

# Practical Implementation of Antibiotic Stewardship: A Pharmacist Approach to Overcoming Barriers

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# USPHS Scientific and Training Symposium

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# Faculty Disclosure

- Employee of Comprehensive Pharmacy Services

# Objectives

- Identify common barriers of antimicrobial stewardship programs
- Formulate solutions to design a practical antimicrobial stewardship service
- Apply specific steps that pharmacists may take to ensure successful outcomes

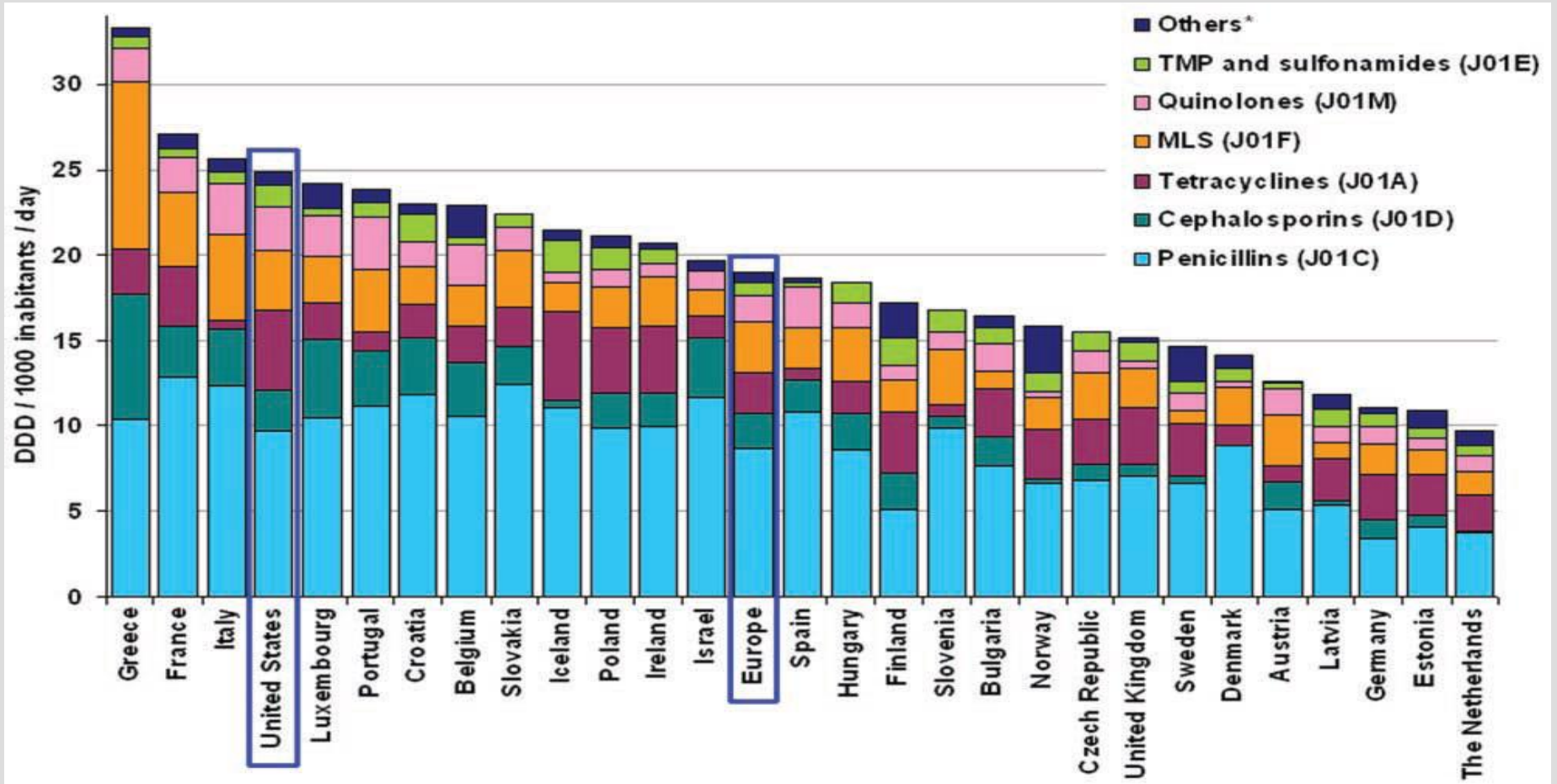
# Stewardship

- Definition: “the careful and responsible management of something entrusted to one’s care”  
[www.webster.com/dictionary/stewardship](http://www.webster.com/dictionary/stewardship)
- Antimicrobial Stewardship is this definition as it applies to anti-infective agents

