Antibiotic Stewardship: The National Perspective

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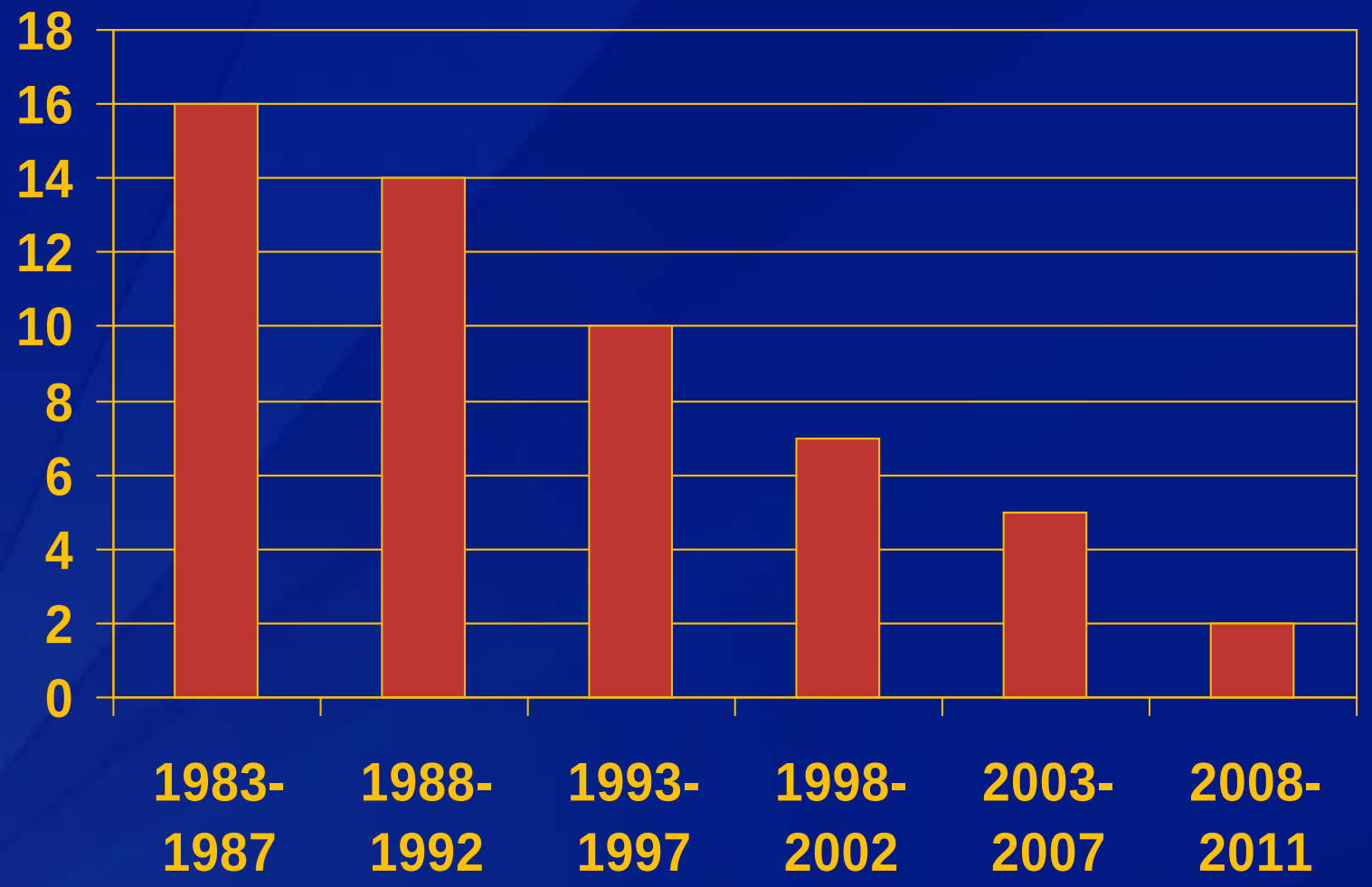
Why We Need Efforts to Improve Antibiotic Use

- We're not getting new ones anytime soon
- Treating infections is more complicated than ever
- Antibiotics are misused
- Antibiotics have adverse effects
- Improving antibiotic use has many benefits

New Antibacterial Agents Approved 1983-2011



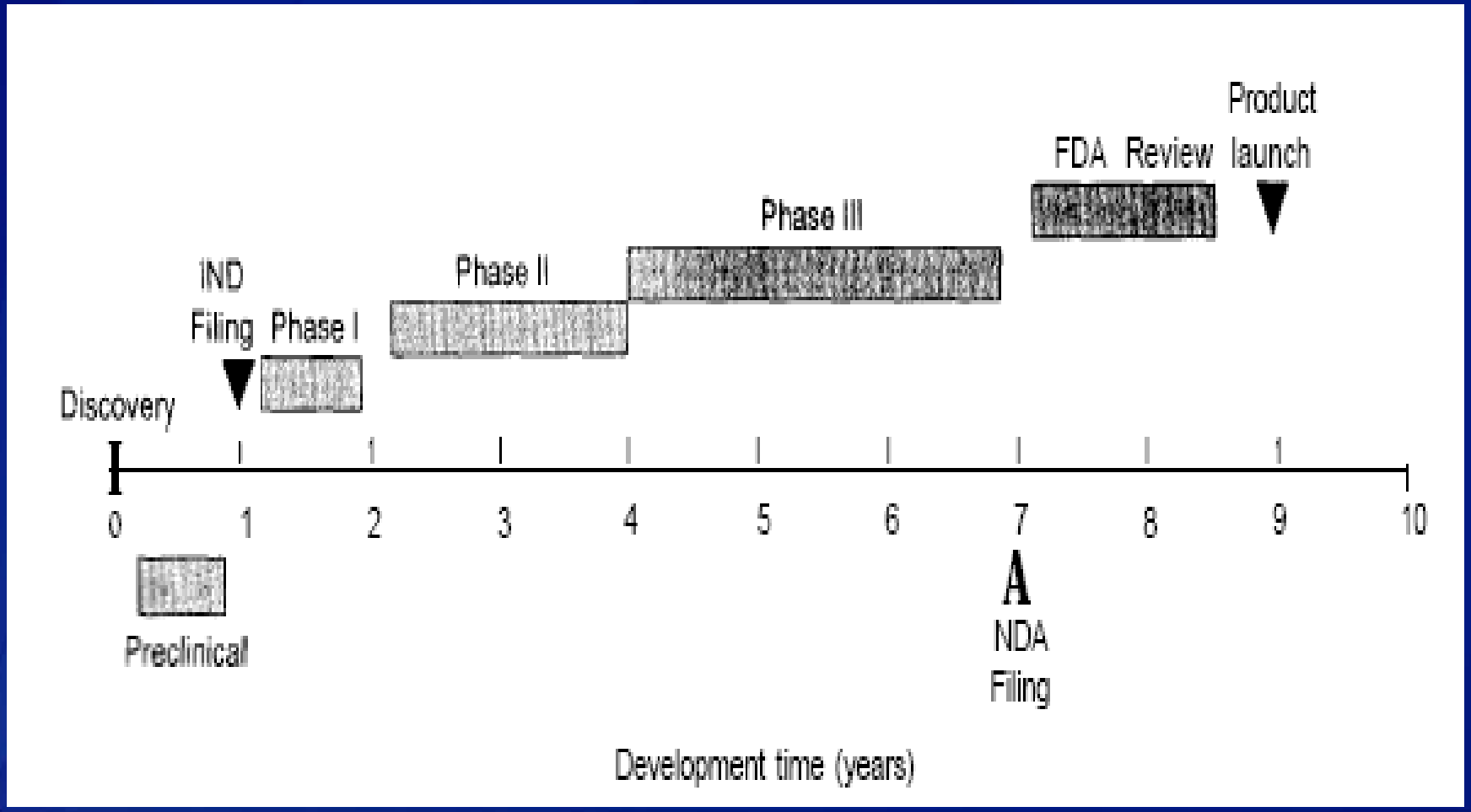
Adapted from Spellberg B et al. *Clin Infect Dis*. 2004;38:1279-86.

The Pipeline is Dry

- Only 15-16 antibiotics are in development
- Only 8 of these have activity against key Gram negative bacteria
- None have activity against bacteria resistant to all current drugs

Boucher HW et al. Clin Infect Dis 2009;48:1–12
European Centre for Disease Prevention and Control/European Medicines Agency Joint Technical Report
http://www.emea.europa.eu/pdfs/human/antimicrobial_resistance/EMEA-576176-2009.pdf

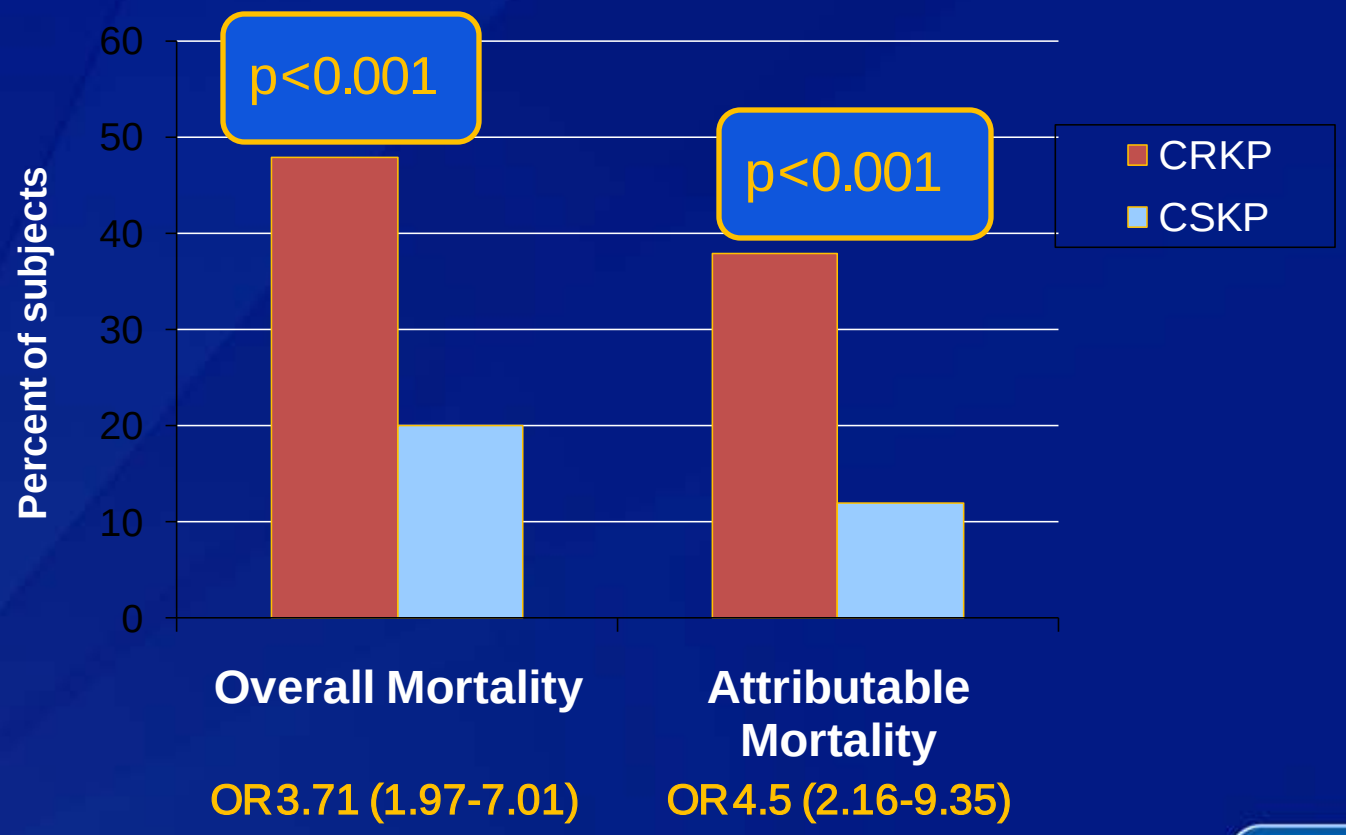
Timeline for Development of a New Antibiotic



Susceptibility Profile: KPC-Producing *K.pneumoniae*

Antimicrobial	Interpretation	Antimicrobial	Interpretation
Amikacin	I	Chloramphenicol	R
Amox/clav	R	Ciprofloxacin	R
Ampicillin	R	Ertapenem	R
Aztreonam	R	Gentamicin	R
Cefazolin	R	Imipenem	R
Cefpodoxime	R	Meropenem	R
Cefotaxime	R	Pipercillin/Tazo	R
Cetotetan	R	Tobramycin	R
Cefoxitin	R	Trimeth/Sulfa	R
Ceftazidime	R	Polymyxin B	MIC >4mg/ml
Ceftriaxone	R	Colistin	MIC >4mg/ml
Cefepime	R	Tigecycline	S

Mortality associated with carbapenem resistant (CR) vs susceptible (CS) Klebsiella pneumoniae (KP)



Patel G et al. Infect Control Hosp Epidemiol 2008;29:1099-1106

Antibiotics are misused in hospitals

- "It has been recognized for several decades that up to 50% of antimicrobial use is inappropriate"
- IDSA/SHEA Guidelines for Antimicrobial Stewardship Programs
- http://www.journals.uchicago.edu/doi/pdf/10.1086/510393

