

# ***Antimicrobial Stewardship***

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# Outline

- Reasons for urgency of Antimicrobial Stewardship Programs (ASPs)
- Understand the purpose, goals, and provide overview of our ASP
- Describe ASPs in key settings
- Summary and case studies

# What is Antimicrobial Stewardship?

“The selection of the optimal antimicrobial agent, route of administration, dose, and duration to provide maximal clinical benefit, while minimizing unintended consequences.”

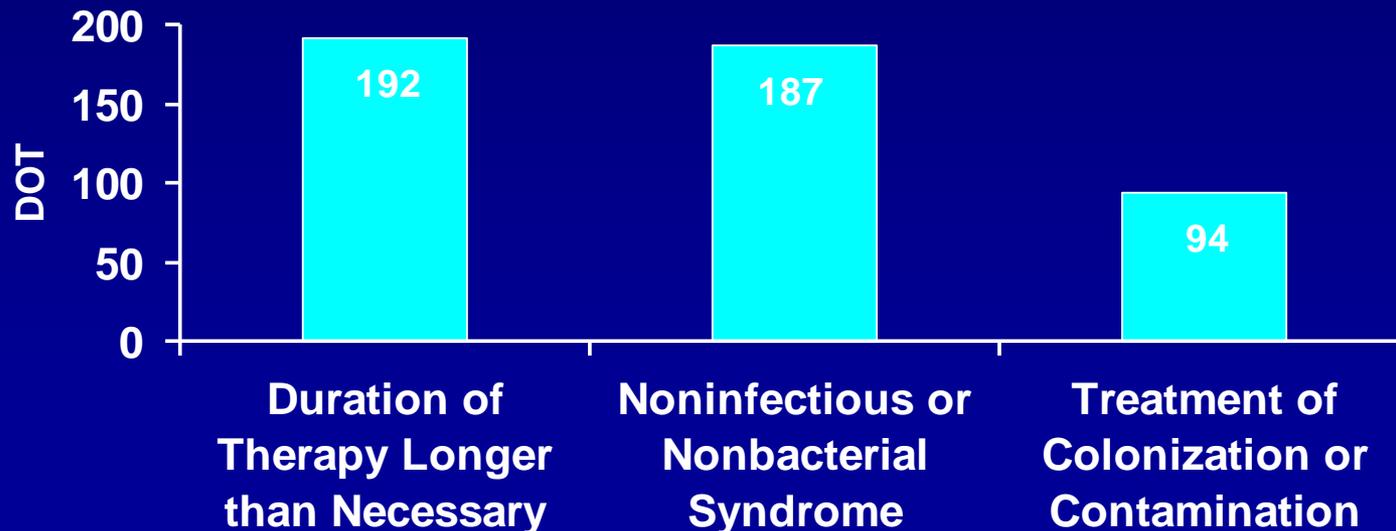
# Why Antimicrobial Stewardship?

- Up to 50% of abx use is inappropriate
  - High quantity, poor quality
- Inappropriate & unnecessary abx use can lead to selection of resistant pathogens
- Antimicrobial resistance continues to increase
- Emergence of antimicrobial resistance leads to significant impact on pt morbidity & mortality, health care costs

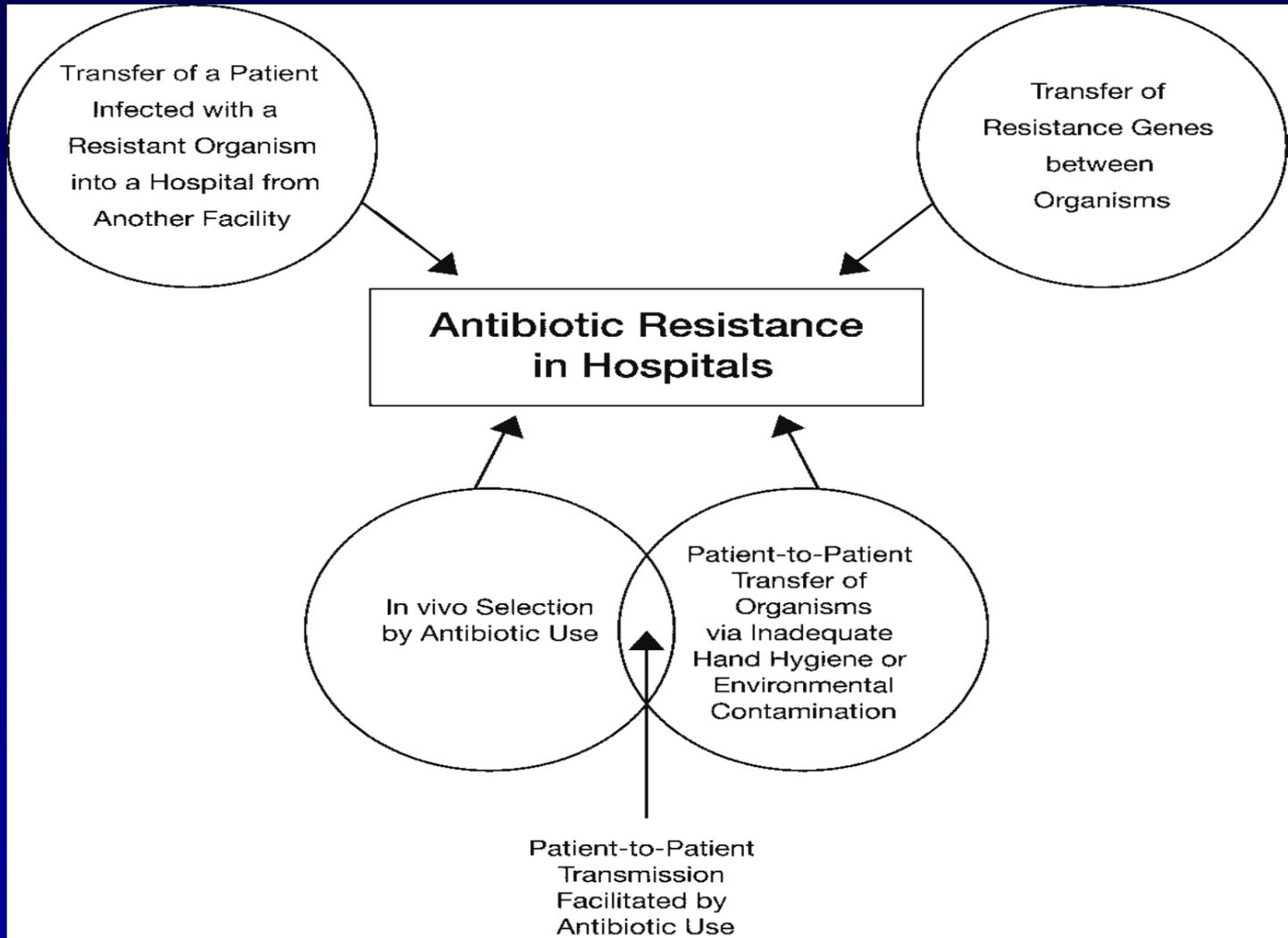
# Unnecessary Use of Antimicrobials in Hospitals

- Prospective observational study conducted in adult inpatients
- 576 (30%) of 1941 total antimicrobial days of therapy (DOT) deemed unnecessary

## Most Common Reasons for Unnecessary DOT



# How We Acquire Antibiotic Resistant Organisms in Hospitals



# Resistance: A Public Health Crisis

## 12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

- 1 Vaccinate
- 2 Get the catheters out
- 3 Target the pathogen
- 4 Access the experts
- 5 Practice antimicrobial control
- 6 Use local data
- 7 Treat infection, not contamination
- 8 Treat infection, not colonization
- 9 Know when to say "no" to vanco
- 10 Stop treatment when cured
- 11 Isolate the pathogen
- 12 Break the chain

Prevent Transmission

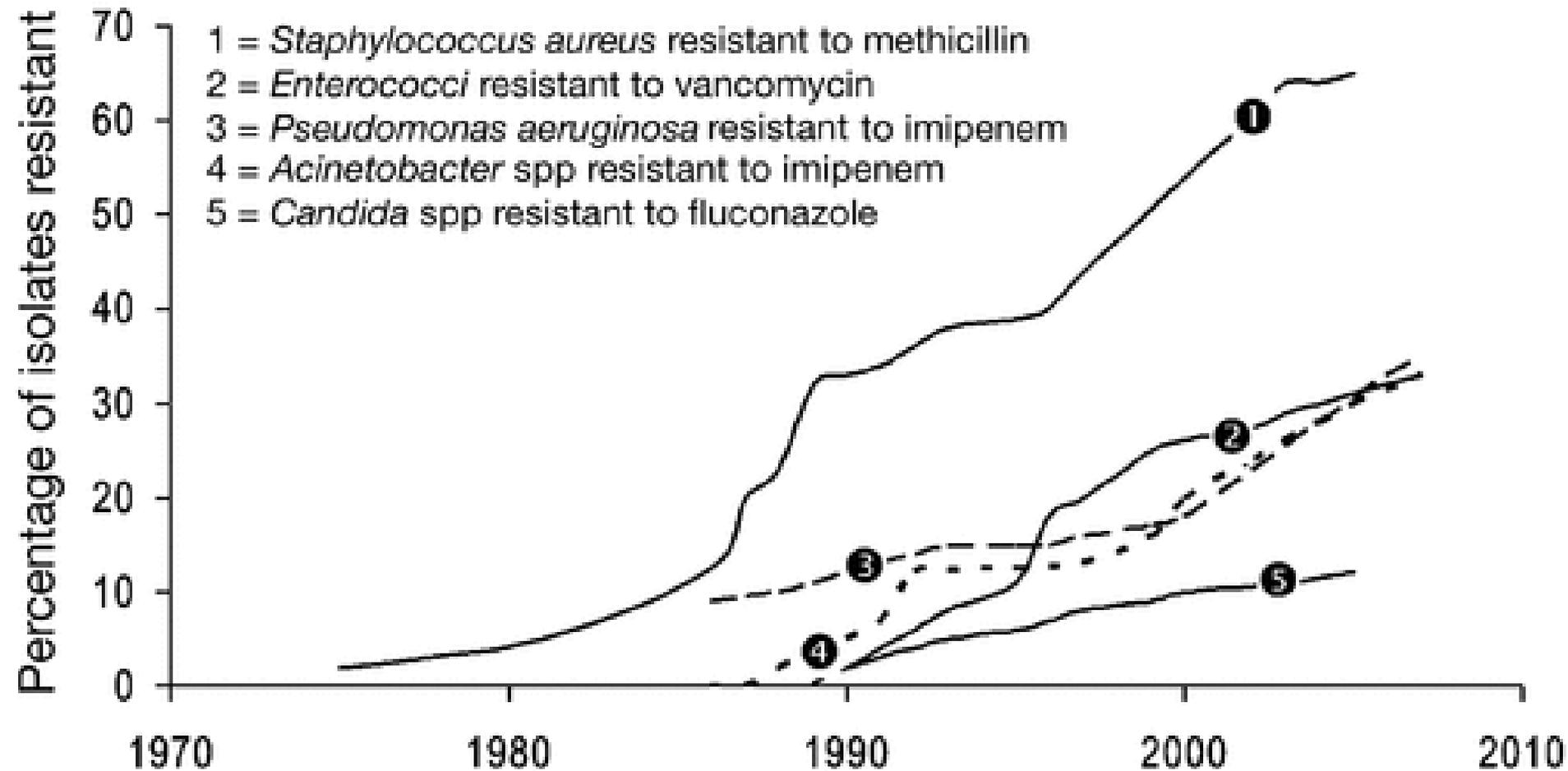
Use Antimicrobials Wisely

Diagnose & Treat Effectively

Prevent Infections

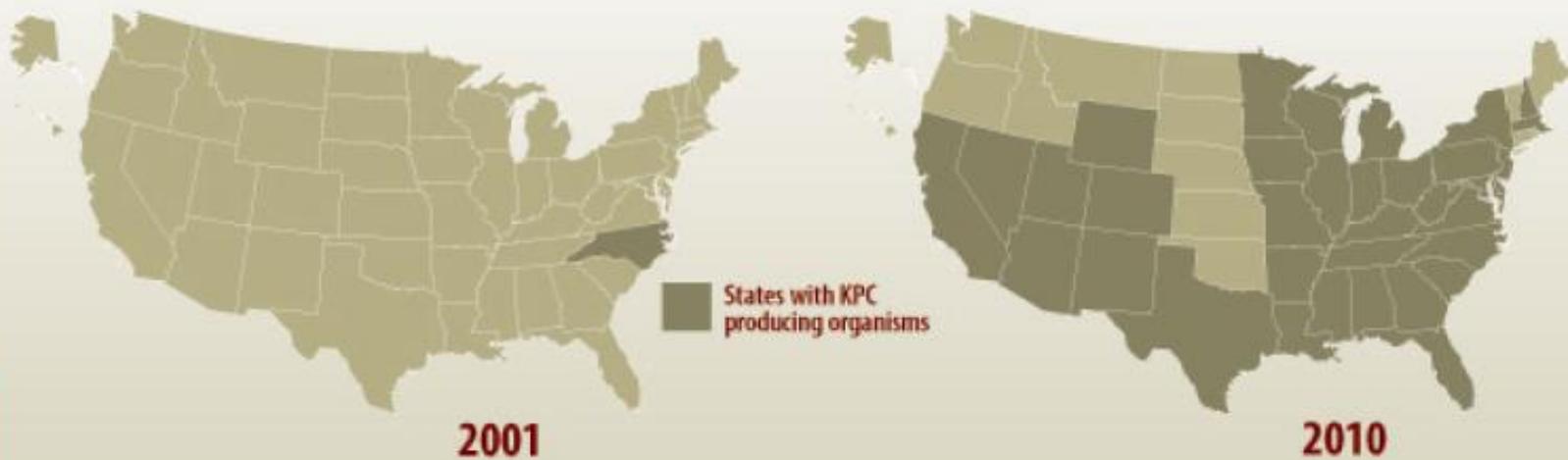


# Antimicrobial Resistance Continues to Increase



# Emergence of KPC Infections

Geographical Distribution of *Klebsiella pneumoniae* carbapenemase (KPC) Infections



**MMWR**<sup>TM</sup>

**Morbidity and Mortality Weekly Report**

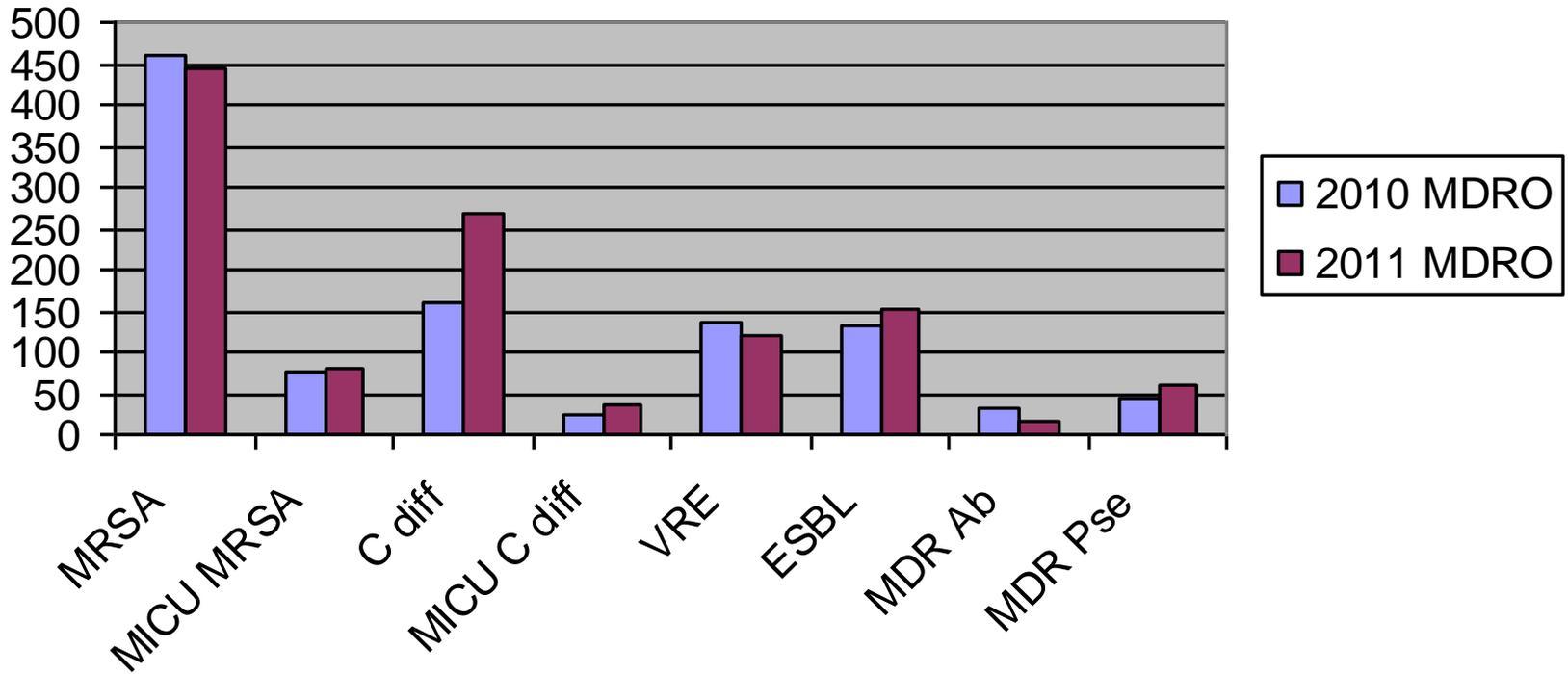
[www.cdc.gov/mmwr](http://www.cdc.gov/mmwr)

**Guidance for Control of Infections  
with Carbapenem-Resistant  
or Carbapenemase-Producing  
*Enterobacteriaceae* in Acute Care  
Facilities**

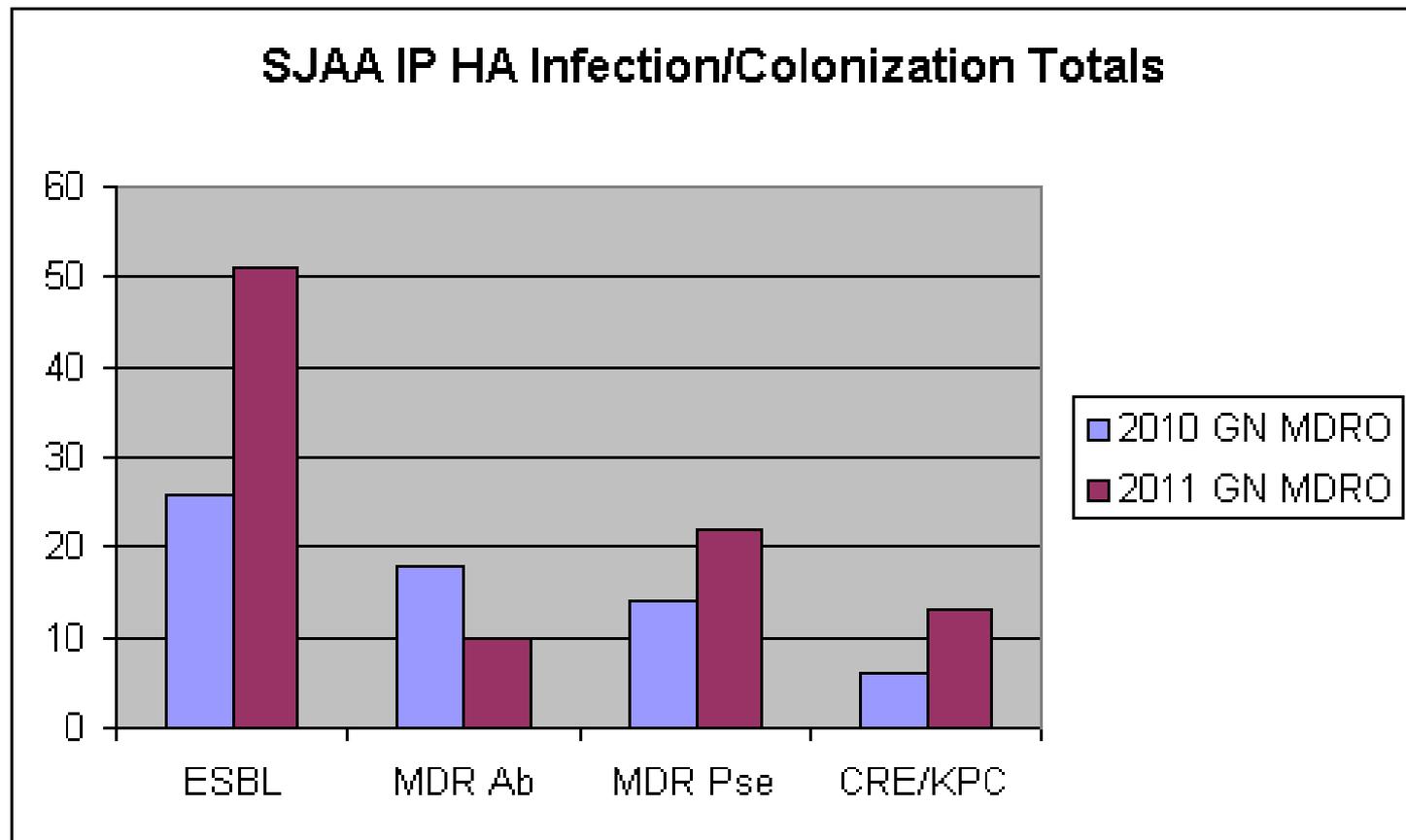
March 20, 2009 / Vol. 58 / No. 10

# Antimicrobial Resistance at SJMH

## Infection/Colonization Totals



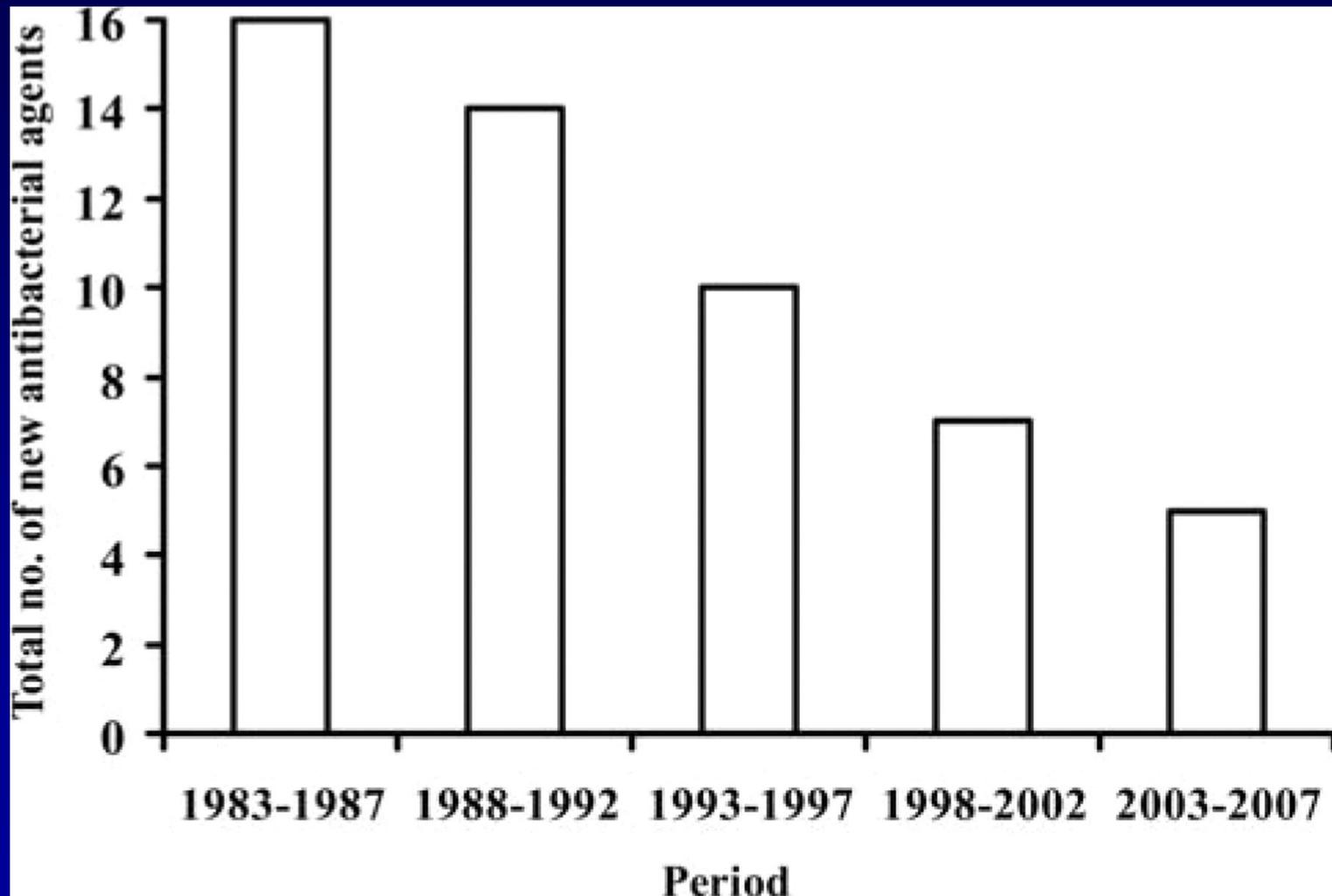
# Antimicrobial Resistance at SJMH



# Costs of Antimicrobial Resistance

- The Chicago Antimicrobial Resistance Project
- 1391 high-risk adults hospitalized at one hospital in 2000
- Evaluated patients with antimicrobial-resistant infections
  - Attributable mortality: 6.5%
  - Excess hospital LOS: 6.4–12.7 days
  - Attributable medical costs: \$18,588–\$29,069 per patient
  - Societal costs: \$10.7–\$15.0 million for all patients at a single hospital

# Antibacterials Approved by the FDA, 1983 - 2007



# Impending Crisis of New Antibiotics

- Last new class of drugs active against GNB, in the 1970s, – “Trimethoprim”
- No new classes of antimicrobials in the foreseeable future
- No new drugs to deal with multi-resistant GNB until 2018
- WHO – “Antibiotic resistance” as one of major threats to human health

1. Bartlett J. *Clin Infect Dis* 2011;53:S4.

2. [http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC\\_DisForm.aspx?ID=444](http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DisForm.aspx?ID=444).

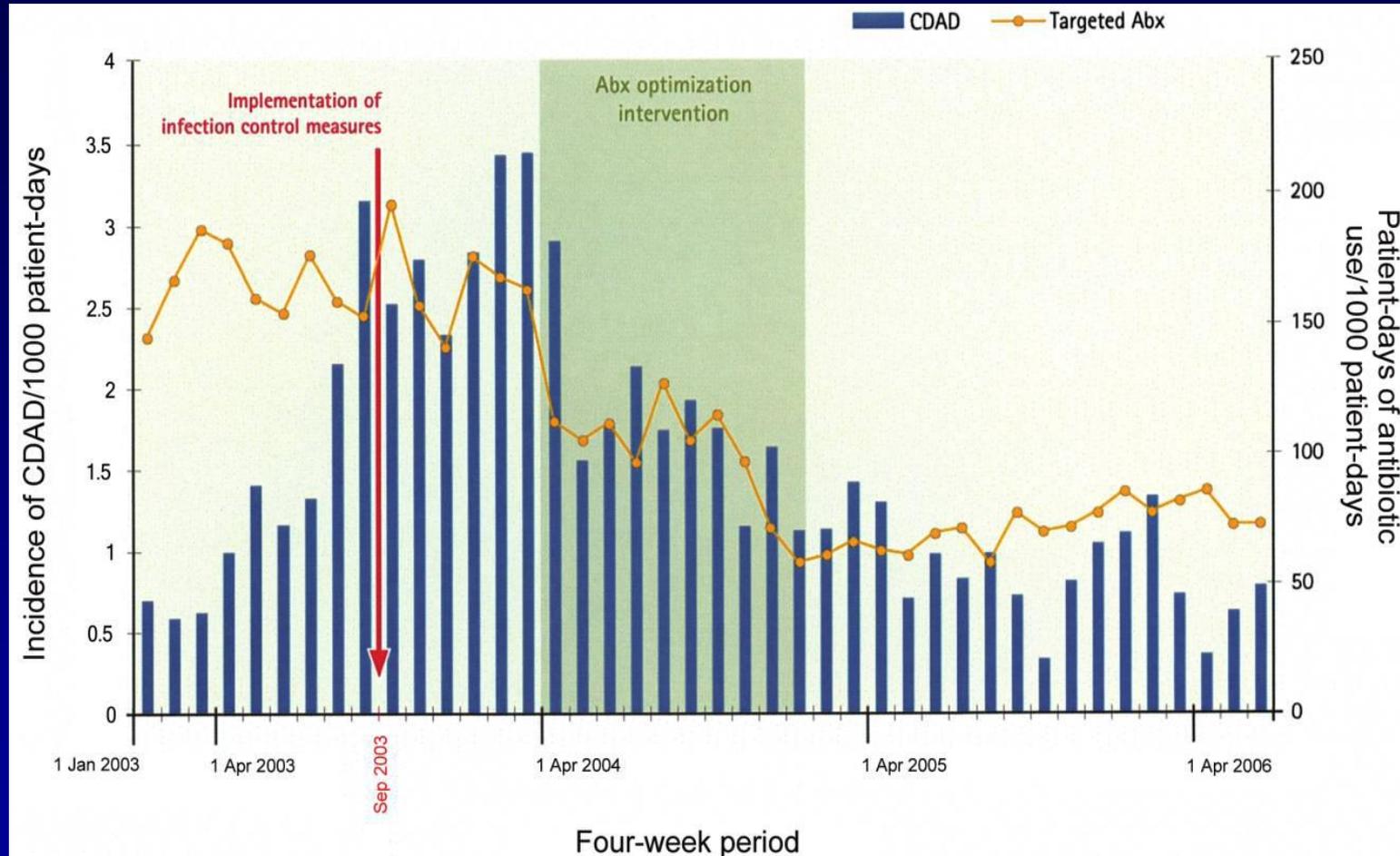
# Evolving Resistance, The “ESKAPE” Organisms

- *Enterococcus faecium*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- *Acinetobacter baumannii*
- *Pseudomonas aeruginosa*
- *Enterobacter* species

# Controlling Resistance?

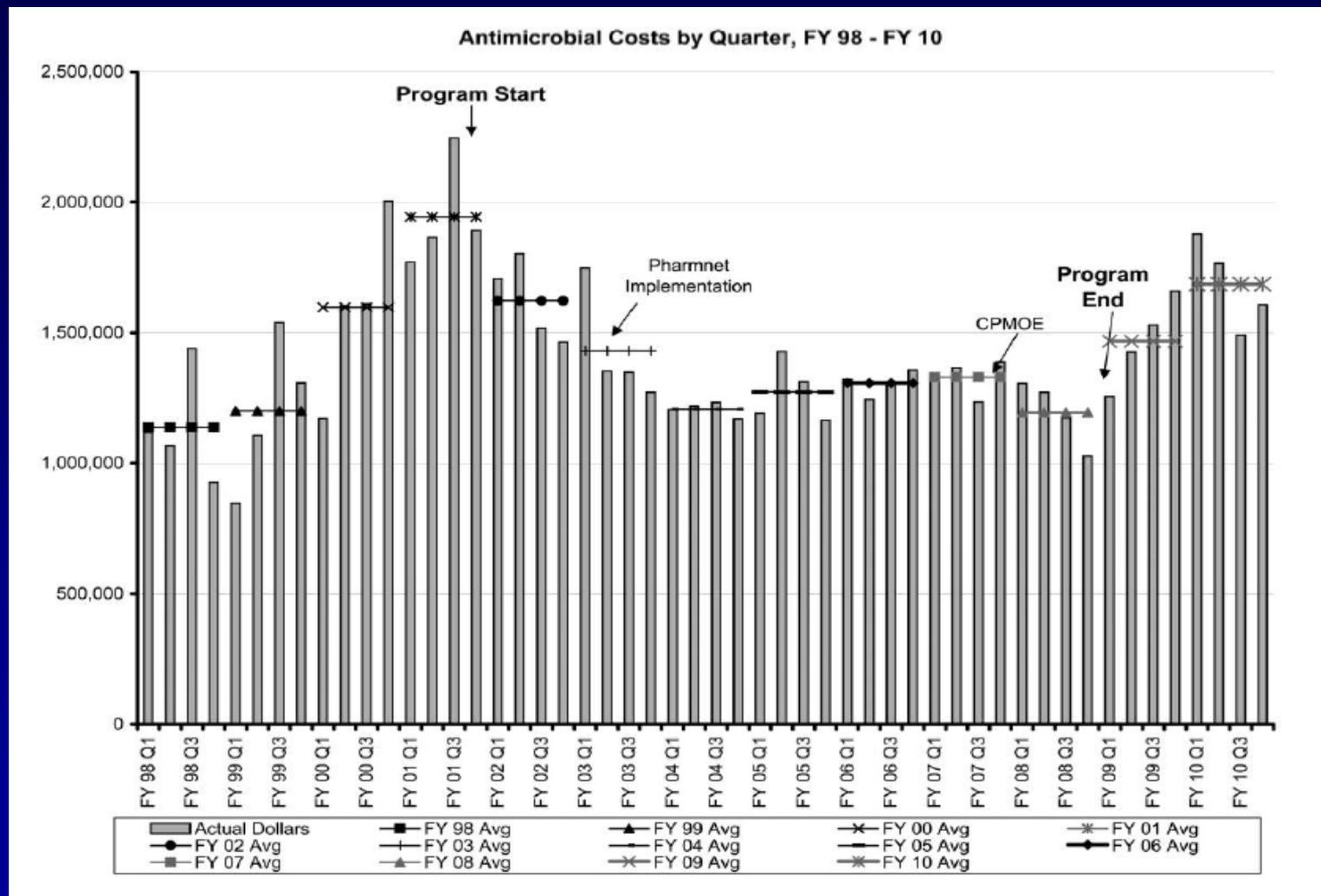
- A combination of BOTH
  - Effective antimicrobial stewardship program
- AND
- Comprehensive infection control program
- Have been shown to limit the emergence and transmission of antibiotic resistant bacteria

# Antimicrobial Stewardship Works

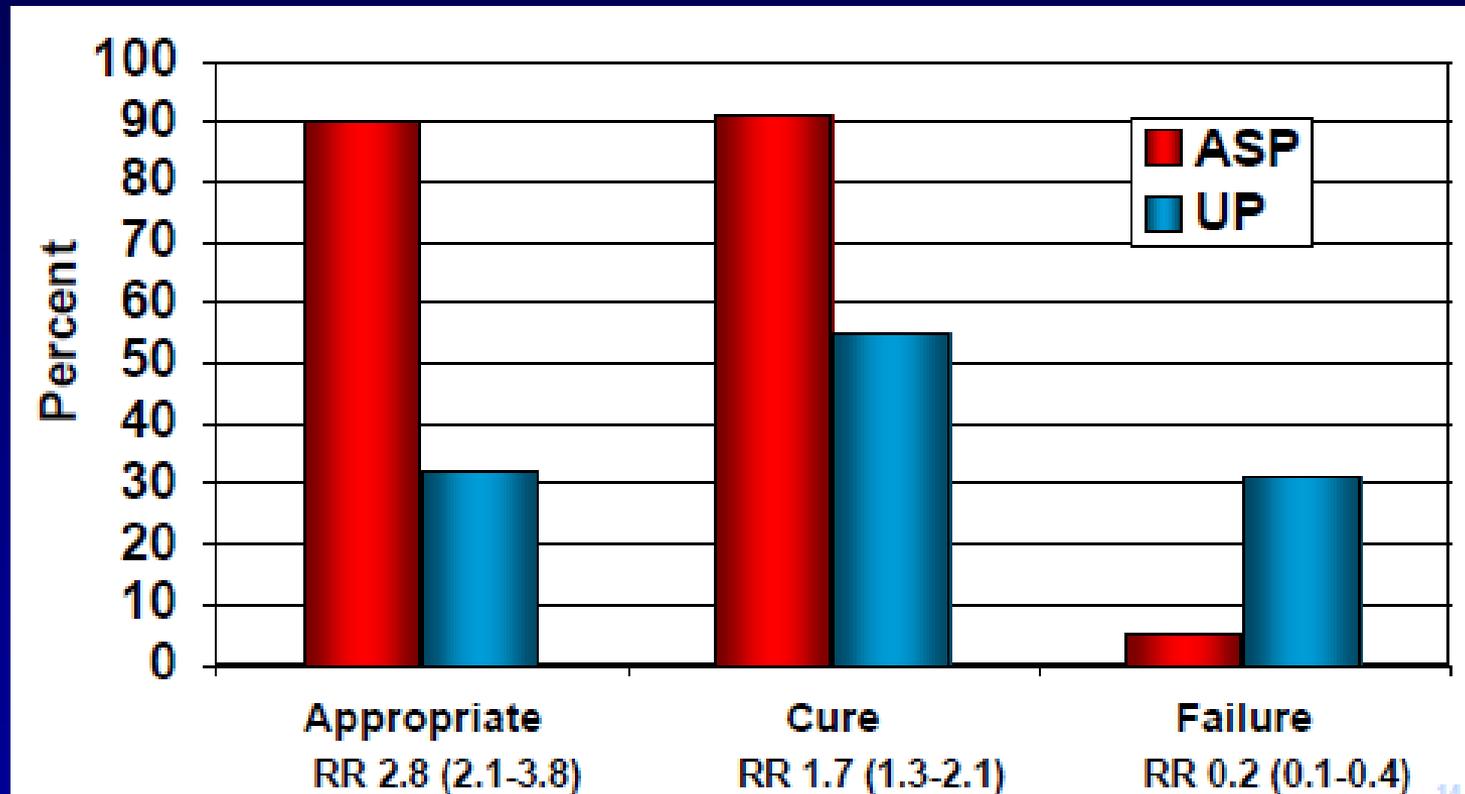


Impact of a Reduction in the Use of High-Risk Antibiotics on the Course of an Epidemic of *Clostridium difficile*-Associated Disease Caused by the Hypervirulent NAP1/027 Strain

# Antimicrobial Stewardship Reduces Costs



# Clinical outcomes better with antimicrobial stewardship program



# Antimicrobial Stewardship Program Goals

- Ensure appropriate antimicrobial use
  - Optimal selection, dose, duration
- Reduce or attenuate advancing antimicrobial resistance
- Improve patient outcomes and reduce adverse events related to antimicrobials
  - Decrease *Clostridium difficile* infection
  - Decrease morbidity and mortality
  - Decrease length of stay
- Decrease healthcare expenditures and antimicrobial costs

# Antimicrobial Stewardship Interventions

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization
- Educations
- Streamlining and de-escalating
- Dose optimization
- Guidelines and clinical pathways
- Parenteral to oral conversion

# Role of the Infection Preventionist

- Daily activities of IPs/HEs vital for ASP
- Implementation of evidenced-based practice and prevention care bundles (hand hygiene, isolation precautions, environmental cleaning, etc)
- No transmission of infection = Avoidance of abx

# Role of the Infection Preventionist

- Identification and surveillance of MDROs
- Monitoring and reporting of trends of MDROs
- Promote high compliance with hand hygiene
- Track and analyze trends in antimicrobial resistance
- Educate multidisciplinary rounding teams about NHSN surveillance definitions of HAIs
- Partners for accountability – share findings with and progress to stakeholders and providers

# SJMH Antimicrobial Stewardship Program

- Focus on restricted abx
  - New starts, duration
- Interventions
  - Approve
  - Stop abx
  - Change/Narrow abx
  - Obtain ID Consult
  - Against ASP advice

# SJMH Antimicrobial Stewardship Program

## ANTIBIOTIC STEWARDSHIP - Intervention

**Instructions:** Click on the **MAROON** headers to sort the table. Currently you can click on Encounter, Start Date, and Patient Name.

\* - Dates must be in the MM/DD/YYYY format

\* - Times must be in military time format (HH:MM) with values between 00:00 and 23:59

Intervention

Follow Up

Completed

Logout

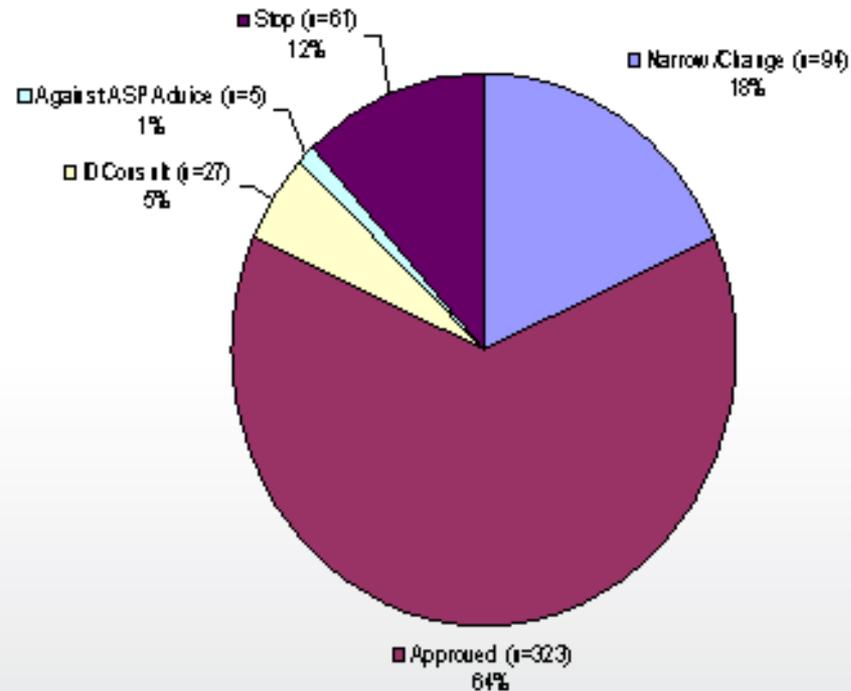
Data Status

Legend: **Approved >= 7 Days** Acknowledgement Needed: + Self Follow Up Reminder: + Add/View Comments: +

|   | Patient Name/<br>Encounter | Unit/<br>Room     | Generic<br>Drug          | Start<br>Date | Attending/<br>Ordering | Intervention<br>Date * | Intervention<br>Time * | Intervention   |        |
|---|----------------------------|-------------------|--------------------------|---------------|------------------------|------------------------|------------------------|--|--------|
| + | [REDACTED]                 | 11 AB/<br>1116-01 | LINEZOLID TAB 600MG      | 6/24/2009     | [REDACTED]             | 6/25/2009              |                        | <input type="radio"/> Approved <input type="radio"/> Get ID Consult <input type="radio"/> Change Dose<br><input type="radio"/> Stop Antibiotics <input type="radio"/> (Narrow)-Change Antibiotics<br>Other: <input type="text"/> | Submit |
| + | [REDACTED]                 | 9BF/<br>0931-01   | AZTREONAM 1<br>GRAM/50ML | 6/23/2009     | [REDACTED]             | 6/25/2009              |                        | <input type="radio"/> Approved <input type="radio"/> Get ID Consult <input type="radio"/> Change Dose<br><input type="radio"/> Stop Antibiotics <input type="radio"/> (Narrow)-Change Antibiotics<br>Other: <input type="text"/> | Submit |

# Outcomes from SJMH ASP

Interventions (n = 510)



## Demographic and clinical characteristics and outcomes of patients pre-ASP compared to patients post-ASP

|  | Period 1<br>N=372 | Period 2<br>N=344 | p     |
|--|-------------------|-------------------|-------|
| Age (yr)   | 64.8<br>(±15.7)   | 62.5<br>(±18.4)   | 0.08  |
| <u>Charlson Comorbidity</u> Count, median (IQR)‡ | 1 (0-2)           | 1 (1-2)           | 0.08  |
| Length of stay, median (IQR)‡ days               | 8.0 (4-8)         | 7.0 (4-7)         | 0.44  |
|  | No. (%)           | No. (%)           |       |
| Males  | 168 (45.2)        | 171 (49.7)        | 0.22  |
| Race (white)                                     | 313 (84.1)        | 299 (86.9)        | 0.29  |
| ICU stay*  | 115 (30.9)        | 94 (27.3)         | 0.29  |
| Ventilator use*                                  | 103 (27.7)        | 46 (13.4)         | <0.01 |
| Receipt of > 1 target antimicrobial              | 47 (12.6)         | 51 (14.8)         | 0.39  |
| Death within 30 days                             | 77 (20.7)         | 55 (16.0)         | 0.11  |
| Readmitted within 30 days                        | 76 (20.4)         | 69 (20.1)         | 0.87  |
| <u>C. difficile</u> infection                    | 46 (12.4)         | 20 (5.8)          | <0.01 |

‡IQR is defined as the mathematical difference between the 75<sup>th</sup> and the 25<sup>th</sup> percentile.

\*Within 2 days of admission.

# Multivariable analysis for association of ASP and patient outcomes

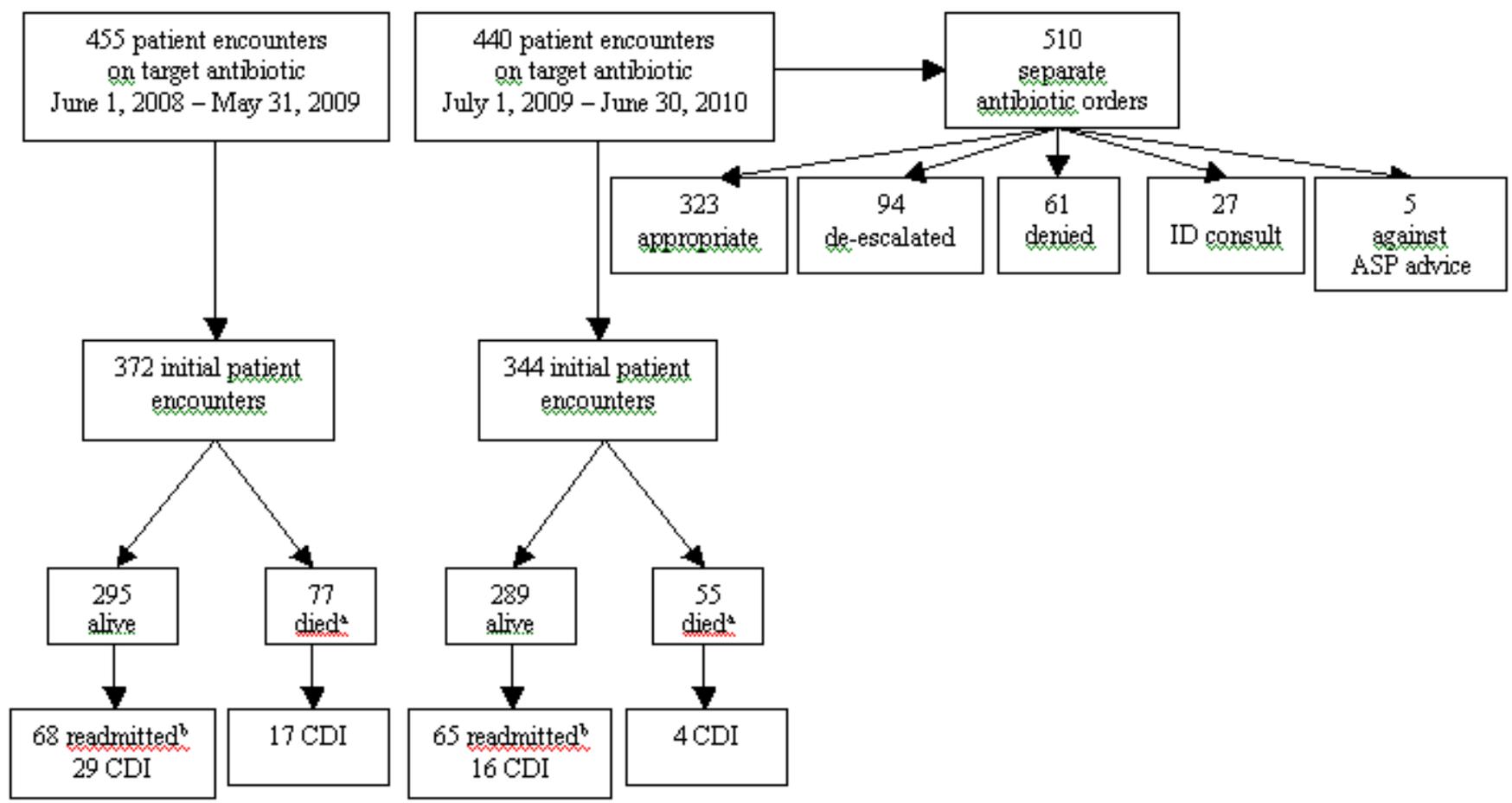
| Model Covariates  | Death within 30 days | p    | Readmission within 30 days | p    | <i>C. difficile</i> Infection | p     |
|---|----------------------|------|----------------------------|------|-------------------------------|-------|
| Age, Race, Sex, ICU Stay†, Vent Use†, 2 <sup>nd</sup> abx*, CCC** | 0.77 (0.50-1.18)     | 0.23 | 0.95 (0.63-1.42)           | 0.80 | 0.46 (0.25-0.82)              | <0.01 |

† Within 2 days of admission.

\*At least 2 target antimicrobials prescribed

\*\*Charlson Comorbidity Count

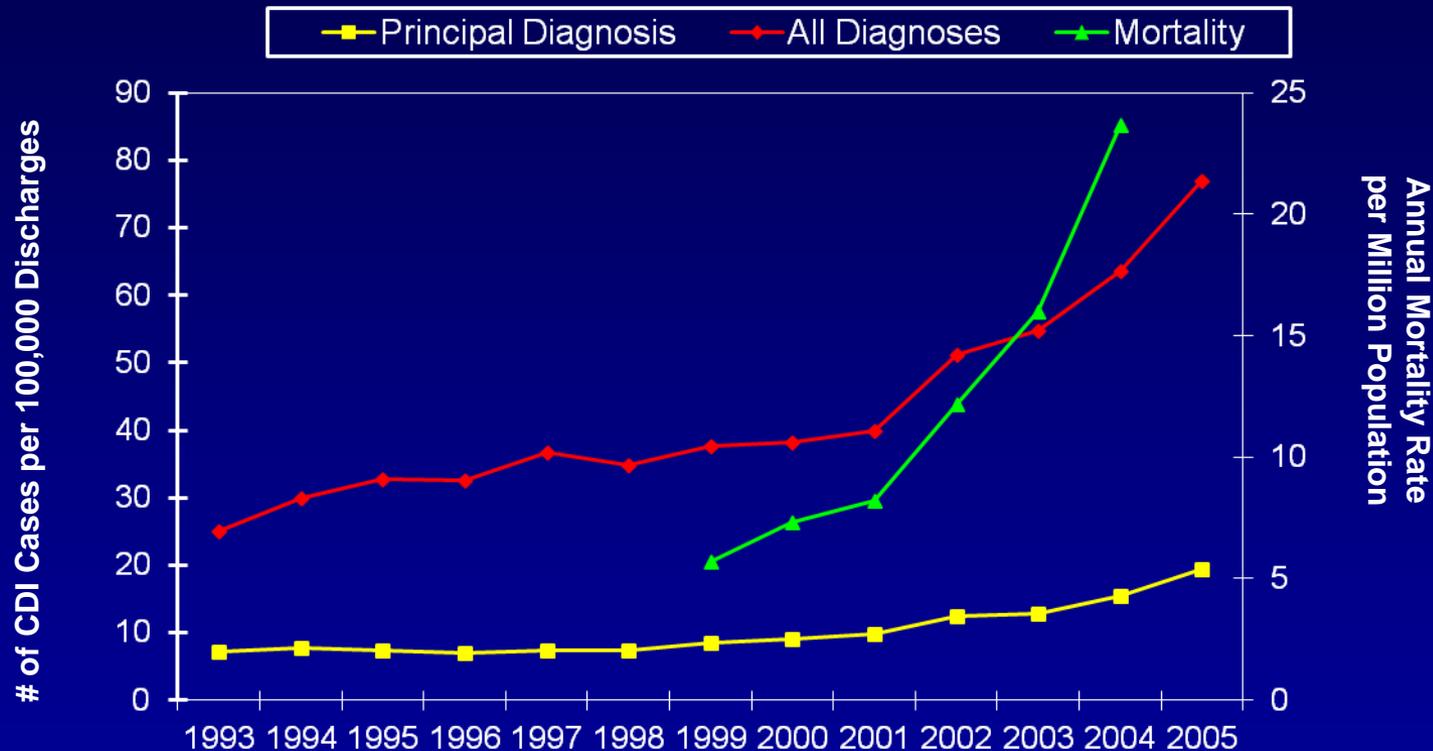
# Flow Diagram of Outcomes from ASP



# Antimicrobial Costs by Fiscal Year

|  | Fiscal year<br>2009 | Fiscal year<br>2010 | Percent<br>change     |
|--|---------------------|---------------------|-----------------------|
| Antimicrobial agents total costs                 | \$1,503,748         | 1,274,837           | -15.2<br>(-\$228,911) |
| Total patient days                               | 147,955             | 144,783             |                       |
| Antimicrobial costs per patient day<br>(average) | \$10.16             | \$8.81              | -13.3                 |
| Targeted antimicrobial agents                    | \$462,404           | \$297,851           | -35.6<br>(-\$164,553) |

# Incidence and mortality of CDI are increasing in US



1. Elixhauser A, et al. Healthcare Cost and Utilization Project: Statistical Brief #50. April 2008. Available at: <http://www.hcup-us.ahrq.gov/reports/statbriefs/sb50.pdf>.

2. Redelings MD, et al. Emerg Infect Dis. 2007;13:1417-1419.

# CMS Inpatient Prospective Payment System

| HAI                              | Target Population                           | Start Date |
|----------------------------------|---|------------|
| CLABSI                           | ICUs  | Jan 2011   |
| SSI                              | Colon and abdominal hysterectomy procedures | Jan 2012   |
| CAUTI                            | ICUs  | Jan 2012   |
| MRSA Bacteremia Lab ID Event     | Facility-wide                               | Jan 2013   |
| <i>C. difficile</i> Lab ID Event | Facility-wide                               | Jan 2013   |
| HCP Influenza Vaccination        | Acute care hospitals                        | Jan 2013   |

# National Efforts on Antimicrobial Stewardship

- SHEA Task Force
- CDC Get Smart Campaign  
[www.cdc.gov/getsmart/](http://www.cdc.gov/getsmart/)
- JTC National Patient Safety Goals  
(NPSG) 07.03.01
- California Senate Bill 739

# LTACs: The Perfect Storm

- Admit complex pts with acute care needs (ventilation weaning, wound care, IV abx)
- Mean duration of 25 days
- Pts with multiple co-morbidities, at risk for colonization with MDROs
- High rates of HAIs
- Implicated in various regional outbreaks of MDROs

# Stewardship in the LTAC

- 60 bed unit in Dallas, Tx
- Weekly chart reviews: ID doc and director of pharmacy
  - Left nonbinding recs in chart
- 15 month intervention period
  - 21% decrease in mean monthly abx use (DDDs/1000 pt days)
  - 28% reduction in mean monthly abx cost/pt day (\$29 to \$20.8)

# Stewardship in the LTAC

- Limitations: no data on outcomes
- Effective stewardship possible with limited resources

# Stewardship at Transitions of Care

- All pts to get parenteral abx seen by ID prior to d/c at Cleveland Clinic
- 244 CoPat consultations
  - 175 (72%) approved
  - 66 (28%) avoided
  - 11% consults avoided abx
- Targeting pts at transitions of care (hospital to community) is an AS strategy

# Future Steps

- Develop systems for appropriate abx use
  1. All orders should have dose, duration, indication
  2. When placing orders, need micro cultures
  3. Abx timeouts in 24 – 48 hrs
- Lead quality initiatives related to abx use (i.e. SCIP)
- Increase collaboration between IP and AS
- Develop ASPs in LTCFs and LTACs

# Surgical Care Improvement Project (SCIP) Infection-Prevention Measures

## Individual SCIP measures

- **INF-1:** patients who received prophylactic antibiotics within 1 h prior to surgical incision (2 h if receiving vancomycin)
- **INF-2:** patients who received prophylactic antibiotics recommended for their specific surgical procedure
- **INF-3:** patients whose prophylactic antibiotics were discontinued within 24 h after surgery end time (48 h for coronary artery bypass graft surgery or other cardiac surgery)
- **INF-4:** cardiac surgery patients with controlled 6 AM postoperative blood glucose level ( $\leq 200$  mg/dL [ $\leq 11.1$  mmol/L])
- **INF-6:** surgery patients with appropriate surgical-site hair removal with clippers or depilatory or those not requiring surgical-site hair removal
- **INF-7:** colorectal surgery patients with immediate postoperative normothermia (first recorded temperature was  $\geq 96.8^\circ\text{F}$  within first 15 minutes after leaving the operating room)

## Composite Measures

- **S-INF-Core:** patient data on all 3 original SCIP measures: INF-1, INF-2, and INF-3
- **S-INF:** all patients with  $\geq 2$  recorded SCIP infection-prevention measures in a single visit (any combination of INF-1, INF-2, INF-3, INF-4, INF-6, and INF-7)

1. Stulberg JJ, et al. JAMA 2010;303:2479-2485.
2. File T, et al. Clin Infect Dis. 2011;53:S15-22.

# Summary

- Primary mission of ASPs is patient safety
- ASPs help assure the appropriate use of antimicrobial therapy
- ASPs can improve pt outcomes, reduce tx costs, & reduce or slow the development of resistant organisms
- A multidisciplinary team approach is essential

# Case # 1

- 83 year old male s/p AAA repair
- Extubated in PACU and tx to the 2000 unit
- 4 days later, develops respiratory distress, SICU tx, and reintubation.
- Further evaluation:
  - New infiltrate on CXR
  - WBC 26.5
  - Tmax 101.9

## Case # 1

- Started on Cefepime and Vancomycin.
  - Has PCN allergy (rash).
- After 1 wk, WBC decreased to 13.7
- Final culture & sensitivities from sputum show:
- Direct Smear: Moderate neutrophils, GNB  
Culture (Final): *Enterobacter aerogenes*

# *Enterobacter aerogenes*

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|                   | <b>MIC</b>  | <b>INT</b> |
|-------------------|-------------|------------|
| ■ Ampicillin/Sulb | 8           | R          |
| ■ Ampicillin      | 16          | R          |
| ■ Aztreonam       | $\leq 1$    | S          |
| ■ Cefazolin       | $\geq 64$   | R          |
| ■ Cefepime        | $\leq 1$    | S          |
| ■ Ceftriaxone     | $\leq 1$    | S          |
| ■ Ciprofloxacin   | $\leq 0.25$ | S          |
| ■ Gentamicin      | $\leq 1$    | S          |
| ■ Meropenem       | $\leq 0.25$ | S          |
| ■ Piper/Tazobac   | $\leq 4$    | S          |
| ■ Tobramycin      | $\leq 1$    | S          |
| ■ Trimeth-Sulfa   | $\leq 20$   | S          |

# Case # 1

- Pt received 72 hours of Cefepime/Vancomycin
  - Readdress abx regimen given cx results
- 
- A. Continue Cefepime and Vancomycin
  - B. Continue Cefepime. D/C Vancomycin.
  - C. De-escalate Cefepime to a different abx. D/C Vancomycin.

# Case # 1

## Take Home Points

- Antibiotic Timeout (reasons for abx use)
- Streamlining and de-escalating
- Duration for abx course
- Clear plans when transitions of care (tx to/from ICUs/discharge summaries/ECFs)

## Case # 2



## Case # 2

- 88 y/o male, hx of dementia, presented with confusion/weakness
- Recent stay at an ECF, presented with foley
- WBC 13.4
- Started on Ceftriaxone → Cefepime/Vancomycin
- Blood cx:  $\frac{3}{4}$  CNS
- Urine cx: alpha hemolytic streptococcus
- U/A 57 WBC, + LE

## Case # 2

- No fevers, exam significant for L knee effusion/pain
- ID c/s stopped all abx
- Underwent arthrocentesis → Pseudogout
- A few days later, started on IV flagyl for CDI
- Changed over to PO flagyl
- D/C back to ECF

## Case # 2

- While at ECF, receives ertapenem for ESBL E. Coli bacteriuria, and then nitrofurantoin for VRE bacteriuria
- Presents 1 month from previous admission with abdominal pain, diarrhea, lethargy, WBC 15.9
- Started on IV ceftriaxone/flagyl
- Seen by ID

## Case # 2

- A. Add po Vancomycin
- B. D/C Ceftriaxone, add po Vancomycin.
- C. Change abx to Zosyn
- D. No treatment

## Case # 2

- Severe CDI
- Pt eventually goes on hospice despite maximal medical tx for a wk

## Case # 2

# Take Home Points

- Aware of adverse effects of abx including CDI, MDRO, etc
- Improved abx use improves pt outcomes
- AS through continuum of care is critical