# Why Stewardship?

- Up to 50% of antimicrobial use is inappropriate (begets resistance)
- New agents and new classes are slow
  - ✓ Increased use of polymyxin
  - ✓ Expansion of desensitization
- Resistant microbes lead to poor outcomes
- Stewardship independently associated with survival
- Government entities now require stewardship
- Medication safety and patient safety

# Antibiotic Use



Clin Infect Dis 2007(44): 1091

# Resistance and Outcomes

<b>Outcome</b>	<b>Uninfected Control Subjects (n=193)</b>	<b>Patients with MSSA SSI (n=165)</b>	<b>Patients with MRSA SSI (n=121)</b>	<b>MSSA group vs. control group</b>	<b>MRSA group vs. control group</b>	<b>MRSA group vs. MSSA group</b>
<b>Death</b>	4 (21)	11 (6.7)	25 (20.7)	.04	<.001	<.001
<b>LOS</b>						
After surgery	5 (3-8)	15 (7-25)	23 (12-38)	<.001	<.001	<.001
After infection	N/A	10 (4-17)	15 (7-30)	N/A	N/A	.001
ICU stay after infection	N/A	0 (0-1)	0 (0-3)	N/A	N/A	.02
<b>Hospital charges</b>	29,455	52,791	92,363	<.001	<.001	<.001

CID 2003; 36:592-8



# Resistance and Outcomes

<b>Characteristic</b>	<b>Cephalosporin Resistant <i>Enterobacter</i> (n=46)</b>	<b>Cephalosporin Susceptible <i>Enterobacter</i> (n=113)</b>	<b>P value</b>
Death	12 (26.1)	15 (13.3)	.06
LOS	29.5 (20-60)	19.0 (13-27)	<.001
Hospital Charges	79,323	40,406	<.001

# Goals of Program

- Limiting inappropriate use
  - ✓ “The most important decision is not what antibiotics to use, but whether to use antibiotics at all”
- Optimizing antimicrobial selection
  - ✓ Dosing
  - ✓ Route
  - ✓ Duration of therapy
- Limiting unintended consequences
  - ✓ Resistance
  - ✓ Adverse drug events
  - ✓ Cost

Quote, Ed Swiatlo

# Program Membership

- Core members
  - ✓ ID physician
  - ✓ ID pharmacist
- Team members
  - ✓ Clinical microbiologist
  - ✓ Information systems specialist
  - ✓ Infection control professional
  - ✓ Hospital epidemiologist
- Collaboration with P&T and hospital administration is essential to success

# Stewardship Strategies

- Prospective Audit and Feedback (Primary Strategy)**
- Formulary Restriction and Preauthorization (Primary Strategy)**
- Education
- Guidelines/Clinical Pathways
- Antibiotic Order Forms
- De-escalation
- Dose Optimization
- IV to PO
- Clinical Laboratory
- Antibiotic Cycling (not recommended)
- Combination Therapy (not recommended)

# Question 1

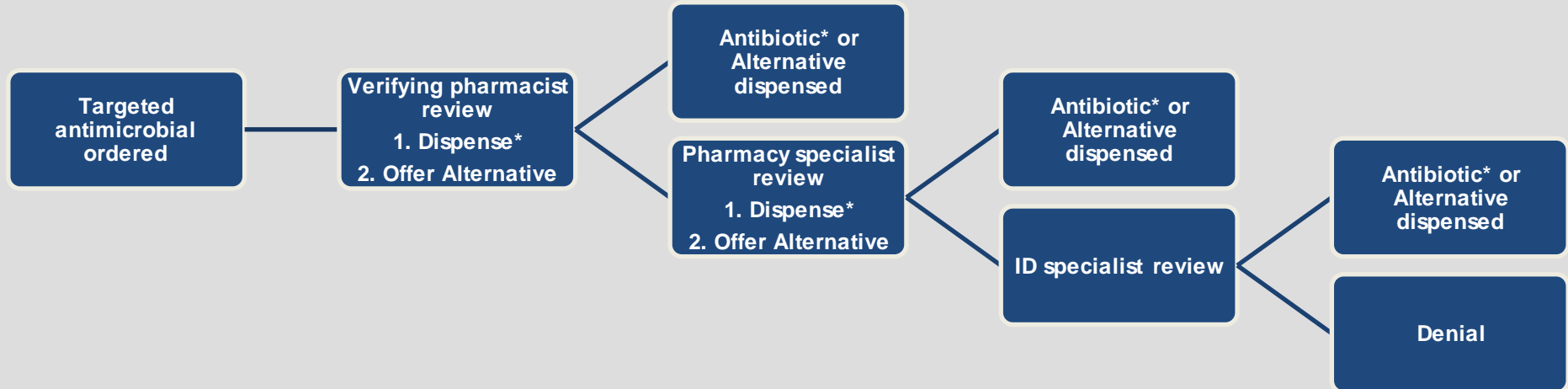
Which is the best primary strategy?

