From Concept to Accomplishments: 7 Years of Antimicrobial Stewardship at CHP

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Disclaimers

- I have no relevant conflict of interests to disclose
- I will NOT discuss off label use of drugs or devices

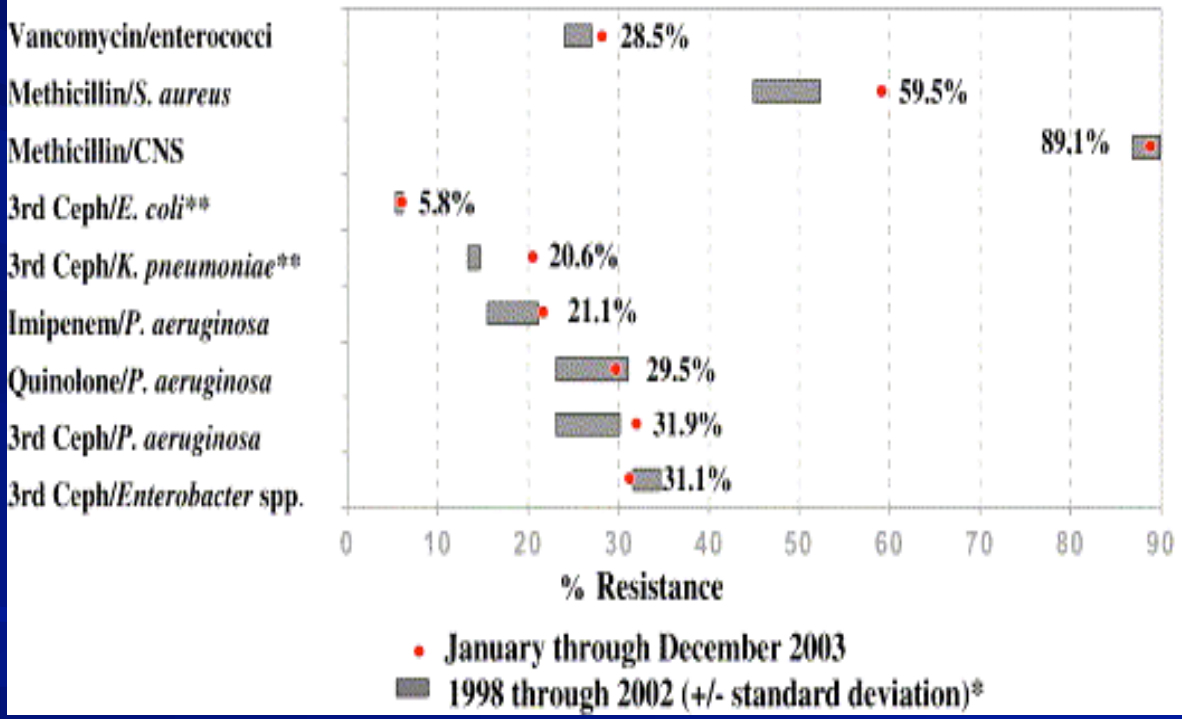
Learning Objectives

- At the end of this talk attendees should be able to:
  - Recognize the historical basis & necessity for antimicrobial stewardship
  - Describe the essential components of antimicrobial stewardship programs nationally & at CHP
  - Understand that antimicrobial stewardship can & has worked at CHP

Outline

- Overview of Trends in Antimicrobial Resistance
- Historical review of the emergence of ASP
  - National Goals
  - Recommended structure
- Antimicrobial Stewardship & CHP
  - “Unique model” built on OUR expertise
  - Overview of accomplishments
- Expanding Goals of Antimicrobial Stewardship at CHP

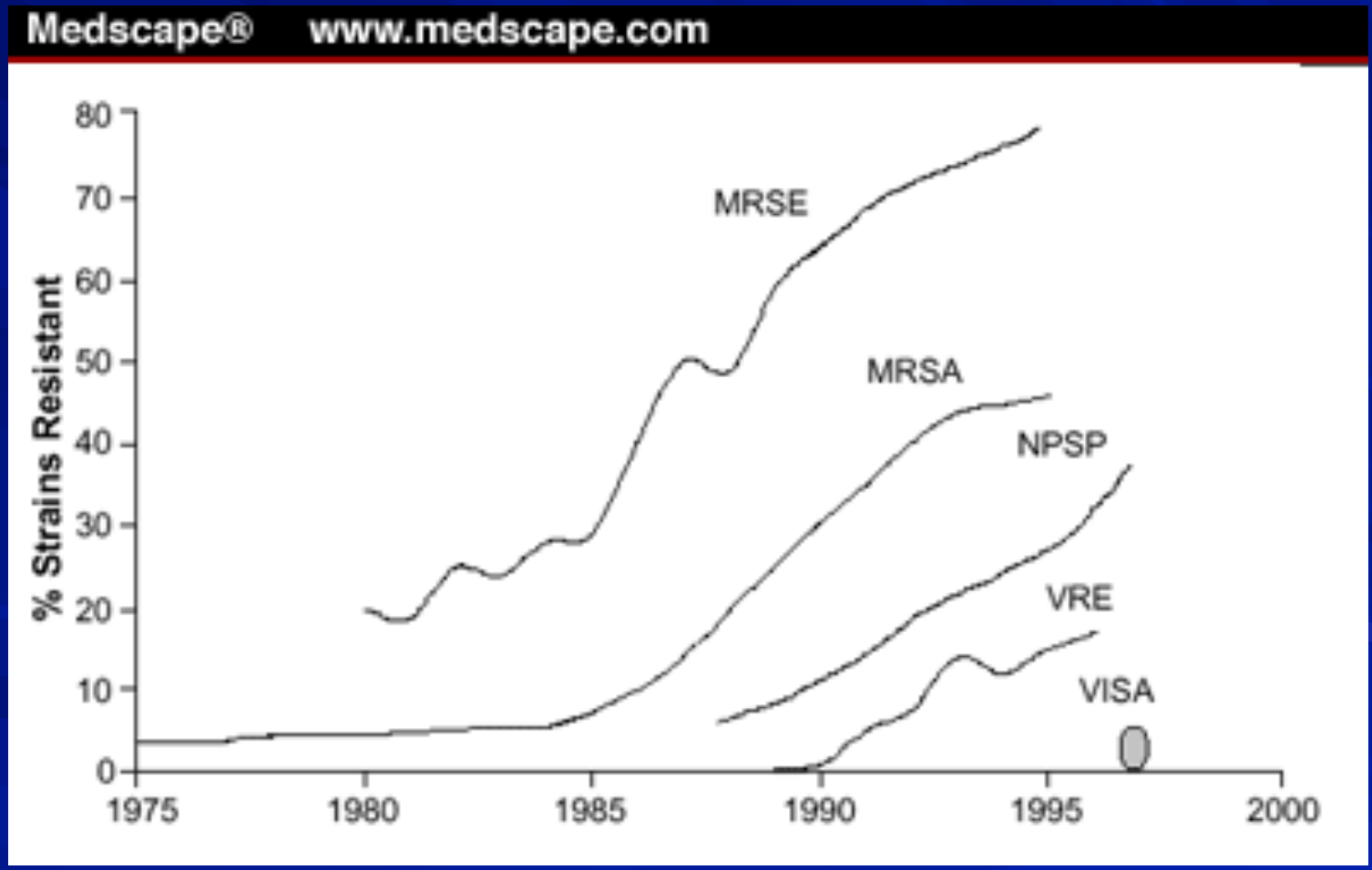
Origins of Antimicrobial Stewardship: Explosion of Antimicrobial Resistance

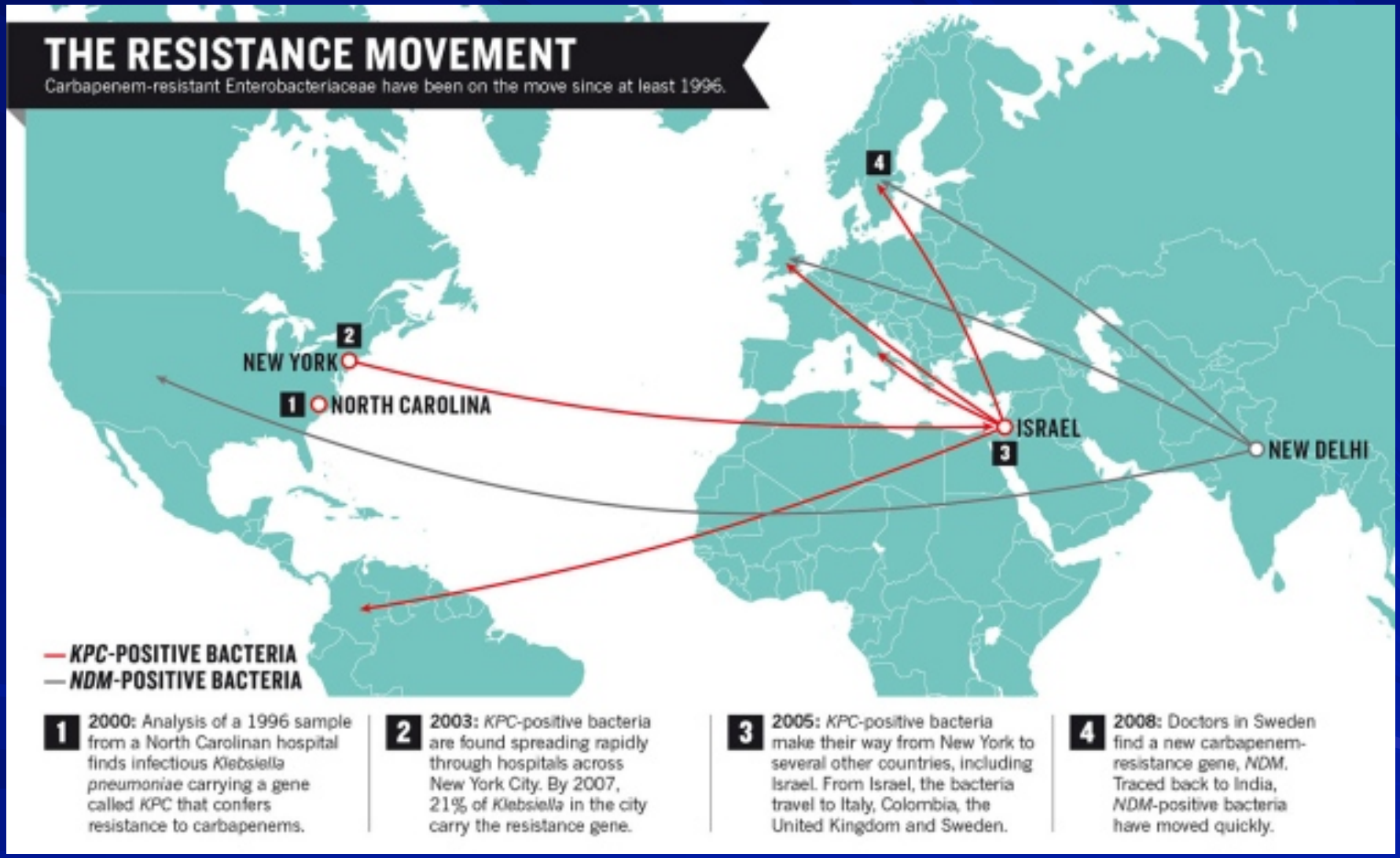


Jan–Dec 2003 No. of Isolates	% increase in resistance (2003 vs 98-02*)
2048	12%
4100	11%
3336	1%
1355	0%
1068	47%
1392	15%
1825	9%
2119	20%
1411	–6%

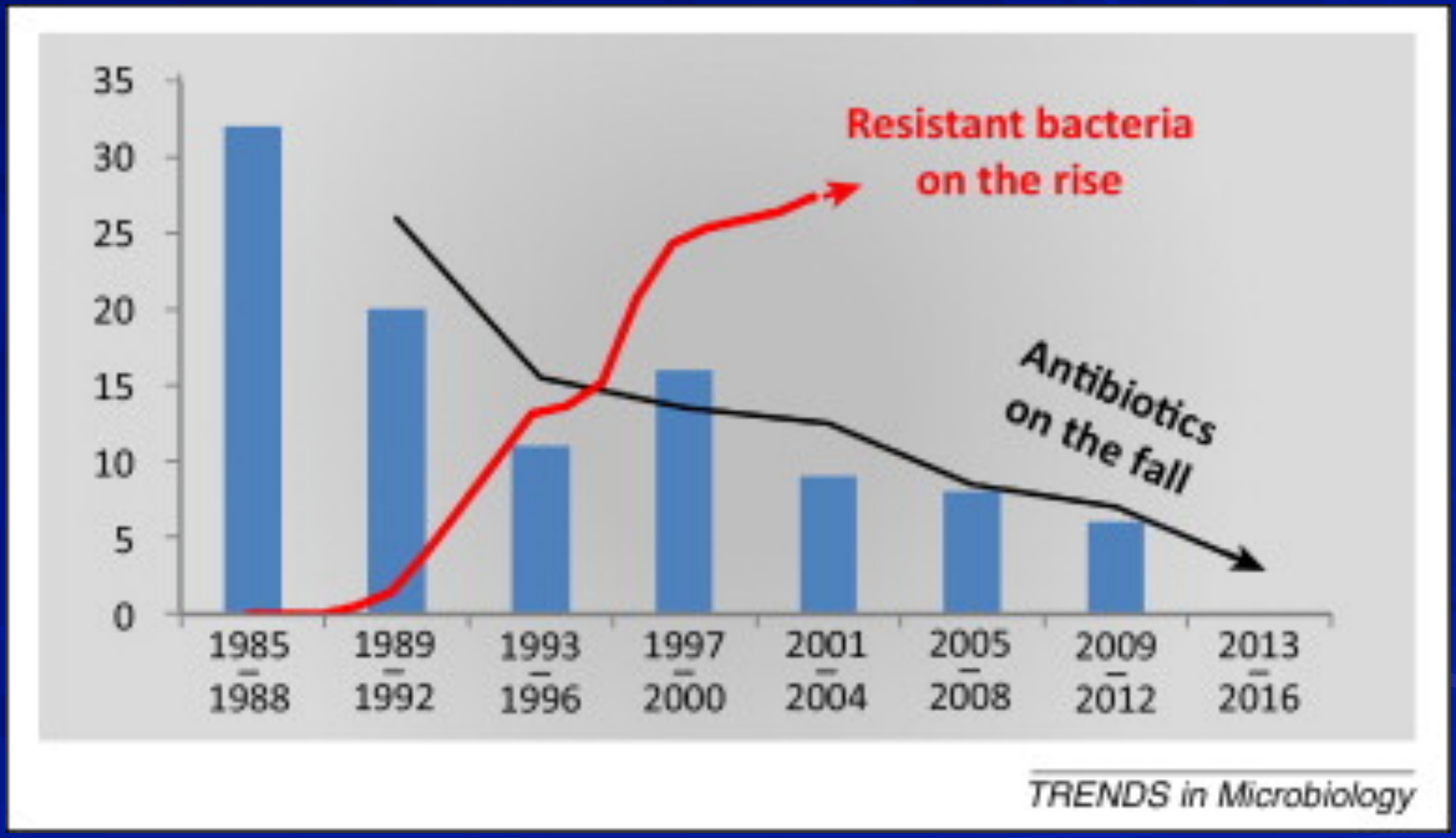
Selected antimicrobial-resistant pathogens associated with nosocomial infections in ICU patients, comparison of resistance rates from 2003 with 1998 through 2002, NNIS system. (Figure from NNIS, 2004).

Origins of Antimicrobial Stewardships: Here Come the Superbugs!




THE RESISTANCE MOVEMENT
Carbapenem-resistant Enterobacteriaceae have been on the move since at least 1996.
4
2
NEW YORK
1
NORTH CAROLINA
ISRAEL
3
NEW DELHI
KPC-POSITIVE BACTERIA
NDM-POSITIVE BACTERIA
1 2000: Analysis of a 1996 sample from a North Carolinan hospital finds infectious Klebsiella pneumoniae carrying a gene called KPC that confers resistance to carbapenems.
2 2003: KPC-positive bacteria are found spreading rapidly through hospitals across New York City. By 2007, 21% of Klebsiella in the city carry the resistance gene.
3 2005: KPC-positive bacteria make their way from New York to several other countries, including Israel. From Israel, the bacteria travel to Italy, Colombia, the United Kingdom and Sweden.
4 2008: Doctors in Sweden find a new carbapenem-resistance gene, NDM. Traced back to India, NDM-positive bacteria have moved quickly.

Trends in Antimicrobial Resistance



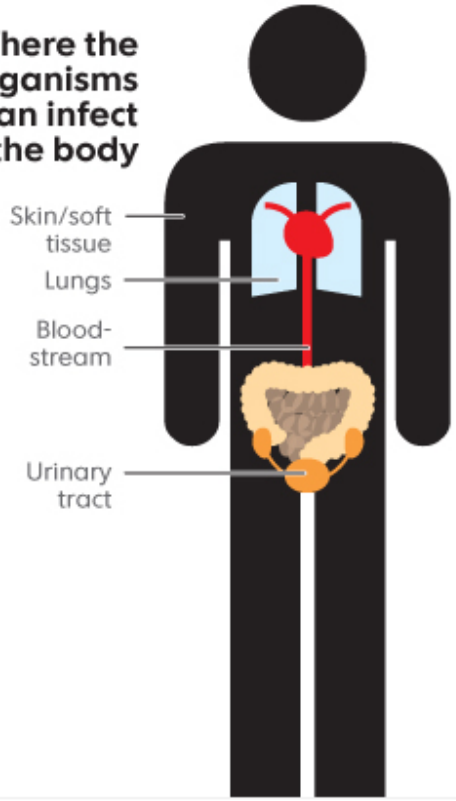
Antimicrobial Resistance in the News: USA Today (3/6/13)

CDC sounds alarm on deadly, untreatable superbugs

DEADLY BACTERIA THAT DEFY DRUGS OF LAST RESORT

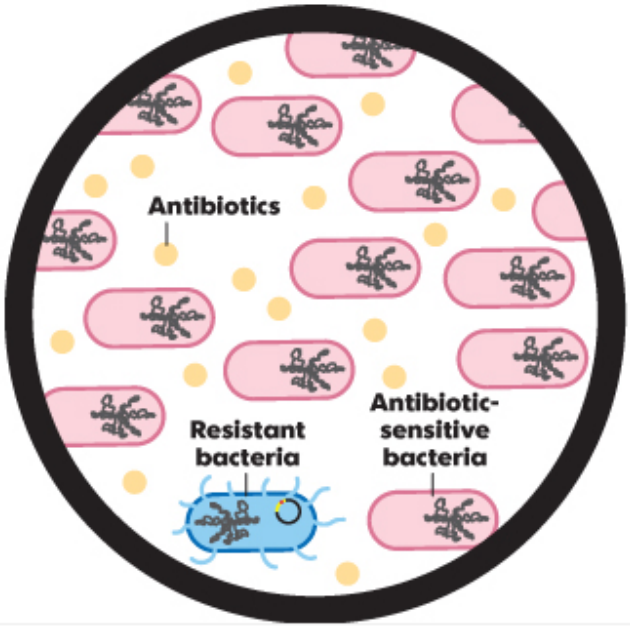
A new family of antibiotic-resistant bacteria, known as CRE, is raising concerns across the medical community because of its ability to cause infections that defy even the strongest antibiotics. The antibiotic resistance is spread by mobile pieces of DNA that can move between different species of bacteria, creating new, drug-defying bugs.

Where the organisms can infect the body



How a resistance gene moves between bacteria

When antibiotic-resistant bacteria are present in the body and antibiotics are introduced ...



NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least **2,049,442** illnesses,

23,000 deaths

**bacteria and fungus included in this report*

+

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses,

14,000 deaths

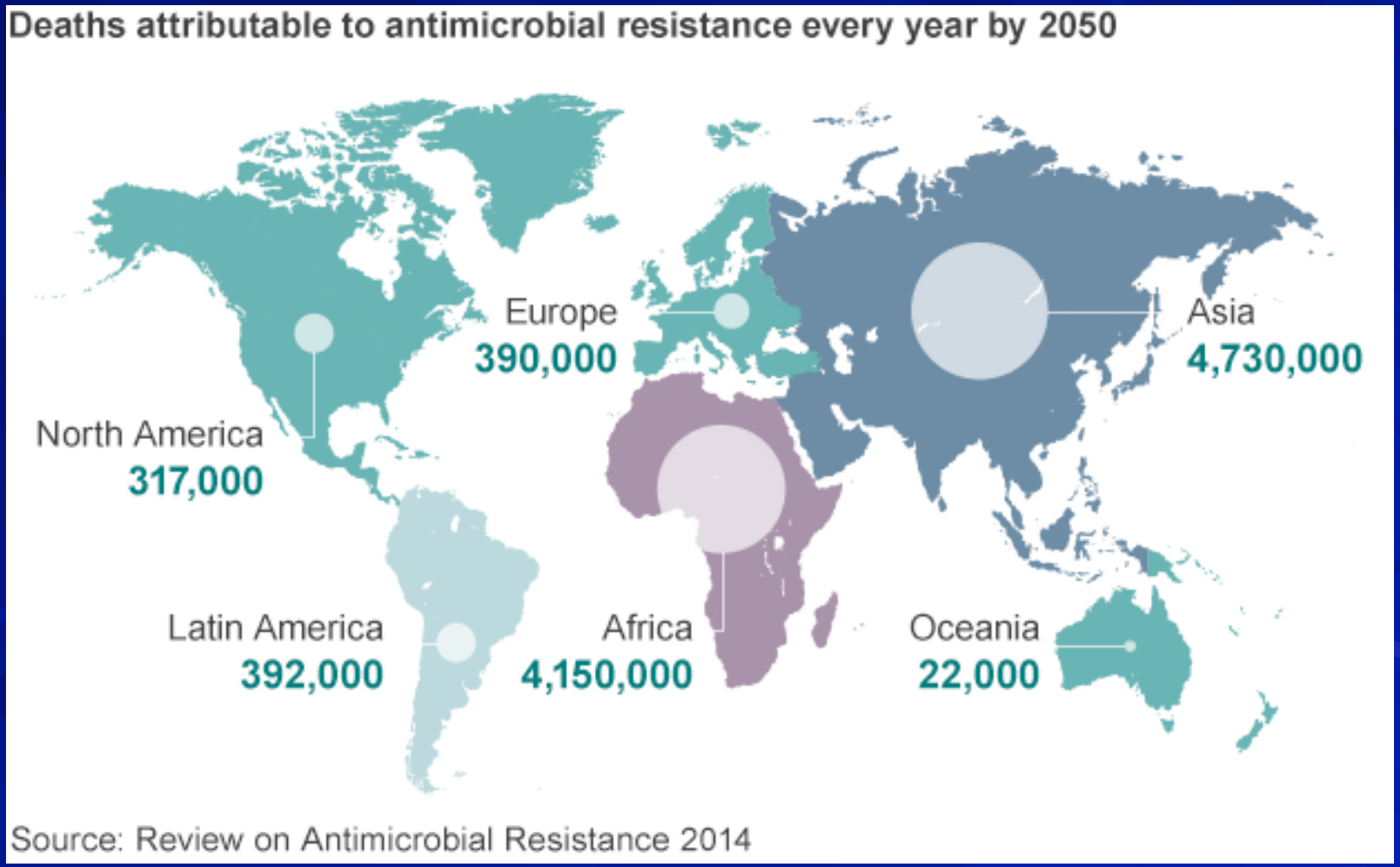
WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS239559

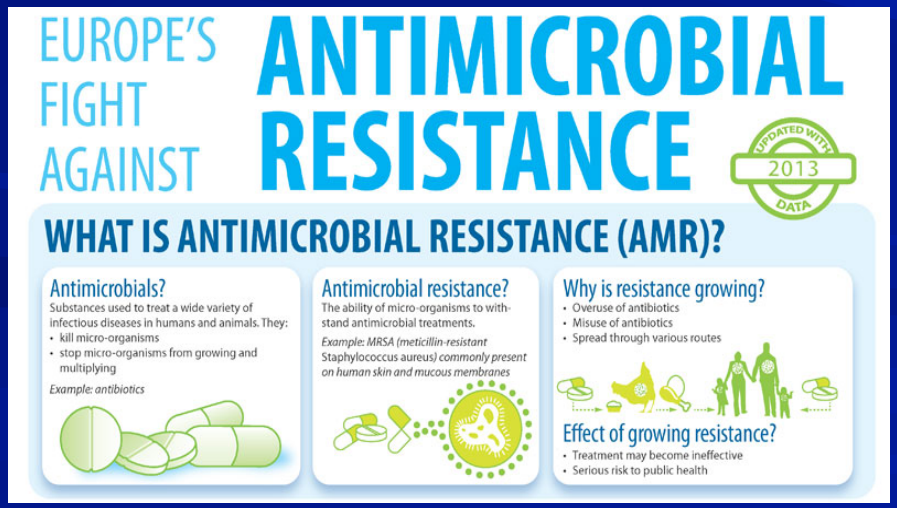
Global Impact of Antimicrobial Resistance



Global Response to Antimicrobial Resistance

Global action plan to combat antimicrobial resistance

World Health Organization



March 2015

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The White House
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For Immediate Release March 27, 2015

FACT SHEET: Obama Administration Releases National Action Plan to Combat Antibiotic-Resistant Bacteria

Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

Judicious use of antibiotics in healthcare and agricultural settings is essential to slow the emergence of resistance and extend the useful lifetime of effective antibiotics. The CDC estimates that up to half of all human antibiotic use is unnecessary or inappropriate. The Action Plan includes activities to foster improvements in the appropriate use of antibiotics (i.e., antibiotic stewardship) by improving prescribing practices across all healthcare settings. , preventing the spread of drug-resistant threats in healthcare facilities and communities, and continuing to eliminate the use of medically-important antibiotics for growth promotion in animals.

By 2020, significant outcomes in this area will include:

- Establishment of antimicrobial stewardship programs in all acute care hospitals and improved antimicrobial stewardship across all healthcare settings.
- Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings.
- Establishment of State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states to monitor regionally important multi-drug resistant organisms and provide feedback and technical assistance to health care facilities.
- Elimination of the use of medically-important antibiotics for growth promotion in food-producing animals.

Four Core Actions to Fight Resistance

(http://www.cdc.gov/drugresistance/pdf/4-2013-508.pd

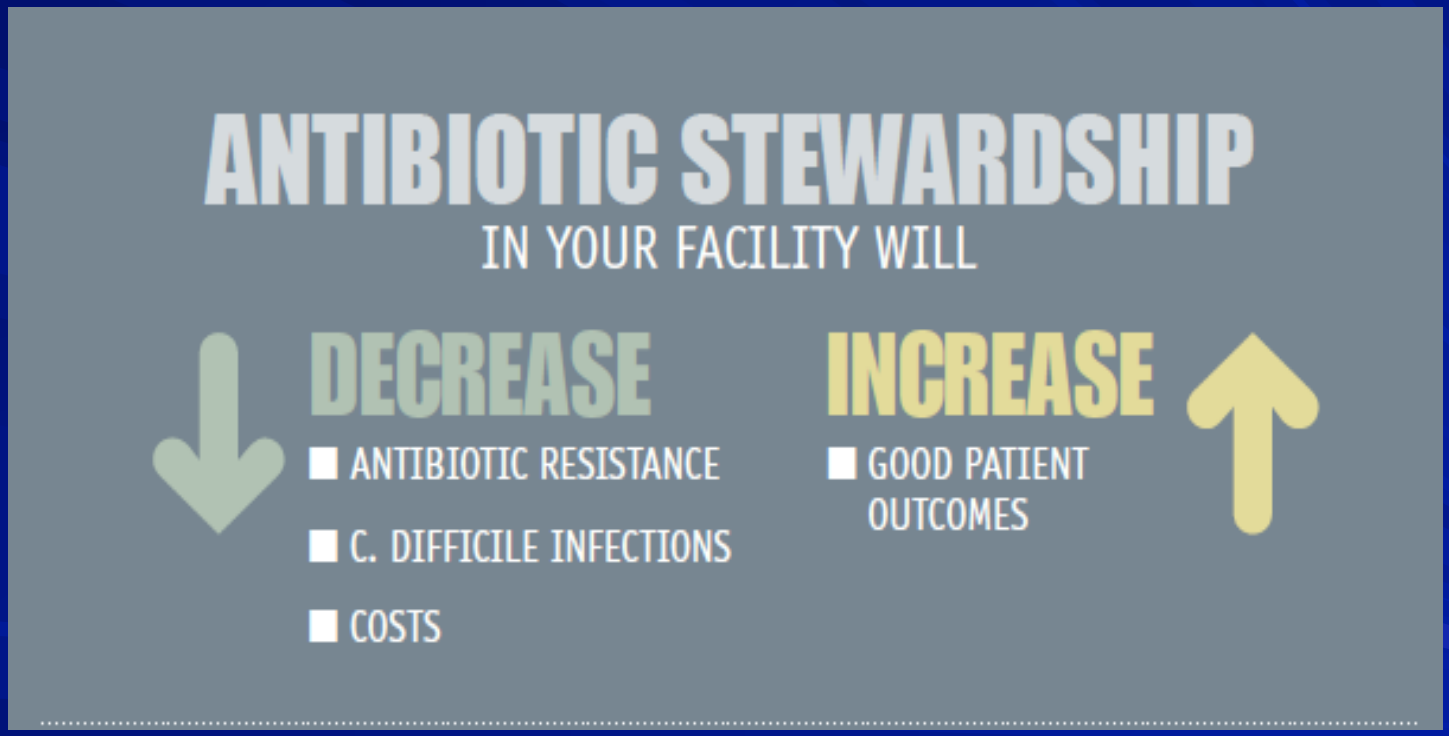
- Preventing infections & the spread of Resistance
- Tracking of rates of resistance over time
- Improving Antibiotic Prescribing/Stewardship
- Developing New Drugs & Diagnostic Tests

Four Core Actions to Fight Resistance

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

What Can Antimicrobial Stewardship DO?



What Can Antimicrobial Stewardship DO?

PROMOTE ANTIBIOTIC BEST PRACTICES— A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN "ANTIBIOTIC TIMEOUT" REASSESSING ANTIBIOTICS AFTER 48–72 HOURS

What Can Antimicrobial Stewardship DO?

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A "WIN-WIN" FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM **SAVED A TOTAL OF $17 MILLION** OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS **IMPROVE PATIENT CARE AND SHORTEN HOSPTIAL STAYS,** THUS **BENEFITING PATIENTS AS WELL AS HOSPITALS**

Antimicrobial Stewardship Strategies

(Newland & Hersh/PIDJ/2010)

- Core strategies
  - Prospective audit with intervention and feedback
  - Formulary restriction and preauthorization
- Supplemental Strategies
  - Education
  - Clinical Guidelines
  - IV to PO conversion
  - Dose optimization
  - Antimicrobial Order Forms


GUIDELINES

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

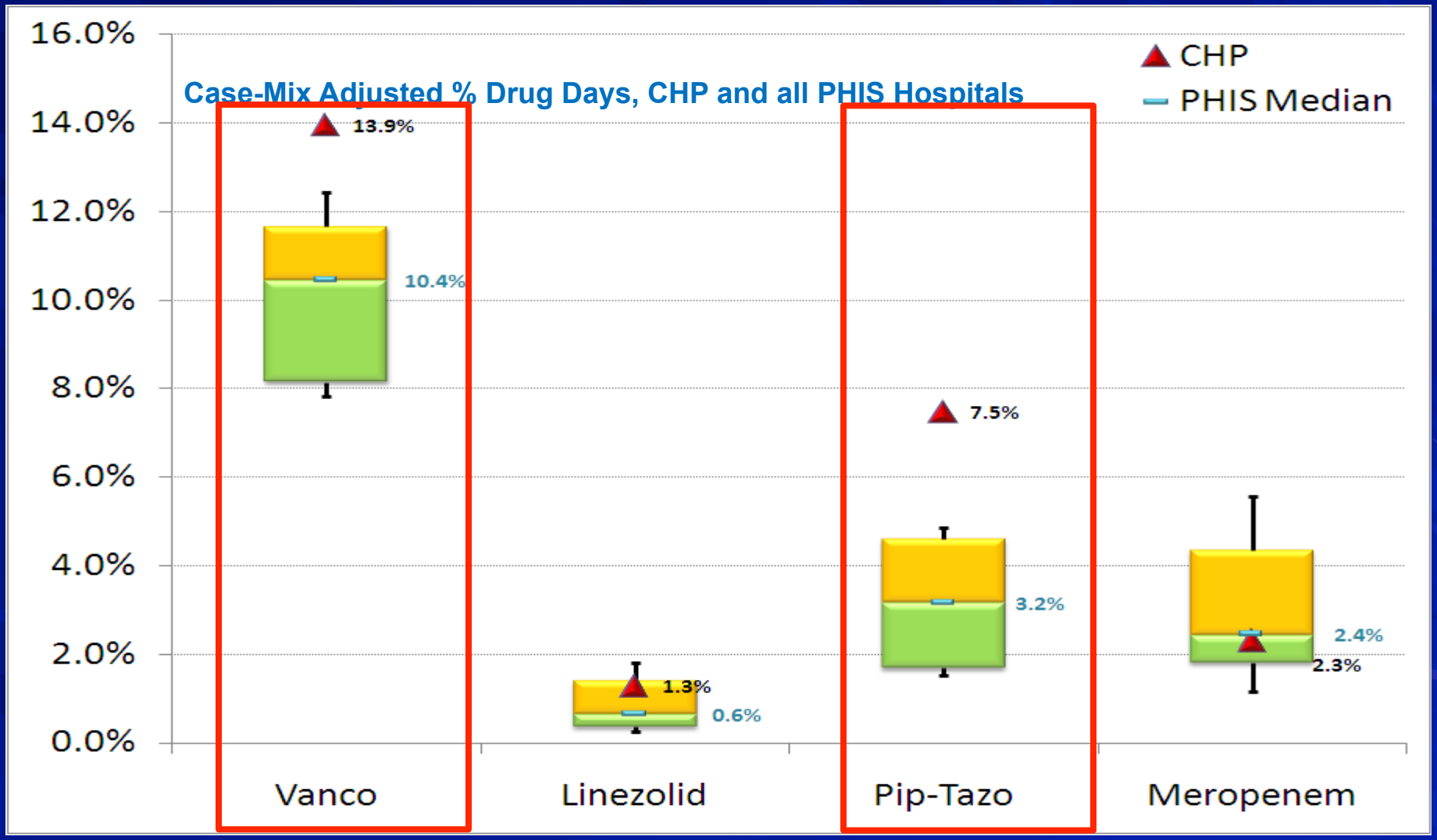
[1]Harborview Medical Center and the University of Washington, Seattle; [2]Maine Medical Center, Portland; [3]Emory University, Atlanta, Georgia; [4]Hines Veterans Affairs Hospital and Loyola University Stritch School of Medicine, Hines, and [5]Stroger (Cook County) Hospital and Rush University Medical Center, Chicago, Illinois; [6]University of Utah, Salt Lake City; [7]Mayo Clinic College of Medicine, Rochester, Minnesota; [8]University of Pittsburgh Medical Center, Pittsburgh, and [9]University of Pennsylvania, Philadelphia, Pennsylvania; [10]William Beaumont Hospital, Royal Oak, Michigan; [11]Ochsner Health System, New Orleans, Louisiana; and [12]University of Miami, Miami, Florida

- Core members of multidisciplinary antimicrobial stewardship team include:
  - ID physician, clinical pharmacist with ID training, clinical microbiologist, an information system specialist, an infection control professional, and hospital epidemiologist
- Collaboration between ASP AND hospital Infection Control and Pharmacy & Therapeutics committees essential
- The support & collaboration of hospital administration, medical staff leadership, and local providers in development and maintenance of ASP is essential
- ID physician and head of pharmacy, as appropriate, should negotiate with hospital administration to obtain adequate authority, compensation, and expected outcomes for the program
- Hospital administrative support for the necessary infrastructure to measure antimicrobial use and to track use on an ongoing basis is essential

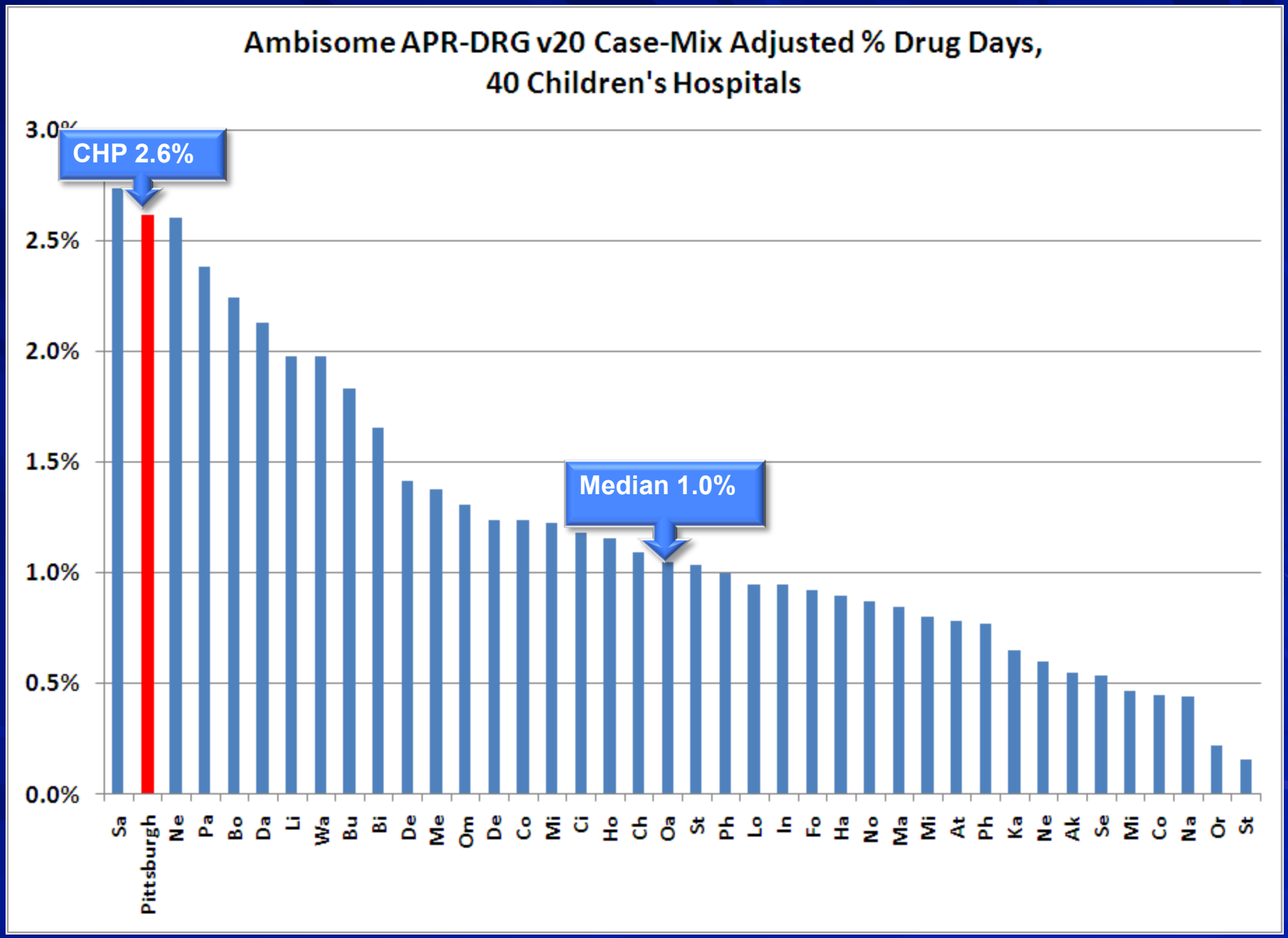
Antimicrobial Stewardship At CHP: Then

- As of 2007, CHP had a long standing requirement for drug approval for "restricted antibiotics" CHP:
  - Some "direction" towards "drugs of choice"
  - No tracking of antibiotic use once approved
  - High prevalence of antimicrobial resistance in ESKAPE pathogens
  - No formal antimicrobial stewardship program

PHIS Antimicrobial Analysis 2007



Levin J, 2007, Unpublished Data



Levin J, 2007, Unpublished Data






ASP AT CHP


Children's | UPMC
Children's | UPMC
Children's | UPMC
Children's | UPMC

Models of ASP:

"Traditional Model" Includes Involvement of:	CHP Model Includes Involvement of:
ID Physician Leader	ID Physician Leader & Full ID Division
Dedicated ASP Pharmacist with ID Training	Team of 7 Service-based Pharmacists
Pharmacy Director	Pharmacy Director
P&T Committee	P&T Committee
Infection Prevention	Infection Prevention
Informatics	Informatics
Hospital Administration	Hospital Administration

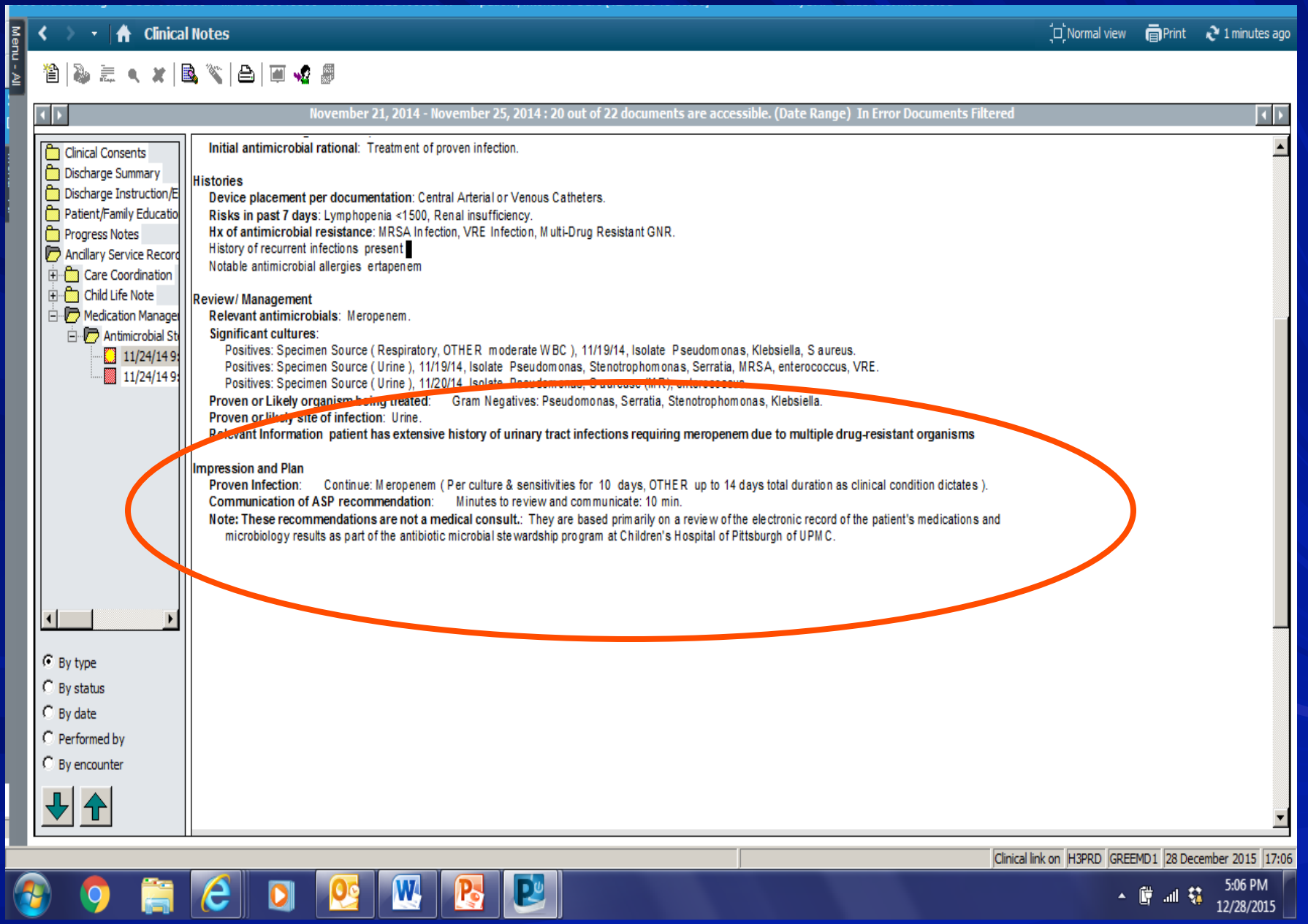
What Makes CHP's ASP Unique?

- Use of Service-based pharmacists
  - Integrated into daily rounding activities for KEY patient populations
  - Already trusted participants in clinical decision making
- Participation of FULL ID Division
  - All Drug Approvals & Weekend/Holiday Day 3 Auditing
  - Global commitment to antimicrobial stewardship
- Leveraged use of EMR & CHP Data warehouse
  - Identify those requiring Day 3 auditing
  - Review patient records & communicate recommendations
  - Continuously track Antimicrobial use to measure impact of program

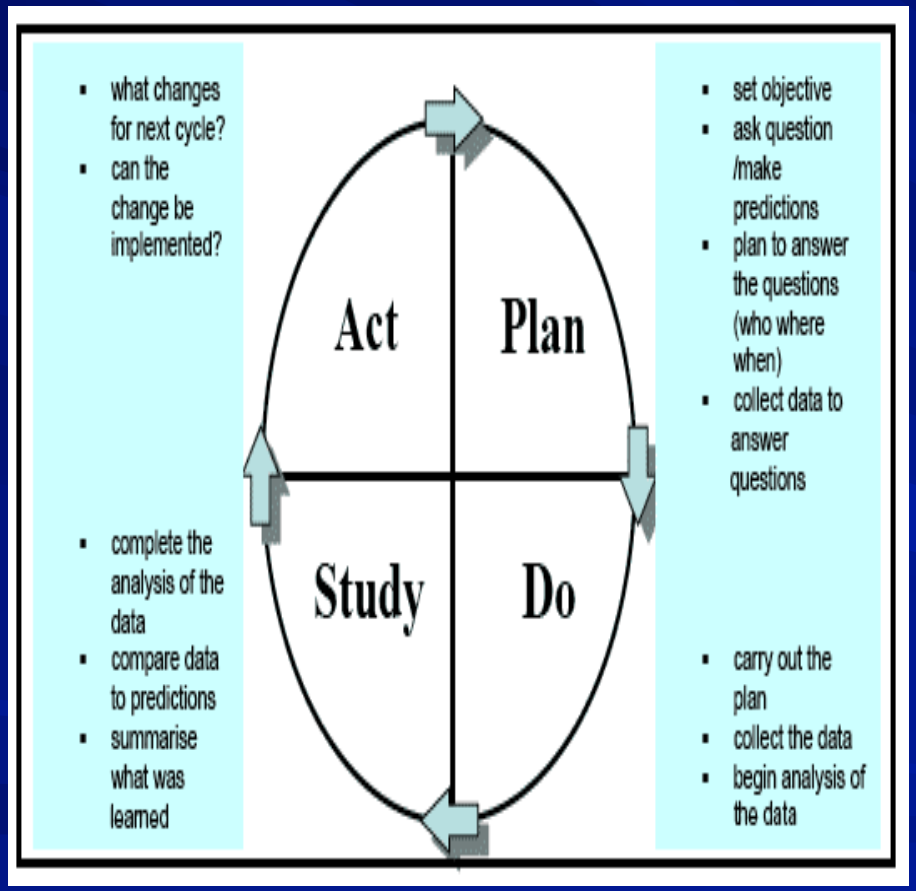
CHP ASP: Development of Guidelines

- Multistep process for development of guidelines for use of “targeted” antimicrobials
- Guideline development includes
  - Review of literature
  - Small group meeting with representatives from key stakeholder groups
  - Development of “draft” guideline followed by review by full stakeholder groups, P & T Committee and Clinical Resource Management Committee
- Once approved, guidelines serve as basis for Day 3 Audits
- Guidelines include:
  - Post-op prophylaxis & antifungal use for Liver & Intestinal Tx
  - Use of ciprofloxacin & vancomycin for IBD patients
  - Use of meropenem (all CHP patient populations)
  - Empiric antimicrobial regimens for surgical infants in NICU
  - Empiric antimicrobial regimens in the CICU

Communicating Recommendations

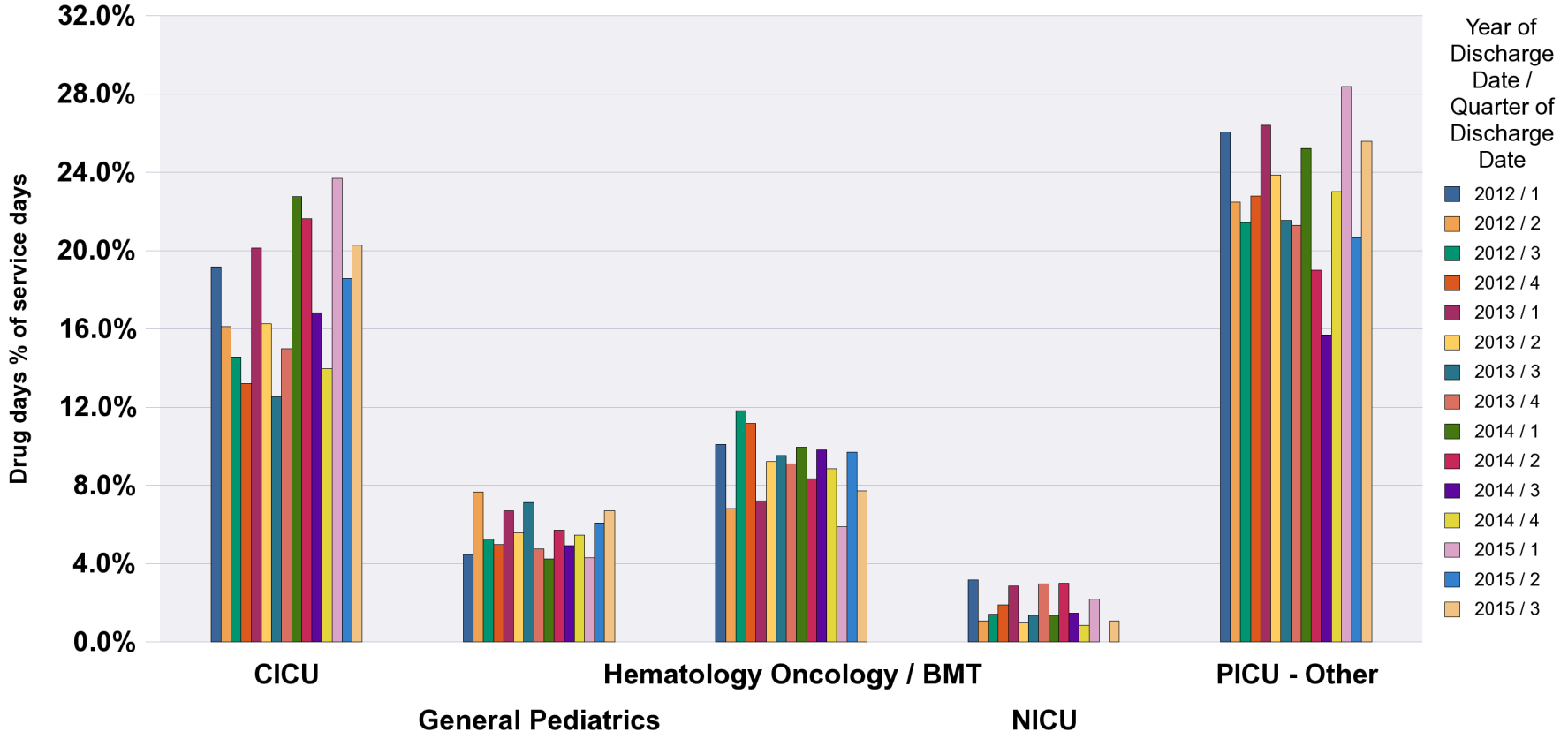


Tracking Results to Enhance Quality



- The **PDSA cycle** is shorthand for testing a change by developing a plan to test the change (Plan), carrying out the test (Do), observing and learning from the consequences (Study), and determining what modifications should be made to the test (Act).

Using CHP Data Warehouse to Track Results over Time



Quarterly reports generated automatically from Data warehouse

Analyzing Results: The role of the Statistician

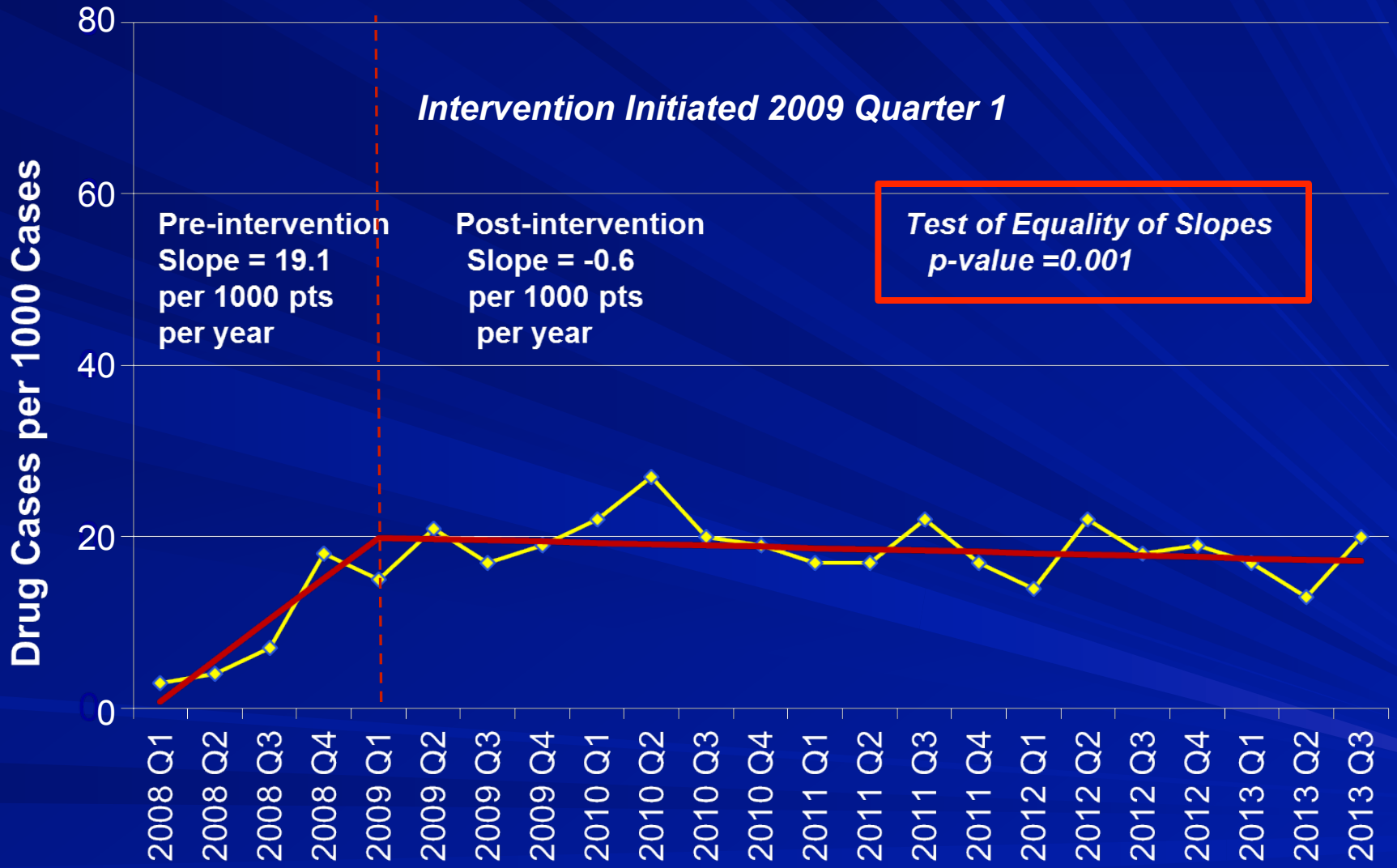
- Interrupted time series: State of the art for analysis
- Essentially compares slope of results over time Before & After intervention
- Illustrates the necessity of statistical support to accurately assess key outcomes
- Maria Mori Brooks, PhD at GSPH to our Rescue

(Thank you Thank you Thank you)

Antimicrobial Stewardship At CHP: Where are we now?

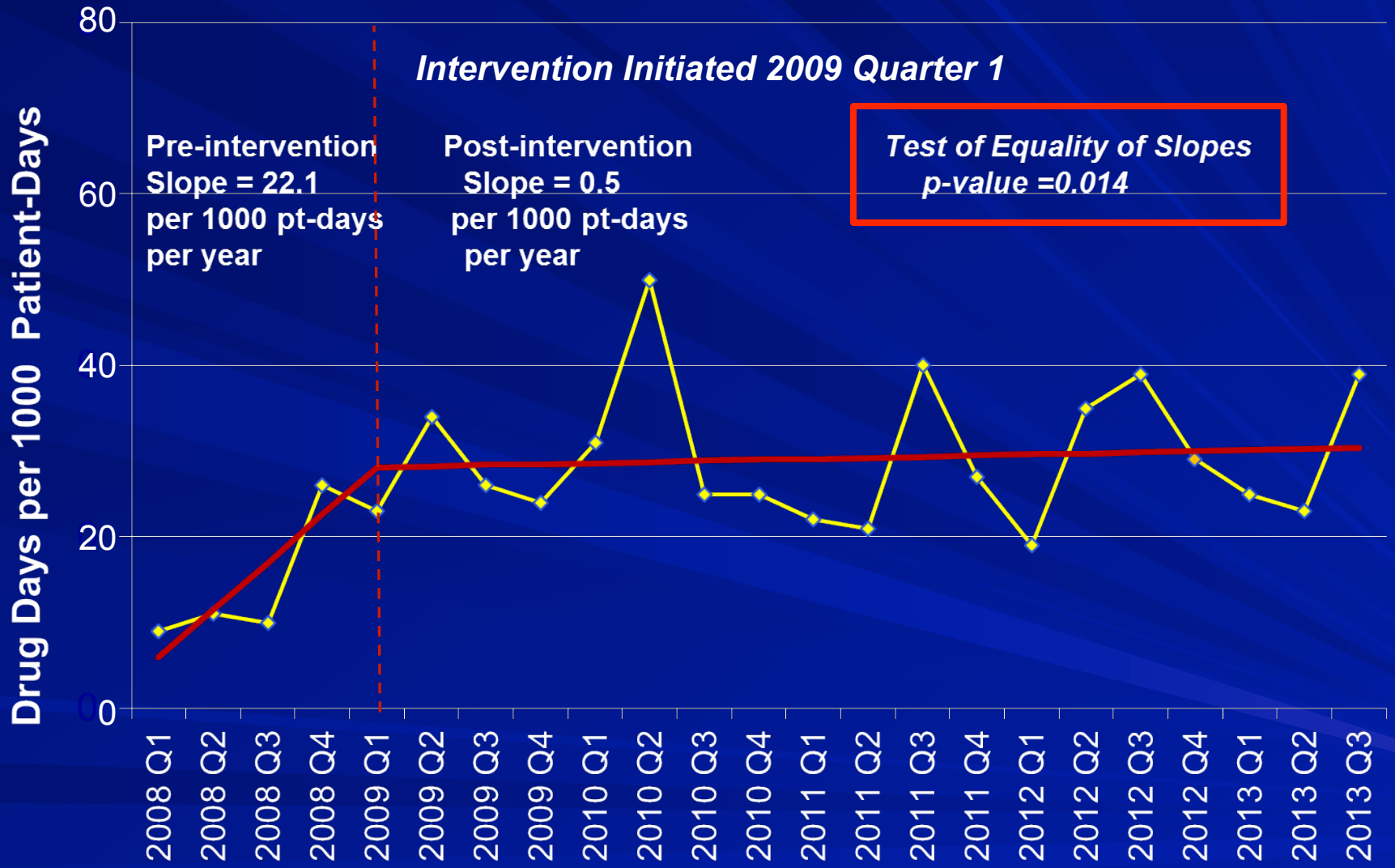
- ASP officially in place for 7 years (January 2009)
- ID Pre-approval for selected antimicrobials continues
- Day 3 Auditing for caspofungin, meropenem & vancomycin
- Guidelines for use of “targeted” antimicrobials developed with stakeholders
- Results reviewed as part of PDSA process on quarterly basis
- Role of ASP established in culture of CHP
- Ongoing question: What should we do next?

Caspofungin Drug Starts



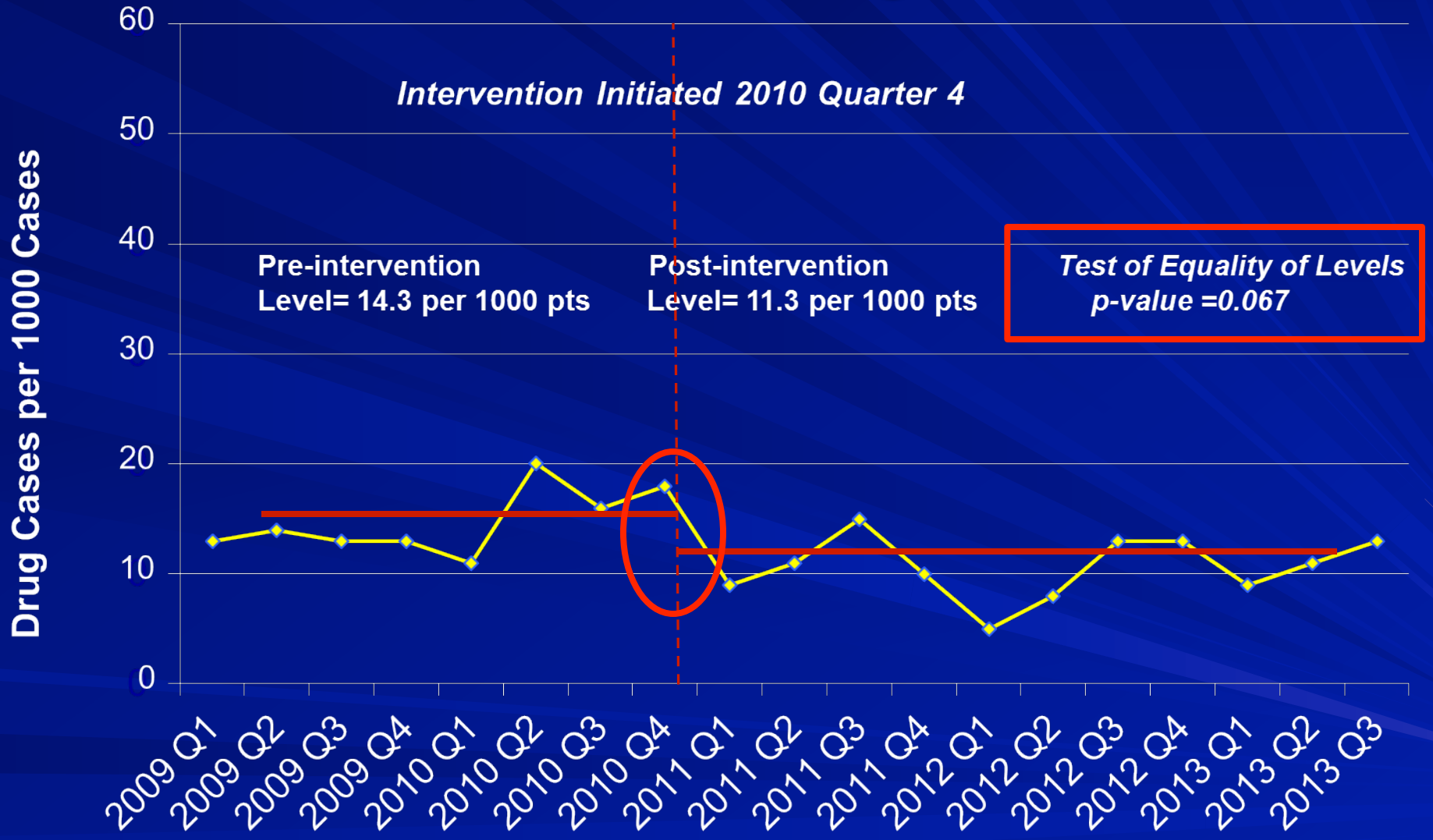
Nguyen-Ha et al, Pediatrics 2016 (In Press)

Caspofungin Drug Use



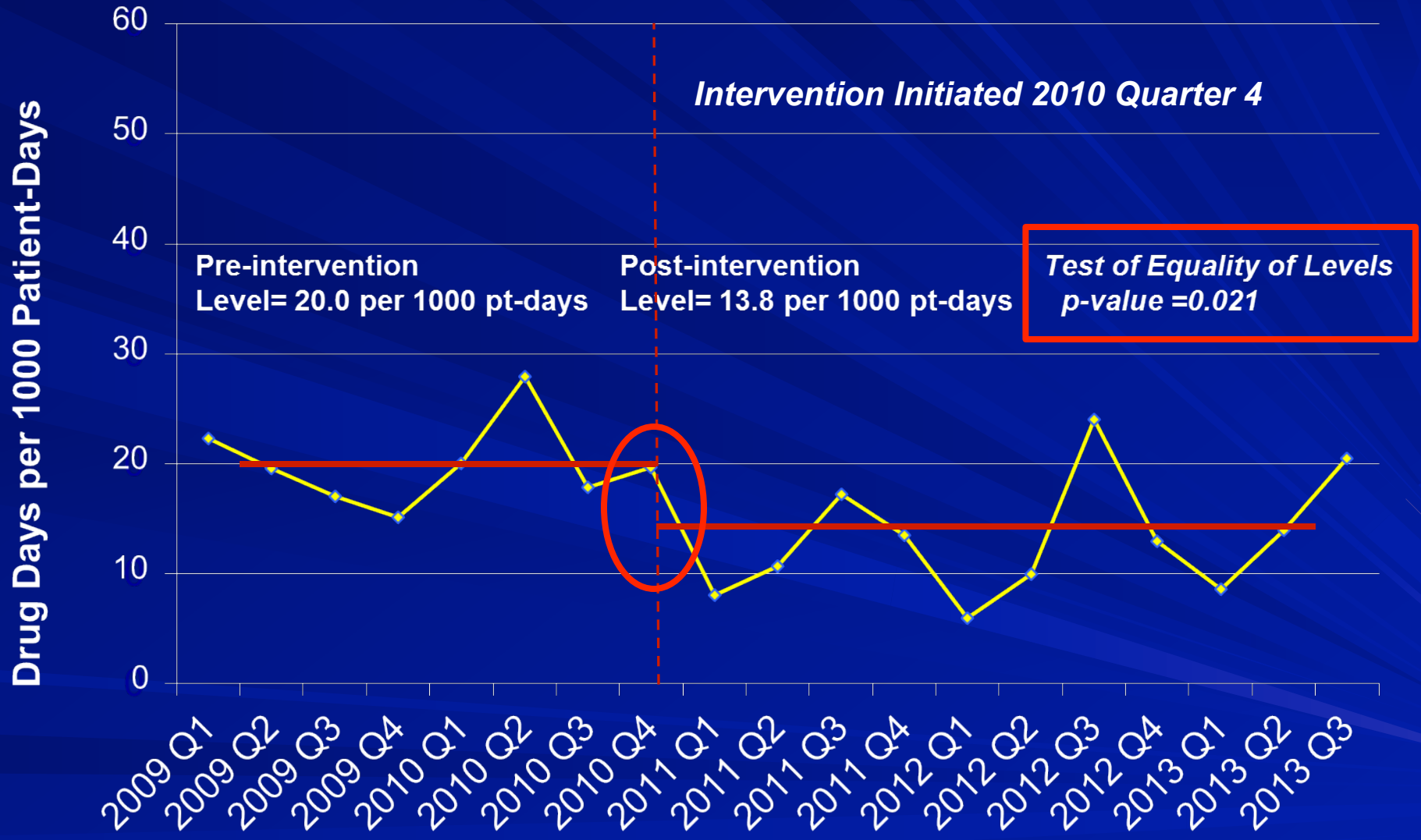
Nguyen-Ha et al, Pediatrics 2016 (In Press)

Meropenem Drug Starts



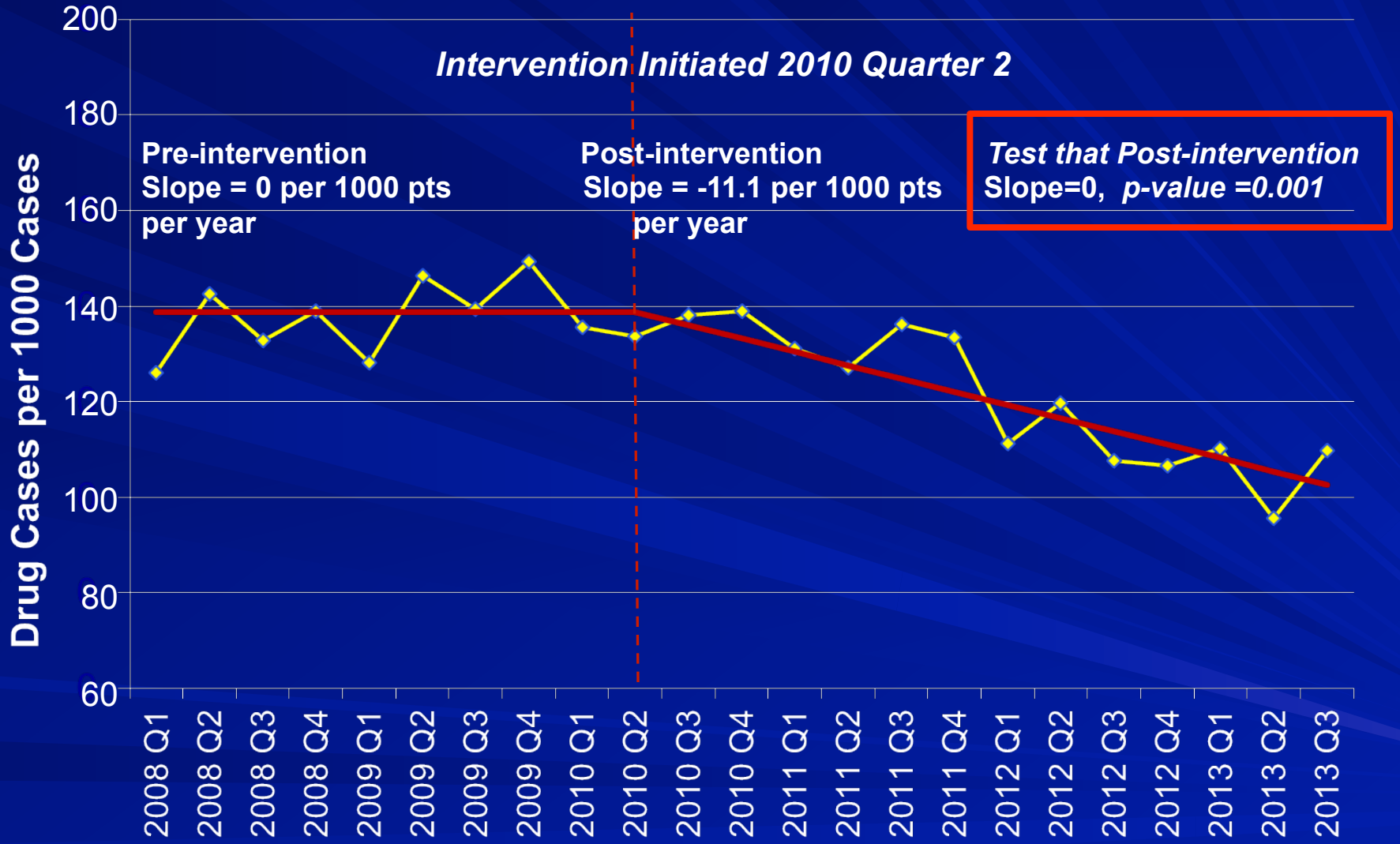
Nguyen-Ha et al, Pediatrics 2016 (In Press)

Meropenem Drug Use



Nguyen-Ha et al, Pediatrics 2016 (In Press)

Vancomycin Drug Starts



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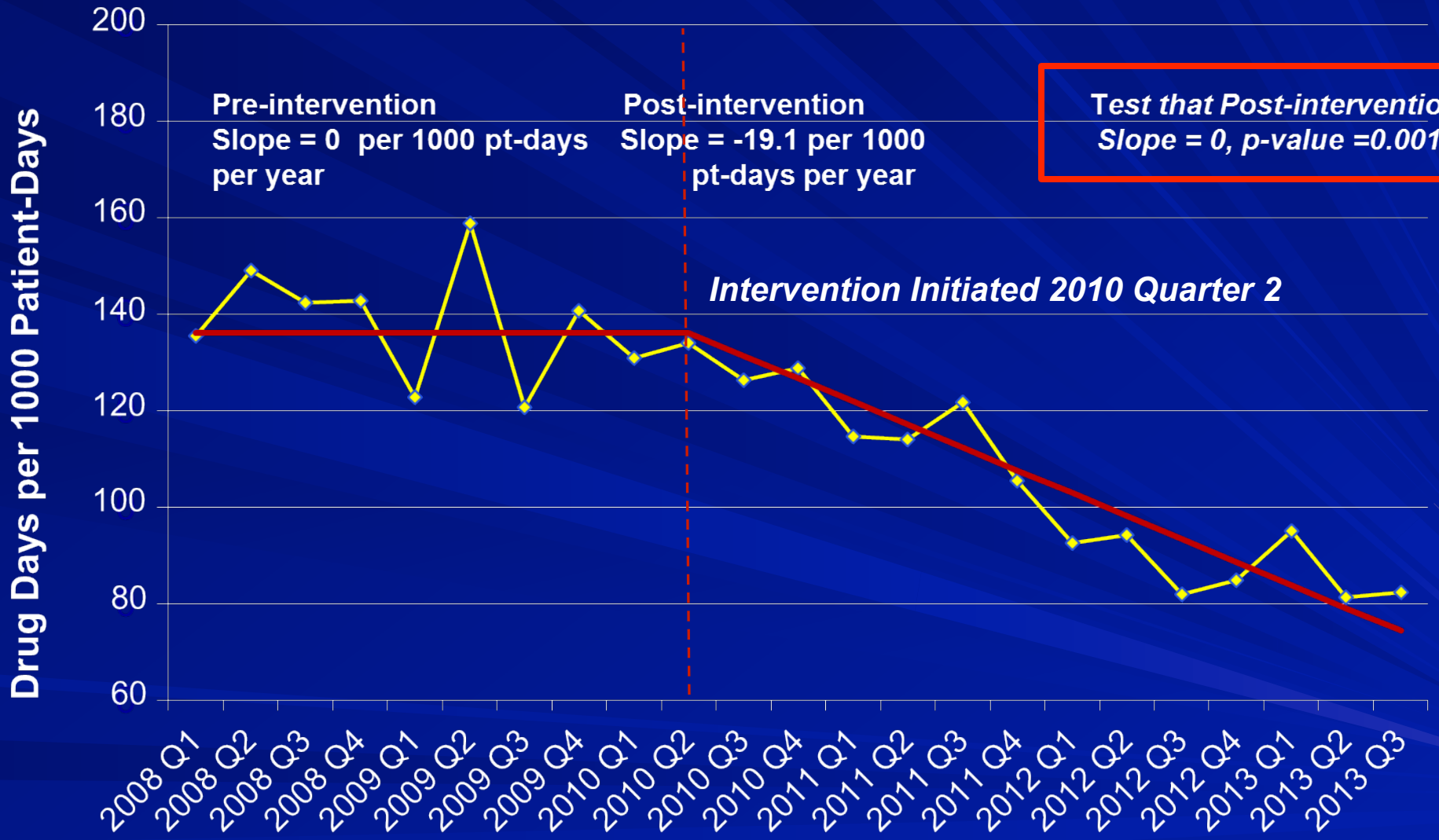
Vancomycin Drug Use

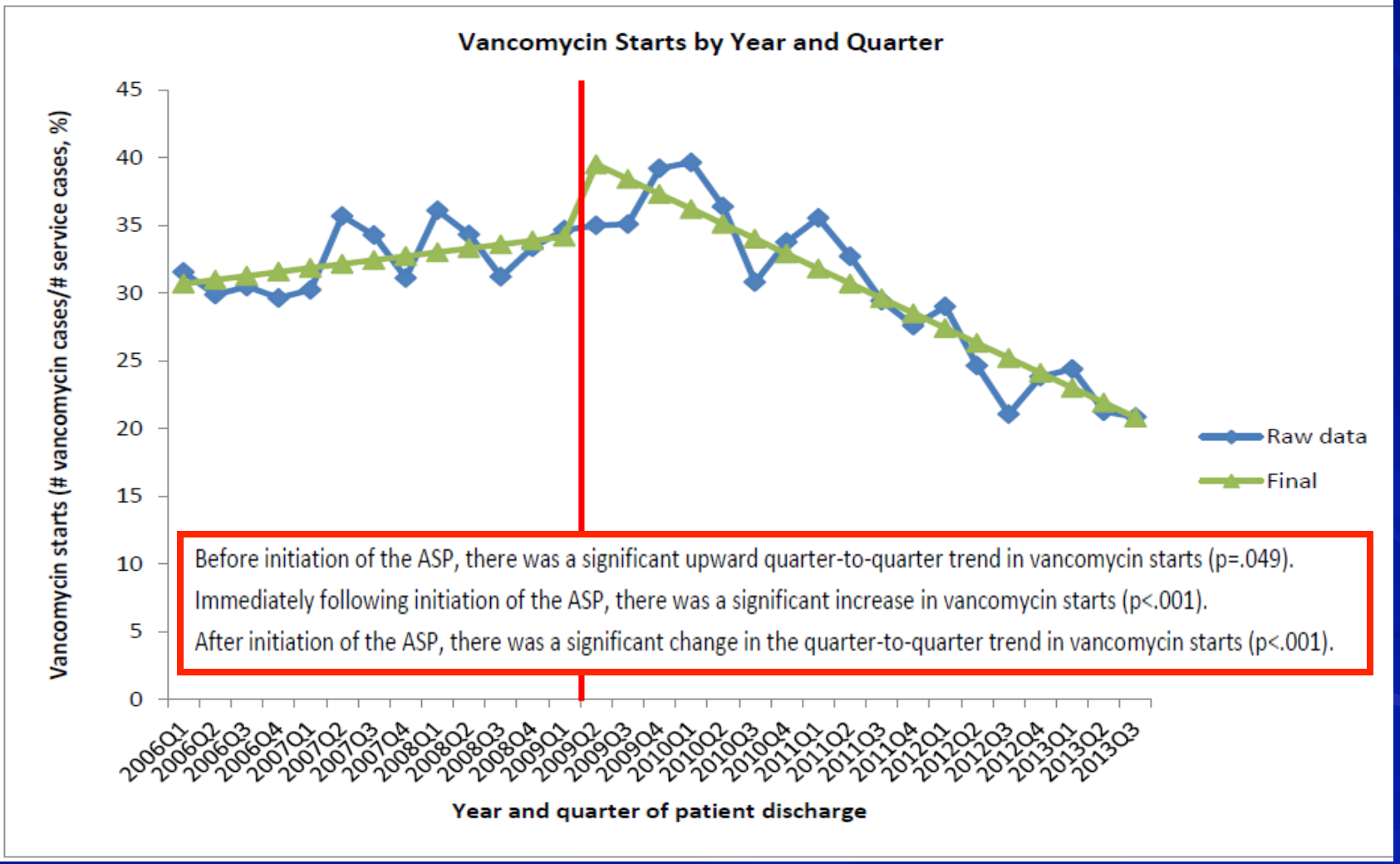


Nguyen-Ha et al, Pediatrics 2016 (In Press)

Vancomycin Starts In ICUs

Results of an Antimicrobial Stewardship Program (ASP) on Vancomycin Prescribing Practices in Pediatric Intensive Care

Drug starts (# drug cases/# service cases, %) – Overall



Crowley et al, (Manuscript In preparation)

