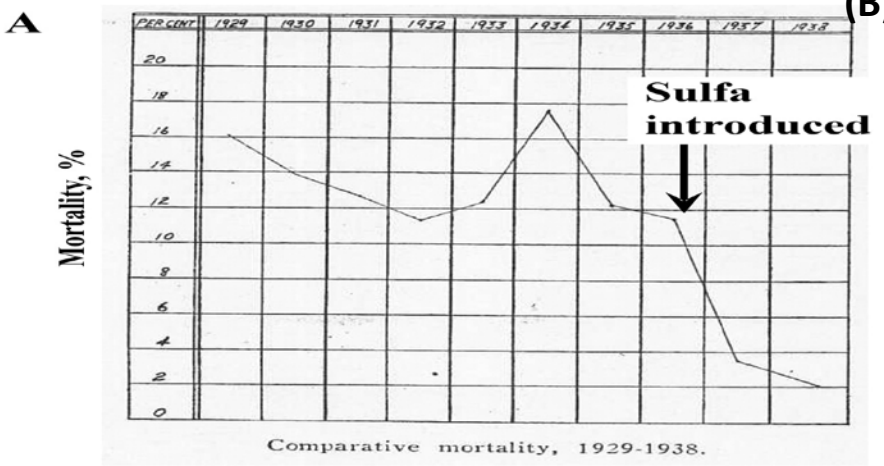
CHI Health

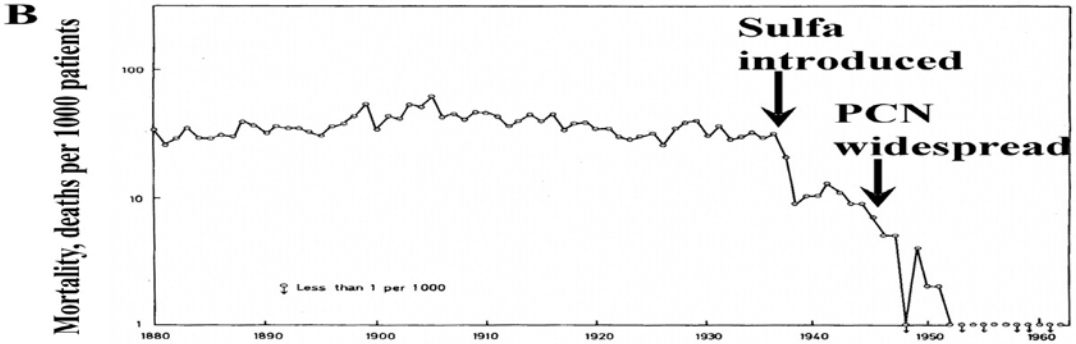
Antimicrobial Stewardship

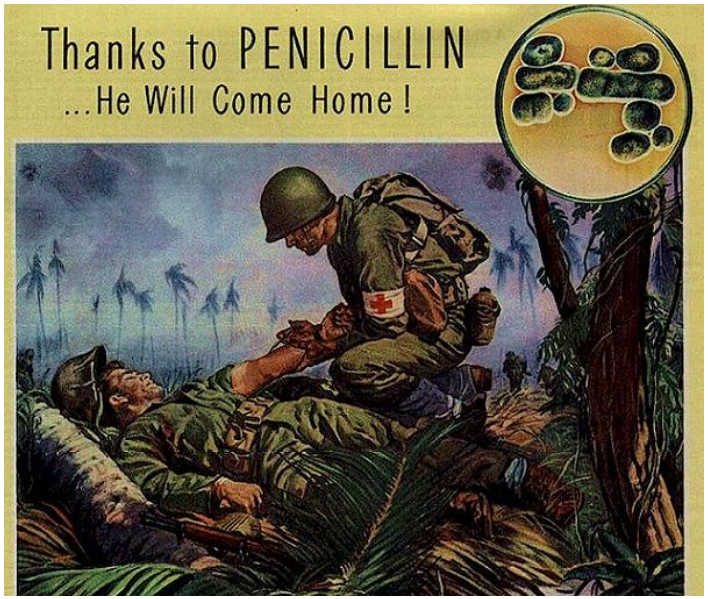
Healthcare Provider Education 2017

Antimicrobial Impact

(A) Mortality rates for erysipelas at Cook County Hospital 1929-1938
(B) Mortality of erysipelas from Norwegian national registry







Spellberg, et al. *Clin Infect Dis*. 2009;49:383-91.

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The Conquest of Infectious Diseases

"Nearly all experts agree, by the year 2000 bacterial and viral diseases will be eliminated; in addition, atherosclerotic heart disease will have been eliminated too." TIME Magazine. Feb 25, 1966

"Its time we close the book on Infectious Diseases."

W.H. Stewart, U.S. Surgeon General, 1969

"I cannot conceive of a need for more infectious diseases experts unless they spend their time culturing each other."

R.G. Petersdorf, M.D. NEJM 1978

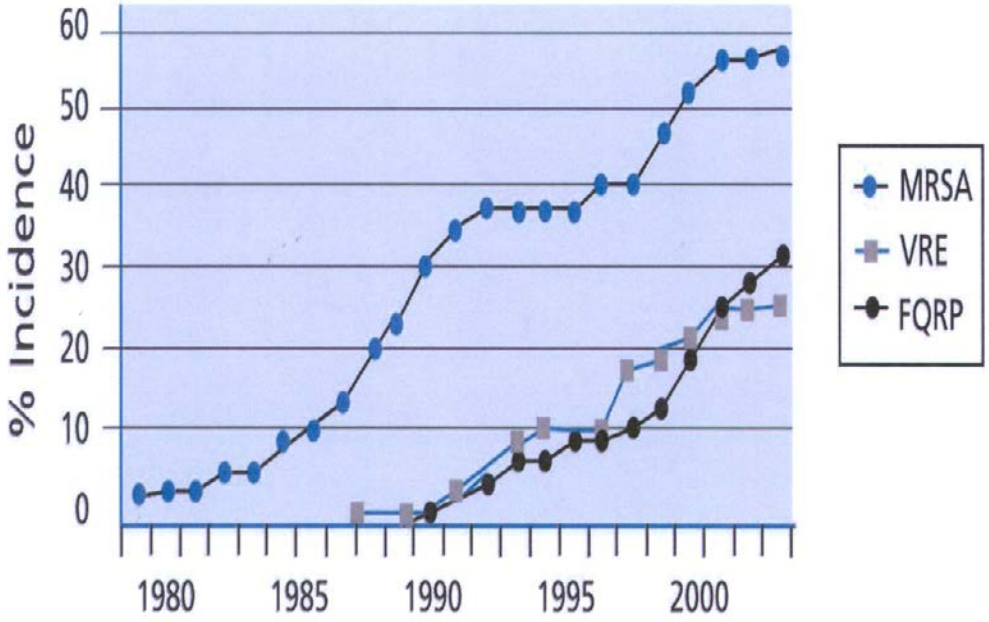

SEPTEMBER 12, 1994 $2.95
TIME
REVENGE OF THE
Killer Microbes
Are we losing the war against infectious diseases?


Super Bug
Dangerous drug-resistant germ spreads across U.S.

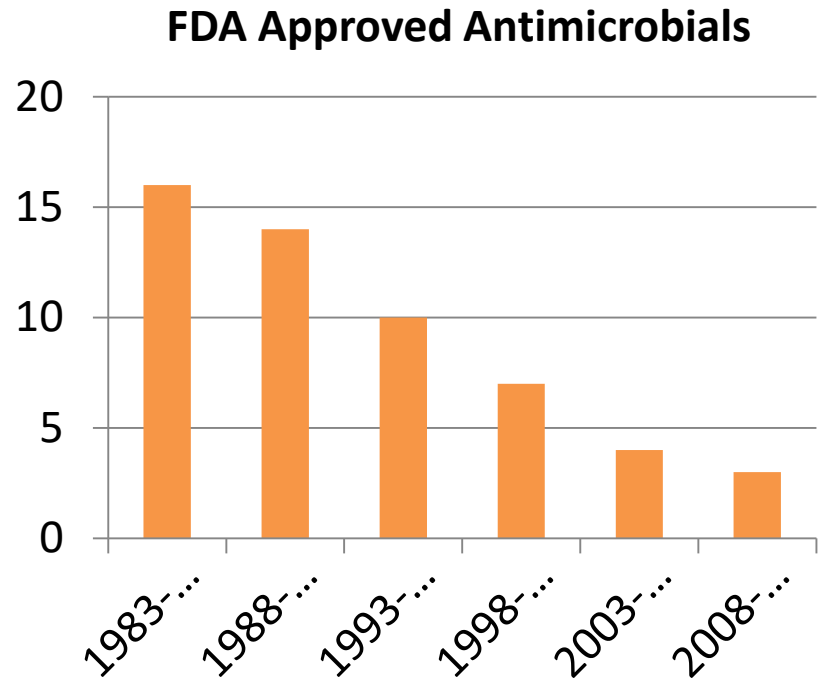

WEDNESDAY, JULY 25,
SUPERBUG DEATH
FREE LILY COLLECTION WORTH £25 FOR EVERY READER
Pick up from
Hospital infection soars by 22 per cent in just three months
1,000 SUPERBUG


o halt spr
kills 4,00
SIS 'TO LAST YEARS'
Cases of C. difficile have tripled since 2001, despite attempts to enforce an NHS crackdown on cleanliness
The worst hospitals
n at significant drop
mber of NHS workers

Antimicrobial Resistance



Source CDC



- Antimicrobial resistance is a growing problem
- Running out of antimicrobial agents
- Results in:
  - Use of less effective, more toxic agents
  - Increased mortality, morbidity, and costs

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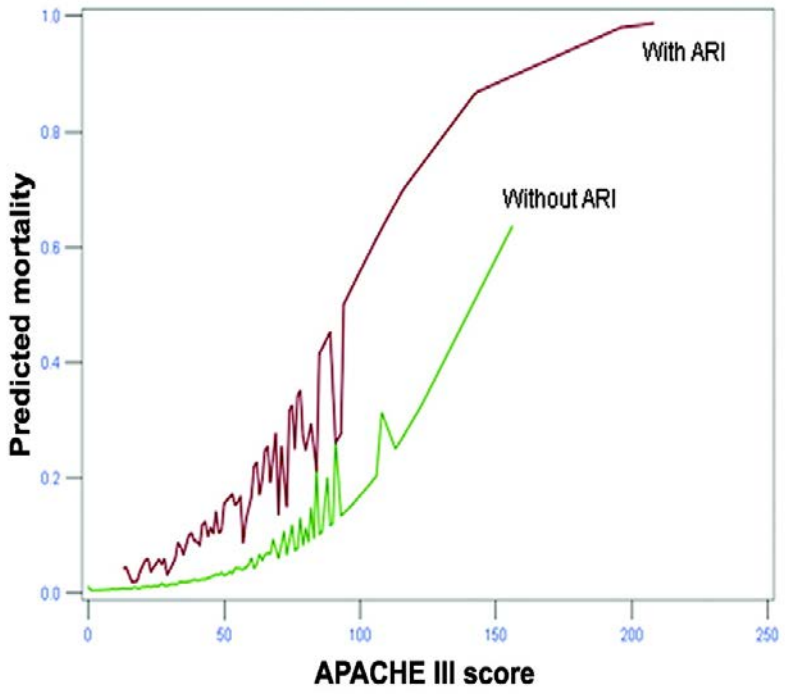
The Cost of Resistance: Bad For Patients, Bad for Healthcare

Analysis of 188 patients with antimicrobial-resistant infections in a group of 1391 hospitalized patients



Medical Costs	• $18,588 to $29,069 per patient
Excess LOS	• 6.4 – 12.7 days
Attributable Mortality	• 6.5%
Overall Increased Cost 1 year	• $13.35 million

Roberts. *Clin Infect Dis*. 2009;49:1175.

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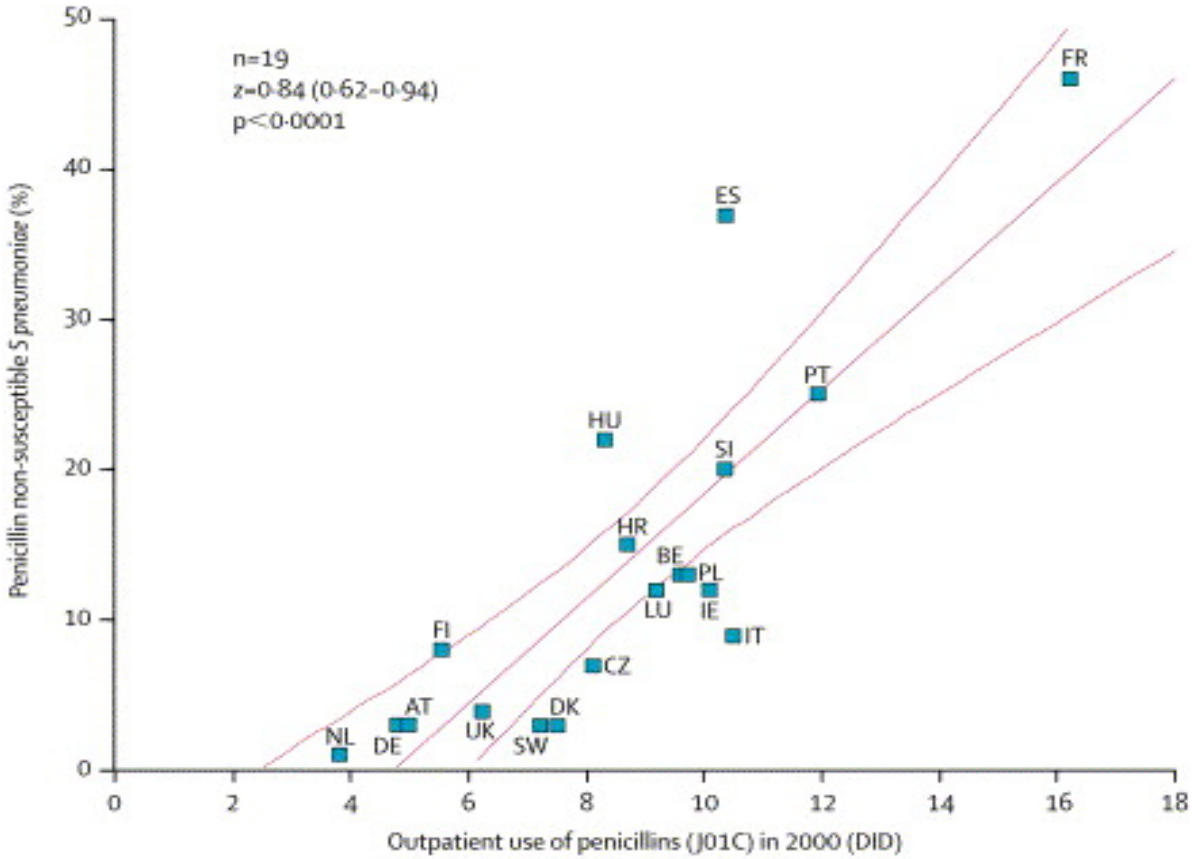
Where Does All This Resistance Come From?



Goossens. *Lancet*. 2005;365:579.

"It is not difficult to make microbes resistant to penicillin… moral: If you use penicillin, use enough."

(Alexander Fleming, Nobel Prize Acceptance Speech, 1945)

"Antibiotic use is the key driver of resistance."

(WHO Global Strategy for Containment of Antimicrobial Resistance, 2000)

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What Do We Do?

- Options
  1. ~~Create new drugs~~
  2. Learn to use what we have more wisely

ANTIMICROBIAL STEWARDSHIP

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What is antimicrobial stewardship (AMS)?

- "coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen including dosing, duration of therapy, and route of administration"

- **Primary goal:** optimize clinical outcomes while minimizing unintended consequences of antimicrobial use
  - effective antimicrobial stewardship **PLUS** infection prevention = limit emergence and transmission of antimicrobial-resistant bacteria

Clin Infect Dis 2016; 62(10):e51-e77.
Clin Infect Dis 2007;44: 159-77.

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Why is AMS important?

- Annually in the United States:
  - 30% of hospital admissions due to infection
  - 2 million people develop hospital acquired infections (HAIs)
- 30-50% of hospitalized patients receive antibiotics
- **50% of antibiotic orders: unnecessary or inappropriate**
- Antimicrobials are usually 30% or more of hospital pharmacy budgets

Pharmacotherapy 1999;19:1369
Clin Infect Dis 2007;44:159

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Antimicrobial Resistance

- Antimicrobial resistance identified by United Nations (UN) leaders as health crisis requiring attention (9/2016)
  - only the fourth time a health issue has been taken up by the UN General Assembly
- Antimicrobial resistance poses a fundamental threat to human health, development, and security
- If not successfully addressed, predict significant social, health, security, and economic repercussions that will seriously undermine the development of countries

High-Level Meeting on Antimicrobial Resistance: UN Headquarters, 21 Sept 2016.
http://www.un.org/pga/71/event-latest/high-level-meeting-on-antimicrobial-resistance/

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Increased Focus on Antimicrobial Stewardship

- Joint Commission released new Antimicrobial Stewardship Standard for all hospitals that requires compliance with starting January 1, 2017

- **Why now?** *Per Joint Commission*:
  - Current scientific literature emphasizes the need to reduce the use of inappropriate antimicrobials in all health care settings due to antimicrobial resistance
  - AMS can help prevent the development of multidrug resistant organisms, and reduce unnecessary drug use and costs associated with expensive, broad-spectrum therapies used to treat HAIs

Joint Commission Perspectives®, July 2016, Volume 36, Issue 7

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AMS Outcomes in Literature

Systematic review of 24 selected studies

- **Decreases seen in:**
  - Antibiotic use
  - Costs
  - Length of therapy
  - Inappropriate use
  - Adverse drug reactions
  - Resistance
- **No increases seen in:**
  - Nosocomial infection rates
  - Length of stay (some studies showed decreased LOS)
  - Mortality

Kaki, et al. J Antimicrob Chemother 2011;66:1223-1230

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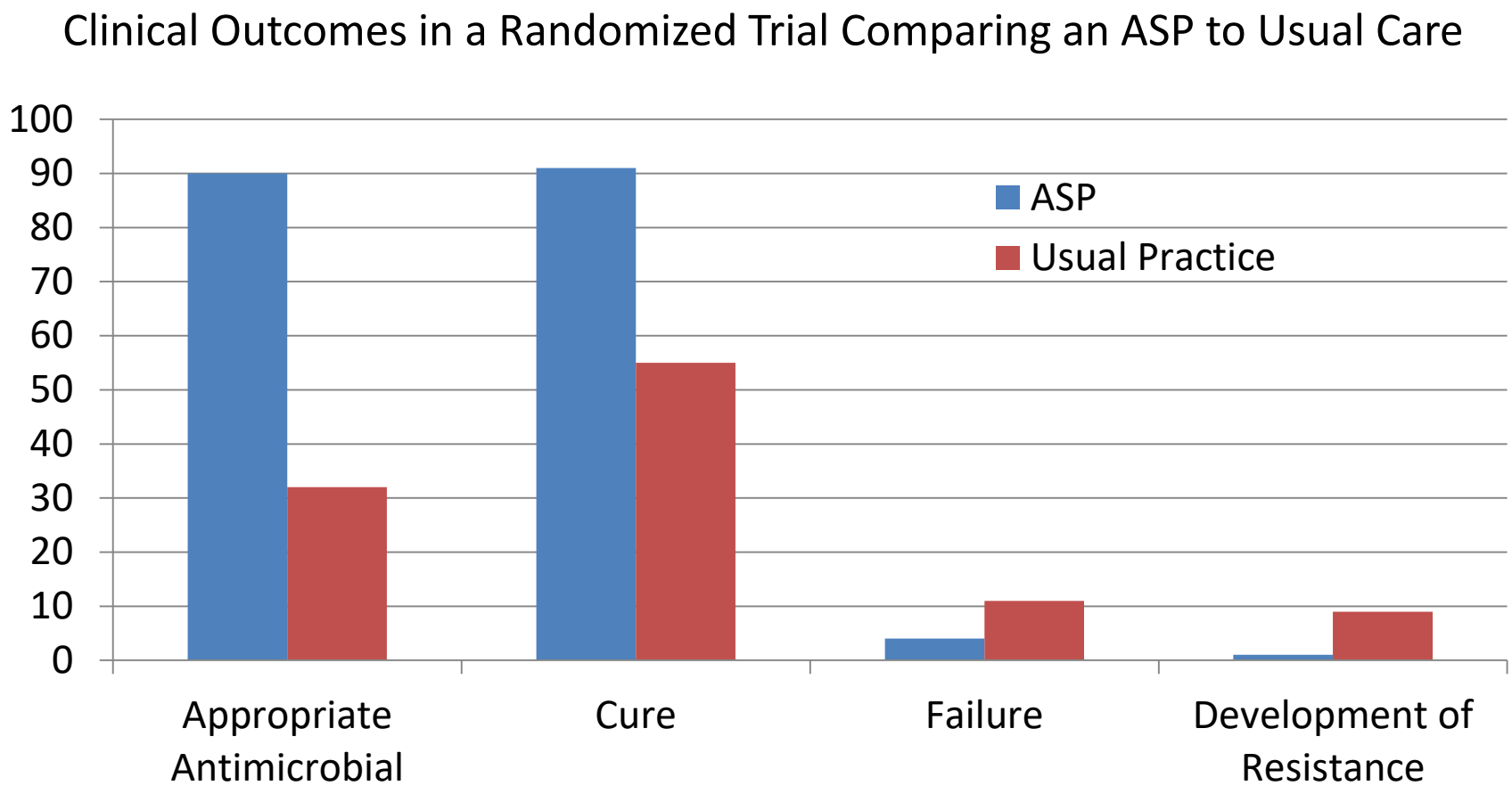
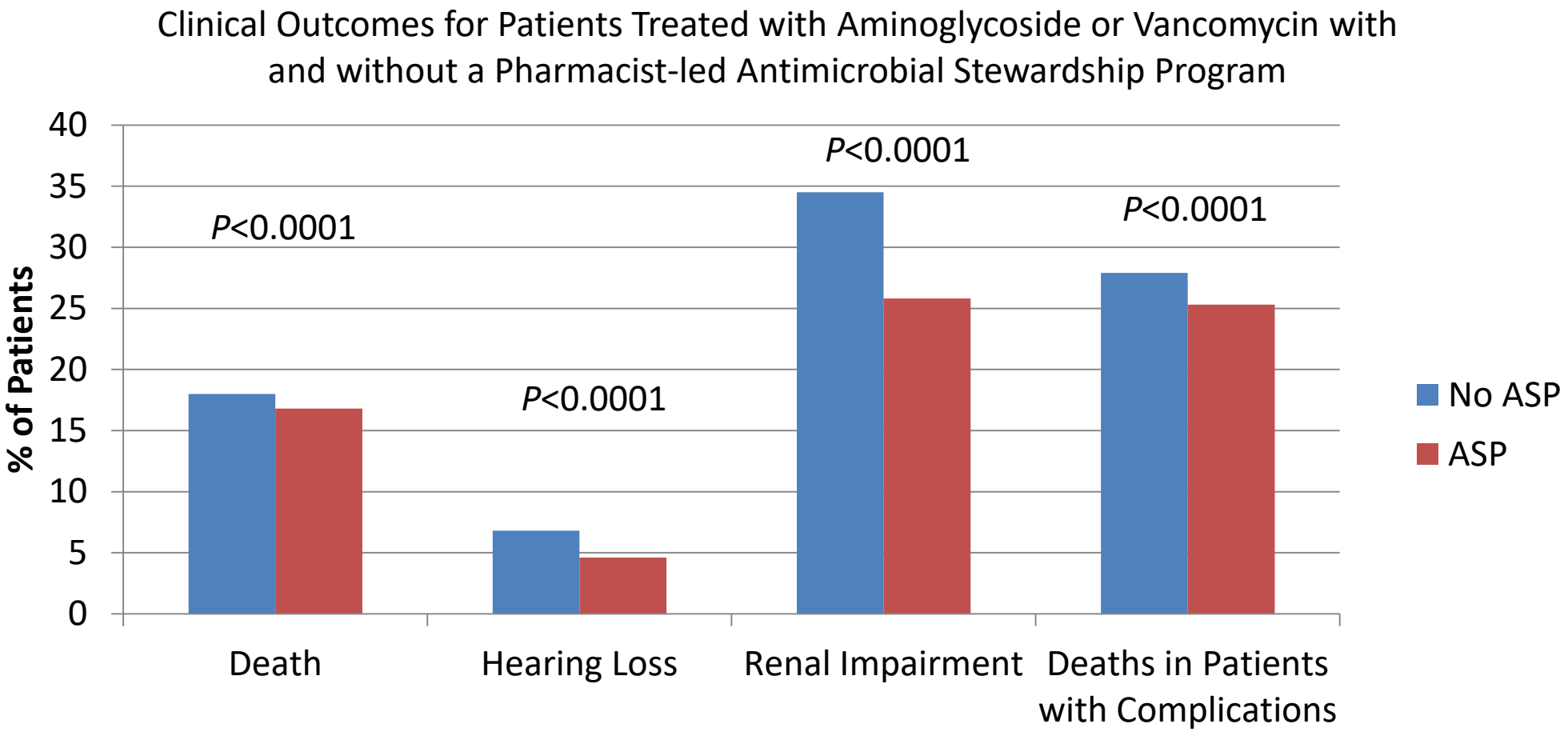
Decreased Toxicity and Improved Clinical Outcomes



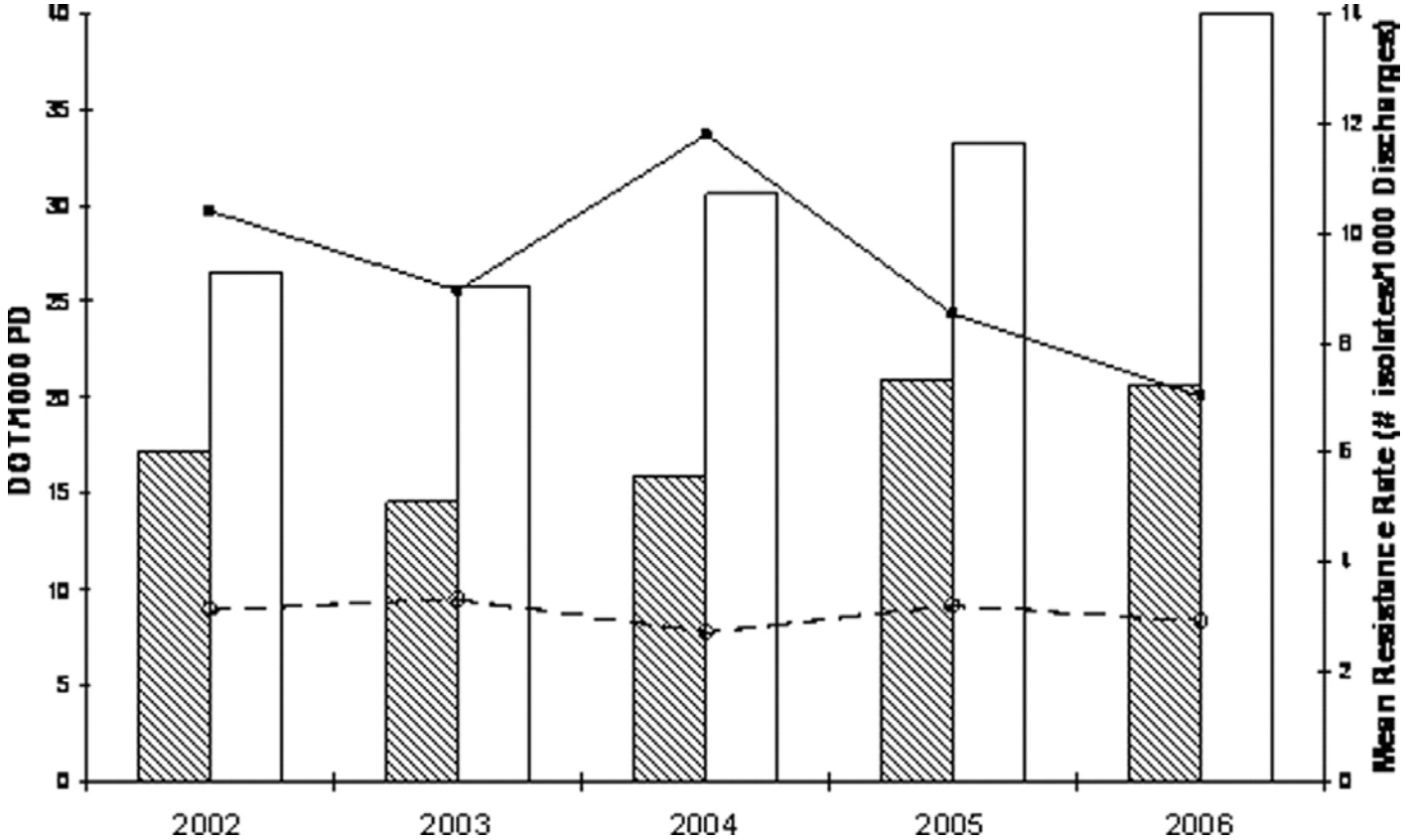
Fishman N. *Am J Med*. 2006;119:S53-61.

Decreased Toxicity and Improve Clinical Outcomes



Bond CA, Raehl CL. *Am J Health-Sys Pharm*. 2005;62:1596-1605.

Carbapenem Restriction and Resistance at 22 Centers



Mean carbapenem use (DOT/1,000 PD) was significantly lower in hospitals that restricted (shaded bars) versus did not restrict (open bars) carbapenems (P = 0.04)

Pakyz, et al. *Antimicrob Agents Chemother*. 2009;53:1983.

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Core AMS Program Strategies

- **Prospective review/audit with feedback**
  - Improve antibiotic use
  - Reduce antibiotic resistance
  - Reduce *Clostridium difficile* infection (CDI) rates
  - No increase in negative patient outcomes

- **Other options to enhance AMS:**
  - Prior Authorization
  - Education
  - Facility-Specific Clinical Practice Guidelines
  - Computerized Clinical Decision Support Systems
  - IV to PO
  - Micro lab – selective/cascade susceptibility reporting, rapid diagnostic testing

Clin Infect Dis 2016; 62(10):e51-e77.

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How to implement AMS program

- Guidelines published by IDSA and SHEA 2016
- **Core members of AMS team:**
  - Infectious disease physician
  - Clinical pharmacist (preferred with ID training)
  - Clinical microbiologist
  - Infection prevention professional
- Need support/collaboration of administration and local providers

Clin Infect Dis 2016; 62(10):e51-e77.

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Ways to Optimize Antimicrobial Use

- Use local hospital/system antibiogram to improve empiric therapy choices for common infections

- Interpret microbiology lab susceptibility report and de-escalate therapy to least broad agent that can treat infection when culture results are known

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ANTIBIOGRAMS - *Interpretative*

- Percent of strains (≥ 30 isolates) tested which are sensitive to a given antibiotic
- Published annually
- **Problems:**
  - duplicate isolates
  - non-pathogens tested
  - sampling bias
  - nosocomial vs community acquired strains
  - retrospective
  - qualitative

ANTIBIOGRAMS - *Example*

CHI Health Laboratories Antibiogram January - December 2015 Data are Percent Susceptible

GRAM NEGATIVE ORGANISM	# of isolates	Amikacin	Ampicillin	Ampicillin/Sulbactam	Aztreonam	Cefazolin[3]	Cefoxitin	Cefepime	Ceftazidime[3]	Ceftriaxone	Cefuroxime	Ciprofloxacin	Clindamycin	Ertapenem	Gentamicin	Levofloxacin	Meropenem[3]	Metronidazole	Nitrofurantoin[1]	Penicillin	Piperacillin/Tazobactam	Tetracycline	Tobramycin	Trimethoprim/ Sulfamethoxazole
Acinetobacter baumannii	86	85		81				65	66	52		50			58	52	81					59	64	56
Bacteroides fragilis group	36			89			72						56					100		0				
Citrobacter freundii	304	100			90			99+	88	86		91		99	90	93	100		94		96	79	90	83
Citrobacter koseri	124	100		93	98	98		100	98	99	81	86		100	98	88	100		84		100	93	100	87
Enterobacter aerogenes	197	100			88			99+	84	82		97		94	98	98	100		21		90	87	99	97
Enterobacter cloacae	447	99+			82			97	82	77		94		93	98	95	99+		27		86	85	97	89
Escherichia coli	9754	99+	54	59	94	92		95	94	94	90	76		100	92	77	100		97		97	75	92	75
Klebsiella oxytoca	374	100		69	91	59		97	96	93	87	92		99+	99+	94	100		94		93	90	99+	96
Klebsiella pneumoniae	1650	99+		83	95	96		96	95	95	91	94		99+	96	97	100		61		97	83	96	90
Morganella morganii	150	99+			92			99	87	88		53		98	80	60	100				100		89	53
Proteus mirabilis	1259	99+	85	93	96	92		98	97	98	97	51		99+	87	58	100				99+		90	69
Providencia rettgeri	50	100			84			98	78	100		84		100	100	88	100				92		100	98
Providencia stuartii	63	100			100			100	93	100		21		95	52	21	100				100		44	71
Pseudomonas aeruginosa	1264	95			74			83	89			69			77	68	86				96		92	
Serratia marcescens	175	99			87			98	85	87		84		98	97	92	98				85	17	93	95
Stenotrophomonas maltophilia[2]	129															79								98

[1] Urine isolates only
[2] Routinely only trimethoprim/sulfamthoxazole and levofloxacin are reported.
[3] Partial year results due to panel change

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ANTIBIOGRAMS - *Interpretative*

- **What are they used for?**
  - Guide empiric therapy to local hospital susceptibility patterns
  - Help clinicians avoid using antimicrobial agents that have higher reported resistance to most likely pathogens for infection being treated (i.e. *E. coli* for UTI)

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When is antimicrobial susceptibility testing (AST) performed in micro lab?

1) Isolate must be clinically significant, i.e. a (potential) pathogen

2) Antimicrobial susceptibility pattern of isolate is unpredictable

3) A standardized method is available for AST performance and interpretation on the isolate

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AST – Very Important Points

- In vitro AST results do not necessarily predict clinical efficacy

- The purpose of AST is to detect phenotypic RESISTANCE → this has a high correlation with clinical failure

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Important AST Definitions

- **MIC** – Minimum Inhibitory Concentration, lowest concentration of antibiotic which prevents growth of the bacteria; µg/mL
- **MIC Breakpoints -** critical antibiotic concentration (µg/mL) that the organism's MIC is compared with, to determine if the organism is susceptible, resistant or intermediate to the antibiotic. Determined by serum or body compartment (e.g. csf) concentration and other PK/PD data, after routine safe doses.
  - ***MIC breakpoints specific for each drug/organism – cannot directly compare MIC results between drugs***

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Important AST Definitions

- **Susceptible** (sensitive) - MIC of the antibiotic against the organism is at or below the susceptible breakpoint; ***the antibiotic has a high probability of clinical effectiveness***

- **Resistant** - MIC of the antibiotic against the organism is at or greater than the resistant breakpoint; ***the antibiotic has a low probability of clinical effectiveness (not recommended for use)***

- **Intermediate** - MIC of the antibiotic against the organism falls between the susceptible and resistant breakpoints; "gray zone", ***the clinical efficacy of antibiotic is questionable (not recommended for use except in extraordinary circumstances)***

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What is YOUR role in AMS?

- Include an indication with every antibiotic order
- Prescribe the narrowest spectrum antibiotic for the condition you are treating
- Review your antibiotic orders every day to make sure they are still indicated and appropriate
- Use evidence based treatment guidelines in determining choice of antimicrobial agent and length of therapy

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Summary

- AMS is now required per CMS in hospital setting starting January 1, 2017
- Can see great outcomes with reduced costs and increase in patient safety and quality of care
- CHI Health hoping to expand AMS in 2017 to more hospital sites
- AMS is a team approach with ID physicians, clinical microbiology, and pharmacy staff working together
- **Core principal for success** → prospective review/audit with feedback and real time education to health care providers