Antimicrobial Stewardship: Concepts & Applications

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UNM HOSPITALS

Objectives

- Explain trends in antimicrobial resistance
- Describe the goals of antimicrobial stewardship programs (ASPs)
- Evaluate strategies used in achieving a successful ASP
- Recognize opportunities to apply antimicrobial stewardship concepts

Audience Survey

- How many of you have an Antimicrobial Stewardship program at your institution?

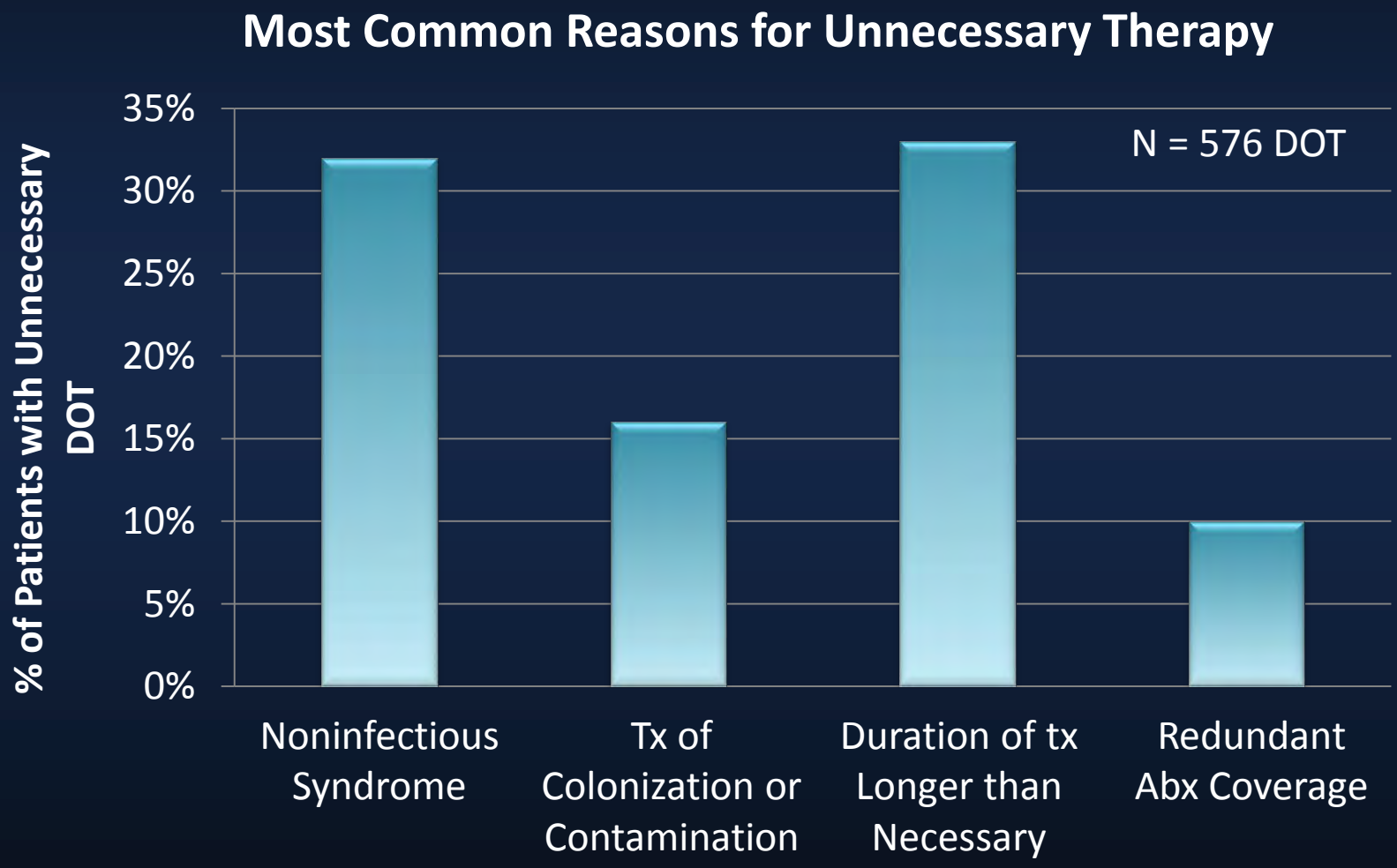
- How many are in the process of implementing Antimicrobial Stewardship at your institution?

Era of Untreatable Infections

New York, NY: A 56 yo septic man in the ICU with blood culture positive for *Acinetobacter baumanni* complex

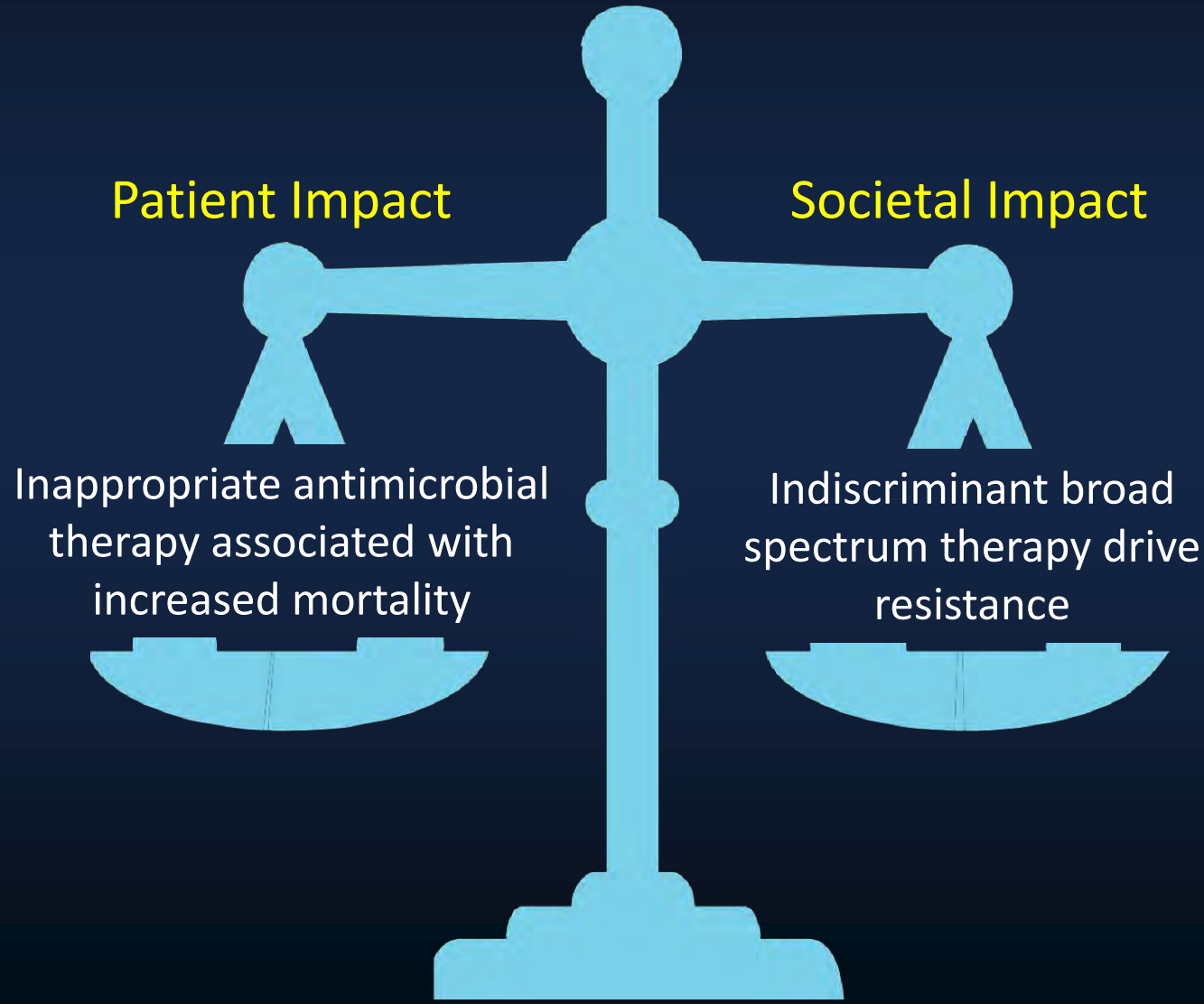
•Pip/tazo	>128/4	Resistant
•Ceftazidime	> 64	Resistant
•Cefepime	> 64	Resistant
•Imipenem	>16	Resistant
•Gentamicin	>16	Resistant
•Amp/sulb	16	Intermediate
•Ciprofloxacin	>4	Resistant
•Amikacin	96	Resistant
•Levofloxacin	>8	Resistant
•SMX/TMP	40	Susceptible
•Polymyxin B	24	Resistant
•Tigecycline	24	Resistant

"50% of antimicrobial use is either unnecessary or inappropriate."

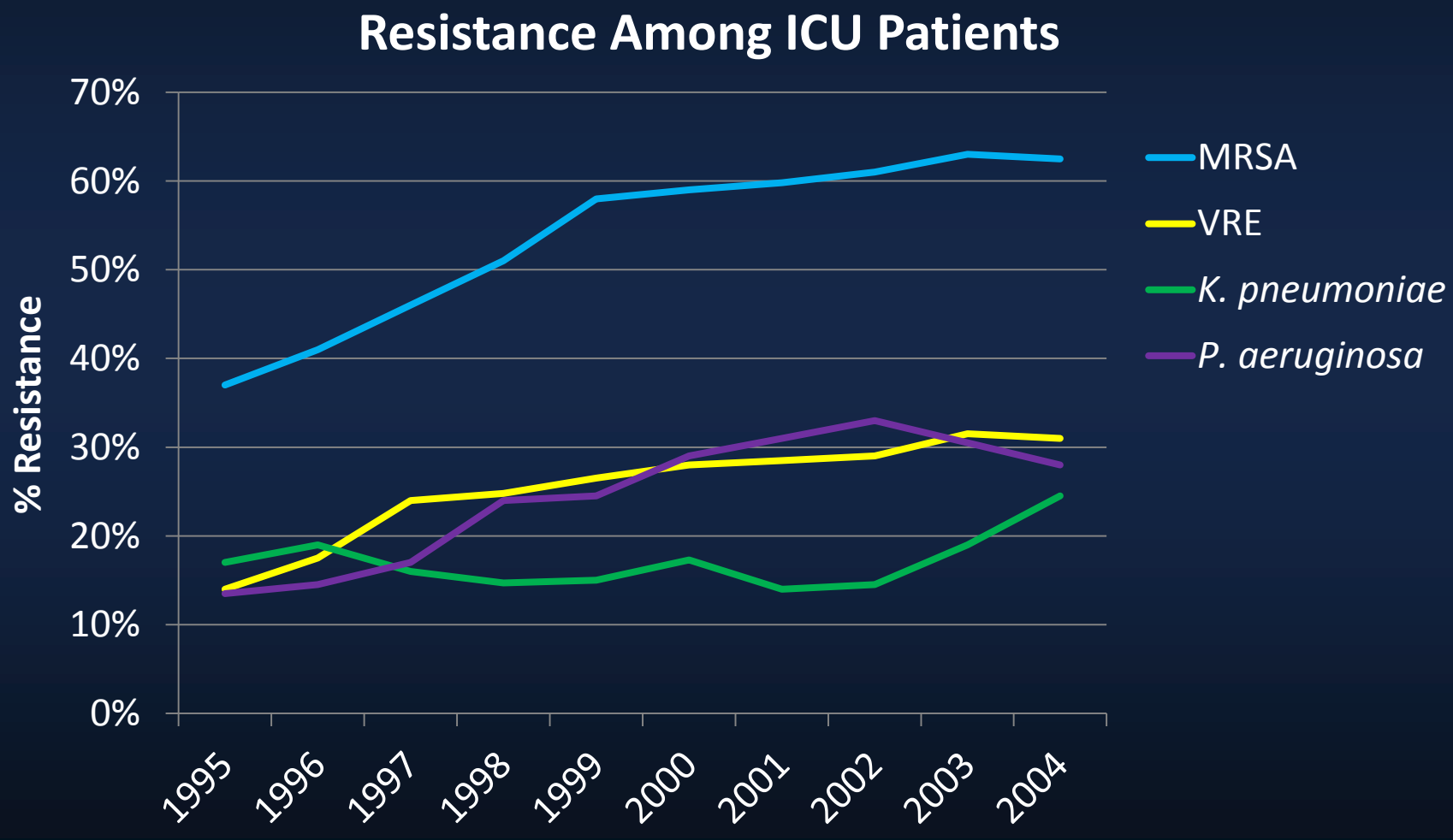


Reimann HA, D'Ambola J. JAMA. 1968;205(7):537.
Hecker MT, et al. Arch Intern Med. 2003;163:972-78.

Balancing the Antimicrobial Impact

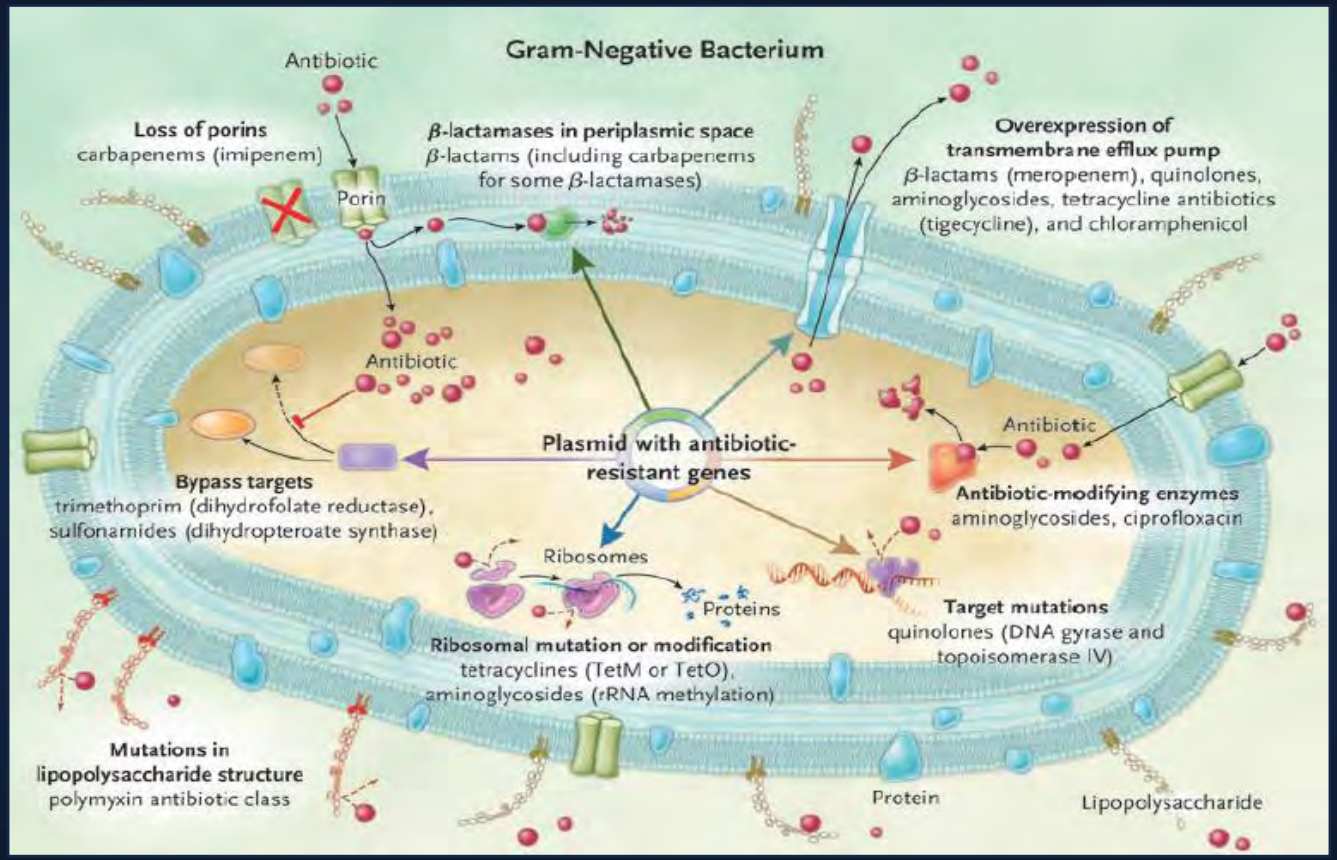


Resistance is on the Rise



CDC National Nosocomial Infections Surveillance (NNIS) Systems, ICU_RESTrend1995-2004.pdf.

Mechanisms of Resistance

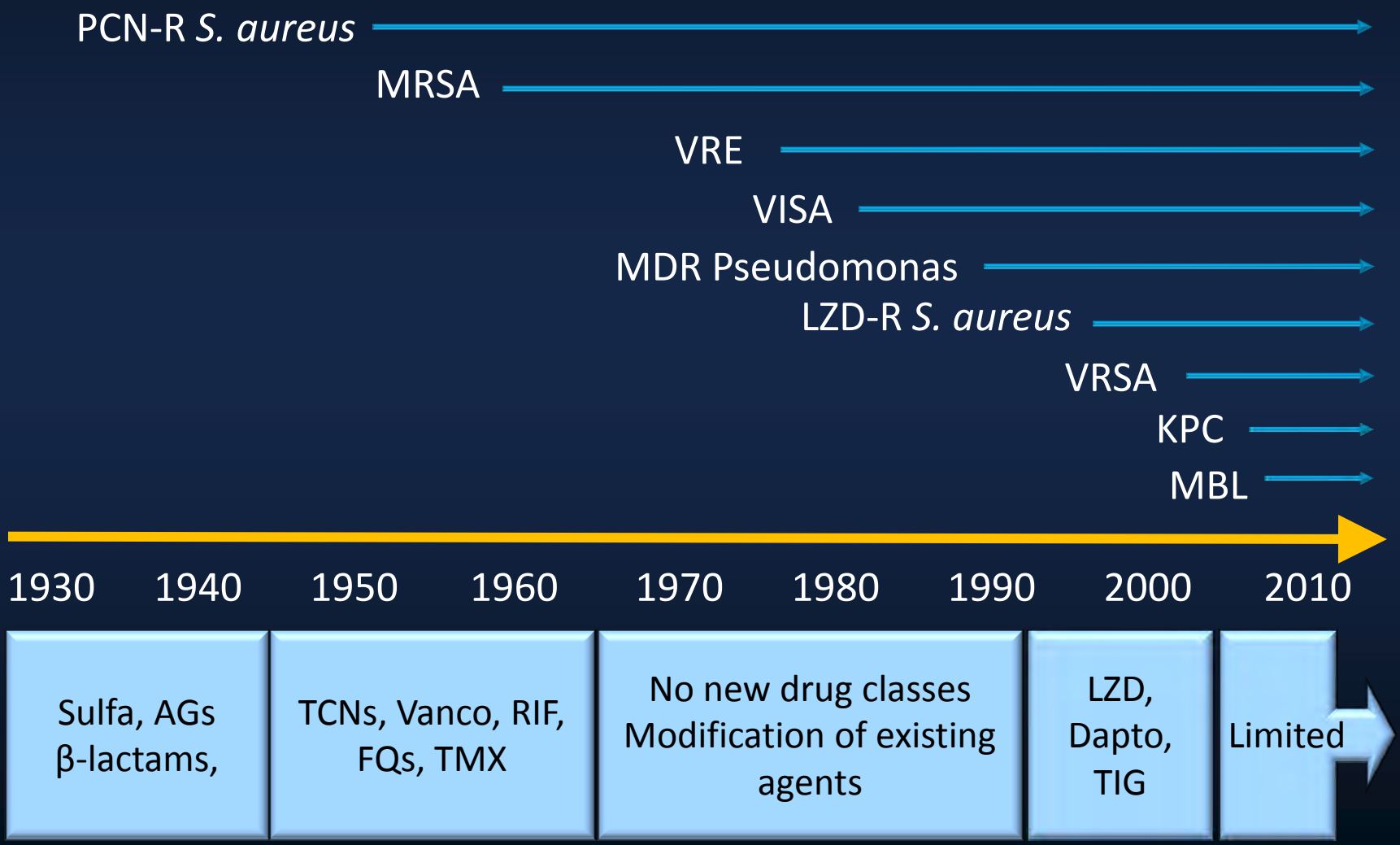


"You must not fight too often with one enemy or you will teach him all your art of war."

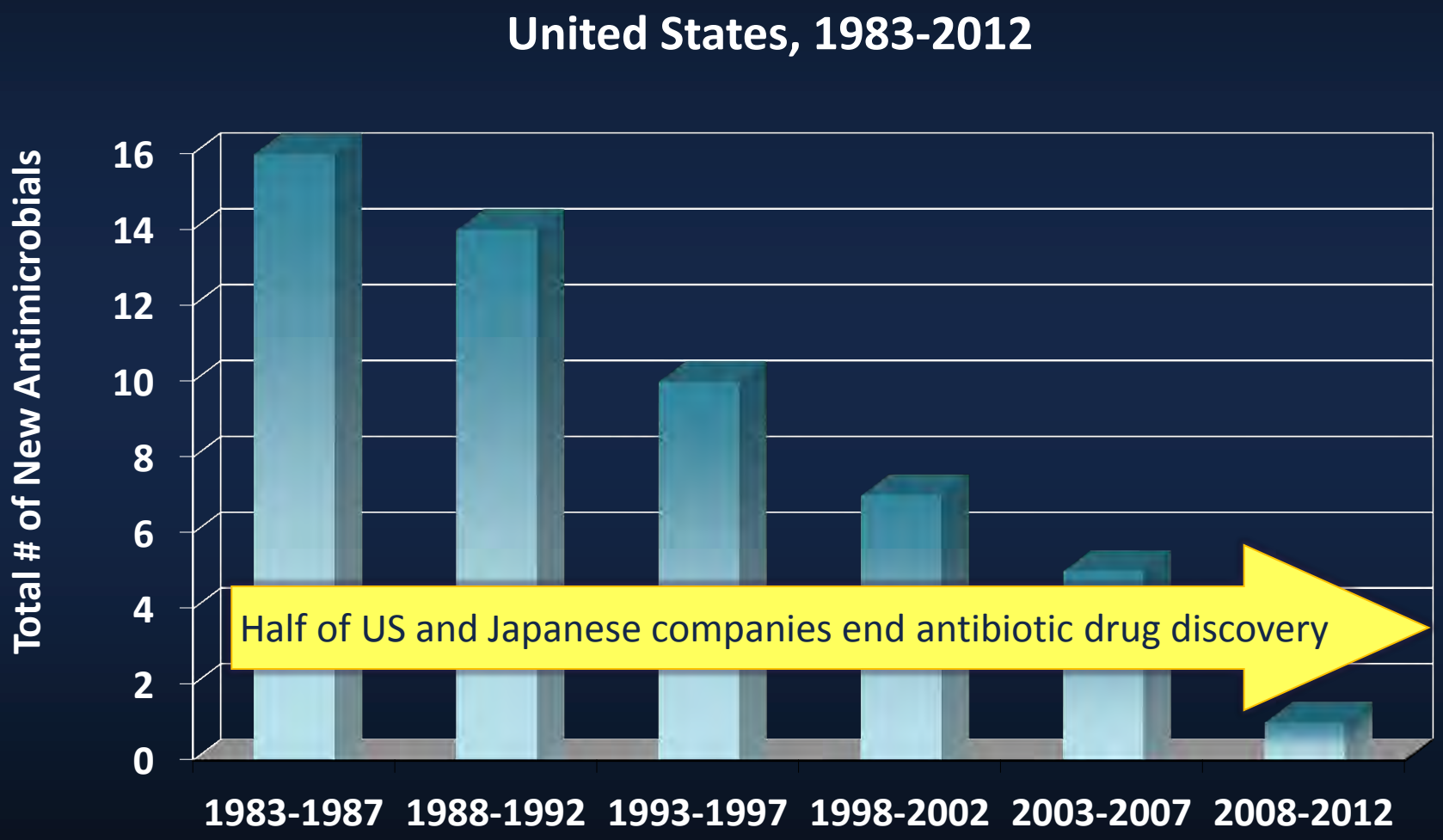
-- Napoleon Bonaparte

Peleg et al. N Engl J Med. 2010; 362-1804-13.

Antimicrobial Resistance Has Surpassed Antibiotic Development



And Then There Were None…



Spellberg B et al. Clin Infect Dis. 2008;46:155-164.

Antimicrobial Stewardship Goals

- Primary Goal:
  - Optimize clinical outcomes while minimizing the unintended consequences of antimicrobial use
- Secondary Goals:
  - Reduce antimicrobial resistance
  - Reduce mortality and length of stay
  - Reduce associated healthcare costs

Antimicrobial Stewardship Components

ASP Core Strategies

Core Strategies	Advantages	Disadvantages
Prospective audit with direct intervention and feedback	• May reduce inappropriate antimicrobial use • Educate to modify future prescribing • Allows prescribers to maintain autonomy	• Difficulty identifying patients with inappropriate therapy and communicating with prescribers
Formulary restriction and preauthorization requirements	• May result in immediate and substantial reduction in antimicrobial use and costs	• May increase staffing requirements • May delay order implementation with potential adverse patient outcomes • May increase use of and resistance to alternative antimicrobial agents • Perceived loss of prescriber autonomy

Dellit et al. Clin Infect Dis. 2007;44:159-77.
Drew et al. Pharmacotherapy. 2009;29:593-607.

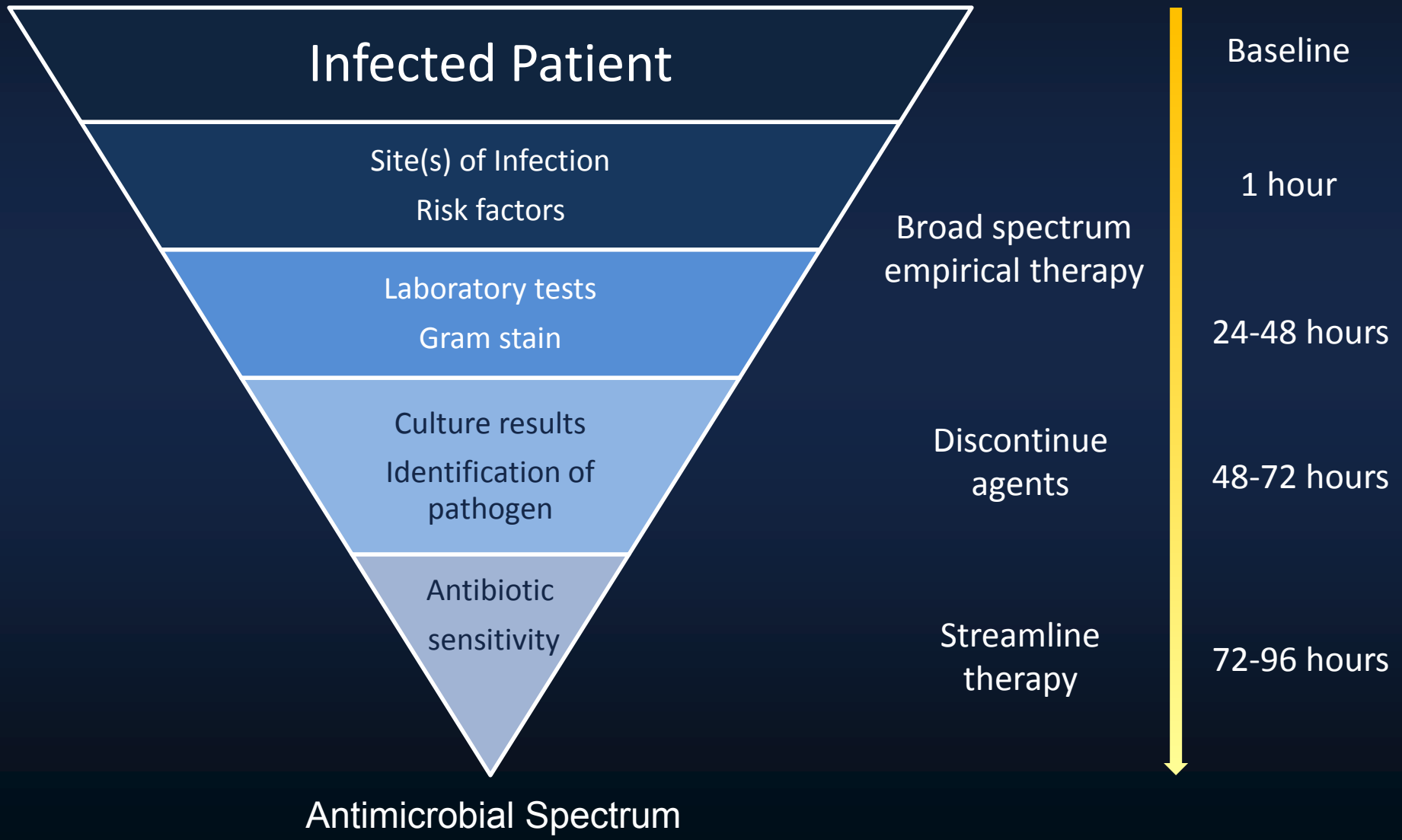
ASP Supplemental Strategies

Supplemental Elements	Advantages	Disadvantages
Education	• May influence prescribing behavior	• Marginally effective when used without active intervention
Evidence based guidelines and clinical pathways	• May improve antimicrobial use and practice variations	• Poor adherence
Streamlining or de-escalation therapy	• Reduces antimicrobial exposure, selection of resistant pathogens, and health care costs	• Prescriber reluctance to de-escalate when cultures are negative and clinical improvement observed
Dose optimization	• Tailors therapy to patient characteristics, pathogen, and PK/PD of antimicrobial	• Nursing concerns regarding incompatibilities and administration
IV to PO conversion	• May decrease length of hospital stay and costs • May reduce complications associated with IV access	• Difficulty identifying patients in whom conversion is appropriate

Dellit et al. Clin Infect Dis. 2007;44:159-77.
Drew et al. Pharmacotherapy. 2009;29:593-607.

Antimicrobial De-escalation

Antimicrobial Treatment Strategy



De-escalating Therapy

- Anticipated Benefits
  - Treatment outcomes are unaltered
  - Beneficial impact on antimicrobial resistance for the institution
  - Decrease in antibiotic related adverse events
  - Reduction in overall antimicrobial costs

Masterton RG. Crit Care Clin. 2011;27:149-62.

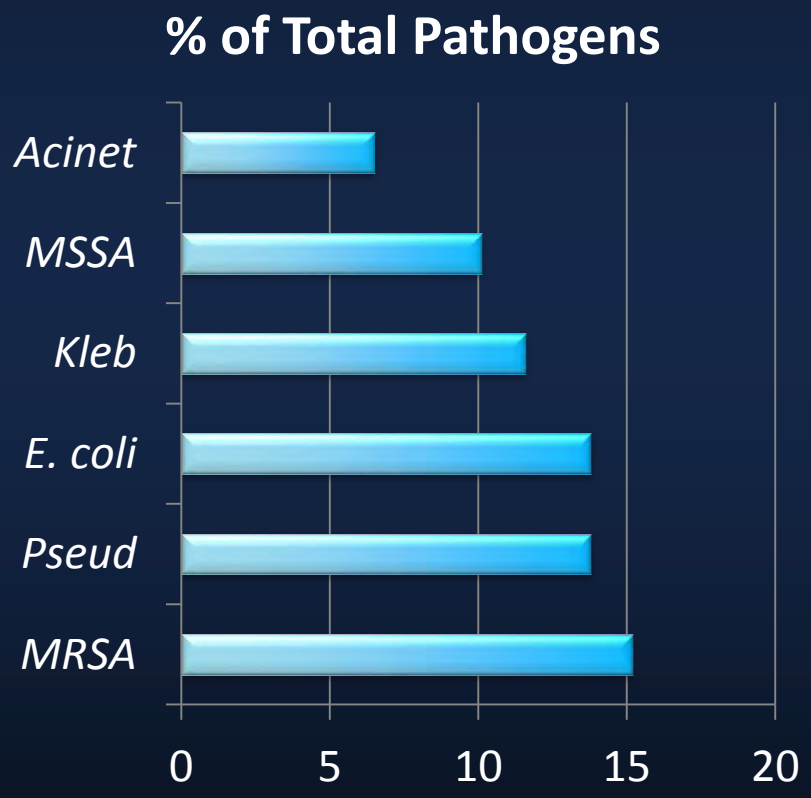
De-escalating Ventilator Associated Pneumonia (VAP) Therapy

- Prospective study in the surgical care ICU at New York Presbyterian Hospital, Weill Cornell Medical Center between 2005-2007
- VAP diagnosed by quantitative broncheoalveolar lavage (BAL) with >10,000 cfu/mL
- Hypothesis
  - De-escalation therapy not associated with increased rates of recurrent pneumonia or mortality

Eachempati SR, et al. J Trauma. 2009;66:1343-8.

