Strategies for Implementing Antimicrobial Stewardship Guidelines

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Objectives

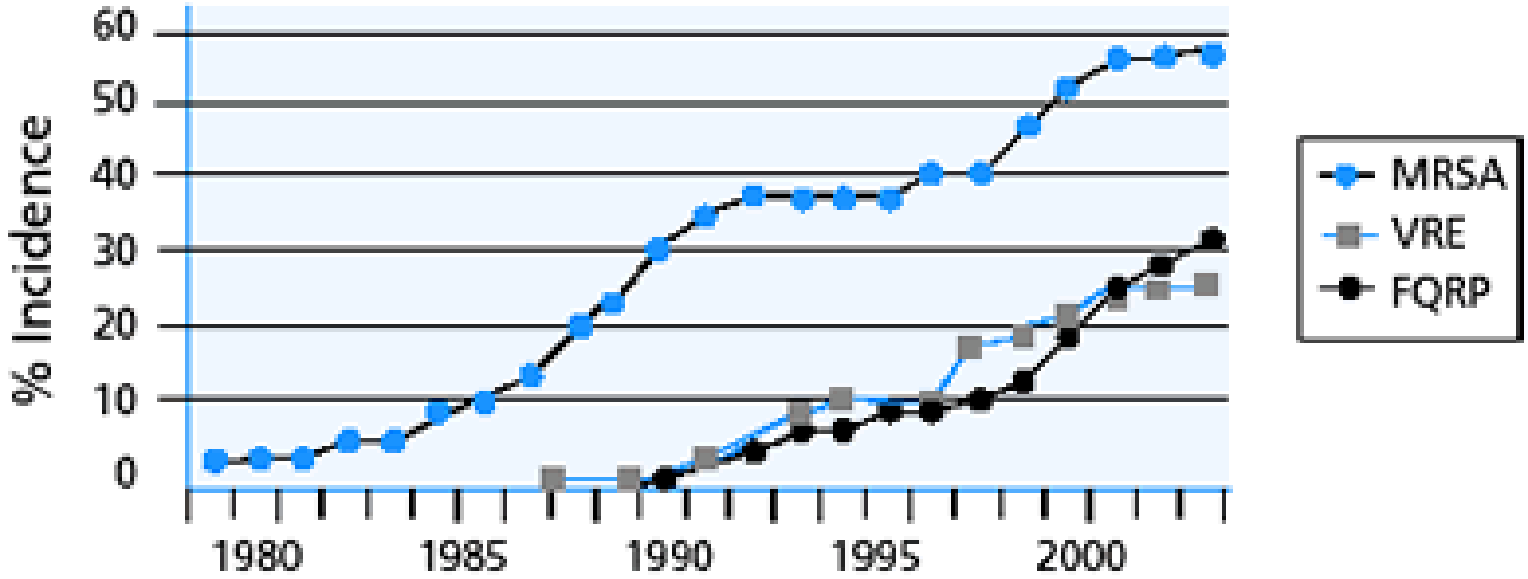
- Identify current antimicrobial practice guidelines
- Discuss strategies for complying with practice standards

Antimicrobial Resistance: a growing problem

- In 2004, approximately 2 million people experienced a hospital-acquired infection
- 90,000 of these infections were fatal
- 1 death every six minutes

Dellit TH. Clin Infect Dis 2007 Jan 15;44(2):159

Resistant Strains Spread Rapidly



Source: Centers for Disease Control and Prevention

MRSA = Methicillin-resistant *Staphylococcus Aureus*
VRE = Vancomycin-resistantant Enterococci
FQRP = Floroquinolone-resistant *Pseudomonas aeruginosa*

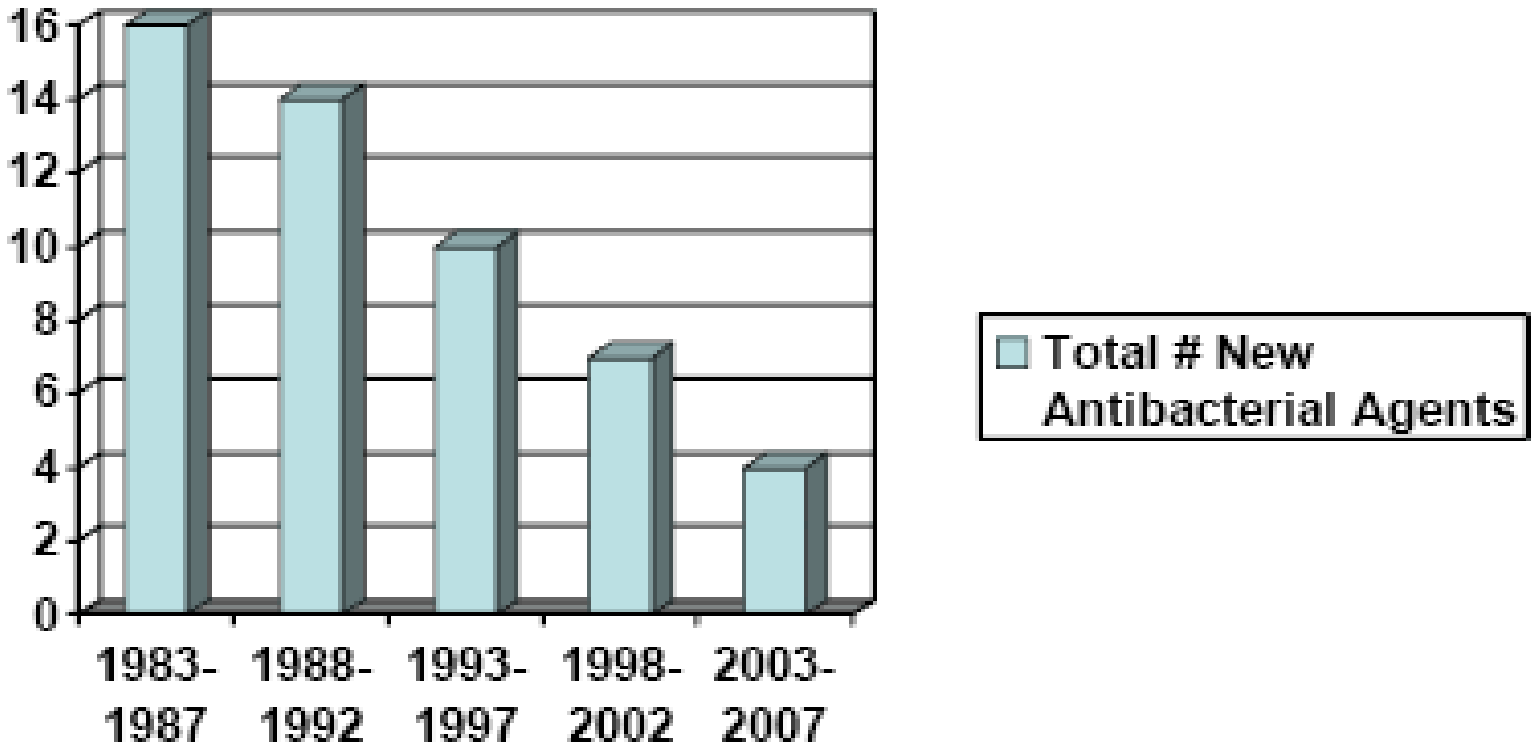
Accessed from http://www.idsociety.org/badbugsnodrugs.html February 1, 2008.

Infectious Diseases Society of America Superbug Hit List

- Methicillin-resistant *Staphylococcus aureus*
- Vancomycin-resistant *Enterococcus faecium* (VRE)
- *Escherichia coli*
- *Klebsiella* species
- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii*

Accessed from http://www.idsociety.org/badbugsnodrugs.html, February 20, 2008

Total Approved Antibacterials: US



Spellberg, et. al., *CID* May 1 2004, Modified

Accessed from http://www.idsociety.org/badbugsnodrugs.html February 1, 2008.

Antibacterials vs. Anti-HIV Agents

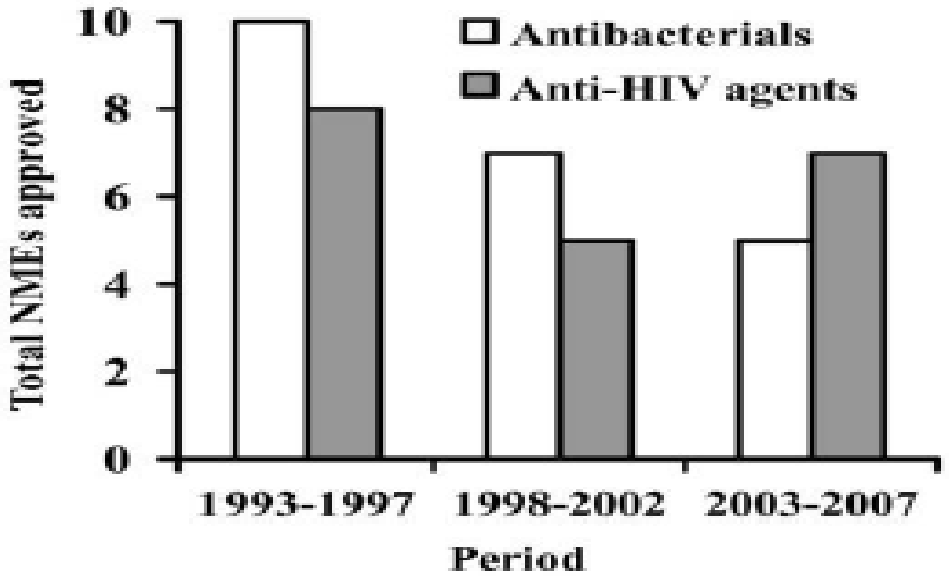


Figure 2. Antibacterial and anti-HIV new molecular entities (NMEs) approved by the US Food and Drug Administration, per 5-year period.

Spellberg, et al. Clin Infect Dis 2008 Jan 15;46:000

New Legislation

- Food and Drug Administration Amendments Act (2007)
- Strategies to Address Antimicrobial Resistance (STAAR) Act
- Research and development tax credits for infectious disease products

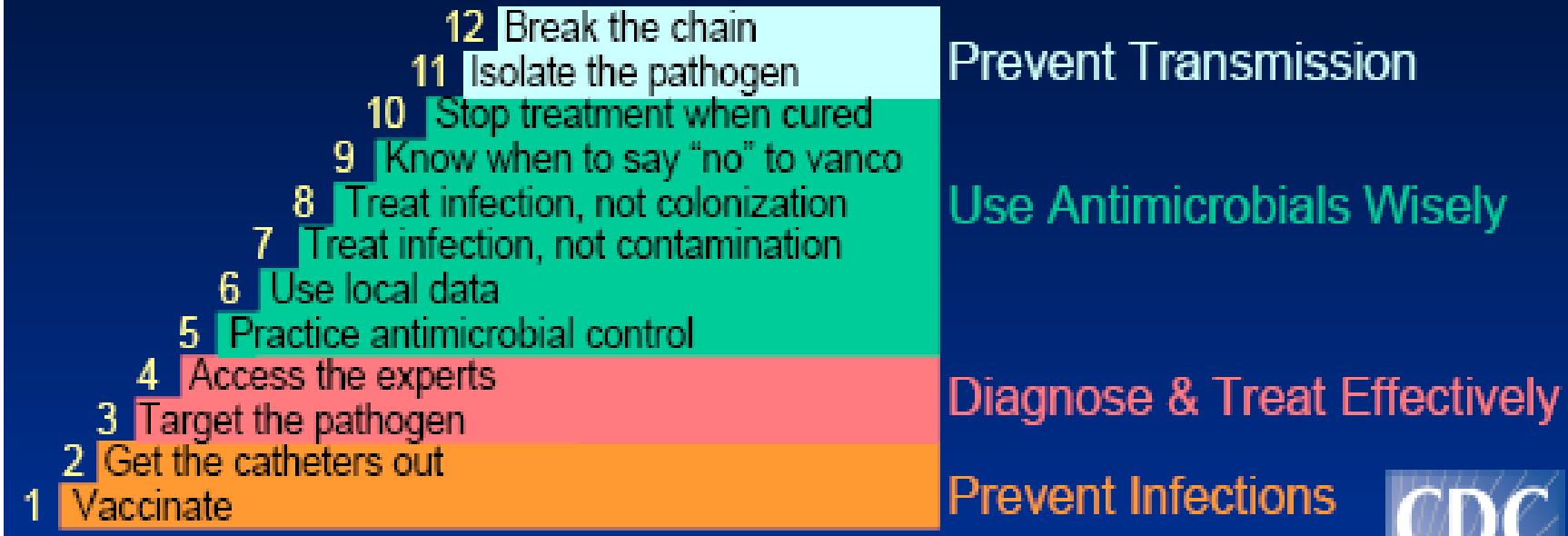
Spellberg, et al. Clin Infect Dis 2008 Jan 15;46:000

Health care professionals are already playing

with antimicrobials

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

Clinicians hold the solution…
Take steps NOW to prevent antimicrobial resistance!



Centers for Disease Control and Prevention (CDC) 12 steps to prevent antimicrobial resistance. http://www.cdc.gov/drugresistance/healthcare/ha/HASlideSet.pdf

The answer:

This activity can result in the best clinical outcome for the treatment **OR** prevention of infection with minimal toxicity and minimal impact on subsequent resistance.





What is: Antimicrobial Stewardship



Antimicrobial Stewardship

Defined:

the optimal **selection**, **dosage, route** and **duration** of antimicrobial treatment.

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Review of Antimicrobial Stewardship

1997: IDSA and Society of Health Care Epidemiology of America publish guidelines for preventing and reducing antimicrobial resistance in hospitals

1999: CDC, FDA, and NIH publish a public health action plan to combat antimicrobial resistance

2002: CDC launches 12 steps to prevent antimicrobial resistance in hospitalized adults campaign

2006: CDC releases Management of Multidrug-Resistant Organisms in Health Care Settings guidelines

2007: IDSA releases guidelines for developing institutional stewardship programs

Just in time?

October 2008: Medicare will stop reimbursement for hospital-acquired conditions deemed preventable. Several of these conditions are infection-related.

Shales DM. Clin Infect Dis 1997;25:584 – 99

Bell D. In: Knobler SL, Lemon SM, Najafi M, Burroughs T, eds. Forum on emerging infections. Washington DC: National Academy Press, 2003.

Centers for Disease Control and Prevention (CDC) 12 steps to prevent antimicrobial resistance. http://www.cdc.gov/drugresistance

Siegel JD. Centers for Disease Control and Prev; 2006: 74

Dellit TH. Clin Infect Dis 2007 Jan 15;44(2):159

Antimicrobial Stewardship

- Primary Goal: to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use
  - Consequences
    - Toxicity
    - Selection of pathogenic organisms
    - Emergence of resistant pathogens
- Secondary goal: to reduce health care costs without adversely affecting the quality of care

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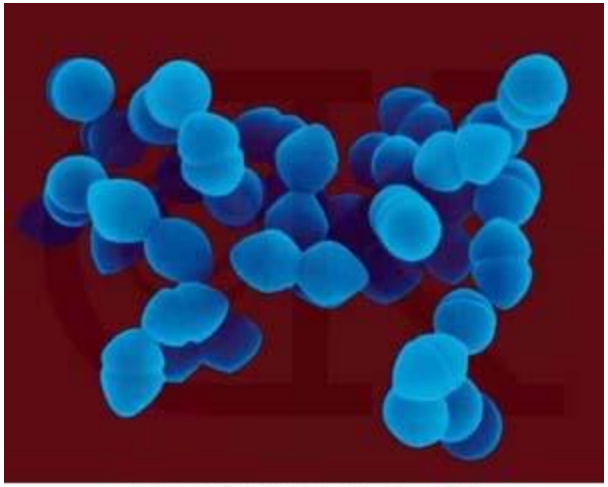
Aspects of antimicrobial stewardship applied…



Vancomycin resistant *E faecium*.
Downloaded from
http://www.buddycom.com/bacteria/gpc/Efaecium.jpg December 17, 2007.

Results of an Antimicrobial Control Program

- University of Kentucky Chandler Medical Center
- Impact of first five years of an ongoing antimicrobial management program (1998 – 2002)
- Report published in American Journal of Health-System Pharmacy in 2005

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Methods

- Formed antimicrobial subcommittee within Pharmacy and Therapeutics committee
  - Representatives from surgery, pediatrics, internal medicine, transplantation, critical care, infectious disease, pharmacy and nursing

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Methods

- Subcommittee responsibilities
  - Develop and implement initiatives to ensure appropriate antimicrobial use
  - Review the existing formulary and recommend cost effective agents that may reduce the selection of resistant nosocomial pathogens

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Cephalosporins

- Ceftazidime and Cefotaxime removed from formulary
  - Association with increased risk of MDR gram negative organisms and VRE
- Ceftriaxone limited to treatment of CAP, meningitis and UTIs
- Penicillin regimens endorsed for most infections
- Cefepime added for nosocomial infections in patients intolerant of PCNs

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Vancomycin

- Internal audit → poor compliance with CDC Hospital Infection Control Practices Advisory Committee (HICPAC) guidelines
    - CDC. Recommendations for preventing the spread of vancomycin resistance. MMWR 1995;44:RR-1
- Mandatory 72-hour stop time unless “vancomycin continuation form” was completed on return of culture and sensitivity data
- Agent was discontinued if patient did not meet criteria within 72 hours
- ID consult required to override automatic discontinuation

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Fluoroquinolones

- Levofloxacin replaced ciprofloxacin as formulary fluoroquinolone (May 2001)
- Ciprofloxacin associated with resistance in multiple common pathogens
- Cost to have both ciprofloxacin and levofloxacin on formulary prohibitively high

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Carbapenems

- Inappropriate use associated with MDR *Pseudomonas aeroginosa* and *Acinetobacter baumannii*
- Use restricted to documented infections with extended-spectrum β-lactamase producing organism or organism otherwise resistant

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Amphotericin B formulations

- All lipid formulations restricted
- ID approval required before use

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Monitoring

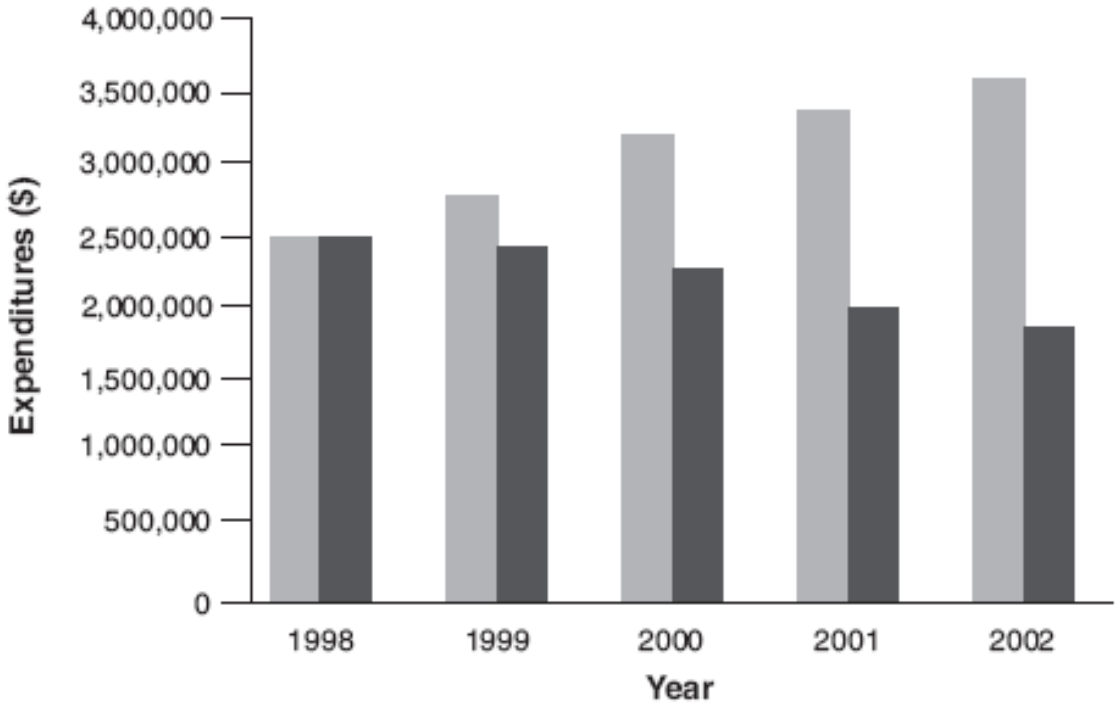
- Susceptibility rates of key pathogens reported on quarterly by clinical microbiology laboratory
- Antimicrobial expenditures reported on quarterly by the pharmacy financial officer
  - Compared with baseline (1998) and adjusted for inflation of drug acquisition costs
  - Purchases also monitored by defined daily doses/1000 patient days

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Expenditures

1998 – 2002 expenditures decreased by 25% (total savings of $1,401,126)

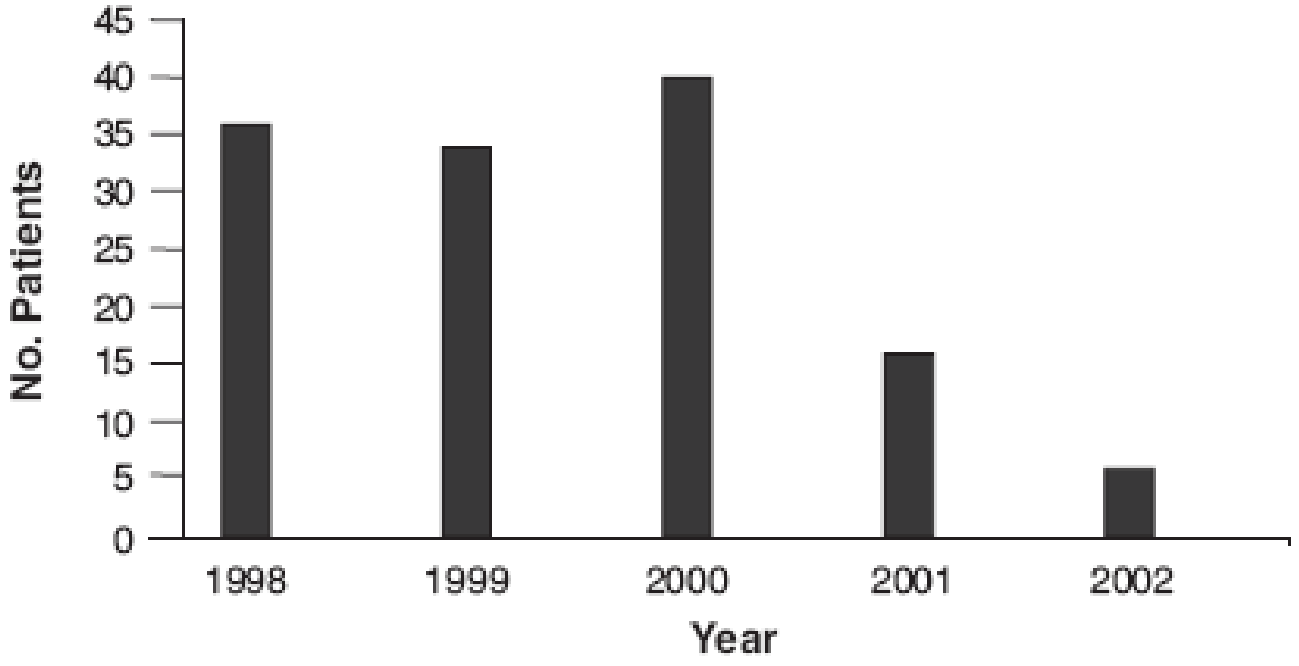
Figure 1. Expected (gray bars) and actual (black bars) antimicrobial expenditures, assuming 10% inflation per year and adjusted for fluctuations in inpatient days.



Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Antimicrobial Susceptibility and Resistance

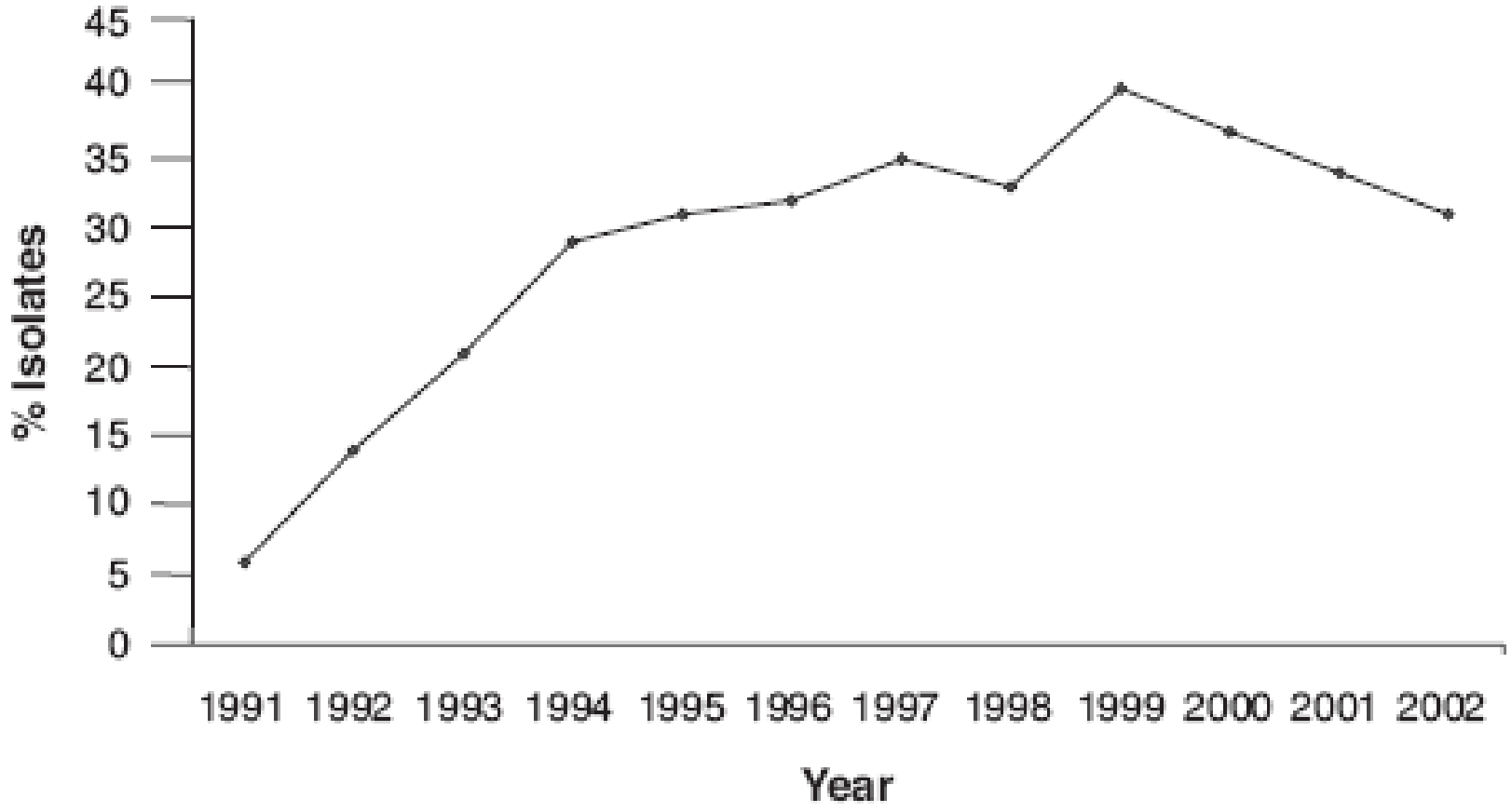
Figure 2. Patients with multidrug-resistant *Pseudomonas aeruginosa* isolates. Multidrug-resistant was defined as susceptible to one or none of the following agents: piperacillin–tazobactam, cefepime, ceftazidime, aztreonam, meropenem, imipenem, tobramycin, gentamicin, amikacin, ciprofloxacin, and levofloxacin. Duplicate patients were excluded.



Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Antimicrobial Susceptibility and Resistance

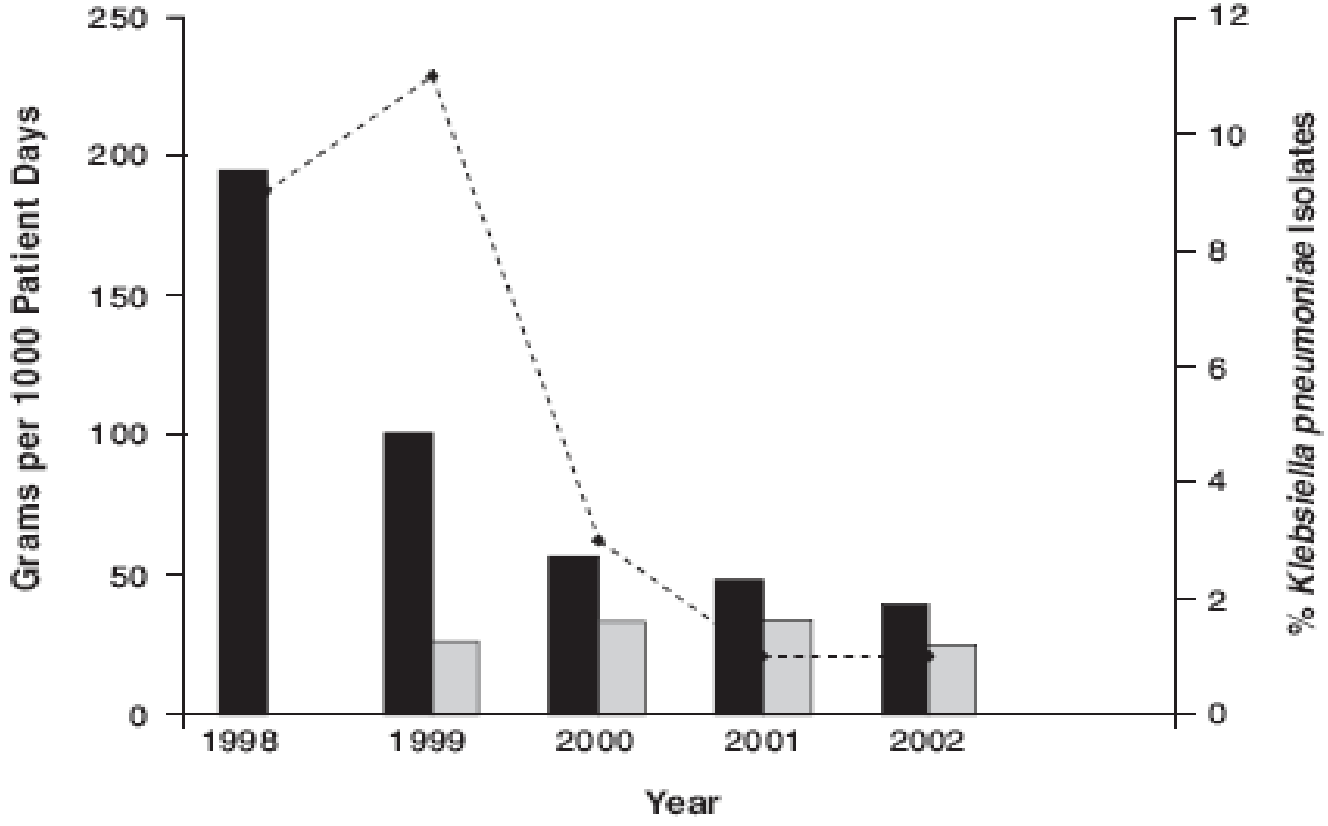
Figure 3. Percentage of all *Staphylococcus aureus* isolates resistant to methicillin.



Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Antimicrobial Susceptibility and Resistance

Figure 4. Defined daily doses per 1000 patient days of third-generation cephalosporins (black bars) and cefepime (gray bars) purchased compared with ceftazidime-resistant *Klebsiella pneumoniae* isolates (dashed line).



Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Tools for Success

- Multidisciplinary team
- Periodic feedback to physicians regarding program's benefits
- Focused goals

Martin et al. Am J Health-Sys Pharm 2005 Apr 1; 62: 732 - 738

Back to the guidelines...

Centers for Disease Control Guidelines for Multidrug-Resistant Organisms in Healthcare Settings (2006).

Siegel JD. Centers for Disease Control and Prev; 2006: 74

Infectious Disease Society of America Guidelines for Developing Institutional Programs to Enhance Antimicrobial Stewardship

Dellit TH. Clin Infect Dis 2007 Jan 15;44(2):159

Centers for Disease Control Guidelines for Multidrug-Resistant Organisms in Healthcare Settings (2006)

- Developed by experts in infection control in conjunction with CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC)

- Stresses the causal relationship between antibiotic use and resistance patterns

Siegel JD. Centers for Disease Control and Prev; 2006: 74

Centers for Disease Control Guidelines for Multidrug-Resistant Organisms in Healthcare Settings (2006)

- Staffing and funding for prevention programs
- Track infection rates
- Use standard infection control practices

Siegel JD. Centers for Disease Control and Prev; 2006: 74

Centers for Disease Control Guidelines for Multidrug-Resistant Organisms in Healthcare Settings (2006)

- Follow guidelines regarding the correct use of antibiotics
- Role of health education campaigns → increased adherence
- Prevention programs customized to specific settings/ local needs

Siegel JD. Centers for Disease Control and Prev; 2006: 74

Infectious Disease Society of America Guidelines for Developing Institutional Programs to Enhance Antimicrobial Stewardship

- Published in the official journal of the IDSA: Clinical Infectious Diseases
- Includes IDSA ranking system for clinical guidelines
- Contains recommendations for hospital-based stewardship programs (no outpatient recommendations)

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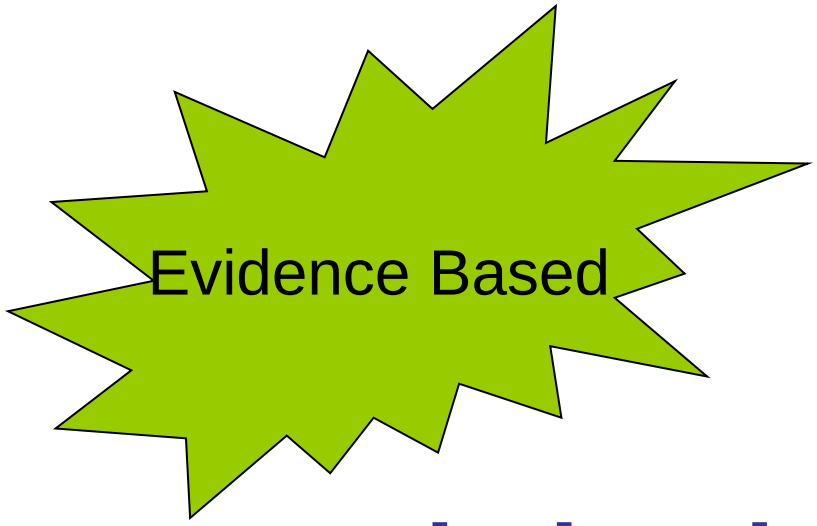

Antimicrobial Stewardship Programs

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IDSA Guidelines: Elements of a successful stewardship program

- Comprehensive program
  - Active monitoring of resistance
  - Fostering of appropriate use
    - Often used as a surrogate marker for impact on resistance
  - Collaboration of effective infection control to minimize secondary spread of resistance

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IDSA Guidelines: Collaborative effort

- Multidisciplinary team

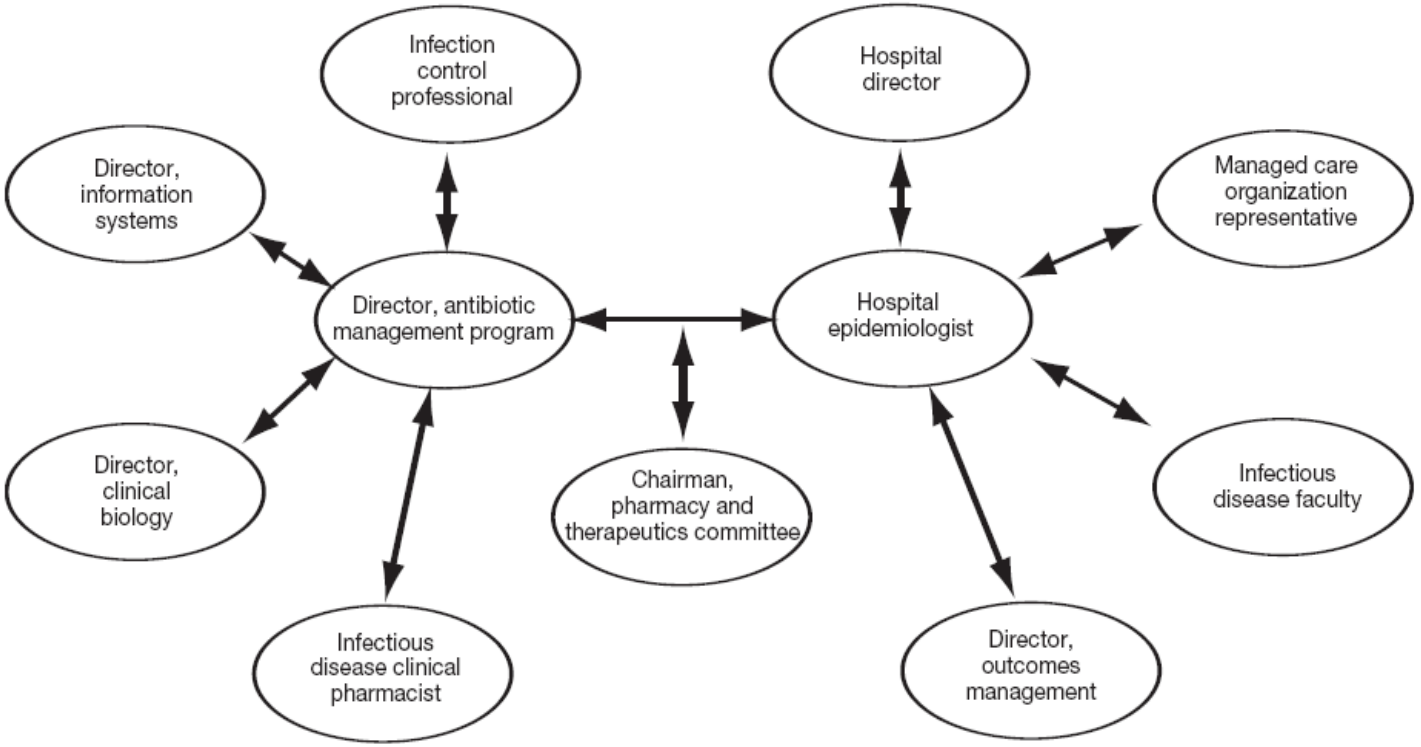

Figure 2. Multidisciplinary members of the antimicrobial stewardship team. (Adapted from reference 6.)

Rybak M. Pharmacotherapy; 27:131S

Infectious Disease Pharmacist

- Qualifications
  - Pharm.D. degree
  - PGY1 Pharmacy Residency
  - Additional training in infectious diseases
    - ID specialty residency preferred
  - Maintain current knowledge base

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Rapp R. 41st ASHP Midyear Clinical Meeting, 2006.

Infectious Disease Pharmacist

- Duties
  - Provide interventional feedback for antimicrobial therapies
  - Collaborate with infectious disease physician
  - Follow clinical outcomes
  - Provide pharmacokinetic services

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Rapp R. 41st ASHP Midyear Clinical Meeting, 2006

Infectious Disease Pharmacist

- Duties, con't
  - Educate hospital staff on appropriate antibiotic usage
  - Precept and mentor pharmacy students, pharmacy practice residents and infectious disease specialty residents
  - Review antibiogram regularly

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Rapp R. 41st ASHP Midyear Clinical Meeting, 2006

IDSA Guidelines: Key Recommendations

- Two proactive core strategies:
  - Prospective audit with intervention and feedback to prescriber
  - Formulary restriction and preauthorization

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Prospective Audit

- ID pharmacist and physician work together
- Select drugs and units
- Review cases and make recommendations within certain time frame after drug is ordered
  - Appropriate drug
    - Bug-drug
    - Streamlining/de-escalation
  - Dose
  - Route

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Formulary Restriction and Preauthorization

- Stewardship team works closely with Pharmacy and Therapeutics Committee to designate restricted drugs and evidence-based indications
- Pager for authorization
- Success depends on who is authorizing
- Challenges:
    - May shift resistance to alternative agent
    - Must monitor trends

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IDSA Guidelines: Additional Recommendations (Level A)

- Education
  - Essential, but insufficient alone
- Development of guidelines and clinical pathways
  - Can improve utilization
  - Can decrease amount of critical thinking

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IDSA Guidelines: Additional Recommendations (Level A)

- Streamlining or de-escalation of therapy
- Dose optimization
- Parenteral to oral conversion

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IDSA Guidelines: Additional Recommendations (Level A)

- Optimization of health care information technology

- Integral role of clinical microbiology lab for rapid return of cultures and sensitivities and trend surveillance

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IDSA Guidelines: Additional Recommendations (Levels B & C)

- Antimicrobial order forms
  - may be an effective component of stewardship
- Computer-based surveillance
  - increased efficiency in targeting interventions, tracking resistance patterns, and identifying nosocomial infections

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IDSA Guidelines: Additional Recommendations (Levels B & C)

- Antimicrobial cycling: insufficient data; not recommended
- Combination therapy: role in certain clinical contexts but routine use not recommended
- Monitor process and outcome measures to determine impact of stewardship program

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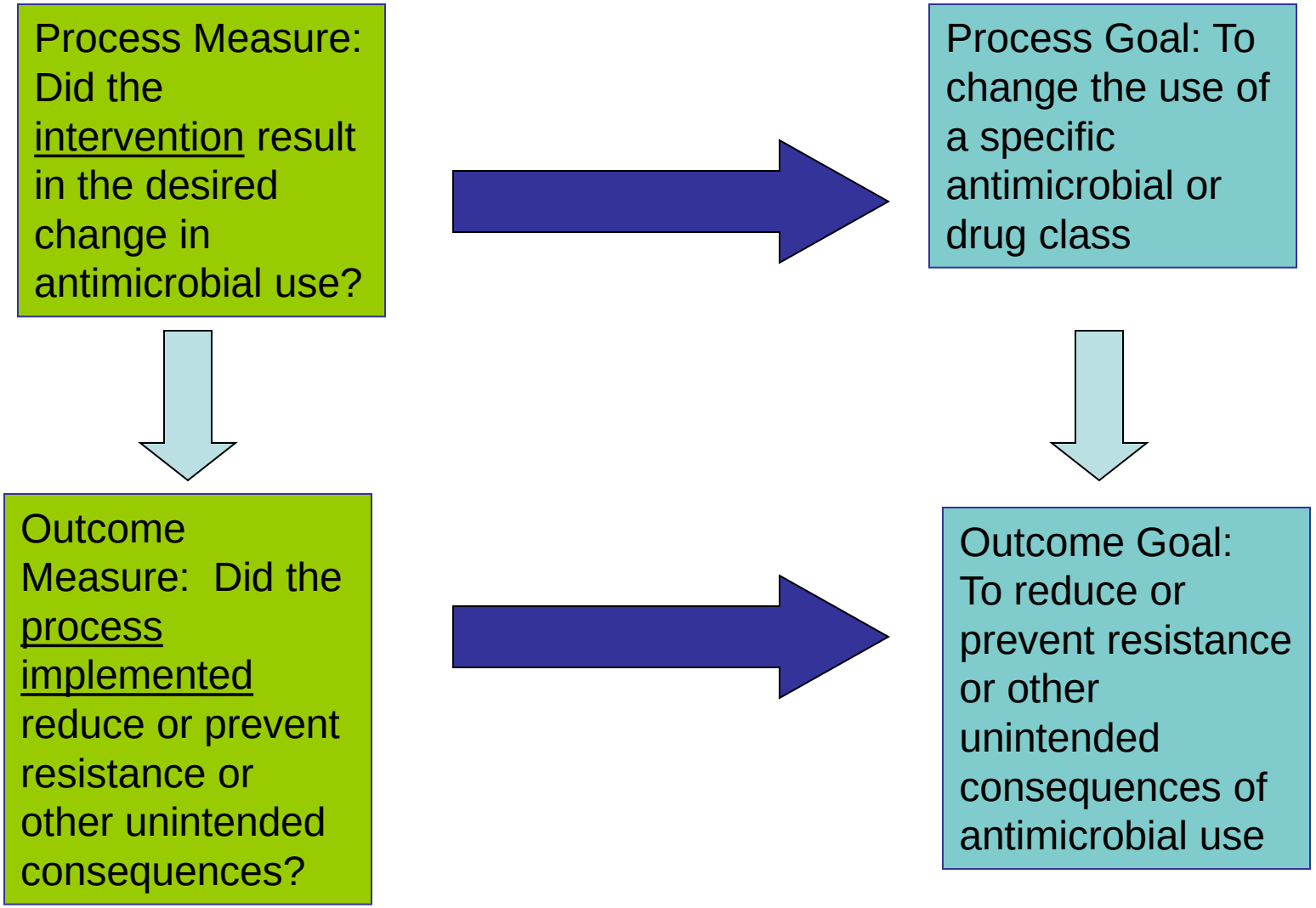
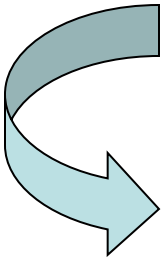
Determining the Impact of Stewardship



Front End Components

- Prior Authorization
- Health care information technology/clinical decision support
- Guidelines/order sets



Antibiotic Order

Back End Components

- Feedback audit
- Streamlining/de-escalation
- Dose optimization
- IV to PO conversion

Future Directions

- Antimicrobial cycling
- Clinical validation of heterogeneous use theory
- Long-term impact of programs
- Bundled programs
- Effectiveness in subpopulations
- Molecular epidemiology to understand the resistance gene pool
- Automated surveillance strategies for nosocomial infections
- Incorporation of stewardship into CPOE

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Getting Started

- IDSA practice guideline
  - Clin Infect Dis 2007 Jan 15;44(2):159
- Assess current climate of use
  - Identify potential barriers
- Develop proposal
- Present proposal to P&T; develop stewardship subcommittee with other hospital team members

McLeod Health Survey

ANTIBIOTIC USE SURVEY
MCLEOD HEALTH

Profession_____ Sub-specialty or unit_____

Rate on a scale from 1-5 (1 = strongly disagree, 5=strongly agree) which of the following you feel are problems limiting the safe and efficacious management of antibiotics at MRMC:

Antibiotics active against resistant organisms are over-used as empiric therapies Ex. Vancomycin or Primaxin® used without cultures confirming resistant organisms or clinical evidence to indicate the presence of resistant organisms	1	2	3	4	5
Empiric therapies are not narrowed on return of culture and sensitivities	1	2	3	4	5
Different services order redundant antibiotics on the same patient	1	2	3	4	5
Lack of familiarity with new antibiotic therapies, indications, and side effects	1	2	3	4	5
Navigation of culture results on Net Access® is time-consuming	1	2	3	4	5
Lack of uniform method for monitoring duration of antibiotic therapy (pharmacy system or charting)	1	2	3	4	5
Hospital antibiogram is difficult to locate	1	2	3	4	5
Hospital antibiogram is difficult to understand	1	2	3	4	5
Sensitivity data from lab is difficult to use	1	2	3	4	5
Clinical microbiology lab resources are difficult to reach	1	2	3	4	5
Infection control techniques are not consistently followed during patient care Ex. Not employing contact precautions for patients on isolation (yellow gowns, gloves, etc.)	1	2	3	4	5
No standardized method of monitoring infection trends by floor or unit	1	2	3	4	5

Please record any additional issues/concerns you have noticed regarding antibiotic management at MRMC:

_____
_____
_____

Rate on a scale from 1-5 (5= strongly agree) which of the following changes would have the greatest impact on improving antibiotic therapy at MRMC:

Implementing a closed-formulary system for certain antibiotics Ex. Reserved antibiotics could only be ordered by consulting pre-designated services	1	2	3	4	5
Implementing a system of prospective audit and intervention of certain antibiotics within 24-hours of starting therapy	1	2	3	4	5
Increased education regarding the appropriate use of certain antibiotic therapies	1	2	3	4	5
Reconciling the return of cultures and sensitivities with selected antibiotic therapies by patient care area or service	1	2	3	4	5
Employing additional clinical pharmacists to follow culture results and make recommendations for antibiotic therapy	1	2	3	4	5
Consolidating the results of all cultures and sensitivities available on Net Access® to one web-page	1	2	3	4	5
Notification of duration of therapy via automatic electronic reminders or purple communication notes	1	2	3	4	5
Restructuring of hospital antibiogram	1	2	3	4	5
Availability of antibiogram at every chart, nurses station, or via a prominent location on the intranet	1	2	3	4	5
Restructuring of sensitivity data from lab to reflect sensitivity to formulary agents	1	2	3	4	5
Target monitoring of infection control improvements institution-wide and report regularly to staff	1	2	3	4	5

Please record additional ideas for improvement below:_____

_____
_____
_____

Getting Started

- IDSA practice guideline
  - Clin Infect Dis 2007 Jan 15;44(2):159
- Assess current climate of use
  - Identify potential barriers
- Develop proposal
- Present proposal to P&T; develop stewardship subcommittee with other hospital team members

Getting Started

- Hire ID physician and pharmacist
- Develop guidelines
- Educate medical staff
- Obtain physician buy-in
- Implement changes
- Track outcomes

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Getting Started: Smaller Institutions

- Scaled-down model
  - LaRocco A. Clin Infect Dis 2003; 37:742-3
- ID physician and clinical pharmacist employed part-time
- Reviewed patients receiving
  - Multiple
  - Prolonged
  - High-cost courses of therapy
- 69% of recommendations accepted
- Cost savings estimated at $177,000


STEWARDSHIP BOARD!

$100

The answer:

The only class of drugs where use in one patient may alter future efficacy in another patient.

What are antimicrobials?

$200

The answer:

- Prevent transmission
- Use antimicrobials wisely
- Diagnose and treat effectively
- Prevent infections

What are the major components to the CDC's 12 steps to reduce antibiotic resistance?

$300

The answer:

A surrogate marker often used by antimicrobial stewardship programs to predict the avoidable impact on community resistance profiles.

What is inappropriate antibiotic use?

$400

The answer:

A core strategy of the IDSA guidelines that allows clinicians to order antibiotics without prior authorization but intervention can occur following treatment initiation.

What is prospective review and intervention?

$500

The answer:

A significant benefit to antimicrobial stewardship programs that results in many programs being self-supporting.

What is cost-savings?

$600

The answer:

This person contributes to the stewardship team by providing interventional feedback to physicians, working closely with the infectious disease physician, providing pharmacokinetic services, and educating hospital staff on appropriate antibiotic use.

Who is the infectious disease pharmacist?

$700

The answer:

Narrowing therapy upon return of cultures and sensitivities to more targeted therapy to decrease antimicrobial exposure and contain cost.

What is streamlining or de-escalation of therapy?

$800

The answer:

Aspect of stewardship that can result in decreased length of stay, reduced hospital costs and fewer potential complications due to prolonged IV access.

What is IV to PO conversion?

$900

The answer:

Amount of antibiotic given that accounts for:

- individual patient characteristics (age, renal function, weight)
- causative organism and site of infection (endocarditis, meningitis, osteomyelitis)
- and pharmacokinetic/dynamic characteristics of the drug

What is dose-optimization?

$1000

The answer:

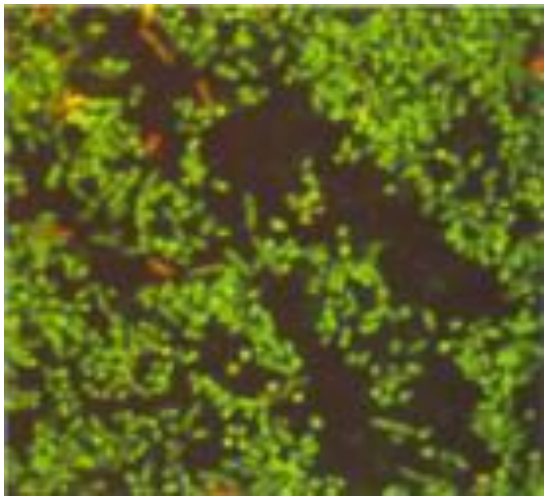
- Prior Authorization
- Health care information technology/ clinical decision support
- Guidelines/order sets

What are front-end components of antimicrobial stewardship?

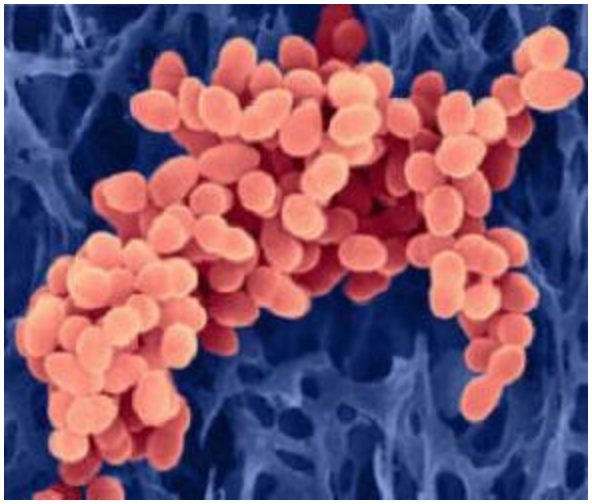
Conclusions

- Antibiotic stewardship programs can result in increased patient safety, improved community resistance profiles, and significant cost savings.
- Stewardship programs should be implemented in all health care facilities as per the 2007 IDSA guidelines.

QUESTIONS



ESBL Klebsiella.
http://www.biomarker.cdc.go.kr:8080/pathogenimg/Klebsiella



MRSA.
http://www.mrsaresources.com/images/MRSA Superbug.JPG