Epidemiology of Carbapenem-Resistant Enterobacteriaceae

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Centers for Disease Control and Prevention

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

INCIDENCE OF CRE IN THE UNITED STATES

Change in CRE Incidence, 2001-2011

	National Nosocomial Infection Surveillance system, Number (%)			National Healthcare Safety Network, Number (%)		
	2001			**2011**		
Organism	Isolates	Tested	Non-Susceptible	Isolates	Tested	Non-susceptible
Klebsiella pneumoniae* and *oxytoca	654	253 (38.7)	4 (1.6)	1,902	1,312 (70.0)	136 (10.4)
E. coli	1,424	421 (29.6)	4 (1.0)	3,626	2,348 (64.8)	24 (1.0)
Enterobacter aerogenes* and *cloacae	553	288 (52.1)	4 (1.4)	1,045	728 (69.7)	26 (3.6)
Total	2,631	962 (36.6)	12 (1.2)	6,573	4,388 (66.8)	186 (4.2)

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Facilities Reporting at least One CRE (CAUTI or CLABSI) to NHSN, First Half of 2012

Facility characteristic	Number of facilities with CRE from a CAUTI or CLABSI (2012)	Total facilities performing CAUTI or CLABSI surveillance (2012)	(%)
All acute care hospitals	181	3,918	(4.6)
Short-stay acute hospital			
Long-term acute care hospital			

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Short-stay acute hospital	145	3,716	(3.9)
Long-term acute care hospital	36	202	(17.8)

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Facility characteristic	Number of facilities with CRE from a CAUTI or CLABSI (2012)	Total facilities performing CAUTI or CLABSI surveillance (2012)	(%)
Hospital bed size			
<100	48	1,609	(3.0)
100-299	46	1,480	(3.1)
300-499	41	541	(7.6)
≥500	45	258	(17.4)
Region			
Northeast	63	658	(9.4)
Midwest	30	927	(3.0)
South	50	1,503	(3.2)
West	29	804	(3.6)

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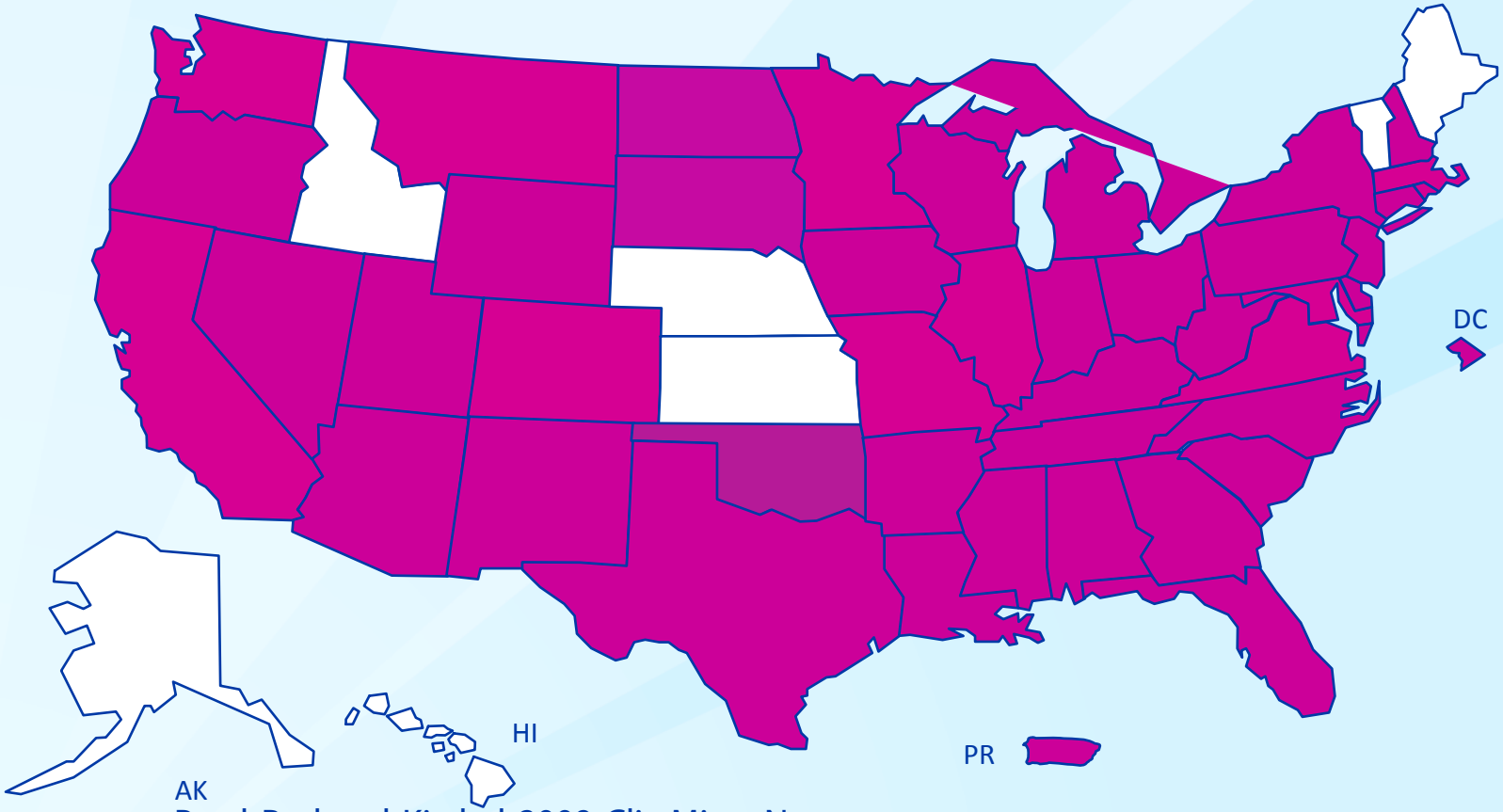
KPC AND NON-KPC CARBAPENEMASES

KPC-producing CRE in the United States



Patel, Rasheed, Kitchel. 2009. Clin Micro News

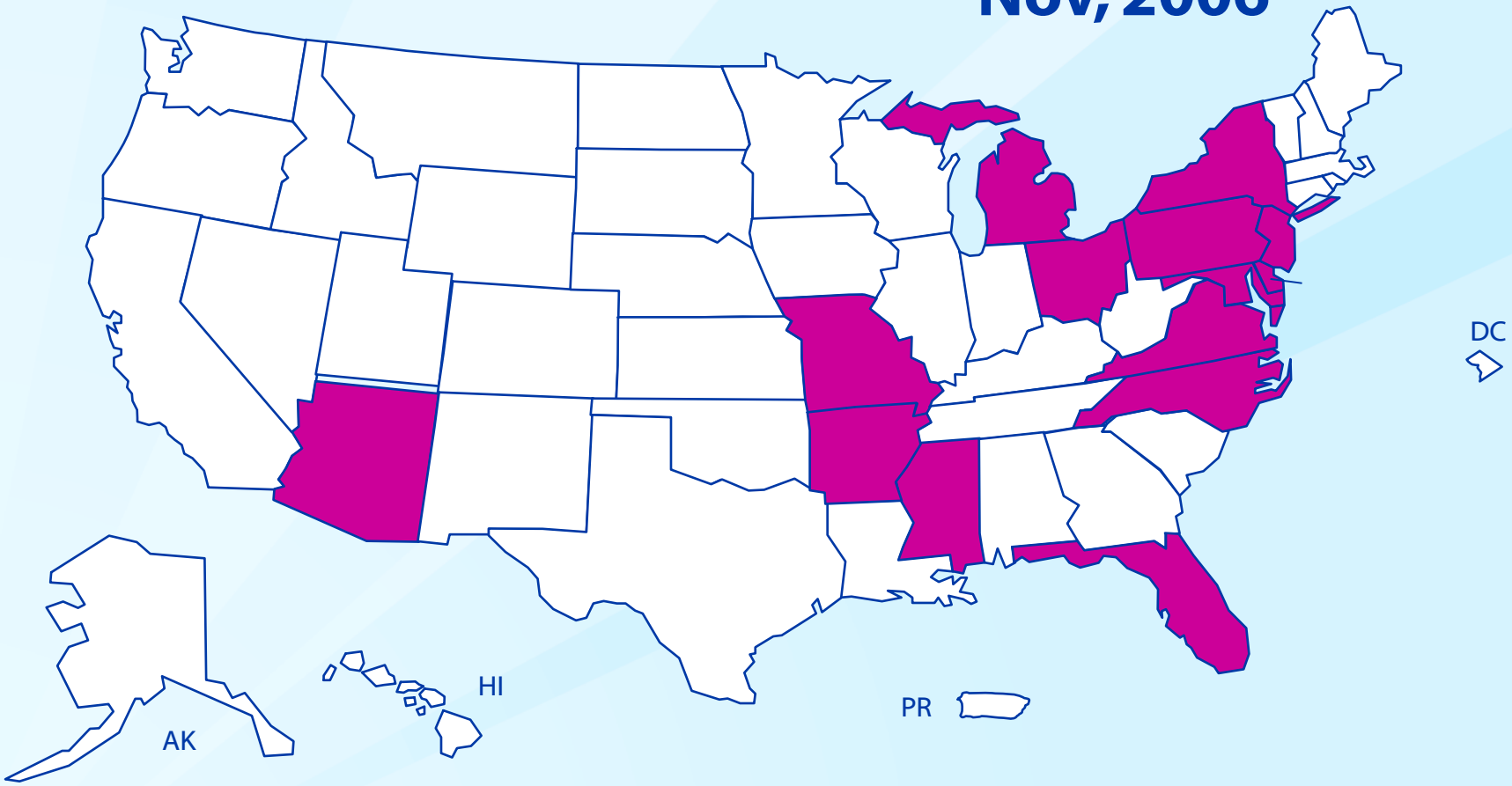
MMWR MMWR Morb Mortal Wkly Rep. 2010 Jun 25;59(24):750.

MMWR Morb Mortal Wkly Rep. 2010 Sep 24;59(37):1212.

CDC, unpublished data

Carbapenemase-producing CRE in the United States

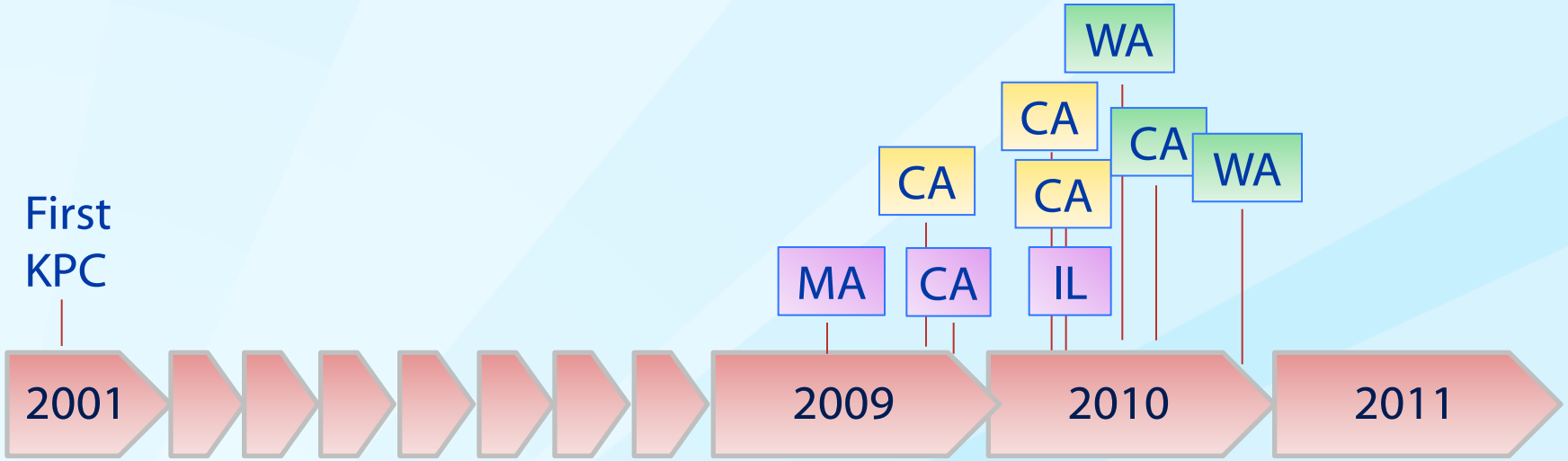
Nov, 2006



Patel, Rasheed, Kitchel. 2009. Clin Micro News

CDC, unpublished data

Emergence of MBLs in the United States

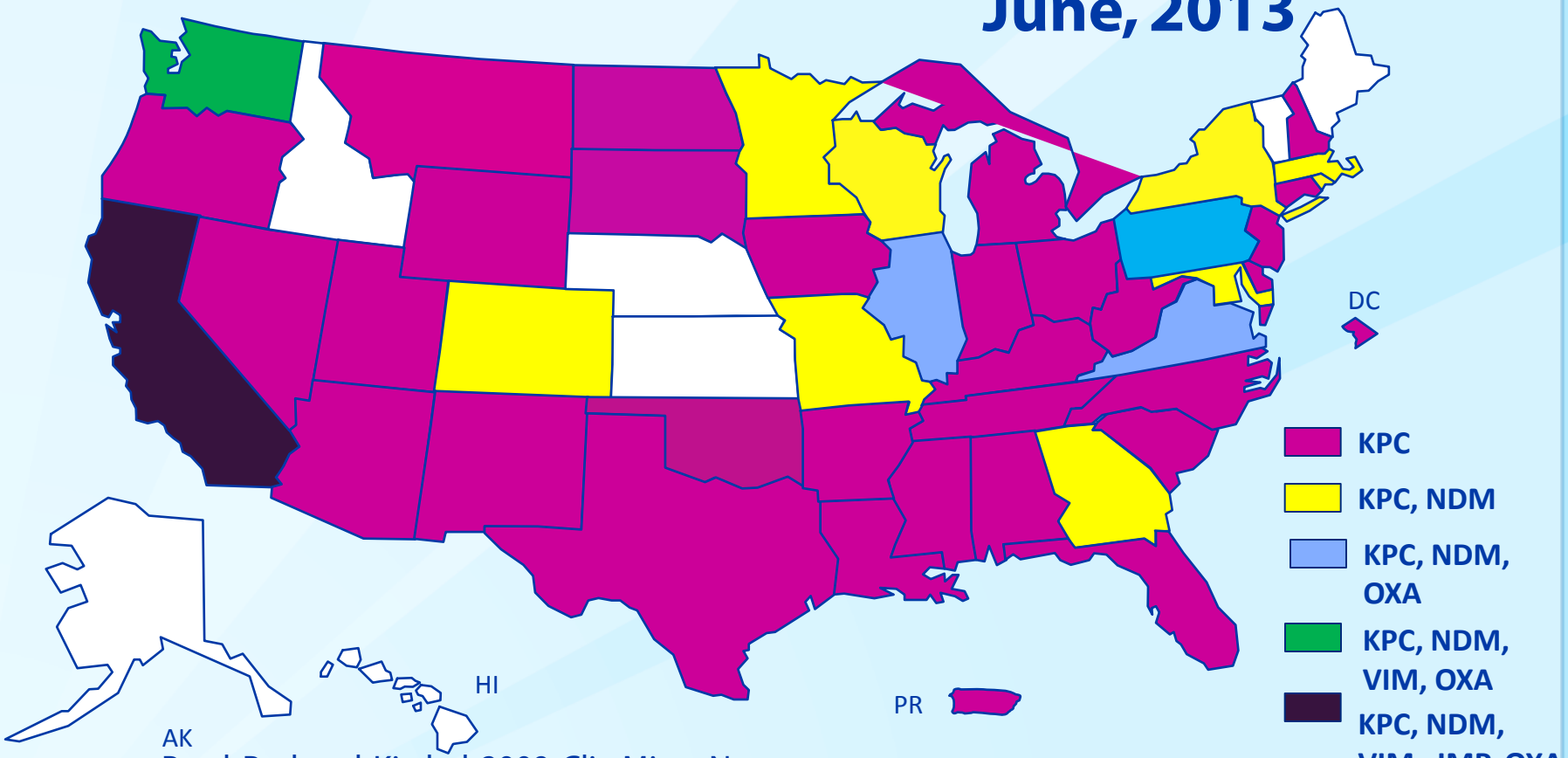


Currently CDC has confirmed (passive surveillance):
-3 IMP-producing CRE
-4 VIM-producing CRE
-10 OXA-48-producing CRE
-41 NDM–producing CRE

NDM
IMP
VIM

Carbapenemase-producing CRE in the United States

June, 2013



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NDM-Producing CRE in The United States

- **41 from 13 states since 2009 (Illinois n=9)**
- **Number by year:**
  - 2009 = 2
  - 2010 = 4
  - 2011 = 5
  - 2012 = 16
  - 2013 (through May 31)=14
- **Organisms (more than one organism for some patients):**
  - *K. pneumoniae* = 23
  - *E. coli* = 19
  - *Morganella* = 1
  - *E. cloacae* = 1
  - *Salmonella enterica* subspecies *enterica* serovar Senftenberg

NDM Exposures

- **20 had overnight healthcare stay outside the US**
  - India, Pakistan, Kenya, Vietnam/Cambodia
  - 2009-2011 - 91% (10/11) had this exposure
  - 2012-2013 – 33% (10/30) had this exposure
- **14 were part of three US hospital outbreaks**
- **Of the remaining 7:**
  - 4/7 had US healthcare exposure (overnight stay)
  - Ethiopian adoptee
  - 4/7with recent travel outside US

POPULATION-BASED SURVEILLANCE (EMERGING INFECTION PROGRAM)

CRE Active Surveillance

State	CR Enterobacteriaceae			Total
	E. coli	*Enterobacter spp.*	*Klebsiella spp.*	
Georgia	8	5	46	59
Minnesota	1	7	2	10
Oregon	0	2	1	3

Kallen et al. ID Week 2012, San Diego

Case Characteristics

Characteristic	CR Enterobacteriaceae (N=72)
Sex (% female)	36 (51%)
Age, median (range)	60 (8-91)
<18	2
>=65	30
Comorbidities	
None identified	5 (7%)

Source of Positive Culture*

Source	CR Enterobacteriaceae (N=72)
Blood	7 (10%)
Peritoneal	3 (4%)
Pleural	0 (0%)
Joint	0 (0%)
Deep Tissue	0 (0%)
Urine	64 (89%)

* Episodes could have positive cultures from more than one source

Culture Location

Most cultures (47/71) taken outside hospital (66%)

- 41/47 (87%) had healthcare exposures
- 6 were community onset without healthcare exposures

Healthcare Exposures Among Community-Onset Cases

Healthcare exposures in prior year (unless otherwise specified)	CR Enterobacteriaceae (N=47)
Hospitalization	34 (72%)
Presence of urinary catheter in 2 days prior	22 (47%)
Long-term care facility	17 (36%)
Surgery	12 (26%)
Presence of other indwelling device in the 2 days prior	11 (23%)
Presence of central line in 2 days prior	9 (19%)
Dialysis	3 (6%)
None	6 (13%)

Case Outcomes

Outcome	CR Enterobacteriaceae (N=72)
Hospitalized	59 (82%)
ICU in 7 days after positive culture	16 (22%)
Died (at discharge or at the end of evaluation)	3 (4%)
Transferred to:	N=69
Non-healthcare facility	27 (39%)
Long-term care facility	29 (42%)
Long-term acute care hospital	6 (9%)
Other hospital	0 (0%)
Unknown	7 (10%)

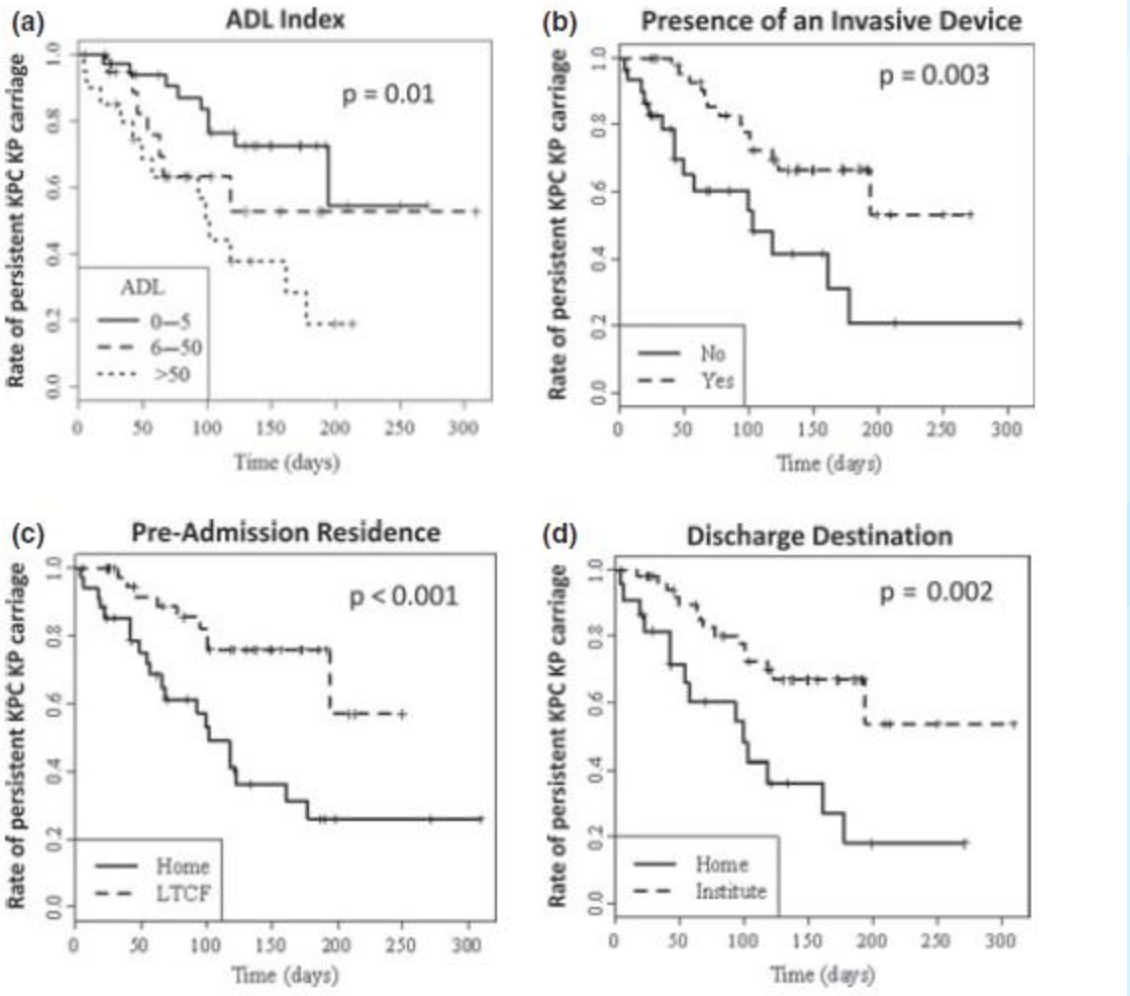
CRE CARRIAGE AND RISK FACTORS

Duration of KPC Carriage

- **97 patients positive beginning in 2009-2010**
- **Time to 1 culture negative (without subsequent positive)**
  - Mean 387 days (312-463)
  - Median 295 days (192-398)
- **Proportion positive by time**
  - 3 mos = 78%
  - 6 mos = 65%
  - 9 mos = 51%
  - 1 year = 39%
- **In multivariable analysis, presence of interval hospitalization and a clinical index culture significant predictors of CRE presence**

Zimmerman FS, et al. AJIC 2013: 190-194

Risk Factors for Persistent KPC Carriage



Persistent carriage: positive 2 or 3 months post-discharge

Feldman et al. Clin Micro and Infect 2012;19:E190-196

Risk Factors for CRE at Readmission

- **Case-control study of 66 patients with CRE**
  - Compared those positive at readmission with those that were negative

TABLE 2. Distribution of the Total Number of Predictors among Carbapenem-Resistant Enterobacteriaceae (CRE) Screen-Positive Case Patients and CRE Screen-Negative Control Patients and the Probability of Having a Positive Screen Test on the Basis of the Total Number of Predictors

No. of predictors	Positive screen test ($n = 23$)	Negative screen test ($n = 43$)	Probability of a positive screen test, % (95% CI)
0	4	24	14.3 (4.0–32.7)
More than 1	19	19	50.0 (33.3–66.7)

NOTE. Predictors included prior fluoroquinolone use (during the 30 days preceding the survey), transfer from an institution or another hospital, and time interval less than or equal to 3 months since the first CRE test. CI, confidence interval.

Schechner V et al. ICHE 2011;32:497-503

Summary: Risks for CRE Carriage

- **Severe illness, presence of devices, poor functional status, ICU admission, receipt of antibiotics**
  - Classes of associated antibiotics include: FQ, carbapenems, cephalosporins (particularly extended-spectrum), and vancomycin
- **Time since last positive culture**
- **Admission from LTACH/acute care hospital (colonization pressure)**

Gasink et al. ICHE 2009; 30:1180-5

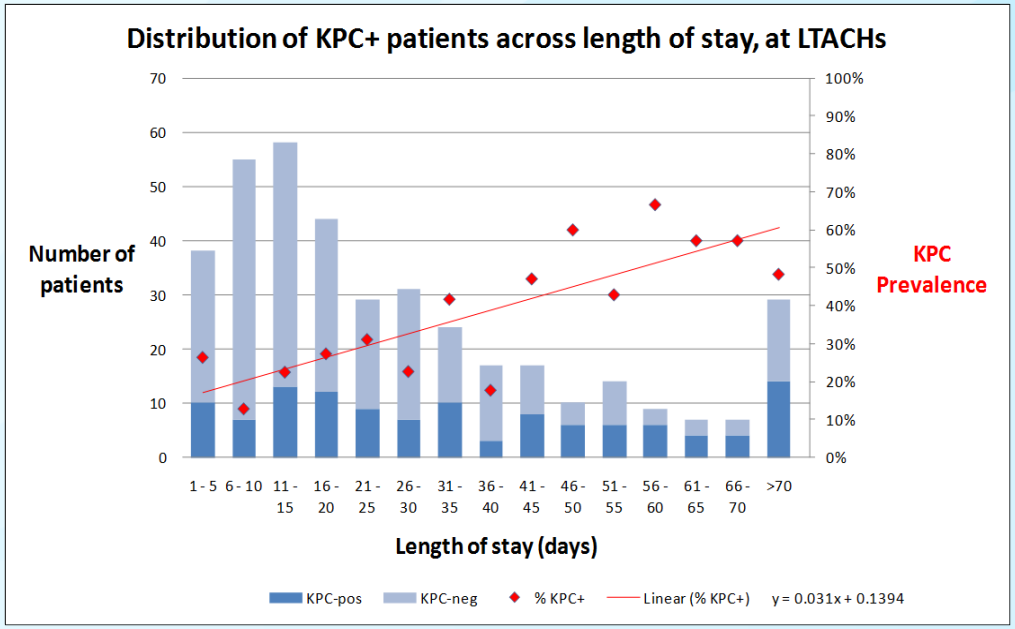
Schwaber et al AAC 2008; 52:1028-33

Marchaim et al. AJIC 2012

LONG-TERM CARE

KPC Point Prevalence Survey - Chicago

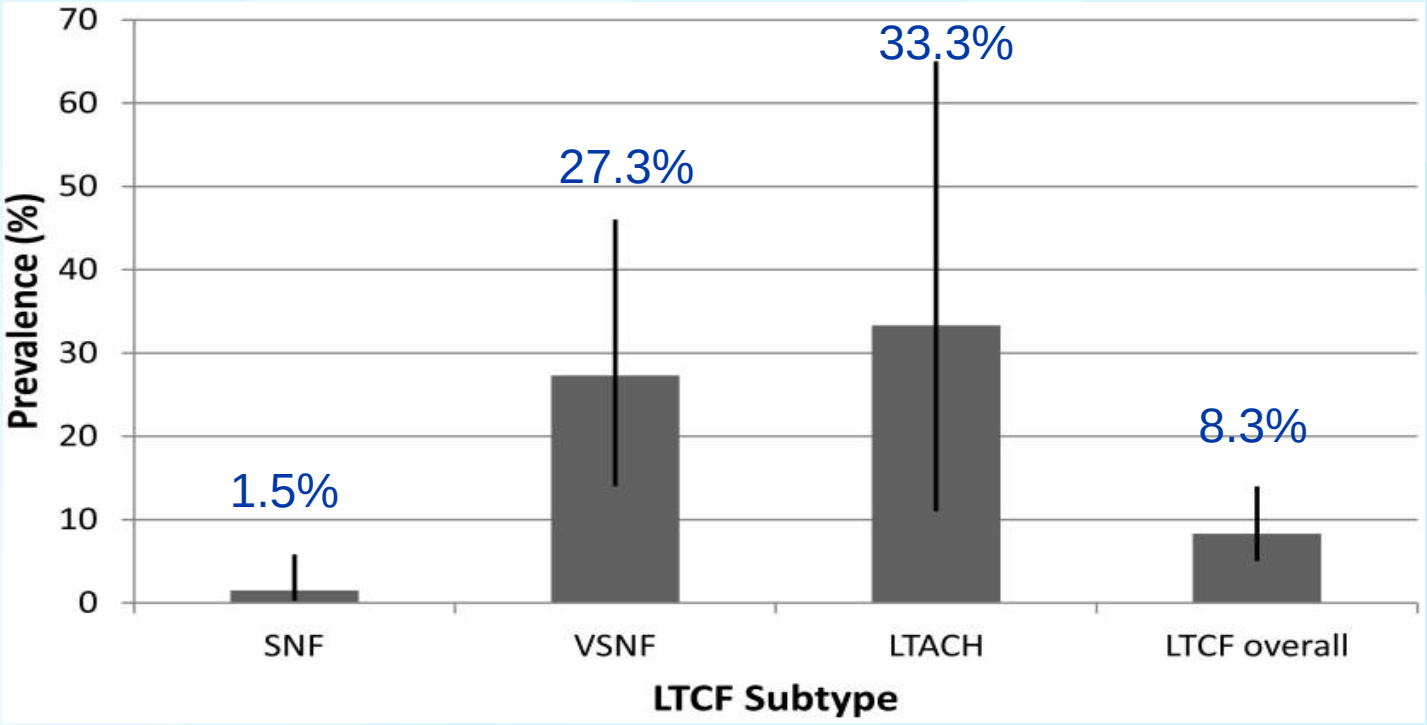
- Hospitals with >10 ICUs and 7 LTACHs
- Two point prevalence surveys (2010 and 2011)
- Results
  - All LTACHs and 15/24 hospitals had at least one patient with KPC
  - In acute care 3.3% of patients colonized (30/909)
  - In LTACH – 30.4% of patients colonized (119/391)



Lin M et al. ID Week 2012 San Diego #396

CRE Prevalence in LTCF: By Type

Prevalence of CRE Carriage at admission to 4 acute care hospitals



0% from those admitted to the community

Prabaker K et al. ICHE 2012; 33:1193-1199

Summary

- **The incidence of CRE has increased between 2001 and 20011**
  - Mostly among *Klebsiella*
  - *Important role of long-term care*
- **NDM-producing isolates are increasingly being reported since early 2012**
- **CRE carriage can be persistent**
  - Particularly among patients with healthcare exposures, recent positive cultures, prolonged exposure to other carriers
- **Population-based surveillance demonstrates**
  - Prevalence varies
  - Most isolates healthcare-associated but collected outside of hospitals
  - Urine important source
  - Overall mortality rates lower than that reported for invasive infections

Thanks for your attention.

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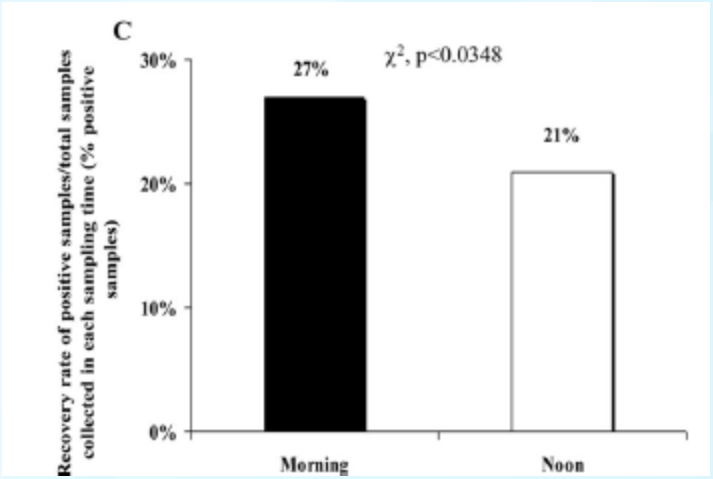
Environment as Source for CRE Transmission

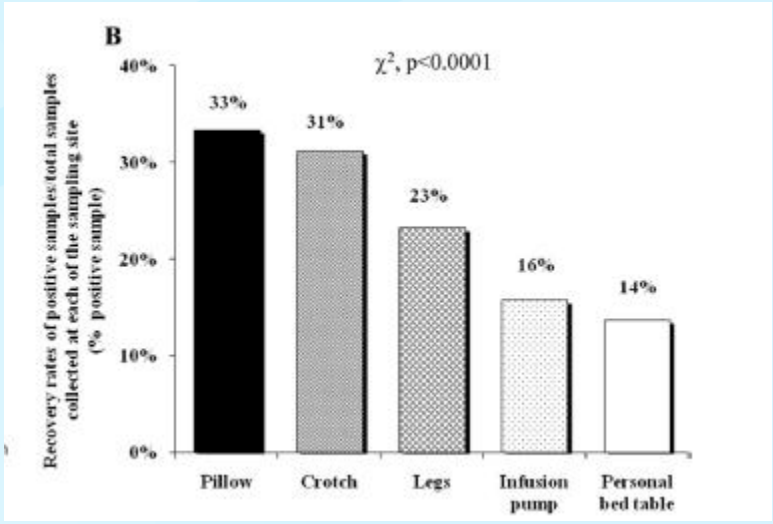
- **Anecdotal associations in outbreaks**
  - Equipment from physical therapy room
- **One study in 6 LTACHs included 371 environmental samples**
  - 2 (0.5%) positive for CRE
  - Bed rail and call button
  - Of note 57 grew other CR Gram-negative bacilli (primarily *Acinetobacter baumannii*)

Thurlow C et al. ICHE 2013;34:56-61

Environment as Source for CRE Transmission

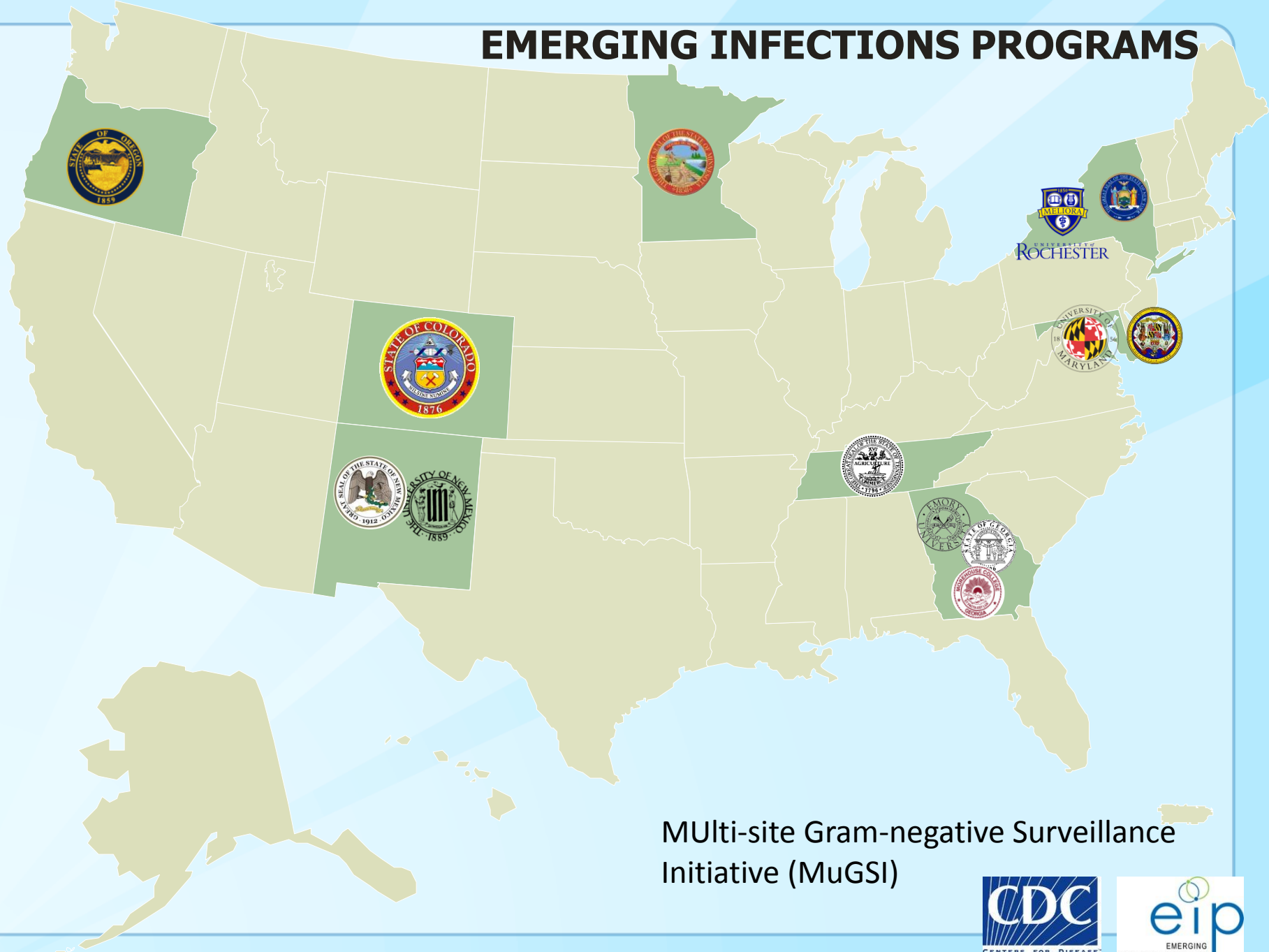
- Cultures of environmental samples from rooms of CRE carriers
- Sampled pillow, groin, legs, bedside table and infusion pump on 2 wards
  - 18% to 29% positive for CRE
- Percent positive higher closer to patient and prior to cleaning





Lerner A et al. J Clin Micro 2013;51:177-181

EMERGING INFECTIONS PROGRAMS

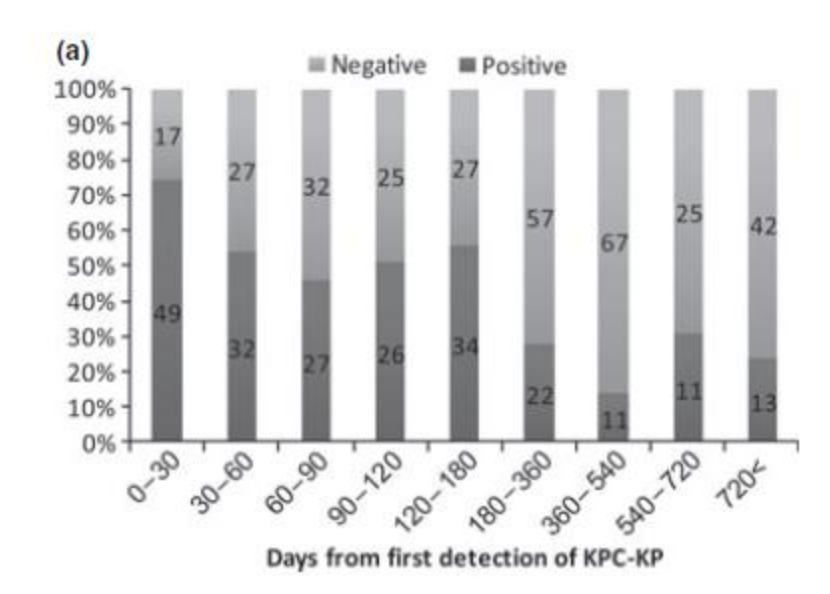


MUlti-site Gram-negative Surveillance Initiative (MuGSI)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

eip
EMERGING INFECTIONS PROGRAMS

Duration of KPC Carriage



- KPC Patients swabbed 5 to 6 times (at discharge, 2 weeks, 1, 2, 3 mos post-discharge)
- Overall resolution of carriage (2 consecutive negatives)
  - 62/125 (52%)
  - 39% of recently identified patient
  - 79% of remotely identified patients (> 4 mos prior)

Feldman et al. Clin Micro and Infect 2012;19:E190-196

Antibiotics as a CRE Risk Factor

TABLE 2. Multivariable Models of Risk Factors for Enterobacteriaceae Isolation, Detroit Medical Center, September 1, 2008, to August 31, 2009

	CRE vs uninfected[b]		ESBL vs uninfected[b]		Susceptible vs uninfected[b]		CRE vs ESBL		CRE vs susceptible		CRE vs all controls combined	
Variable[a]	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Any antibiotic exposure in previous 3 months	11.4 (2–64.3)	.006	1.7 (0.7–4.1)	.24			5.2 (1.4–19.4)	.015	12.3 (3.3–45)	<.001	7.1 (1.9–25.8)	.003
Permanent residency in institution	1.04 (0.2–4.5)	.96	1.3 (0.5–3.6)	.56	0.15 (0.05–0.5)	.002	2.1 (1–4.2)	.05	5.3 (2.1–12.9)	<.001	2.6 (1.3–5.3)	.01
Isolation of resistant bacteria in previous 6 months[c]	15.3 (4.2–55.6)	<.001	8.25 (2.7–25.7)	<.001	6.6 (1.9–23.3)	.003	1.7 (0.76–3.7)	.2	1.8 (0.7–4.7)	.23	2.9 (1.4–5.7)	.003
Dependent functional status in background	1.4 (0.5–4.4)	.55	5.6 (2.1–14.7)	.001	2.6 (1.1–6.4)	.03			2.0 (0.7–6.2)	.2	1.6 (0.6–4)	.33
ICU stay in previous 3 months	3.9 (1.3–12.4)	.02	5.2 (2.1–13.2)	.001	3.0 (1.2–7.2)	.02			1.6 (0.6–4)	.34	1.36 (0.7–2.7)	.37
Recent (6 months) invasive procedure	4.2 (1.2–15)	.03	1.2 (0.4–3.4)	.76	3.2 (1.3–8)	.01	2.8 (1.1–7.6)	.04			2.7 (1.1–7.1)	.04
Charlson weighted index comorbidity ≥3	3.1 (0.8–11.8)	.1	1.1 (0.4–2.7)	.87	2.2 (0.94–5)	.07	2.4 (1.03–5.6)	.04	4.8 (1.9–12.5)	.001	3.1 (1.4–7)	.006

NOTE. CI, confidence interval; CRE, carbapenem-resistant Enterobacteriaceae; ESBL, extended-spectrum β-lactamase–producing Enterobacteriaceae; ICU, intensive care unit; OR, odds ratio.

[a] If a variable was not significant in bivariate analysis, it was not forced into the multivariable model.

[b] Part of the case-case-control analysis.

[c] Includes methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, ESBL-producing Enterobacteriaceae, *Acinetobacter baumanni*, and *Pseudomonas aeruginosa*.

Marchaim D et al., ICHE 2012;33:817-830

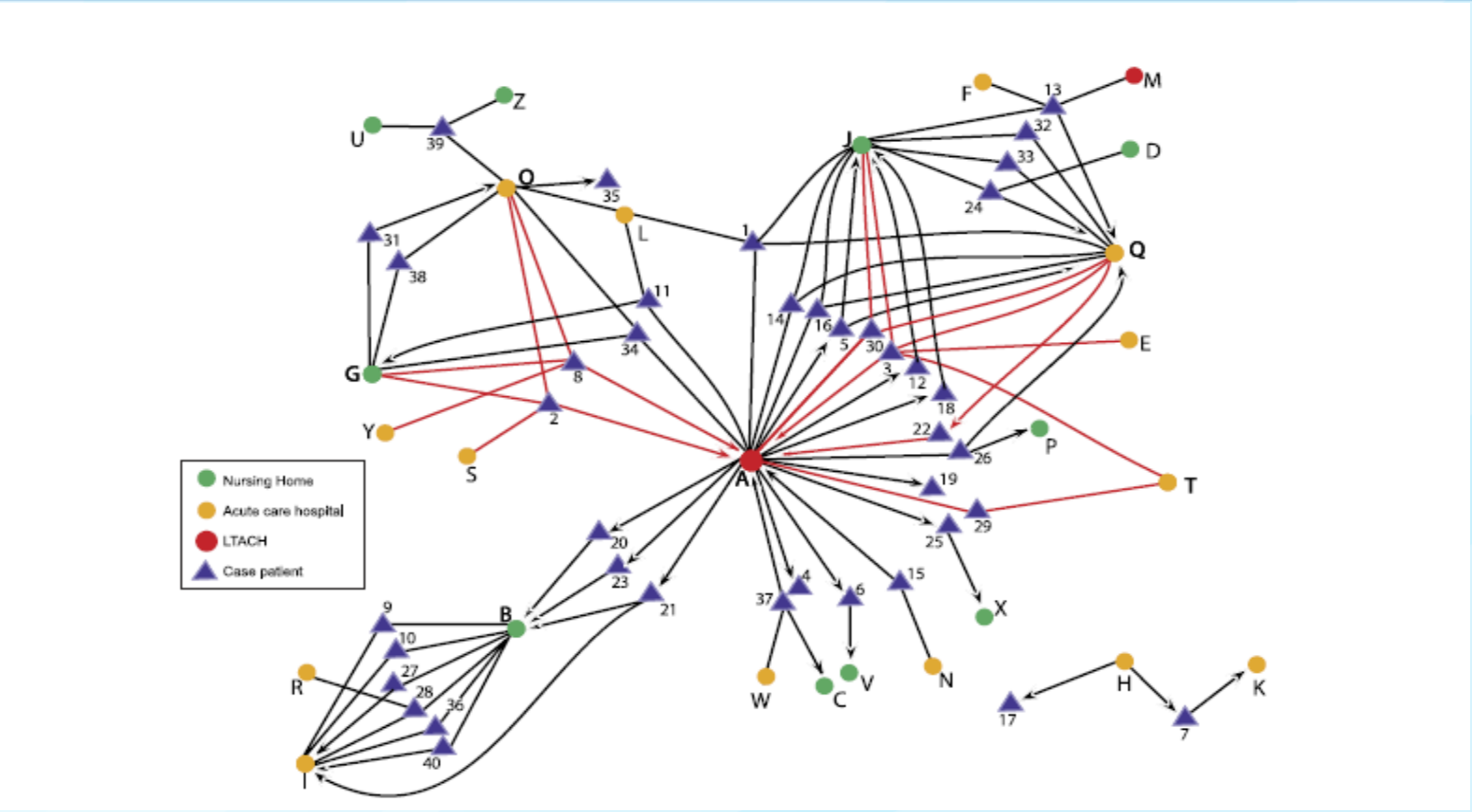
ENTEROBACTERIACEAE AND HEALTHCARE-ASSOCIATED INFECTIONS

Pathogens Reported to NHSN 2009-2010

	Overall percentage	CLABSI	CAUTI	VAP	SSI
E.					
K.					
P. aeruginosa	8% (5)	4%	11%	17%	6%
Enterobacter spp.	5% (8)	5%	4%	9%	4%

These three groups of organisms make up about 25% of organisms reported to NHSN Device and Procedure module

Sievert D, et al. Infect Control Hosp Epidemiol 2013; 34: 1-14



KPC outbreak in Chicago, 2008

- Of 40 KPC patients, only 4 definitively acquired KPC in acute care hospital
- Most (60%) linked to 1 LTACH

Won et al. Clin Infect Dis 2011;53:532-540

Risk for Transmission

- **NDM outbreak in Canada**
  - 9 cases in 15 months, Index patient had care in India
  - Case-control study of transmission cases compared to exposed patients (roommates, ward mates, environmental contacts) that did not acquire NDM
  - Duration of exposure and exposure to certain antimicrobials (Pen, FQ, macrolides, TMP/SMX, vancomycin, carbapenems) were significant risks
  - Exposure time was 26.5 days vs 6.7 days

Lowe C et al. ICHE 2013;34:49-55