- A. Prospective audit and feedback
- B. Criteria based antibiotics
- C. Antibiotic restriction

# Primary Strategies

- Prospective audit and feedback (PAF)
  - ✓ Targeted antimicrobials reviewed for appropriateness before dispense
    - Smaller hospitals review within 24-48 hours
- Criteria-based antibiotics
  - ✓ Targeted antimicrobials held unless patient meets specific criteria
    - Requires an override procedure
    - Criteria must be firm (i.e. no “other indication” box)
- Antibiotic restriction
  - ✓ Targeted antimicrobials require specialist approval
    - Fallen out of favor
    - Creates an unsavory hierarchy
    - Consult intimidation

# Prospective Audit vs. Criteria



\*Overrides at any level reviewed monthly/quarterly

# Prospective Audit vs. Criteria

## Prospective Audit

- Pros
  - Effective
  - Thorough
- Cons
  - Time consuming
  - Slow results

## Criteria/Restriction

- Pros
  - Most effective
  - Fast results
- Cons
  - Tends to cause more conflict
  - More time to finalize protocol



# Preauthorization

- Comparison of three programs
  - ✓ Hospital-wide preauthorization
  - ✓ Preauthorization for non Intensive Care Units (ICU)
  - ✓ Post dispensary review
- Endpoint – consumption of piperacillin/tazobactam, fluoroquinolones, carbapenems, broad-spectrum cephs

Program	Consumption DDD/1000PD
Hospital-wide preauthorization	109.3
Preauthorization non-ICU	179.2
Post dispensary review	168.5

- Only hospital-wide preauthorization decreased resistance

# Prospective Audit vs. Criteria

- Before and after study of restriction vs. restriction/PAF

## Criteria

Aztreonam  
Ceftazidime  
Cefepime  
Levofloxacin  
Meropenem  
Piperacillin/tazobactam  
Vancomycin  
Antifungals

## Criteria/PAF

Criteria:  
Aztreonam  
Ceftazidime  
Levofloxacin  
Meropenem  
Antifungals

PAF:  
Cefepime  
Piperacillin/tazobactam  
Vancomycin

# Prospective Audit vs. Criteria

- Gram (-) agents moved to PAF increased significantly (p=0.03)
  - ✓ Those kept on Criteria decreased
  - ✓ Overall use increased (p<0.001)
- Length of stay increased (p=0.016)
- Length of stay after first antimicrobial dose increased (p=0.004)

# Question 1

Which is the best primary strategy?

- A. Prospective audit and feedback
- B. Criteria based antibiotics
- C. Antibiotic restriction

# Education

- Includes physicians, pharmacists, mid-level practitioners, administrators, nurses, etc.
- Effective, but short-lived, results
- Plan something every 90 days, at least
  - ✓ Live presentations
  - ✓ Newsletters
  - ✓ Section meetings
  - ✓ Note: Education should do beyond P&T; use a variety of settings

# Guidelines

- Guidelines and Clinical Pathways
  - ✓ Should contain formulary agents with limited resistance liability
  - ✓ Ideal to contain deescalation advice and stop dates
    - Antibiotic revisit
    - Goal: > 80% antibiotics written with a stop date
- Antibiotic Order Forms
  - ✓ Useful for restricted or criteria based antibiotics
  - ✓ Require vetting by pharmacy and/or stewardship team
  - ✓ Can be useless without follow-up
  - ✓ Maximize computerized physician order entry

# De-escalation

- Very powerful
- Review all antibiotics at 48-72 hours
- Make a decision
  - ✓ Stop therapy
  - ✓ Narrow therapy
  - ✓ Change therapy
  - ✓ Continue therapy
  - ✓ Set a stop date
- Can/should deescalate in culture negative infection
- Can/should fix culture practices if not optimized

# Additional Strategies

- Dose Optimization
  - ✓ Underdosing leads to resistance
  - ✓ Overdosing increases side effects
- IV to PO
  - ✓ Gets patients out of the hospital sooner
  - ✓ Fewer line manipulations
  - ✓ Automatic conversion
    - Less work
    - Higher conversion rate

Laing, et al. JAC 1998;42:107 Przbylski et al. Pharmacotherapy 1997;17(2):271



# Clinical Laboratory

- Using an active antibiogram

✓ Not just for unseen publication

✓ Explore MIC changes

**Demo Hospital**  
January 2014 - December 2014

This data is a guide to empiric antibiotic therapy only. Streamlining post C&S results are necessary to prevent the emergence of resistant pathogens.

Microorganism	Number of Isolates	Aminoglycosides				Penicillins				Cephalosporins				Carba-penems		Fluoro-quinolone		Miscellaneous										
		Amikacin	Gentamicin	Gentamicin Synergy	Tobramycin	Ampicillin	Ampicillin/sulbactam	Oxacillin	Penicillin (meningitis)	Penicillin (non-meningitis)	Piperacillin/tazobactam	Cefazolin	Cefotaxime	Ceftriaxone	Cefepime	Ertapenem	Meropenem	Ciprofloxacin	Levofloxacin	Aztreonam	Clindamycin	Daptomycin	Linezolid	Nitrofurantoin	Sulfamethoxazole/Trimethoprim	Tetracycline	Vancomycin	
<b>Gram Negative Organisms<sup>a</sup></b>																												
<i>Acinetobacter baumannii</i>	51	67	40	-	51	-	47	-	-	-	-	-	-	35	-	45	31	35	-	-	-	-	-	-	40	-	-	
<i>Enterobacter cloacae</i>	116	98	96	-	95	-	-	-	-	80	-	72	81	95	91	95	88	88	80	-	-	-	-	30	88	-	-	
<i>Escherichia coli</i>	1322	99	88	-	93	40	52	-	-	96	85	88	94	96	82	99	67	67	95	-	-	-	-	95	73	-	-	
<i>E. coli</i> (urine only)	704	99	87	-	90	35	46	-	-	96	85	89	95	96	-	99	68	68	-	-	-	-	-	97	65	-	-	
<i>Klebsiella pneumoniae</i>	417	97	90	-	93	-	84	-	-	95	90	92	94	96	91	99	92	92	92	-	-	-	-	45	89	-	-	
<i>Proteus mirabilis</i>	291	95	91	-	94	61	71	-	-	95	82	92	95	96	88	93	61	61	85	-	-	-	-	-	73	-	-	
<i>Pseudomonas aeruginosa</i>	420	89	78	-	87	-	-	-	-	88	-	-	-	81	-	85	61	56	61	-	-	-	-	-	-	-	-	
<i>Serratia marcescens</i>	618	98	92	-	93	-	-	-	-	89	-	90	94	99	98	99	90	90	93	-	-	-	-	-	89	-	-	
<b>Gram Positive Organisms</b>																												
<i>Enterococcus faecalis</i>	540	-	-	54	-	98	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100	100	-	-	26	100
<i>Enterococcus faecium</i>	82	-	-	81	-	17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	85	96	-	-	32	31
<i>Staphylococcus aureus<sup>b</sup></i>	1302	-	-	-	-	-	54	-	-	-	54	-	52	-	-	-	-	58	-	78	99	100	-	98	95	100	-	
<i>Staphylococcus epidermidis</i>	220	-	-	-	-	-	25	-	-	-	25	-	-	-	-	-	-	23	-	98	99	96	-	45	78	99	-	
<i>Streptococcus pneumoniae<sup>c</sup></i>	68	-	-	-	-	-	-	45	84	-	-	-	82	-	-	87	-	99	-	100	-	100	-	100	-	62	77	100
<i>Viridans Streptococcus<sup>d</sup></i>	8	-	-	-	-	87	-	-	-	-	-	-	100	-	-	-	-	100	-	87	-	-	-	-	-	63	100	-

a using updated breakpoints for carbapenems, aztreonam, and cephalosporins  
b positive D-test assumed resistant for clindamycin  
c combined 2013 and 2014 to get above 30 isolates  
d less than 30 isolates reported, susceptibility results may be inaccurate  
e used automated report and manually validated for results

## Question 2

Rapid diagnostics are critical to antibiotic stewardship.

A. True

B. False

# Utilizing Rapid Diagnostics

- May rule out infection earlier in admission
  - ✓ Leading to a decrease in antibiotic use
  - ✓ No changes in mortality or adverse events
  - ✓ Arch Intern Med 2011;171(15):1322
- If staff unwilling to make clinical changes based on results, limited utility
  - ✓ Do not discontinue based on WBC, temp, RR, symptoms, etc.
  - ✓ Crit Care Med 2012;40(8):2304
- