CRE Detect and Protect Crash Course

Illinois Infection Prevention and CRE Workshop

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Disclosures

- I have nothing to disclose

I want to cover:

- What is CRE and XDRO?
- The roles we each play
- What happens after a CRE case is reported?

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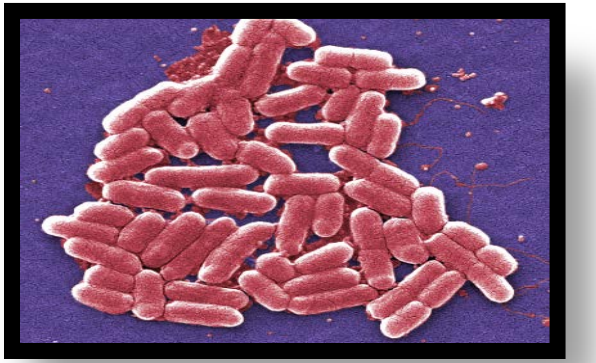
What is CRE?

Carbapenem
Resistant
Enterobacteriaceae

Carbapenem:
Class of broad-spectrum antibiotics

Resistant:
Bacteria with mutations that make antibiotics ineffective



Enterobacteriaceae:
Family of bacteria that includes *Escherichia coli*, *Klebsiella sp.*, *Enterobacter*

CRE is

- KPC
- NDM
- OXA
- VIM
- IMP

CRE is **not**…

- VRE
- Pseudomonas
- Acinetobacter
- ESBLs

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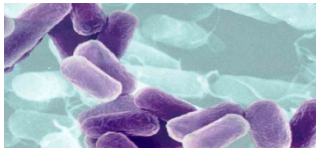
Why is CRE such a big deal?

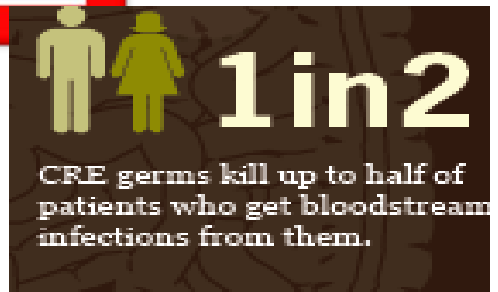


- Deadly infection
- Few treatment options (if any)
- Spreading quickly

HAZARD LEVEL
URGENT

These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (C. difficile), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)



http://www.cdc.gov/drugresistance/threat-report-2013/

What is the XDRO registry?

XDRO = e**X**tensively **D**rug **R**esistant **O**rganisms

XDRO registry = where CRE is reported in Illinois*

Began: November 1, 2013

Required to report:

- Acute care hospitals
- Long-term acute care hospitals
- Long-term care facilities
- Laboratories

* Illinois healthcare facilities and laboratories are required to report CRE to the XDRO registry per 77 Ill. Adm. Code 690, Control of Communicable Diseases Code.

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But wait, let's take a step back…

We all have a role to play:

State Health Department (IDPH)

Local Health Departments

Health Care Facilities

Laboratories

Other?

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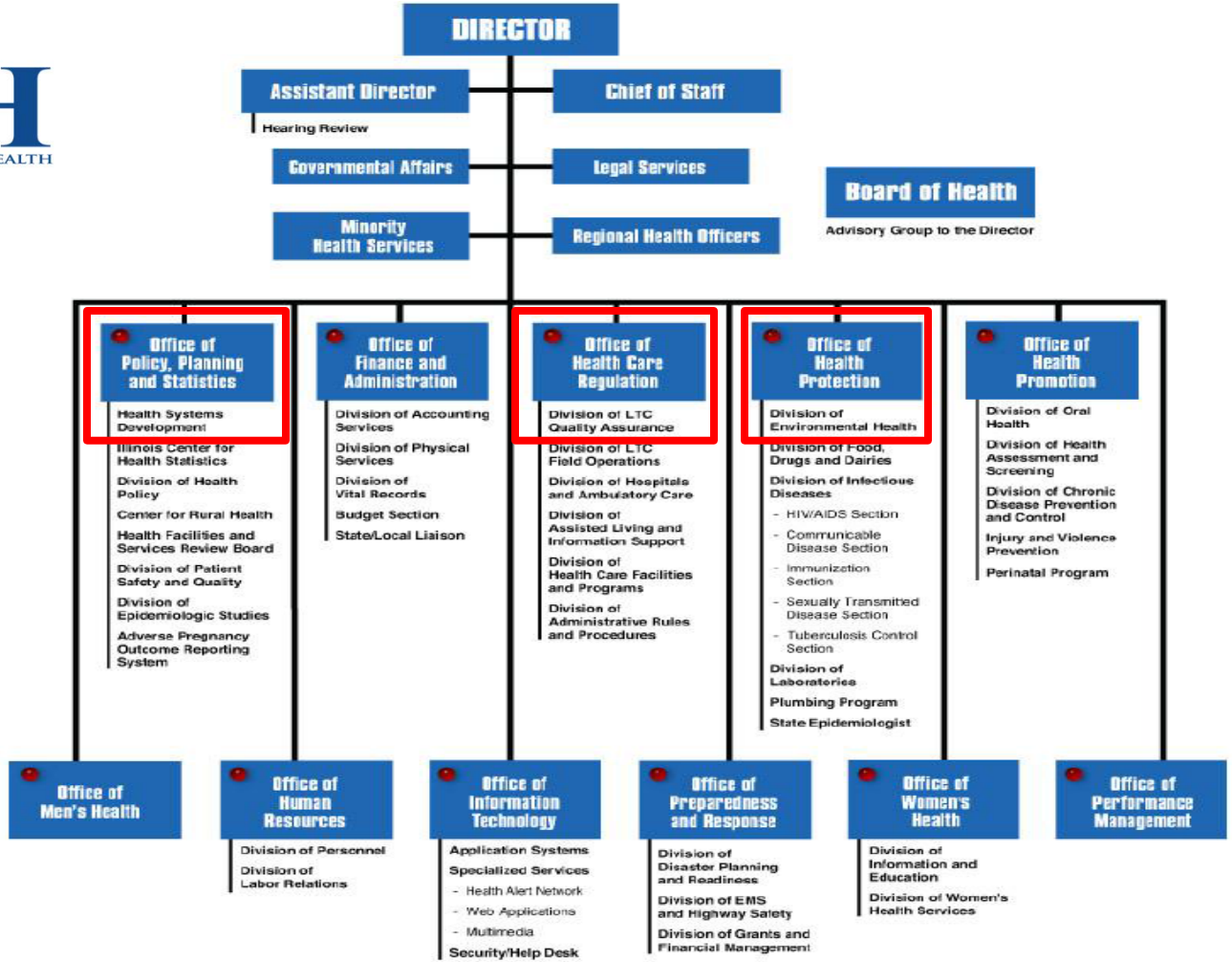

IDPH Office of Health Care Regulation

License, inspect or certify those that must comply with state and federal regulations.

May include:

- Ambulatory surgical treatment centers (ASTCs)
- Certified nurse aides
- Health maintenance organizations (HMOs)
- Home health agencies
- Hospices
- Hospitals
- Laboratories
- Nursing homes
- Physical therapists in independent practice
- Poison control resource centers
- Pregnancy termination centers
- Rural health clinics
- Sperm and tissue bank

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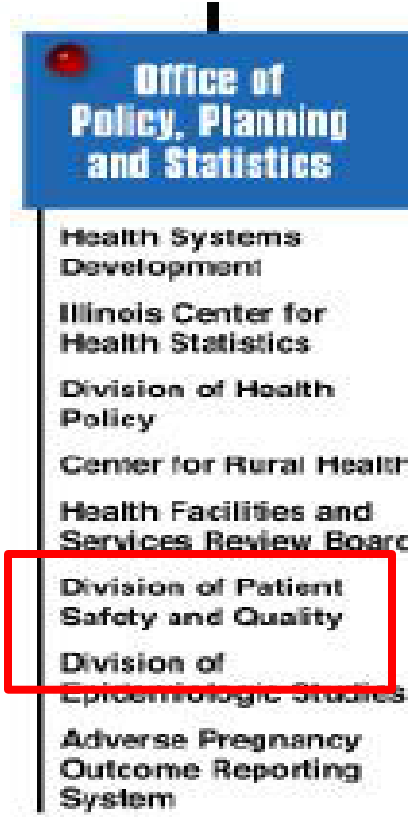
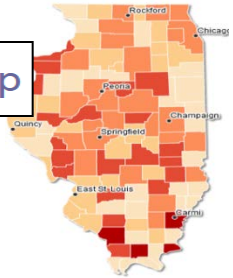


IDPH Division of Patient Safety and Quality

- Promotes health care transparency
- Collects and reports health care provider data
- **Develops and implements programs for improving the quality and value of health care**

Illinois Hospital Report Card
and Consumer Guide to Health Care

Illinois Public Health Community Map



XDRO registry

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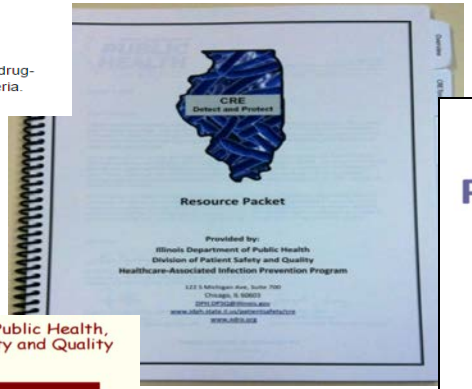
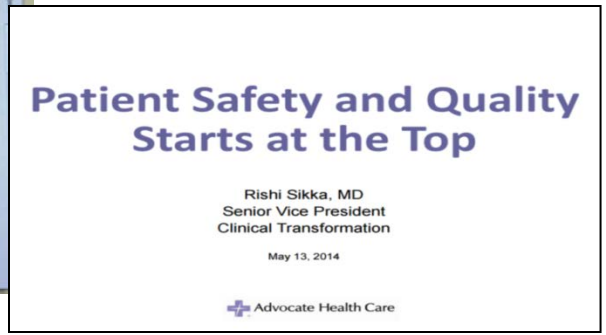
CRE "Detect and Protect" Campaign

- 30 stakeholder CRE Taskforce
- 6 webinars: 605 people
- 2 packets: 470 facilities
- 2 websites
- 1 Press release
- 3 regional workshops





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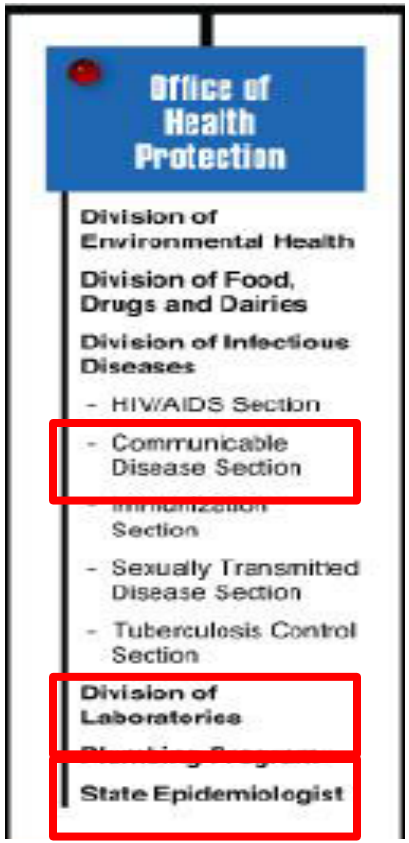
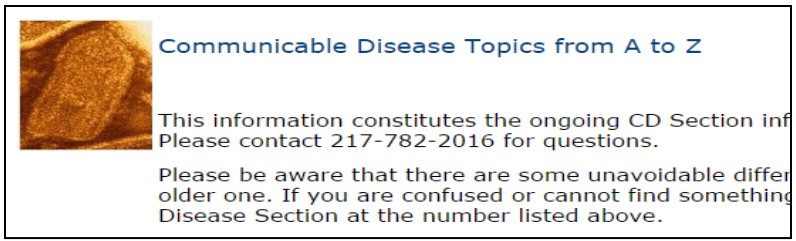
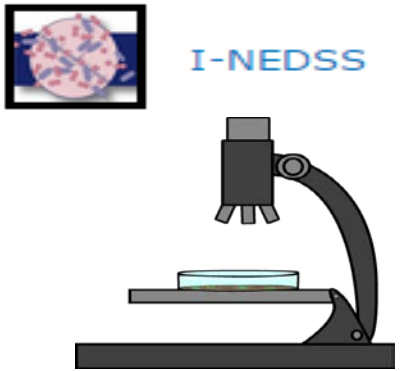
IDPH Division of Infectious Disease



- Protect people from infectious diseases through disease surveillance, analysis, immunization, and education

- Mandated reporting of certain infectious diseases to Illinois' National Electronic Disease Surveillance System (I-NEDSS)





IDPH and Local Health Departments

- Local Health Departments are typically the first point of contact

- Health care facilities are organized by Local Health Department jurisdictions

Local → State → Federal

HEALTHY CHICAGO
CHICAGO DEPARTMENT OF PUBLIC HEALTH

→

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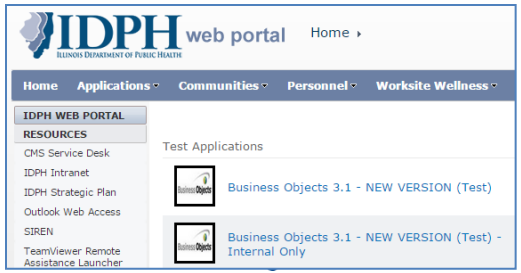
→

CDC

If I work at a Local Health Dept…

- Refer facilities to report CRE to the XDRO registry
- Notify IDPH about unusual CRE (e.g. NDM), or potential CRE clusters
- Investigate clusters in collaboration with IDPH
- Facilitate communication when patients are transferred
- Refer facilities to CDC CRE Toolkit guidelines
- Maintain vigilance for clusters of CRE via INEDSS B.O.
- Refer CRE questions to IDPH CRE Team



If I work at a Health Care Facility…

- Communicate with the lab about CRE testing
- Report CRE cases to the XDRO registry
- Use the XDRO registry to query for admitted patients/ residents
- Use the XDRO registry (or some other method) to keep track of CRE patients/ residents
- Contact your local health department about unusual CRE or potential CRE clusters
- Implement appropriate infection control measures according to the CDC CRE Toolkit*

*http://www.cdc.gov/hai/organisms/cre/cre-toolkit/

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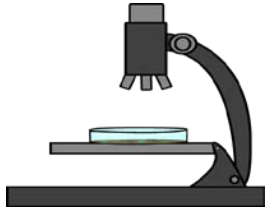
If I work at a Laboratory…



- Communicate with your facilities about what type of CRE testing you do
- Report CRE cases to the XDRO registry
- Submit your first five CRE isolates to IDPH labs for validation testing (by 7/31/15)
- Submit any unusual CRE (e.g. NDM) to IDPH labs to send to CDC for confirmatory testing*

*Coordinate with your Local Health Department

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What happens after CRE cases are reported to the XDRO registry?

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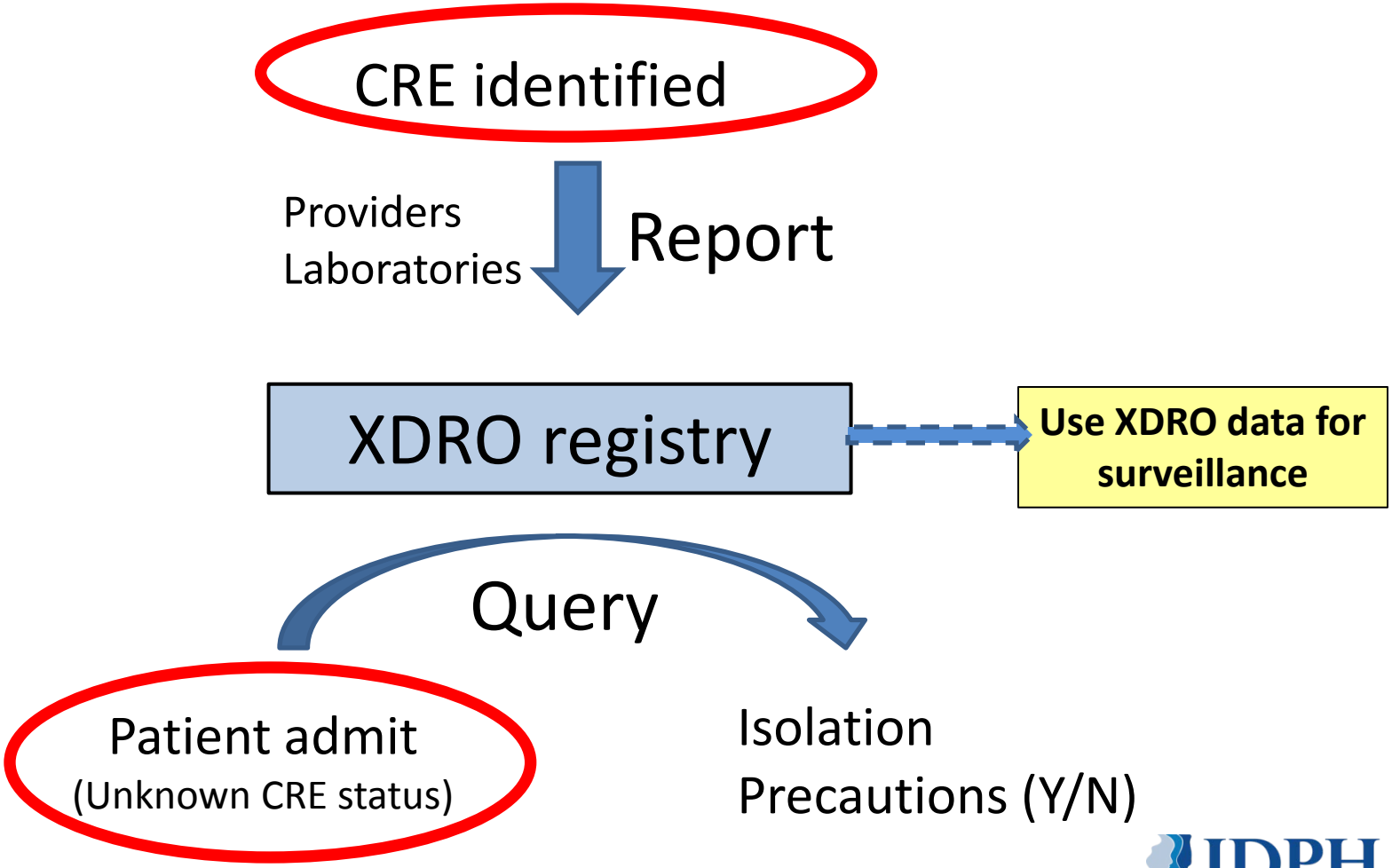
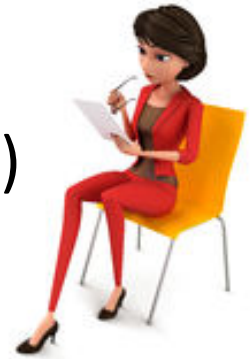

CRE identified
Providers
Laboratories
Report
XDRO registry
Use XDRO data for surveillance
Query
Patient admit
(Unknown CRE status)
Isolation
Precautions (Y/N)

Once CRE cases are in the XDRO registry…

- Health Departments review the cases
  - Look for anything unusual (e.g. NDM, clusters)
  - Follow-up as necessary



- IDPH does not publicly report CRE cases by facility

- For now, CRE cases are in the XDRO registry indefinitely

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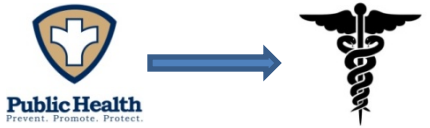
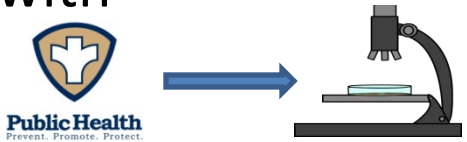
What happens if there is an unusual CRE or potential cluster?

1. IDPH will contact the local health department with jurisdiction over the involved facility

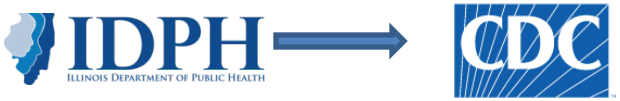
2. Local health department (or IDPH) will follow up with the healthcare facility to gather more information



3. Local health department (or IDPH) may follow up with the laboratory that identified the CRE



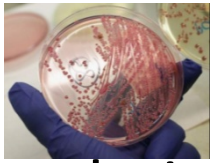
4. IDPH will notify CDC (as necessary)



More information for a CRE case

- Foreign travel
- Foreign healthcare exposure
- Invasive procedures
- Past medical history

- Dates and locations of previous healthcare facility exposure
- Surveillance cultures



- Adherence to CDC CRE Toolkit recommendations

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Closing up a CRE case

- Make sure facilities know what to do to prevent spread of CRE
- Summary report to local health departments, IDPH, and CDC, as necessary

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Who do I call for questions about CRE?

If you're a **Health Care Facility** or **Laboratory**, start with your Local Health Department

If you're a **Local Health Department**, contact IDPH CRE Team:

Mary Alice Lavin, Hektoen (MaryAlice.Lavin@illinois.gov)

Jodi Morgan (Jodi.Morgan@illinois.gov)

Angela Tang, Hektoen (Angela.Tang@illinois.gov)

Robynn Cheng Leidig (Robynn.Leidig@illinois.gov)

When in doubt, call IDPH Division of Infectious Diseases at 217-785-7165 or email dph.xdroregistry@illinois.gov

Websites: www.xdro.org; www.idph.state.il.us/patientsafety/cre/

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Recognizing Carbapenem-Resistant *Enterobacteriaceae*: Crash Course for Non-Microbiologists

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Department of Medical Laboratory Science
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July 28, 2015

Disclosures

- Research support through the CDC Chicago Prevention Intervention Epicenter (C-PIE), RA Weinstein, PI and MK Hayden, Co-I
- Industry sponsored grants/contracts (Cepheid)
- Unpaid research (AdvanDx)

Objectives

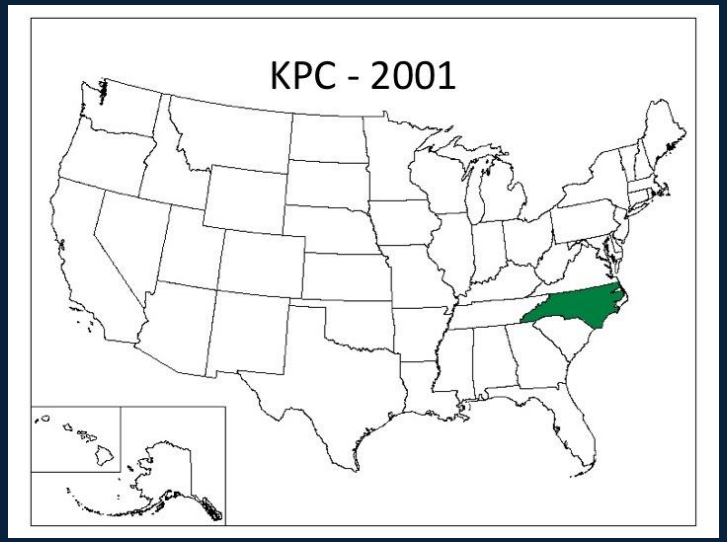
By the end of this presentation, the learner will be able to:

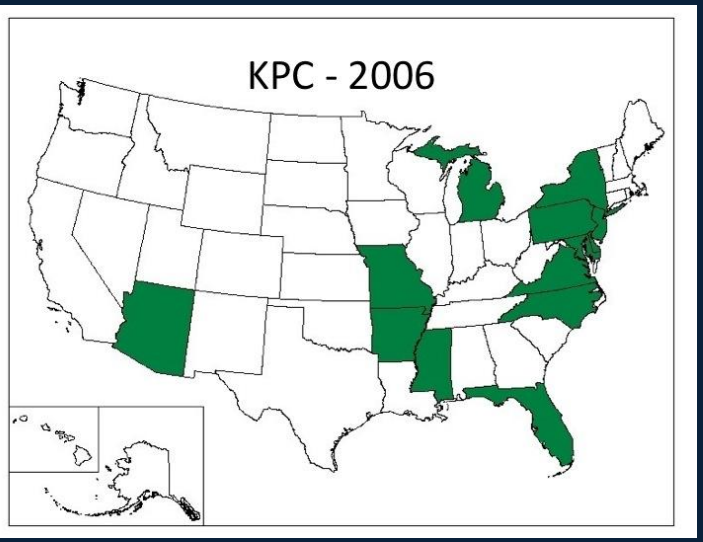
1. Define Carbapenem-Resistant *Enterobacteriaceae* (CRE)
2. Discuss laboratory techniques used to identify CRE
3. Distinguish between different mechanisms of carbapenem resistance

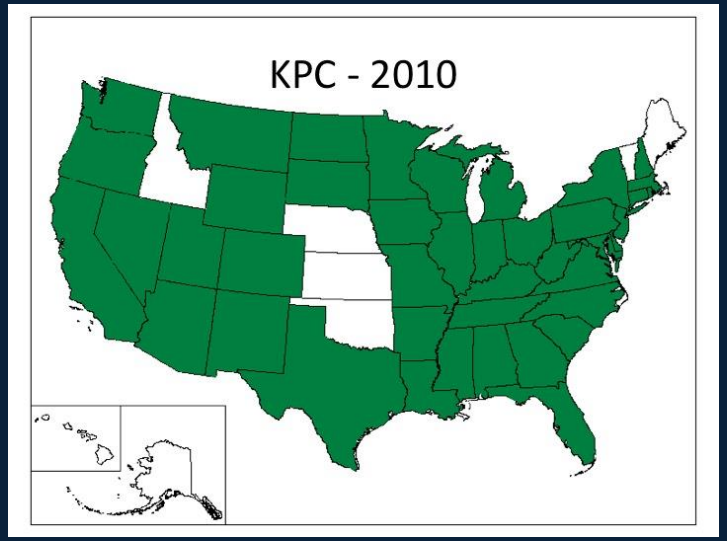
Carbapenem-Resistant *Enterobacteriaceae*

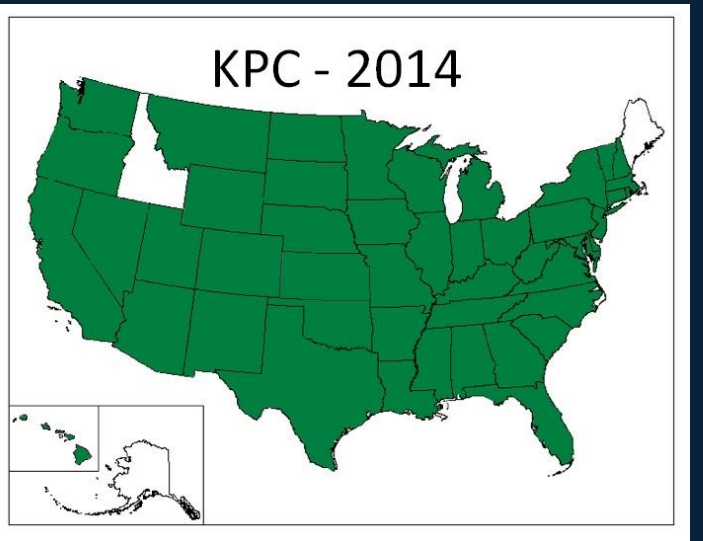
- CRE are serious public health threat
  - *Klebsiella pneumoniae* carbapenemase (KPC) is the most common worldwide

http://www.cdc.gov/drugresistance/biggest_threats.html


KPC - 2001

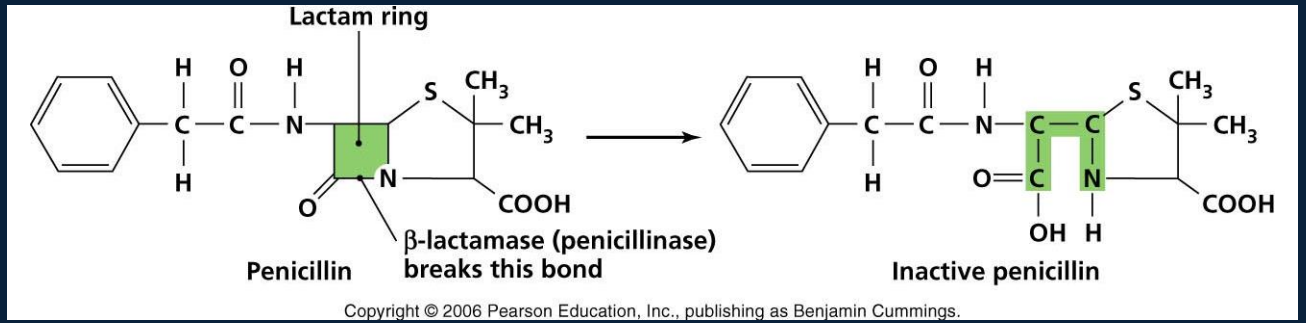

KPC - 2006


KPC - 2010


KPC - 2014

Carbapenems

- Imipenem
- Meropenem
- Ertapenem
- Doripenem

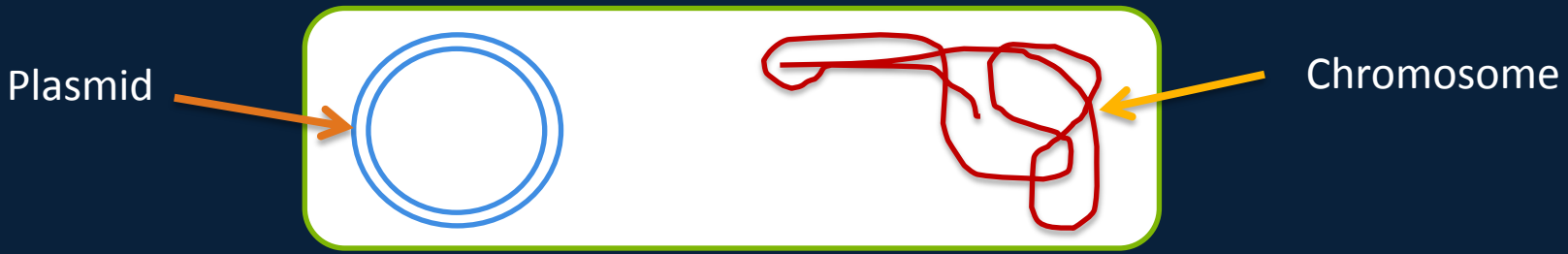


Carbapenemases

- Carbapenem-hydrolyzing beta-lactamases that confer carbapenem resistance
- The carbapenemases have been organized based on amino acid homology into the Ambler molecular classification schema
  - Class A, C, and D share a serine residue in the active site
  - Class B enzymes require the presence of zinc for activity

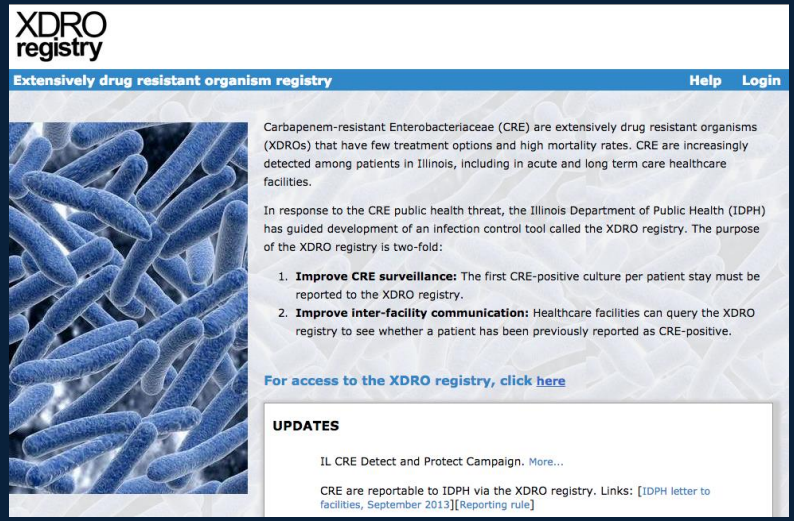
Carbapenemases

Ambler Class	Carbapenemase	Location of gene	Dissemination potential	Activity	Predominant Species
A	KPC	Plasmid	High	All β-lactams	*K. pneumoniae*
B	NDM-1	Plasmid	High	All β-lactams except aztreonam	*K. pneumoniae, E. coli*
D	OXA-48	Plasmid	High	Carbapenems, except 3rd gen cephalosporins	*K. pneumoniae, E. coli, E. cloacae*



Mandated Reporting in Illinois

- IDPH amended the Control of Communicable Diseases Code (77 Ill. Adm. Code 690) Rules to require reporting of CRE
- Began November 1, 2013
- XDRO Registry for CRE



Enterobacteriaceae

- *Enterobacteriaceae* are a large family of enteric Gram-negative bacilli

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Citrobacter* spp.
- *Enterobacter* spp.

- Other genera: *Proteus, Providencia, Serratia*

Defining CRE for the XDRO Registry

1. Molecular test (e.g. PCR) specific for a carbapenemase gene (e.g. *bla*$_{KPC}$, *bla*$_{NDM}$)

2. Phenotypic test (e.g. modified Hodge test) specific for carbapenemase production

3. E. coli or Klebsiella spp. only: non-susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime)

What is PCR?

- Polymerase chain reaction
- Laboratory method developed to rapidly generate copies of nucleic acids (DNA or RNA)
- Bacterial colony provides the template (DNA)
- Series of primers and probes specific for carbapenemase gene will bind to and recognize complementary sequence in bacterial DNA, if present
- Rapid cycles of denaturing, annealing, and extending will generate exponential copies of region of interest
- Fluorescent threshold → positive result

PCR

Pros

- Quick turn-around time
- Specific for carbapenemase
- Definitive
- Can multiplex targets into single assay (e.g. KPC/NDM)
- Does not require viable organisms

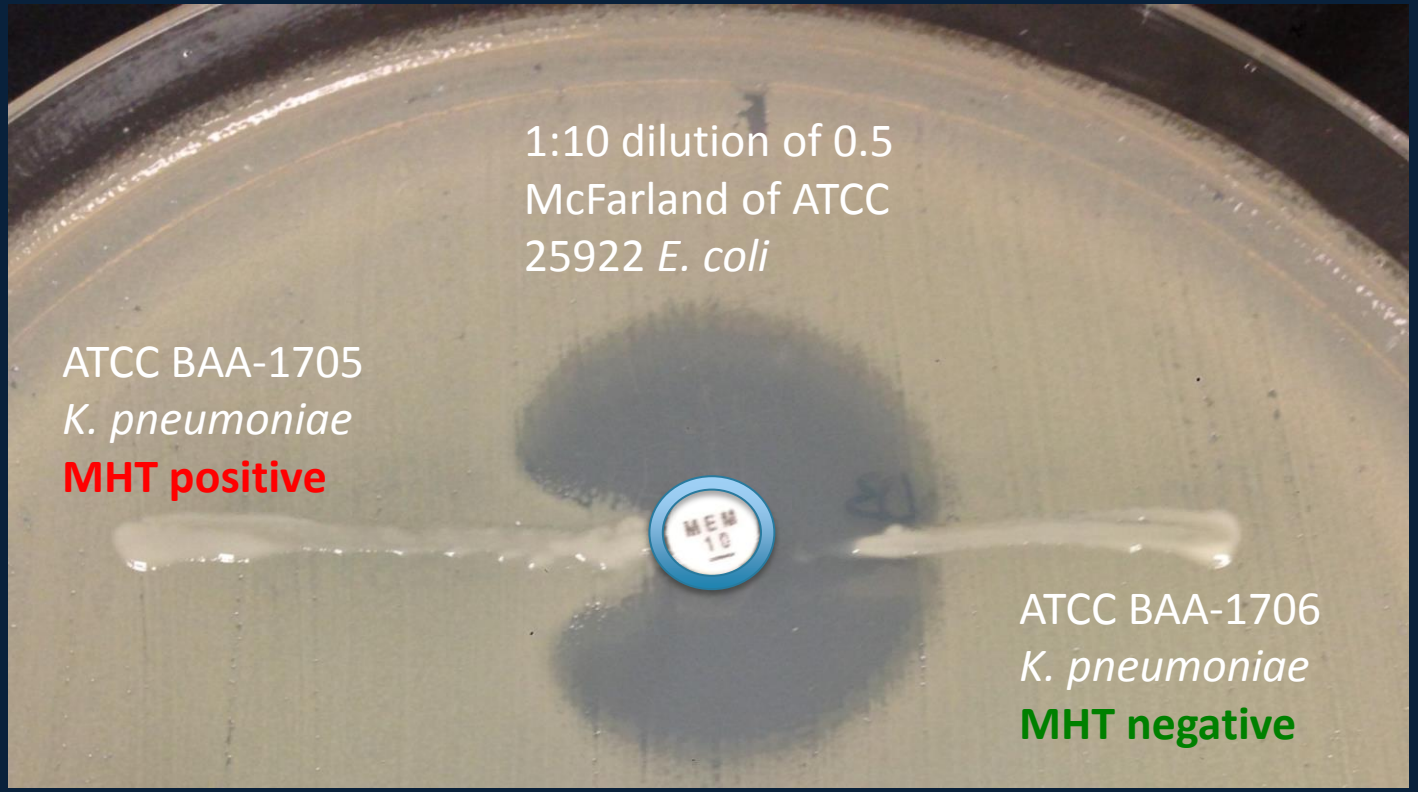
Cons

- Expensive
- High-complexity testing
- Organisms not available for additional testing, epidemiologic studies

Phenotypic Test: Modified Hodge

- Uses a pan-susceptible *E. coli* (indicator) to create a lawn of confluent growth on a Mueller Hinton agar plate
- Carbapenem disk applied to center of plate (meropenem or ertapenem)
- Suspicious isolates struck from center of disk to edge of plate
- Examine after 18-24 hour incubation for a growth of *E. coli* around the isolate streak

Modified Hodge Test



Modified Hodge Test

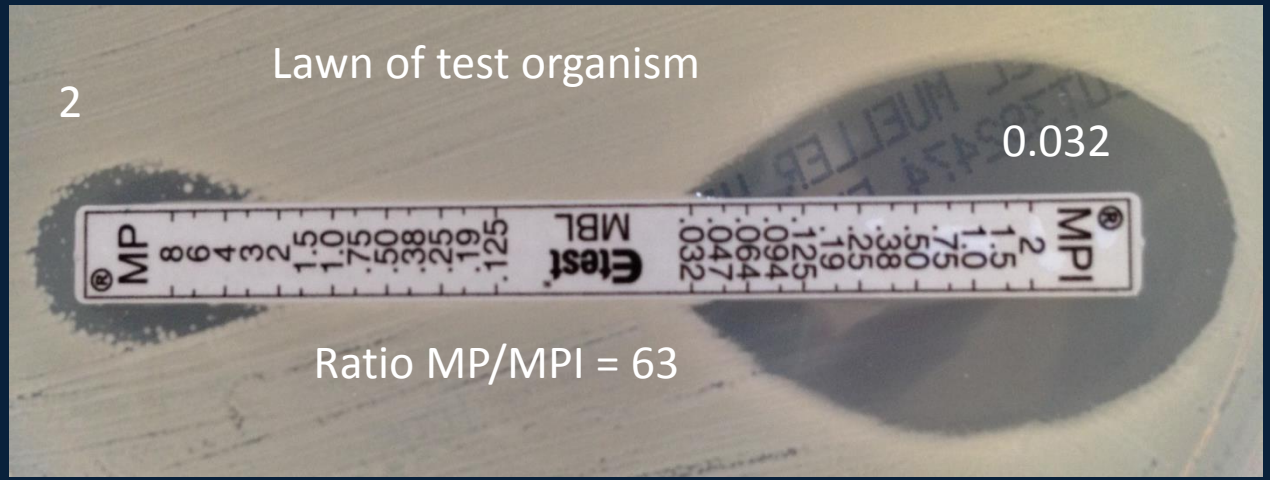
Pros

- Inexpensive
- Easy to perform
- Organisms available for additional testing

Cons

- Requires additional overnight incubation
- Not specific
- Lacks sensitivity for MBLs (e.g. NDM)

MβL Etest® Phenotypic Screening

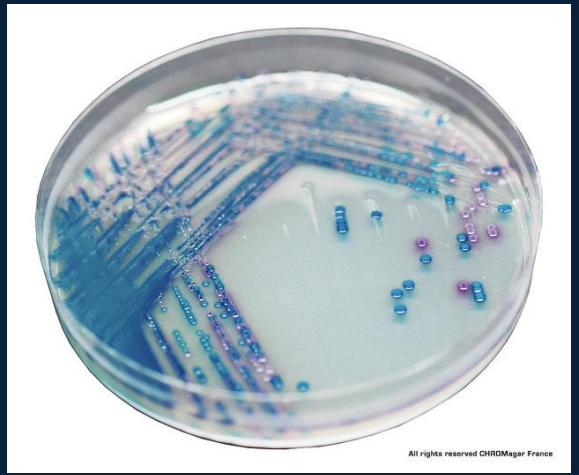


- Presence of MβL indicated by a reduction of the MP MIC by ≥ 3 doubling dilutions in the presence of EDTA
- Phenotypic method requires confirmation

Chromogenic Media

- CHROMagar™ KPC – research use only
- Brilliance™ CRE agar – not for sale in US
- chromID® CARBA agar
- HardyCHROM™ CRE agar

- Inexpensive and convenient
- No definitive ID
- Does not provide mechanism
- Studies with various sensitivity, specificity



Suspect KPC from a Micro Report

1 Klebsiella pneumoniae

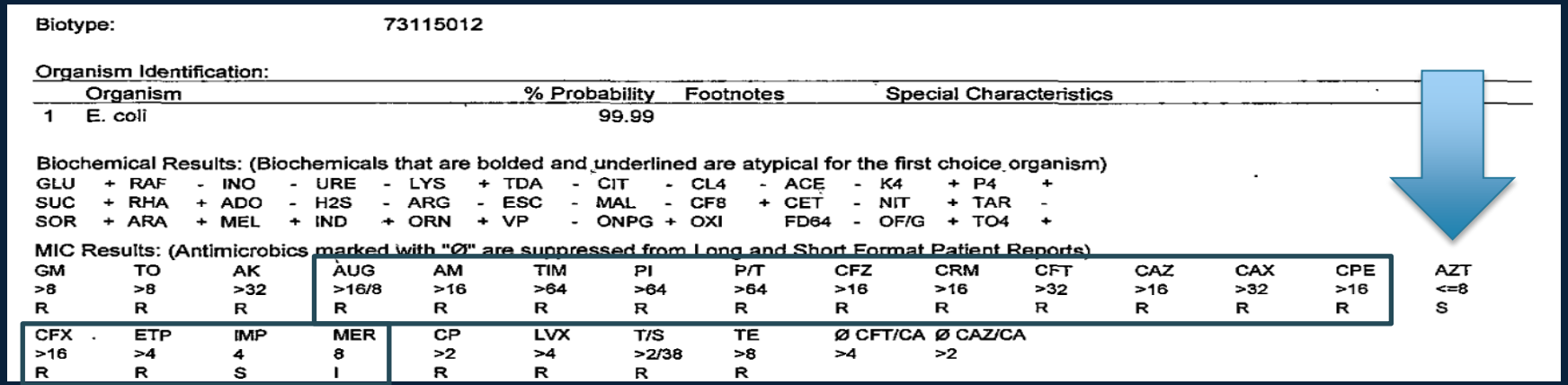
1 K. pneumoniae

Drug	MIC	Interps	Origin
Gentamicin	<=4	S	
Tobramycin	>8	R	
Amikacin	>32	R	
Amox/K Clav	>16/8	R	
Ampicillin	>16	R	
Ticar/K Clav	>64	R	
Piperacillin	>64	R	
Pip/Tazo	>64	R	
Cefazolin	>16	R	
Cefuroxime	>16	R	
Cefotaxime	>32	R	
Ceftazidime	>16	R	
Ceftriaxone	>32	R	
Cefepime	>16	R	
Aztreonam	>16	R	
Cefoxitin	>16	R	
Ertapenem	>4	R	
Imipenem	>8	R	IMP ENT R
Meropenem	>8	R	
Ciprofloxacin	>2	R	
Levofloxacin	>4	R	
Trimeth/Sulfa	>2/38	R	
Tetracycline	8	I	

- *Enterobacteriaceae*
- Non-susceptible to all β-lactam antibiotics
  - Penicillins
  - Cephalosporins
  - Cephamycins
  - Monobactams
  - Carbapenems

bla$_{KPC}$ PCR = POSITIVE

Suspect NDM from a Micro Report



Biotype: 73115012

Organism Identification:

	Organism	% Probability	Footnotes	Special Characteristics
1	E. coli	99.99		

Biochemical Results: (Biochemicals that are bolded and underlined are atypical for the first choice organism)

GLU	+	RAF	-	INO	-	URE	-	LYS	+	TDA	-	CIT	-	CL4	-	ACE	-	K4	+	P4	+
SUC	+	RHA	+	ADO	-	H2S	-	ARG	-	ESC	-	MAL	-	CF8	+	CET	-	NIT	+	TAR	-
SOR	+	ARA	+	MEL	+	IND	+	ORN	+	VP	-	ONPG	+	OXI		FD64	-	OF/G	+	TO4	+

MIC Results: (Antimicrobics marked with "Ø" are suppressed from Long and Short Format Patient Reports)

GM	TO	AK	AUG	AM	TIM	PI	P/T	CFZ	CRM	CFT	CAZ	CAX	CPE	AZT
>8	>8	>32	>16/8	>16	>64	>64	>64	>16	>16	>32	>16	>32	>16	<=8
R	R	R	R	R	R	R	R	R	R	R	R	R	R	S

CFX	ETP	IMP	MER	CP	LVX	T/S	TE	Ø CFT/CA	Ø CAZ/CA
>16	>4	4	8	>2	>4	>2/38	>8	>4	>2
R	R	S	I	R	R	R	R		

- *Enterobacteriaceae*
- Non-susceptible to all β-lactam antibiotics
  - except aztreonam

$bla_{\text{NDM-1}}$ PCR = POSITIVE

Suspect OXA-48 from a Micro Report

01 Klebsiella pneumoniae

01 K. pneumoniae

Drug	MIC	Interps
Gentamicin	>8	R
Tobramycin	<=4	S
Amikacin	>32	R
Amox/K Clav	>16/8	R
Ampicillin	>16	R
Amp/Sulbactam	>16/8	R
Pip/Tazo	>64	R
Cefazolin	>4	R
Cefuroxime	>16	R
Cefotaxime	8	R
Ceftriaxone	8	R
Cefepime	<=4	S
Ertapenem	>2	R
Imipenem	2	I
Meropenem	8	R
Ciprofloxacin	>2	R
Levofloxacin	>4	R
Trimeth/Sulfa	<=2/38	S
Tetracycline	>8	R
Tigecycline	<=2	S

- *Enterobacteriaceae*
- Non-susceptible to β-lactam antibiotics
- Remains susceptible to 4th generation cephalosporin

bla$_{\text{OXA-48}}$ PCR = POSITIVE

Summary

- XDRO Registry is tracking Carbapenem-resistant *Enterobacteriaceae* (CRE)
- Report isolates based off molecular, phenotypic or susceptibility test results
  - Reporting using only AST data is valid only if isolate is *E. coli* or *Klebsiella* spp.
- Some patterns in susceptibility profiles may suggest a particular mechanism, but must to be confirmed

Questions

Acknowledgements

Don Blom
Manon Haverkate
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Monica Sikka
Caroline Thurlow
Shayna Weiner
Robert Weinstein

Contact Information

- Questions? Comments? Troubleshooting?

Nicholas Moore

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312-942-4629

Carbapenem-Resistant Enterobacteriaceae

Illinois' XDRO Registry

William Trick, MD
Cook County Health & Hospitals System
Chicago CDC Prevention Epicenter

July 28, 2015

I have nothing to disclose.

Orinoco area of Amazonas state, Venezuela

The microbiome of uncontacted Amerindians

- Highest diversity microbiome ever reported
- All *E. coli* pan-susceptible
- Harbor bacteria with resistance genes
    - Poised for mobilization when exposed to pharmacologic levels of antibiotics

A History of Overuse

Alexander Fleming discovered penicillin in 1928, doctors first prescribed it in the U.S. in 1942, and by 1945 Fleming was already warning about the risk of resistant bacteria—a prediction that became all too true over the following decades.

Total pounds of antibiotics produced, for use in humans and animals, in the U.S.

1942
First U.S. patient treated with penicillin

1944
2,650 pounds produced

1946
Feeding antibiotics to farm animals shown to speed their weight gain

1947
Penicillin-resistant infections reported

1958
Vancomycin approved to treat penicillin-resistant bacteria

1960s
Antibiotic-resistant salmonella identified in food animals and humans

1968
MRSA, a bacteria resistant to several antibiotics, first identified in a U.S. hospital patient

1977
FDA proposes revoking uses of penicillin and tetracyclines in animal feed

1986
Vancomycin-resistant enterococci (VRE) reported

1994
83 million pounds produced
Congress stops collecting data on total antibiotic production after this year

1997
MRSA contracted outside of hospital kills first person in the U.S.

1999
Synercid approved to treat certain vancomycin-resistant bacteria

2003
World Health Organization says feeding antibiotics to farm animals harms human health; Institute of Medicine recommends banning medically important antibiotics for growth promotion in food production

2005
FDA blocks use of a fluoroquinolone antibiotic in poultry because of resistance

2013
CDC reports at least 23,000 people per year die from resistant infections, including MRSA

1945 1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015

…Sustainable control of aggressive weeds is going to occur only when natural, intact ecosystems are restored…

Keely J, Conservation Biology, 2006

An un-natural creation

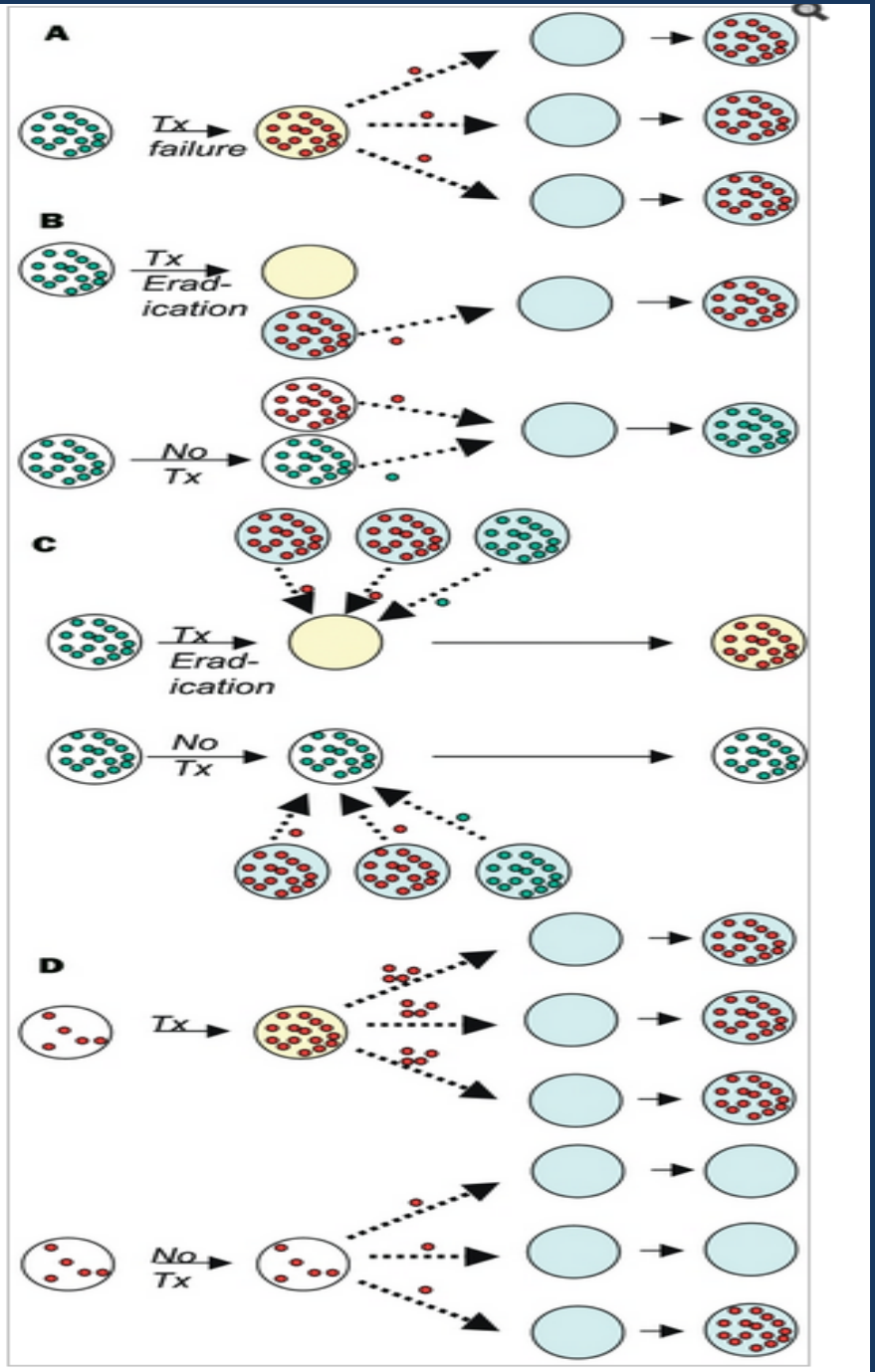
BLOOD CULTURE (PERIPHERAL) (Abnormal):
PROCEDURE: BLOOD CULTURE (PERIPHERAL)
SOURCE: BLOOD
COLLECTED: [redacted]

---------- FINAL REPORT ----------

FINAL REPORT [redacted]
GROWTH OF GRAM NEGATIVE RODS
FINAL IDENTIFICATION: KLEBSIELLA PNEUMONIAE
This isolate demonstrates carbapenemase production.
Carbapenems, cephalosporins, and penicillins are
unlikely to be effective in treatment of serious
infections. Contact precautions required.

---------- SUSCEPTIBILITY TESTING ----------

		K PNEUMO		
	MIC mcg/ml	MIC INTERP	MIC mcg/ml	ET INTERP
TRIMETH/SULFA	>2/38	RESISTNT		
CEFAZOLIN	>16	RESISTNT		
TIGECYCLINE			1.00	SUSCEPT
LEVOFLOXACIN	>4	RESISTNT		
CEFOXITIN	16	INTERMED		
PIP/TAZOBACTAM	>64	RESISTNT		
TICARCIL/K CLAV	>64	RESISTNT		
CEFTRIAXONE	>32	RESISTNT		
GENTAMICIN	<=4	SUSCEPT		
TOBRAMYCIN	>8	RESISTNT		
AMIKACIN	16	SUSCEPT		
IMIPENEM	8	RESISTNT		
MEROPENEM	>8	RESISTNT		
CEFEPIME	16	RESISTNT		
COLISTIN			.38	SUSCEPT
A ERTAPENEM	>4	RESISTNT		


A
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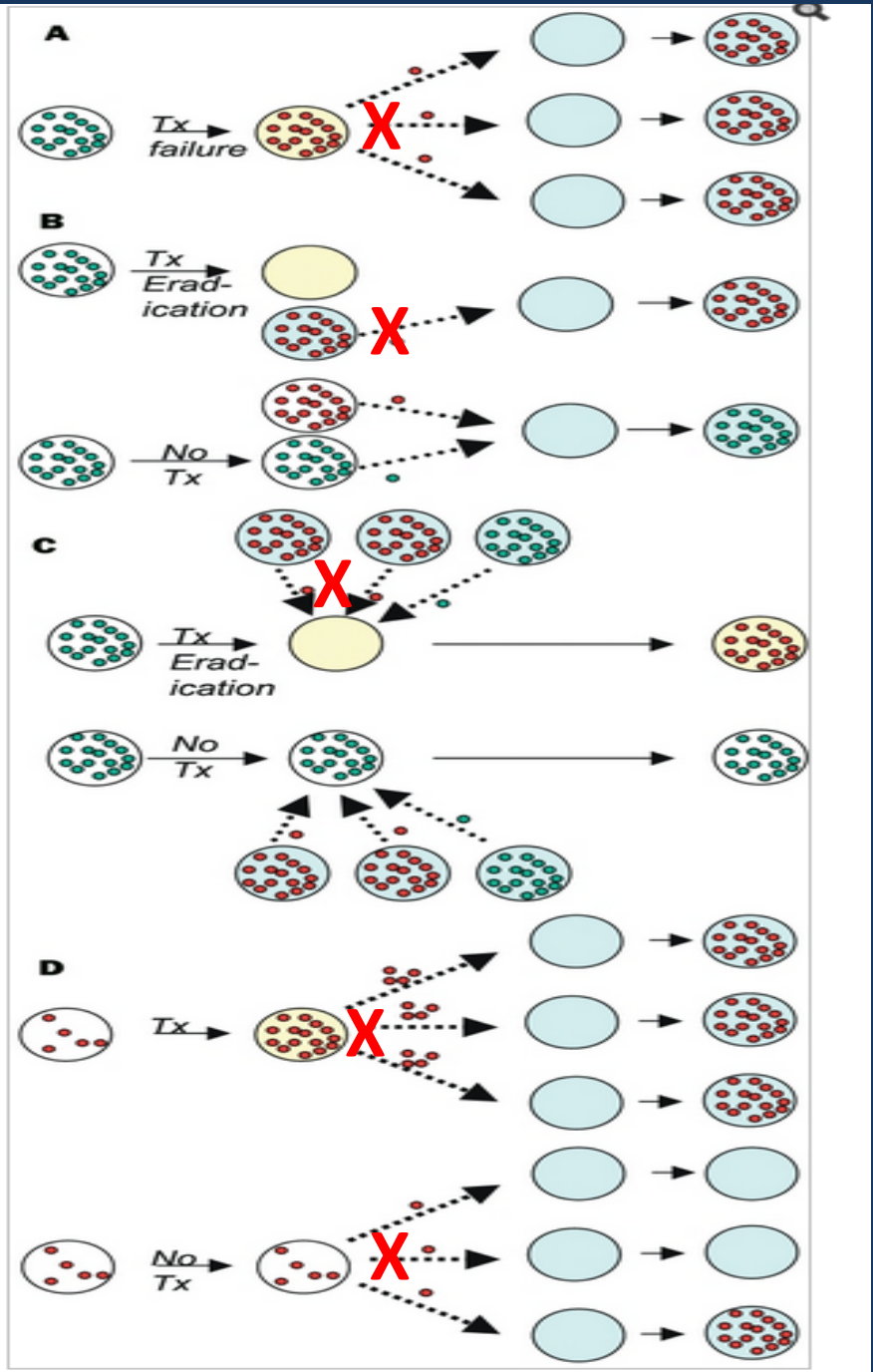
A
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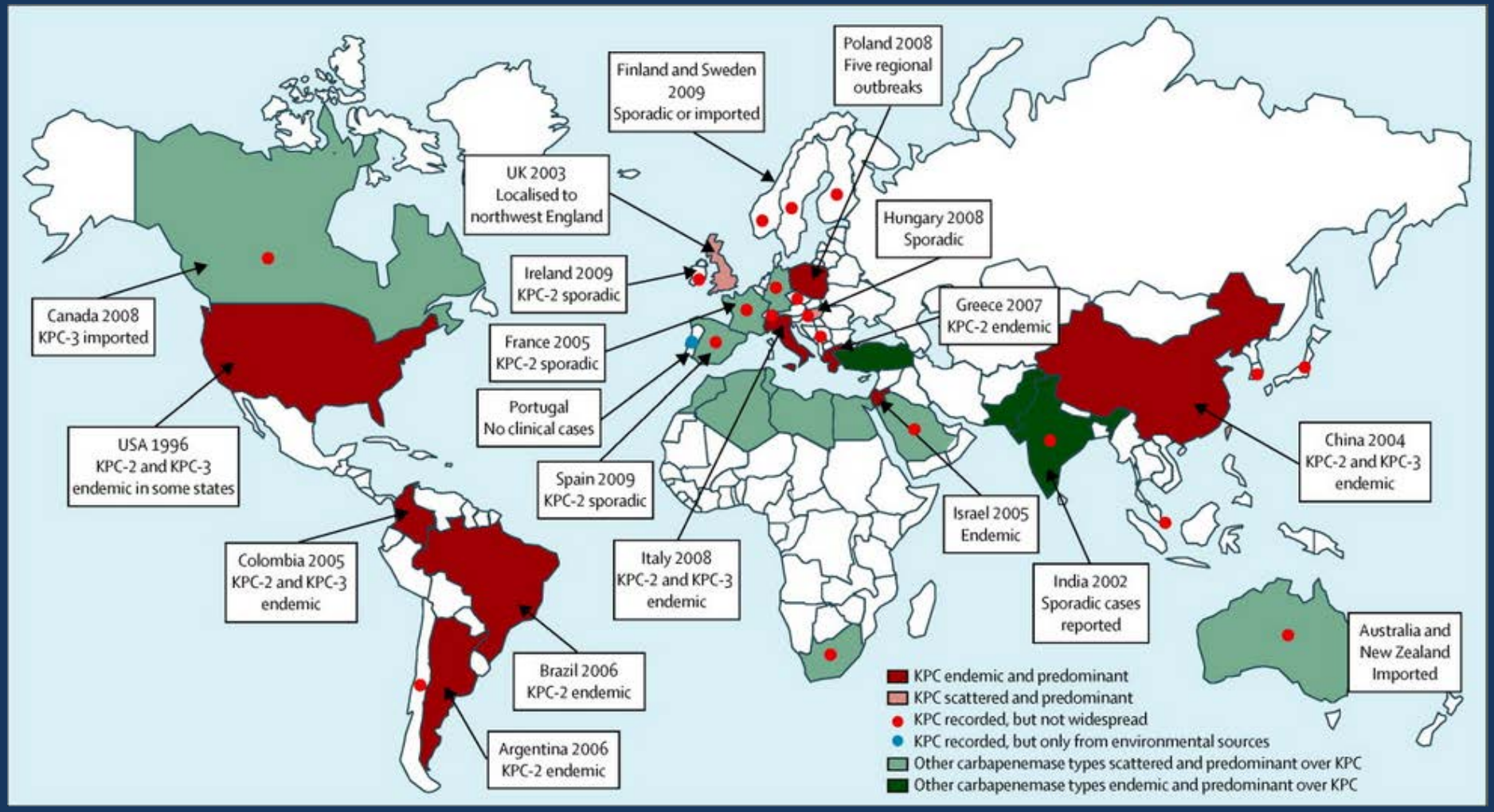
Tx

KPC global spread



Munoz-Price LS et al. Lancet ID. 2013

NDM global distribution

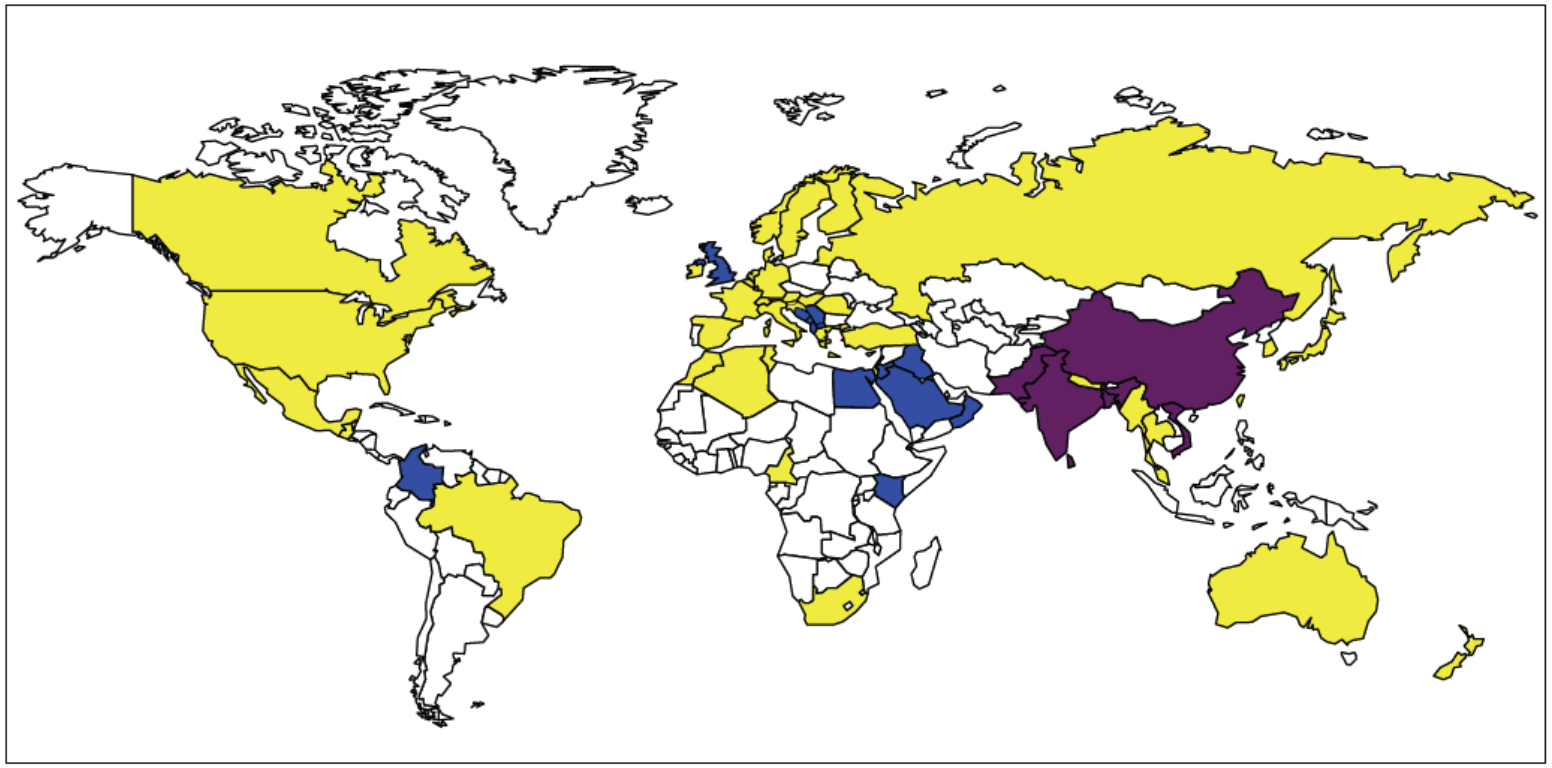


FIGURE 2: Geographical distribution of NDM producers.

Dortet et al. BioMed Res Int. 2014

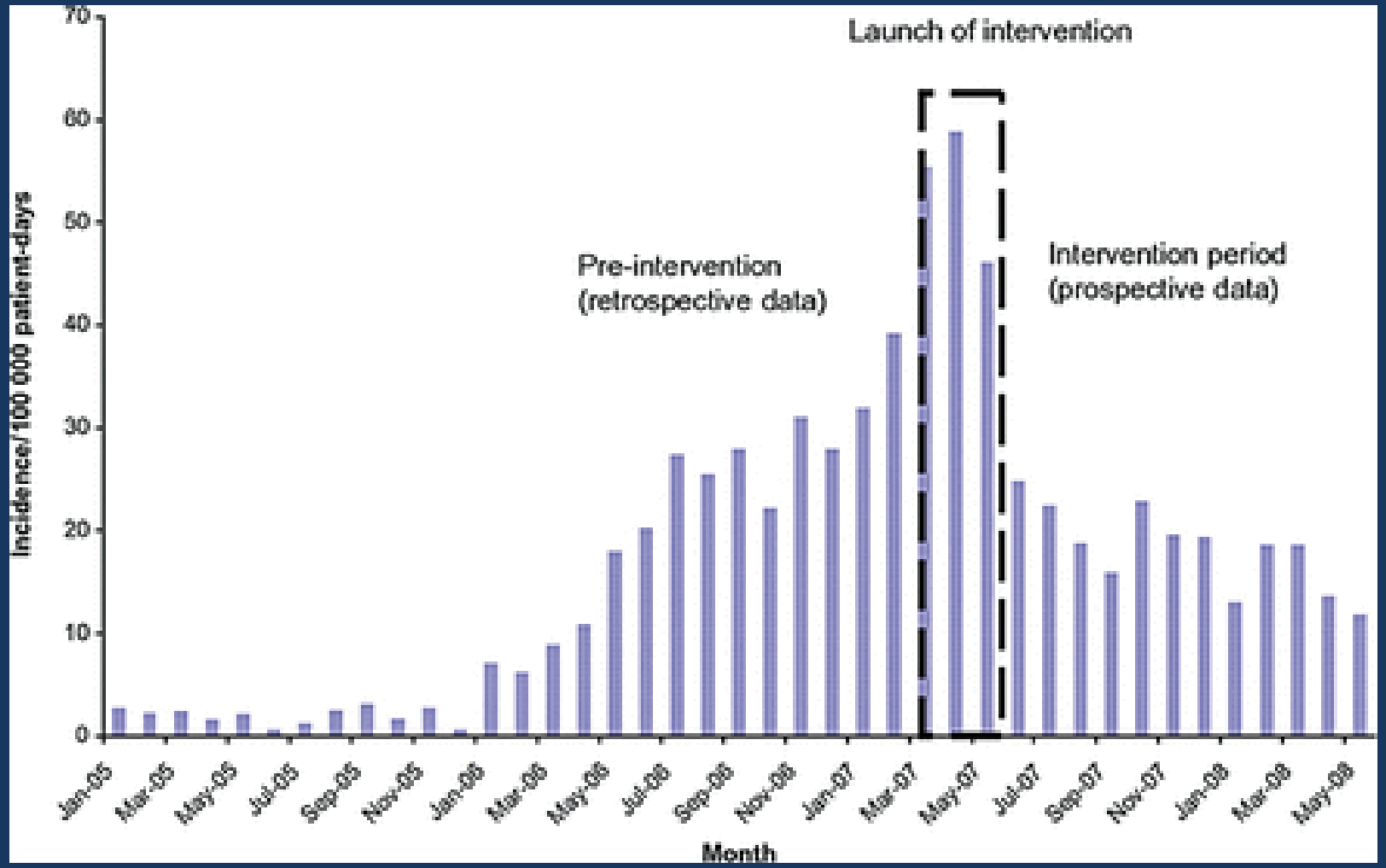

SOUTH DAKOTA
WISCONSIN
Minneapolis
Sioux Falls
Sioux City
IOWA
Cedar Rapids
NEBRASKA
Chicago
Omaha
Des Moines
Davenport
MISSOURI
KANSAS
Kansas City
ILLINOIS
29
90
35
80
70

TABLE 3. PREVALENCE OF COLONIZATION WITH VANCOMYCIN-RESISTANT ENTEROCOCCI AMONG PATIENTS OR RESIDENTS OF 30 ACUTE CARE AND LONG-TERM CARE FACILITIES IN THE SIOUXLAND REGION IN JULY AND AUGUST 1997, OCTOBER 1998, AND OCTOBER 1999.*

	1997	1998	1999	1999 VERSUS 1997† RELATIVE RISK (95% CI)	1999 VERSUS 1997† P VALUE
	no. of patients (%)				
All	40 (2.2)	26 (1.4)	9 (0.5)	0.2 (0.1–0.5)	<0.001
Acute care	10 (6.6)	9 (5.5)	0	0	<0.001
Long-term care	30 (1.7)	17 (1.0)	9 (0.5)	0.3 (0.2–0.7)	0.001

National Intervention to Reduce Incidence of CRE:

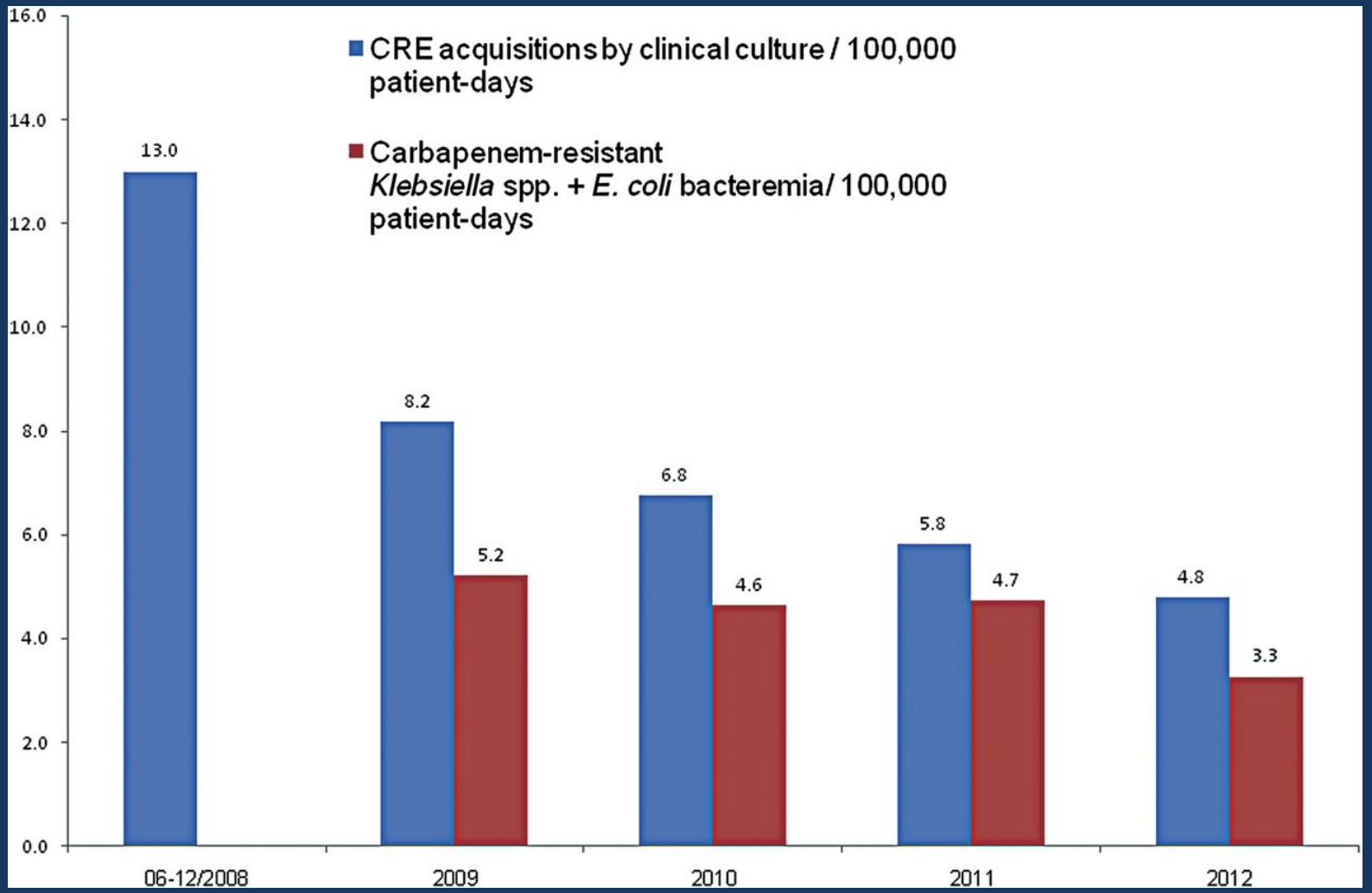
Clinical Cultures at Acute Care Hospitals.



Schwaber et al. Clin Infect Dis. 2014

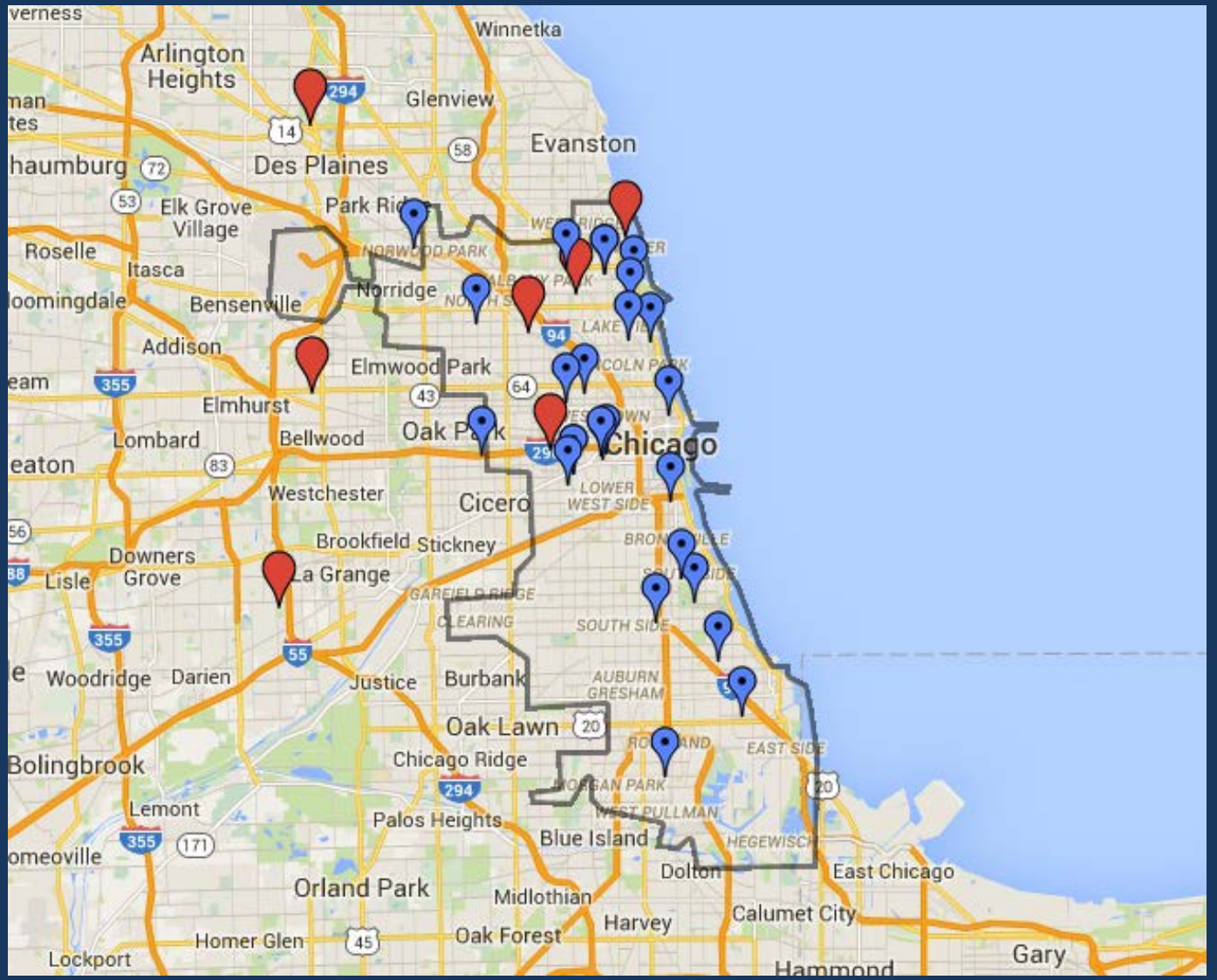
National Intervention to Reduce CRE:

Clinical Cultures & Bacteremia, Acute Care Hospitals



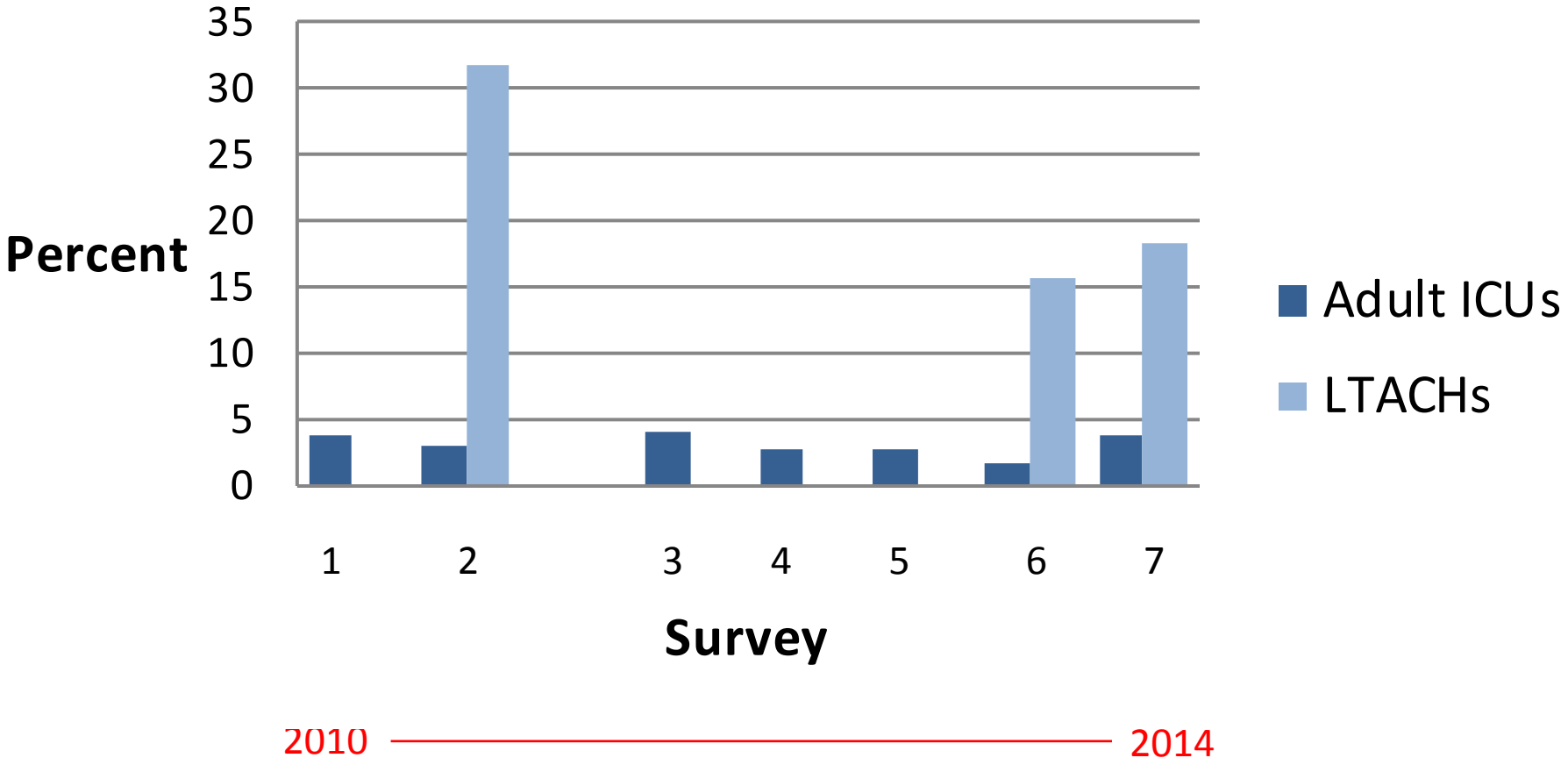
Schwaber et al. Clin Infect Dis. 2014

REALM project - KPC

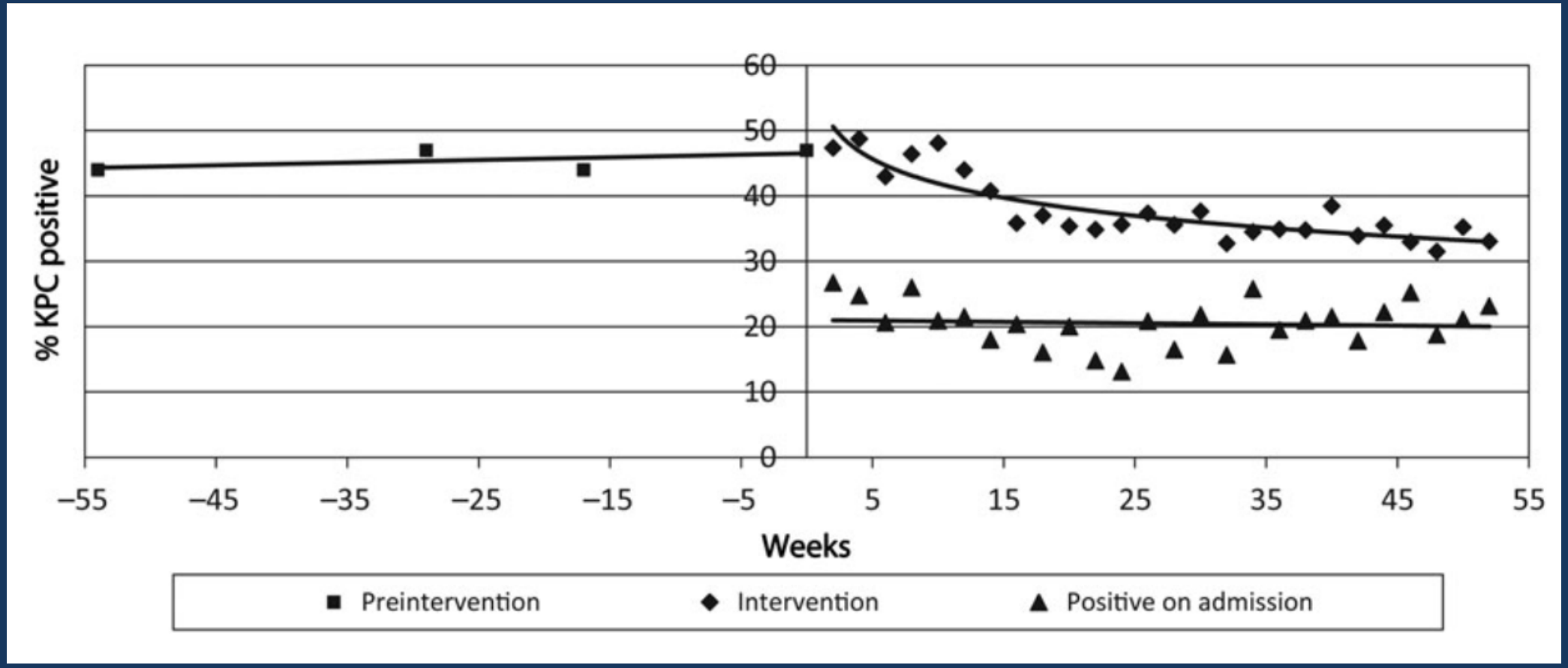


- Hospital ICUs (blue), LTACHs (red):

Prevalence of KPC colonization among ICU vs. LTACH patients



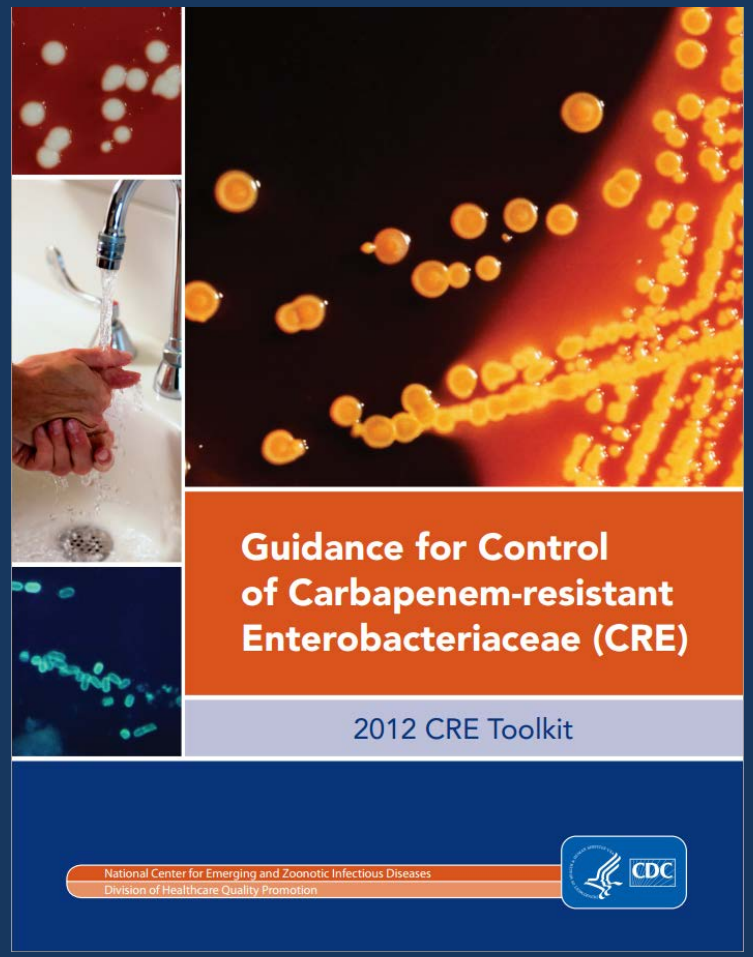
KPC Intervention for LTACHs



Hayden, Clin Infect Dis, 2015

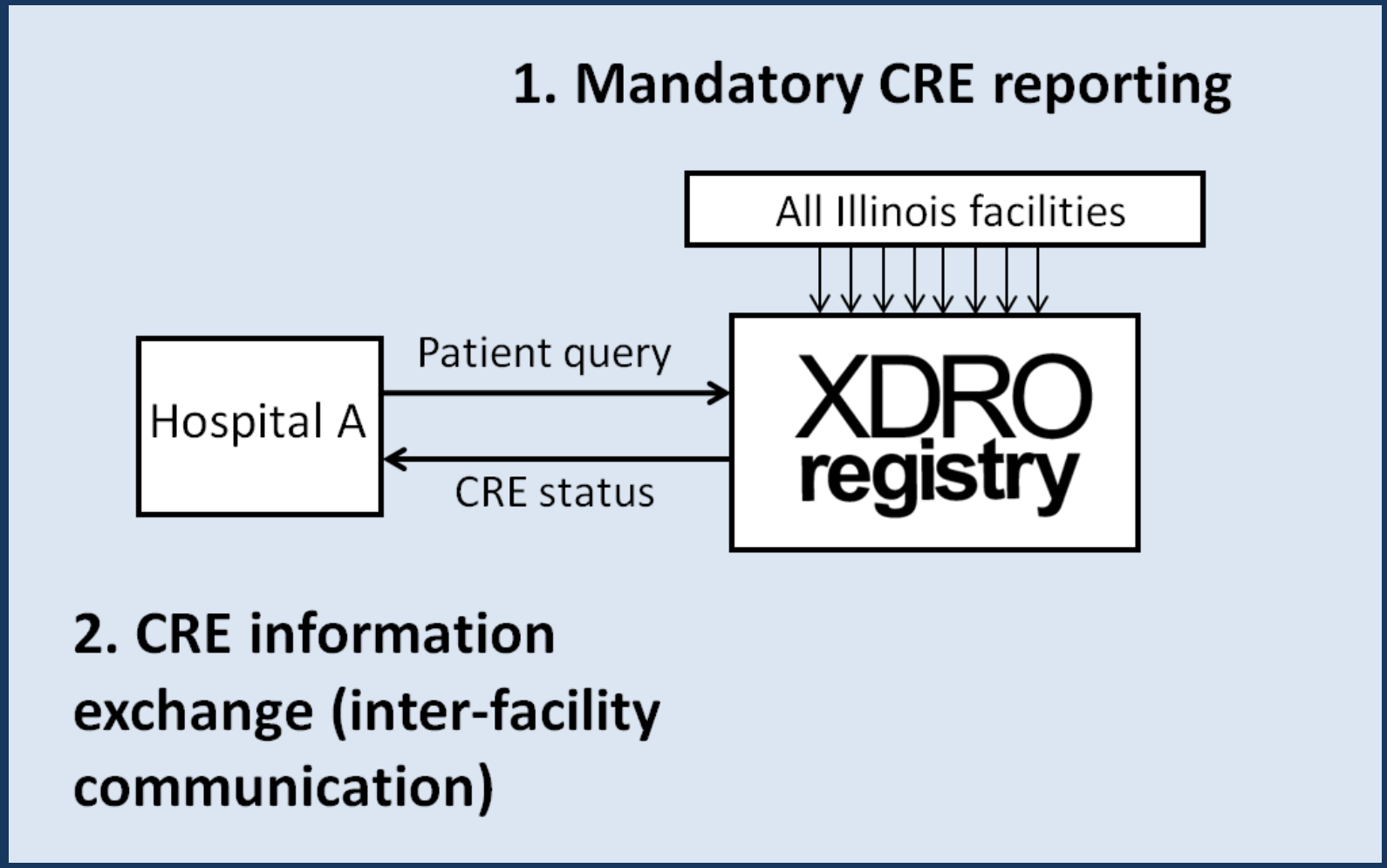
Illinois’ CRE Control efforts: Detect and Protect

“Detect and Protect”



- Detect: Identify all patients with CRE
- Protect: Maintain CRE-colonized patients in isolation precautions throughout the healthcare system

XDRO registry overview



Participants: Illinois hospitals including LTACHs (142), nursing homes (784), laboratories

Illinois CRE definition: Enterobacteriaceae with one of the following test results:

1. Molecular test (e.g., PCR) specific for carbapenemase

OR

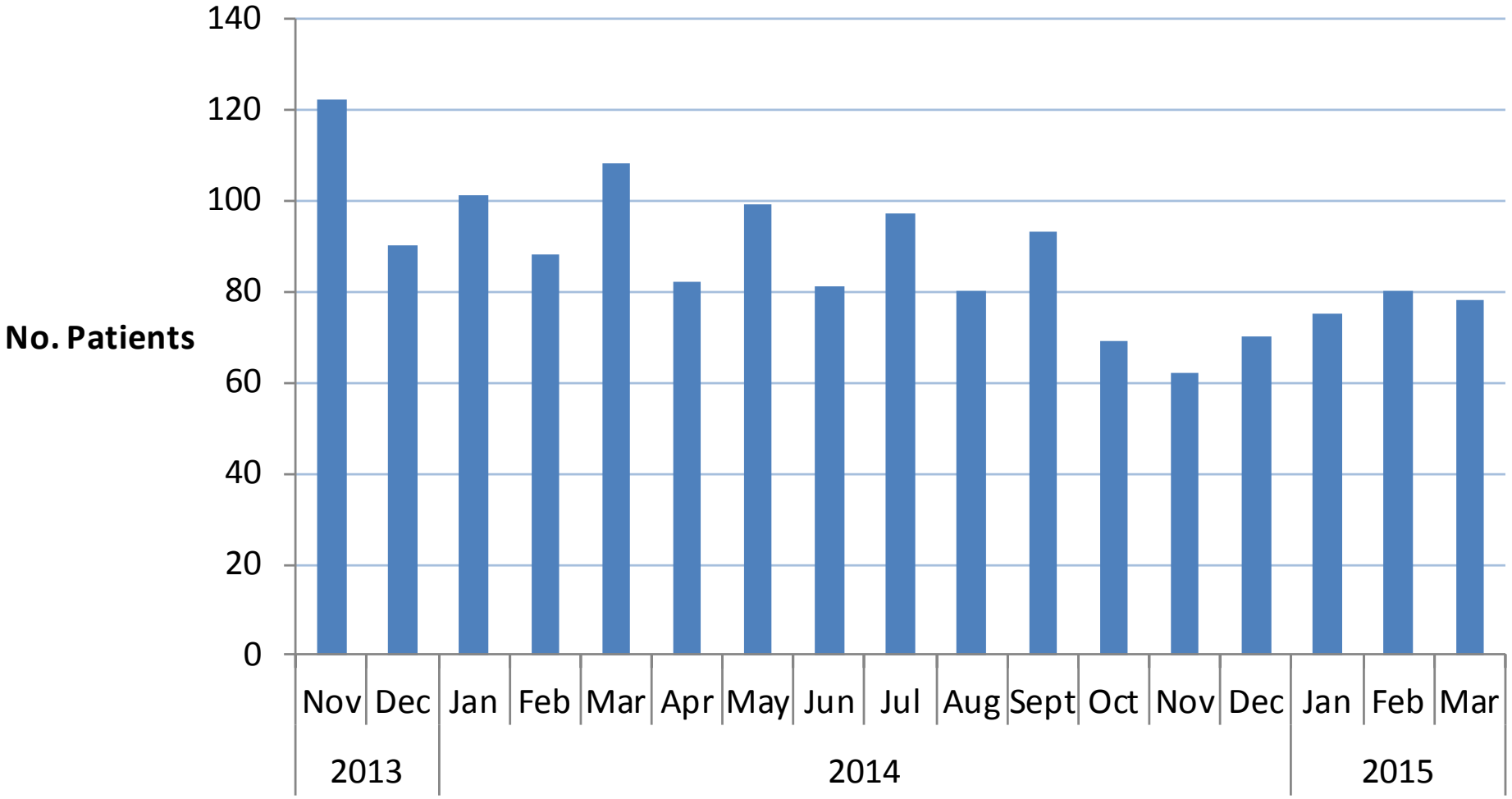
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production

OR

3. For ***E. coli*** **and** ***Klebsiella*** species only: non-susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime).

Report 1st CRE event per patient per encounter

Unique patients reported to XDRO registry



XDRO registry, year 1

Reporting

- Unique reports: 1,557 reports
- Unique patients: 1,095
- Reporting facilities: 175

115	Acute hospitals
5	LTACHs
46	SNFs
7	reference labs
2	Outpatient clinics

Querying

- 30 unique facilities query the registry/month

XDRO registry summary, 2014

Characteristics of ALL submitted reports	N	%
Culture Type		
Clinical	1254	80
Screening	301	20
Organism		
Klebsiella spp.	1347	86
E. coli	103	7
Enterobacter spp.	77	5

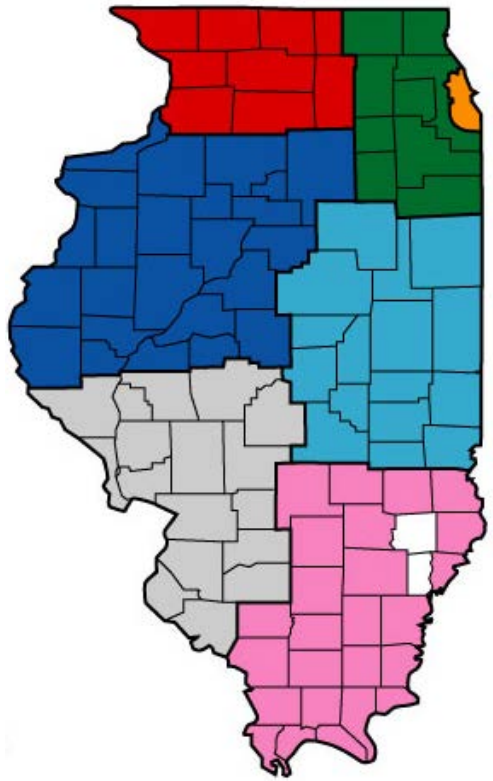
Data from IDPH

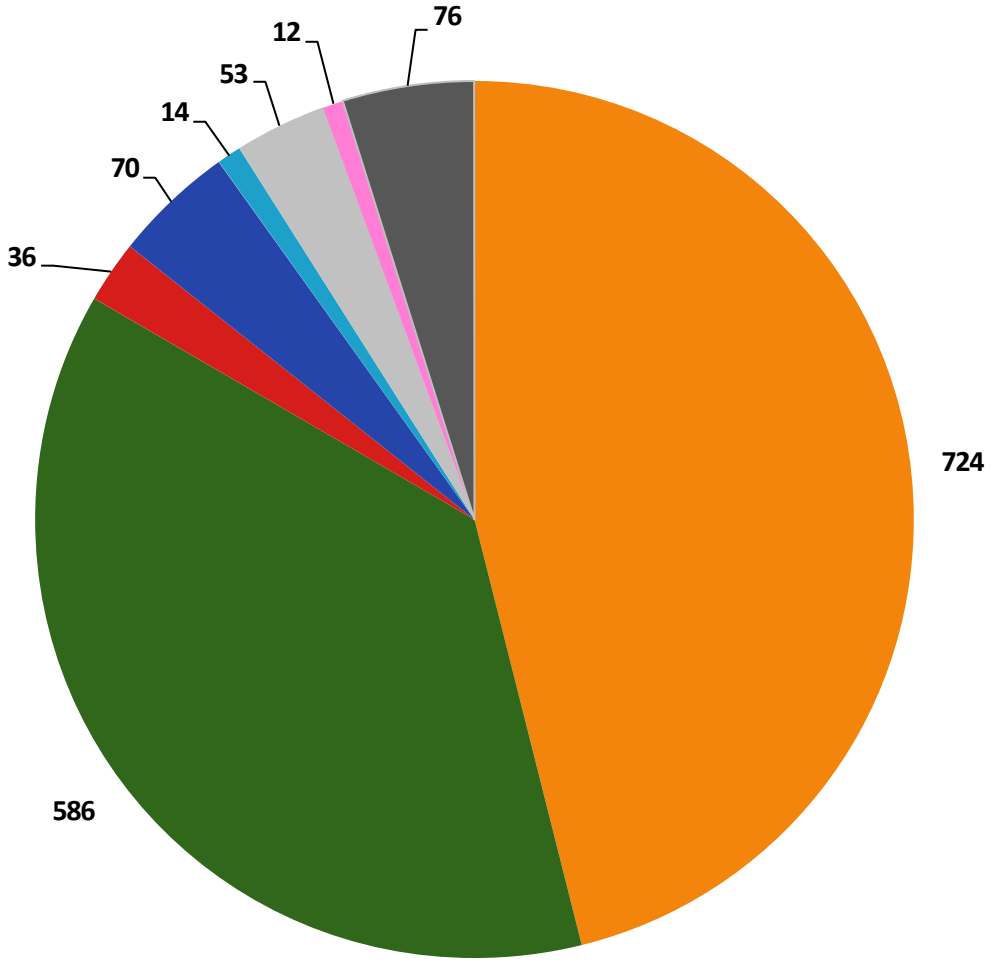
XDRO registry summary, 2014 (cont)

Characteristics of ALL submitted reports	N	%
Type of testing performed*		
1) Molecular test*	397	25
2) Phenotypic test*	751	48
3) Susceptibility test ONLY	449	29
Unknown	29	2
Mechanism of resistance (applies only to reports with molecular test)		
KPC	363	91
NDM	11	3

*≥1 response accepted per isolate

All XDRO reports by region





- City of Chicago
- West Chicago
- Rockford
- Peoria
- Champaign
- Edwardsville
- Marion
- Missing/Unknown

Data from IDPH

XDRO data access for LHDs

- Local health departments
  - Access through I-NEDSS
- E-mail dph.xdroregistry@illinois.gov for user form or questions about access

Lab Validation results, 134 isolates (1/1/15 – 4/25/15)

- 115 (86%) Carbapenemase-producing *Enterobacteriaceae*
  - 111 (97%) KPC PCR+
  - 2 (2%) NDM PCR+
  - 2 (2%) OXA-48-like

- 10 (8%) carbapenem-resistant *Enterobacteriaceae*
  - 9 *Enterobacter* spp, 1 *E. coli*

- 3 (2%) carbapenem-resistant *Acinetobacter*/*Pseudomonas*
- 6 (5%) carbapenem-susceptible *E. coli*

Courtesy of M. Hayden

Lab validation – moving forward

- Current protocol:
  - Send first consecutive CRE isolates of 2015 to IDPH until quota (n=5) met

- Proposed protocol for 2016
  - Send 5 consecutive CRE isolates for 2016
  - For confusing isolates, lab can send an additional 5 CRE isolates

Automated Queries

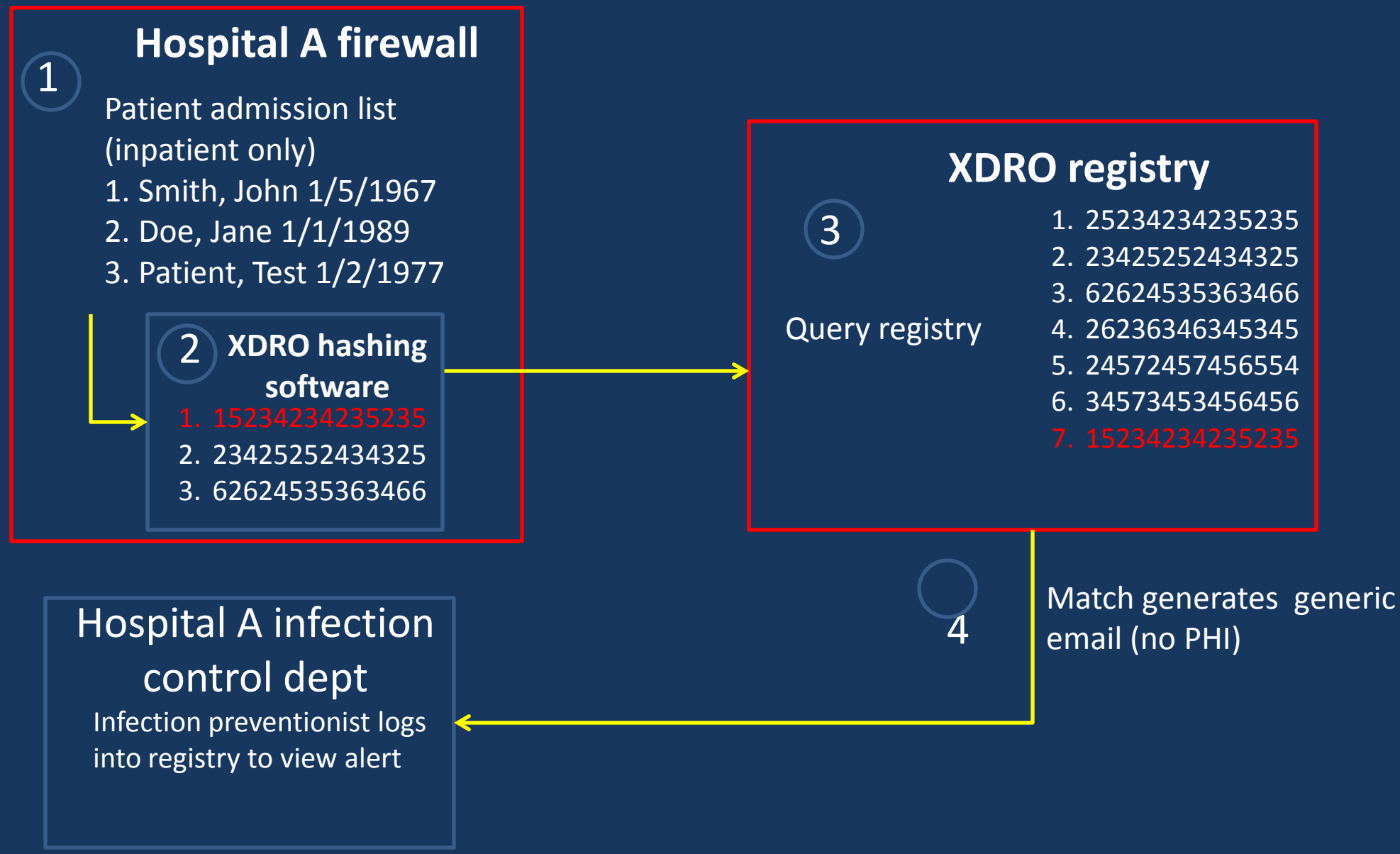
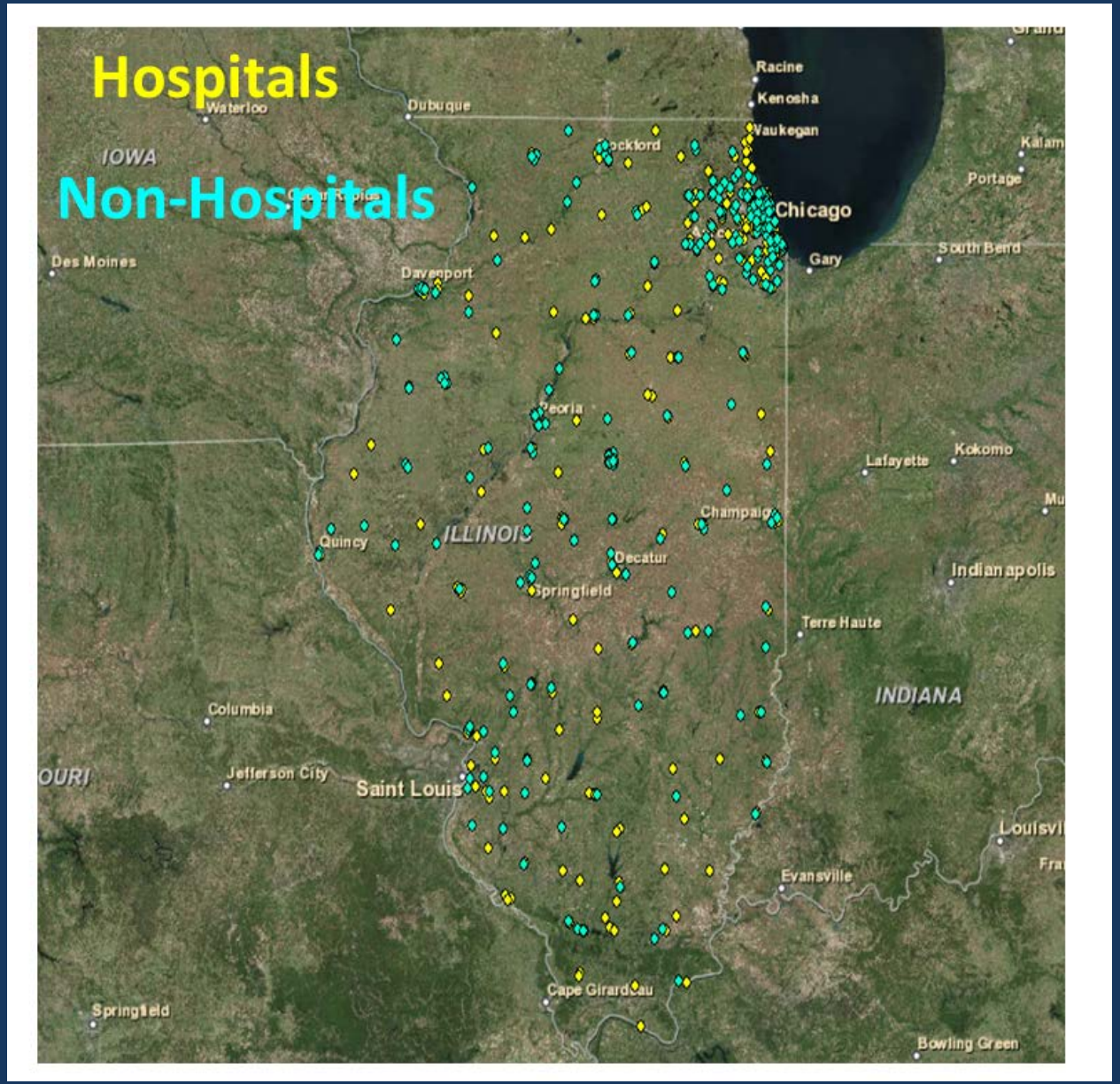


TABLE 1. Compliance with Infection Control Guidelines in 13 Post-Acute Care Hospitals as Noted on 3 Site Visits

Variable	2008	2010	2011	*P*
Infection control consultant	62	85	92	.055
Hand hygiene[22]				
Presence of ABHR in each room	85	92	100	.146
ABHR at site of care	15	54	85	<.001
Presence of antiseptic soap	15	92	85	<.001
Presence of sink in each room	23	31	46	.164
Paper towel availability	69	85	100	.032
Compliance audits	0	46	77	<.001
Appropriate use of barrier precautions in context of standard precautions[23]				
Gloves	31	69	92	.001
Gowns	54	77	77	.208
Masks	38	62	69	.118
CRE prevention program				
Placement of colonized patients in single rooms or cohorting	77	85	100	.082
Use of gown and gloves in contact isolation	46	92	100	.001
Designated medical equipment	92	100	100	.221
Admission screening cultures	15	69	77	.002
Contact screening	38	77	100	.001
Discontinuation of isolation per standard protocol	15	46	100	<.001
Total infection control score (average, out of possible 16)	6.8	11.6	14.0	<.001

NOTE. Data are percentage of compliant hospitals ($n = 13$), unless otherwise indicated. ABHR, alcohol-based hand rub; CRE, carbapenem-resistant Enterobacteriaceae.

Detection of CRE Clusters in Illinois



Summary

- CRE control can be successful
  - Coordinated approach
  - Improve detection and inter-facility communication (XDRO registry)
  - Local action
  - Antibiotic stewardship too!

Thank you

Illinois' Infection Control Community

Illinois Dept. of Public Health
Allison Arwady
Craig Conover
Mary Driscoll
Robynn Leidig
Erica Runningdeer
Michael Ray

Hektoen Institute
Mary Alice Lavin
Angela Tang

Chicago Dept. of Public Health
Stephanie Black
Sarah Kemble

CDC Prevention Epicenter
Wei (Vicky) Gao
Mary Hayden
Michael Lin
Robert Weinstein

CDC
John Jernigan
Alex Kallen

Bad Bugs, No Drugs?

An Ongoing Battle against MDR and XDR Pathogens

Janak Koirala, MD MPH FACP FIDSA
Professor of Medicine and Division Chief
Division of Infectious Diseases
Southern Illinois University School of Medicine

SIU School of Medicine

Disclosures

- **Clinical trials:**
  - Bayer
  - Cempra
  - Insmed
  - Pfizer
  - Theratechnologies

- **Lab research:**
  - MMC Foundation

Objectives

- **Describe significant multidrug resistant (MDR) and extensively drug resistant (XDR) organisms.**
- **Review changing epidemiology of MDR and XDR pathogens and their impact on healthcare.**
- **Discuss prevention and control through implementation of antimicrobial stewardship program and infection control practices.**

“Bad Bugs”

Gram Positive Cocci

- **Enterococci:** ***E. faecalis, E. faecium***

  Vancomycin resistance — ***Example:*** **VRE**

- ***Staphylococcus aureus***

  Oxacillin resistance — ***Example: MRSA***

  Vancomycin resistance — ***Examples:*** **VISA, VRSA**

- ***Streptococcus pneumoniae***

  Penicillin resistance — ***Example:*** **PRSP**

Gram Negative Rods

- **Enterobacteriaeceae**
  - ***Escherichia coli***
  - ***Klebsiella pneumoniae, K. oxytoca***
  - ***Enterobacter cloacae, E. aerogenes***
- ***Pseudomonas aeruginosa***
- ***Acinetobacter baumannii***
- ***Stenotrophomonas maltophilia***
- ***Burkholderia cepacia***

MDR, XDR and PDR Gram Negative Rods

- **Multi-drug resistant (MDR)**

  Resistance to 3 or more classes of antibiotics generally active against GNR including:

  - **Aminoglycosides**
  - **Extended-Spectrum penicillins**
  - **Carbapenems**
  - **Cephalosporins**
  - **Fluoroquinolones**

- **Extensively-drug resistant (XDR)**

  Resistance to all classes of antibiotics except polymyxins

- **Pan-drug resistant (PDR)**

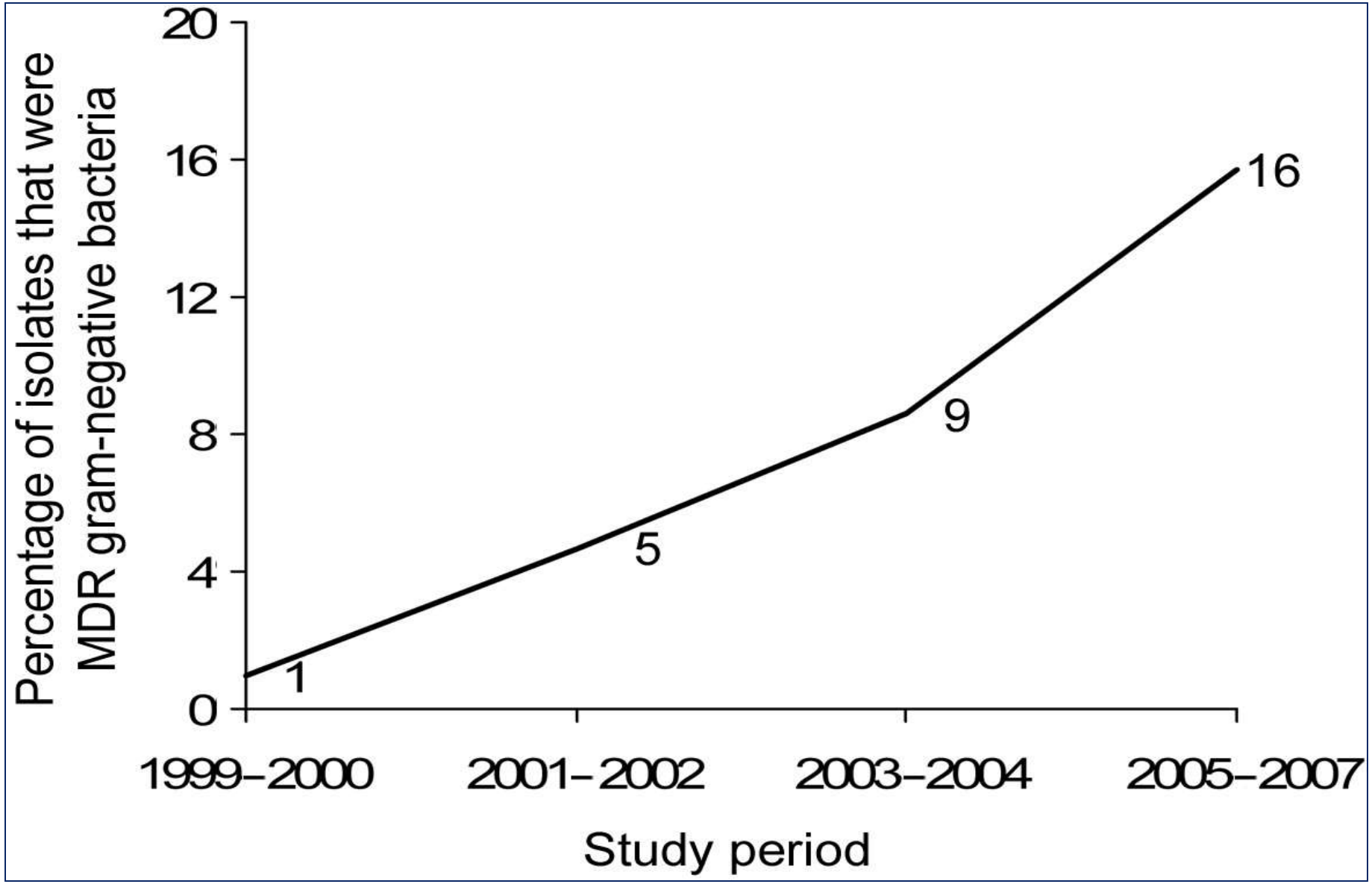
  Resistance to all classes of antibiotics including polymyxins

MDR Gram Negative Infections

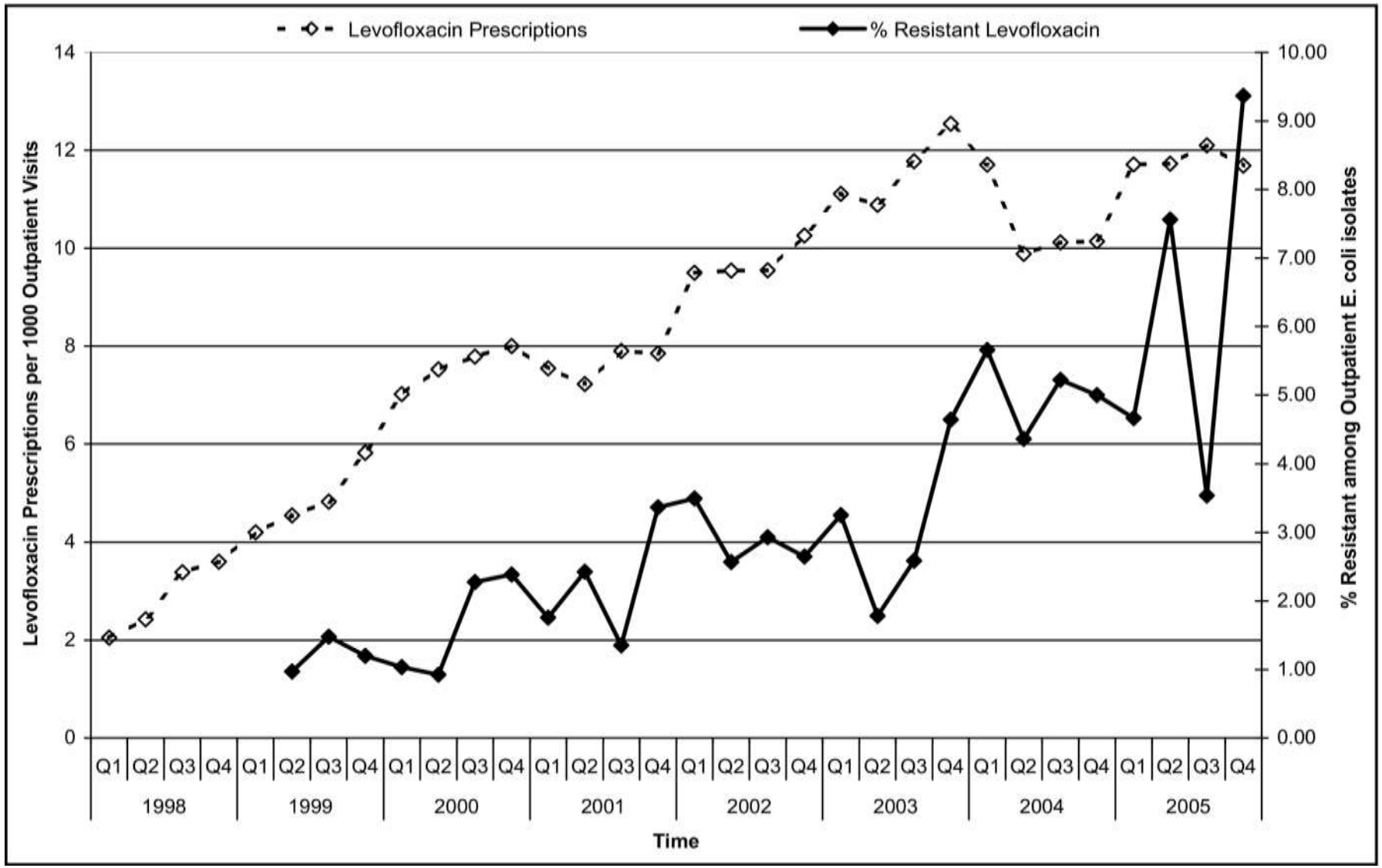
- **Increasing resistance**
  - Extended-spectrum β-lactamase production
  - Carbapenemase production
- **Rising at a steady rate over past decade**
  - One of the biggest challenges of the decade
  - WHO recognizes it as one of the major threats to human health

MDR GNR from bloodstream (within 48 hours)

(Pop-Vicas et al, Infect Control Hosp Epidemiol 2009)

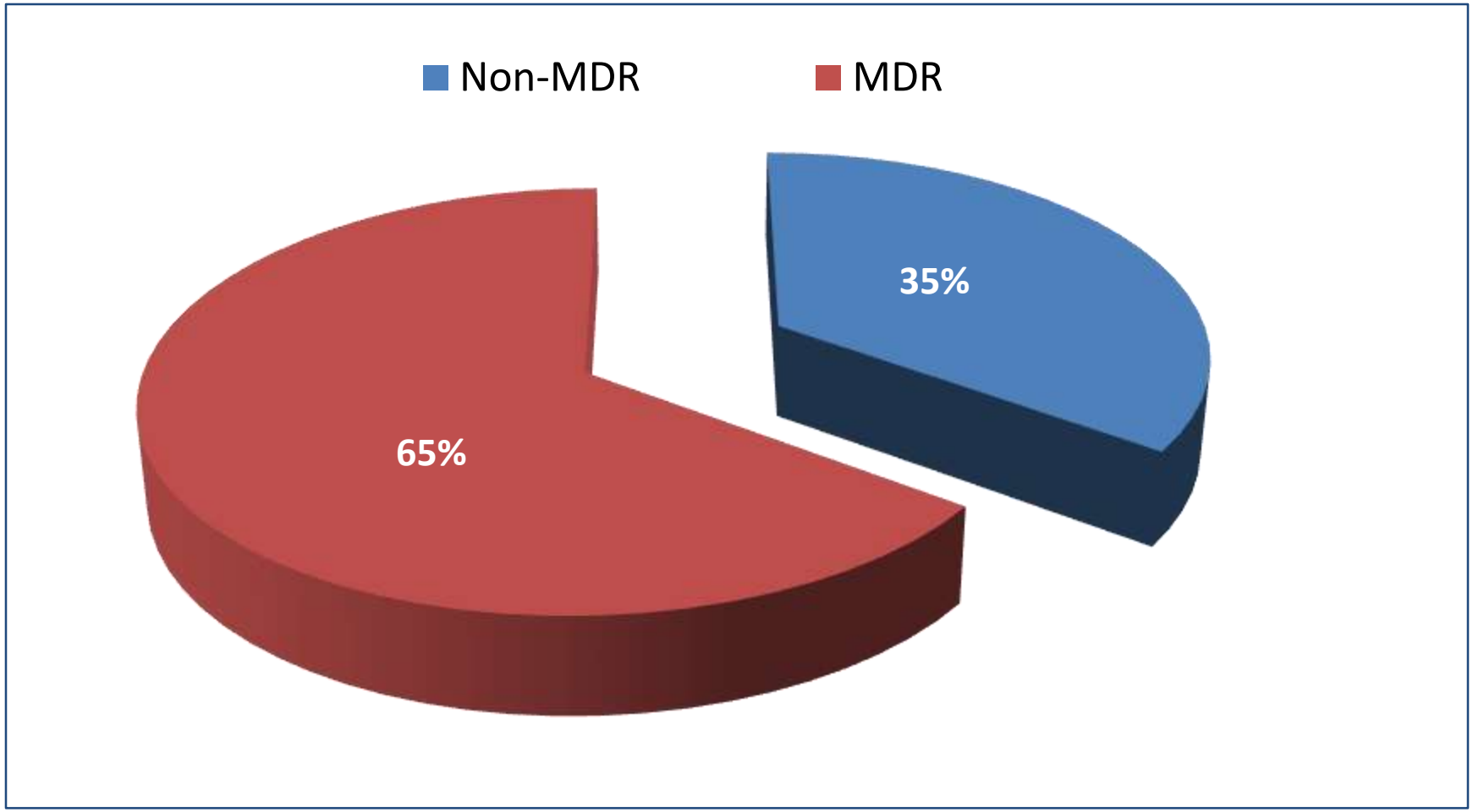


Emergence of Fluoroquinolone Resistance in Outpatient Urinary *E coli Isolates*



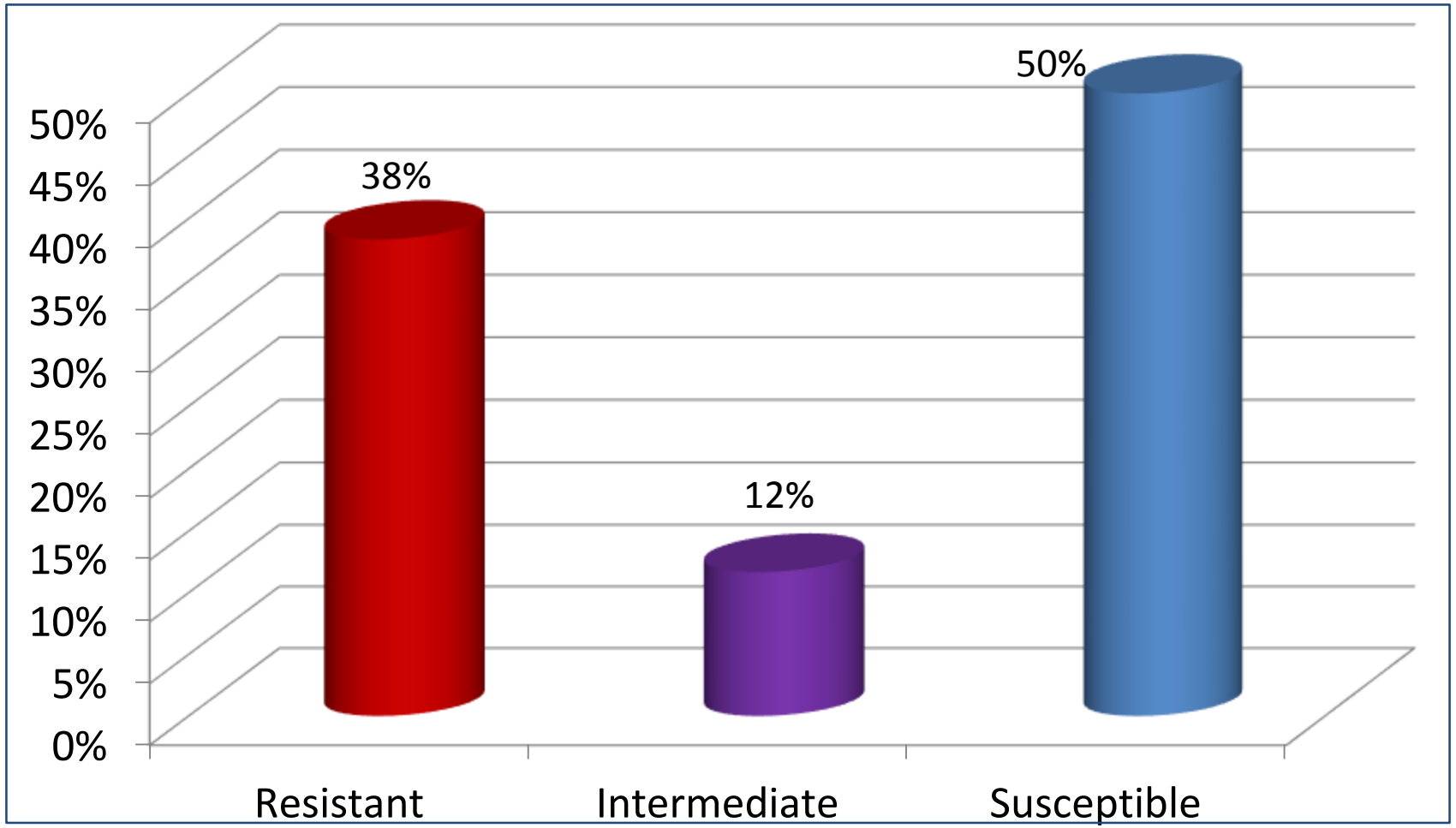
(Luke Johnson et al, Am J Med, Oct 2008)

Distribution of MDR vs. Non-MDR strains of *Acinetobacter baumannii* (N=60)



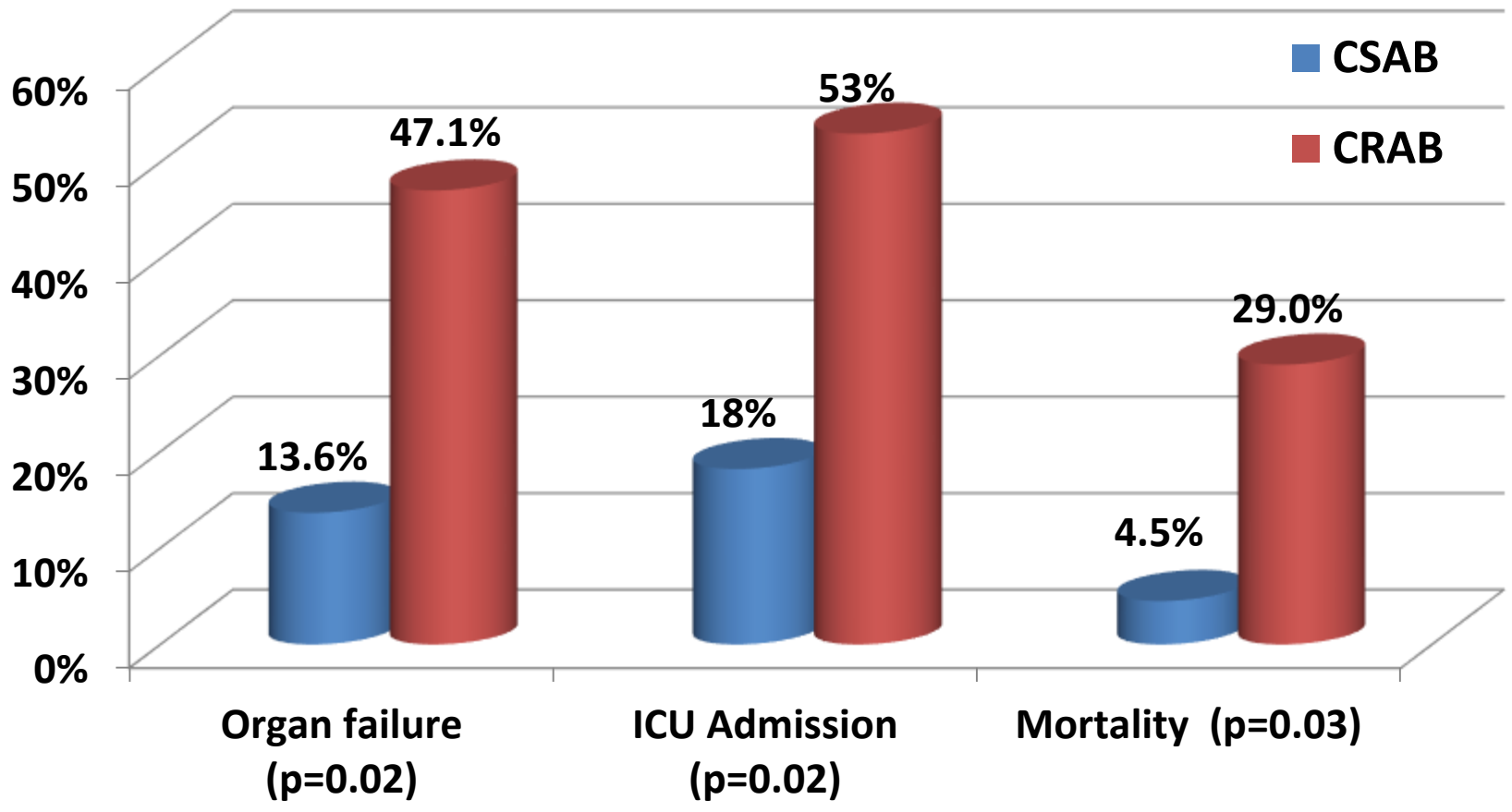
(Tyagi & Koirala, ISID 2010)

Acinetobacter baumannii: Susceptibility to imipenem (N=60)



(Tyagi & Koirala, ISID 2010)

Comparison of clinical outcomes in carbapenem sensitive vs. resistant *A. baumannii* (N=60)



(Tyagi & Koirala, ISID 2010)

Study conclusions

This study confirms that in comparison to the carbapenem-susceptible *A. baumannii* (CSAB), carbapenem-resistant *A. baumannii* (CRAB) infections are significantly associated with:

- severe morbidity
- prolonged hospitalization
- prolonged ICU admissions
- increased mortality

Carbapenem-resistant Enterobacteriaceae (CRE)

- high levels of resistance to antibiotics
- CRE is associated with high mortality rates
  - up to 50% in some studies
- Examples: *E. coli, Klebsiella spp*, *Enterobacter spp*
  - normal gut bacteria
- Infection examples:

Ventilator-associated pneumonia	intubation
Catheter related UTI	urinary catheters
Blood stream infections	IV catheters

Carbapenem-resistant Enterobacteriaceae (CRE) : Previous CDC Definition 2012

- **Nonsusceptible** to one of the following carbapenems: doripenem, meropenem, or imipenem

AND

- **Resistant** to all of the following third-generation cephalosporins: ceftriaxone, cefotaxime, ceftazidime

Note: *This CRE surveillance definition was based upon the 2012 Clinical and Laboratory Standards Institute (CLSI) breakpoints for carbapenems.*

Carbapenem-resistant Enterobacteriaceae (CRE) : Updated CDC Definition 2015

- **Resistant to imipenem, meropenem, doripenem, or ertapenem**

  <u>OR</u>

- **Documentation that the isolate possess a carbapenemase**

<u>Two types based on mechanism</u>

- **CP-CRE:** Production of carbapenemases e.g. KPC, NDM, etc
- **Non-CP-CRE:** mechanisms other than carbapenemase production; such as most commonly- production of beta-lactamases (e.g., AmpC) in combination with alterations in the bacteria's cell membrane (e.g., porin mutations)

Carbapenemases

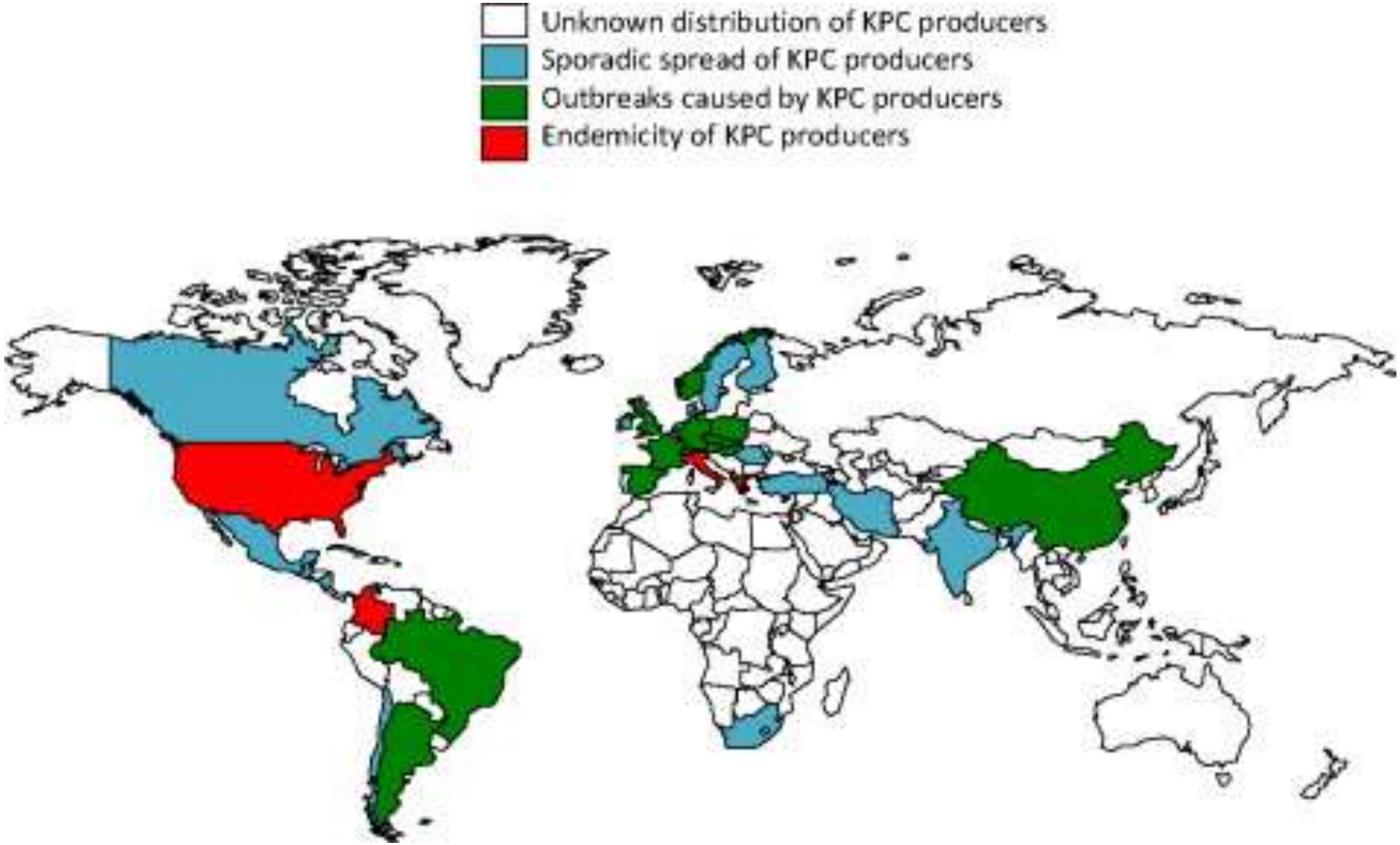
Class	Details
Class A	Inhibited by clavulanic acid, e.g. **KPC**, SME, IMI/NMC-A, GES
Class B	Metallo-enzymes, e.g. IMP (SE Asia), VIM (Europe), **NDM**
Class C	CMY-10
Class D	**OXA**-type

(Source: Gould IM. Int J Antimicrob Agents. 2008 Aug 29)

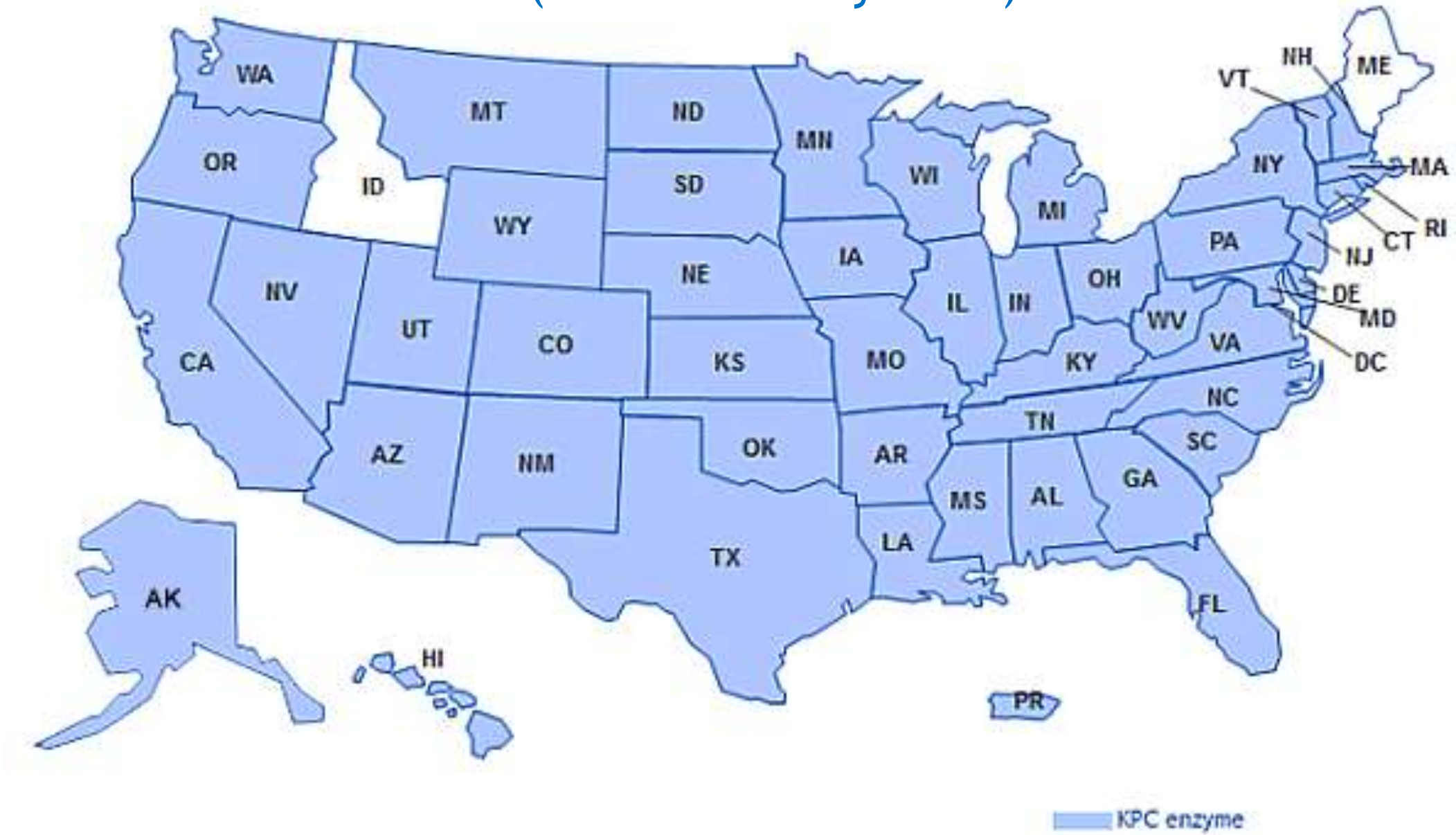
Carbapenemase Examples

- ***Klebsiella pneumoniae* Carbapenemase (KPC)**
  - confers carbapenem resistance
  - often carry genes that confer high levels of resistance to other antimicrobials
  - “Pan-resistant” KPC-producing strains have been reported
  - prevalent in North and South America, Europe (Italy, Greece), Asia (China, Israel)

KPC Distribution: World (Normann, CMI 2014)



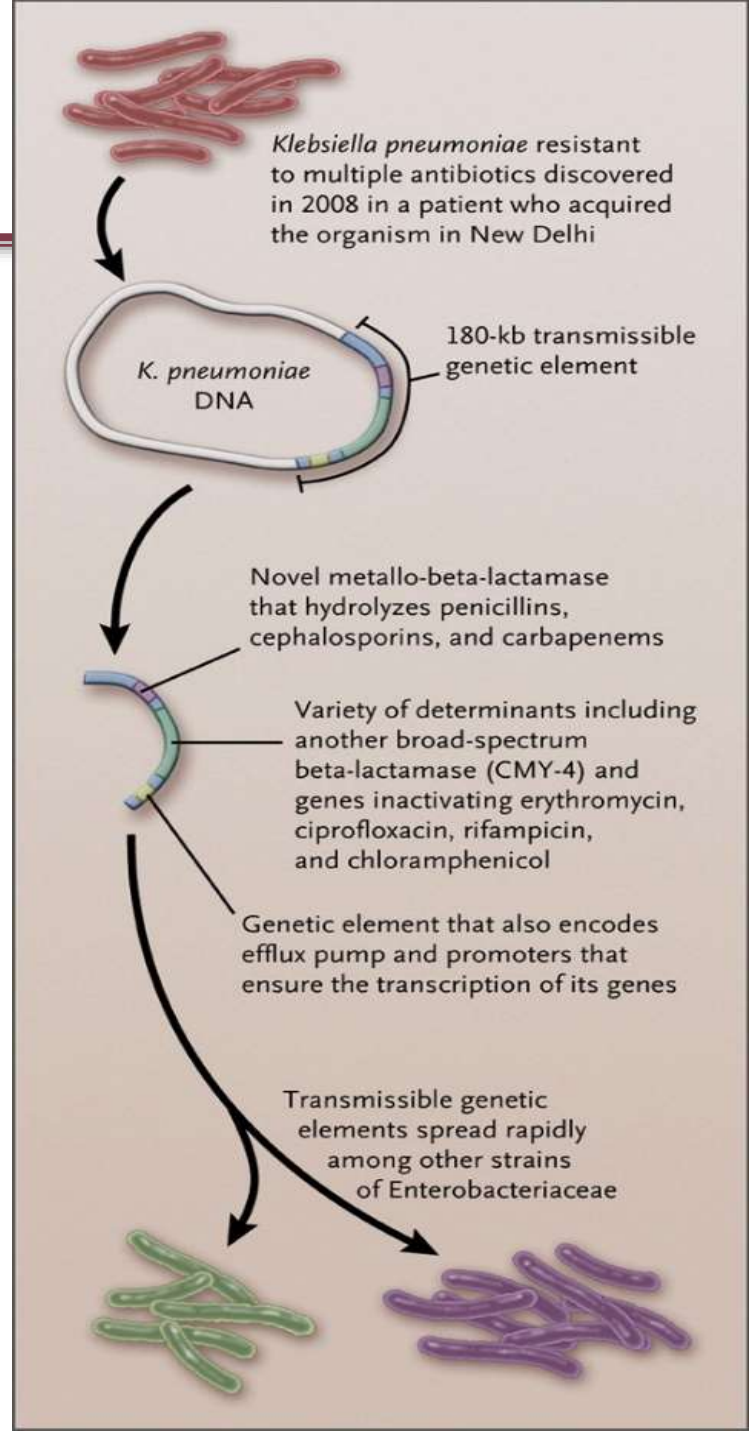
States with KPC-producing CRE isolates reported to the CDC (as of February 2015)



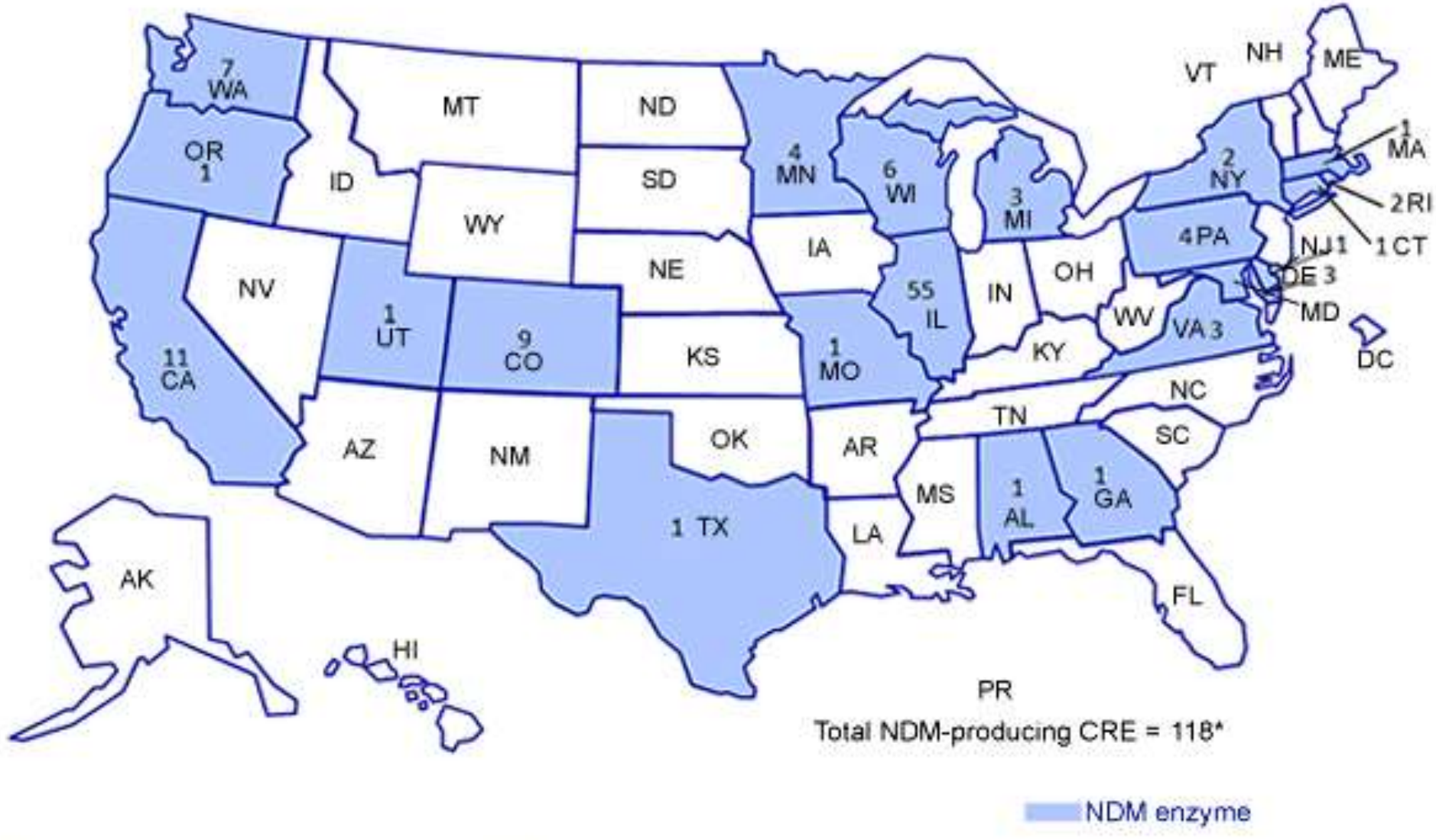
Carbapenemase Examples

- **New Delhi metallo-beta-lactamase (NDM)**
  - First reported in 2008 in a Swedish patient who was previously hospitalized in Delhi
  - Primarily found in Enterobacteriaceae (particularly in *E. coli* and *K. pneumoniae*), and less often in *Acinetobacter* spp.
  - Currently, 12 different variants (NDM-1 to NDM-12)
  - highest incidence in India, Pakistan, China, England, Balkans

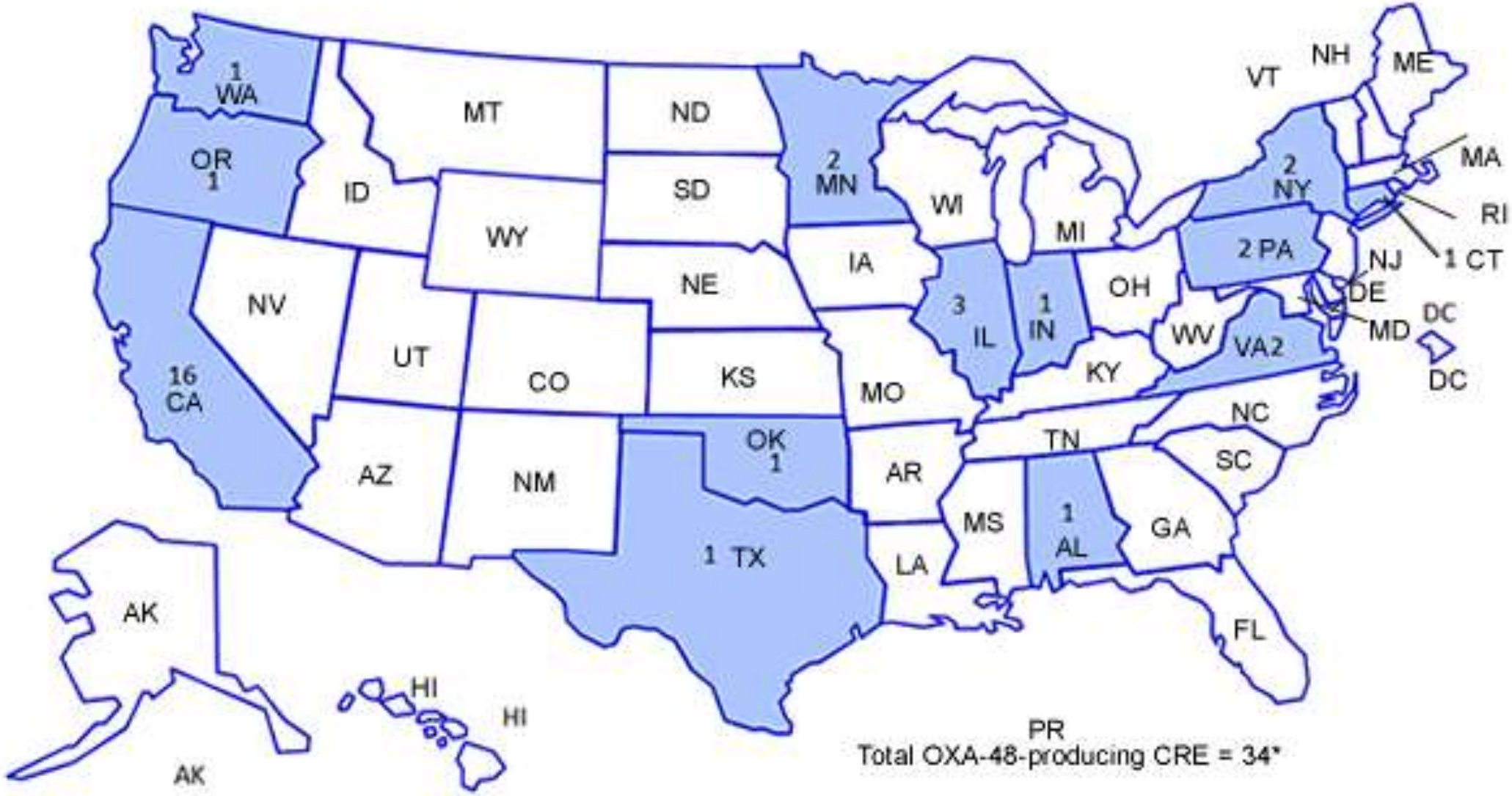
(Moellering RC Jr. , N Engl J Med 2010)



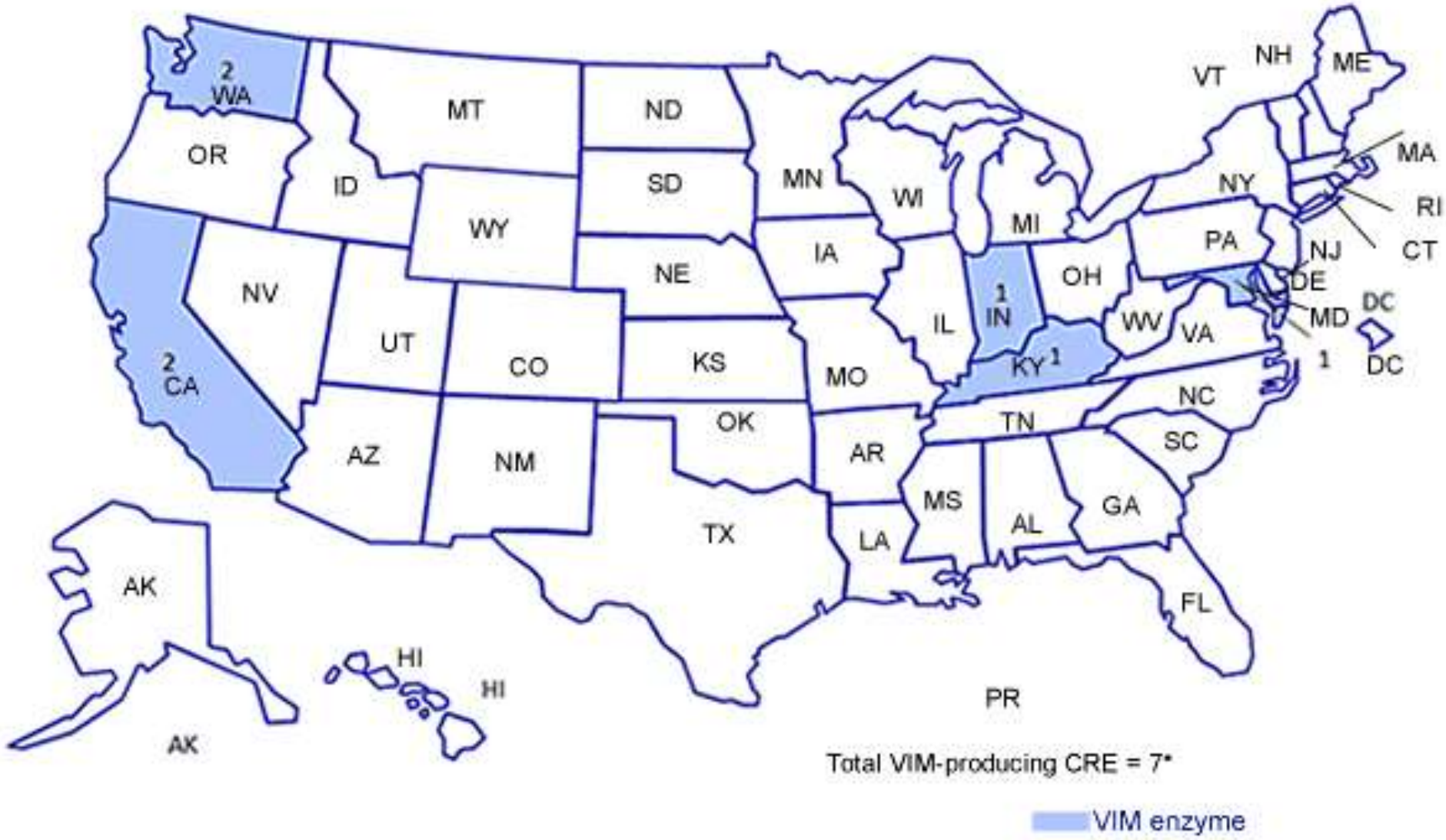
NDM-producing CRE isolates reported to the CDC (as of January 2015, by state)



OXA-48-type carbapenemase producing CRE isolates reported to the CDC (as of January 2015, by state)

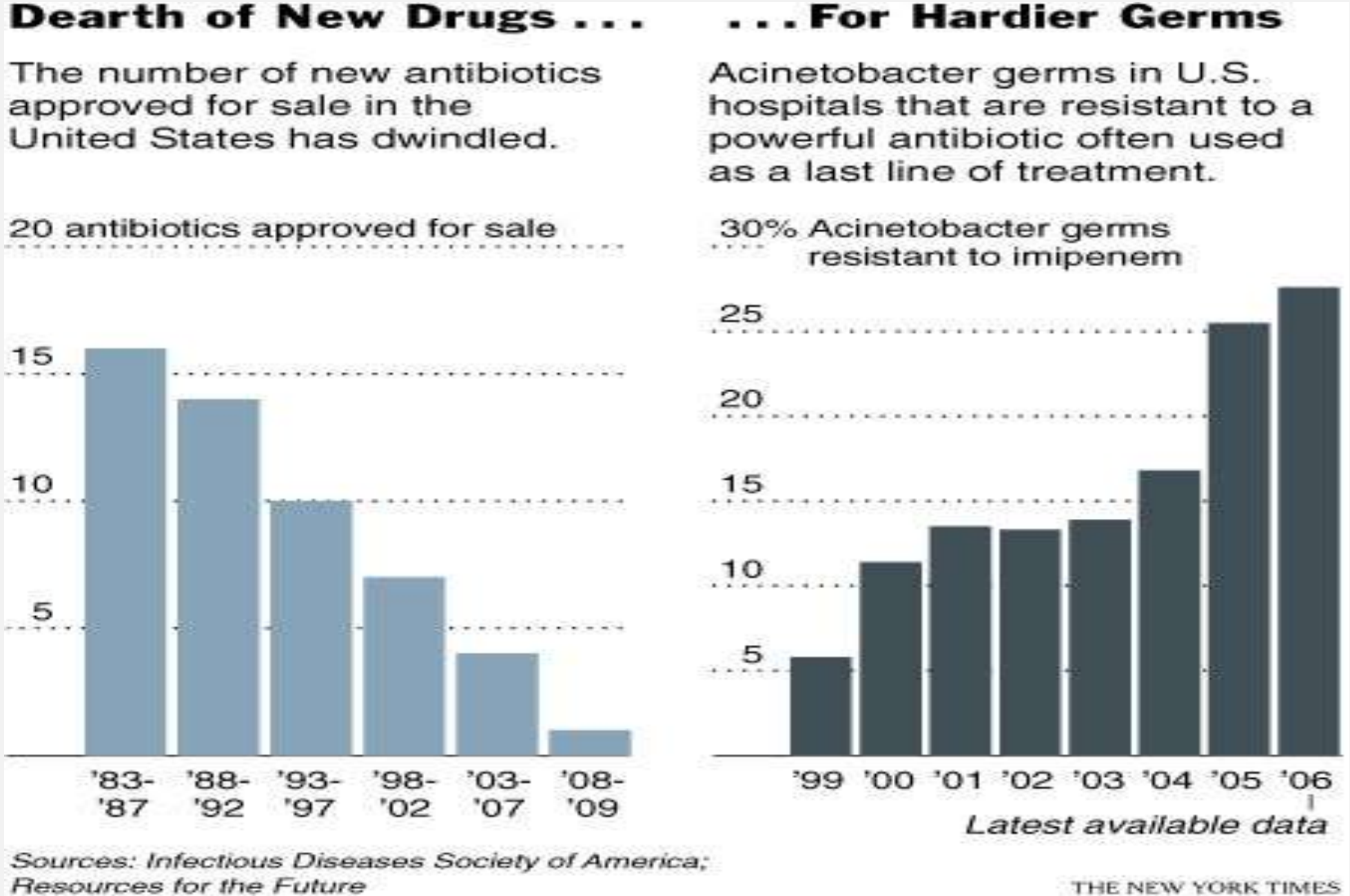


VIM-producing CRE isolates reported to the CDC (as of January 2015, by state)

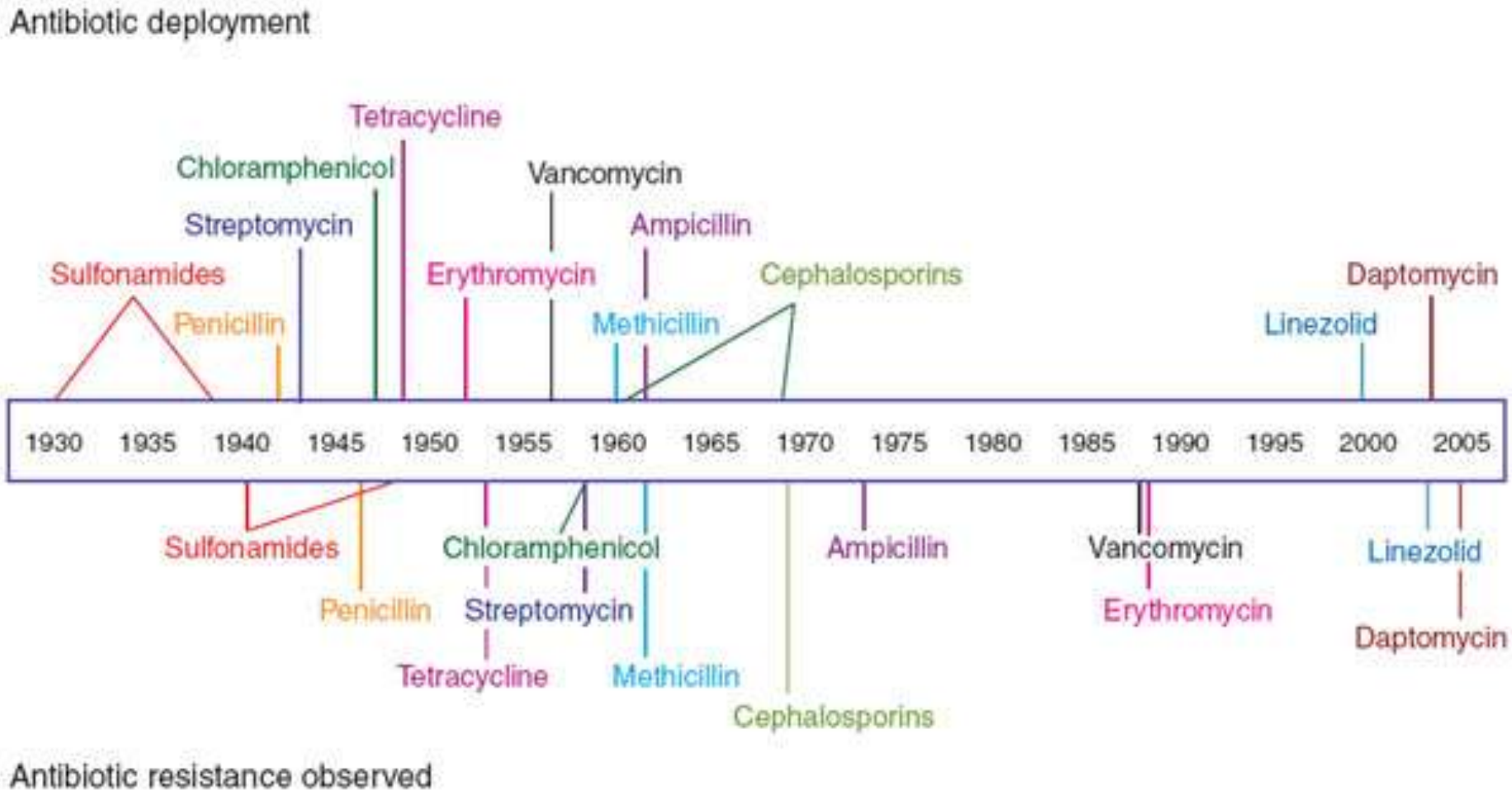


No Drugs?

The New York Times (February 27, 2010)



Antibiotic Resistance Timeline



(Source: Clatworthy, et al. Nature Chemical Biology, 2007)

"Bad Bugs, No Drugs: No ESKAPE!"

- **IDSA Campaign:**

  "As antibiotic discovery stagnates, a public health crisis brews"

- **IDSA's 10 x '20 Initiative:** Challenges scientific community to develop 10 new drugs by 2020 against

  ESKAPE : **E**nterococci
  Staphylococci
  Klebsiella
  Acinetobacter
  Pseudomonas
  Enterobacter

Antimicrobial agents for MDRO: limited options

MDR Organisms	**Treatment options** (examples)
MRSA →**VISA**	vancomycin, linezolid, daptomycin
VRE	linezolid, daptomycin, tigecycline
Klebsiella→**KPC**	ertapenem, ciprofloxacin
Pseudomonas	ciprofloxacin, piperacillin-tazobactam, ceftazidime, cefepime, imipenem, amikacin
Acinetobacter	imipenem, polymyxins
Stenotrophomonas	trimethoprim-sulfamethoxazole

Newer Antibiotics: New classes

- Oxazolidinones: Linezolid, Tedizolid
- Lipopeptide: Daptomycin
- Glycylcycline: Tigecycline
- Lipoglycopeptide: Telavancin
  Dalbavancin, Oritavancin
- Fluroketolide: Solithromycin
- Cephalosporin (5^{th} gen): Ceftaroline

Newer Antibiotics: Older Classes

- Cephalosporins+BLI: Ceftazidime+avibactam
  Ceftolozane+Tazobactam
- Lipid Aminoglycosides: Liposomal Amikacin (inhalational)

“How can we improve use of antibiotics and slow down resistance?”

Healthcare Associated Infection
Risk factors

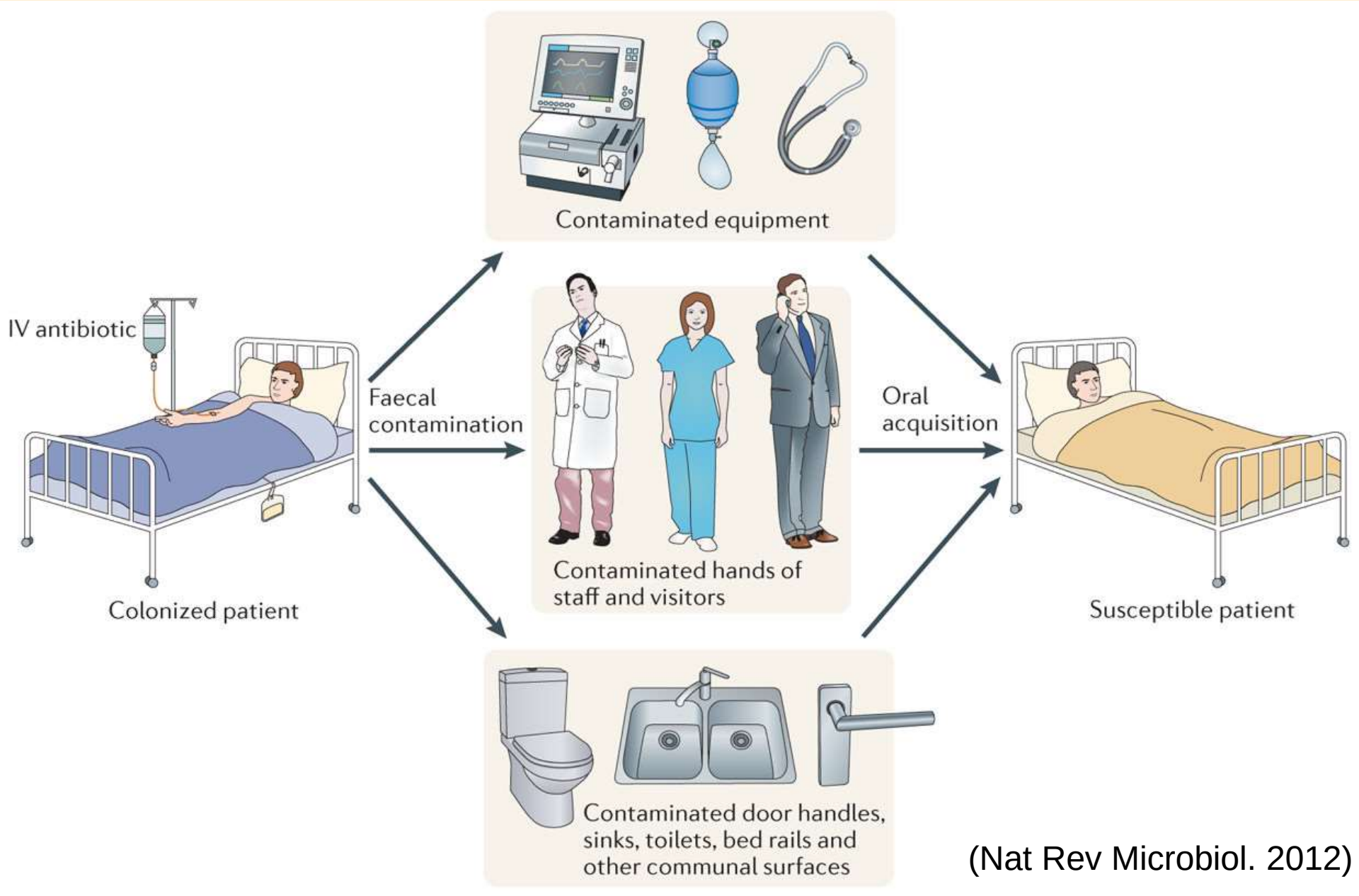
- Surgical procedures
- Injections: intravascular, intra-articular, intrathecal, etc
- Contamination of the healthcare environment
- Transmission between patients and HCWs
- Overuse or improper use of antibiotics

Transmission

- MDROs are carried from one person to another via the hands of health care personnel
- Hands are easily contaminated during the process of care-giving or from contact with environmental surfaces in close proximity to the patient.

  For example:
  - Patients may have diarrhea and the reservoir of the MDRO is the gastrointestinal tract
  - Patients bed sheet, surfaces of the bed rails, and surfaces of the furniture in the room may have microorganisms

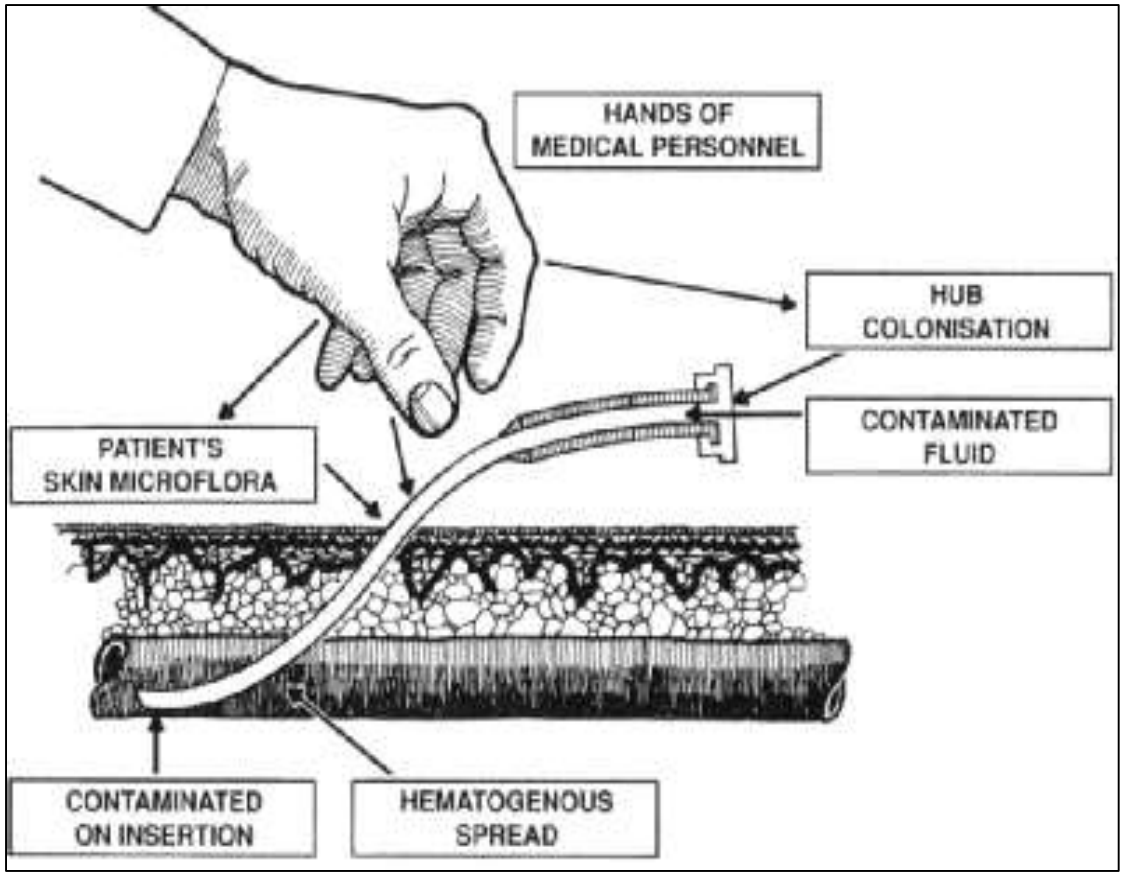
Nosocomial Transmission



(Nat Rev Microbiol. 2012)

Healthcare Associated Infection
Risk factors

- Use of indwelling medical devices
  - Bloodstream catheters
  - Urinary catheters
  - Endotracheal tube
  - Prosthetic joints
  - Prosthtic valves
  - Implant devices: pacemaker, AICD, shunts, pumps, etc.



Rapid global dissemination of CRE genes

Attributed to a combination of 3 major social and microbiological mechanisms:

- international travel
- patient-to-patient transmission
- interspecies transfer of resistant genes; e.g.

  KPC resistance elements are often flanked by transposons and are carried on transferable plasmids of GNRs

  Many plasmids that carry KPC resistance elements concurrently carry other plasmid-mediated resistance elements, such as quinolone (QnrA and QnrB) and aminoglycoside (rmtB) resistance

MDRO Prevention Strategies

Four parallel strategies:

- Infection prevention
- Prompt diagnosis and treatment
- Prudent use of antimicrobials
- Prevention of transmission

CRE Prevention Strategies: Core Measures (CDC 2012)

1. Hand hygiene

Promote hand hygiene

Monitor hand hygiene adherence and provide feedback

Ensure access to hand hygiene stations

CRE Prevention Strategies: Core Measures (CDC 2012)

2. Contact Precautions

Acute care

Place CRE colonized or infected patients on Contact Precautions (CP)

Preemptive CP might be used for patients transferred from high-risk settings

Educate healthcare personnel about CP

Monitor CP adherence and provide feedback

Develop lab protocols for notifying clinicians and IP about potential CRE

Long-term care

Place CRE colonized or infected residents that are high-risk for transmission on CP

For patients at lower risk for transmission, use Standard Precautions

CRE Prevention Strategies: Core Measures (CDC 2012)

3. Patient and staff cohorting

When available cohort CRE colonized or infected patients and the staff that care for them even if patients are housed in single rooms

If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence)

4. Minimize use of invasive devices

5. Laboratory notification

CRE Prevention Strategies: Core Measures
(CDC 2012)

6. Promote antimicrobial stewardship

7. Screening

Screen patient with epidemiologic links to unrecognized CRE colonized/infected patients

Conduct point prevalence surveys of units containing unrecognized CRE patients

8. Healthcare personnel education

CRE Prevention Strategies (CDC 2012)
Supplemental Measures for facilities with CRE transmission

1. Conduct active surveillance testing

Screen high-risk patients at admission and periodically during their facility stay for CRE

Preemptive CP can be used while results of admission surveillance testing are pending

Consider screening patients transferred from facilities known to have CRE at admission

2. Chlorhexidine bathing

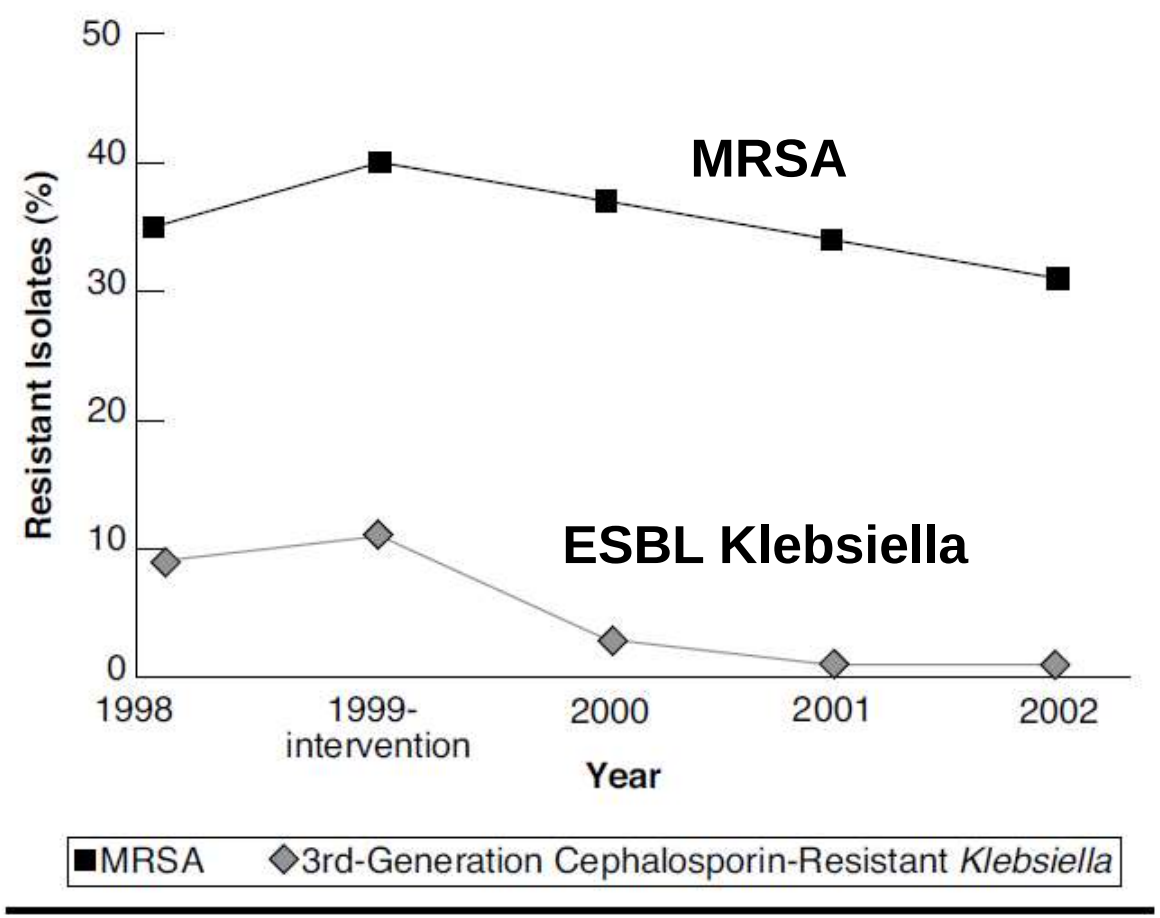
Bathe patients with 2% chlorhexidine

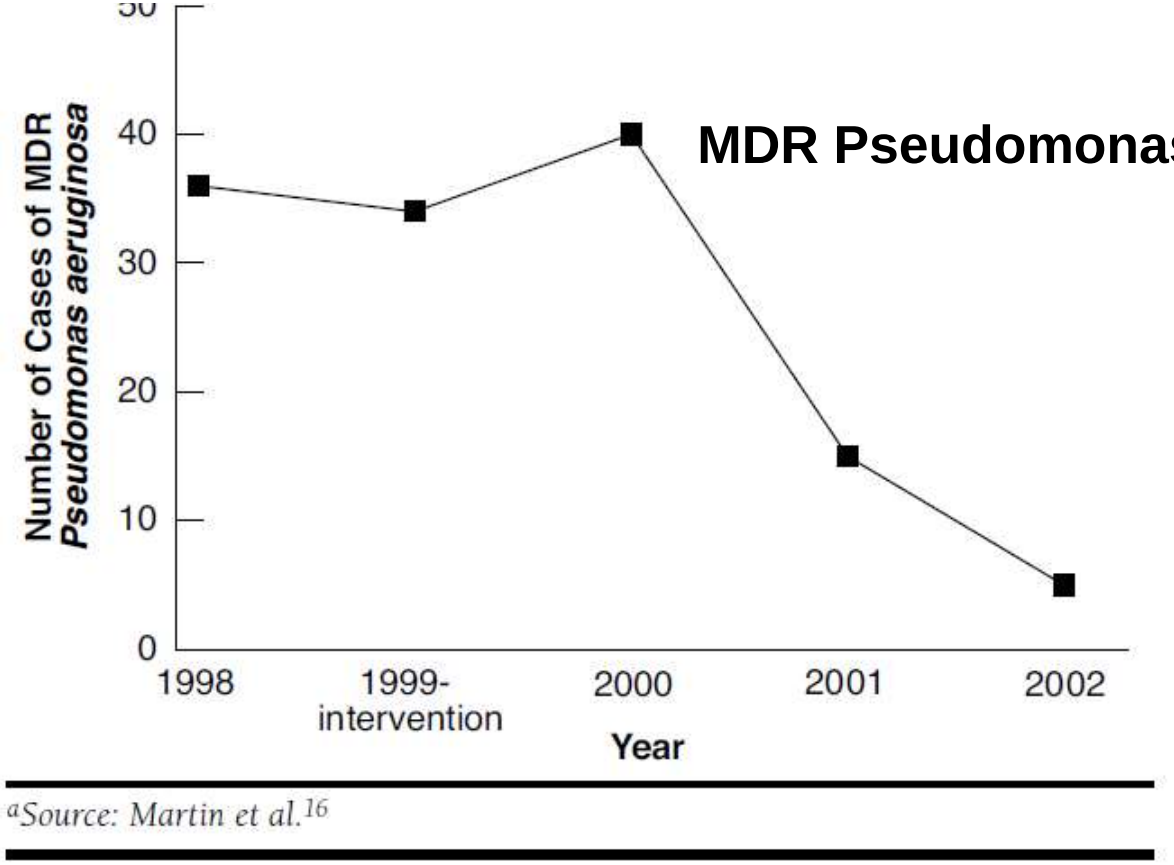
Antibiotic Stewardship

1. Appropriate antimicrobial agent, correct dose & right duration
   - **Four Ds of optimal antimicrobial therapy:**

     right **D**rug, right **D**ose, right **D**uration, **D**e-escalation
2. Prevention of antimicrobial overuse, misuse & abuse
3. Minimize antimicrobial usage to prevent emergence of resistance
4. Switch intravenous antibiotics to oral
5. Develop protocols and guidelines

Impact of Formulary Restriction and Pre-Authorization on MRSA, ESBL Klebsiella, and MDR Pseudomonas

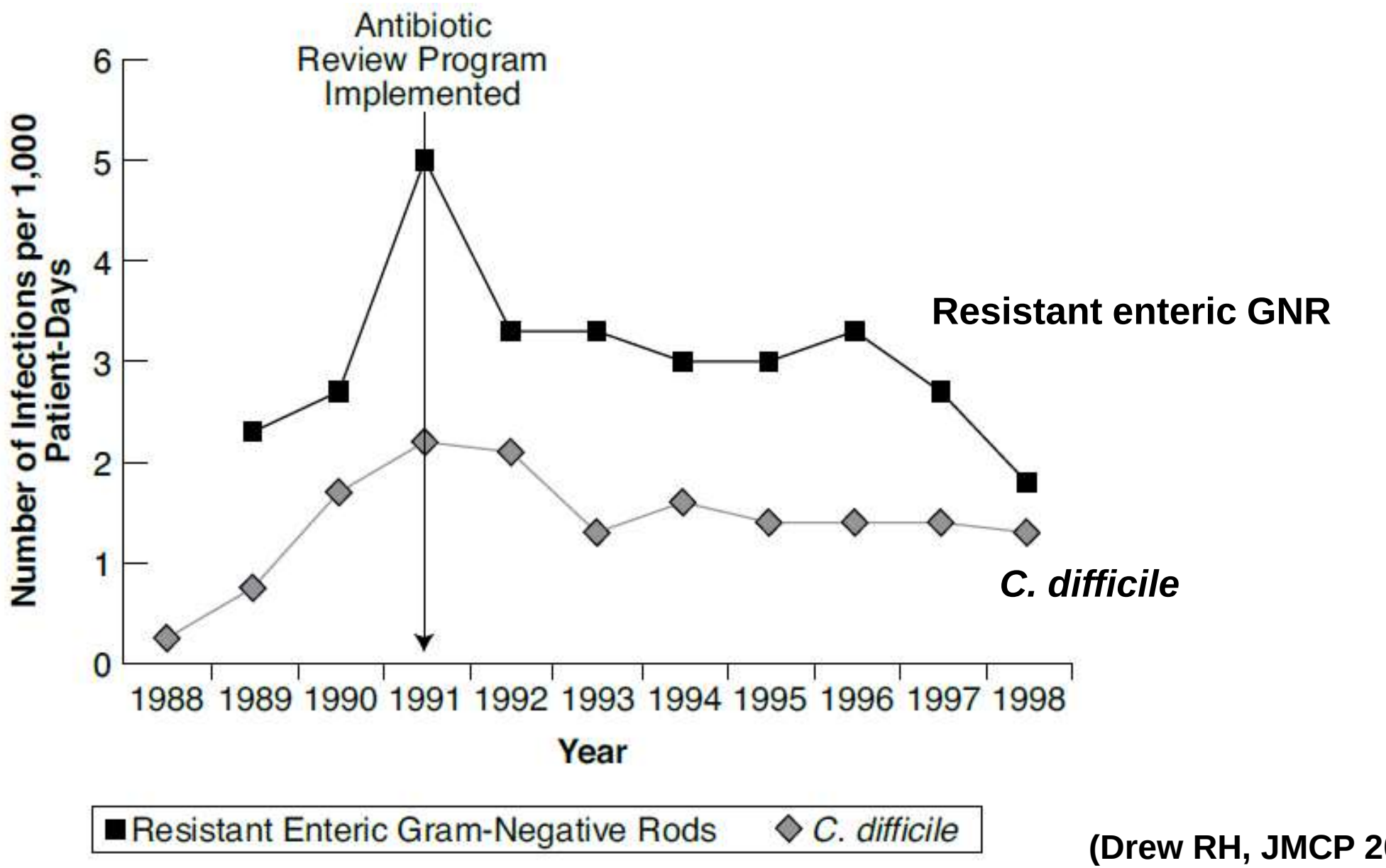




[a]Source: Martin et al.[16]

(Drew RH, JMCP 2009)

Impact of Prospective Audit with Intervention and Feedback



(Drew RH, JMCP 2009)

MDRO Control interventions

Environmental measures

- The potential role of environmental reservoirs, such as surfaces and medical equipment, in the transmission of VRE and other MDROs has been the subject of several reports
- A common reason for finding environmental contamination with an MDRO is the lack of adherence to facility procedures for cleaning and disinfection
- Strategies may include:
  - use of dedicated noncritical medical equipment
  - assignment of dedicated cleaning personnel to the affected patient care unit
  - increased cleaning and disinfection of frequently-touched surfaces; e.g., bedrails, charts, bedside commodes, doorknobs, etc.

WAAAR: World Alliance Against Antimicrobial Resistance

1. Awareness of all stakeholders, including the general public
2. Organization of a financed national plan for containment of resistance in every country
3. Permanent access to antibiotics of assured quality
4. Cautious, controlled, and monitored usage of antibiotics
5. Infection prevention
6. Use of diagnostic tests
7. Education and information
8. Surveillance of consumption of and resistance to antibiotics
9. Promotion of basic and applied research for development of new drugs
10. Inclusion of antibiotics in the UNESCO's intangible cultural heritage

Concluding Remarks

- ✓ MDR and XDR GNRs are becoming increasingly common pathogens in the healthcare environment
- ✓ CRE are a real major threat for causing potentially deadly outbreaks in healthcare institutions and communities
- ✓ There is a gap in innovation and discovery of new antibiotics
- ✓ It is important to have a planned, controlled, and monitored usage of antibiotics through antibiotic stewardship programs in both inpatient and outpatient settings
- ✓ An effective infection prevention program plays the most vital role to control these pathogens

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Detect and Protect – Establishing an Infection Prevention and Control Plan for Carbapenem Resistant Enterobacteriaceae

Mary Alice Lavin, RN, MJ, CIC

Hektoen Institute, LLC

July 28, 2015

Disclosures

- This presentation was developed in conjunction with the Illinois Department of Public Health. The opinions, viewpoints, and content may not necessarily represent the position of the Illinois Department of Public Health.

- I have nothing to disclose.

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Objectives

- List proactive interventions for preventing and controlling Carbapenem Resistant Enterobacteriaceae.
- Identify the components of a Carbapenem Resistant Enterobacteriaceae risk assessment.
- Describe the steps to take following identification of a patient with Carbapenem Resistant Enterobacteriaceae.

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Key Elements - 2012

- Recognizing Carbapenem Resistant Enterobacteriaceae (CRE) are epidemiologically important
- Understanding the prevalence in the region
- Identifying colonized and infected patients when they present to the facility
- Implementation of regional and facility based interventions for control

http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html

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Core Interventions

(AKA - Back to the Basics)

- Hand Hygiene
- Contact Precautions
- Healthcare Worker Education
- Appropriate Device Use
- Cohorting
- Lab Notification
- Antimicrobial Stewardship
- Screening epidemiologically linked contacts
- Interfacility Communication

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Core Interventions

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Supplemental Interventions

- Active surveillance testing
- Chlorhexidine bathing
  - 51% decrease in *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae (P<.001)
    - Effectiveness may vary by skin site
    - Patients with diarrhea had an increased risk for inguinal colonization
    - Patients with a tracheostomy were colonized at the neck
    - Gently but firmly scrubbing with a CHG cloth for 20 seconds may be necessary for CHG bathing to be an effective component of a control program

Lin, Michael Y., et al. The effectiveness of routine daily chlorhexidine gluconate bathing in reducing Klebsiella pneumoniae Carbapenemase–producing Enterobacteriaceae skin burden among long term acute care hospital patients. Infect Control Hosp Epidemiology 2014;35(4): 440-442.

Proactive Interventions

- Aggressive control
  - Retrospective lab review for missed cases
    - Point prevalence surveys
  - Proactive screening of certain patient populations at admission
    - Presumptive Contact Precautions

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Key Elements - 2013

- Supplemental testing for CRE identified in a patient who had an overnight stay in a healthcare facility outside the United States

- Consideration for performing rectal screening cultures on patients who received care in a healthcare facility outside of the United States and isolating them until results are available

http://emergency.cdc.gov/han/han00341.asp

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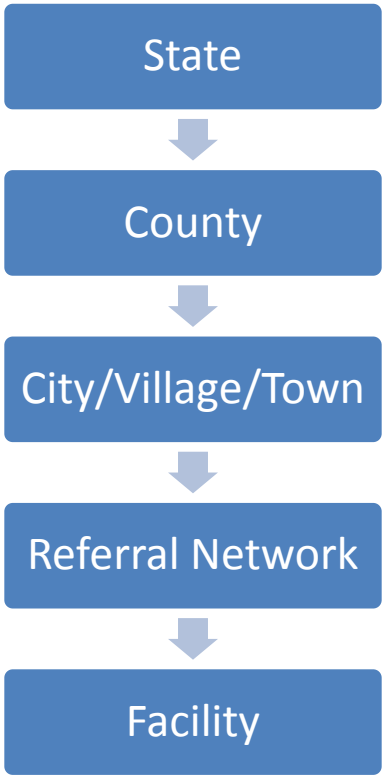
Risk Assessment



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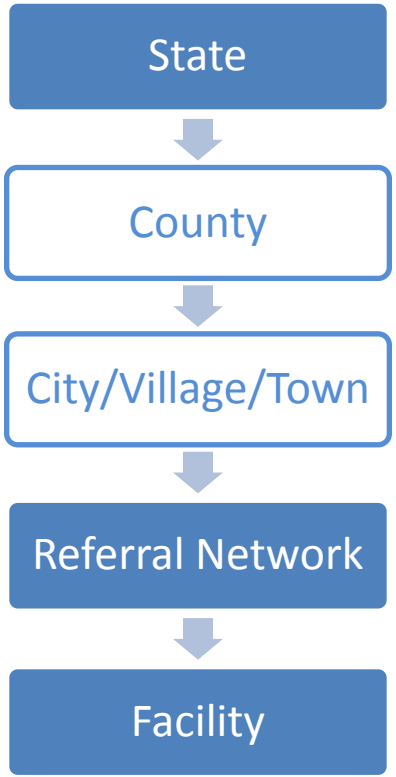
Risk Assessment



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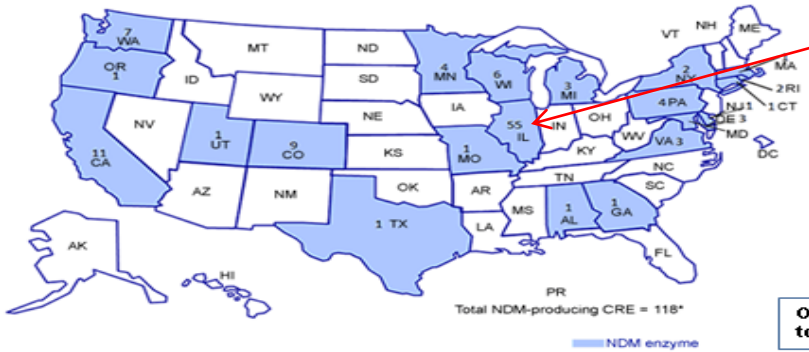
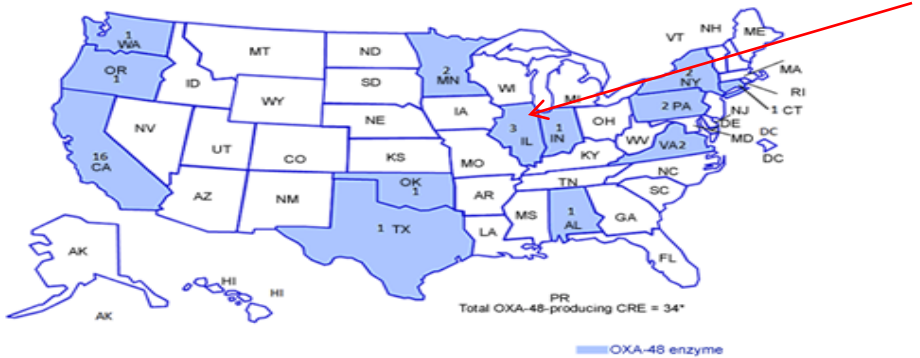
State

NDM-producing Carbapenem-resistant Enterobacteriaceae (CRE) isolates reported to the Centers for Disease Control and Prevention (CDC) as of January 2015, by state



This map was last updated on January, 2015

OXA-48-Type-producing Carbapenem-resistant Enterobacteriaceae (CRE) isolates reported to the Centers for Disease Control and Prevention (CDC) as of January 2015, by state



This map was last updated on January, 2015

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

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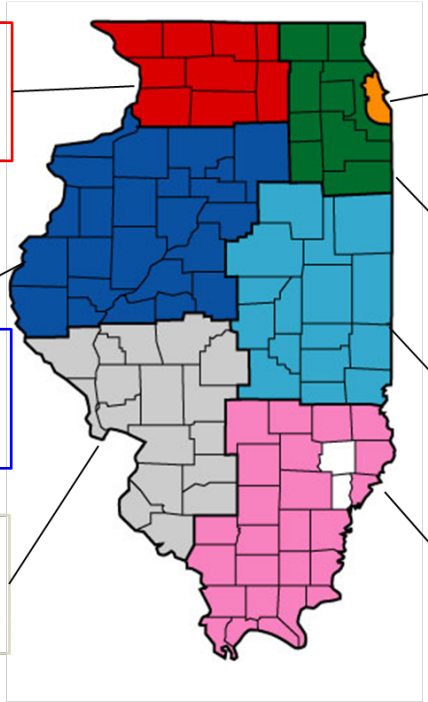
State

All XDRO reports by IDPH region, 2014
N=1,571



Rockford
(n=36; 2%)

Chicago
(n=724; 46%)

West Chicago
(n=586; 37%)

Peoria
(n=70; 4%)

Champaign
(n=14; 1%)

Edwardsville
(n=53; 3%)

Marion
(n=12; 1%)

Unknown/missing (n=76; 5%)

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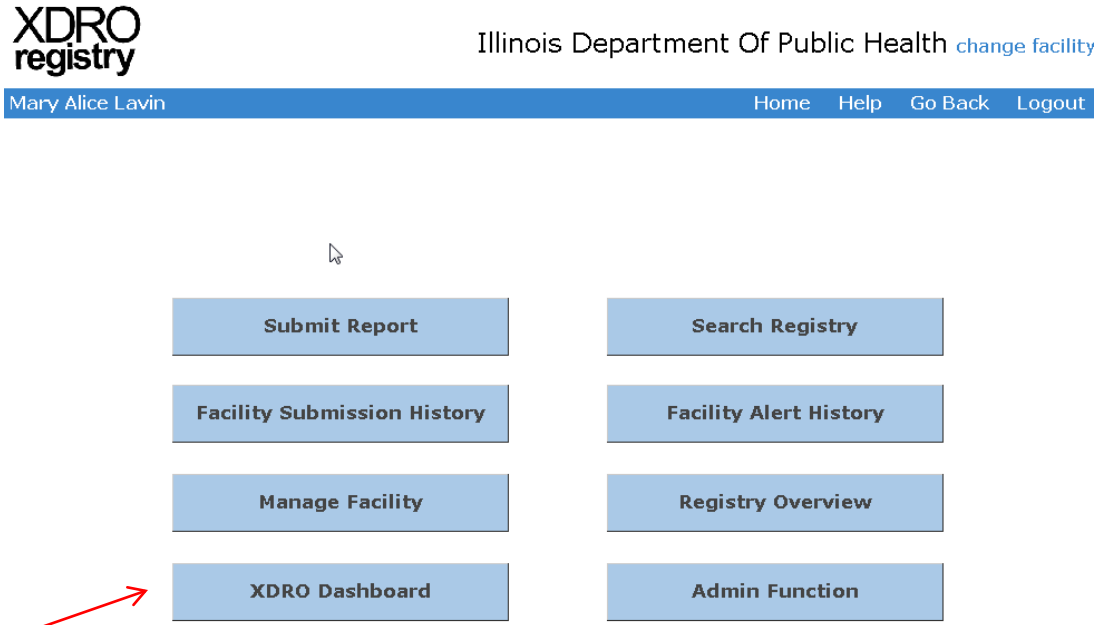
State



https://www.xdro.org/index.html

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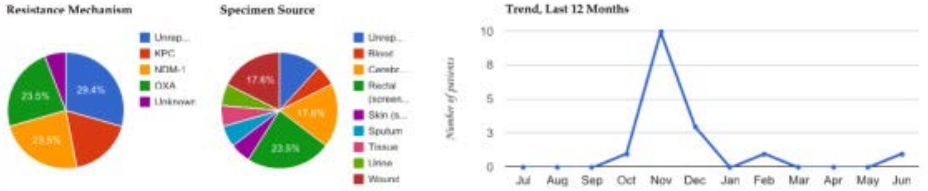
State

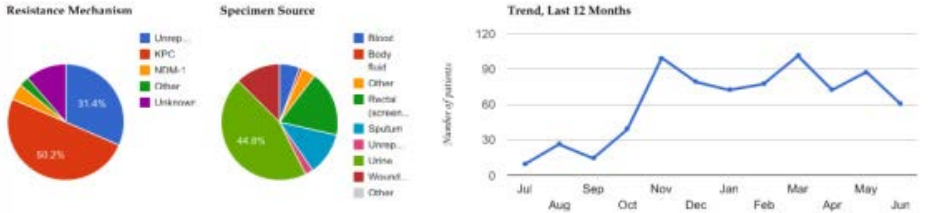
XDRO Report

Facility Data [a]



Entire Dataset

State Data [b]



Entire Dataset

a: The facility level report removes all duplicates regardless of time. A duplicate is defined at the level of the patient and facility, using the patient's first name, last name, and date of birth.

b: The state level report removes all duplicates regardless of time and facility. A duplicate is defined at the level of the patient, using the patient's first name, last name, and date of birth.

https://www.xdro.org/index.html

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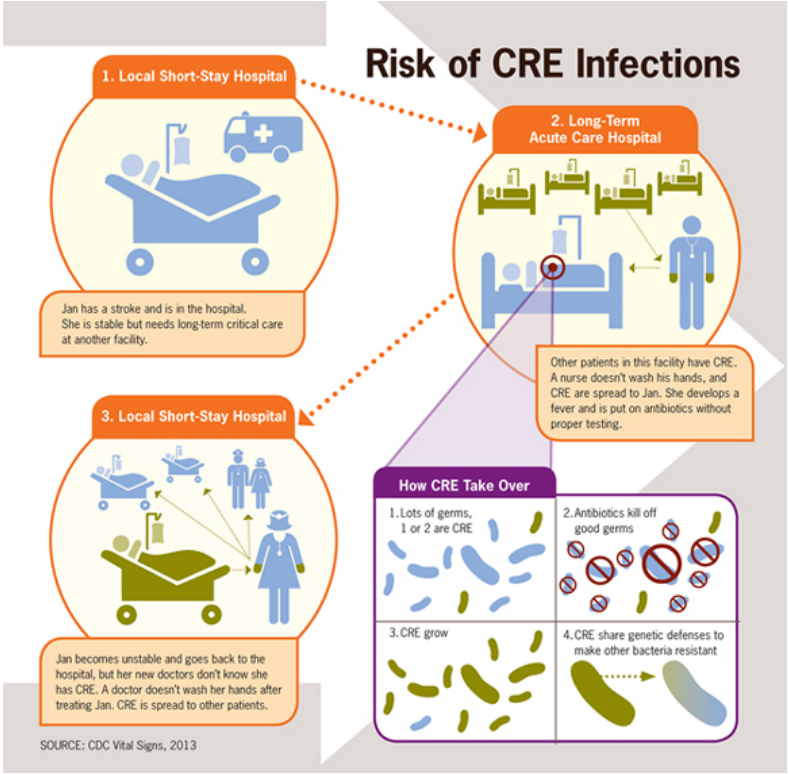
Referral Network



Additional reading:

Lin, Michael Y., et al. "The importance of long-term acute care hospitals in the regional epidemiology of Klebsiella pneumoniae Carbapenemase–producing Enterobacteriaceae." *Clinical infectious diseases* (2013).

Won, Sarah Y., et al. "Emergence and rapid regional spread of Klebsiella pneumoniae carbapenemase–producing Enterobacteriaceae." *Clinical infectious diseases* 53.6 (2011): 532-540.

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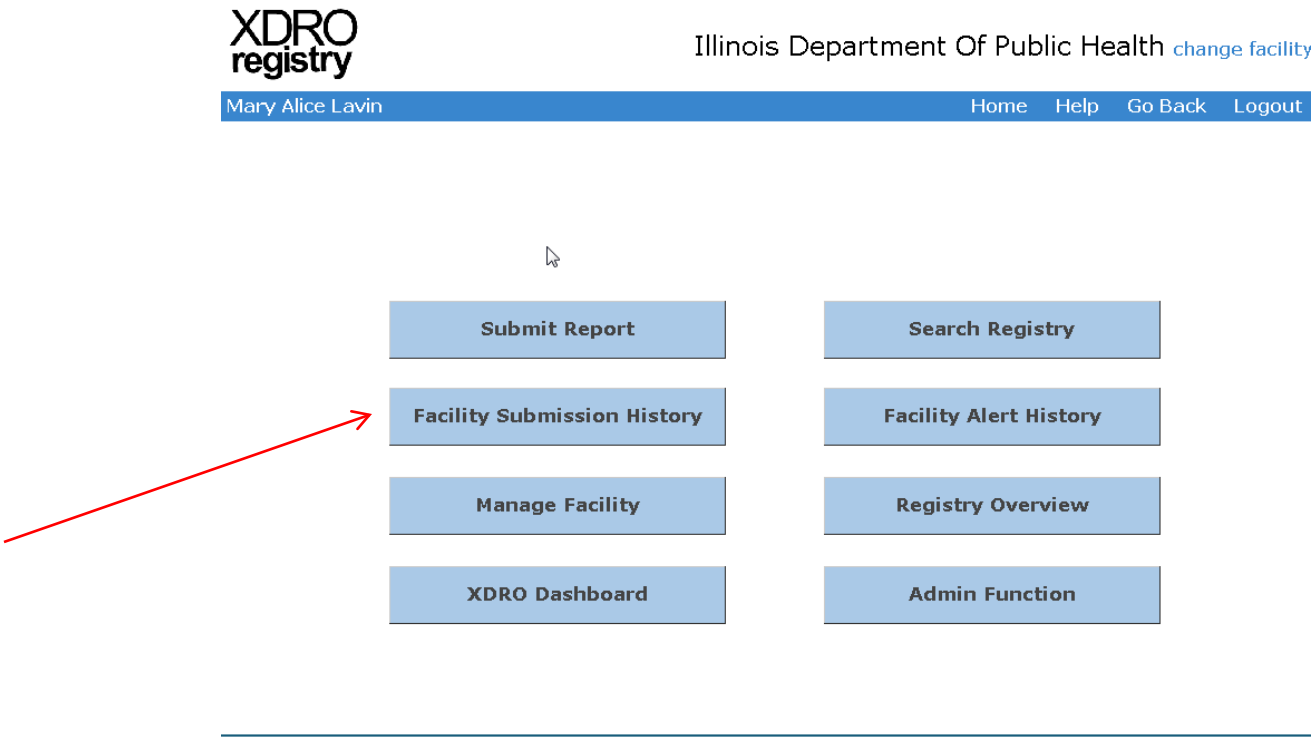
Facility



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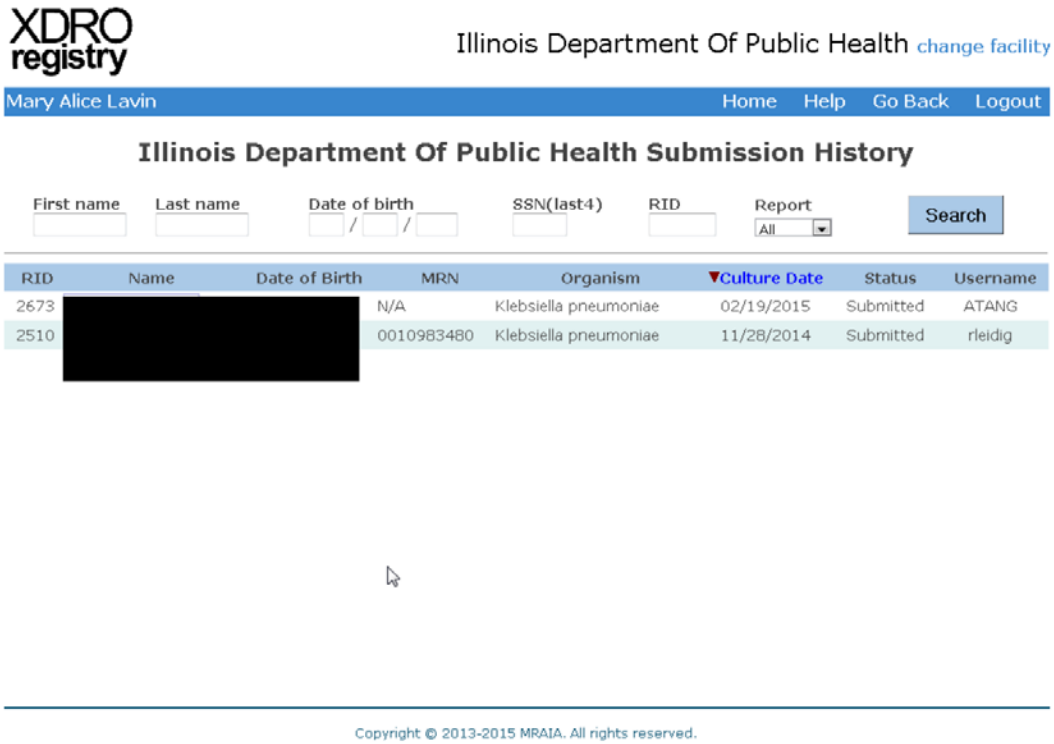
Facility



https://www.xdro.org/index.html

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Facility

Look Back and Active Surveillance Cultures

- Lab information system review of Enterobacteriaceae
  - Review susceptibility
  - Consider additional testing if not previously performed and isolates available
- Active surveillance culture order sets
  - ICU admission
  - “Patients at risk”
  - Based on admission source

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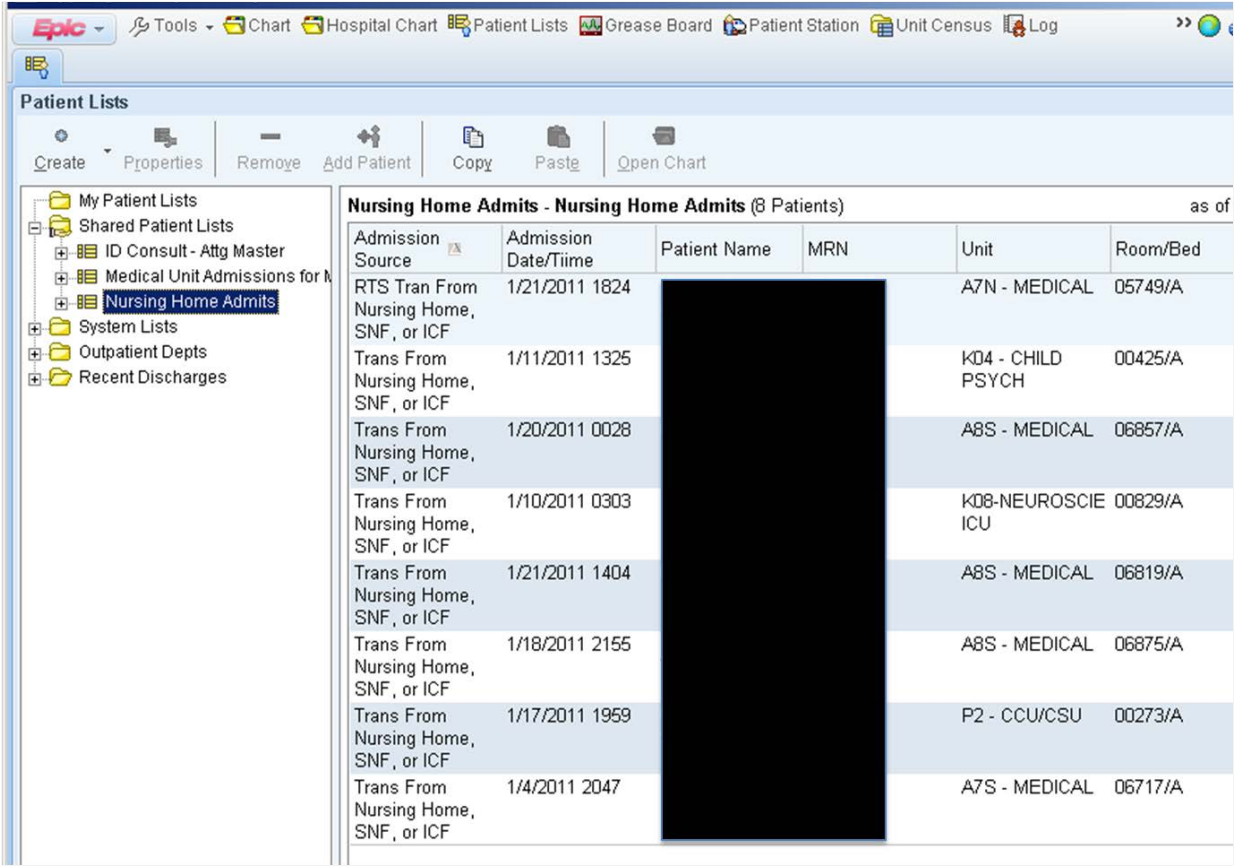

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Active Surveillance Cultures

- Admission screening of patients on high risk units
- Ring surveillance
  - Index patient
  - All epidemiologically linked patients
- Retrospective search
  - CRE positive patients who had spent 24 or more hours on the same ward as a new CRE patient (case patient)before they were identified as CRE positive

Fitzpatrick, M. Outcomes of an enhanced surveillance program for Carbapenem-resistant Enterobacteriaceae Infect Control Hosp Epidemiol 2014;35(4):419-422

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Active Surveillance Cultures

- Results of admission screening
  - 29 of 63 positive patients were already on contact precautions
  - 14 patients triggered ring surveillance
    - 174 patients were screened with 3 new patients identified.
    - The three patients grew different organisms than the index patient and therefore did not represent transmission
- Results of retrospective search
  - 7 possible transmissions occurred from 6 case patients
  - The case patients all had positive clinical cultures

Fitzpatrick, M. Outcomes of an enhanced surveillance program for Carbapenem-resistant Enterobacteriaceae Infect Control Hosp Epidemiol 2014;35(4):419-422

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Active Surveillance Cultures

- Conclusions
  - Ring surveillance identified unrecognized cases
  - Because ring surveillance is a single point in time, it may not identify all possible transmissions
  - Patients with active CRE infections may be more likely to transmit CRE than patients with asymptomatic colonization
  - Study had limitations

Fitzpatrick, M. Outcomes of an enhanced surveillance program for Carbapenem-resistant Enterobacteriaceae Infect Control Hosp Epidemiol 2014;35(4):419-422

Case Response and Investigation

- Prompt initiation of Contact Precautions
- Assessment of potential exposures
  - Source for transmission
    - Contact Precautions/length of time to Contact Precautions
    - Invasive procedures
    - CRE positive clinical culture
  - Ring surveillance cultures
  - Resulting in transmission
    - Invasive procedures
    - Invasive devices

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Ongoing and Proactive Interventions

- Feedback and feed-forward of information
  - Internal
    - Flagging of medical records
    - SBAR, warm hands offs, ticket to ride
    - XDRO Registry
  - External
    - Inter-facility Infection Prevention Transfer Form
    - Transfer form
    - Discharge/transfer summary
    - XDRO Registry
- Program reassessment

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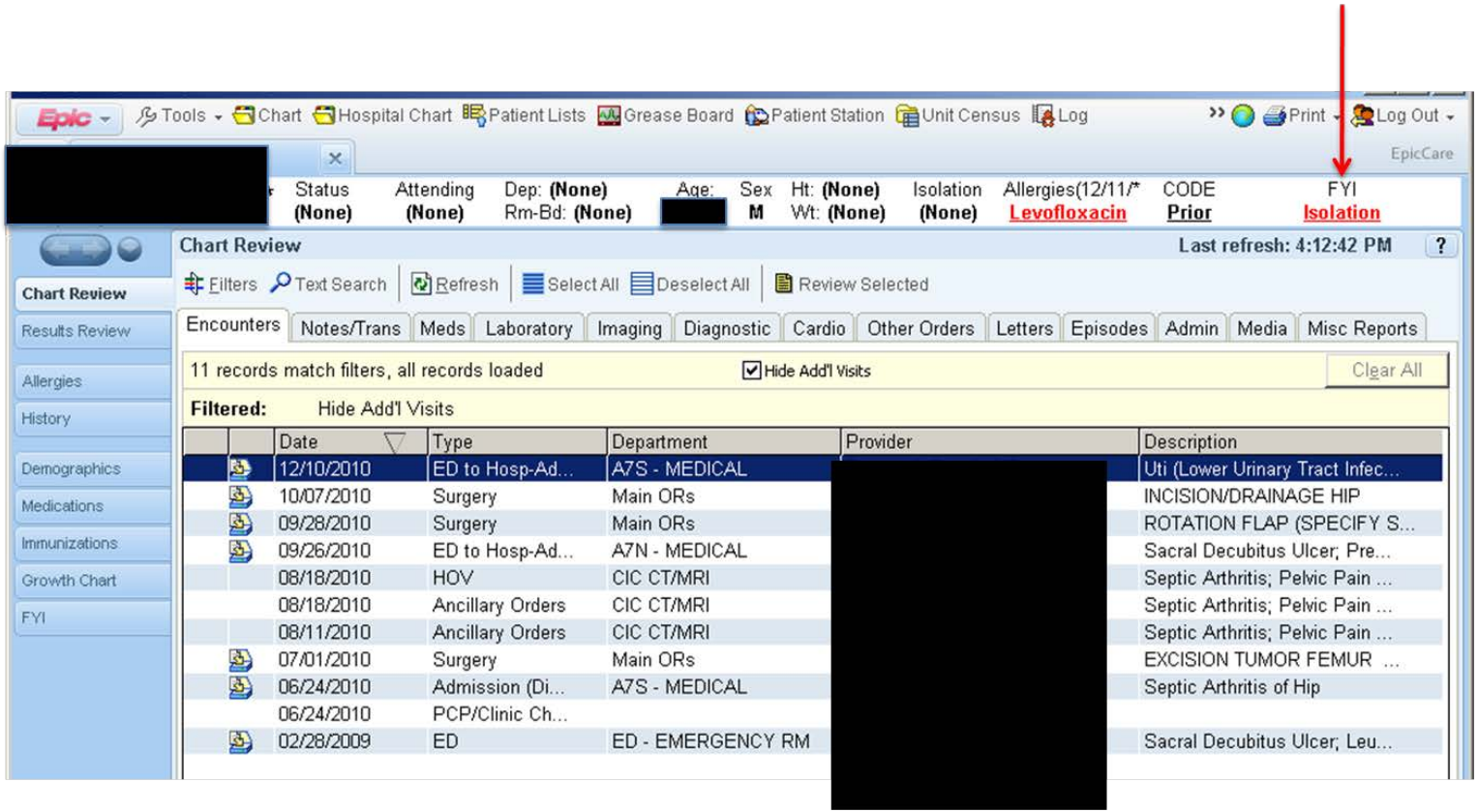

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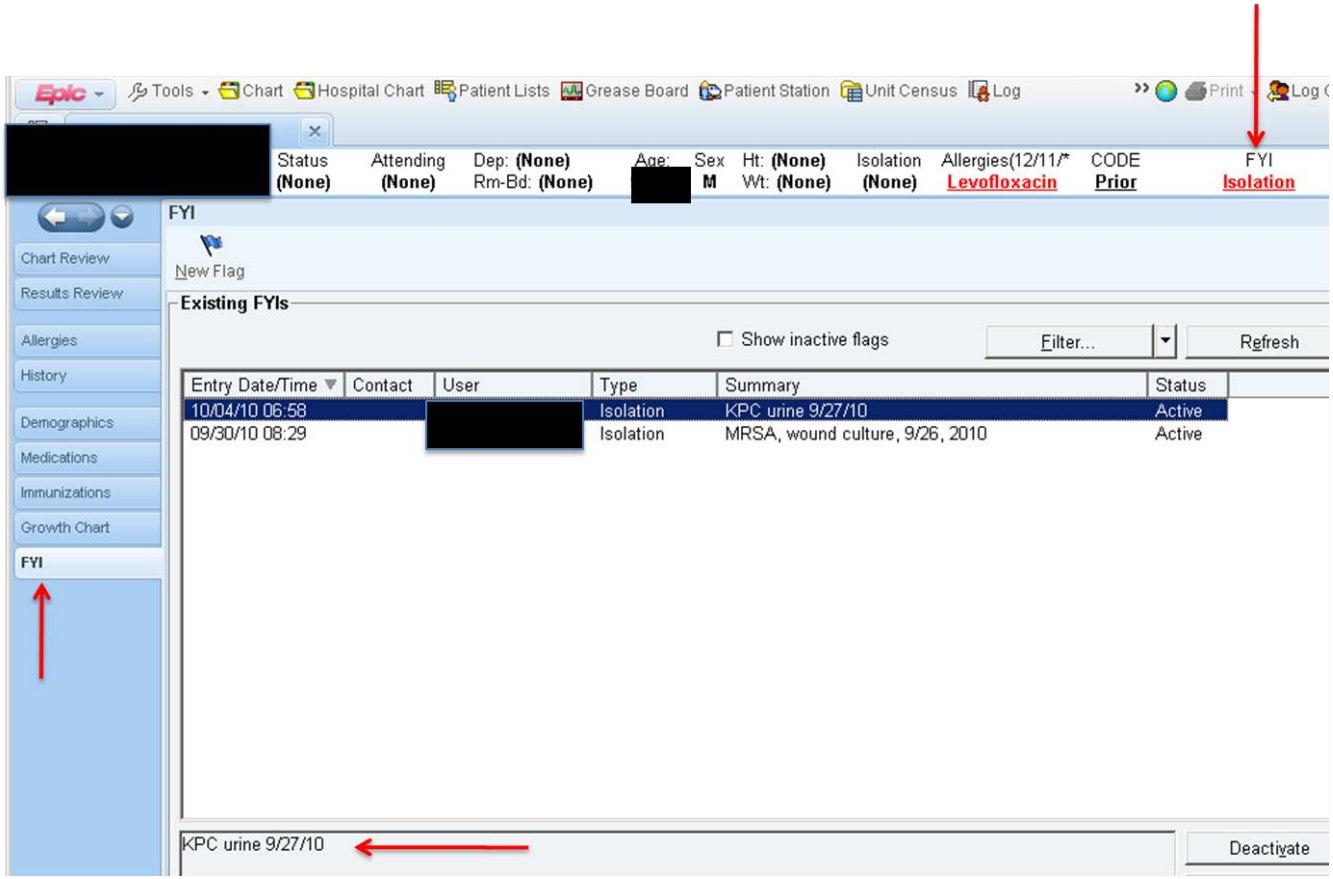

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Inter-facility Infection Prevention Transfer Form

When transferring patient/resident, please complete to the best of your ability to assist with care transitions.

Patient Information

Last Name _____ First Name _____

Date of Birth ____/____/____

Isolation Precautions

The patient currently requires the following type(s) of isolation precautions.

- ☐ Contact precautions. Reason: _____
- ☐ Droplet precautions. Reason: _____
- ☐ Airborne precautions. Reason: _____

☐ The patient DOES NOT require isolation.

Infection/Colonization History (check all that apply)

- ☐ MRSA (Methicillin-resistant *Staphylococcus aureus*)
- ☐ VRE (Vancomycin-resistant enterococci)
- ☐ *Clostridium difficile*
- ☐ Any MDRO gram-negative bacteria (multidrug-resistant). If known, please also specify:
  - ☐ Carbapenem-resistant *Enterobacteriaciae* (examples: *Klebsiella* or *E. coli* with KPC, NDM-1)
  - ☐ *Acinetobacter*, multidrug-resistant
  - ☐ ESBL (extended spectrum beta-lactamase) bacteria
  - ☐ *Pseudomonas aeruginosa*, multidrug-resistant
- ☐ Respiratory Illness (influenza, adenovirus, etc., suspected or confirmed) — Droplet Precautions
- ☐ Respiratory Illness (tuberculosis , etc., suspected or confirmed) — Airborne Precautions
- ☐ Any other pathogen requiring isolation. Please list: _____

Sending Facility Information

Facility Name _____ Unit _____

Address _____ Phone _____

Person Completing Form

Name/Title _____

Phone _____

Email/Fax _____

Infection Prevention Designee

Name _____

Phone _____

Email/Fax _____

Please send copies of any relevant microbiology cultures, medication administration record (MAR) or physician order sheet (POS), and immunization documentation.

Version 1.2 3/11/11

http://cookcountypublichealth.org/files/pdf/facility-transfer-form.pdf

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ILLINOIS DEPARTMENT OF PUBLIC HEALTH

Conclusions

- Control of CRE requires coordination among all stakeholders
- A risk assessment can guide the program and interventions at the facility level
- Success for one is success for all with communication as the key

IDPH
Illinois Department of Public Health

Additional Resources

- CDC. 2012 CRE Toolkit - Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE) http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html (Note: currently being revised.)
- CDC. Vital signs: Carbapenem-resistant Enterobacteriaceae. MMWR Morb Mortal Wkly Rep 2013;165-170.
- ECRI Institute. CRE and Duodenoscope Resource Center, Guidance on reprocessing of ERCP endoscopes linked to the superbug outbreak https://www.ecri.org/resource-center/Pages/Superbug.aspx
- Ostrowsky BE, Trick WE, Sohn AH et al. Control of vancomycin-resistant *enterococcus* in health care facilities in a region. N Eng J Med 2001;344(19):1427-33.
- Parker VA, Logan CK, Currie B. Carbapenem-Resistant *Enterobacteriaceae (CRE) Control and Prevention Toolkit. (Prepared by Boston University School of Public Health and Montefiore Medical Center under Contract No. 290-2006-0012-I.) AHRQ Publication No. 14-0028. Rockville, MD: Agency for Healthcare Research and Quality. April 2014.* http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cretoolkit/cretoolkit.pdf

IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

Questions

maryalice.lavin@illinois.gov

IDPH
Illinois Department of Public Health

Antimicrobial Stewardship: The OSF Experience

J Gavin Cotter MD MPH
Director Antimicrobial Stewardship
Assistant Professor of Clinical Medicine
Infectious Disease

Full Disclosure of Presenter Financial Interests or Relationships

- I declare that I or my immediate family do not have a financial interest or other relationship with any manufacturer/s of a commercial product/s which may be discussed at the conference.

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Antimicrobial Stewardship Definition

Rational, systematic approach to the use of antimicrobial agents in order to achieve optimal outcomes

- Optimal Outcomes
  - Achievement of cure
  - Avoidance of medication toxicity
  - Avoidance of Adverse affects (ie. *Clostridium Difficile*)
  - Reduction of antimicrobial selection pressure limiting antimicrobial resistance

Dellit T.H., et al. "Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship." *Clinical Infectious Diseases* (2007) 44: 159–77.

OSF Healthcare

- Owned and operated by The Sisters of the Third Order of St. Francis, Peoria, Illinois.
- 11 acute care facilities
- 1 Hospice House
- OSF Prompt Care
- 2 Colleges of Nursing
- OSF Medical Group

OSF HealthCare

OSF Healthcare: Hospitals

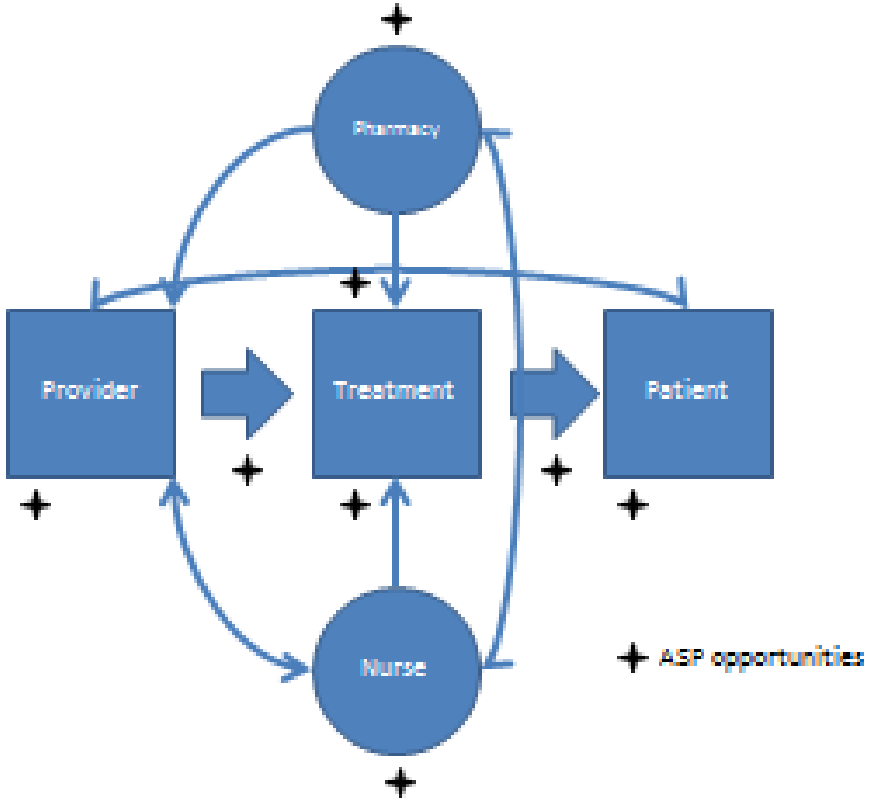
- **Saint James-John W Albrecht Medical Center**
  - Pontiac, IL
  - Beds: 42
- **Saint Joseph Medical Center**
  - Bloomington, IL
  - Beds: 149
- **Saint Luke Medical Center**
  - Kewanee, IL
  - Beds: 25
- **Saint Francis Medical Center**
  - Peoria, IL
  - Beds: 609
- **Holy Family Medical Center**
  - Monmouth, IL
  - Beds: 23
- **Saint Anthony's Health Center**
  - Alton, IL
  - Beds: 203
- **Saint Mary Medical Center**
  - Galesburg, IL
  - Beds: 90
- **Saint Elizabeth Medical Center**
  - Ottawa, IL
  - Beds: 97
- **Saint Anthony Medical Center**
  - Rockford, IL
  - Beds: 254
- **St. Francis Hospital and Medical Group**
  - Escanaba, MI
  - Beds: 25
- **Saint Paul Medical Center**
  - Mendota, IL
  - Beds: 25

OSF HealthCare

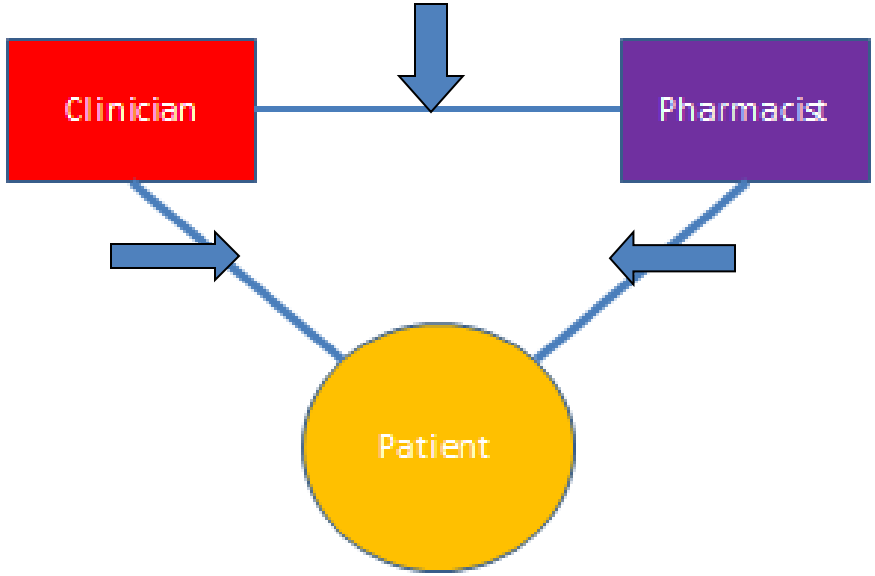
Aims

- To create a formalized Inpatient ASP at OSF SFMC.
- To support pre – existing inpatient efforts within OSF Healthcare and transition these efforts into formalized Inpatient ASPs.
- To create new inpatient ASPs within OSF Healthcare.
- To develop an Ambulatory ASP within OSF Healthcare.

Antibiotic Utilization Process



OSF Antimicrobial Stewardship Program: Fractal



Clinician: MD/DO(Attending/Resident/Intern), NP, PA, Nursing

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Data Gathering Sources

- EMR
- Pharmacy
- Billing Data
- TheraDoc®
- Chart Review
- Other

EMR review also revealed…

- “Continue antimicrobials until course completed.”
- “Most likely viral. We will continue the antibacterial.”
- “Patient with colitis possibly due to C. difficile. Will empirically start Levo and Flagyl”
- “Viral Bronchitis Day #7/14 Levaquin.”
- “Allergy to PCN. Continue Augmentin.”

Where are we now?

IDSA Policy Statement: Combating Antimicrobial Resistance 2011

GET SMART
Know When Antibiotics Work

CDC 2009 Know when Antibiotics Work Campaign

10x'20

IDSA Policy Statement: The 10x'20 Initiative Inaugural Statement; April 2010

THE WHITE HOUSE
WASHINGTON

National Action Plan to Combat Antibiotic Resistant Bacteria; May 2015

EU Policy Options. Office of Health Economics

Literature Review: Interventions

- Prospective audit with interaction and feedback
- Restriction
  - Formulary
  - Pre authorization
- Education
- De-escalation
- Guidelines and Clinical Pathways
- Order Sets
- IV to PO conversion
- Dose optimization
- Computer Decision Support

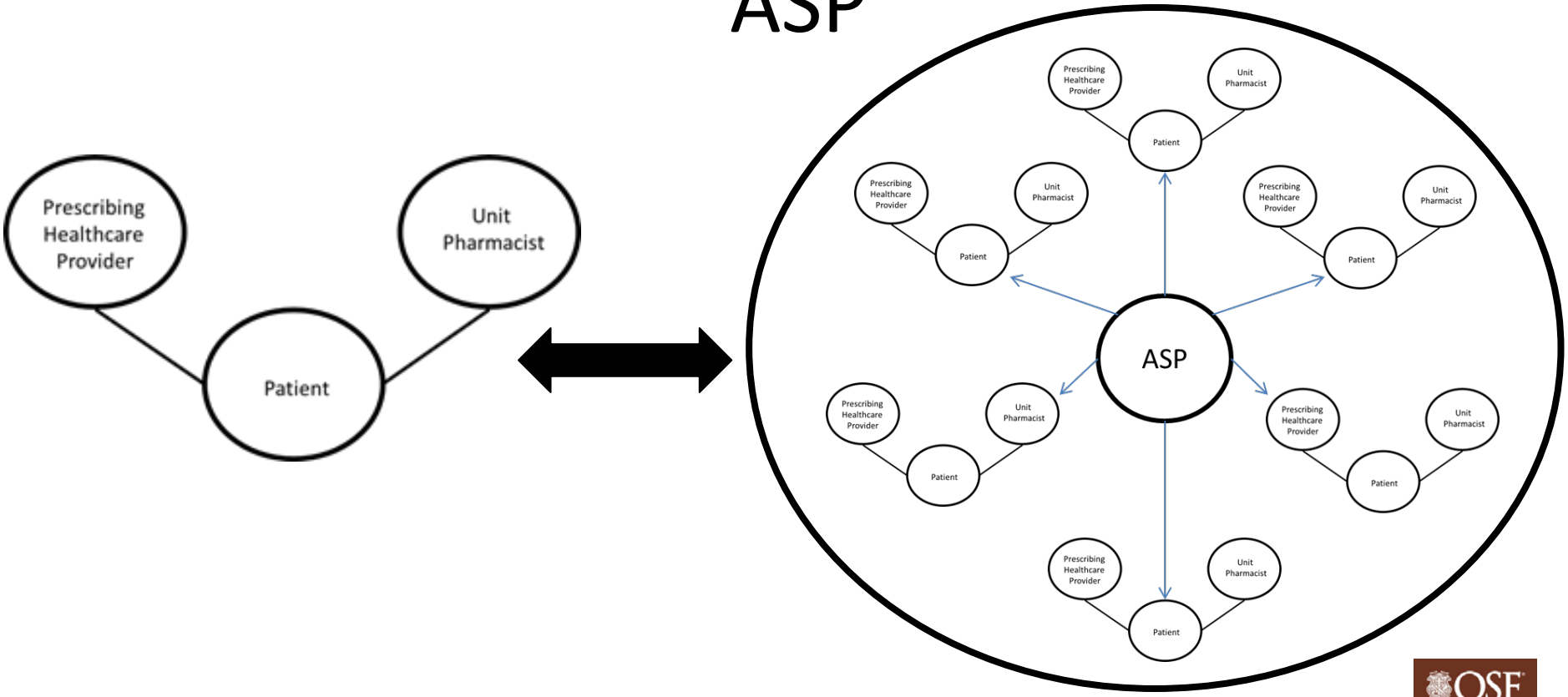
OSF HealthCare

All systems are perfectly designed to get the results they are getting.

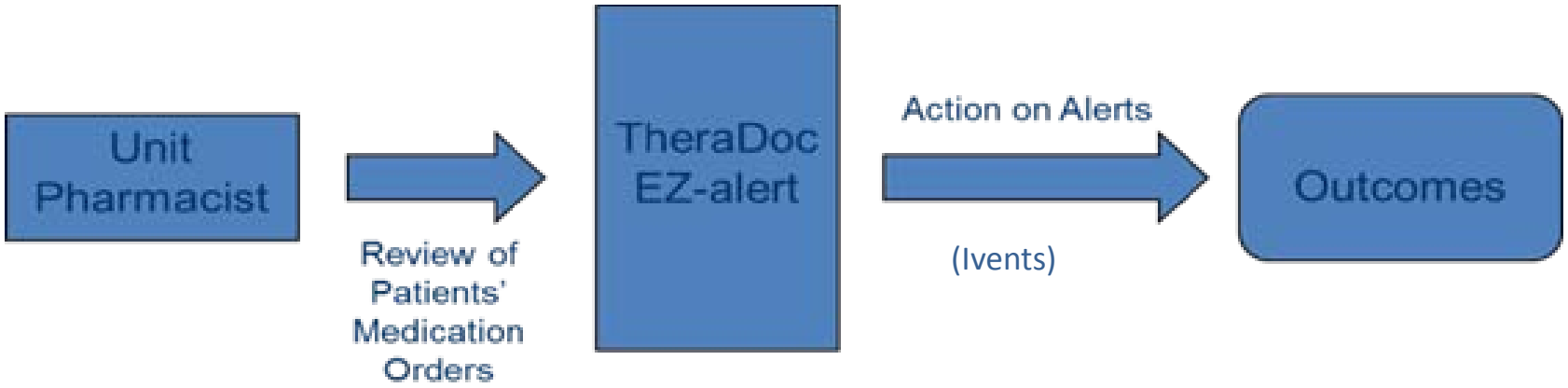
Paul Batalden, MD

OSF HEALTHCARE

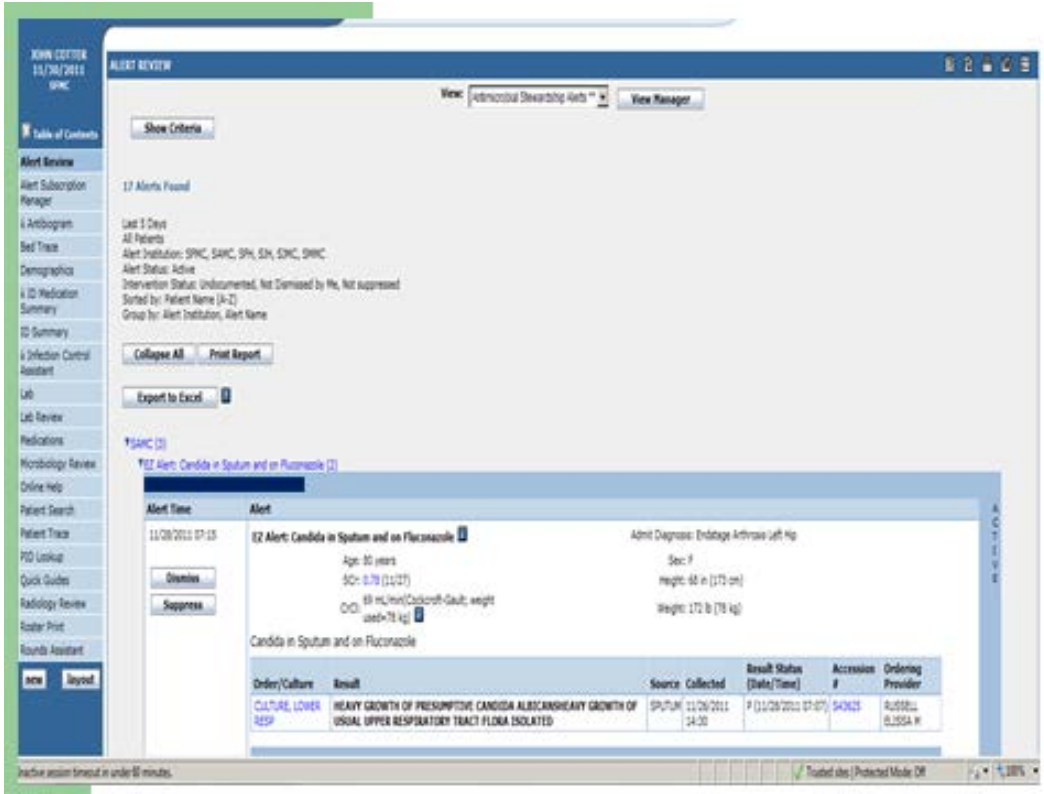
AS Fractal and the decentralization of ASP



New ASP Process: Pharmacy



TheraDoc® EZ-Alert Screen Shot and Example EZ-Alerts



- Candida in Sputum and on Fluconazole
- Flagyl and double coverage
- On Cefepime and enterobacter or pseudomonas with MIC >= 4
- On Levaquin and Ciprofloxacin MIC >=1 for e. coli, pseudomonas, or strep pneumonia
- On Vancomycin and MRSA with MIC >= 2
- On Zosyn with enterobacter or pseudomonas with MIC >= 32
- Strep pneumonia Urine Ag positive
- Urine LE neg and pos urine culture on antibiotics

Therapeutic mismatches:

- Susceptibility known
- De-escalation
- No positive Bacterial cultures
- No Positive Fungal cultures
- Redundant Anaerobic spectrum therapy
- Redundant Antifungal spectrum therapy
- Redundant Beta-lactam therapy
- Redundant Staphylococcal therapy

- Targeted Drugs:
  - Ampho B
  - Acyclovir IV
  - Aztreonam
  - Cefepime
  - Daptomycin
  - Ertapenem,
  - Levofloxacin
  - Linezolid
  - Meropenem
  - Pip/tazo
  - Tigecycline
  - Vancomycin
  - Voriconazole.

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Create a simple vision

"Right drug for the right bug,
at right dose/duration/indication."

Establish a Sense of Urgency

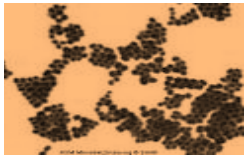
- Communication:
  - Told Stories
  - Presented Facts
  - Shared Plans – “partnerships not punitive”
  - Listened – Attitudes/Knowledge/Beliefs

- Positive Peer Pressure

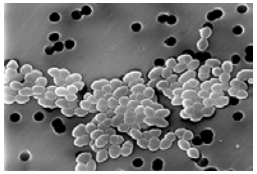
Once upon a time….

- Mrs Jones was a 80yo female.
- Admitted for elective surgical intervention.
- Given appropriate prophylactic antimicrobial.
- No stop date on antimicrobial – continued > 7 days post operatively.
- Clinical condition worsened.
- Diagnosis: Toxic megacolon secondary to Clostridium difficile.

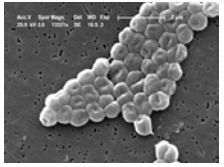
Bad Bugs



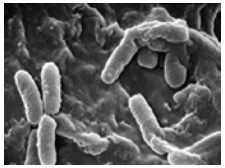
Methacillin Resistant Staphyloccous (MRSA)



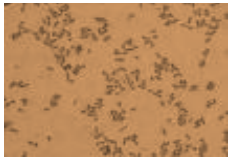
Vancomycin Resistant Enterococci (VRE)



Acinetobacter baumannii bacteria



P. Aeruginosa – Multi-Drug Resistant (MDR)



Extended Spectrum Beta-lactamase (ESBL)
- E. Coli

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Carbapenem Resistant Enterobacteraciae (CRE)

Culture & Susceptibility

KLEBSIELLA PNEUMONIAE

Antibiotic	Sensitivity	Result
Amikacin	Susceptible	16 SUSCEPTIBLE
Ampicillin	Resistant	>=32 RESISTANT
Ampicillin/sulbactam	Resistant	>=32 RESISTANT
Aztreonam	Resistant	>=64 RESISTANT
Cefazolin	Resistant	>=64 RESISTANT
Cefotetan	Resistant	RESISTANT
Ceftazidime	Resistant	>=64 RESISTANT
Ceftriaxone	Resistant	16 RESISTANT
Gentamicin	Resistant	>=16 RESISTANT
Levofloxacin	Resistant	>=8 RESISTANT
Meropenem	Resistant	8 RESISTANT
Nitrofurantoin	Resistant	256 RESISTANT
Tobramycin	Resistant	>=16 RESISTANT
Trimeth/Sulfamethoxazole	Resistant	160 RESISTANT
cefepime	Resistant	RESISTANT

Comments KLEBSIELLA PNEUMONIAE

>100,000 COL/ML KLEBSIELLA PNEUMONIAE INFECTION CONTROL ALERT - THE ORGANISM ISOLATED IS MULTIDRUG-RESISTANT. PATIENTS WITH THIS ORGANISM MUST BE ISOLATED.

Lab and Collection

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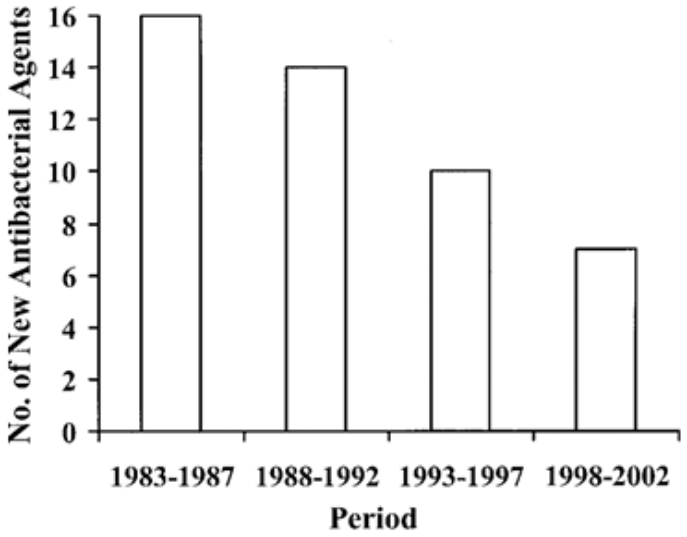
New antibacterial agents approved in the United States, 1983–2002

New antibacterial agents approved in the United States, 1983–2002, per 5-year period.



Spellberg B et al. Clin Infect Dis. 2004;38:1279-1286

Clinical Infectious Diseases

OSF HealthCare

Infection Cost

- “Antibiotic-resistant infections cost the US Healthcare System in excess of $20 billion annually.”

APUA/Cook County Hospital 2000

- “The annual cost to the US health care system of antibiotic-resistant infections is $21 billion to $34 billion and more than 8 million additional hospital days.”

CID 2011;52(S5):S397-428

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Action

- Order sets
  - PNA – CAP/HCAP
  - Sepsis
- TheraDoc® EZ-Alerts
- SCIP
- Drug Reviews
- C diff Work Group
- EDUCATION!!!
- Branding – “The antibiotics people.”
- Ambulatory ASP

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Community Acquired Pneumonia-Outpatient Oral Antibiotics - Adult ED

☐ azithromycin (ZITHROMAX) tablet 500 mg	250 mg, Oral, ONCE For 1 Doses
☐ doxycycline (VIBRAMYCIN) capsule 100 mg	100 mg, Oral, ONCE For 1 Doses
☐ levofloxacin (LEVAQUIN) tablet 750 mg	750 mg, Oral, ONCE For 1 Doses

COMMUNITY ACQUIRED PNEUMONIA, NON-ICU TREATMENT - ADULT

NON-ICU TREATMENT - ADULT

Select Both (Primary Regimen):

☐ cefTRIAXone (ROCEPHIN) injection 1 g	1 g, Intravenous, EVERY 24 HOURS For 7 Days Dilute with 10 mL normal saline
☐ AZITHROMYCIN PO PANEL	**"Followed by" Linked Panel**
☐ azithromycin	500 mg, Oral, ONCE For 1 Doses
☐ azithromycin	250 mg, Oral, DAILY Starting tomorrow For 4 Doses

OR Pick a Quinolone (Alternative Regimen): (Single Response)

○ levofloxacin (LEVAQUIN) PO	750 mg, Oral, DAILY For 5 Days Pharmacy to adjust dose based on Creatinine Clearance

OR: Select These Two:

☐ ampicillin-sulbactam (UNASYN) IVPB - 3g, IVPB	3 g, Intravenous, EVERY 6 HOURS For 7 Days, for 30 Minutes Covers Aspiration. Pharmacy to adjust dose based on Creatinine Clearance.
☐ AZITHROMYCIN PO PANEL	**"Followed by" Linked Panel**
☐ azithromycin	500 mg, Oral, ONCE For 1 Doses
☐ azithromycin	250 mg, Oral, DAILY Starting tomorrow For 4 Doses

COMMUNITY ACQUIRED PNEUMONIA ICU TREATMENT - ADULT

ICU TREATMENT - ADULT

Select these two:

☐ cefTRIAXone (ROCEPHIN) 2 g IVPB	2 g, Intravenous, EVERY 24 HOURS For 7 Days, for 30 Minutes
☐ AZITHROMYCIN CAP IV/PO PANEL	**"Followed by" Linked Panel**
☐ azithromycin	500 mg, Oral, DAILY For 3 Doses

OR Select these two:

☐ cefTRIAXone (ROCEPHIN) 2 g IVPB	2 g, Intravenous, EVERY 24 HOURS For 7 Days, for 30 Minutes
☐ levofloxacin (LEVAQUIN) IVPB 750 mg/150 mL	750 mg, Intravenous, EVERY 24 HOURS For 7 Days, for 90 Minutes Pharmacy to adjust dose based on Creatinine Clearance

OR: Select These Two

☐ ampicillin-sulbactam (UNASYN) IVPB - 3g, IVPB	3 g, Intravenous, EVERY 6 HOURS For 7 Days, for 30 Minutes Covers Aspiration. Pharmacy to adjust dose based on Creatinine Clearance.
☐ AZITHROMYCIN CAP IV/PO PANEL	**"Followed by" Linked Panel**
☐ azithromycin	500 mg, Oral, DAILY For 3 Doses

OR If Beta-Lactam Allergic, Select these Two, plus Pharmacy consult:

☐ levofloxacin (LEVAQUIN) IVPB	750 mg, Intravenous, DAILY For 7 Days, for 90 Minutes

OSF HEALTHCARE

HEALTHCARE ASSOCIATED PNEUMONIA (HCAP) - HOSPITAL ACQUIRED PNEUMONIA (HAP)

REFERENCE: TABLE 2 OF INFECTIOUS DISEASE SOCIETY OF AMERICA/AMERICAN THORACIC SOCIETY 2005 HEALTHCARE ACQURIED PNEUMONIA GUIDELINES -
ADULT: RISK FACTORS FOR HEALTHCARE ASSOCIATED PNEUMONIA (HCAP) / HOSPITAL ACQUIRED PNEUMONIA (HAP):

A) Residence in a nursing home or extended care facility B) Hospitalization for 2 days or more in the preceding 90 days C) Chronic Dialysis within 30 days
D) Antimicrobial therapy in preceding 90 days (significant exposure) E) Home infusion therapy (including antibiotics) F) Home wound care
G) Immunosuppressive disease and/or therapy

INFECTIOUS DISEASE SOCIETY OF AMERICA/AMERICAN THORACIC SOCIETY 2005 HEALTHCARE ACQURIED PNEUMONIA GUIDELINES - ADULT: **URL:** http://www.thoracic.org/statements/resources/mtpi/guide1-29.pdf

#1 Anti-Pseudomonal Agent Base (Select One) - Adult

☐ cefipime (MAXIPIME) IVPB 2 g	2 g, Intravenous, EVERY 8 HOURS, for 30 Minutes Pharmacy to adjust dose based on Creatinine Clearance
☐ piperacillin-tazobactam (ZOSYN)	4.5 g, Intravenous, EVERY 6 HOURS Covers Aspiration. Pharmacy to adjust dose based on Creatinine Clearance.
☐ meropenem (MERREM) injection 500 mg	0.5 g, Intravenous, EVERY 6 HOURS 1. Dilute with 10 mL normal saline. 2. Alternative: Reserve for use if history of Multidrug resistant pathogen(s). 3. Covers Aspiration. 4. Pharmacy to adjust dose based on Creatinine Clearance.

#2 Double Coverage for Pseudomonas (Select all):

Note on Sensitivities - July 2012: 1) Sensitivities of Pseudomonas to Levofloxacin is 59% in the ICU at SFMC, and around 70% at the other OSF hospitals.
2) Sensitivity of Pseudomonas to Tobramycin is around 88% at SFMC, and high 90s at the other OSF hospitals. .

☐ tobramycin (NEBCIN) IVPB	7 mg/kg, Intravenous, EVERY 24 HOURS, for 60 Minutes Pharmacokinetic dosing
☐ IP Consult to Pharmacy - for Pharmacokinetic Tobramycin dosing	Reason for Consult?: Pharmacokinetic Tobramycin dosing
☐ levofloxacin (LEVAQUIN) IVPB 750 mg	Intravenous, DAILY, for 90 Minutes Pharmacy to adjust dose based on Creatinine Clearance

#3 If suspect MRSA or post-influenza pneumonia is present, Select One:

☐ vancomycin (VANCOCIN) IVPB	15 mg/kg, Intravenous, EVERY 12 HOURS, for 120 Minutes Pharmacokinetic dosing
☐ IP Consult to Pharmacy - for Pharmacokinetic vancomycin dosing	Reason for Consult?: Pharmacokinetic vancomycin dosing Reason for consult: Pharmacokinetic Vancomycin dosing

#4 If Severe Beta-lactam Allergic, Select Both of the following and see #3 if need to add MRSA coverage: (Severe reaction = swelling, anaphylaxis, shortness of breath, etc.)

☐ aztreonam (AZACTAM) 2 g IVPB	2 g, Intravenous, EVERY 8 HOURS, for 30 Minutes Alternative: Use if anaphylaxis to penicillins or cephalosporins is reported.
☐ levofloxacin (LEVAQUIN) IVPB 750 mg	750 mg, Intravenous, DAILY For 7 Days, for 90 Minutes Pharmacy to adjust dose based on Creatinine Clearance

ASPIRATION PNEUMONIA (Highly Suspected, Witnessed, or Visualized)

Aspiration - No Nosocomial Risk Factors

☐ ampicillin-sulbactam (UNASYN) IVPB	3 g, Intravenous, EVERY 6 HOURS, for 30 Minutes Pharmacy to adjust based on Creatinine Clearance

Aspiration - Nosocomial Risk Factors Present

RISK FACTORS FOR HEALTHCARE ASSOCIATED PNEUMONIA (HCAP) / HOSPITAL ACQUIRED PNEUMONIA (HAP):

A) Residence in a nursing home or extended care facility B) Hospitalization for 2 days or more in the preceding 90 days C) Chronic Dialysis within 30 days
D) Antimicrobial therapy in preceding 90 days (significant exposure) E) Home infusion therapy (including antibiotics) F) Home wound care
G) Immunosuppressive disease and/or therapy

☐ piperacillin-tazobactam (ZOSYN)	4.5 g, Intravenous, EVERY 6 HOURS Pharmacy to adjust dose based on creatinine clearance.

Aspiration - Beta-Lactam Allergy, No Nosocomial Risk Factors

☐ clindamycin (CLEOCIN) IVPB 600 mg	600 mg, Intravenous, EVERY 8 HOURS, for 30 Minutes

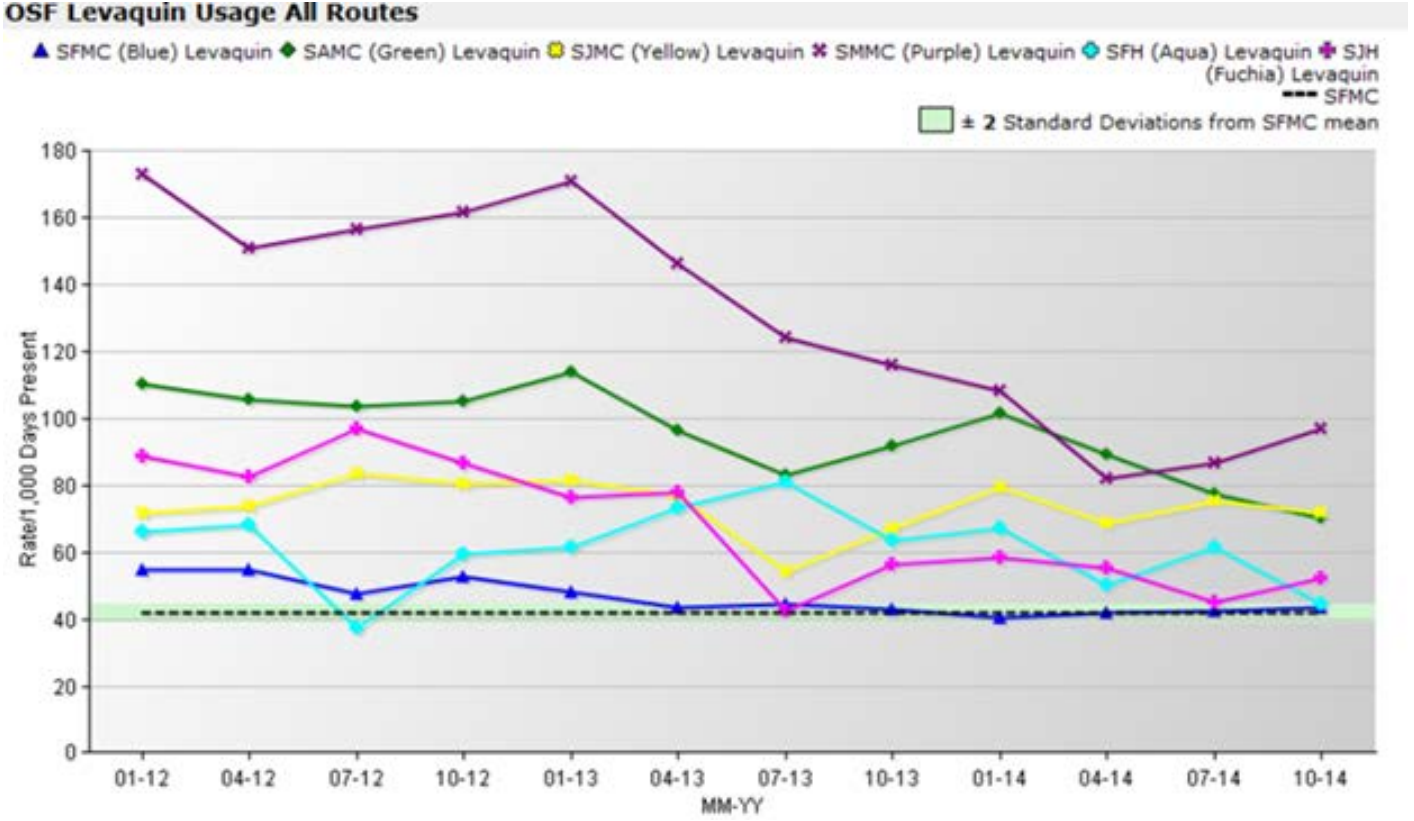
Aspiration - Beta-Lactam Allergy, With Nosocomial Risk Factors Present

Always select two druge: 1. Clindamycin to cover Anaerobic organisms. 2. Either aztreonam or levofloxacin to cover Aerobic organisms.

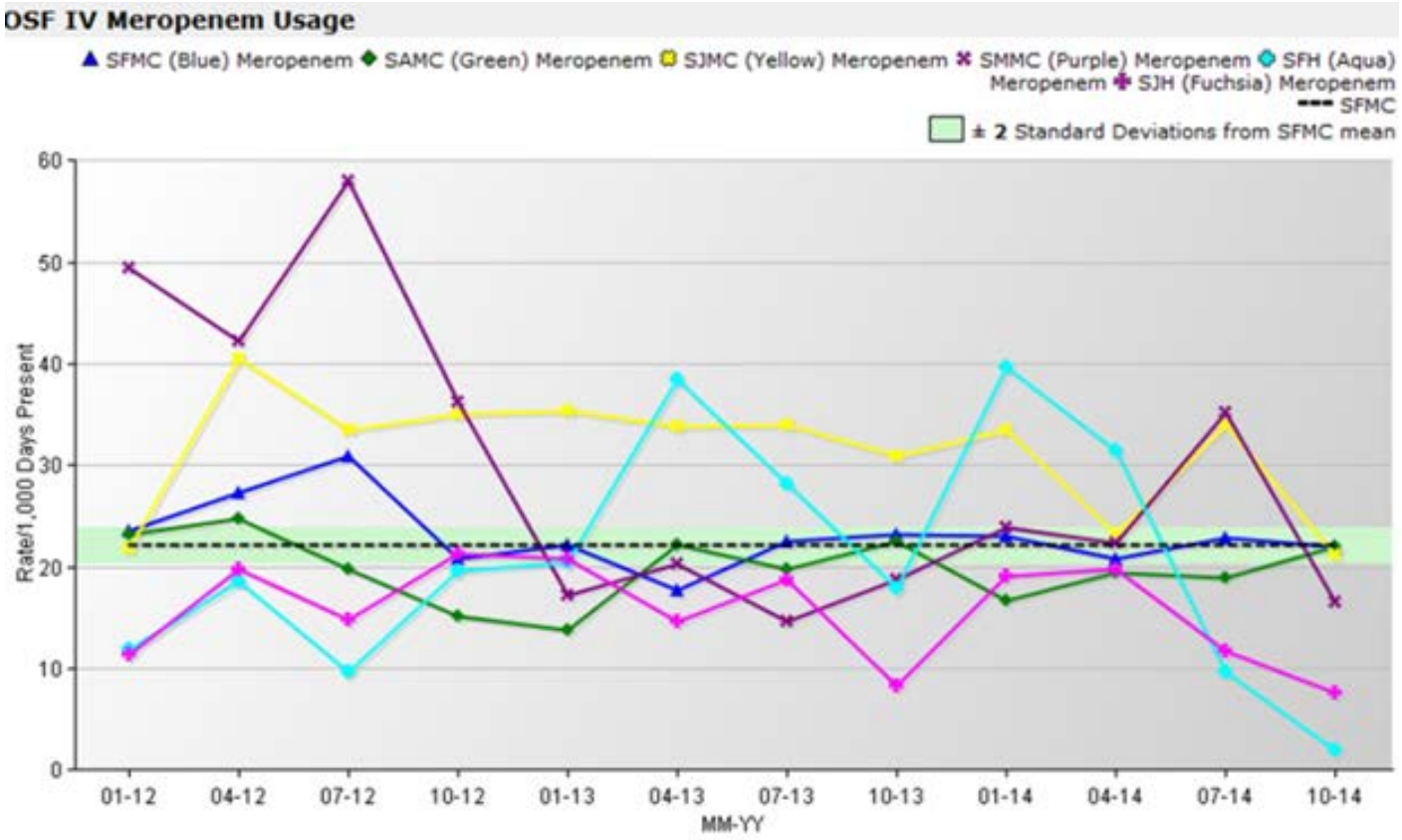
☐ clindamycin (CLEOCIN) IVPB 600 mg	600 mg, Intravenous, EVERY 8 HOURS, for 30 Minutes
☐ aztreonam (AZACTAM) IVPB 2 GM	2 g, Intravenous, EVERY 8 HOURS
☐ levofloxacin (LEVAQUIN) IVPB 750 mg	Intravenous, EVERY 24 HOURS, for 90 Minutes

OSF HealthCare

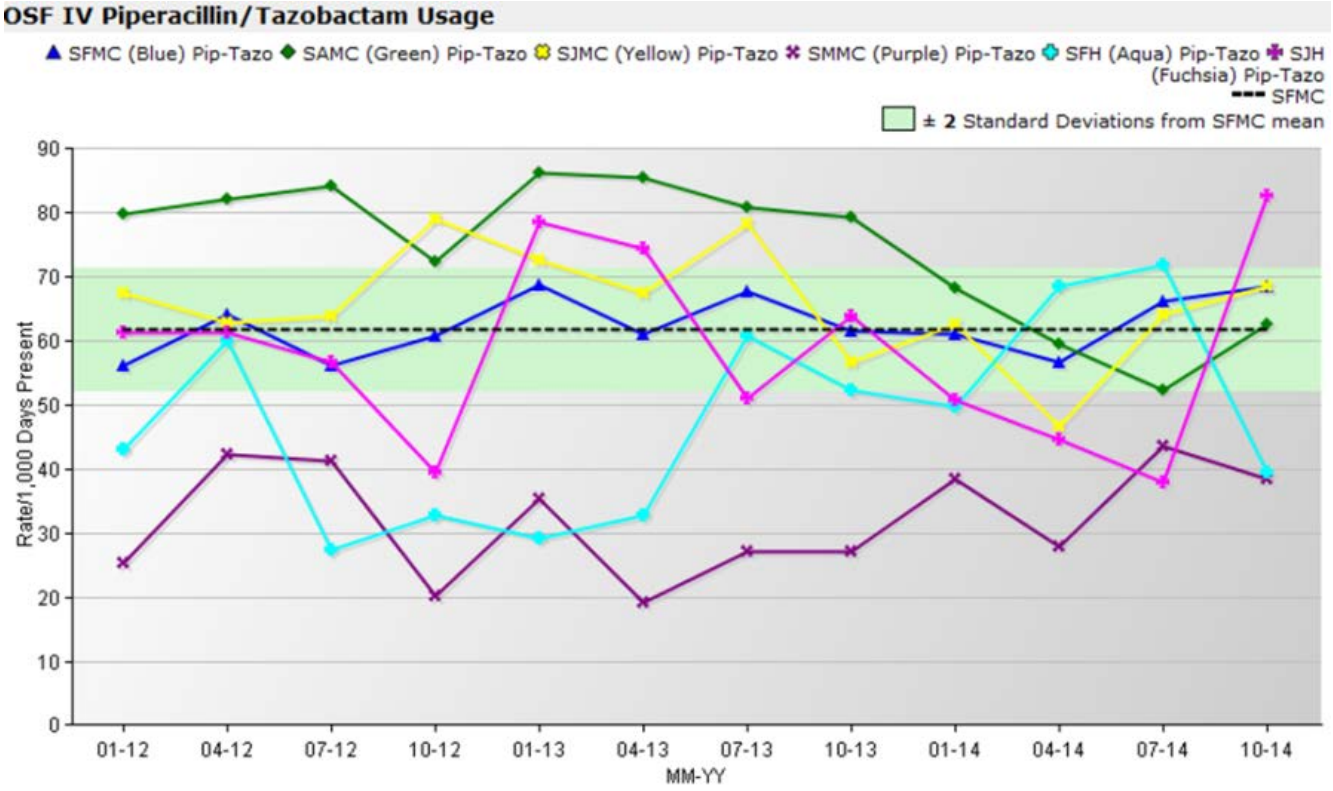
OSF Levaquin Utilization: 2012-2014



OSF Meropenem Utilization: 2012-2014



OSF Piperacillin/Tazobactam Utilization: 2012-2014

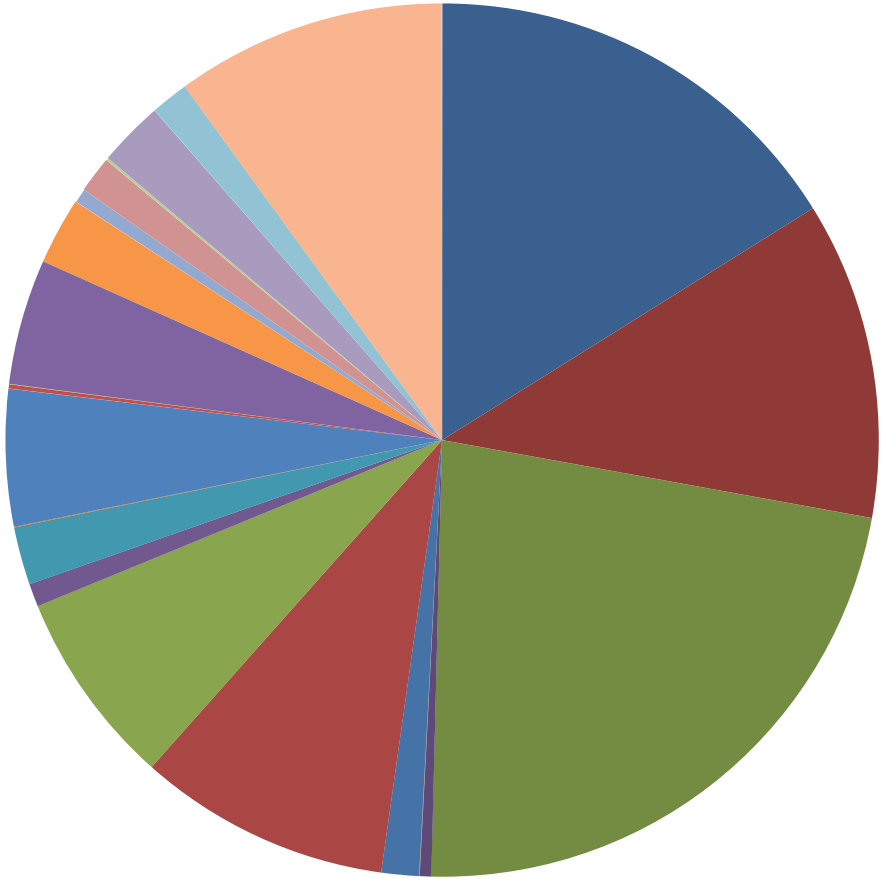


Outpatient Antimicrobial Utilization Review

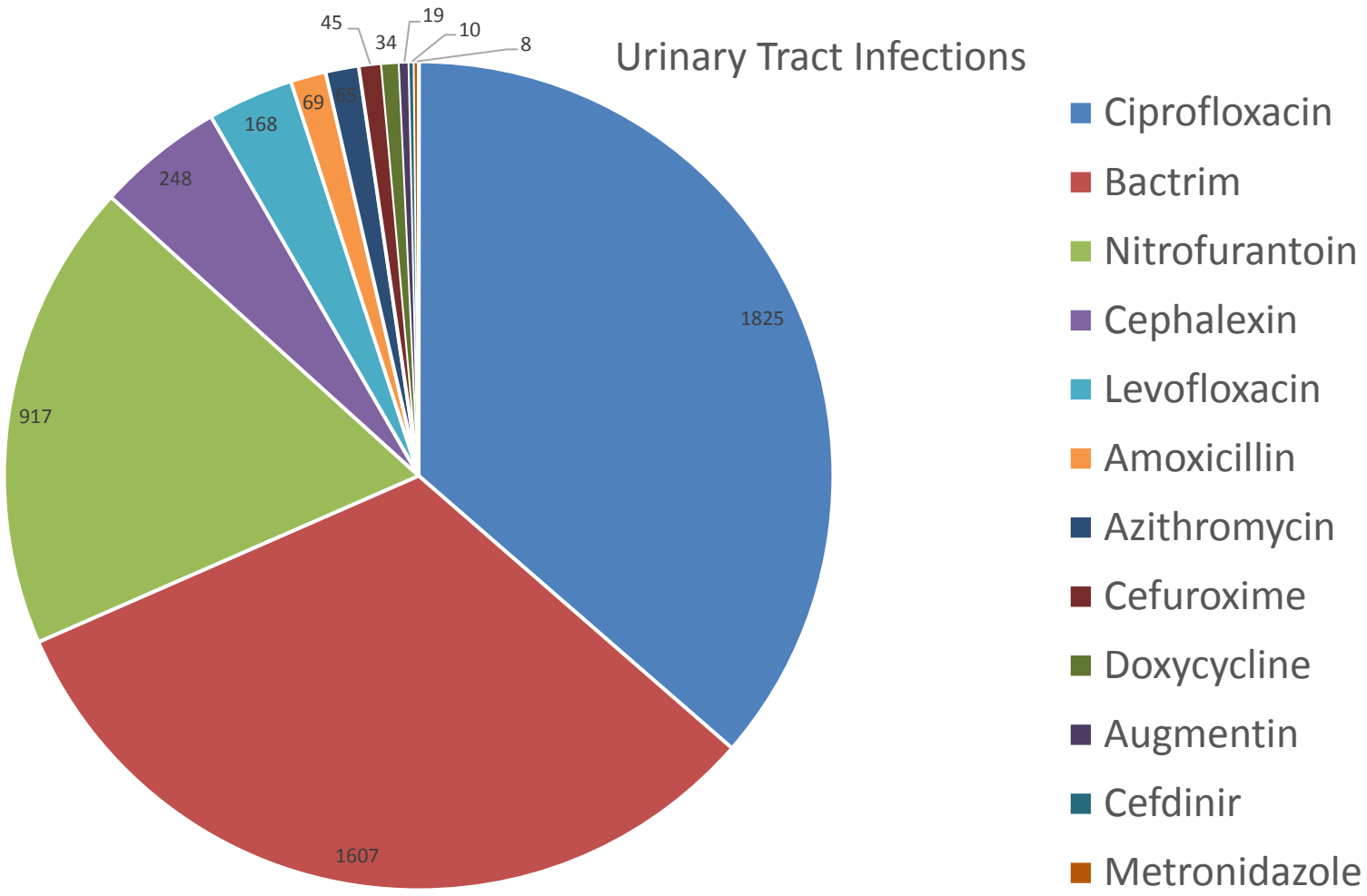
OSF HealthCare

Antibiotic Utilization in Percent

Total Abx Prescriptions = 65,535



- AMOXICILLIN
- AMOXICILLIN-POT CLAVULANATE
- AZITHROMYCIN
- CEFDINIR
- CEFPODOXIME PROXETIL
- CEFTIN
- CEFUROXIME AXETIL
- CEPHALEXIN
- CIPROFLOXACIN
- CLARITHROMYCIN
- CLINDAMYCIN
- DICLOXACILLIN
- DOXYCYCLINE
- Erythromycin
- FOSFOMYCIN
- LEVOFLOXACIN
- LINEZOLID
- METRONIDAZOLE PO
- METRONIDAZOLE Top
- MINOCYCLINE
- MOXIFLOXACIN
- NITROFURANTOIN
- PENICILLIN V
- SULFAMETHOXAZOLE-TRIMETHOPRIM


Urinary Tract Infections
1825
1607
917
248
168
69
55
45
34
19
10
8
Ciprofloxacin
Bactrim
Nitrofurantoin
Cephalexin
Levofloxacin
Amoxicillin
Azithromycin
Cefuroxime
Doxycycline
Augmentin
Cefdinir
Metronidazole

Antibiogram

Gram negative rods (a)

Percent Susceptible		PENICILLINS				CEPHEMS			LACTAMS			AMINOGLYC's			OTHERS			Urine Only	
	No. Tested (b)	Ampicillin	Piperacillin	Amp/Sulbactam	Pip/Tazobactam	Cefazolin	Cefotaxime	Cefepime	Aztreonam (c)	Imipenem	Meropenem	Gentamicin	Tobramycin	Amikacin	Ciprofloxacin	Levofloxacin	Trimeth/Sulfamethox	1ST GENERATION Ceph's [oral]	Nitrofurantoin
Achromobacter xylosoxidans	16	–	–	–	88	–	–	0	0	81	69	0	0	0	0	44	81	–	–
Acinetobacter baumannii	11	–	–	80	–	–	–	50	–	–	80	60	60	70	50	60	60	–	–
Burkholderia cepacia (d,e)	3	Ceftazidime 33%				–	Minocycline 67			–	67	–	–	–	–	–	100	–	–
Citrobacter freundii	32	0	–	0	90	0	86	100	79	100	100	97	100	100	97	97	81	–	94
Citrobacter koseri	27	0	–	0	100	100	100	100	100	100	100	100	100	100	100	96	100	–	73
Enterobacter aerogenes	39	0	–	0	70	0	65	100	85	100	100	100	100	100	95	95	97	–	5
Enterobacter cloacae	83	0	–	0	91	0	85	96	85	100	100	98	98	100	98	98	93	–	37
Escherichia coli	1022	47	–	61	90	83	89	96	89	100	100	88	87	99	74	74	67	–	94
Klebsiella oxytoca	41	7	–	85	100	66	100	100	100	100	100	100	100	100	95	95	93	–	71
Klebsiella pneumoniae	237	0	–	84	95	87	92	94	90	100	100	95	91	96	88	87	80	–	22
Morganella morganii	14	0	–	21	100	0	100	100	100	–	–	79	93	100	100	–	79	–	0
Proteus mirabilis	90	77	–	89	100	95	93	98	97	–	–	86	88	100	80	–	69	–	0
Proteus vulgaris (d)	4	0	–	75	50	0	–	100	100	100	100	100	100	100	100	100	50	–	0
Pseudomonas aeruginosa	354(f)	–	–	–	87	–	–	78	67	81	84	79	94	91	70	65	–	–	–
Ps. aeruginosa CF mucoid (e)	88(f)	–	84	Ticarcillin 81%			–	81	73	65	74	–	88	–	58	–	–	–	–
Ps. aeruginosa CF non-mucoid (e)	63(f)	–	76	Ticarcillin 61%			–	66	59	49	58	–	56	–	39	–	–	–	–
Salmonella spp. (d)	2	100	–	–	–	Ceftriaxone 100%		–	–	–	–	–	–	–	100g	–	100	–	–
Serratia marcescens	58	0	–	0	100	0	100	100	100	97	97	100	93	100	91	97	95	–	0
Stenotrophomonas maltophilia	46	–	–	Ticarcillin/Clavulanate 42%			–	–	–	–	–	–	–	–	–	82	93	–	–
Cost		$$	$$	$	$$	$	$	$	$$$	$$$	$$	$	$	$	$	$	$	$	$

(a) Until final identifications are available, reports describe gram negative rods as lactose-fermenters (LF; such as E.coli, Klebsiella, Enterobacter, Citrobacter); non-lactose fermenters (NLF, such as Proteus, Serratia, Salmonella, Shigella), or non-fermenters (NF, such as Pseudomonas, Acinetobacter, Stenotrophomonas, and others, most of which are intrinsically more resistant to many antibiotics).

(b) Not all isolates tested against every antibiotic listed.

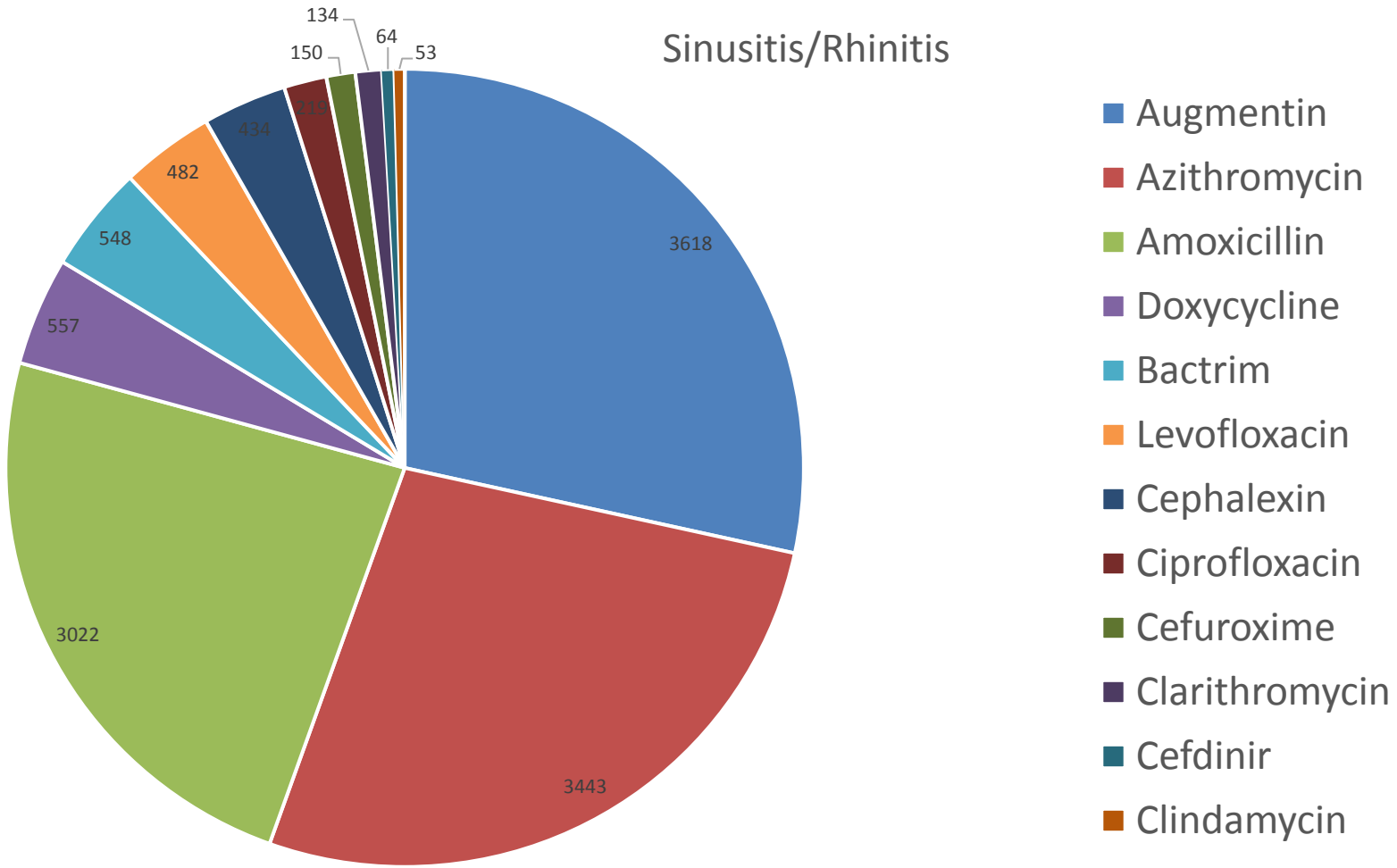
(c) Unlike aztreonam, aminoglycosides have synergistic activity with β-lactams (ex: piperacillin, ampicillin) against aerobic gram negative rods and enterococci. Aztreonam should only be used for treating documented infections due to susceptible organisms in patients with anaphylactic reactions to β-lactams. In patients with renal insufficiency, aminoglycosides can be administered safely when doses are adjusted for patient's renal function. For information on dosing, including single daily dosing, please contact a Clinical Pharmacist (beeper # available from unit secretary).

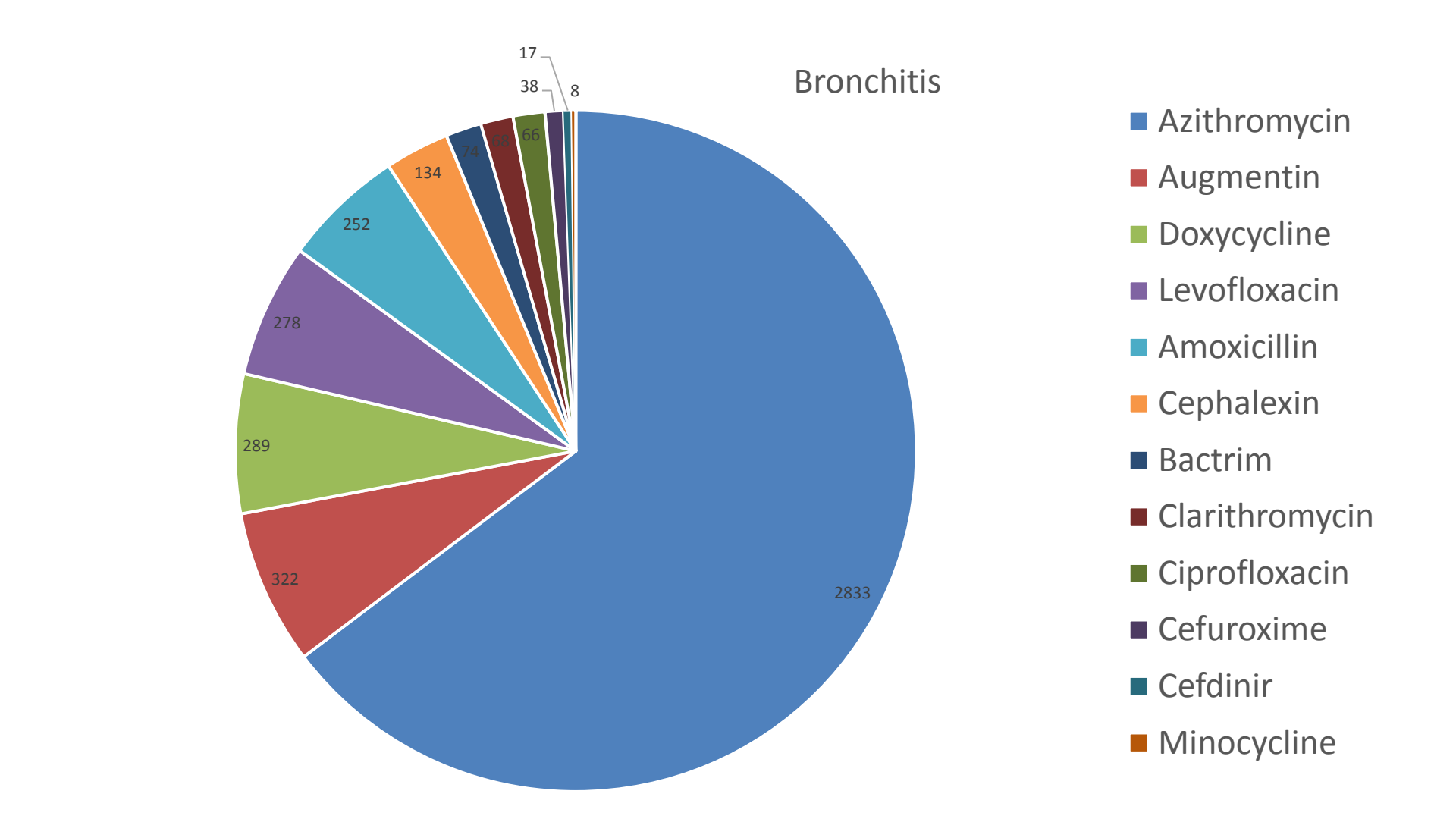
(d) Data from isolate totals <10 may be statistically unreliable.

(e) Cystic fibrosis patient isolates tested by disk diffusion.

(f) Pseudomonas aeruginosa isolates not corrected for duplicates.

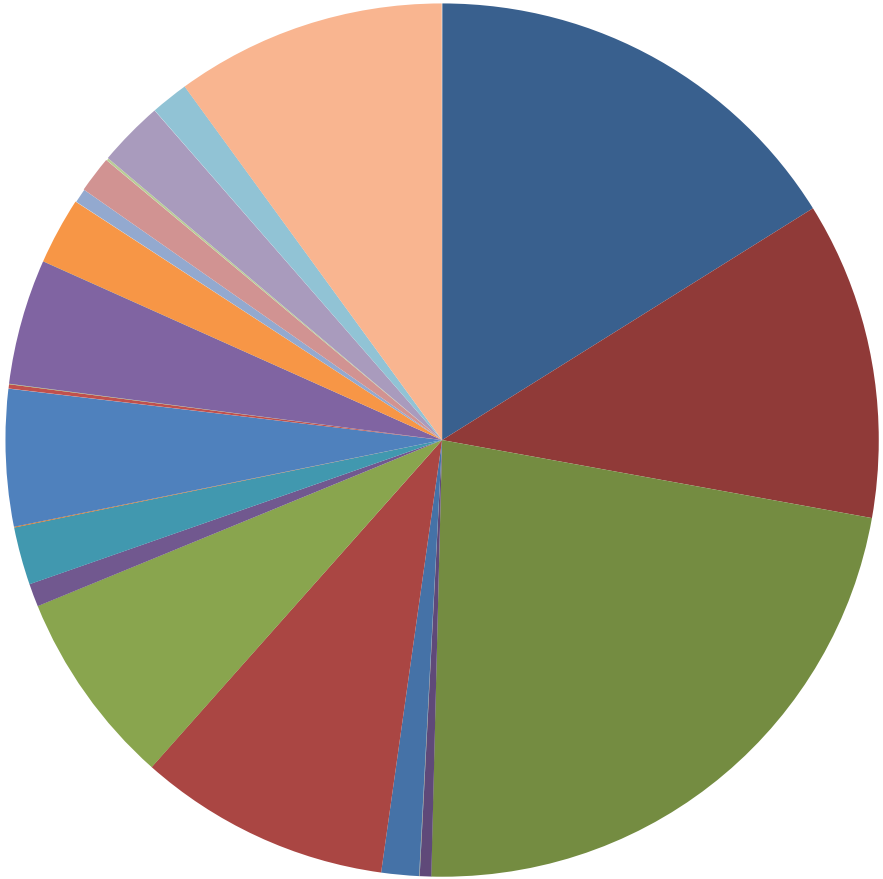
(g) Infectious Diseases consultation strongly recommended for determining treatment of Salmonella species recovered from blood.


Sinusitis/Rhinitis
3618
3443
3022
557
548
482
434
219
150
134
64
53
Augmentin
Azithromycin
Amoxicillin
Doxycycline
Bactrim
Levofloxacin
Cephalexin
Ciprofloxacin
Cefuroxime
Clarithromycin
Cefdinir
Clindamycin


Bronchitis
2833
322
289
278
252
134
74
68
66
38
17
8
Azithromycin
Augmentin
Doxycycline
Levofloxacin
Amoxicillin
Cephalexin
Bactrim
Clarithromycin
Ciprofloxacin
Cefuroxime
Cefdinir
Minocycline

Antibiotic Utilization in Percent

Total Abx Prescriptions = 65,535



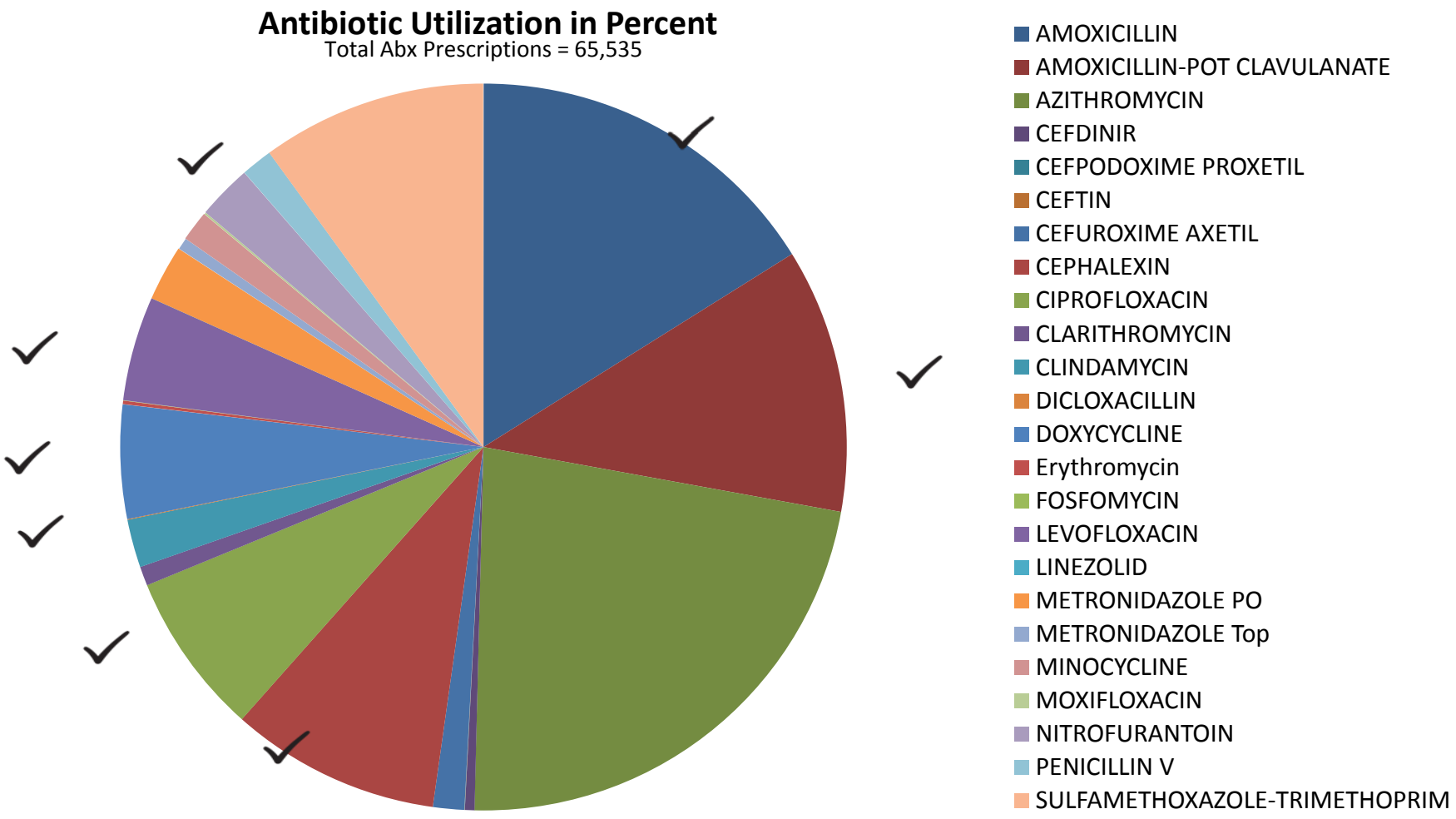
- AMOXICILLIN
- AMOXICILLIN-POT CLAVULANATE
- AZITHROMYCIN
- CEFDINIR
- CEFPODOXIME PROXETIL
- CEFTIN
- CEFUROXIME AXETIL
- CEPHALEXIN
- CIPROFLOXACIN
- CLARITHROMYCIN
- CLINDAMYCIN
- DICLOXACILLIN
- DOXYCYCLINE
- Erythromycin
- FOSFOMYCIN
- LEVOFLOXACIN
- LINEZOLID
- METRONIDAZOLE PO
- METRONIDAZOLE Top
- MINOCYCLINE
- MOXIFLOXACIN
- NITROFURANTOIN
- PENICILLIN V
- SULFAMETHOXAZOLE-TRIMETHOPRIM

Antibiotics and Risk Potential for Developing *C. Difficile*

High	Medium	Low
Clindamycin	Sulfametoxazole/ Trimethoprim (Bactrim®)	Aminoglycosides
Fluoroquinolones	Macrolides	Metronidazole
Cephalosporins	Tetracyclines	Vancomycin IV
Ampicillin/Amoxicillin	Other Penicillins	Rifampin

- All antibiotics have the potential to cause C. difficile infection

OSF HealthCare


Antibiotic Utilization in Percent
Total Abx Prescriptions = 65,535
AMOXICILLIN
AMOXICILLIN-POT CLAVULANATE
AZITHROMYCIN
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CIPROFLOXACIN
CLARITHROMYCIN
CLINDAMYCIN
DICLOXACILLIN
DOXYCYCLINE
Erythromycin
FOSFOMYCIN
LEVOFLOXACIN
LINEZOLID
METRONIDAZOLE PO
METRONIDAZOLE Top
MINOCYCLINE
MOXIFLOXACIN
NITROFURANTOIN
PENICILLIN V
SULFAMETHOXAZOLE-TRIMETHOPRIM


The Future

Questions

Antimicrobial Stewardship Basics for Long Term Care

Disclosure Statement

I have nothing to disclose

What is antimicrobial stewardship?

- According to SHEA (Society for Healthcare Epidemiology of America) antimicrobial stewardship refers to a “a set of coordinated strategies to improve the use of antimicrobial medication with the goal of enhancing patient health outcomes, reducing resistance to antibiotics and decreasing unnecessary costs”.

We are all guilty!

We have used antibiotics too much and not always appropriately and now we are dealing with *Clostridium difficile*, MRSA, VRE, CRE and the trend will continue unless…..

We

It

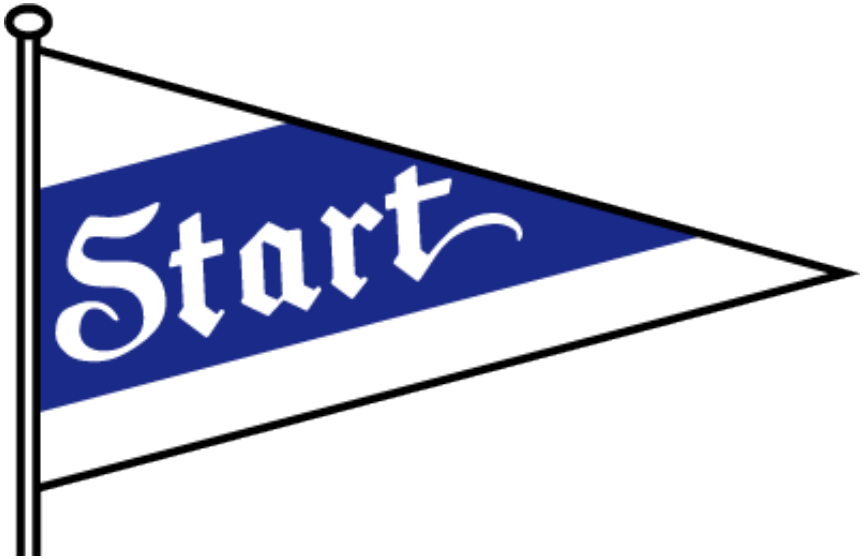
Now!!!!

I wish it was as easy as pressing a button, but it will require work!


not so
easy

It will take ALL of us to make it happen!

So where do we start?



We must:

- Get signed up for the XDRO registry
- Adopt good antimicrobial stewardship traits
  - Learn how to determine if a “true” infection is present and if treatment is needed – teach your staff
  - Track and trend antibiotic usage
- Conduct surveillance
- Develop a facility plan

Get signed up for the XDRO Registry

It’s as easy as pie!

Not as good as pie, but as easy as eating it!!

Get signed up for the XDRO Registry (continued)

- Go to https://www.xdro.org/ and look for access for the XDRO registry and click on that link

Get signed up for the XDRO Registry (continued)

- It will take you to a new page. Look for - New users and click on the New Users link. Once you agree to the terms it will take you to a form. You must fill out the form to create a new username and select the box to access the application “INEDSS (Disease Surveillance) System/XDRO registry”

Get signed up for the XDRO Registry (continued)

Remember the password!!!!

Get signed up for the XDRO Registry (continued)

At the bottom you will see:

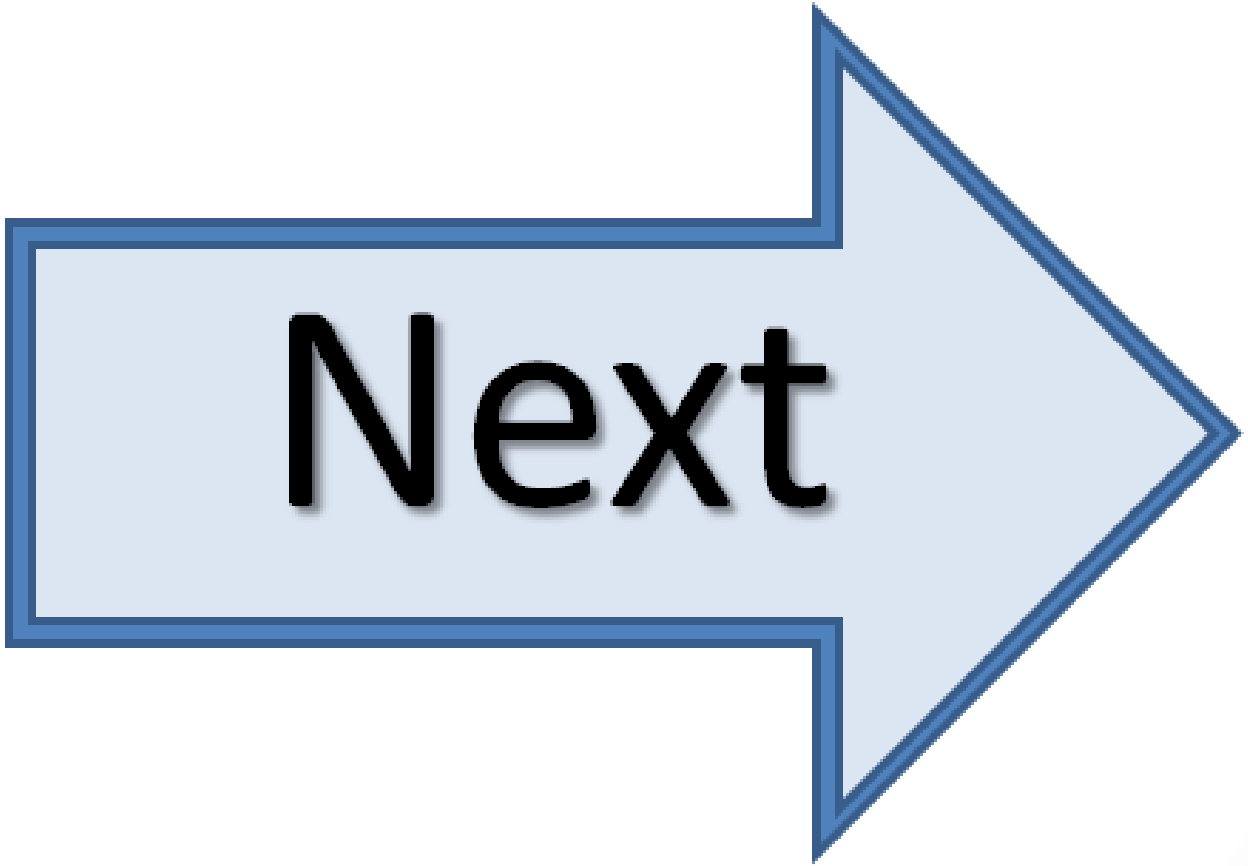
PRA E-mail: * select from the Portal Registration Authority list:

Click on that Portal Registration Authority link. It will open a new box where you can enter a keyword to search for your facility.

Get signed up for the XDRO Registry (continued)

It takes a while to get portal access, but just be patient.

Once you have access you will be able to use the XDRO registry with ease!


Next

Adopt good antimicrobial stewardship traits

Learn how to determine if a “true” infection is present and if treatment is needed

Assess

Assess

Assess

Learn how to determine if a “true” infection is present and if treatment is needed

A condition change requires assessment
Our elders have multiple co-morbidities.
Symptoms could mean a variety of things
Know your resident
Don’t jump the gun on antibiotics
What should we do first
Treat appropriately
Follow McGeer Criteria

Track and trend antibiotic usage

- Review antibiotic usage on at least a monthly basis
- Work with your pharmacist and pharmacy to help you track and trend antibiotic usage
- Meet with physicians
- Talk with family members
- Educate everyone!!!!

Educate Everyone!!!!

Conduct surveillance

- Surveillance is key
- Are we doing everything we can to reduce infections?
- If we find a concern do we address it timely?
- Are your employees reporting their symptoms to you when they are calling off work?
- Are we cleaning appropriately?
- Do we handle linens correctly?
- Are we using the correct chemicals to clean and disinfect – do they have kill claims for things like c.diff spores?

You MUST be out there watching – and not with **rose colored** glasses!

Get involved – communicate!

Develop a facility plan

You should build a team and create a plan to reduce infections in your facility by:

- Following hand hygiene requirements
  - Example – Utilize a QI process for observing hand hygiene – we use a process surveillance monitoring tool for these observations

Develop a facility plan

- Good cleaning and disinfecting
  - Started a “Pen Light Program” to monitor cleaning and disinfecting

Develop a facility plan

- Appropriate laundry handling
  - Put a process in place to wash isolation linens on an isolation cycle

Develop a facility plan

- Using antibiotics appropriately
  - Work closely with your pharmacy and your pharmacist to monitor and track antibiotic use

Develop a facility plan

- Isolating appropriately
  - Have created Isolation posters with staff pictures to draw attention to the need for isolation in a particular area

Good things can happen when you begin to adopt some of the principles we just reviewed.

By using some of the principles I have just mentioned and working together my company reduced UTIs in 2014:

- 1st Quarter 2014 = 505
- 2nd Quarter 2014 = 376
- 3rd Quarter 2014 = 319
- 4th Quarter 2014 = 299

The numbers are still coming down!

We can all make a difference!

Now Go…..

This is the time for action!

And please……

Wash your hands!!!!


Thank You!

Contact Information

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INFECTION CONTROL MONTHLY LOG

Facility: _____ **Month/Year:** _____

Resident										
Room #										
Admit Date										
Onset Date										
Site										
Culture: Yes (List date) -or- No										
Lab or x-ray date										
Organism										
Precautions Used: (In addition to Standard Precautions): Contact = C Droplet = D Airborne= A										
Antibiotic										
Nosocomial: Yes (List date) -or- No										
Were Re-Cultures or repeat x-rays or labs done: Yes (List Date) -or- No										
Resolve Date										
Report to IDPH: Yes (List date) -or- No										

***Notify Nursing Field Supervisor prior to reporting any infections to IDPH.**

Total # of Infections: Urine: _____ Respiratory: _____ GI: _____ Skin: _____ Ear: _____ Eye: _____ Blood: _____ Other:

_____

PROCESS SURVEILLANCE

(Circle appropriate month and complete surveillance and document outcome and action taken on both items listed under that month.)

January/April/July/October

1. Minimizes exposure to a potential source of infection (eg. Room placement, use of isolation precautions)
2. Uses Personal Protective Equipment (PPE) when indicated

February/May/August/November

3. Uses appropriate hand hygiene prior to and after all procedures:
4. Ensures that appropriate sterile techniques are followed; for example, that staff:
   - Use sterile gloves, fluids, and materials, when indicated, depending on the site and the procedure
   - Avoid contaminating sterile procedures
   - Ensure that contaminated/non-sterile items are not placed in a sterile field

March/June/September/December

5. Ensures that reusable equipment is appropriately cleaned, disinfected, or reprocessed
6. Uses single-use medication vials and other single use items appropriately (proper disposal after every single use)

_____ Outcome: _____

_____

_____

Action Taken: _____

_____

_____ Outcome: _____

_____

_____

Action Taken: _____

_____

MONTHLY OUTCOME SURVEILLANCE DATA ANALYSIS

1) Are any identified trends noted (3 or more cases of same infection in specific area in building)? Yes No
   _____
2) Is there one case of any highly communicable infection? Yes No
   _____
3) Is there any commonality of staff in infected residents? Yes No
   _____
4) Are any MDROs noted?
   a. MRSA? #: _____ Area: _____
   b. VRE? #: _____ Area: _____
   c. C-Diff? #: _____ Area: _____
5) Seasonal variance? Yes No _____
6) Comparisons from previous month: _____
7) Antibiotic review completed? Yes No _____
8) Employee Infection Record reviewed? Yes No _____

Conclusion: _____

_____

_____

_____

INFECTION CONTROL PROCESS SURVEILLANCE MONITORING

Date: _____ Time: _____ Conducted by: _____

Surveillance Item	Compliance				Comments
	Yes	No	Not Known	N/A	
Exposure Monitoring – Minimizes exposure to a potential source of infection. **January / April / July / October**					
Are residents co-horted in rooms with other residents with same infection?					
Are private rooms utilized if necessary?					
Are resident rooms (environment) clean?					
Are Isolation rooms being cleaned with correct cleaner?					
Are “Isolation Precautions” posted when appropriate?					
Is equipment clean (i.e. bedpans, urinals, etc.)?					
Is resident clean and dry with good hygiene?					
Is hand washing witnessed before and after resident care?					
Are resident’s hands being washed?					
Are gloves used and changed as needed?					
Is there safe handling of blood and infectious fluids?					
Are soiled items disposed of or handled properly?					
Are “Biohazard” signs available and used?					
Are PPE available and used appropriately?					
Is there monitoring for nosocomial infections?					
Is prevention considered?					
Are infection rates evaluated?					
PPE – Uses Personal Protective Equipent (PPE) when indicated. **January / April / July / October**					
Are gowns/aprons available?					
Are gloves available?					
Are masks available?					
Is eyewear in locations where they can be easily found?					
Are solutions for cleaning up blood/body fluid spills available?					
Are needle boxes available?					
Is there adequate room in needle boxes?					
Are gloves used and changed as needed?					
Can employees answer questions about availability of barrier equipment?					
Are appropriate PPE used based on isolation need?					
Are hand washing procedures followed?					
Are employees aware of Standard Precautions?					

Surveillance Item	Compliance				Comments
	Yes	No	Not Known	N/A	
Hand Hygiene – Uses appropriate hand hygiene prior to and after all procedures. **February / May / August / November**					
Is hand washing witnessed before and after resident care and at any time hands become soiled?					
Is hand washing witnessed before and after procedures?					
Are hands washed after removal of gloves?					
Are resident's hands being washed?					
Sterile Techniques – Ensures that appropriate sterile techniques are followed: • Use of sterile gloves, fluids and materials, when indicated, depending on the site and the procedure • Avoid contaminating sterile procedures • Ensure that contaminated / non-sterile items are not placed in a sterile field **February / May / August / November**					
Are sterile gloves, fluids and materials used for sterile procedures?					
Are sterile fields maintained as sterile throughout procedure?					
If contamination occurs, is problem corrected and a sterile field once again maintained?					
Do contaminated and sterile items remain separate?					
Do contaminated or non-sterile items remain free of the sterile field?					
Cleaning / Disinfecting / Reprocessing – Ensures that reusable equipment is appropriately cleaned, disinfected, or reprocessed. **March / June / September / December**					
Is reusable equipment (B/P cuffs, stethoscopes, thermometers, etc.) appropriately cleaned, disinfected or reprocessed after use?					
Single Use Items – Uses single-use medication vials and other single use items appropriately (proper disposal after every single use). **March / June / September / December**					
Are single use medication vials used?					
Are single use items used as needed for residents in isolation?					
Are single use items disposed of properly after every single use?					

Central Illinois Infection Prevention and CRE Workshop, Springfield, IL

CRE and CPO: Methods for Detection and Pitfalls to Avoid

Angella Charnot-Katsikas, MD
Assistant Director, Clinical Microbiology and Immunology Laboratories
Department of Pathology
The University of Chicago
July 28, 2015

THE UNIVERSITY OF CHICAGO MEDICINE

Disclosures

- None

Objectives

By the end of this presentation, the learner will:

1. Describe the major types of CRE
2. Understand the difference between CRE and CPO
3. Review approaches for detecting and reporting CRE and avoiding common pitfalls
4. Evaluate your laboratory's readiness for assessing CRE-positive specimens

Terms….

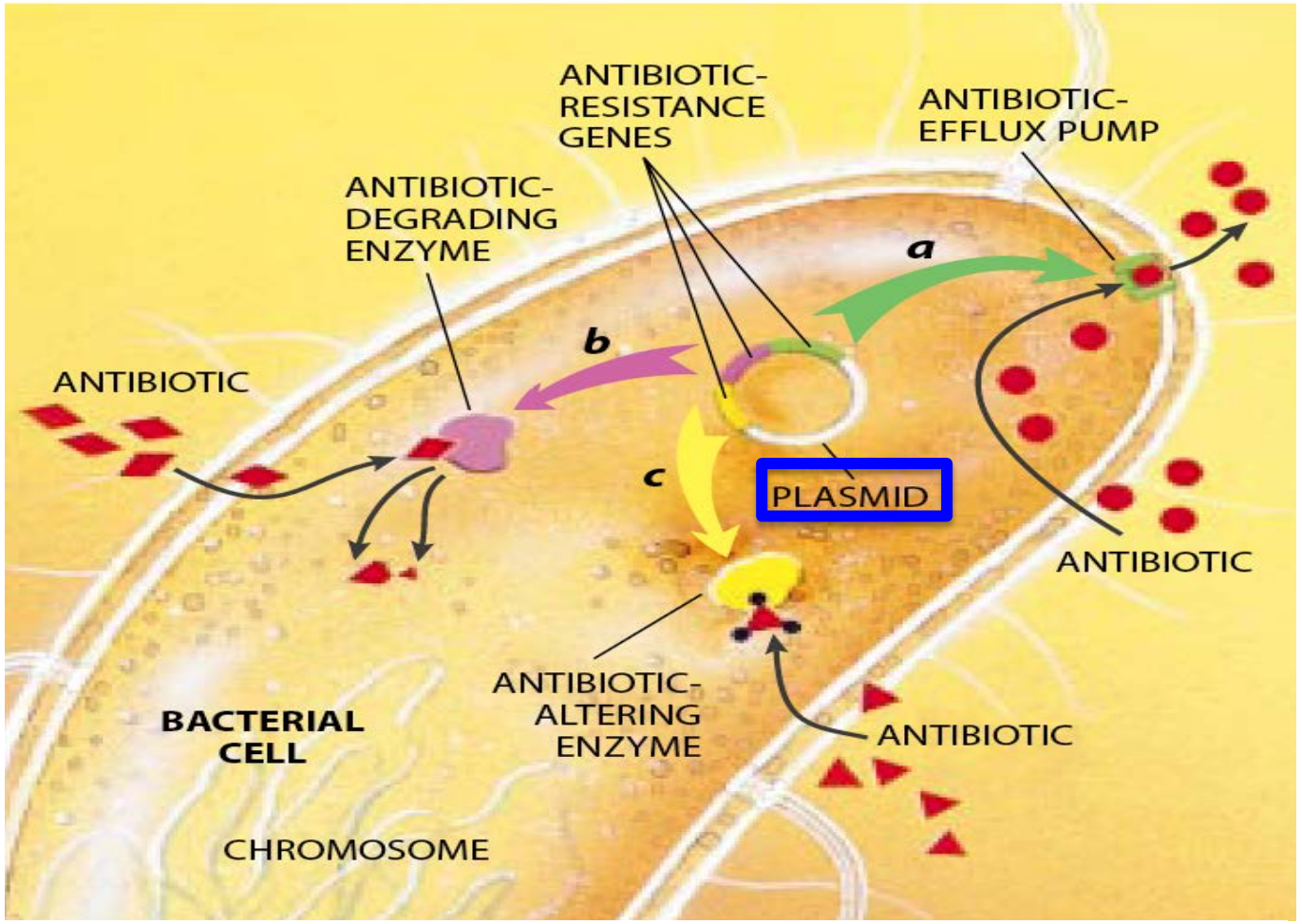
- Carbapenem
- Carbapenemase
- Carbapenem-Resistant *Enterobacteriaceae* “CRE”
- Carbapenemase-Producing Organism “CPO”

Carbapenems & Carbapenemases

- Carbapenems: β-lactam drugs that end in "penem"
  - Ertapenem
  - Imipenem
  - Meropenem
  - Doripenem
- Carbapenem*ases*: enzymes that break down carbapenem drugs

The Many Faces of Carbapenem Resistance

- **Carbapenem Resistance – a phenotype**
  - Many mechanisms involved…porin mutations, enzyme production, efflux pumps, etc.
    - ie Carbapenem-Resistant *Enterobacteriaceae* "CRE"
  - **Carbapenem*ase*-Producing Organism "CPO" – a specific mechanism**
    - *Enterobacteriaceae* and non-*Enterobacteriaceae*
      - KPC, NDM,OXA
      - MDRO



ANTIBIOTIC-RESISTANT BACTERIA owe their drug insensitivity to resistance genes. For example, such genes might code for "efflux" pumps that eject antibiotics from cells (*a*). Or the genes might give rise to enzymes that degrade the antibiotics (*b*) or that chemically alter—and inactivate—the drugs (*c*). Resistance genes can reside on the bacterial chromosome or, more typically, on small rings of DNA called plasmids. Some of the genes are inherited, some emerge through random mutations in bacterial DNA, and some are imported from other bacteria.

http://www.orion-group.net/journals/Journals/Vol1_Sep1998/7.htm

The β-lactam family of antibiotics

Penicillins	Cephalosporins	Cephamycins	Carbapenems	Monobactams
Benzyl-penicillin	Cephalothin 1st	Cefoxitin	Imipenem	Aztreonam
Methicillin	Cefamandole 2nd	Cefotetan	Meropenem	
Ampicillin	Cefuroxime 2nd	Cefmetazole	Ertapenem	
Carbenicillin	Cefotaxime 3rd		Doripenem	
Mezlocillin	Ceftazidime 3rd			
Ticarcillin	Ceftriaxone 3rd			
	Cefepime 4th			

KPCs hydrolyze all

Penicillins
Cephalosporins
Cephamycins
Carbapenems
Monobactams

Slide courtesy of Dr. Paul Schreckenberger

Summary – gram negative β-lactamases

β-lactamase Category	Molecular (Ambler) Class	Examples	Key Features of the class*	Found in
ESBL	A (serine)	CTX-M SHV TEM	Activity against penicillins, 1st through 3rd-generation cephalosporins and aztreonam; Susceptible to clavulanic acid & cephamycins	*Enterobacteriaceae*; other gram negative organisms such as *N.gonorrhoeae* and *H.influenza*
AmpC	C (serine)	ACC, FOX LAT, MOX	Activity against cephamycins (cefoxitin); Resistant to clavulanic acid; Susceptible to cefepime & carbapenems; Can be induced by β-lactam agents	SPACE bugs (discussion in text) *E.cloacae*
Carbapenemase (all have activity against the carbapenems & cephamycins are resistant to clavulanic acid); all are serious infection control threats	A (serine)	KPC, IMI, SME	Weaker carbapenemase hydrolyzers; May be inhibited by boronic acid and partially inhibited by clavulanic acid	*Enterobacteriaceae* esp *K.pneumoniae* and *E.coli;* SME in *Serratia marcescens;* *A. baumannii;* *P. aeruginosa*
	B (metallo β-lactamases, "MβLs"; zinc at active site)	NDM, VIM, IMP, GIM, SPM-1	Strong carbapenemase hydrolyzers; Do not inactivate aztreonam; Inhibited by EDTA but not clavulanic acid or boronic acid	*A. baumannii; P. aeruginosa*; *Enterobacteriaceae*
	D (serine)	OXA	Weak carbapenem hydrolysis; high activity against oxacillin; susceptible to aztreonam; not inhibited by EDTA, boronic acid and clavulanic acid	*A. baumannii; P. aeruginosa*; *Enterobacteriaceae*

Adapted from Bush and Jacoby. Antimicrob Agents Chemother. 2010; 54(3)

Antibiotics affected by different Resistance Mechanisms

Antibiotic	ESBL	AmpC	CRE / CPO	
			KPC	MBL
Ampicillin	X	X	X	X
Ampicillin/Sulbactam		X	X	X
Aztreonam*	X	X	X	
Cefazolin	X	X	X	X
Cefoxitin (not reported)		X	X	X
Cefepime	X		X	X
Ceftazidime	X	X	X	X
Ceftriaxone	X	X	X	X
Ertapenem			X	X
Imipenem*			X	X
Meropenem			X	X
Piperacillin*	X	X	X	X
Piperacillin/Tazobactam*		X	X	X

Carbapenem*ase*

- Isolate likely to be resistant to all carbapenems and other β-lactam agents

- Infection Control emergency

A serious public health threat

- *Klebsiella pneumoniae* carbapenemase (KPC) is the most common worldwide
- Increased morbidity and mortality

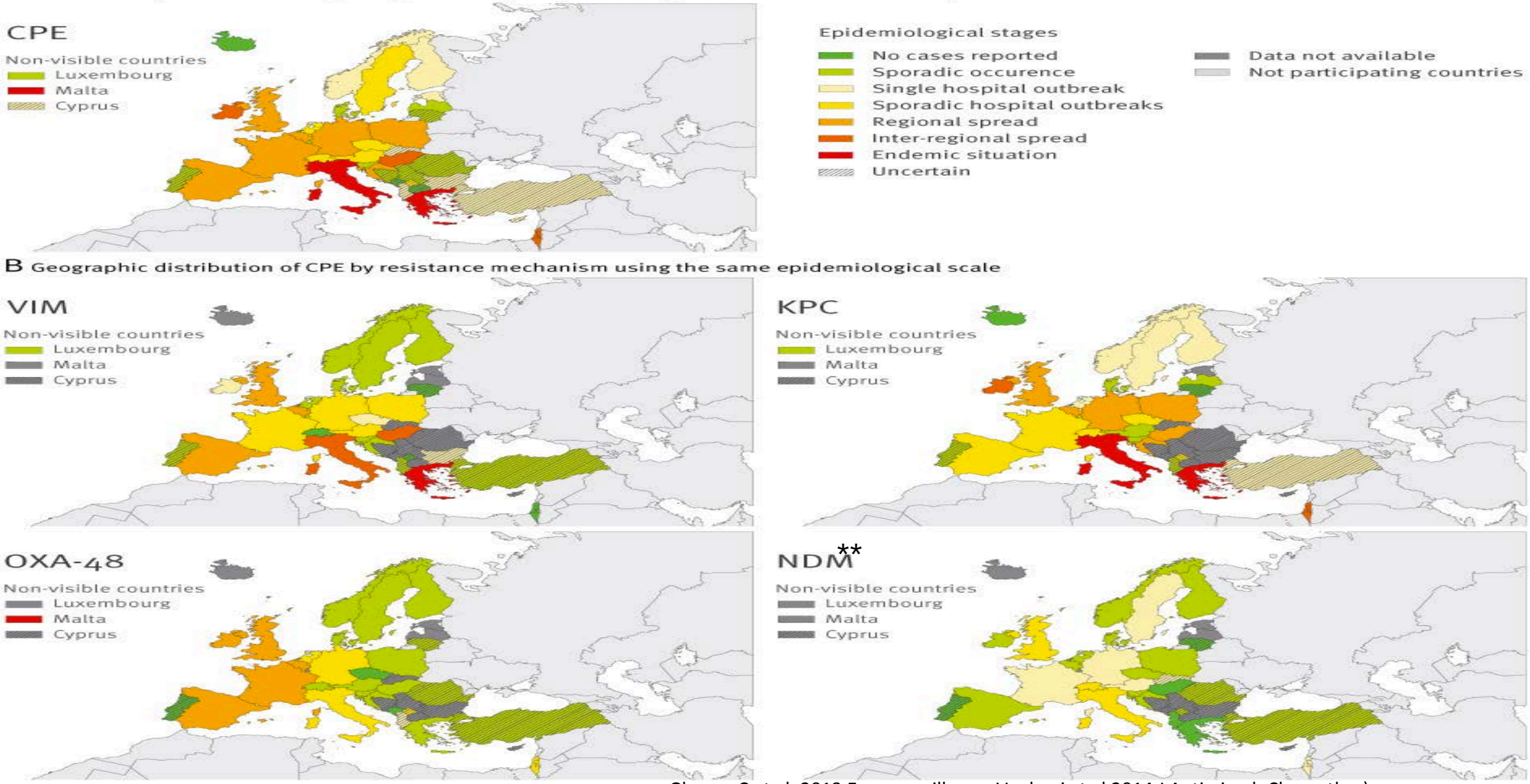
World Health Organization ANTIMICROBIAL RESISTANCE Global Report on Surveillance. 2014. http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf?ua=1.

A serious public health threat globally

FIGURE

Occurrence of carbapenemase-producing *Enterobacteriaceae* (CPE) in 39 European countries based on self-assessment by respective national experts, 2013

A Overall European situation regarding CPE using an epidemiological scale of nationwide expansion

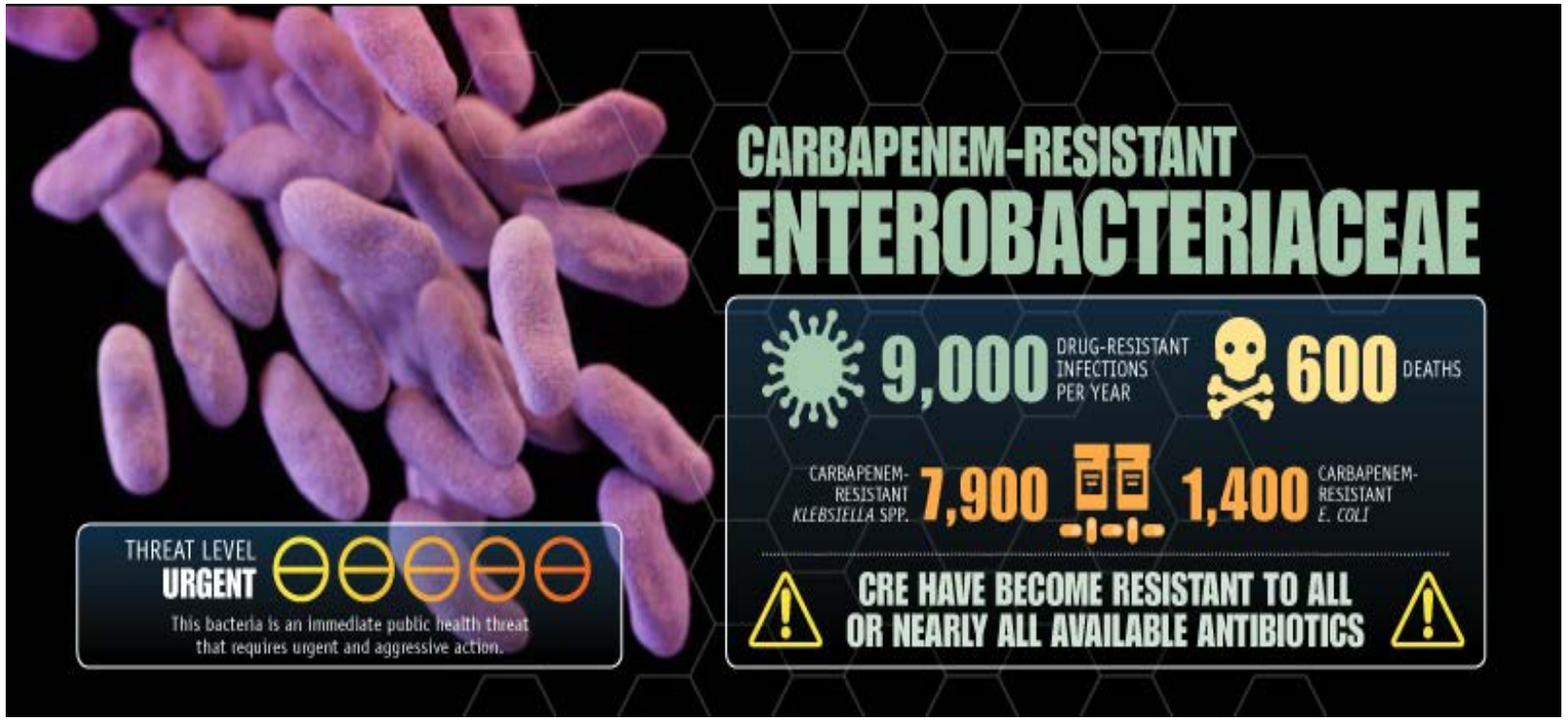


Glasner C et al. 2013 Eurosurveillance; Voulgari et al 2014 J Antimicrob Chemother)

A serious public health threat at home

- In the US, > 2 million people are sick every year with antibiotic-resistant infections, with at least 23,000 dying (CDC, Antibiotic Resistance Threats in the United States, 2013)
  - Level of concern :
    - CRE is ‘urgent’
    - MDRO Acinetobacter, ESBL, MRSA, & VRE are ‘serious’

CRE



http://www.cdc.gov/drugresistance/biggest_threats.html

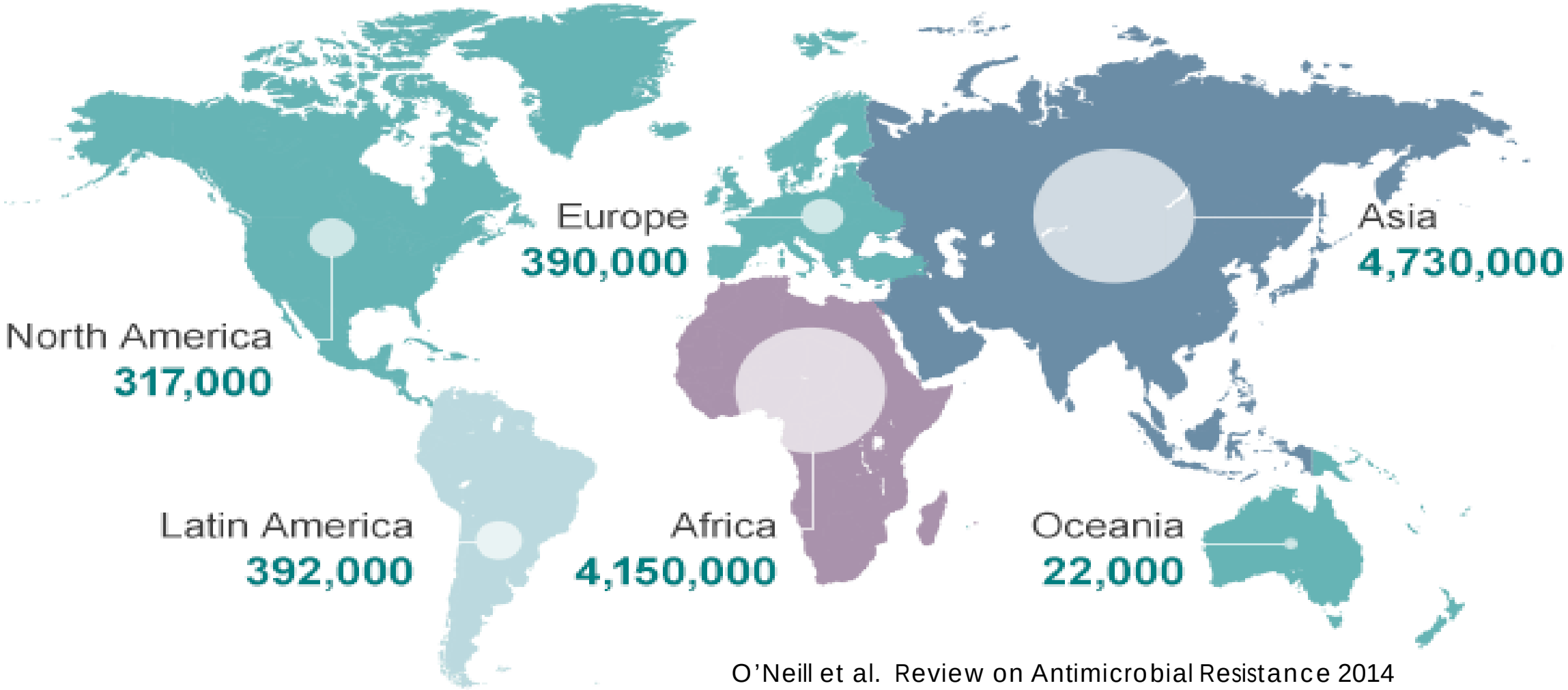
Mortality due to *K.pneumoniae* bloodstream infections

Infection related mortality

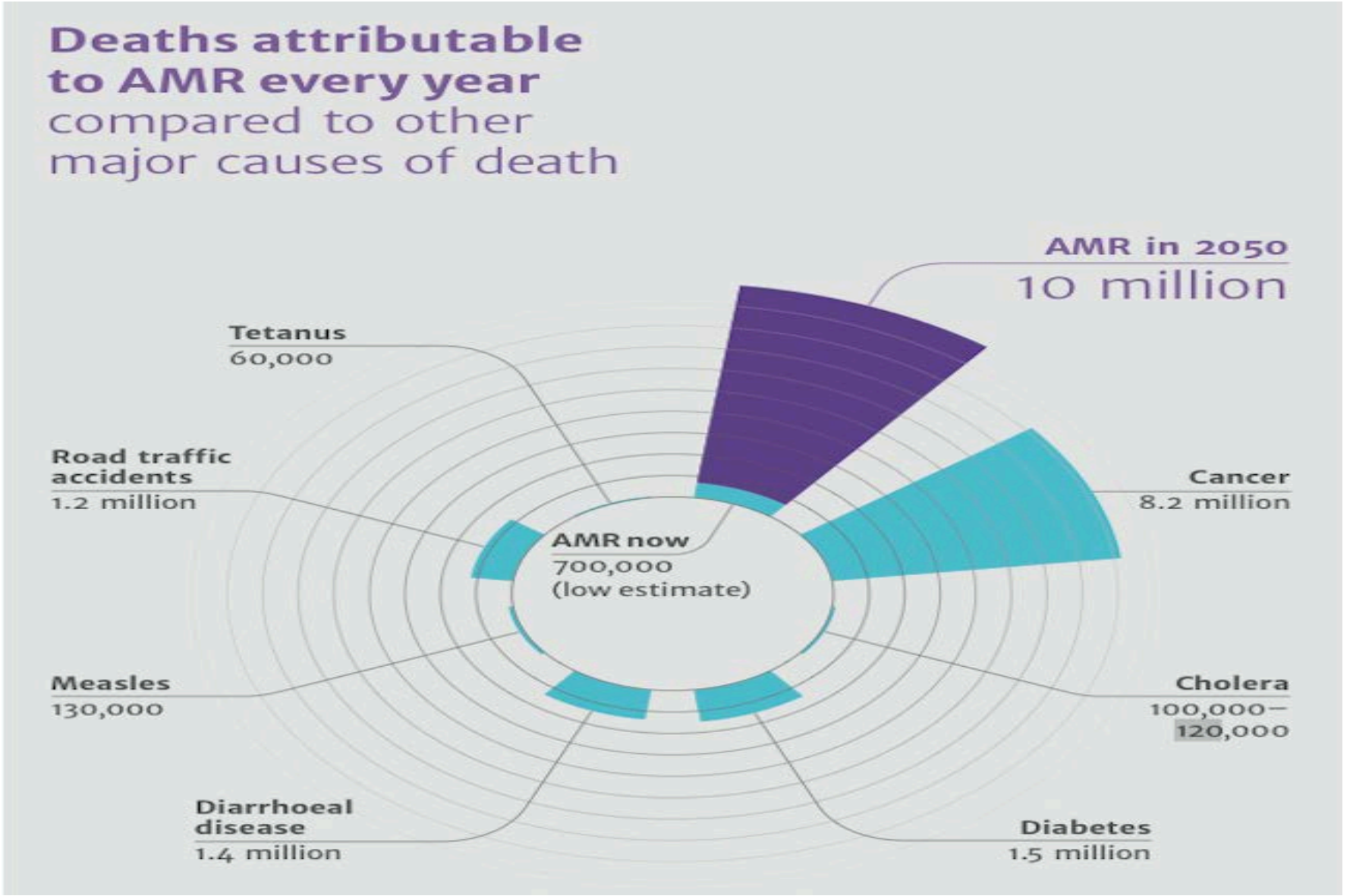
- Susceptible 17%
- ESBL + 22%
- CRE + 48%

Benn-David et al, Clin Microiol Infect 2012;
Neuner EA et al DMID 2011

Projections….
Deaths attributable to antimicrobial resistance every year by 2050



O'Neill et al. Review on Antimicrobial Resistance 2014



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O'Neill et al. Review on Antimicrobial Resistance 2014

Definitions, definitions….

For *E.coli, Klebsiella & Enterobacter spp*

- CSTE/CDC then (2012):

Non-susceptible to imipenem, meropenem, or doripenem AND Resistant to all 3rd gen cephalosporins tested

  - *difficult implementation*
  - *Missed cases (KPCs resistant only to ertapenem; OXA-48 NOT resistant to 3rd gen cephalosporins)*

- CSTE/CDC now:

Resistant to imipenem, meropenem, doripenem **OR ertapenem OR documentation of carbapenem*ase***

"Resistant"; + ertapenem; - cephalosporins

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http://www.cdc.gov/hai/organisms/cre/definition.html

The change…

- MAY increase the measured CRE prevalence particularly since the addition of ertapenem and confirmatory testing is not required
  - *Enterobacter spp* may be R to ertapenem but are not necessarily CRE

CDC Suggestions

- If an isolate fits the new CDC definition…
  - **Lab Test** for carbapenemase (phenotype or genotype)
    - IF test -, then implement basic infection control (IC) measures (hand hygeine, contact precautions, etc)
    - IF test +, then implement intensive infection control measures (basic IC + screening cultures, patient/staff cohorting, etc)

OR

  - **Automatically consider isolate to be a CPO-CRE** and implement intensive infection control measures
    - Consider cost:benefit (more IC interventions but less lab testing and less info on epidemiology)

CDC Suggestions

OR….

Do something in-between (this can get tricky)

- Test only for *less* likely CR-CPOs (*E.coli* and *Enterobacter* spp) instead of all (*K.pneumoniae*)
- Test only isolates in areas where CR-CPOs are less likely to be found geographically
- Test only islates R to one carbapenem, instead of those R to all

Reporting in Illinois - Mandatory

- Per the Control of Communicable Diseases Code 77 Ill. Adm. Code 690, IDPH requires reporting of **CRE**
- XDRO Registry for CRE began November 1, 2013
- Phenotype or Genotype (molecular) confirmation tests are accepted

Defining CRE for the XDRO Registry

Only report 1st CRE event/patient/*encounter*

For the Enterobacteriaceae (E. coli, Klebsiella, Enterobacter, Proteus, Citrobacter, Serratia, Morganella, or Providentia species):

1. Molecular test (e.g. PCR) for a carbapenemase gene (e.g. bla_{KPC}, bla_{NDM})

OR

2. Phenotypic test (e.g. Modified Hodge test) for carbapenemase production

OR

3. For E. coli or *Klebsiella* spp. only: Non-Susceptible to ONE of the carbapenems (doripenem, meropenem, or imipenem) **AND** Resistant to ALL third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime)

Note: ignore ertapenem for this definition

https://www.xdro.org/reporting-rule.html

Standardization of definitions

- Important!
- Apples to apples comparison among facilities and states
- Correct data and tracking

Still working on it state by state….

Stay tuned for any IL modifications!

Screen vs Confirm

Screen

MICs/Interpretations

Confirm

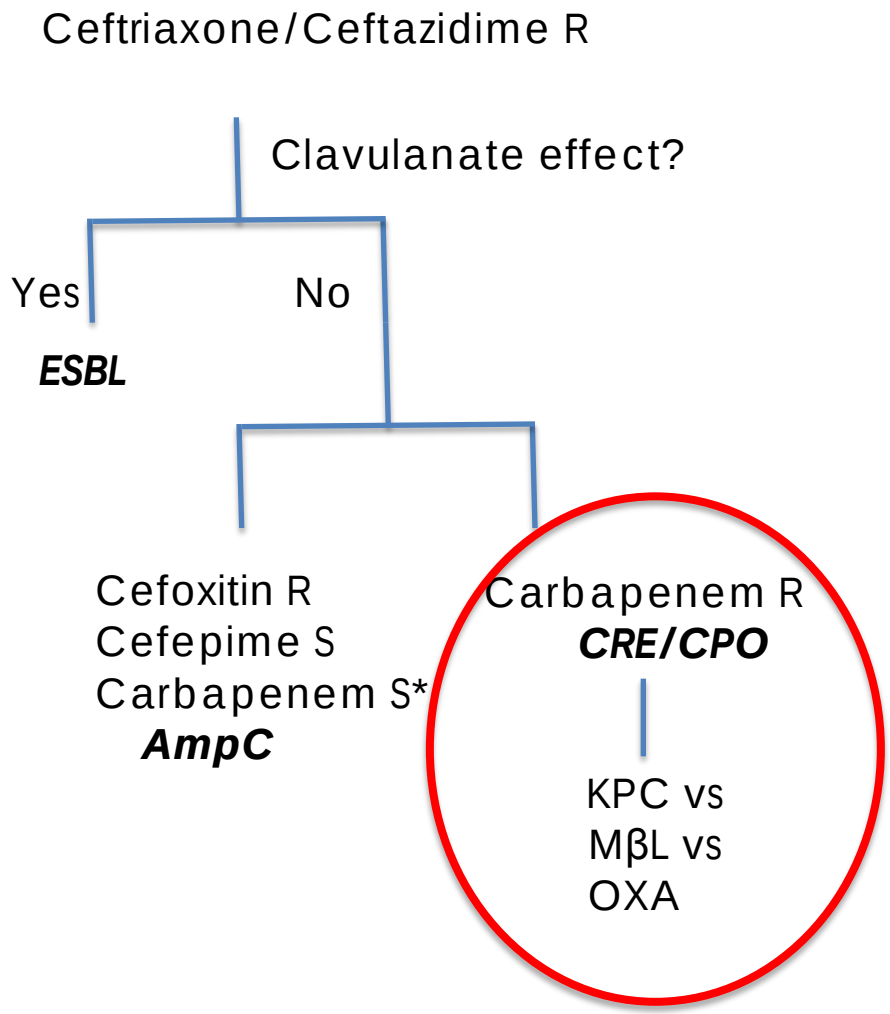
Phenotype

- Inhibitor based tests
- Colorimetric
- MALDI

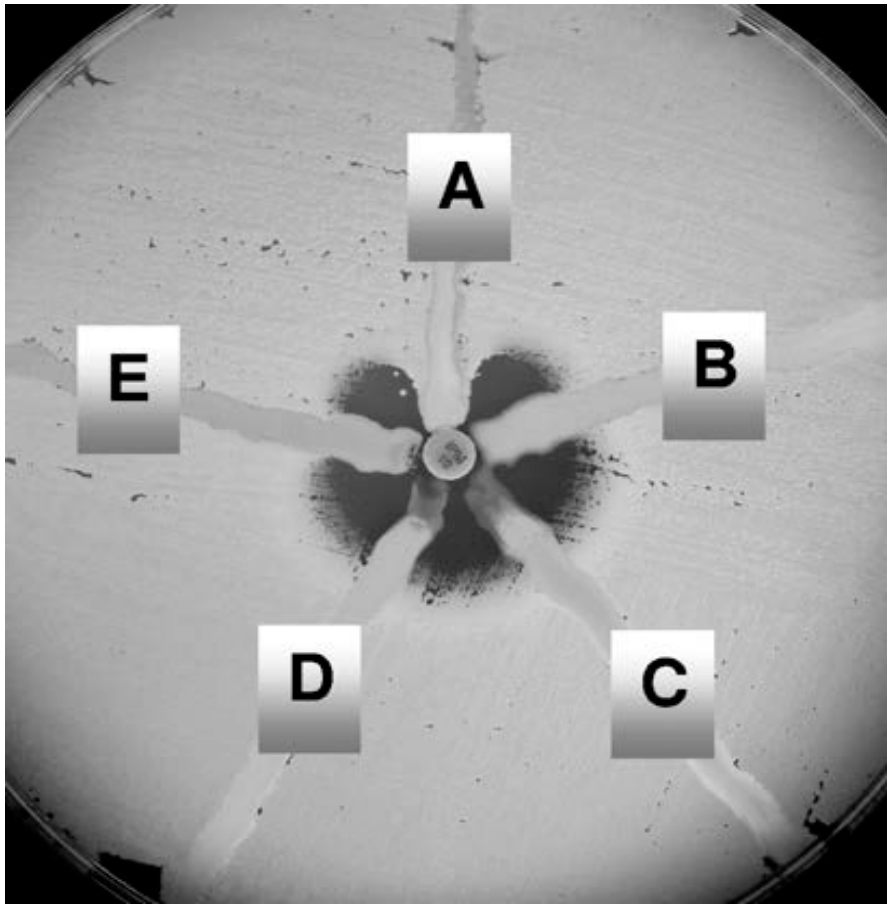
Genotype/Molecular

Confirming: Phenotypic Tests

Sample Algorithm



Modified Hodge Test (MHT)
for Enterobacteriaceae



Which is the KPC producer?

Isolate A

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Anderson KF et al. JCM 2007 Aug;45(8):2723-5.

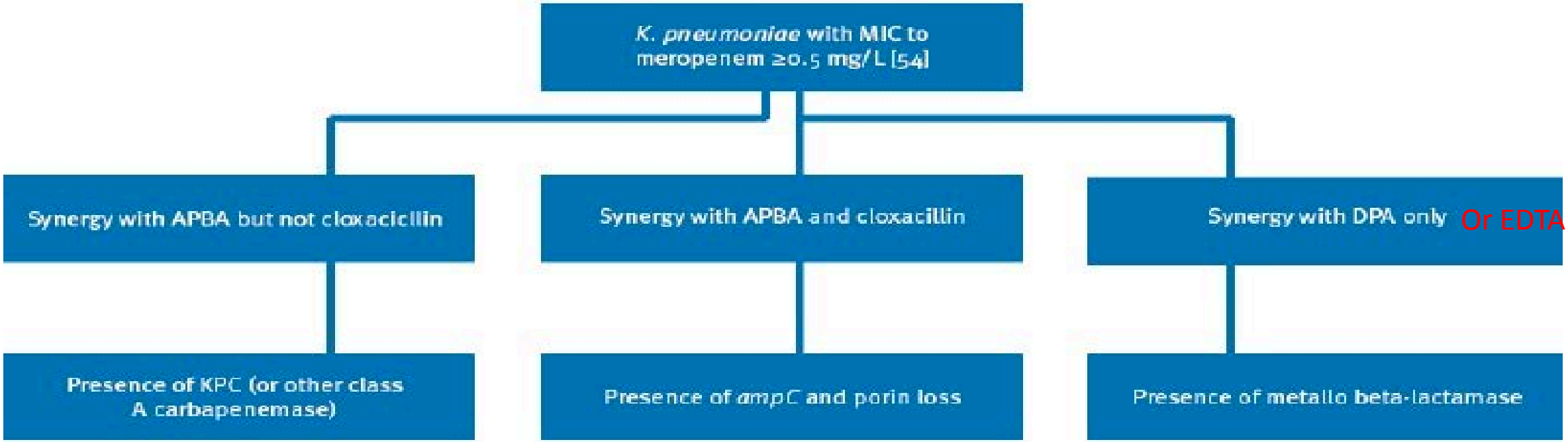
Metallo beta-lactamase (MBL) Test

- Testing:
  - a double-ended Etest strip ; one end has an Imipenem gradient and the other has Imipenem + EDTA
  - MBL activity can be negated by metal chelators such as EDTA.
  - A difference in MIC of ≥ 3 $\log_2$ (≥8) indicates the presence of MBL.
  - Can also do combination EDTA/boronic disk testing…

EUROROUNDUPS

Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts

Algorithm for disk diffusion synergy tests to detect Carbapenem Non Susceptible Enterobacteriaceae

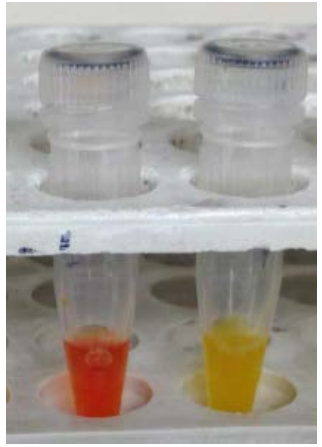


APBA = aminophenyl boronic acid (β lactamase inhibitor)
DPA = dipicolinic acid (metal chelating agent)

Grundmann H and the CNSE Working Group. Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts. Euro Surveill. 2010;15(46):pii=19711.

Other Phenotypic Tests

- **Colorimetric**
  - Carba NP
    - Good for KPC, NDM, VIM, SPM, SME
    - Not so good for OXA (False Neg)
    - Can use for *P.aeruginosa* and *Acinetobacter*
  - NEO-Rapid CARB Kit by Rosco Diagnostica (Hardy, Key Scientific) - NOT FDA
    - Prob w/ NDM + *A.baumannii*
  - RAPIDEC® CARBA NP (bioMerieux) - NOT FDA
    - Detects carbapenemases but no differentiation
  - EPI-CRE® (Pilots Point, Sarasota, FL) - NOT FDA
    - Sens/spec 100% (Siesar and Schreckenberger, Abstract, ASM 2015)



+

- **MALDI-TOF**
  - Similar sens/spec to Carba NP but increased sens when used with NH4HCO3
  - Problems with OXA-48

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Slide courtesy of Dr. Paul Schreckenberger

Confirming:
Molecular Tests

- Biofire (KPC only)
- Nanosphere (KPC, NDM, OXA, IMP & VIM)
- BD Max, Cepheid, Check Points (non-FDA; all detect KPC, NDM, and OXA-48; later two also detect IMP and VIM)

- *Only detect genes that recognized by the available probes*
  - *Can miss detection of new enzymes*

CLSI M-100 S25, 2015

- Continues to endorse confirmation of carbapenemase production by MHT, Carba NP, or molecular assay for infection control and epidemiologic purposes

Pitfalls to avoid

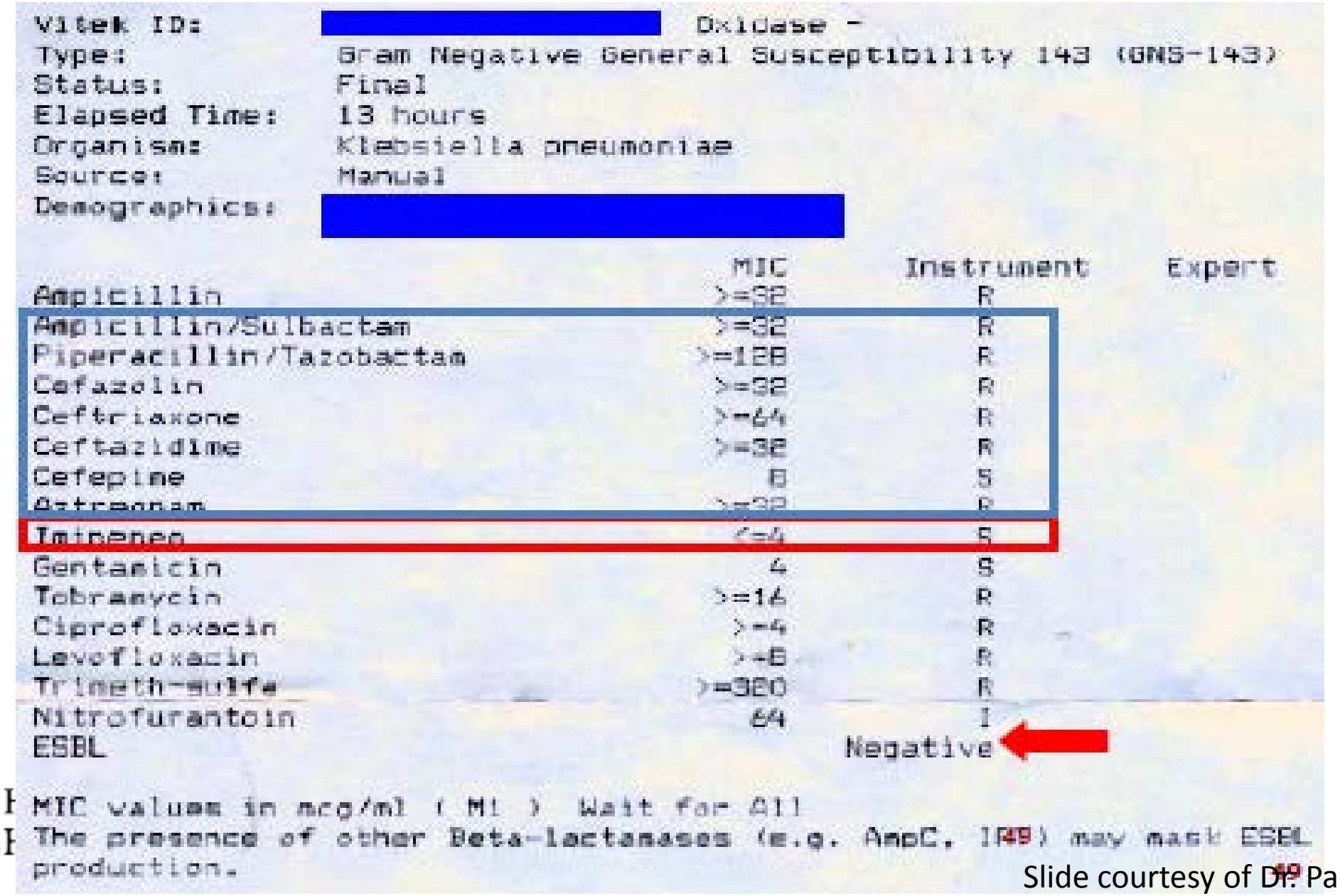
Pitfalls… tests & drug-bug combinations used for testing

- Imipenem disk test - not a good screen
- Imipenem MIC - cannot use as a screen for *Proteus/ Providencia/Morganella* due to intrinsically elevated MICs
  - higher MICs with imipenem vs. *P. mirabilis* due to reduced binding of drug by PBP

Important but *NOT an IC emergency….*

Resistance is NOT due to carbapenemases

Pitfall – systems/cards used for testing

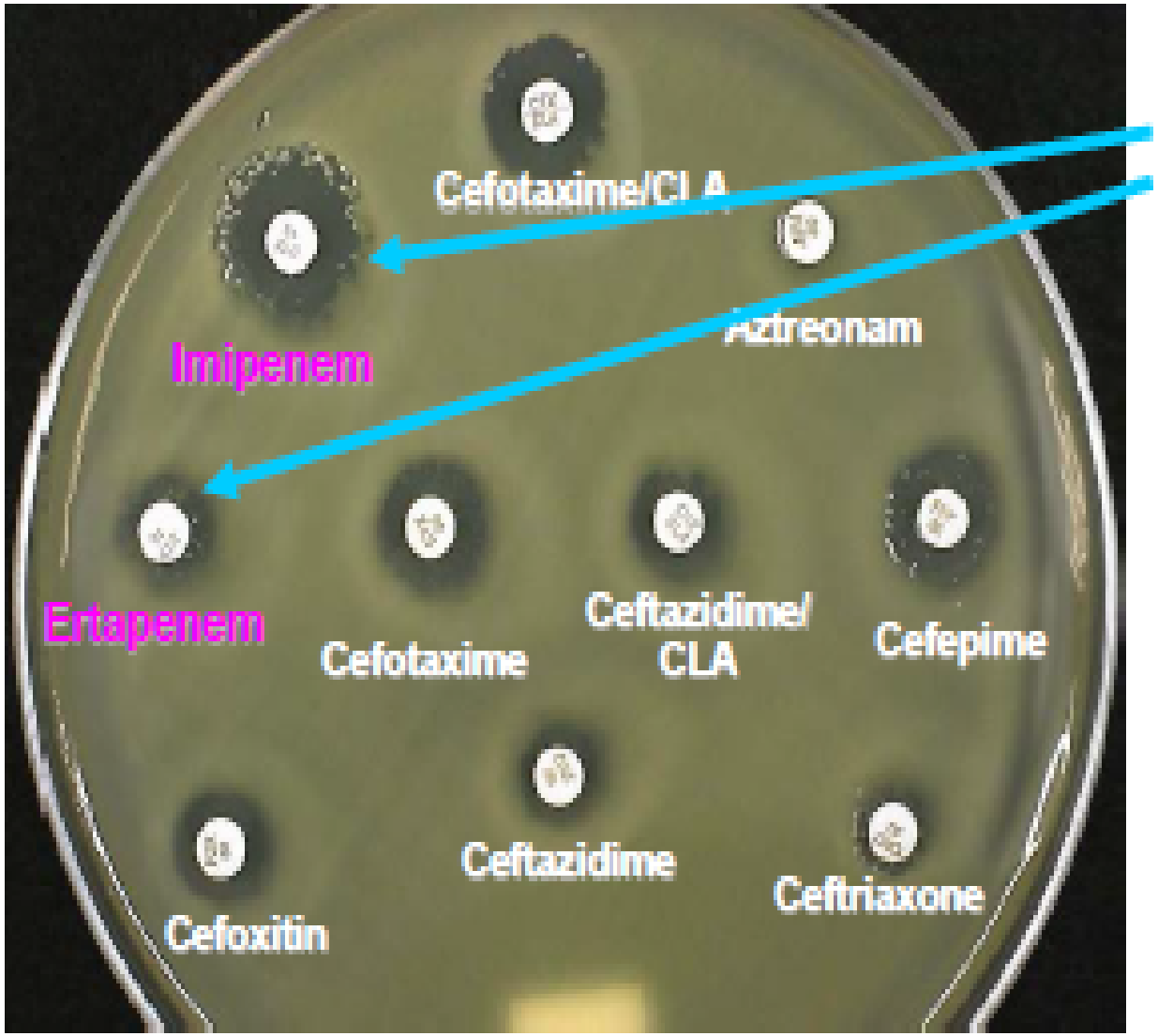


Vitek ID: [redacted] Oxidase -
Type: Gram Negative General Susceptibility 143 (GNS-143)
Status: Final
Elapsed Time: 13 hours
Organism: Klebsiella pneumoniae
Source: Manual
Demographics: [redacted]

	MIC	Instrument	Expert
Ampicillin	>=32	R	
Ampicillin/Sulbactam	>=32	R	
Piperacillin/Tazobactam	>=128	R	
Cefazolin	>=32	R	
Ceftriaxone	>=64	R	
Ceftazidime	>=32	R	
Cefepime	8	S	
Aztreonam	>=32	R	
Imipenem	<=4	S	
Gentamicin	4	S	
Tobramycin	>=16	R	
Ciprofloxacin	>=4	R	
Levofloxacin	>=8	R	
Trimeth-sulfa	>=320	R	
Nitrofurantoin	64	I	
ESBL		Negative	

MIC values in mcg/ml (MI) Wait for All
The presence of other Beta-lactamases (e.g. AmpC, IR49) may mask ESBL production.

Slide courtesy of Dr. Paul Schreckenberger

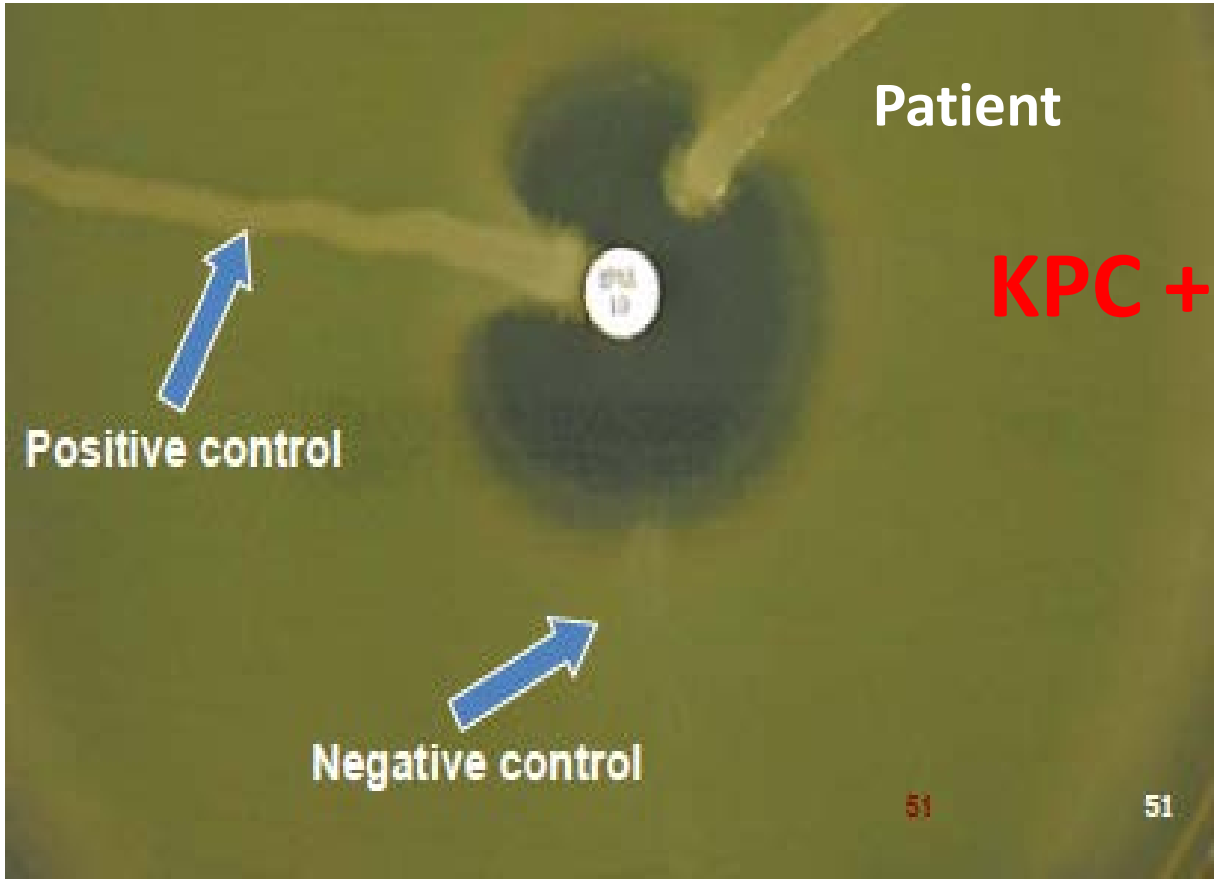


Imipenem - S
Ertapenem - R

Suggests possible KPC which should be confirmed with Hodge test or sent to reference lab for confirmation

Slide courtesy of Dr. Paul Schreckenberger

And in fact….



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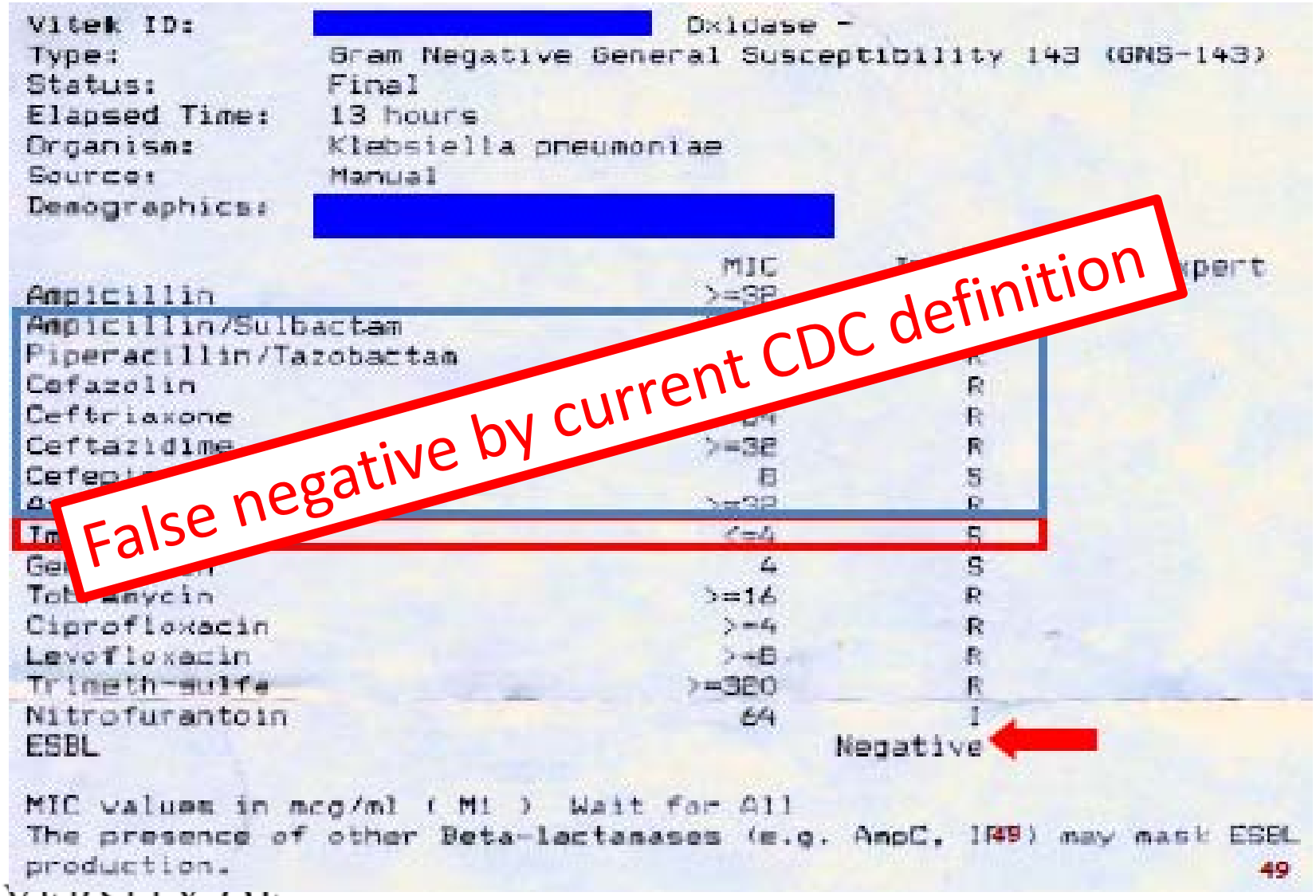
Pitfall – systems/cards used for testing



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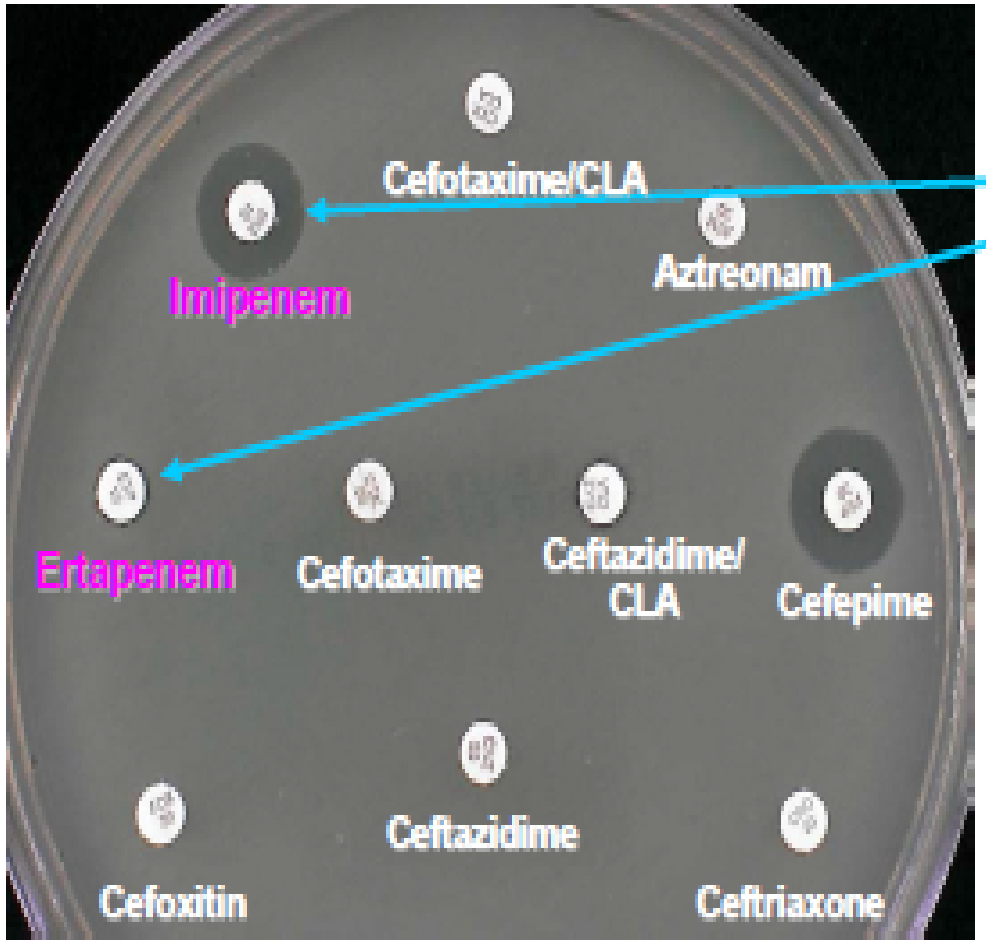
Slide courtesy of Dr. Paul Schreckenberger

Pitfalls… Breakpoints used

- Impacts screening by automated methods
- Impacts reporting – do you change your results based on additional testing?
- Previous example:
  - If using former CLSI/FDA breakpoints you may still change all carbapenems to R
  - If using new CLSI/FDA breakpoints report interpretations as tested
  - **Either way, you wouldn't necessarily know if you didn't do a confirmatory test**
  - **Either way, report as CRE** –probable KPC type. Implement infection control measures accordingly
  - **REPORT TO XDRO REGISTRY**

Pitfalls… .*Enterobacter spp (E.cloacae)*



Imipenem - S
Ertapenem - R

Suggests possible KPC which should be confirmed with Hodge test or sent to reference lab for confirmation

Slide courtesy of Dr. Paul Schreckenberger

But in this case….

- MHT –
- So….What is this?

Chromosomal AmpC with a porin mutation = carbapenem R

….

So is resistant to carbapenems

but

is NOT a CPO

&

is NOT to be reported to XDRO – recall current definition (slide 24)!

*But note: would be reported **if** we followed CDC definition (slide 19)!*

Pitfalls…imperfect confirmatory tests

- False positive MHT:
  - Hyper AmpC producers + porin mutation
- "False" Negative MHT
  - MBL
  - not specific
    - Good for KPC +
    - OXA +/- (may be MHT *and* MBL negative)
    - Note: OXA-48 (and other OXA) may also remain S to 3rd/4th generation cephalosporins

Pitfalls…

- *P. aeruginosa* and *A.baumannii* : both have CPO's yet these are not reported under the current XDRO Registry definition

For More Information

- http://www.cdc.gov/labtraining/master_courses.html
- https://www.xdro.org/
- http://www.cdc.gov/hai/organisms/cre/definition.html

Thank you!

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