VAP De-escalation Outcomes

VAP Pathogens Isolated



De-escalation Outcomes

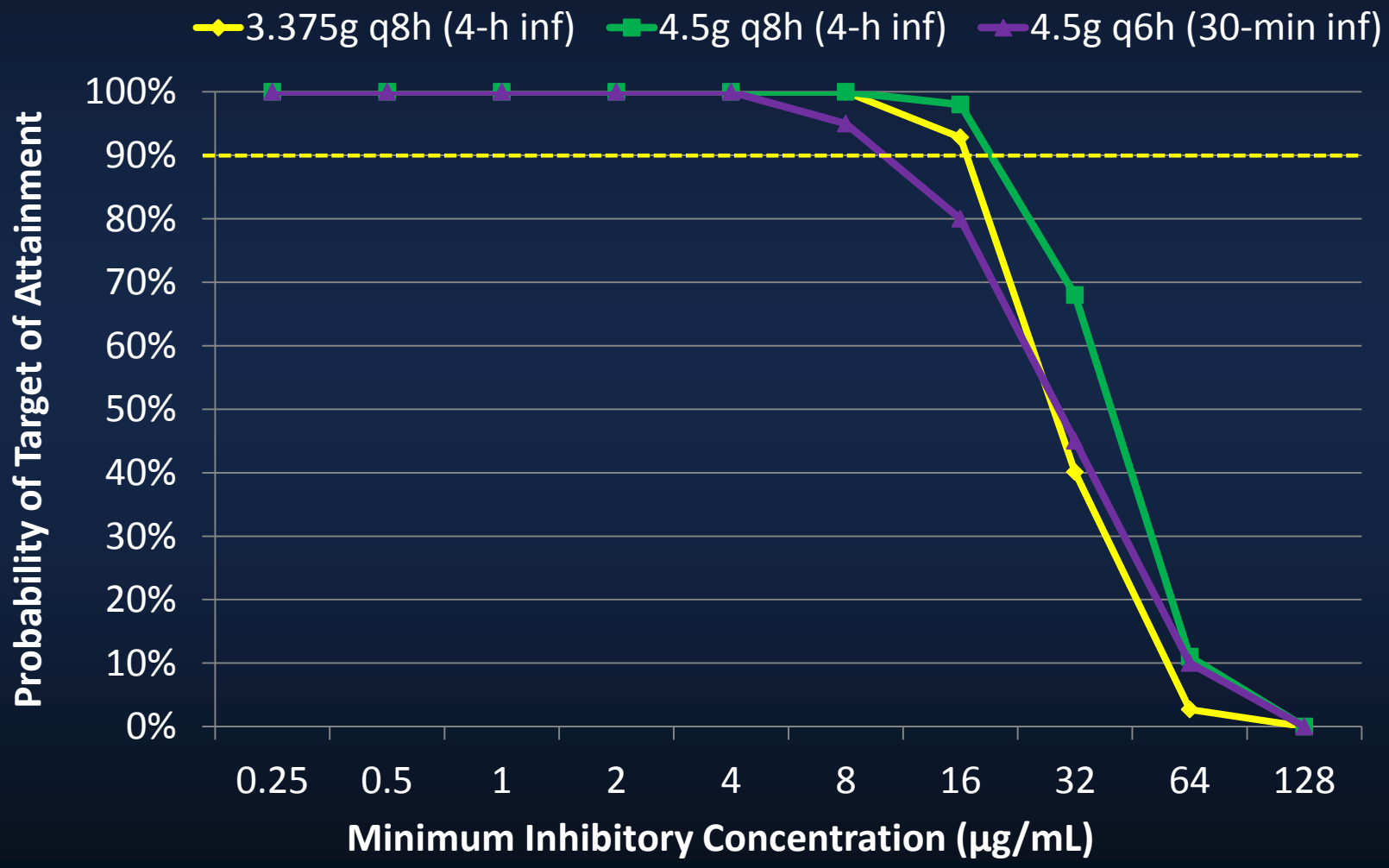
	De-escalation (N = 77)	Non De-escalation (N = 57)	*P*-value
Age	64.1 ± 2.2	63.4 ± 2.6	0.81
APACHE III	79.8 ± 3.2	85.5 ± 3.1	0.22
RP	27.3%	35.1%	0.35
Mortality	33.8%	42.1%	0.32

RP = Recurrent pneumonia

Eachempati SR, et al. J Trauma. 2009;66:1343-8.

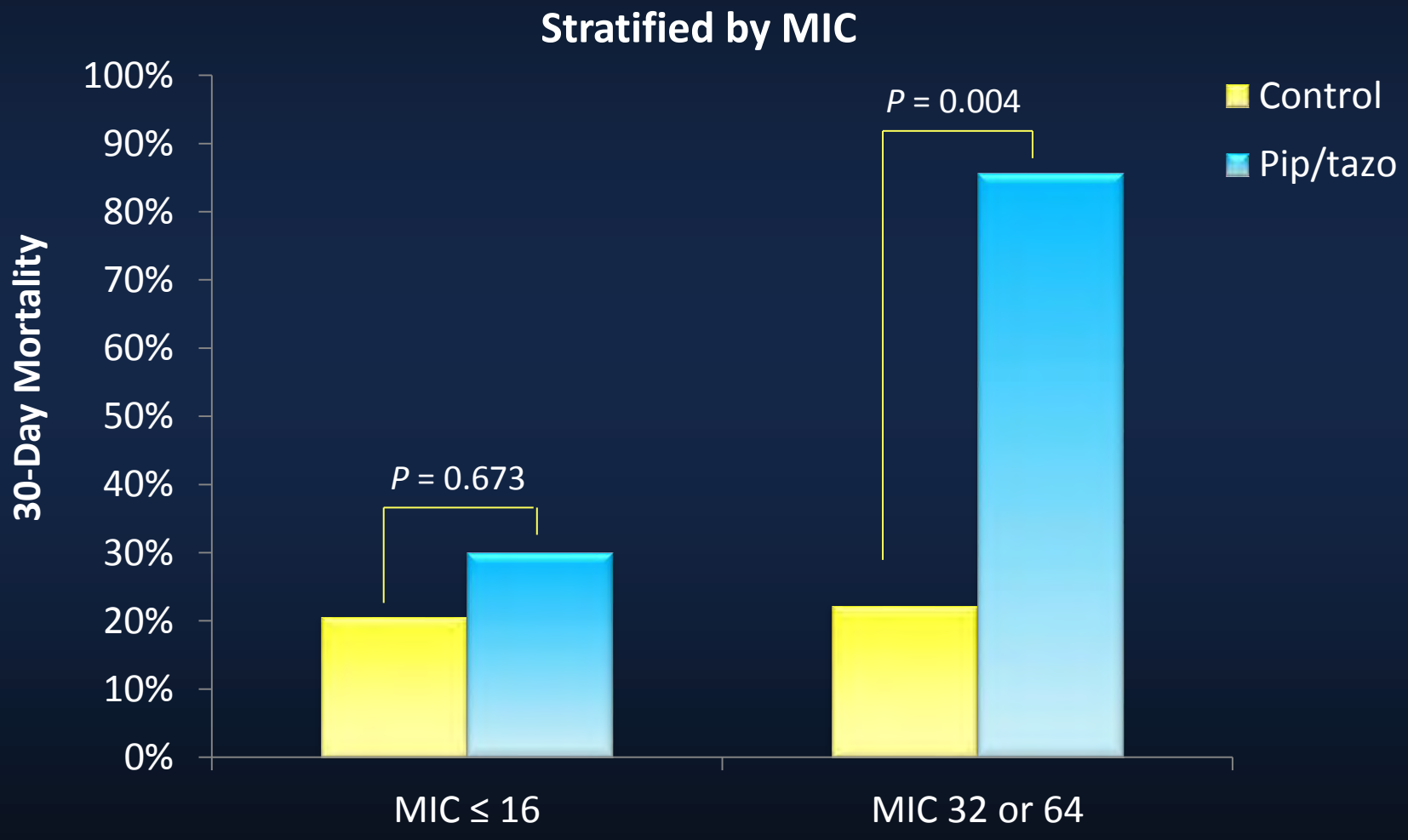
Dose Optimization

Probability of Bactericidal Exposure for Pip/tazo



Kim A, et al. Pharmacotherapy 2007;27:1490-1497.

30-Day Mortality Among Patients with *P. aeruginosa* Bacteremia



Tam VH, et al. Clin Infect Dis. 2008:46(15):862-7.

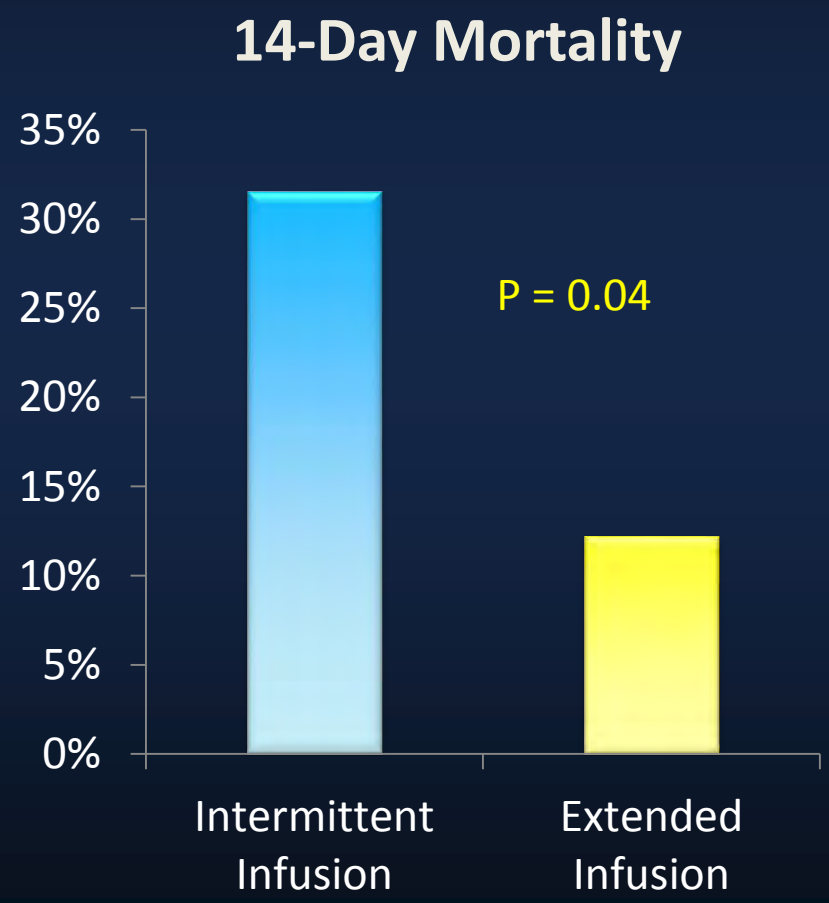
Clinical Implementation of Extended Infusion Piperacillin/tazo

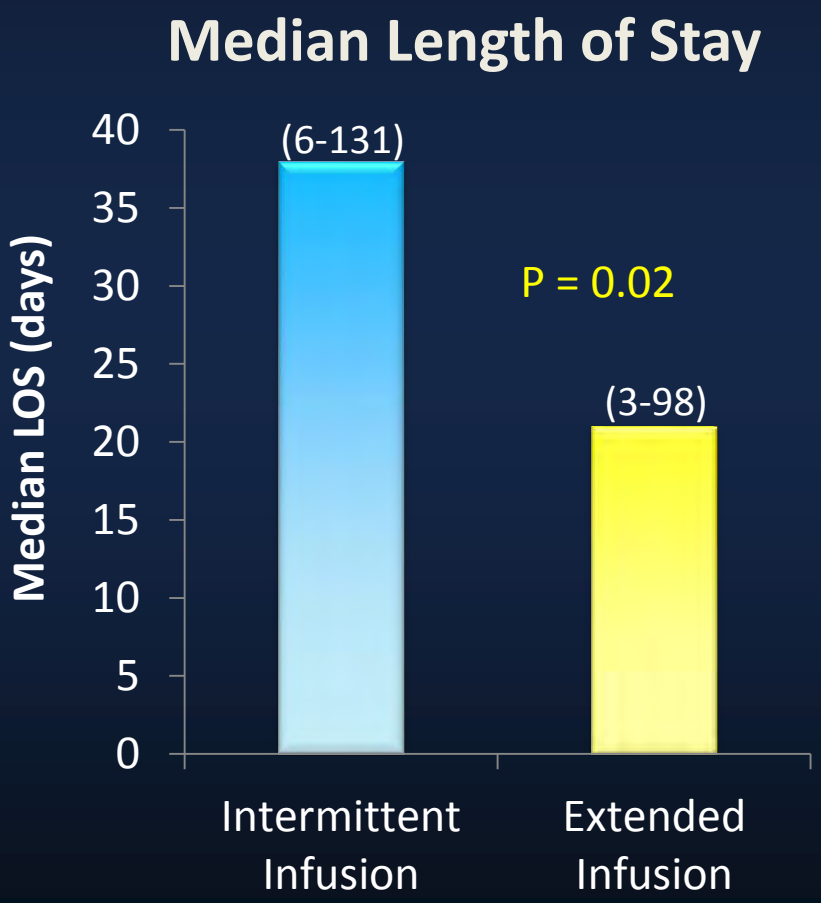
- In 2002, an automatic hospital-wide substitution of pip/tazo was implemented at Albany Medical Center
  - Pip/tazo 3.375 g IV q8h, infused over 4-hours
  - Replaced traditional intermittent infusions of 3.375 g IV q4-6h, infused over 30 min
- Measured pre- and post-implementation outcomes
  - 14-day mortality
  - Length of hospital stay (LOS)

Lodise et al. Clin Infect Dis. 2007;44(1):357-63.

P. aeruginosa Bacteremia
4-h infusion of pip/tazo 3.375 g IV q8h

Patients with APACHE II ≥ 17





Lodise TP, et al. Clin Infect Dis. 2007;44(1):357-63.

Clinical Impact

Clinical & Economical Impact of ASPs

Pharmacist-Managed Antimicrobial Prophylaxis in Surgical Patients

	ASP (N = 162)	No ASP (N = 698)	Increase (%)	*P*-value
No. of patient days	456,698	1,644,596	10.21	< 0.001
Postoperative Infections (%)	1.13	1.72	34.3	< 0.001
Mean drug charges ($)	4,029	4.321	7.2	0.005
Mean laboratory charges ($)	2,721	2,795	2.7	0.0056
Death (%)	2.7	4.1	52.1	< 0.0001

Bond CA, et al. Am J Health Syst Pharm. 2007;64:1935-42.

Impact of Non-ID Trained Pharmacists

	Mean ± SD Expenditure ($)		Cost Savings ($)†	
	Baseline	Intervention	Daily	Yearly
Ceftazidime	115 ± 47	80 ± 27	35	12,775
Imipenem	299 ± 84	232 ± 112	67	24,455
Levofloxacin	497 ± 35	448 ± 31	49	17,885
Pip/tazo	2,110 ± 134	2,037 ± 11	73	26,645
Vancomycin	1,221 ± 79	1,008 ± 9	213	77,745

†Extrapolated savings based on cost data during intervention period

- Grady Memorial Hospital in Atlanta, GA
- Prospective audit with intervention and feedback of non-ICU patients
- Mortality, LOS, and re-admissions were similar for both periods
- Emergence of resistance decreased from 9.5% to 5% ($P = 0.06$)

DiazGranados CA, et al. Am J Health-Syst Pharm. 2011;68:1691-2.

Future Directions

- Expand antimicrobial stewardship to:
  - Pediatrics
  - Long term care facilities
  - Ambulatory care
  - Rural and community hospitals
  - Education of other healthcare professionals
- Antimicrobial stewardship reimbursment incentives

Healthcare Associated Infections: National Targets & Metrics

Metric	Source	National 5-Year Prevention Target
Bloodstream Infections	NHSN	50% reduction
C. difficile Infections	NHSN	30% reduction
Urinary Tract Infections	NHSN	25% reduction
MRSA bacteremia (hospital)	NHSN	25% reduction
Surgical Site Infections	NHSN	25% reduction

NHSN = National Healthcare Safety Network

Targets may soon be incentives for hospital re-imbursement

http://www.hhs.gov/ash/initiatives/hai/nationaltargets/index.html#hospital

Barriers to Antimicrobial Stewardship

- Lack of trained personnel
- Medical literature access
- Knowledge of updated guidelines/practices
- Lack of leadership supporting antimicrobial stewardship

Informal Infectious Diseases Educational Opportunities

- Identify a mentor with ID expertise
- Attend rounds with an ID physician
- “Shadow” a clinical microbiologist
- Join ID professional organizations
- Attend ID professional meetings
- Subscribe to ID list serves
- Sign up for electronic table of content alerts to ID journals
- Read basic primers, review articles, and practice guidelines on ID topics

Rapp RP, et al. http://onlinece.ashpadvantage.com/stewardship.stewardship-white-paper.pdf.

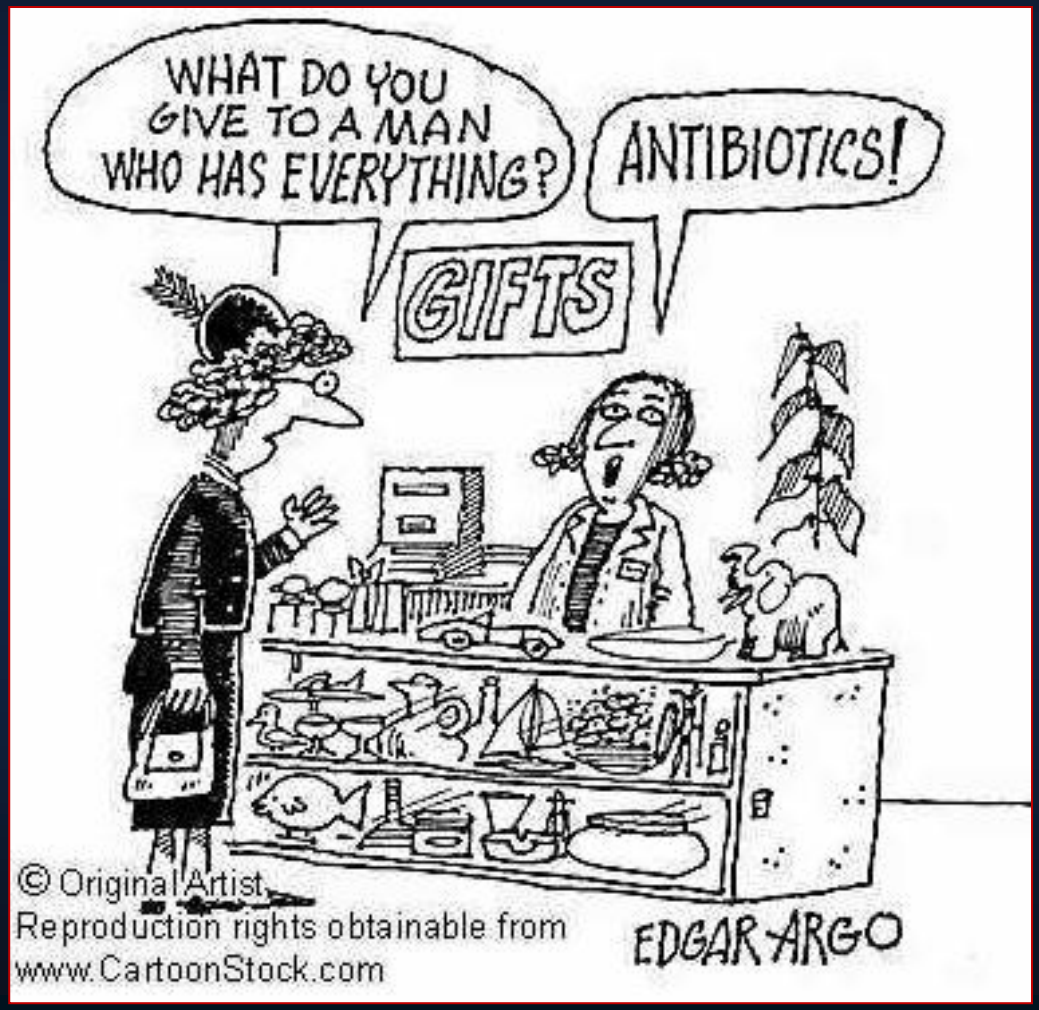
ASP Certificate Programs

- Advances knowledge base of
  - Clinical microbiology
  - Pharmacokinetic/pharmacodynamics
  - Infectious disease state management
- Combination of self-study, webinars, and practice skills components
- Available Programs:
  - Society of Infectious Disease Pharmacists (SIDP)
  - Making a Difference in Infectious Diseases (MAD-ID)

Conclusions

- Inappropriate antimicrobial use drives antimicrobial resistance
  - Affects public health, patient care and safety
- New antimicrobial agents to combat resistance is lacking
- Antimicrobial stewardship is needed to preserve our current antimicrobial agents

Questions?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GIFTS
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