

# CRE: Chicago-Area Epidemiology and Control Efforts

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# Outline

- Overview of CRE
- Epidemiology and control of KPC
- Epidemiology of emerging NDM

# *Enterobacteriaceae*

- Large family of bacteria – normal intestinal flora
- Examples: *E coli*, *Klebsiella* spp, *Enterobacter* spp, *Serratia* spp., *Citrobacter* spp, *Proteus* spp
- Common cause of community infections and healthcare-associated infections
- $\beta$ -lactam antibiotics (penicillin derivatives) first-line treatment

# $\beta$ -Lactam Antibiotics Active Against *Enterobacteriaceae*

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Penicillin	Cephalosporin	Cephameycin	Monobactam	Carbapenem
Ampicillin	Cephalexin	Cefoxitin	Aztreonam	Imipenem
Amoxicillin	Cefazolin	Cefotetan		Meropenem
				Doripenem
Piperacillin	Cefuroxime			Ertapenem
Ticarcillin	Ceftazidime			
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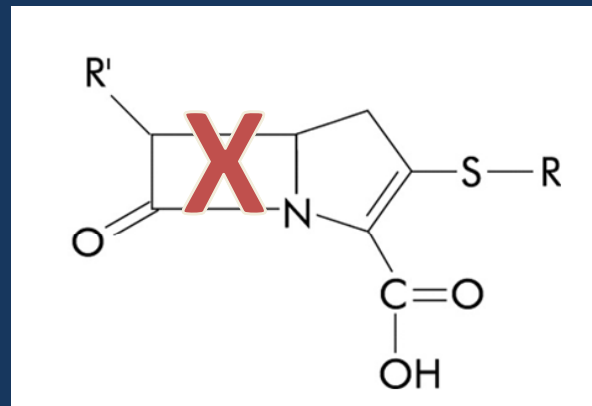
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Ceftazidime

Ceftriaxone

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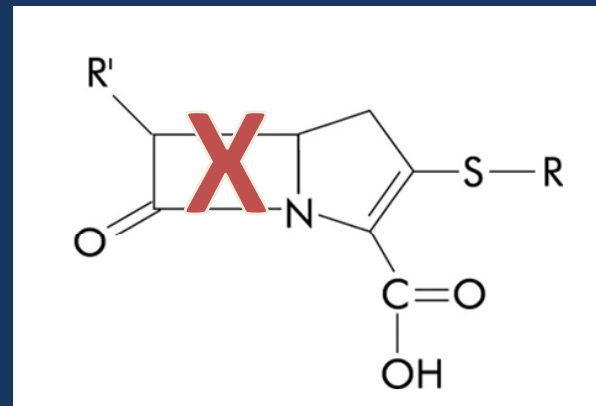
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# Diversity of Carbapenemases in *Enterobacteriaceae*

Carbapenemase	Ambler structural class	Predominant species	Carbapenem MICs	Location of gene	Dissemination potential
KPC	A	<i>K pneumoniae</i>	Variable	Plasmid	High
NDM	B	<i>K pneumoniae</i> , <i>E coli</i>	Variable	Plasmid, chromosome	High
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Adapted from: Adler A and Carmeli Y. mBio 2011, 2(6):e00280-11.

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\*KPC+ strains often XDR

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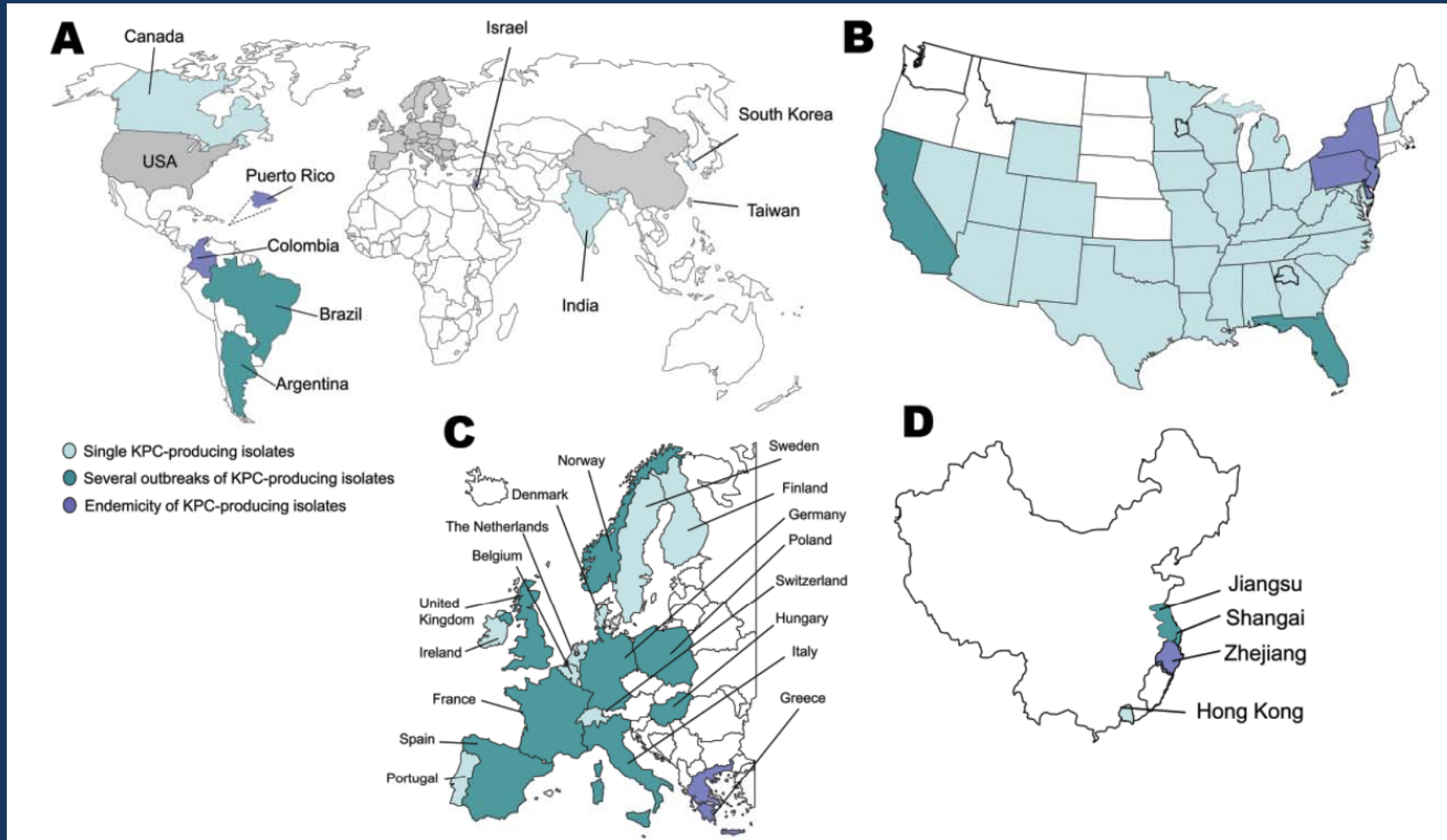
# Epidemiology of KPC-Producing *Enterobacteriaceae*

- Healthcare-associated infections
  - UTI, BSI, pneumonia, wound infections
- Patient-to-patient transfer via healthcare worker hands
- Risk factors
  - Healthcare exposure, medical devices, co-morbid conditions, antibiotics
- Attributable mortality 30% - 50%

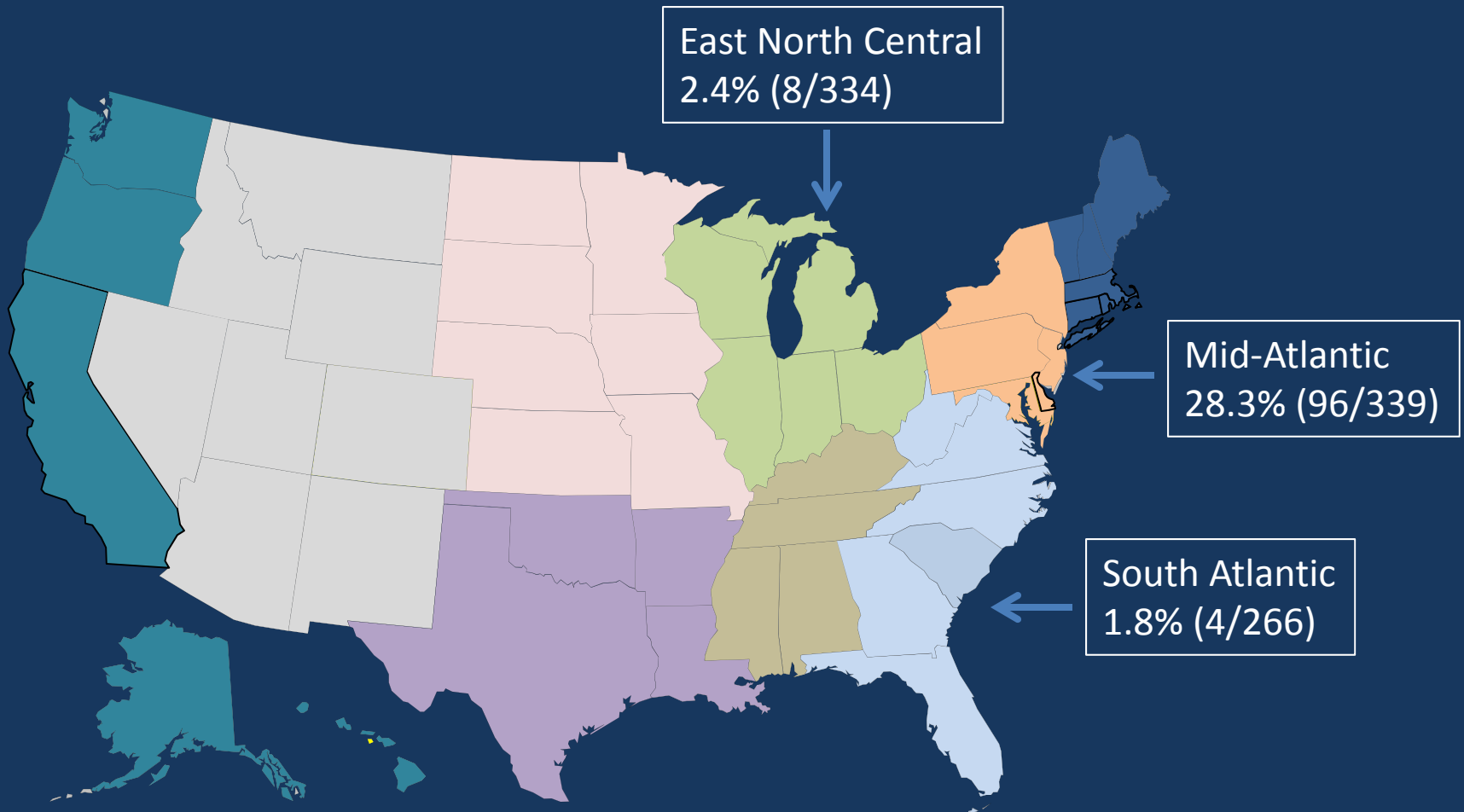
# Origin of KPC

- First KPC from North Carolina 1996
- Restricted to East Coast of US for next 10 years
- Rapid global spread since 2005
  - *K pneumoniae* ST258

# Worldwide Dissemination of KPC



# KPC-producing *K pneumoniae*, US Trends SENTRY 2007-09



# KPC+ *Enterobacteriaceae* in Israel

- 2005: KPCs first encountered but rarely seen
- 2006: Nationwide clonal outbreak of KPC+ *K. pneumoniae* ST 258
  - Rapid spread
  - Pockets of high prevalence but overall 1%-5%



# National Intervention to Control KPC: Israel

- National Task Force with authority to collect data and intervene as needed
- Mandatory reporting
- Mandatory isolation of hospitalized KPC carriers
  - Contact precautions (index and subsequent admissions)
  - Cohort nursing

Epidemiology and Control of KPC-  
Producing *Enterobacteriaceae*: Chicago

# KPC in Chicago

- KPC first recognized in Chicago area in December 2007
- Patient transferred to a west suburban hospital from a skilled nursing facility in Northwest Indiana



# KPC in Chicago

- May 2008, first KPC case at Rush case at Rush
- Transferred from acute care hospital in Northwest Indiana



# Outbreak Investigation

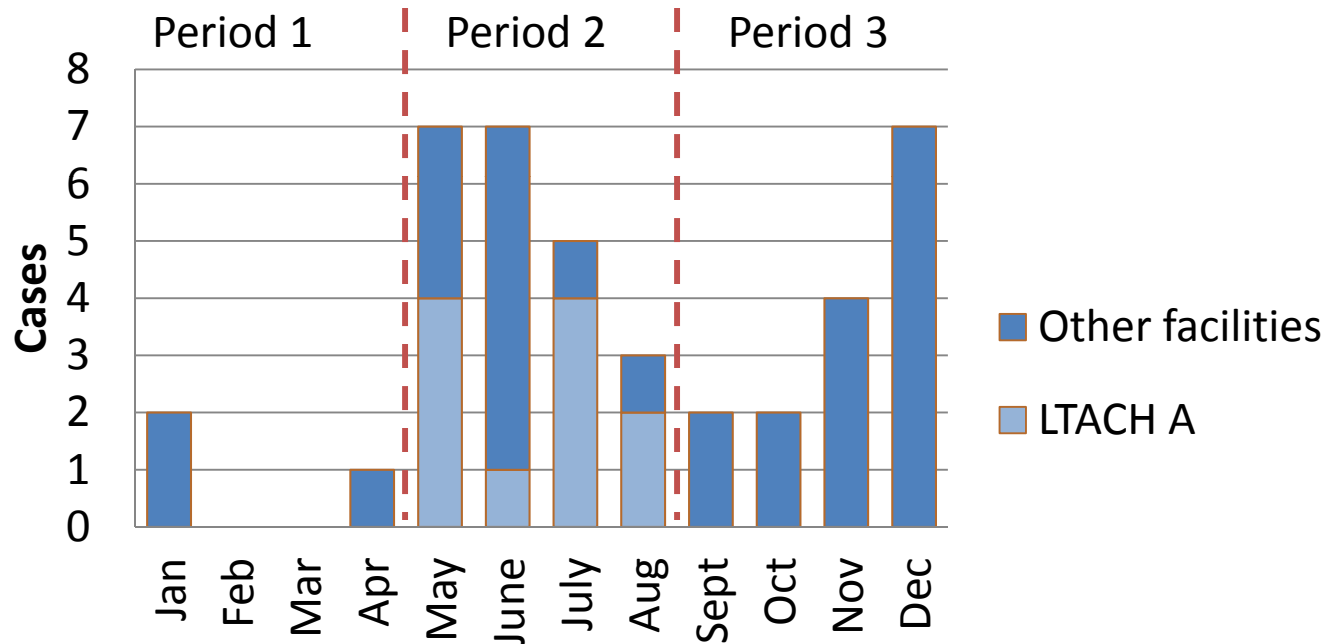
- Case finding: Any CRE
  - 1/1/2008 – 12/31/2008
  - Surveyed results of 5 regional and hospital clinical microbiology laboratory databases in 4 counties
    - ≈25,000 Enterobacteriaceae isolates

# Outbreak Investigation

- Medical record review
- Microbiologic analysis of available isolates
  - ID and susceptibility
  - *bla*<sub>KPC</sub> PCR & DNA sequence analysis, PFGE, MLST
- “Exposure network analysis”

# Epidemic Curve January-December, 2008

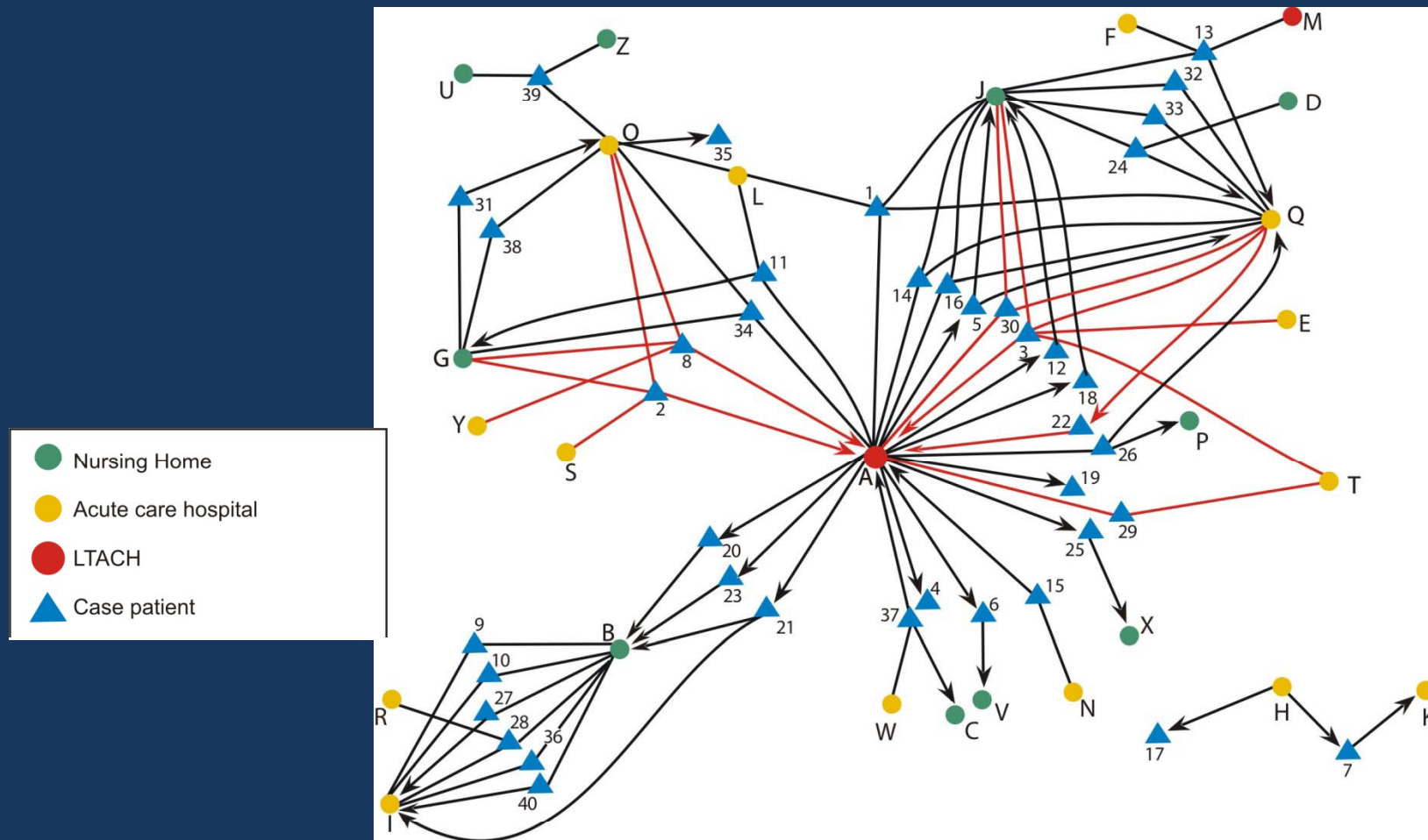
## 40 cases



Won SY et al. CID 2011; 53:532.

Munoz-Price LS et al. ICHE 2010, 31:341.

# Emergence and Rapid Regional Spread of KPC



Won SY et al. CID 2011; 53:532.



# Surveillance for KPC REALM Project

- A voluntary MDRO surveillance network of hospitals
  - Acute care hospitals in Chicago with  $\geq 10$  ICU beds
  - LTACHs in Cook County
- Serial point prevalence culture surveys every 6 months
- KPC surveillance began 2010

# REALM Project Results, 2010-2011

- 24 of 25 eligible hospitals and 7 of 7 eligible LTACHs participated in the surveys

# REALM Project Results, 2010-2011

Facility type	KPC positive (n)	Total (N)	Percent (95% CI)
Acute care hospital adult ICUs	30	909	3.3 (2.2 – 4.7)
LTACHs	119	391	30 (26 – 35)

- 15 of 24 acute care hospitals had KPC-colonized patients
- 7 of 7 LTACHs had KPC-colonized patients

# Is long-term care residence a risk factor for KPC colonization on admission to acute care hospitals in Chicago?

- Cross-sectional study of patients transferred from long-term care facilities to 4 Chicago area acute care hospitals
- Matched 1:1 to community patients by age, admitting clinical service, and admission date
- November 2010 - June 2011

# Is long-term care residence a risk factor for KPC colonization on admission to acute care hospitals in Chicago?

- Rectal swab culture for KPC within 3 days of acute care hospital admission
- Medical records reviewed

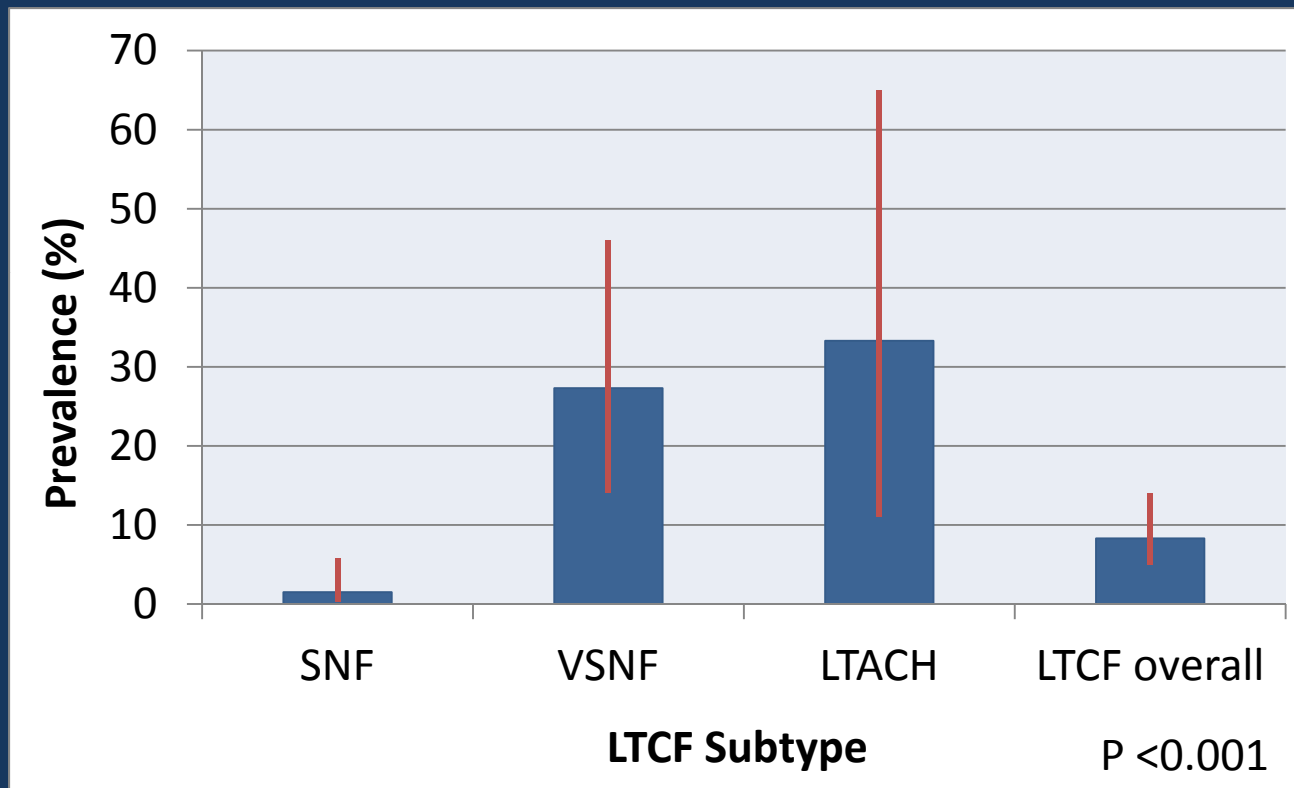
# Is long term care residence a risk factor for KPC colonization on admission to acute care hospitals in Chicago?

	LTCF Patients (N=180)	Community Patients (N=180)
Prevalence of KPC	15 (8.3%)	0 (0%)

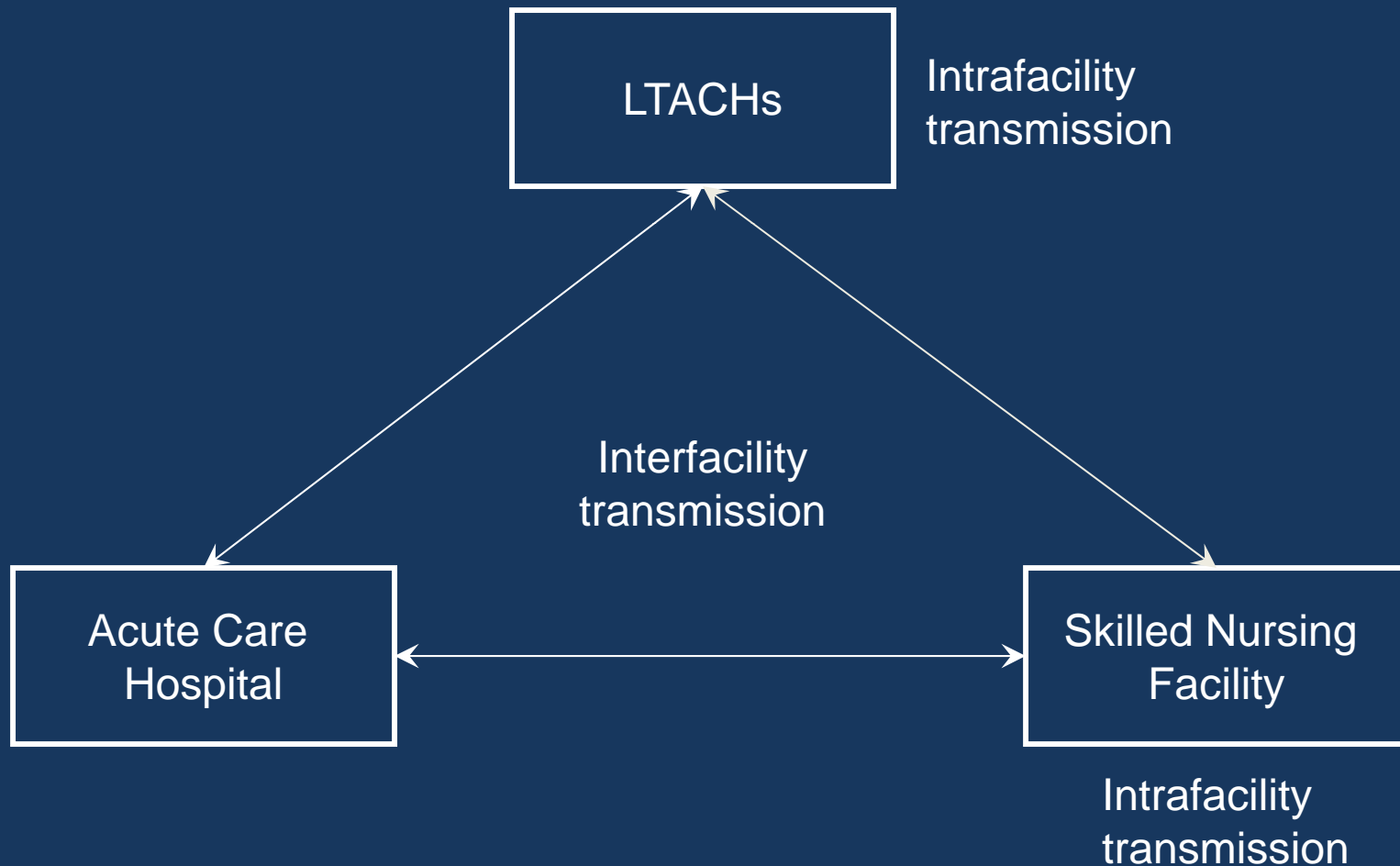
P < 0.001

- 15 patients admitted from 7 different LTCFs

# KPC Prevalence Differed among Patients Admitted from Different Types of LTCFs



# Hypothesis: Epidemiology of Regional KPC Spread





# Regional KPC Control Plan

- Decrease cross-transmission of KPC in high-prevalence healthcare facilities
  - Infection prevention bundle
- Improve communication of KPC status among transferring healthcare facilities

# Development of Infection Prevention Bundle

- Is patients' skin contaminated/colonized with KPC?
- Is inanimate healthcare environment contaminated with KPC?

# Anatomic Sites of Patient Colonization and Environmental Contamination with KPC

- Cross-sectional culture survey
- 6 LTACHs in Cook County
- February 2011 – June 2011
- Sites cultured
  - Patients' skin
  - Non-skin sites
  - Environmental surfaces in patients' rooms and common areas

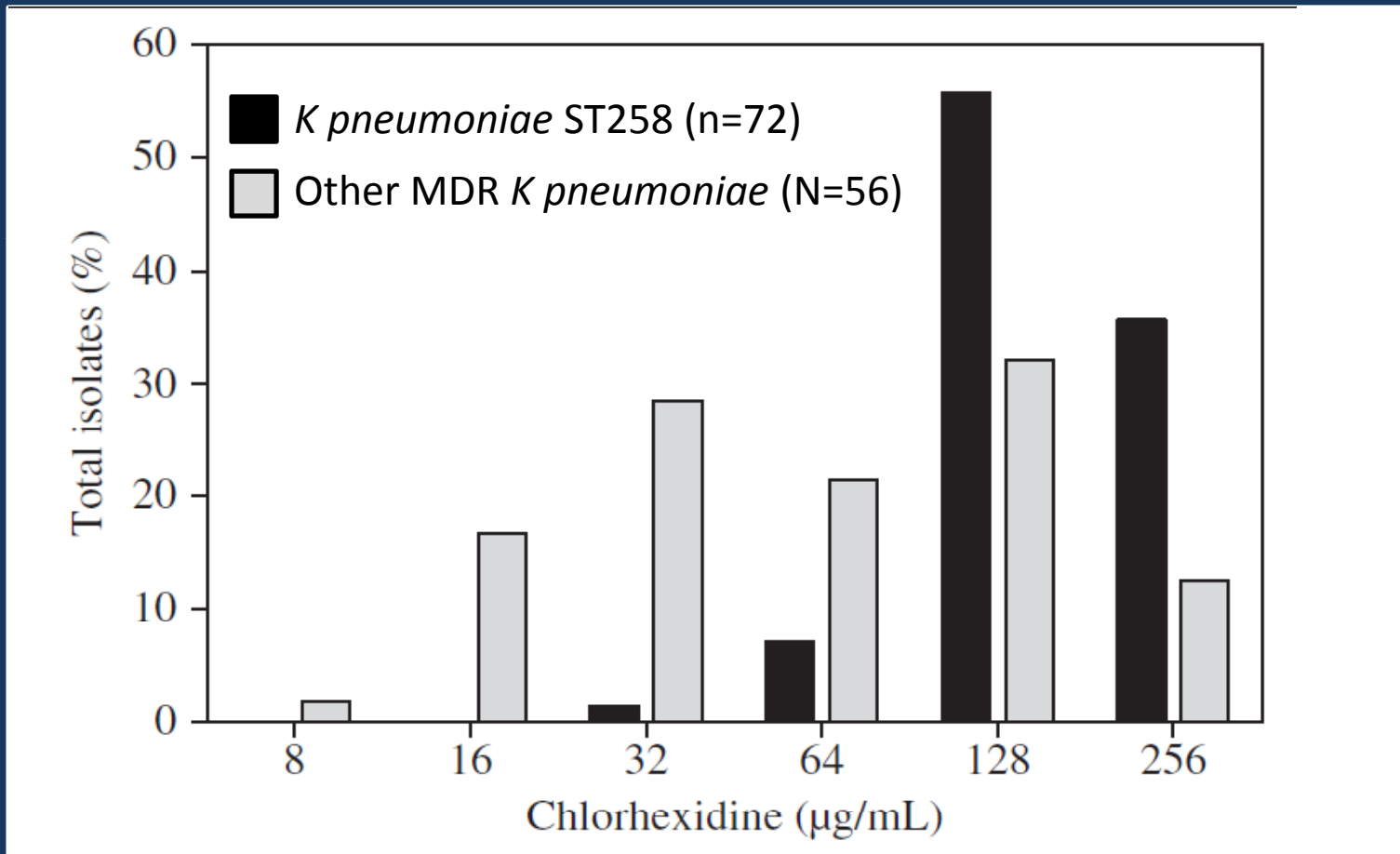
# KPC Common on Skin

- 33 patients cultured
- 24 patients any anatomic site KPC-positive
  - 23 (96%) patients  $\geq 1$  skin site KPC-positive
    - 19 (79%) inguinal area
    - 18 (75%) axillae
    - 6 (25%) upper back
    - 6 (25%) antecubital fossae
  - 49/96 (51%) skin cultures KPC-positive

# KPC Rare in Environment

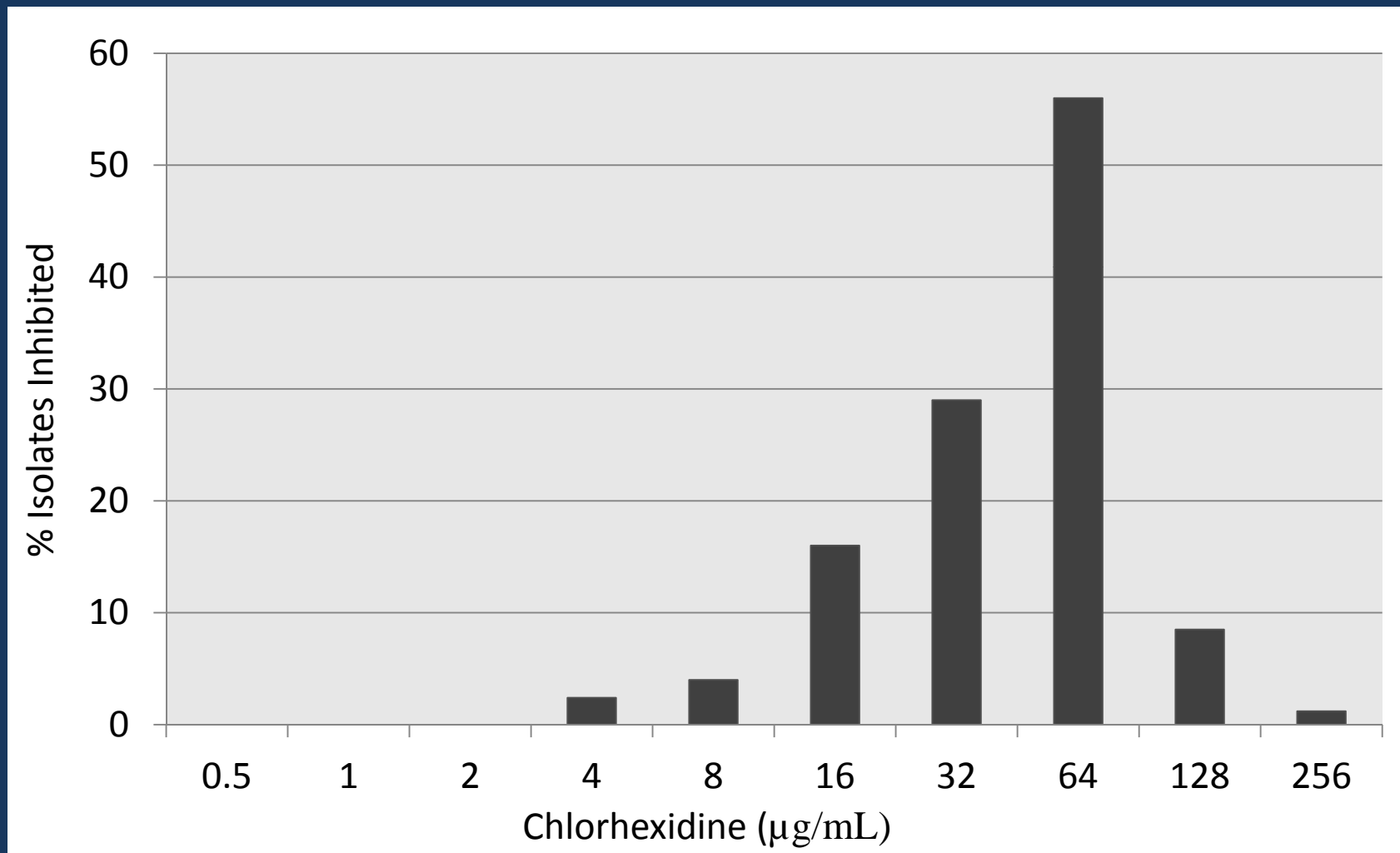
- 371 environmental surfaces cultured
  - 2 (0.5%) sites grew KPC-positive *K pneumoniae*
  - 57 (15%) grew other carbapenem-resistant gram-negative bacteria
    - 53 *Acinetobacter baumannii*
    - 2 *Pseudomonas aeruginosa*
    - 1 *Achromobacter xylosoxidans*
    - 1 *Chryseobacterium indologenes*

# Reduced Susceptibility of *K pneumoniae* ST258 to Chlorhexidine



Naparstek L et al JHI 2012, 81:15.

# KPC-Positive *K pneumoniae* (N=82)



Thurlow CJ et al. Infect Control Hosp Epidemiol; 2013; 34:56.

# Regional KPC Control Project: KPC Control in LTACHs

- KPC Control Bundle
  - Active surveillance
    - Admission and periodic surveillance
  - Geographic separation of patients
    - Cohort floor or private rooms
  - Patient skin antisepsis
    - Daily CHG bathing
  - Strengthen basic infection prevention measures
    - Healthcare worker hand hygiene



# Regional KPC Control Project: KPC Control in LTACHs

- Design: Stepped wedge randomized cluster
- 4 of 7 LTACHs in Cook County enrolled

		Time (2-month intervals)				
		1	2	3	4	5
LTACH	1	0	X	X	X	X
	2	0	0	X	X	X
	3	0	0	0	X	X
	4	0	0	0	0	X

- 12-18 month intervention

# Regional KPC Control Project: KPC Control in LTACHs

- Primary outcome: KPC prevalence in LTACHs
- Secondary outcomes
  - KPC incidence in LTACHs
  - HAI incidence in LTACHs
  - Incident KPC infections in LTACHs
  - KPC prevalence in acute care hospital ICUs

# New Delhi Metallo- $\beta$ -lactamase (NDM)

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Adapted from: Adler A and Carmeli Y. mBio 2011, 2(6):e00280-11.

# Global Spread of NDM



Johnson AP and Woodford N; J Med Microbiol 2013, 62:499.

# Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study



Timothy R Walsh, Janis Weeks, David M Livermore, Mark A Toleman

## Summary

**Background** Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum  $\beta$ -lactamases are known to be circulating in the Indian community. We therefore measured the prevalence of the NDM-1 gene in drinking water and seepage samples in New Delhi.

**Methods** Swabs absorbing about 100  $\mu$ L of seepage water (ie, water pools in streets or rivulets) and 15 mL samples of public tap water were collected from sites within a 12 km radius of central New Delhi, with each site photographed and documented. Samples were transported to the UK and tested for the presence of the NDM-1 gene, *bla*<sub>NDM-1</sub>, by PCR and DNA probing. As a control group, 100  $\mu$ L sewage effluent samples were taken from the Cardiff Wastewater Treatment Works, Tremorfa, Wales. Bacteria from all samples were recovered and examined for *bla*<sub>NDM-1</sub> by PCR and sequencing. We identified NDM-1-positive isolates, undertook susceptibility testing, and, where appropriate, typed the isolates. We undertook Inc typing on *bla*<sub>NDM-1</sub>-positive plasmids. Transconjugants were created to assess plasmid transfer frequency and its relation to temperature.

**Findings** From Sept 26 to Oct 10, 2010, 171 seepage samples and 50 tap water samples from New Delhi and 70 sewage effluent samples from Cardiff Wastewater Treatment Works were collected. We detected *bla*<sub>NDM-1</sub> in two of 50 drinking-water samples and 51 of 171 seepage samples from New Delhi; the gene was not found in any sample from Cardiff. Bacteria with *bla*<sub>NDM-1</sub> were grown from 12 of 171 seepage samples and two of 50 water samples, and included 11 species in which NDM-1 has not previously been reported, including *Shigella boydii* and *Vibrio cholerae*. Carriage by enterobacteria, aeromonads, and *V cholera* was stable, generally transmissible, and associated with resistance patterns typical for NDM-1; carriage by non-fermenters was unstable in many cases and not associated with typical resistance. 20 strains of bacteria were found in the samples, 12 of which carried *bla*<sub>NDM-1</sub> on plasmids, which ranged in size from 140 to 400 kb. Isolates of *Aeromonas caviae* and *V cholerae* carried *bla*<sub>NDM-1</sub> on chromosomes. Conjugative transfer was more common at 30°C than at 25°C or 37°C.

**Interpretation** The presence of NDM-1  $\beta$ -lactamase-producing bacteria in environmental samples in New Delhi has important implications for people living in the city who are reliant on public water and sanitation facilities. International surveillance of resistance, incorporating environmental sampling as well as examination of clinical isolates, needs to be established as a priority.

*Lancet Infect Dis* 2011;  
11: 355–62

Published Online

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See [Comment](#) page 334

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Correspondence to: Prof Timothy R Walsh, Centre for Clinical Research (UQCCR) | Level 8, Building 71/918 Royal Brisbane Hospital, Herston QLD 4006, Australia  
t.r.walsh@uq.edu.au

# NDM in US

- 41 NDM+ patients from 13 states
  - First patient 2009
  - 14 patients YTD 2013
- Species
  - 22 *K pneumoniae*
  - 19 *E coli*
  - 1 *Morganella morgannii*
  - 1 *E cloacae*
  - 1 *K pneumoniae/Salmonella sp*

\*Data courtesy of Alex Kallen, MD, CDC

# NDM in US

- 41 NDM+ patients
  - 20 inpatient healthcare exposure outside of US
  - 14 from 3 US hospital transmission outbreaks
  - 4 South Asian heritage + inpatient healthcare exposure in US
  - 1 travel (India) + inpatient healthcare exposure in US
  - 1 inpatient healthcare exposure in US only
  - 1 travel only (Ethiopia)

\*Data courtesy of Alex Kallen, MD, CDC



# NDM in Illinois

- 8 NDM patients from Illinois
  - Tied with Colorado for most cases
- Recent cluster in metropolitan Chicago

\*Data courtesy of Alex Kallen, MD, CDC

# Metro Chicago NDM Cluster\*

- 4 NDM+ patients identified March 2013
- No international travel
- Exposure to 1 acute care hospital
  - Subsequent screening at acute care hospital has not identified additional NDM+ patients

\*Data courtesy of Michael Vernon (SCCDH) and Judith Conway (IDPH)

# Metro Chicago NDM Cluster

- 4 NDM+ patients had subsequent exposure to 5 long term care facilities
- 200 LTCF patients screened
- 1 roommate of a case NDM-1 positive
- TOTAL: 5 NDM+ patients in Chicago cluster

\*Data courtesy of Michael Vernon (SCCDH) and Judith Conway (IDPH)

# Metro Chicago NDM Cluster

- All isolates *E coli*
  - 2 urine
  - 1 sputum
  - 1 wound
  - 1 rectal swab
- All isolates closely related by PFGE
  - Unrelated to earlier NDM+ *E coli* isolates from IL

\*Data courtesy of Michael Vernon (SCCDH) and Judith Conway (IDPH)

# Conclusions

- Most CRE in Chicago are KPC-producers
- KPC-producing *Enterobacteriaceae* are endemic in metropolitan Chicago
- Prevalence of KPC in majority of acute care hospital ICUs in Chicago is low and stable

# Conclusions

- A bundled intervention introduced to 4 Chicago area LTACHs was successful in reducing KPC prevalence, incidence and number of KPC+ clinical cultures at the LTACHs
- Together, these findings suggest that KPC-producing *Enterobacteriaceae* can be controlled in our region

# Conclusions

- NDM is emerging in Chicago area
  - Sporadic cases
    - International travel
  - Nosocomial cluster
- Needs close monitoring
- Can no longer assume that all CRE in Chicago are KPC!

# Team KPC

- Don Blom
  - Carolyn Gould
  - David Hines
  - Alex Kallen
  - Sarah Kemble
  - Michael Lin
  - Karen Lolans
  - Rosie Lyles-Banks
  - Nicholas Moore
  - Silvia Munoz-Price
  - Kavitha Prabaker
  - Monica Sikka
  - Caroline Thurlow
  - Shawn Vasoo
  - Shayna Weiner
  - Bob Weinstein
  - Sarah Won
- 
- CDC coop. agree. 1U54CK000161 (Weinstein)
  - CDC contract no. 200-2011-M-41103 (Hayden)
  - Foglia Family Foundation



Thank you!