CRE and *C. difficile*: Is Your Healthcare Facility Implementing the Necessary Approach to Stop the Spread?

Clinician Outreach and Communication Activity (COCA) Webinar

August 20, 2015

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Planners have reviewed content to ensure there is no bias. This presentation will not include any discussion of the unlabeled use of a product or products under investigational use.

Objectives

At the conclusion of this session, the participant will be able to:

- **Discuss the current state of antibiotic-resistant bacteria in U.S. healthcare facilities**
- **Identify mechanisms that can be used to identify gaps in antibiotic stewardship and help charter a course of action to decrease the spread of antibiotic-resistant infections**
- **Describe how healthcare organizations and public health can collaborate to stop the spread of antibiotic-resistant germs and *C. difficile* between facilities**

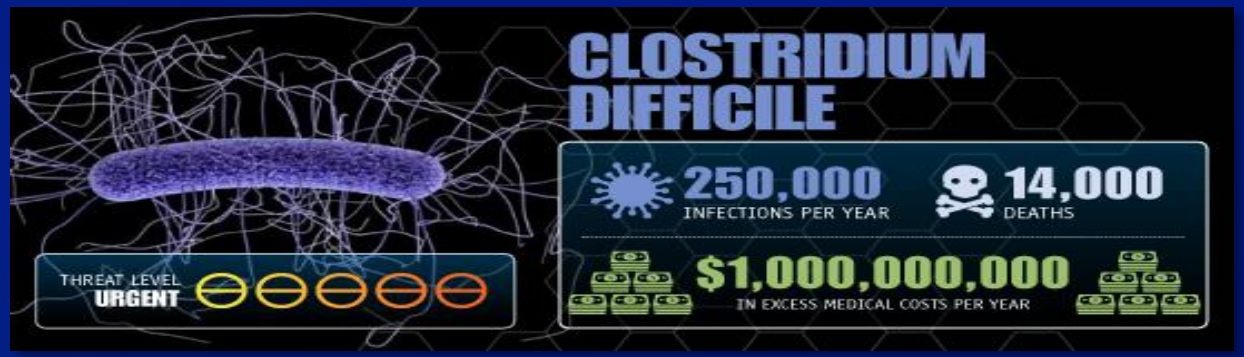
TODAY'S MODERATOR & PRESENTER

Arjun Srinivasan, MD

Associate Director
Healthcare-Associated Infection Prevention
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention (CDC)

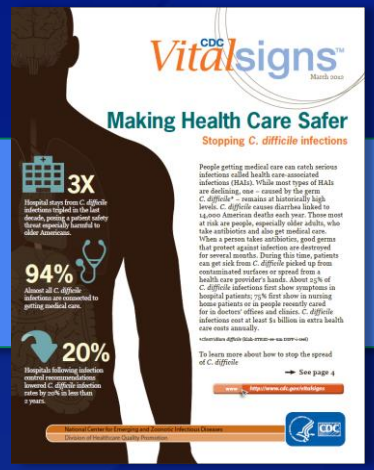
Antibiotic Resistance in the U.S.

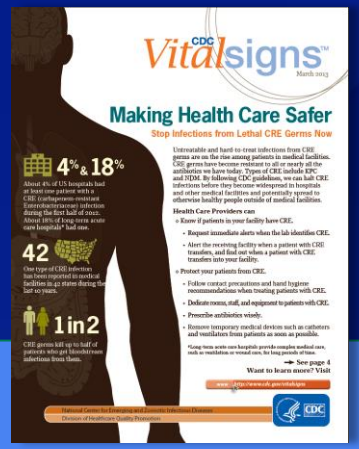
- Sickens **>2 million** people/year
- Kills at least **23,000** people/year, plus **14,000**/year from *C. difficile*
- **>$20B**/year in health care costs
- Threat to economic stability
- Need to act now or even drugs of last resort will soon be ineffective

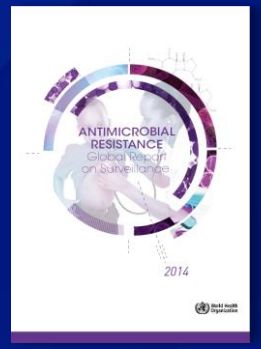


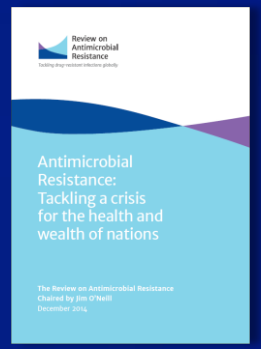
Challenge. Action. Change.

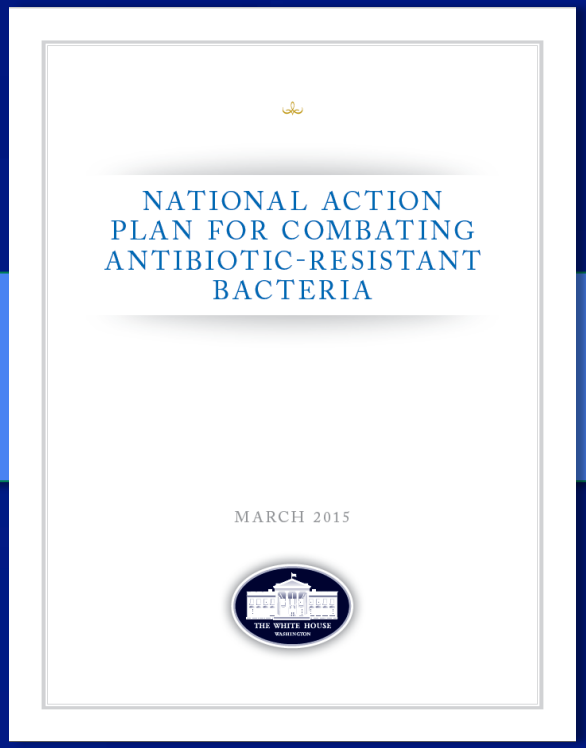
2012 2013 2014 2015







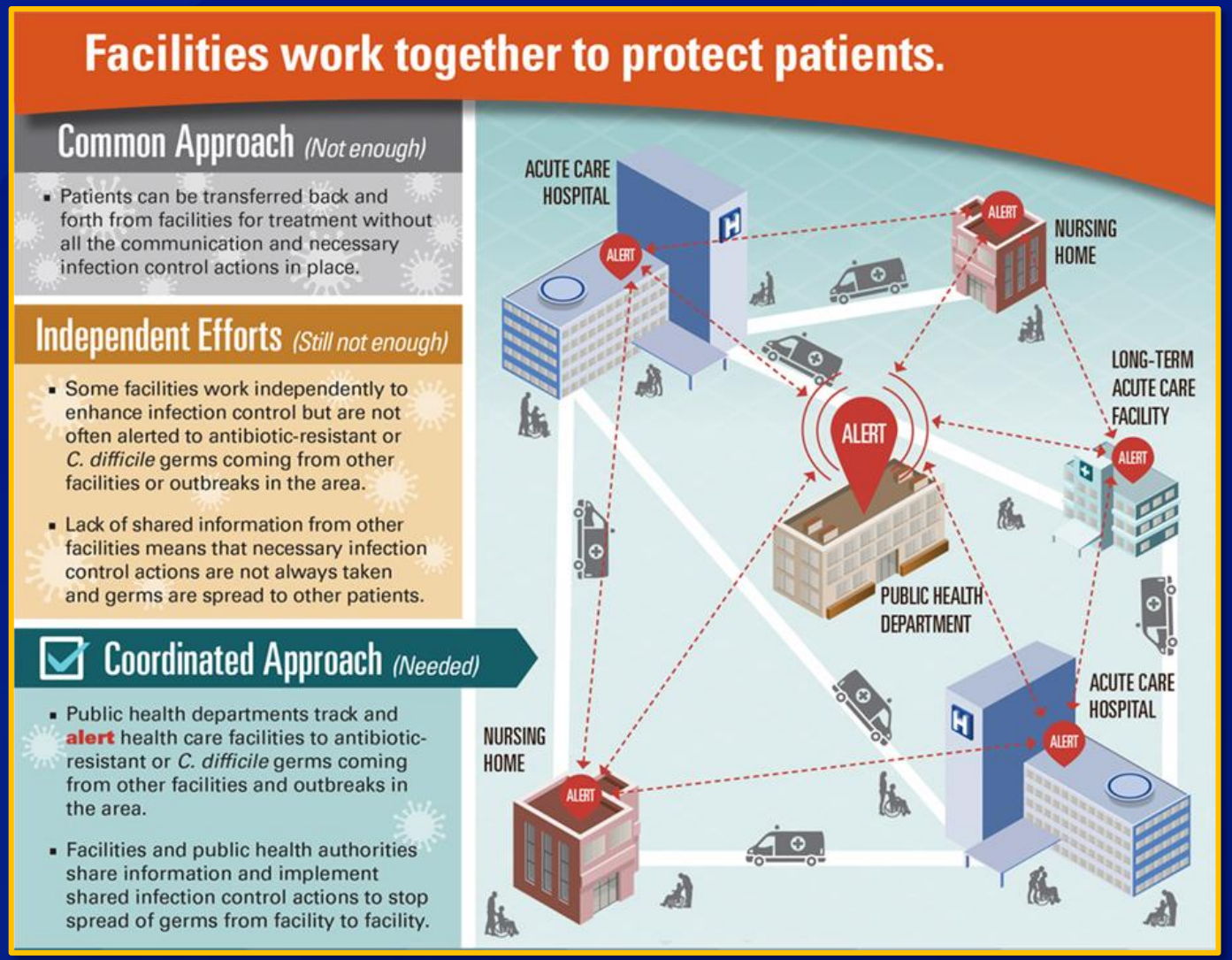




Antibiotic Stewardship: A Coordinated Approach

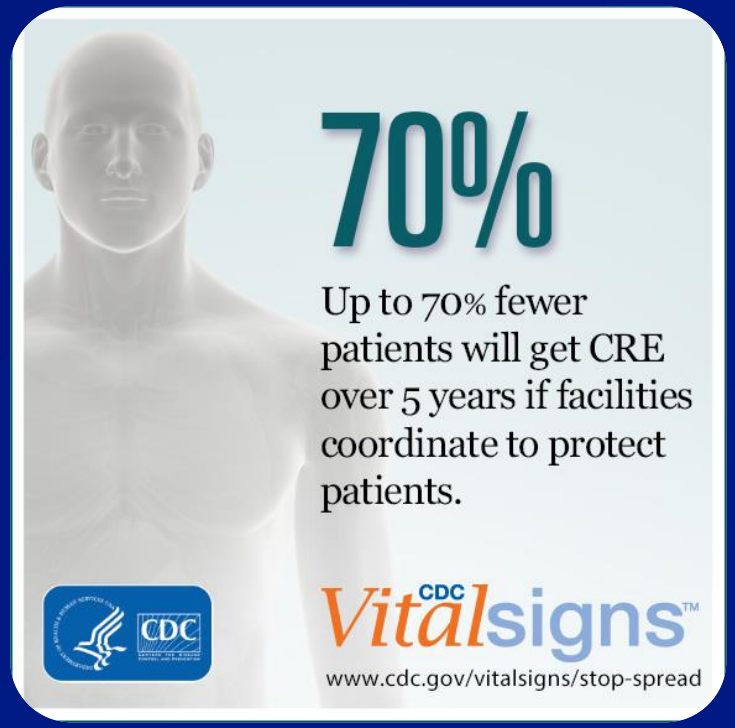
Key actions needed:

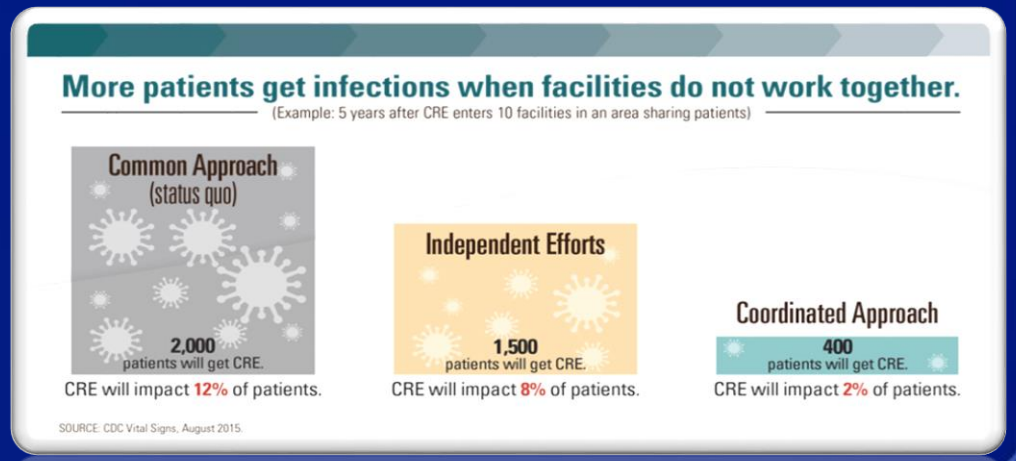
- Infection control
- Stewardship
- Surveillance



Forward Looking Approach: Investments Needed

- Now we have a clear sense not only how bad the problem is, but also what needs to be done, and what the benefits of doing it will be
- Now it is up to Congress to support the resources needed to protect Americans from drug-resistant bacteria and the risk of a post-antibiotic age that undermines many life-saving procedures of modern medicine





What We Can Do Right Now?

TODAY'S PRESENTER

Robert A. Weinstein, MD
C Anderson Hedberg MD Professor of Internal Medicine
Chief Academic Officer
Rush University Medical Center

TODAY'S PRESENTER

Sara Cosgrove, M.D., M.S., FSHEA, FIDSA
Associate Hospital Epidemiologist
Director, Antimicrobial Stewardship Program
Associate Professor of Medicine
Johns Hopkins University School of Medicine

The Chicago Experience with Regional Spread and Control of Carbapenem-resistant Enterobacteriaceae (CRE)

Robert A. Weinstein, MD

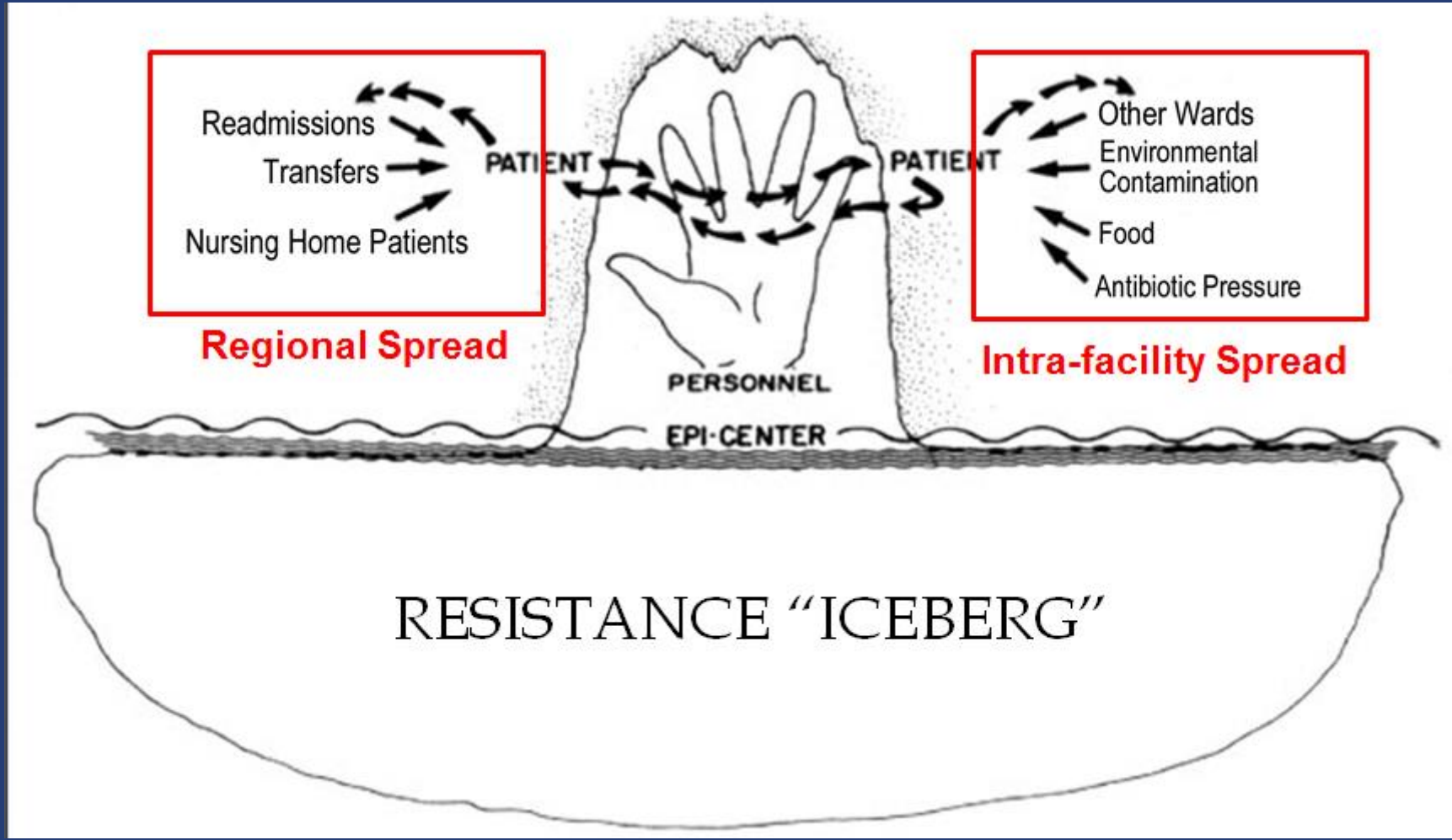
August 20, 2015

Cook County Health & Hospitals System
Rush Medical College

Disclosures: Sage Inc (Remote) & CDC (Current) Funding

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry

Resistance Bad — Control Measures Are Based on Epidemiology



Adapted from Weinstein & Kabins, *Am J Med* 1981; 70:449-54

This Is Not A New Problem

Multiple Antibiotic–Resistant *Klebsiella* and *Escherichia coli* in Nursing Homes

Janis Wiener, MD
John P. Quinn, MD
Patricia A. Bradford, PhD
Richard V. Goering, PhD
Catherine Nathan, MS
Karen Bush, PhD
Robert A. Weinstein, MD

Context Infections caused by ceftazidime sodium–resistant gram-negative bacteria that harbor extended-spectrum β-lactamases (ESBLs) are increasing in frequency in hospitals in the United States.

Objectives To report a citywide nursing home–centered outbreak of infections caused by ESBL-producing gram-negative bacilli and to describe the clinical and molecular epidemiology of the outbreak.

Design Hospital-based case-control study and a nursing home point-prevalence survey. Molecular epidemiological techniques were applied to resistant strains.

Settings A 400-bed tertiary care hospital and a community nursing home.

Patients Patients who were infected and/or colonized with ceftazidime-resistant *Escherichia coli*, *Klebsiella pneumoniae*, or both and controls who were admitted from nursing homes between November 1990 and July 1992.

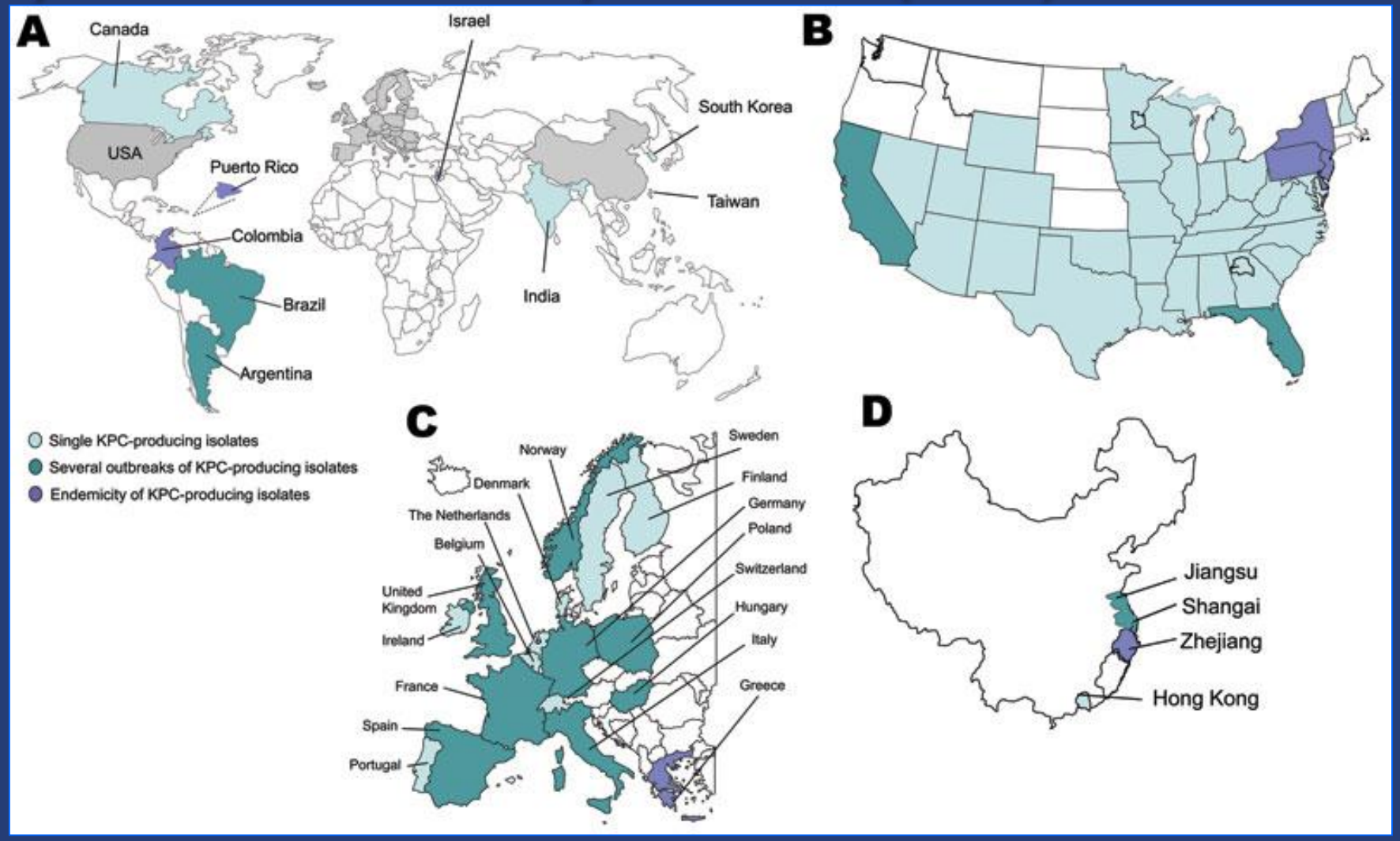
Main Outcome Measures Clinical and epidemiological factors associated with colonization or infection by ceftazidime-resistant *E coli* or *K pneumoniae*; molecular genetic characteristics of plasmid-mediated ceftazidime resistance.

Results Between November 1990 and October 1992, 55 hospital patients infected or colonized with ceftazidime-resistant *E coli*, *K pneumoniae*, or both were identified. Of the 35 admitted from 8 nursing homes, 31 harbored the resistant strain on admission. All strains were resistant to ceftazidime, gentamicin, and tobramycin; 96% were resistant to trimethoprim-sulfamethoxazole and 41% to ciprofloxacin hydrochloride. In a case-control study, 24 nursing home patients colonized with resistant strains on

ANTIBIOTIC RESISTANCE AMONG nosocomial pathogens is a cause of major concern.[1-3] Three aspects of this problem have been particularly challenging: the frequent emergence of resistance to the newest antibiotics; the presence of antibiotic resistance genes on bacterial plasmids, which may be transferred among different bacterial species; and the spread of resistant bacteria among patients not only in the hospital but also in the community.

Wiener et al, *JAMA* 1999; 281:517-23

Worldwide Geographic Distribution of *Klebsiella pneumoniae* Carbapenemase (KPC) Producers

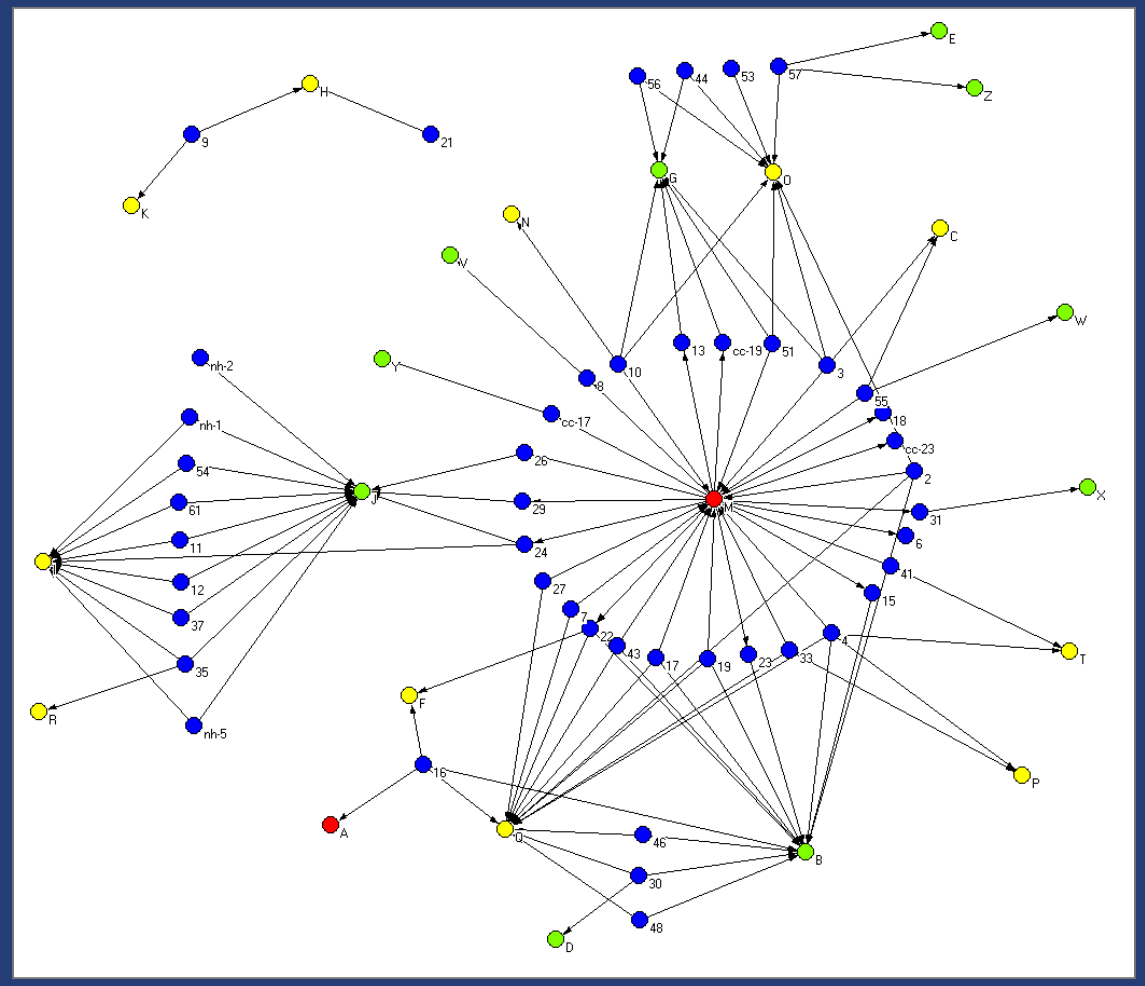


Nordmann et al, *Emerg Infect Dis* 2011; 17(10):1791-8

Emergence & Rapid Regional Spread of *K pneumoniae* Carbapenemase-Producing Enterobacteriaceae

Hospital and Long-term Care Interrelations

Social Network depiction of LTACH, Nursing Home, & Hospital spread of KPC (Carbapenem-resistant *Klebsiella pneumoniae)*



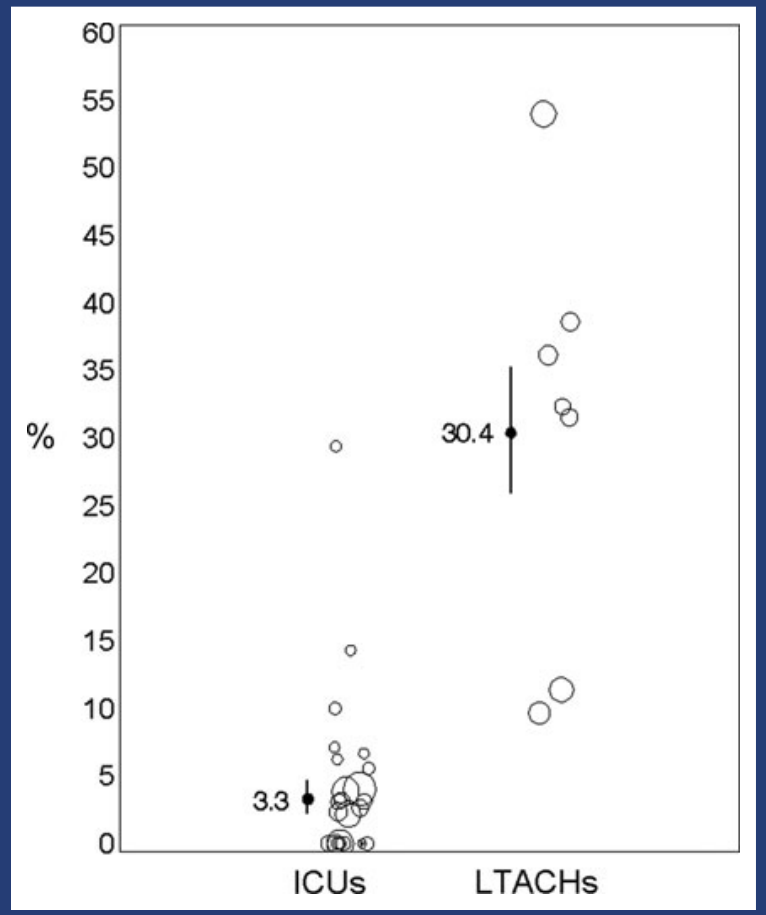
LEGEND

- LTACH
- NURSING HOME
- ACUTE HOSPITAL
- PATIENT

LTACH, Long term acute care hospital; MDRO, Multidrug resistant organism

Won et al, *Clin Infect Dis* 2011; 53(6):532-40

The Importance of Long-term Acute Care Hospitals in the Regional Epidemiology of *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae (KPC)



KPC colonization prevalence 9-fold higher in LTACHs than in short-stay acute care hospital adult ICUs

LTACH, Long-term acute care hospital; ICU, intensive care unit

Lin et al, *Clin Infect Dis* 2013; 57(9):1246–52.

Developing Control Measures --The Fecal Patina?
KPC Common on Skin but Rare in Most Environmental Sites of LTACH Patients

- 22/24 (92%) patients ≥1 skin site KPC-positive
  - 49/96 (51%) skin cultures KPC-positive
- 2/371 (0.5%) environmental sites in patient rooms or common areas grew KPC
- Environmental site of concern: SINKS?

KPC, *Klebsiella pneumoniae* carbapenemase;
LTACH, long-term acute care hospital

Thurlow et al, *Infect Control Hosp Epidemiol* 2013; 34(1):56-61.

Prevention of Colonization and Infection by *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae in Long-term Acute-Care Hospitals

Mary K. Hayden,[1,2] Michael Y. Lin,[1] Karen Lolans,[2] Shayna Weiner,[1] Donald Blom,[1] Nicholas M. Moore,[3] Louis Fogg,[4] David Henry,[5] Rosie Lyles,[6] Caroline Thurlow,[1] Monica Sikka,[1] David Hines,[7] and Robert A. Weinstein[1,6]; for the Centers for Disease Control and Prevention Epicenters Program

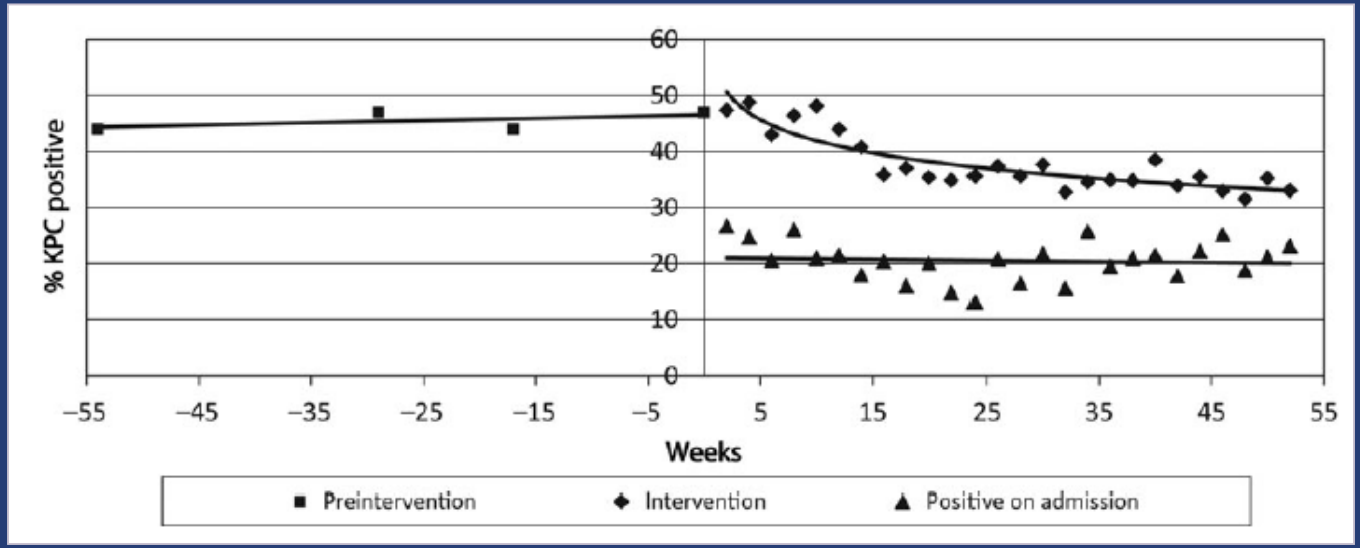
Departments of [1]Medicine, Division of Infectious Diseases, [2]Pathology, [3]Medical Laboratory Science, and [4]Nursing, Rush University Medical Center, [5]Department of Biostatistics, University of Illinois School of Public Health, [6]Department of Medicine, Division of Infectious Diseases, Cook County Health and Hospital System, and [7]Metro Infectious Disease Consultants LLC, Chicago, Illinois

		Staggered Introduction of Intervention				
		February 1, 2010 – November 27, 2011	November 28, 2011 – February 4, 2012	February 5, 2012 – April 8, 2012	April 9, 2012 – June 17, 2012	June 18, 2012 – June 30, 2013
LTACH	A	0	X	X	X	X
	B	0	0	X	X	X
	D	0	0	0	X	X
	C	0	0	0	0	X

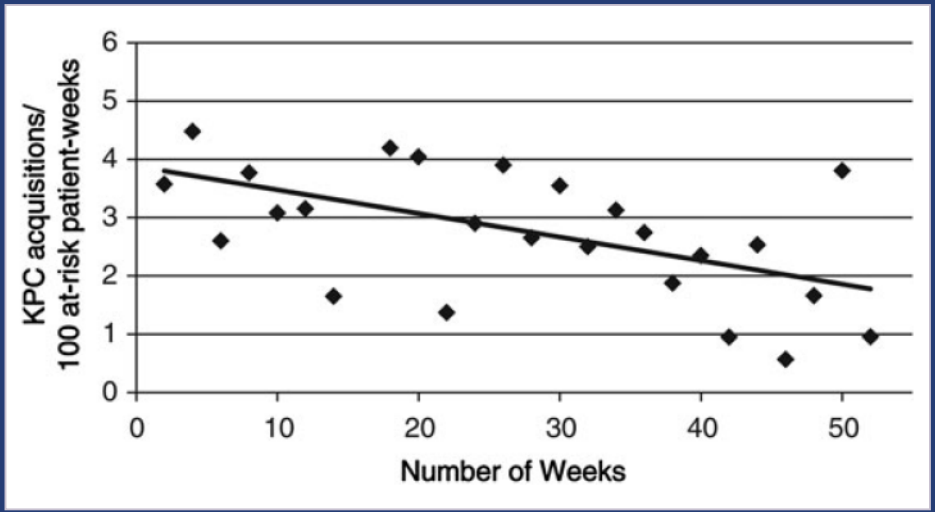
X = Intervention Bundle Introduced

Hayden et al, *CID* 2015; 60:1153-61

Prevalence rate of KPC–producing Enterobacteriaceae rectal colonization



Incidence rate of KPC–producing Enterobacteriaceae rectal colonization during the intervention period



Intervention Bundle

- Admission & every other week rectal culture screening
- Contact precautions; cohorts or private rooms
- Daily bathing with
- chlorhexidine-impregnated cloths
- HCW education & adherence monitoring

Hayden et al, *CID* 2015; 60:1153-61

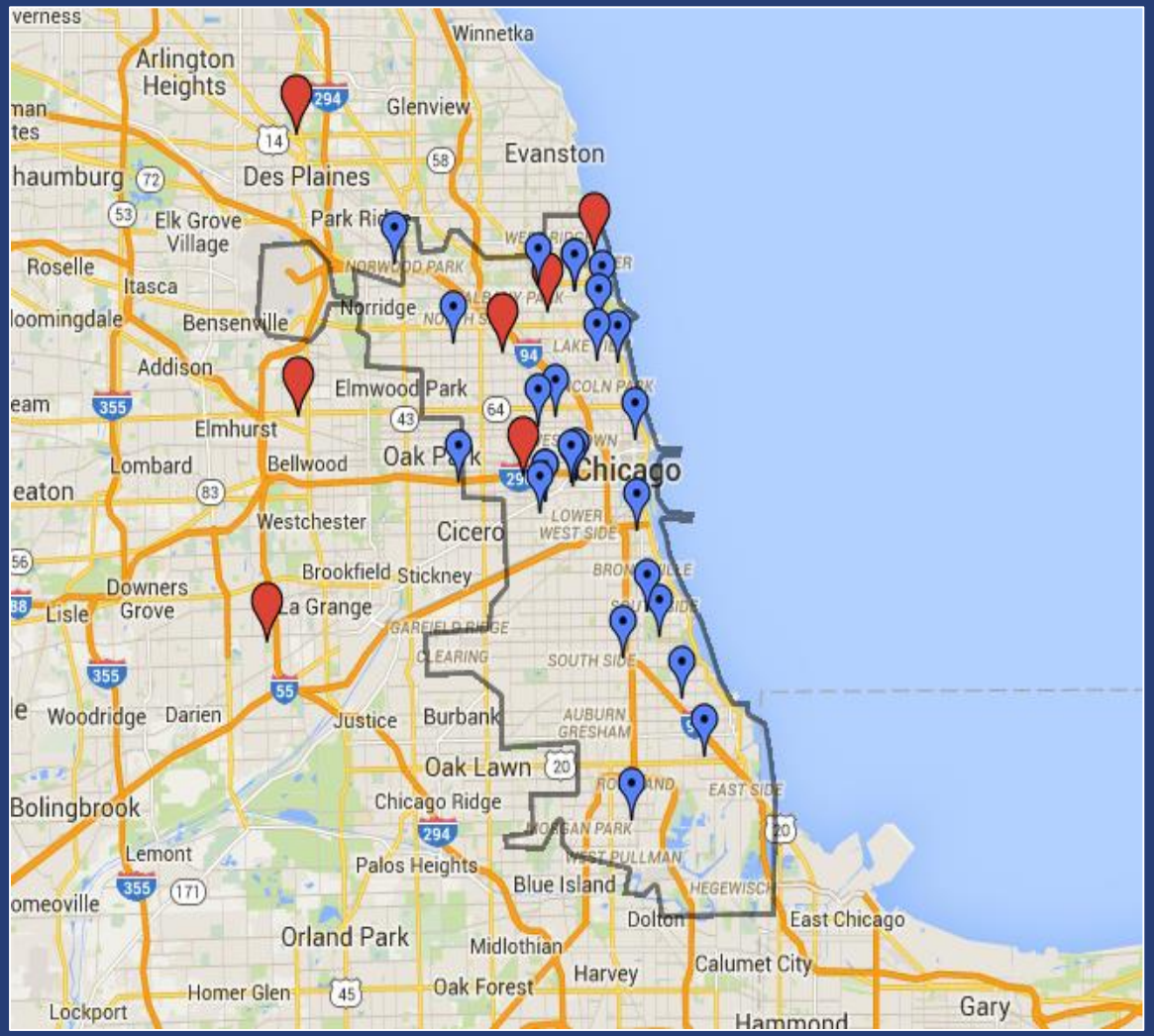
Effect of Bundled Intervention on Positive Clinical Cultures at 4 LTACHs

	Pre-Intervention		Intervention		
	No. of events	Events/ 1000 pt-days	No. of events	Events/ 1000 pt-days	P-value
KPC in any clinical culture	656	3.7	285	2.5	.001
KPC bloodstream infection	165	0.9	48	0.4	.008
Bloodstream infection due to any pathogen	2004	11.2	870	7.6	.006

LTACH, long-term acute care hospital;
KPC, *Klebsiella pneumoniae* carbapenemase

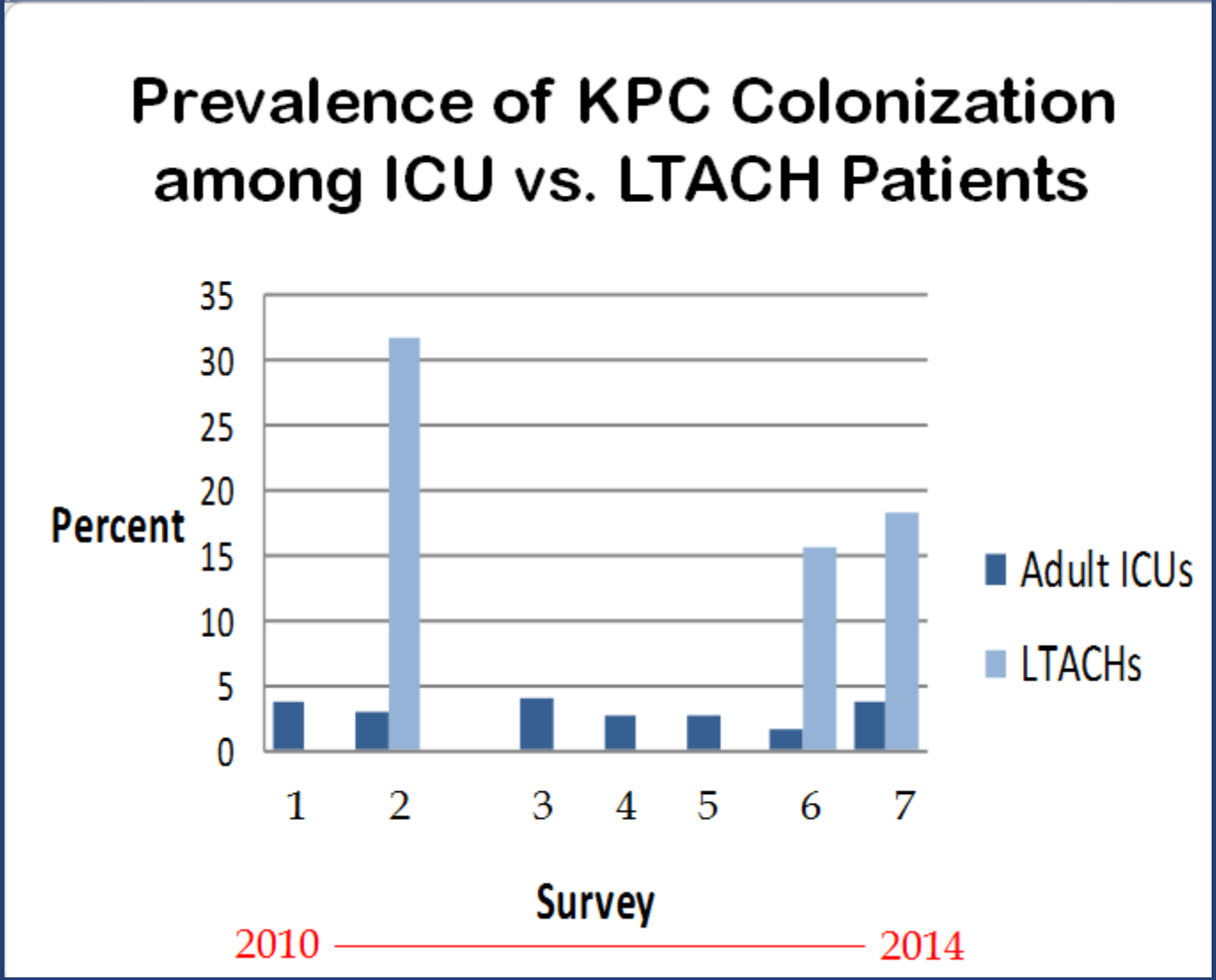
Hayden et al, *CID* 2015; 60:1153-61

REALM Project – ICU & LTACH Surveillance for KPC



Hospital ICUs (blue)
LTACHs (red)

REALM, Regional Evaluation of Legislative Mandate to screen patients for MRSA; LTACH, Long-term acute care hospital; KPC, *Klebsiella pneumoniae* carbapenemase



KPC, *Klebsiella pneumoniae* carbapenemase; ICU, Intensive Care Unit; LTACH, Long-term acute care hospital

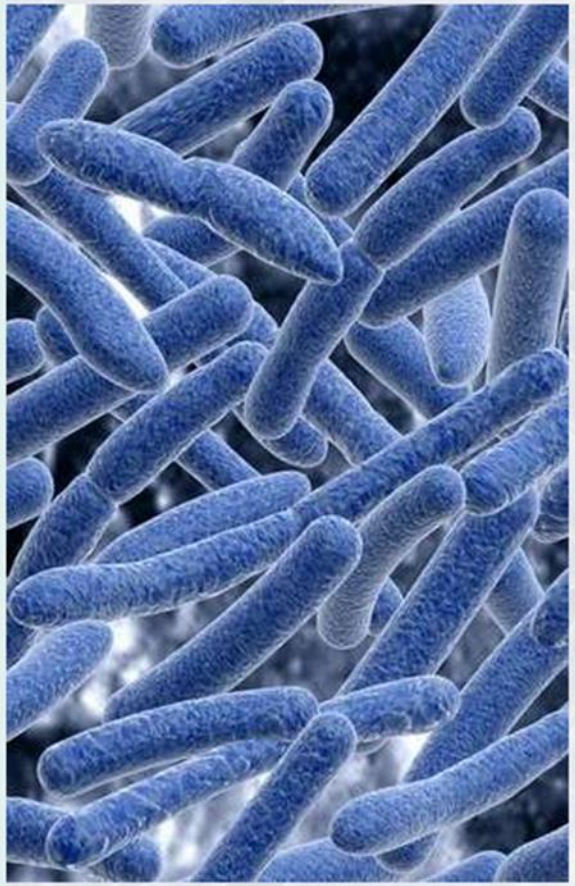
REALM data courtesy of Michael Lin, MD, MPH; unpublished data, not for distribution

Firefox | XDRO | Registry

XDRO registry

Extensively drug resistant organism registry

Help Login



Carbapenem-resistant Enterobacteriaceae (CRE) are extremely drug resistant organisms (XDROs) that have few treatment options and high mortality rates. CRE are increasingly detected among patients in Illinois, including acute and long term care healthcare facilities.

In response to the CRE public health threat, the Illinois Department of Public Health (IDPH) has guided development an infection control tool called the XDRO registry. The purpose of the XDRO registry is two-fold:

1. **Improve CRE surveillance:** The first CRE-positive culture per patient stay must be reported to the XDRO registry.
2. **Improve inter-facility communication:** Healthcare facilities can query the XDRO registry to see whether a patient has been previously reported as CRE-positive.

For access to the XDRO registry, click here

UPDATES

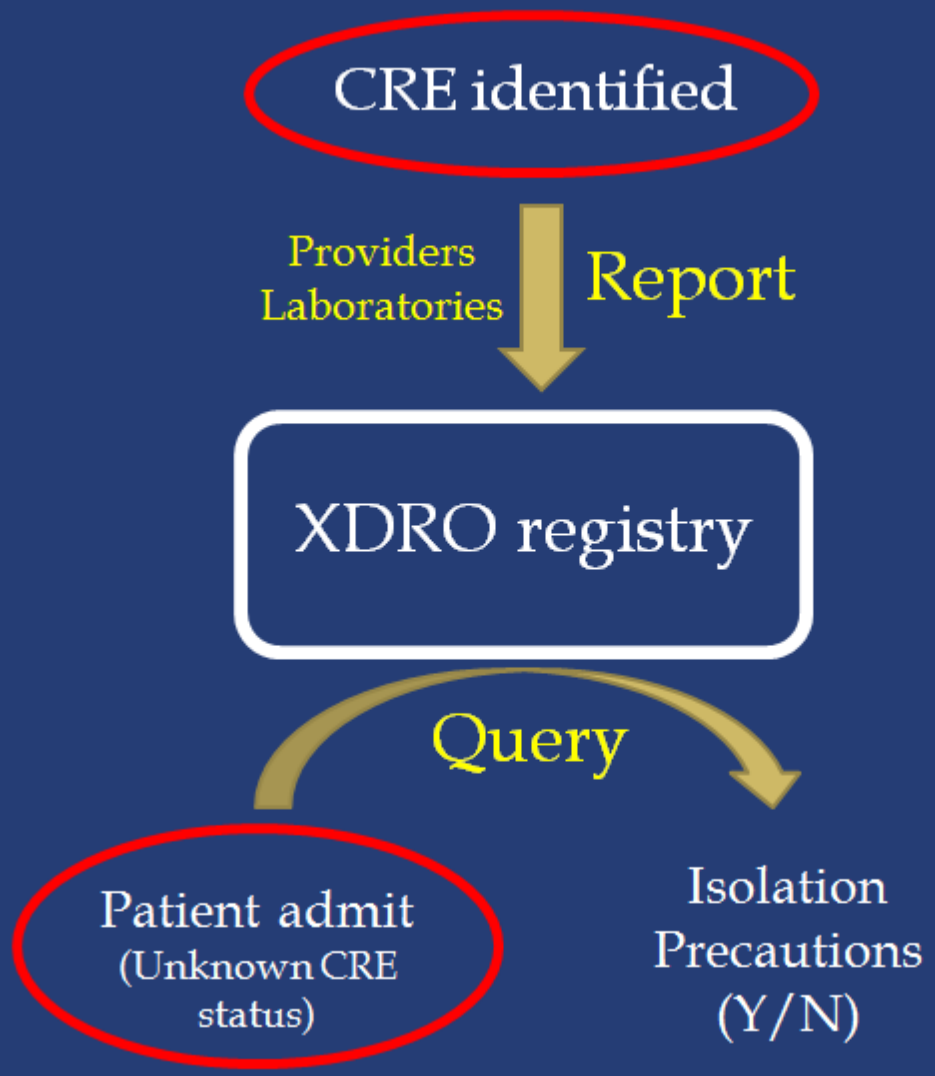
IL CRE Detect and Protect Campaign. More...

CRE are reportable to IDPH via the XDRO registry. Links: [IDPH letter to facilities, September 2013][Reporting rule]

XDRO registry orientation webinar [Slides][Recording]

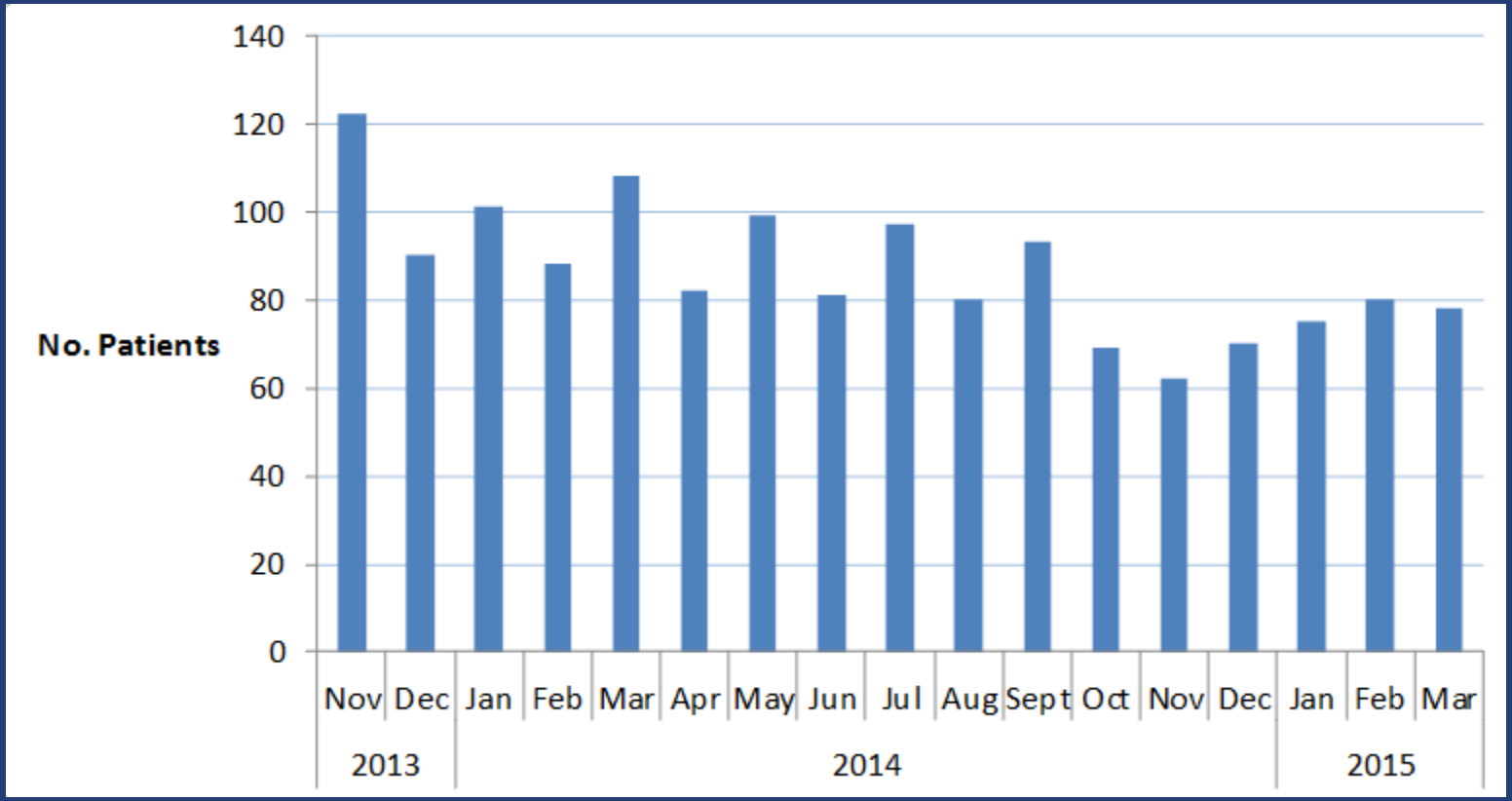
CDC guidance on control of CRE: [The 2012 Toolkit]

The XDRO registry is a product of collaboration between IDPH, Medical Research Analytics and Informatics Alliance (MRAIA), and the Chicago CDC



CRE, Carbapenem-resistant Enterobacteriaceae

Unique CRE-Infected Patients Reported to Statewide XDRO Registry



CRE, Carbapenem-resistant Enterobacteriaceae

Bottomline

- Develop Controls Based on Epidemiology
  - Traditional control measures work
  - But spread of resistant bacteria among acute care, long-term acute care, & skilled nursing facilities is common
  - So, controls must be applied regionally (& beyond)
- Resistance Must be Tracked Regionally (& Beyond)
  - Our approach — Citywide culture surveys (REALM Project) & Statewide XDRO registry

ASK THE AUDIENCE

Antimicrobial Stewardship

Sara Cosgrove, MD, MS

Associate Professor of Medicine, Division of Infectious Diseases

Director, Johns Hopkins Hospital Antimicrobial Stewardship Program

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry

Outline

- Importance of antibiotic stewardship
- Implementation of antibiotic stewardship in a single facility
- Antibiotic stewardship interventions to decrease CDI
- Implementation of antibiotic stewardship across multiple healthcare facilities

Why Does Antibiotic Stewardship Matter?

- Although antibiotics have saved countless lives, their use is not benign or risk neutral
- Antibiotic resistance occurs in populations and individual patients
- At least 5% of hospitalized patients experience an adverse reaction
  - Rash
  - Nephrotoxicity
  - *C. difficile* infection
- Few new antibiotics are being developed
- At least 30% of antibiotics used in hospitals are incorrect or not needed

Executive Order -- Combating Antibiotic-Resistant Bacteria

EXECUTIVE ORDER

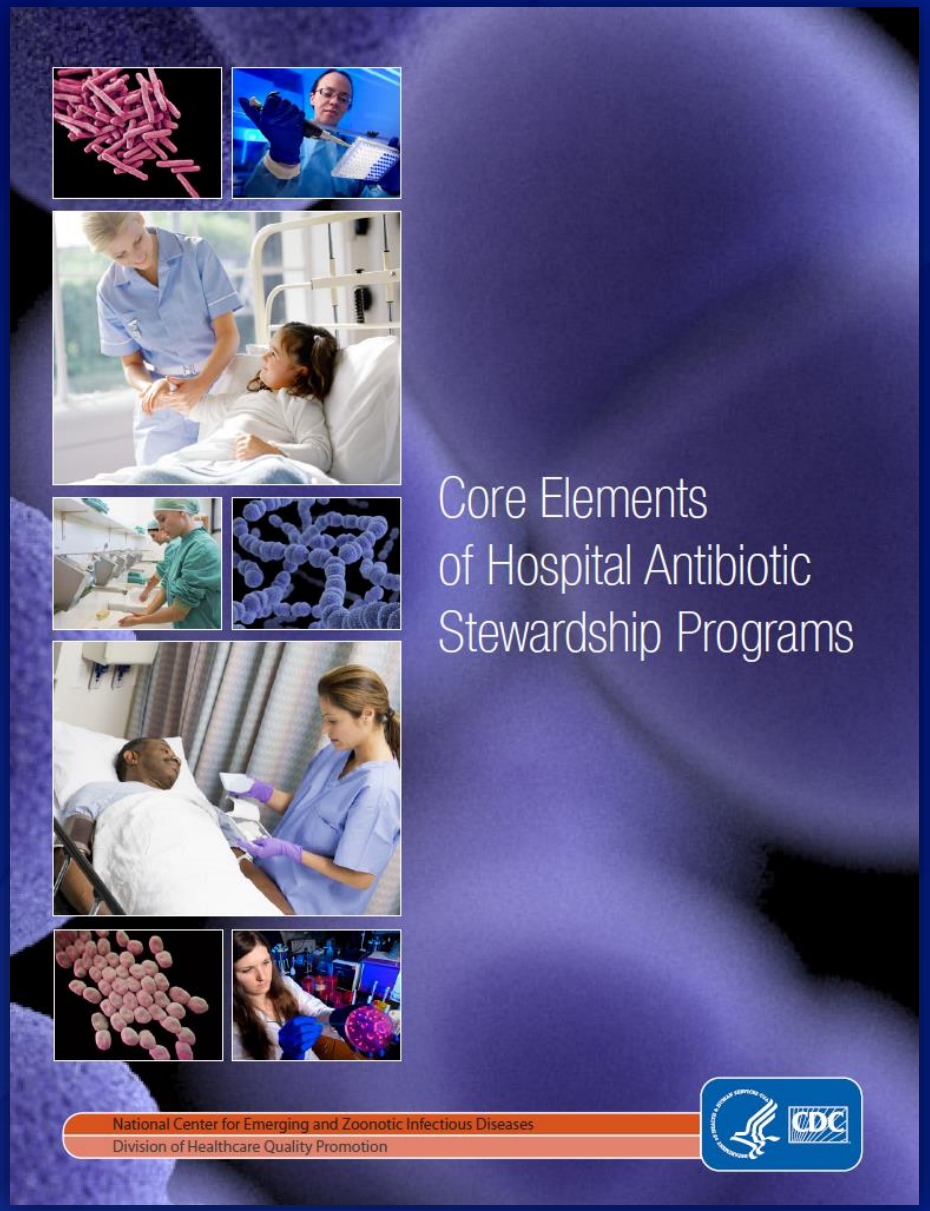
COMBATING ANTIBIOTIC-RESISTANT BACTERIA

By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

Sec. 5. Improved Antibiotic Stewardship. (a) By the end of calendar year 2016, HHS shall review existing regulations and propose new regulations or other actions, as appropriate, that require hospitals and other inpatient healthcare delivery facilities to implement robust antibiotic stewardship programs that adhere to best practices, such as those identified by the CDC. HHS shall also take steps to encourage other healthcare facilities, such as ambulatory surgery centers and dialysis facilities, to adopt antibiotic stewardship programs.

BARACK OBAMA

THE WHITE HOUSE,
September 18, 2014.



Summary of Core Elements of Hospital Antibiotic Stewardship Programs

- **Leadership Commitment:** Dedicating necessary human, financial and information technology resources.
- **Accountability:** Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective.
- **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- **Action:** Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. "antibiotic time out" after 48 hours).
- **Tracking:** Monitoring antibiotic prescribing and resistance patterns.
- **Reporting:** Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff.
- **Education:** Educating clinicians about resistance and optimal prescribing.

Available at http://www.cdc.gov/getsmart/heathcare/implemenation/core-elements.html.

Two Levels of Implementation

- **Implementation of the program itself**
  - Leadership support
    - Financial
    - Intellectual
      - Public declaration that the work is important
      - Willingness to hold prescribers accountable
  - Determination of personnel
    - Program leadership
    - Program support
  - Access to antibiotic use data

- **Implementation of interventions to improve antibiotic use**
  - Guideline development
  - Targeted interventions
  - Feedback to prescribers

AS Interventions to Reduce CDI

- All antibiotics can cause CDI
  - Most commonly implicated: clindamycin, 2nd/3rd generation cephalosporins, quinolones, carbapenems
  - Risk proportional to amount of antibiotic exposure
- Interventions to reduce exposure to these agents likely to impact CDI rates over time
  - Where are these agents used in your institution?
    - Surgical prophylaxis
    - Community-acquired pneumonia (CAP)
    - Urinary tract infection/asymptomatic bacteriuria (ASB)
    - Carbapenem use in patients not at risk for MDRGN
  - Emphasize avoiding unnecessary starts (ASB), narrowing therapy (CAP, carbapenems), reduced durations (UTI, CAP, prophylaxis)

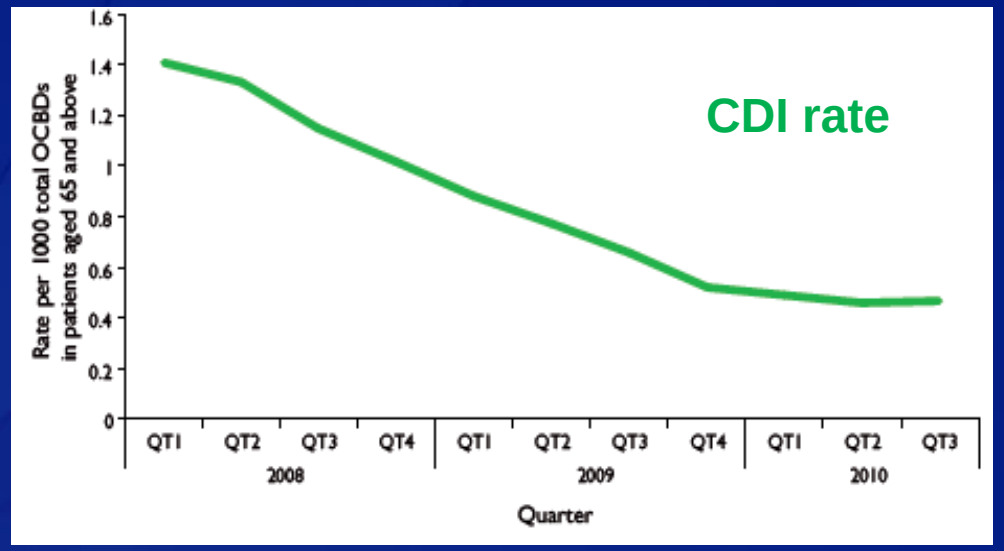
AS Interventions to Reduce CDI

- Other considerations
  - Aggressive reduction in one class of antibiotics can lead to increases in other classes
  - Use of proton pump inhibitors associated with 1.4-2.8x increased risk of CDI
  - Over-testing for CDI
    - PCR-based testing detects colonization and infection
      - ~20% of hospitalized patients colonized
    - Not all hospital-acquired diarrhea is caused by CDI
  - Infection control interventions very important also

Experience from Scotland

2008: Implementation of ASP in all hospitals

Focus on reduction in use of fluoroquinolones and 3rd generation cephalosporins



- Statistically significant decreases in:
  - 3rd generation cephalosporins resistance in *E. coli* (2-3% decreased across class)
  - Fluoroquinolone resistance in *P. aeruginosa* (12% to 6%)
- No statistically significant increases in resistance to other antibiotics

Implementation Across Multiple Healthcare Facilities: Safety in Numbers

Slides courtesy of Elizabeth Dodds-Ashley, PharmD

Summary Statement

Unity Health System

UR MEDICINE
MEDICINE of THE HIGHEST ORDER

ROCHESTER GENERAL HEALTH SYSTEM

C. diff Prevention Collaborative Antimicrobial Stewardship Workgroup

Thursday, April 10, 2014

DID YOU KNOW? On a single day in Rochester, NY:

- **1 in 5 (20%)** hospitalized patients receiving antibiotics for treatment of urinary tract infections (UTI) had no documented symptoms of UTI[1]

AND

- **5 in 6 (86%)** hospitalized patients receiving antibiotics for UTI did not meet criteria for UTI treatment [1,2]

Summary Recommendations

To minimize exposure to antimicrobials that may increase patients' risk for developing subsequent *C. difficile* infection, the stewardship workgroup recommends the following:

AVOID OVERTESTING & TREATING ASYMPTOMATIC BACTERIURIA

Order a urinalysis and urine culture only in cases where one of the following are met:

1. SIRS criteria without readily apparent alternative source of infection
2. Fever AND ≥ 1 urinary symptom* are present
3. ≥ 2 urinary symptoms* are present

MENTAL STATUS CHANGES ALONE ARE NOT SUFFICIENT INDICATION TO TEST THE URINE
DO NOT TREAT ASYMPTOMATIC BACTERIURIA IN MOST PATIENTS

*Urinary tract symptoms: dysuria, urgency, flank pain, shaking chills, new onset urinary incontinence, frequency, gross hematuria, suprapubic pain[2]

References:

1. Stone ND, Ashraf MS, Calder J et al. Infect Control Hosp Epidemiol 2012;33:965-77/
2. Loeb M, Brazil K, Lohfeld. BMJ 2005;331:669.

Community Acquired Pneumonia Intervention

Doxycycline for CAP – A Rochester City-Wide Collaborative C difficile Prevention Strategy

The RGH Infection Prevention (IP) and Antimicrobial Stewardship Program (ASP) participate in a Rochester city-wide Clostridium difficile Prevention Collaborative whose focus is to reduce the incidence of C difficile in our community. The collaborative agreed to initiate a uniform antibiotic intervention across all four Rochester hospitals (RGH, Unity Hospital, Strong Memorial Hospital, and Highland Hospital) for Community Acquired Pneumonia (CAP) that consists of two goals:

1. to reduce the use of fluoroquinolones, a drug class well-recognized for their associated high-risk for C difficile
2. to encourage use of doxycycline when applicable as doxycycline has recently been described as having a potentially protective role against C

From this, the ASP teams suggest that for patients hospitalized with non-ICU CAP, moxifloxacin be reserved for patients with severe penicillin allergies only. Those with no allergy, or mild to moderate penicillin (and no cephalosporin) allergy, a beta-lactam with PO doxycycline is the preferred treatment regimen. Three oral beta-lactam regimens with doxycycline are also provided below.

The ASP team would like to emphasize that these recommendations are for empiric therapy of non-ICU CAP.

- Patients admitted to ICU or MAT unit should continue to be prescribed either a macrolide (i.e. azithromycin) or moxifloxacin according to guidelines for empiric coverage of Legionella.
- The microbiologic evaluation for the bacterial pathogen should still be performed, such as

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