beta$-lactamase, KPC-3, in a New York medical center. *Antimicrob Agents Chemother* 2004;48(12):4793–4799.
26. Weisenberg S, Morgan D, Espinal-Witter R, et al. Clinical outcomes of patients with *Klebsiella pneumoniae* carbapenemase–producing *K. pneumoniae* after treatment with imipenem or meropenem. *Diagn Mircrobiol Infect Dis* 2009;64(2):233–235.
27. Ben-David D, Maor Y, Keller N, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. *Infect Control Hosp Epidemiol* 2010;31(6):620–626.
28. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant *Klebsiella*

*pneumoniae* in intensive care unit patients. *Infect Control Hosp Epidemiol* 2008;29(10):966–968.
29. Schechner V, Kotlovsky T, Tarabeia J, et al. Predictors of rectal carriage of carbapenem-resistant Enterobacteriaceae (CRE) among patients with known CRE carriage at their next hospital encounter. *Infect Control Hosp Epidemiol* 2011;32(5):497–503.
30. Clinical and Laboratory Standards Institute (CLSI). *M100-S20 Enterobacteriaceae Susceptibility—Cephalosporin and Carbapenem Breakpoint Revisions.* Wayne, PA: CLSI, 2010.
31. Duffy J, Sievert D, Rebman C, et al. Effective state-based surveillance for multidrug-resistant organisms related to health care–associated infections. *Public Health Rep* 2011;126(2):176–185.
32. Saidel-Odes L, Polacheck H, Peled N, et al. A randomized, double-blind, placebo-controlled trial of selective digestive decontamination using oral gentamicin and oral polymyxin E for eradication of carbapenem-resistant *Klebsiella pneumoniae* carriage. *Infect Control Hosp Epidemiol* 2012;33(1):14–19.
33. Bonomo R. Multiple antibiotic-resistant bacteria in long-term-care facilities: an emerging problem in the practice of infectious diseases. *Clin Infect Dis* 2000;31(6):1414–1422.
34. Centers for Disease Control and Prevention. Carbapenem-resistant *Klebsiella pneumoniae* associated with a long-term–care facility—West Virginia, 2009–2011. *MMWR Morb Mortal Wkly Rep* 2011;60(41):1418–1420.
35. Endimiani A, DePasquale J, 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(5):1102–1110.
36. Tenover F, Kalsi R, Williams P, et al. Carbapenem resistance in *Klebsiella pneumoniae* not detected by automated susceptibility testing. *Emerg Infect Dis* 2006;12(8):1209–1213.
37. Anderson K, Lonsway D, Rasheed J, et al. Evaluation of methods to identify the *Klebsiella pneumoniae* carbapenemase in Enterobacteriaceae. *J Clin Microbiol* 2007;45(8):2723–2725.
38. Tan T, Ng L. Comparison of three standardized disc susceptibility testing methods for colistin. *J Antimicrob Chemother* 2006; 58(4):864–867.
39. Centers for Disease Control and Prevention (CDC). *Inter-Facility Infection Control Transfer Form for States Establishing HAI Prevention Collaboratives Using ARRA Funds.* Atlanta: CDC, 2010. http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf. Accessed August 24, 2012.