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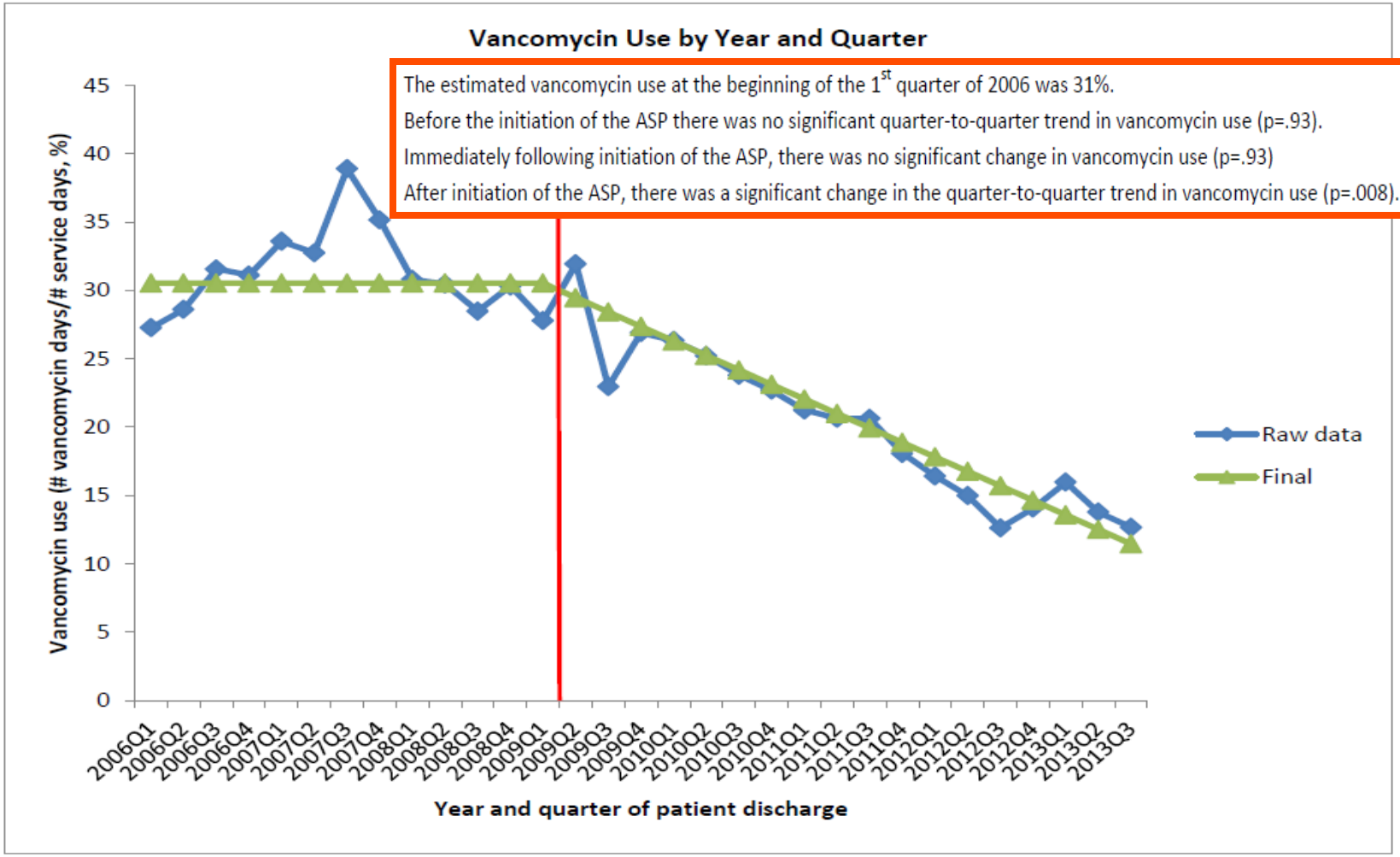
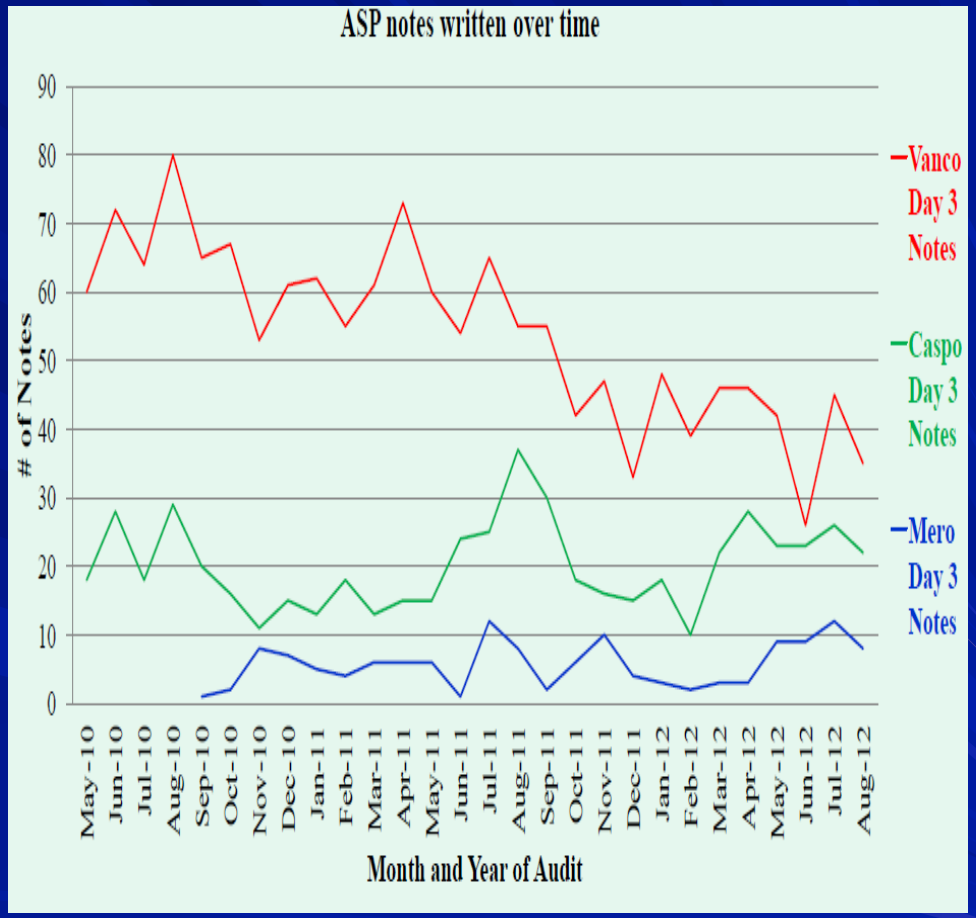


Crowley et al, (Manuscript In preparation)

Monitoring Acceptance of ASP Recommendations

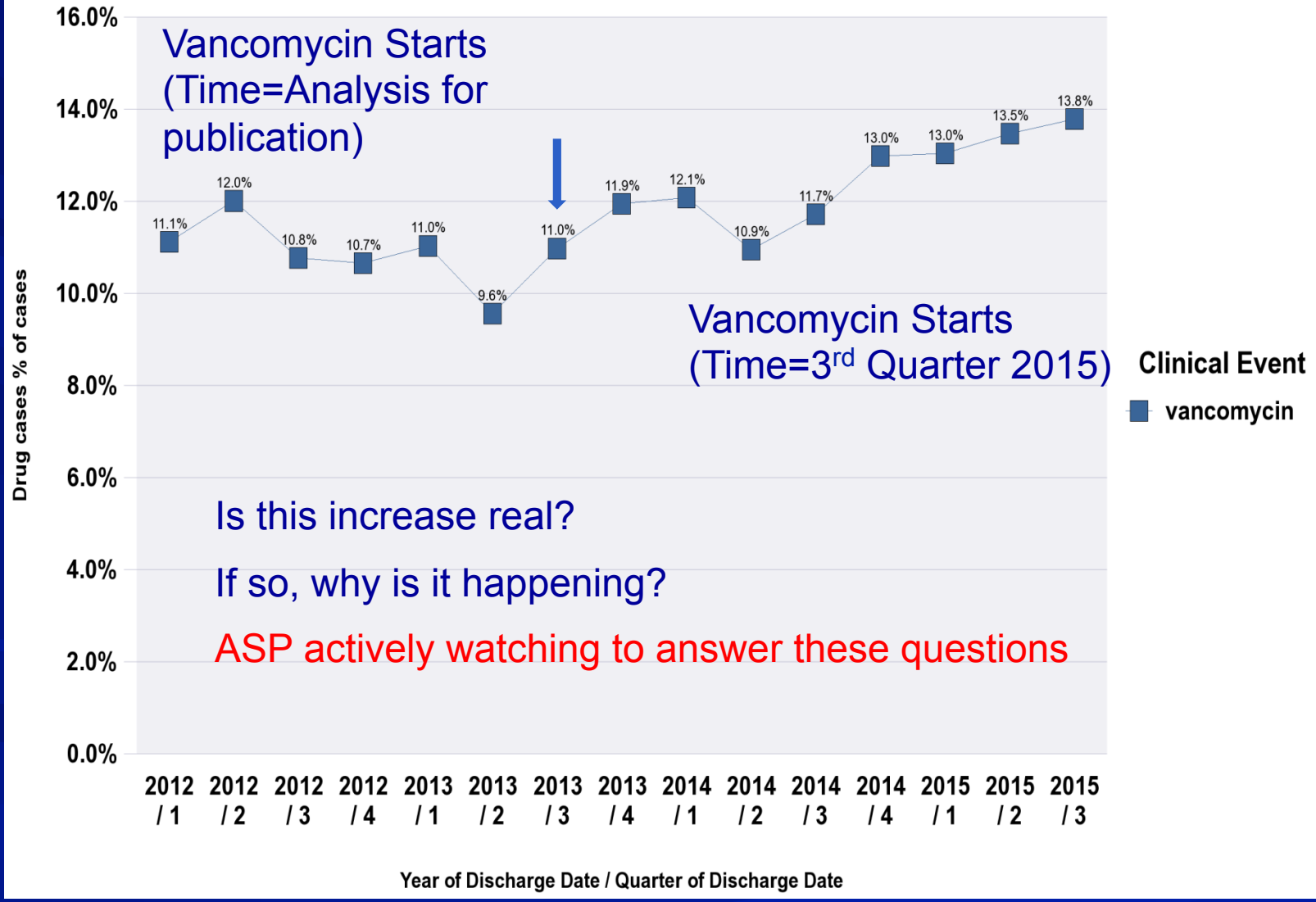
- Recommendation "accepted" when followed within 24 hours of completion of eNote.
- Compliance: % ASP recommendations accepted/ # eNotes written in 3 month "audit" period for each drug
- Overall acceptance rate of 90%, 93% &100% for recommendations relating to vancomycin, caspofungin & meropenem, respectively.



Decline in ASP notes over time suggests that clinicians are making decisions in advance of audit note

Nguyen-Ha et al, Pediatrics 2016 (In Press)

Maintaining Stewardship Overtime Requires Ongoing Attention



Maintaining Stewardship: Should other drugs be restricted or audited?

Journal of the Pediatric Infectious Diseases Society Advance Access published July 13, 2015

Brief Report

Piperacillin-Tazobactam Usage at a Tertiary Pediatric Hospital: An Antimicrobial Stewardship Review

Andrew B. Janowski,[1] Marian G. Michaels,[2] Judith M. Martin,[2] and Michael D. Green[2]
[1]Department of Pediatrics, St. Louis Children's Hospital, Missouri; and [2]Department of Pediatrics, Children's Hospital of Pittsburgh of UPMC, Pennsylvania

Table 2. Panel Assessment of the Utilization of Piperacillin-Tazobactam at Initiation and at 72-Hour Review Mark

Piperacillin-Tazobactam Initiated	200, N (%)
• Agreed with initiation	186 (93)
• Disagreed with initiation	14 (7)
Piperacillin-tazobactam discontinued before or at 72 hours	110 (55)
• Agreed with discontinuation	104 (94.5)
• Disagreed with discontinuation	6 (5.5)
Piperacillin-tazobactam continued beyond 72 hours	90 (45)
• Agreed with continuation	67 (74.4)
• Disagreed with continuation	23 (25.6)

CONCLUSIONS

In summary, this systematic chart review provides insight into the indications for piperacillin-tazobactam initiation and continuation at 72 hours. Our results suggest that a review at 72 hours could reduce usage and provide cost savings. This study may serve as a guide for determination of which antibiotics require formal approval at initiation or should be audited at 72 hours for reassessment.

Not Calculated:
COST of ASP effort to audit a drug used as much as piperacillin/ tazobactam?

ASP at CHP: What's Next?

- Potential Initiatives:
  - Work with DRG to identify targets for guidelines and stewardship in treatment of hospitalized children with community acquired infection
  - Work with CCP & GAP to identify targets for guidelines and stewardship in ambulatory treatment of community acquired infection in children
- Continue to review data & seek opportunities for cost-effective stewardship in all settings

Recognizing the CHP ASP

- TDM
  - Don Berry
  - Kelli Crowley
  - Elizabeth Ferguson
  - Denise Howrie
  - Bill Mcghee
  - Tan Nguyen
  - Carol Vetterly
  - Emily Polischuck
  - Jen Shenk
- Pharmacy
  - Jeff Goff
- Medical Director's Office
  - Ann Thompson
- Infectious Diseases
  - Brian Campfield
  - Toni Darville
  - Michael Green
  - Jim Levin
  - Ling Lin
  - Judy Martin
  - Marian Michaels
  - Andy Nowalk
  - Terri Stillwell
  - John Williams
  - ID Fellows
- GSPH Biostatistics
  - Maria Mori Brooks
  - Jong-Hyeon Jeong
  - Marcia Kurs-Lasky

Questions?


need to know
ANTIBIOTIC RESISTANCE IS NOT COMING IT IS HERE RIGHT NOW
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE
need to know
THE DISCOVERY OF PENICILLIN WAS SO IMPORTANT IT WAS AWARDED A NOBEL PRIZE
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE
need to know
ANTIBIOTICS ARE LOSING THEIR POWER
ANTIBIOTIC
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE
need to know
ANTIBIOTIC RESISTANCE KNOWS NO GEOGRAPHICAL BOUNDS
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE
need to know
ANTIBIOTICS WON'T MAKE YOUR COLD OR FLU BETTER FASTER
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE
need to know
DON'T ASK FOR ANTIBIOTICS WHEN YOU DON'T NEED THEM
WINTERISCOMING.NPS.ORG.AU
NPS MEDICINEWISE

Thank you to all CHP Clinicians and Stakeholders for your support and contributions to CHP Stewardship Efforts!