Antibiotic are misused in a variety of ways

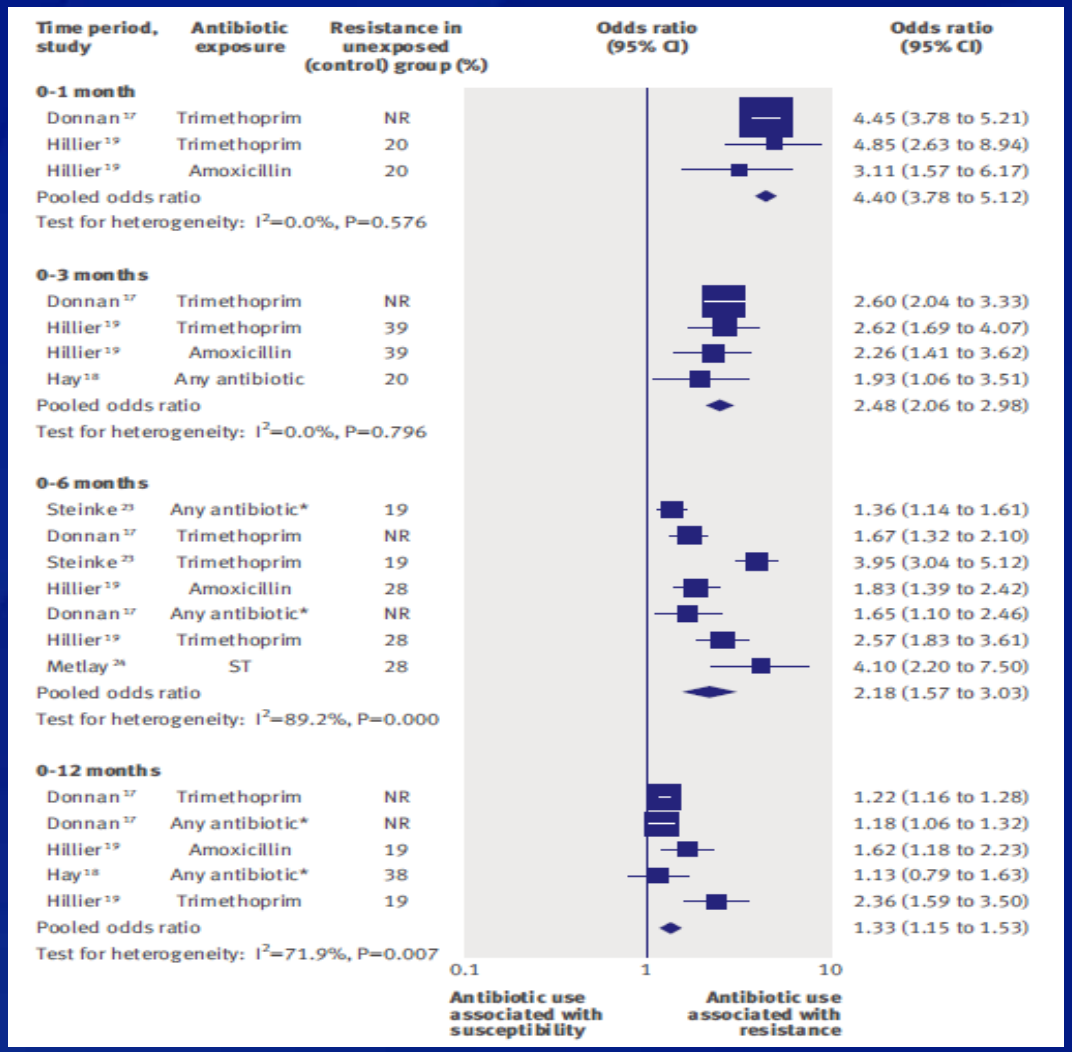
- Given when they are not needed
- Continued when they are no longer necessary
- Given at the wrong dose
- Broad spectrum agents are used to treat very susceptible bacteria
- The wrong antibiotic is given to treat an infection

Antibiotics Have Side Effects

- In 2008, there were 142,000 visits to emergency departments for adverse events attributed to antibiotics.[1]
- National numbers not available for in-patients, but adverse events can be even more serious: hearing loss, renal failure, bone marrow suppression.

1. Shehab N et al. Clinical Infectious Diseases 2008; 15:735-43

Effect of antibiotic prescribing on antimicrobial resistance in individual patients



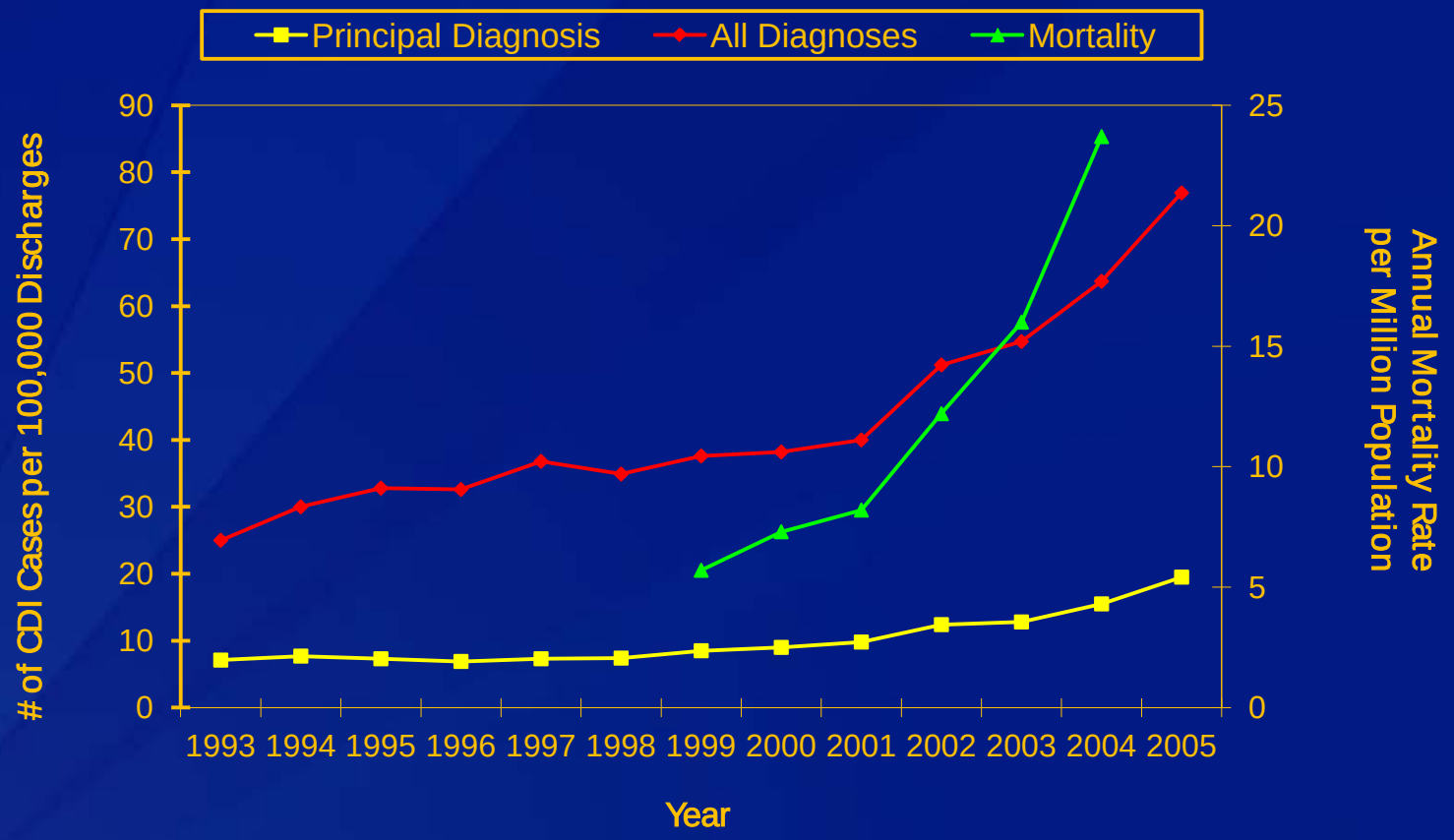
Costelloe C et al. *BMJ.* 2010;340:c2096.

Antibiotics Have Side Effects *C. difficile*

- **Antibiotic exposure is the single most important risk factor for the development of *Clostridium difficile* associated disease (CDAD).**
  - Up to 85% of patients with CDAD have antibiotic exposure in the 28 days before infection[1]

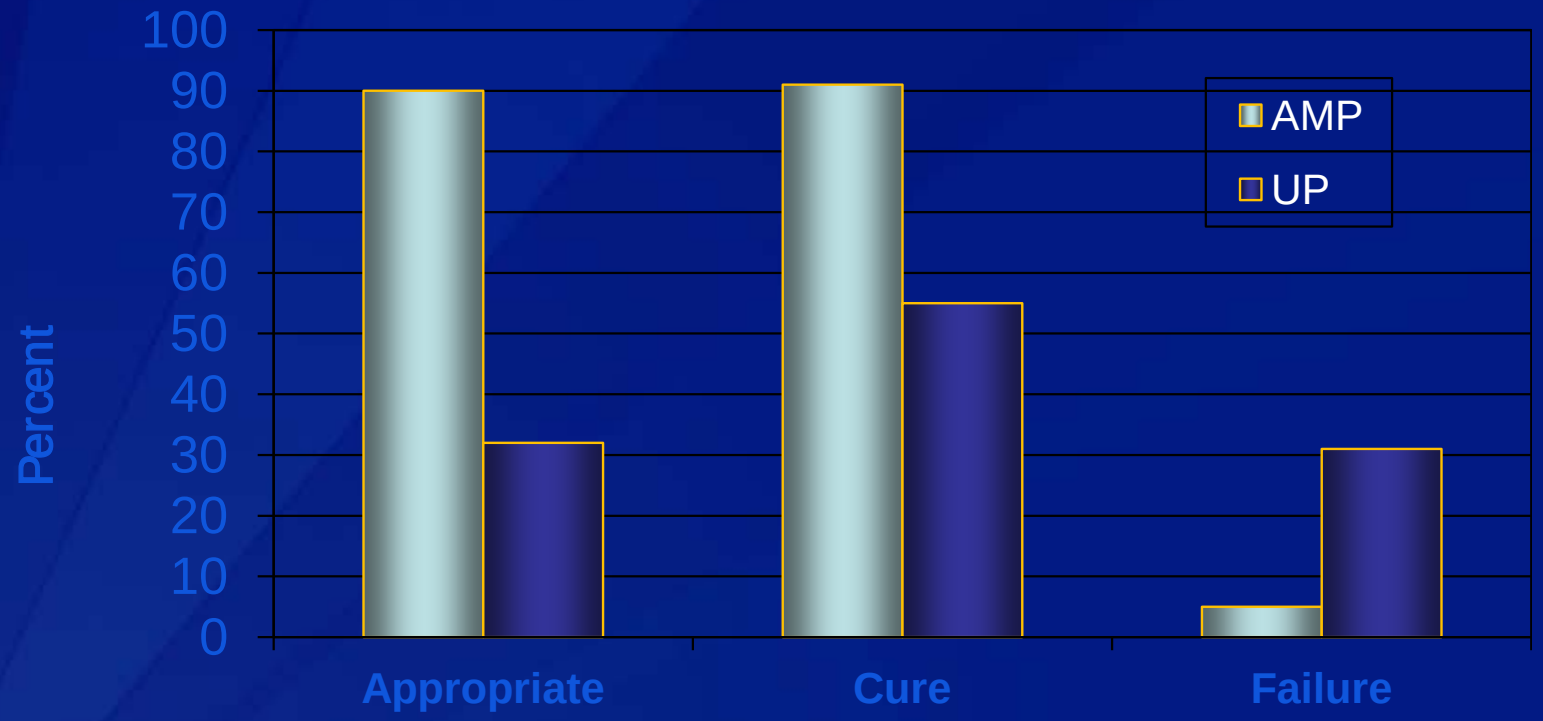
1. Chang HT et al. *Infect Control Hosp Epidemiol 2007;* 28:926–931.

C difficile Incidence and Mortality Are Increasing



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. Accessed March 10, 2010.
Redelings MD, et al. Emerg Infect Dis. 2007;13:1417-1419.

Clinical outcomes better with antimicrobial management program



RR 2.8 (2.1-3.8) RR 1.7 (1.3-2.1) RR 0.2 (0.1-0.4)

AMP = Antibiotic Management Program
UP = Usual Practice

Fishman N. *Am J Med.* 2006;119:S53.

Stewardship Optimizes Patient Safety: Improved Surgical Prophylaxis

- Intervention to standardize surgical prophylaxis
  - Simplify drug options
  - Standardize dosing
  - Improve timing
- Results
  - All doses correct
  - Reduction in dosing after incision (20% to 7%)
  - Annual cost savings $112,000

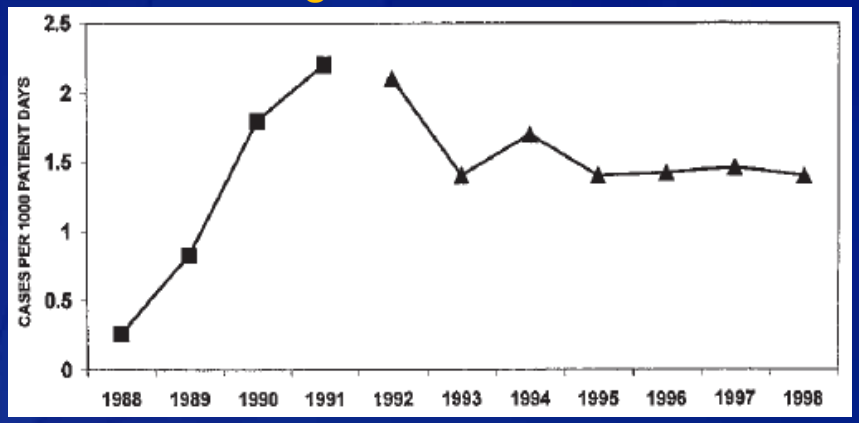
Table I Use of antimicrobial agents for perioperative antibiotic prophylaxis before and after implementation of the new guideline

Antimicrobial agent	Before new guideline	After new guideline
	N (%)	*N* (%)
Co-amoxiclav	70 (45.8)	–
Cefamandole	34 (22.2)	–
Cefazolin	24 (15.7)	135 (91.8)
Flucloxacillin	16 (10.5)	–
Cefuroxime	4 (2.6)	1 (0.7)
Cefuroxime + metronidazole	3 (2.0)	–
Cefazolin + metronidazole		11 (7.5)
Amoxicillin	1 (0.7)	–
Clindamycin	1 (0.7)	–
Total procedures	153 (100)	147 (100)

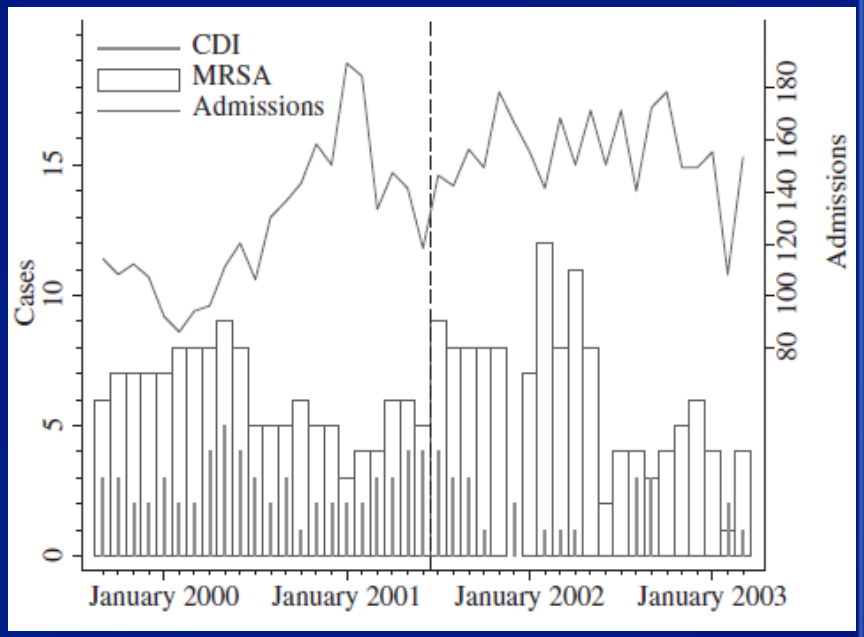
Willemsen I et al. J Hosp Infect. 2007;67:156-160.

Stewardship Optimizes Patient Safety: Decreased *C. difficile* Infection

- Carney hospital
  - Review of broad spectrum agents followed by form on patient's chart with recommendations
  - 7 day automatic stop orders for antibiotics
  - Exclusion of pharmaceutical detailing



- 3 acute care wards for elderly at a English tertiary center
  - Restriction of broad spectrum agents



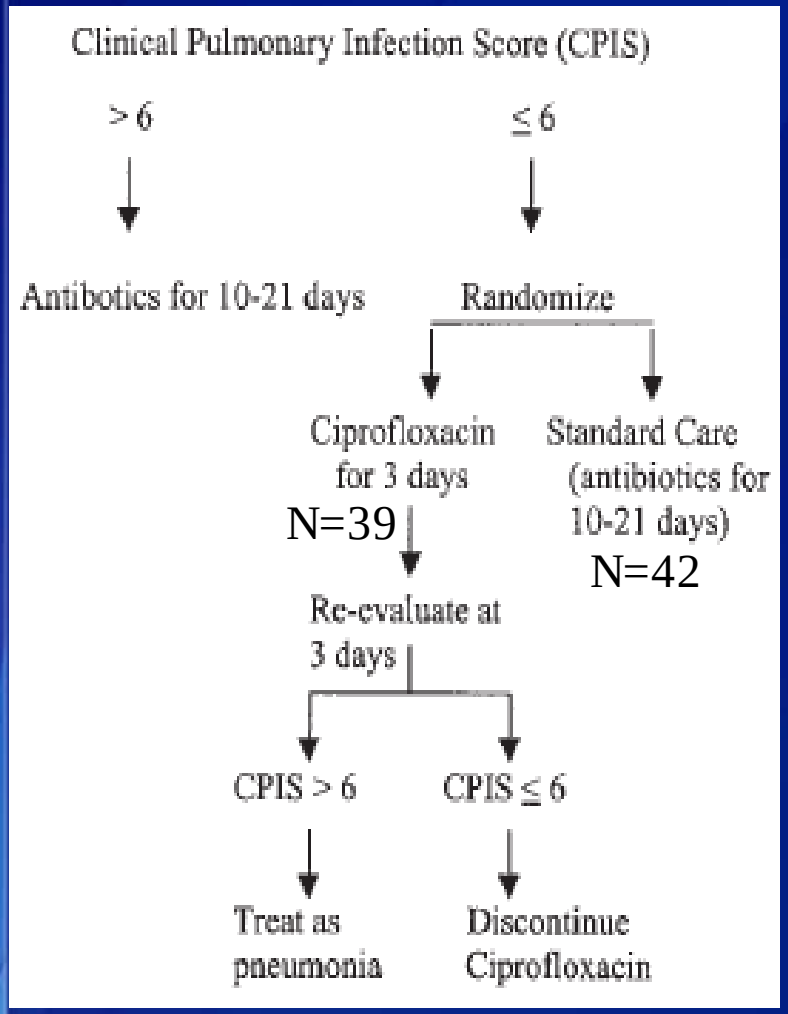
Carling P et al. Infect Control Hosp Epidemiol. 2003;24:699
Fowler S et al. J Antimicrob Chemother. 2007;59:990.

Stewardship Optimizes Patient Safety: Improved Renal Dosing

- Clinical decision support system to appropriately dose based on renal function implemented using academic detailing
- Results
  - Appropriate dosing of gentamicin increased from 63% to 87%
  - Appropriate dosing of vancomycin increased from 47% to 77%
  - Appropriate use of gentamicin therapeutic monitoring increased from 70% to 90%

Roberts GW et al. J Am Med Inform Assoc. 2010;17:308-12.

Stewardship Optimizes Patient Safety: Decreased Patient-Level Resistance



	Cipro	Standard
Antibiotic duration	3 days	10 days
LOS ICU	9 days	15 days
Antibiotic resistance/ superinfection	14%	38%

Study terminated early because attending physicians began to treat standard care group with 3 days of therapy

Singh N et al. *Am J Respir Crit Care Med.* 2000;162:505-11.

Stewardship Decreases Resistance

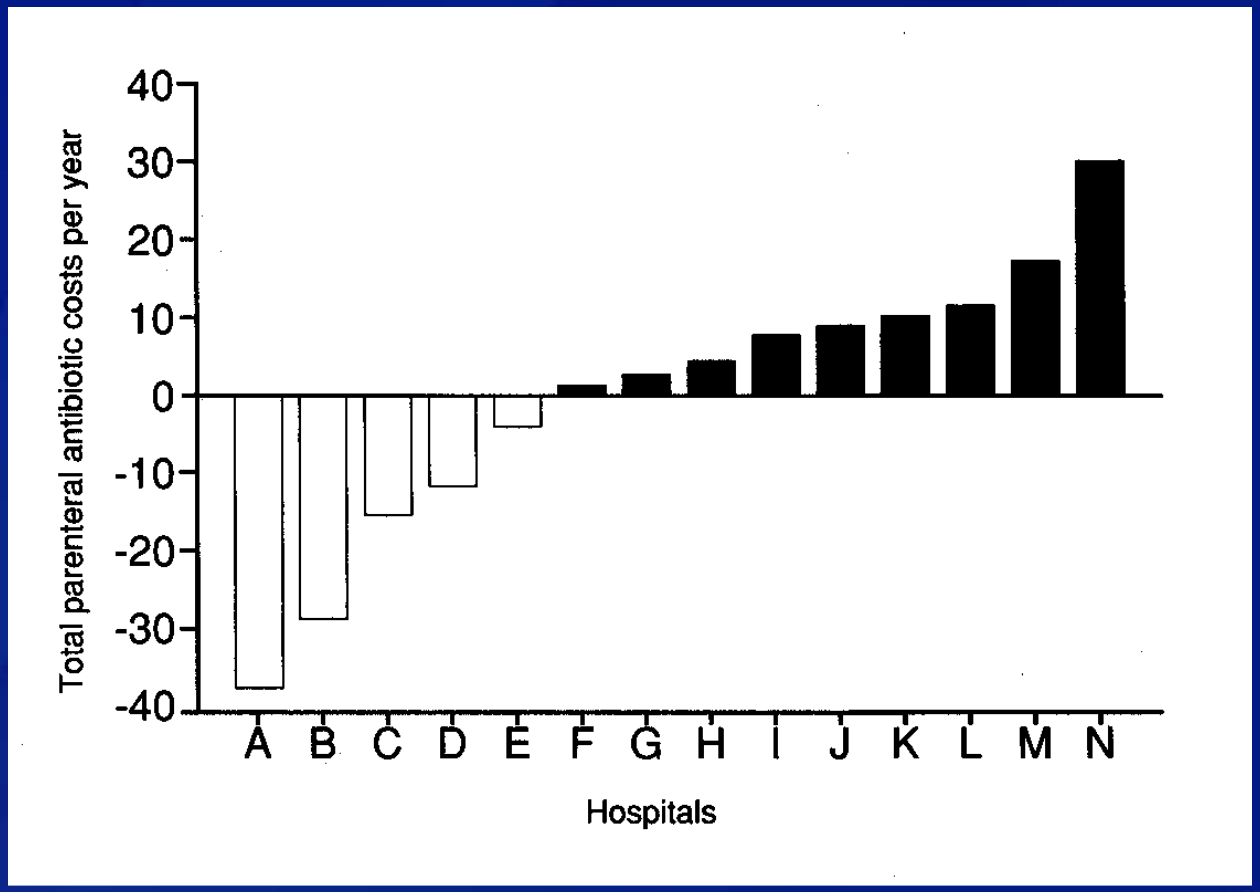
- Ben Taub General Hospital, 1994
- ID faculty held approval pager 24/7
  - All broad-spectrum antibiotic required approval (ticar/clav, imipenem, aztreonam, ceftazidime, ciprofloxacin, ofloxacin, amikacin, IV fluconazole)
- Increased susceptibility of Gram negatives

P. aeruginosa susceptibilities, 1/93-12/93 vs. 7/94-6/95

Ticar/clav	Imipenem	Aztreonam	Ceftazidime	Cipro
83 → 89	83 → 95	70 → 88	76 → 92	83 → 87

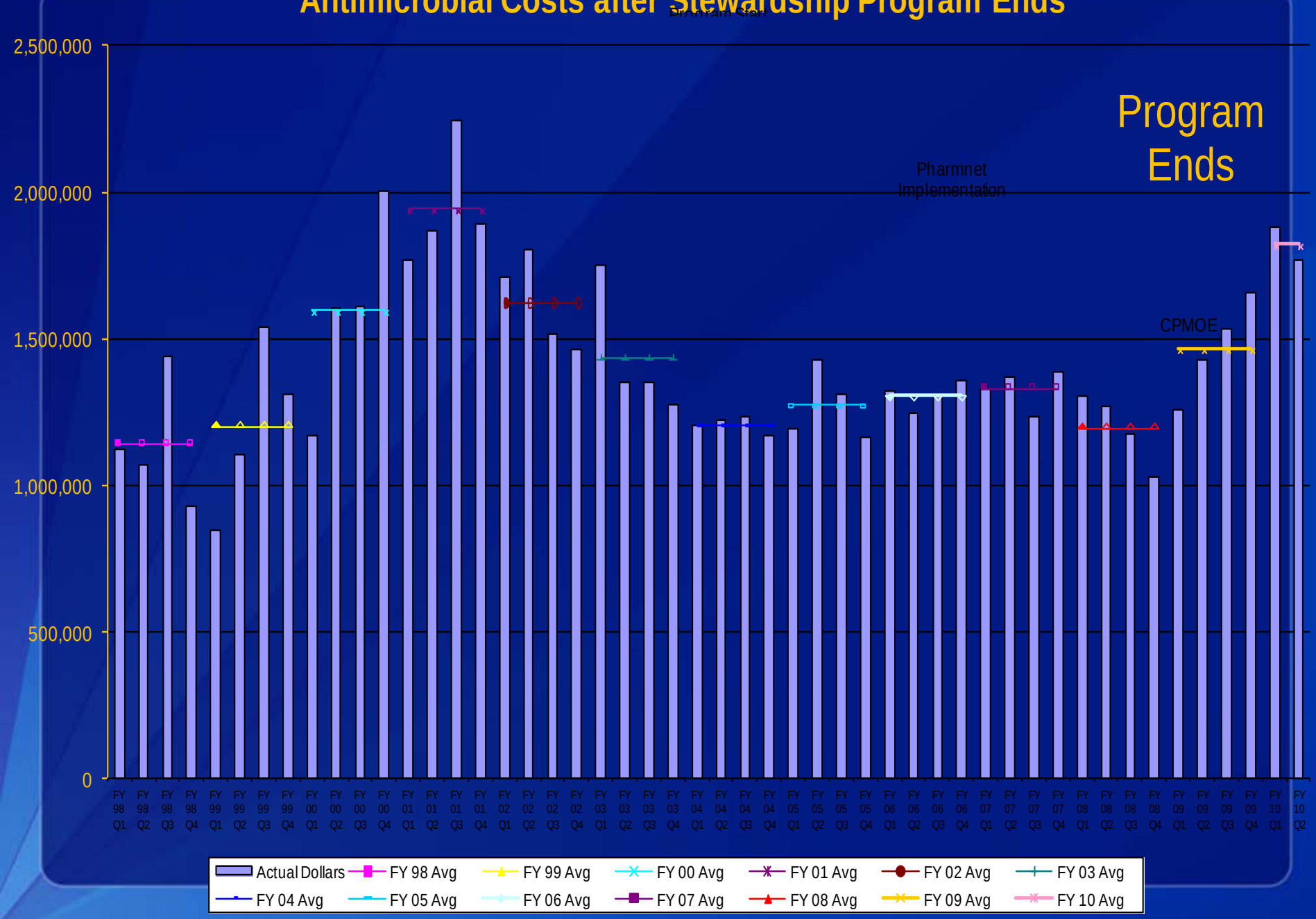
White et al. *Clin Infect Dis.* 1997;25:230

Total costs of parenteral antibiotics at 14 hospitals



Carling et. al. CID,1999;29;1189.

Antimicrobial Costs after Stewardship Program Ends



Antibacterial Agents with the Greatest Increase in Costs

	FY08	FY09	Increase	% Change
Pip/Tazo	877,809	1,339,270	461,460	53%
Linezolid	343,725	499,845	156,120	45%
Daptomycin	102,944	254,294	151,350	147%
Carbapenems	405,181	548,737	143,556	35%
Tigecycline	187,305	274,554	87,248	47%
Total	**1,916,964**	**2,642,146**	**999,736**	**52%**

Standiford HC et al. Abstract #666 "Antimicrobial Stewardship: The Cost of Discontinuing a Program" Presented at the Fifth Decennial International Conference on Healthcare-Associated Infections, Atlanta, GA, March 18-22, 2010.

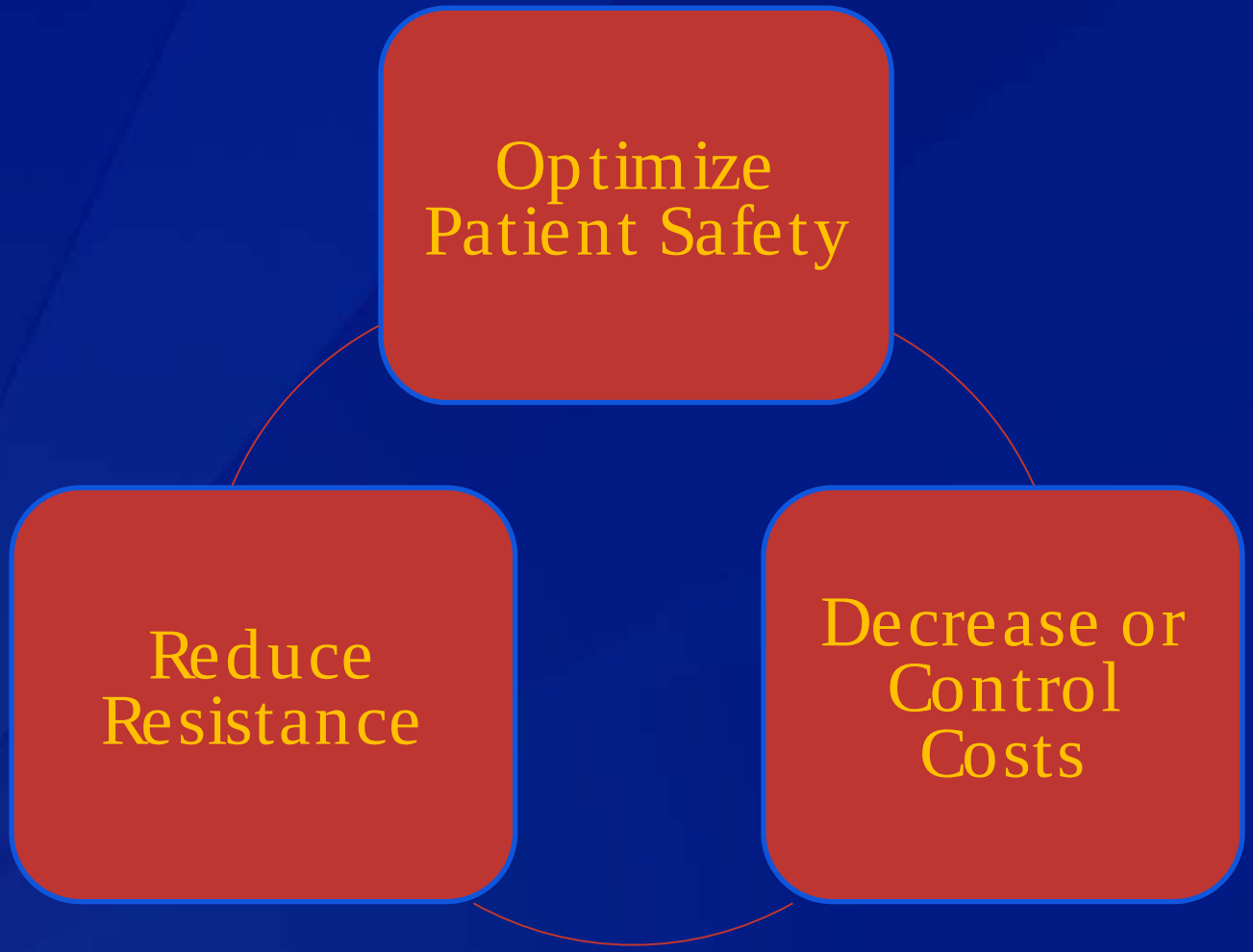
Antimicrobial Stewardship

Antimicrobial Stewardship refers to processes designed to measure and optimize the appropriate use of antimicrobials by selecting the appropriate agent, dose, duration of therapy and route of administration. The major objectives of antimicrobial stewardship are to achieve optimal clinical outcomes, to minimize toxicity and other adverse events, and to minimize the development of antimicrobial resistance. Antimicrobial stewardship may also reduce excessive costs attributable to inappropriate or unnecessary therapy, suboptimal outcomes, toxicity and other adverse events, and antimicrobial resistance.

Antimicrobial Stewardship

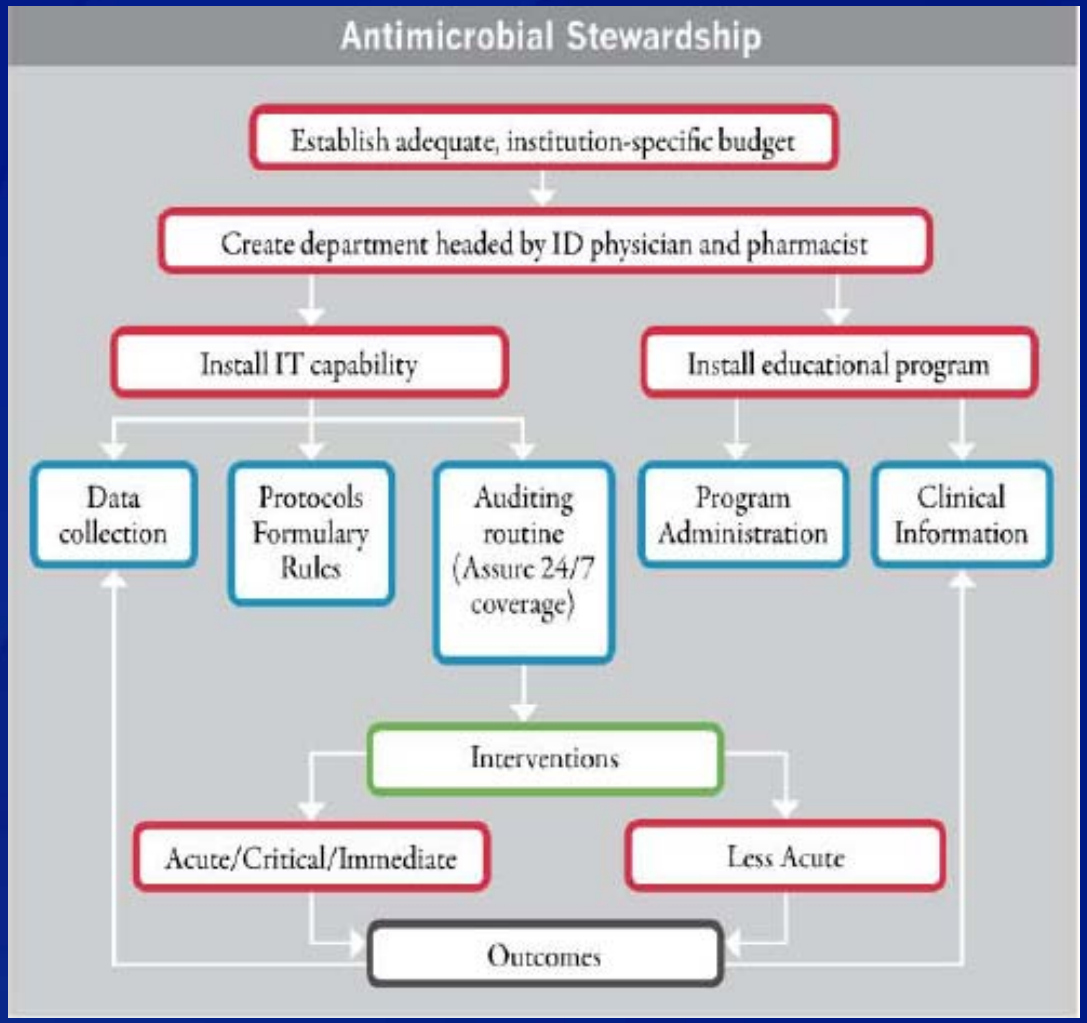
- Making people eat their peas.

Goals of Antimicrobial Stewardship



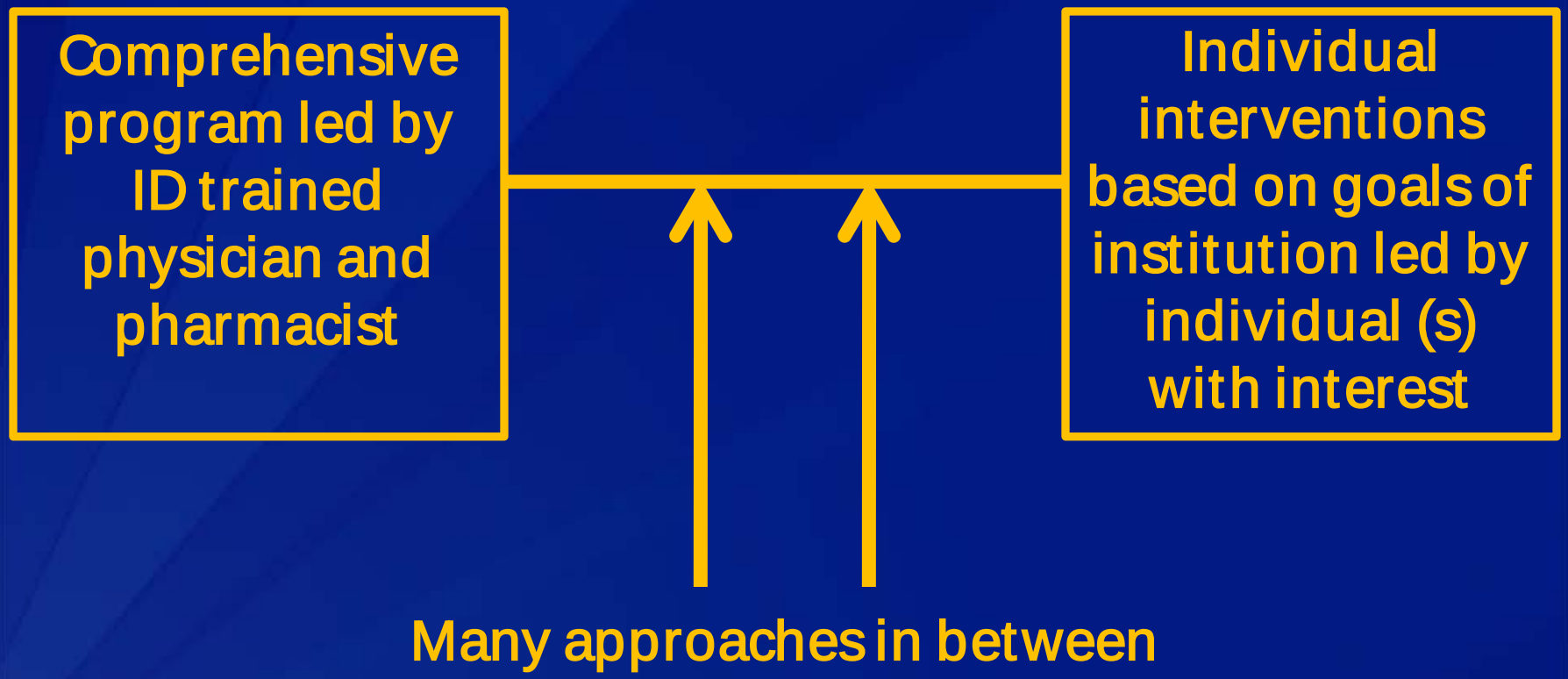
What Do Stewardship Programs Look Like?

The Original Model



Dellit TH et al."Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship" Clin Infect Dis 2007;44:159-77.

The New Model: A Spectrum of Activities



Who Can Be A Steward?

- Not realistic to expect that all institutions have ID trained physicians and pharmacists
- Basic requirements: interest in stewardship/patient safety/performance improvement and basic knowledge of antibiotics
  - Alternatives to ID physician: hospitalist, microbiology director, surgeon, intensivist
  - Alternatives to ID pharmacist: pharmacist with advanced training (e.g. critical care, medicine), pharmacist who has attended a training program in stewardship
  - All must be given some time to dedicate to activities
- Activities can be tailored to comfort level

Key Stakeholders

Hospital Administration

Prescribers

Pharmacy
Microbiology
Infection Control
Information Technology

Goals of Hospital Administration

- Decrease and control costs
- Regulatory compliance
  - IPPS Rules
  - Core measures (e.g. CAP)
- Stay competitive
  - Public reporting pressures
- Optimize patient safety
  - Most definitely, if it decreases costs
  - Otherwise depends on the climate in the institutions
- Reduce resistance
  - In your dreams

Stewardship Pitch for Hospital Administration

- Emphasize potential for cost-savings
  - External and internal data
    - Reduction in antibiotic costs
    - Reduction in LOS
- Emphasize how stewardship can help fulfill other missions
  - Patient safety
  - Regulatory compliance

Goals of Prescribers

- Give what they want to give
- Optimize patient safety
  - Hard to argue against
- Reduce resistance
  - If they are feeling public-healthy that day
- Regulatory compliance
  - Sometimes compelling, esp. to surgeons
- Decrease and control costs
  - In your dreams

Stewardship Pitch for Providers

- You are not trying to tell them what to do, you are trying to make their lives better
  - Help with bug/drug mismatch
  - Help with dosing
  - Help with IV to PO switch for earlier discharge
  - Prevent adverse events: drug interactions, allergies, *C. difficile*
- Anecdotes can be compelling
- Education can be a carrot
  - Do you know about the most recent endocarditis prophylaxis guidelines? Let me give you a quick summary!
- Recruit thought leaders in different specialties to support and reiterate your message

Where Can I Begin? Find Your Allies

- Pharmacy staff will be central to making any effort work.
- They might be the driving force for the effort.
- You don't have to have ID trained pharmacists.

Find Your Allies

- Infection control staff are a key ally.
- They are very aware of C difficile and resistance issues.
- They review lots of culture results and might be seeing problems.
- Stewardship work fits perfectly with what they are already doing to reduce infections.

Find Your Allies

- Critical to have a "physician champion" who is willing to help you work with physicians.
- Does NOT have to be an Infectious Disease attending.
- Only need someone with an interest in improving antibiotic use.
- Hospitalists can be a great choice.

Find Your Allies

- It's also really helpful to have an advocate within your administration.
- Might be useful to talk with pharmacy and get some cost data to share with them.
- Can be useful to meet with them as a team: physician, infection control, pharmacy.

Where Can I Begin?

- Assess your situation- talk to providers
- What are problems in your hospital?
  - C difficile? Other Adverse drug reactions to antibiotics? Resistance?
- What would people like help with when it comes to antibiotics?
  - Dosing? IV to PO conversion? Treatment of specific conditions?
- What expertise is available to you?

Getting Started- Assess Your Situation

- Review some charts of patients who got antibiotics to see if any issues emerge:
  - Are providers getting cultures before starting therapy?
  - Are people using culture results? Especially blood cultures and other sterile sites?
  - Are patients getting unneeded duplicate therapy (2 anaerobic drugs)?

Getting Started- Assess Your Situation

- If you have available expertise
  - Review the treatment of some common infections: pneumonia, urinary tract infections
  - Do patients being treated for these infections actually meet criteria for an infection?
  - Are treatment durations in line with evidence?

Pick Something

- Bring your team together to review whatever data you've gathered and use that to try and pick some intervention.
- START SMALL
- START SMALL
- START SMALL
- Only do what you are most comfortable doing.
- Only do what appeals locally.

Pick Something- Examples

- Review antibiotics on all patients with positive blood cultures.
- Choose some "never" combinations of antibiotics and intervene when those are prescribed.

Pick Something- Examples

- Develop some diagnosis and treatment guidelines for common infections.
- Pneumonia
- Urinary tract infections

Measure Something

- No matter what you pick, develop a plan to monitor what's happening.
- List of cases where blood culture results prompted different therapy.
- List of cases where unneeded duplicate therapy was stopped.
- Review charts to assess compliance with treatment guidelines.

Feed Back the Data

- Summarize your data and share it with anyone who will listen.
- Especially key to share with leadership.
- Summary format- keep it short and bullted.
- Use shiny paper.

Summary

- "Some is not a number, soon is not a time"
- We need to take concrete steps to improve in-patient antibiotic use- NOW.
- We can improve antibiotic use in any facility- we just need to learn more about how.
- I would love the chance to both support and learn from your efforts to do this.

http://www.cdc.gov/getsmart/healthcare/

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion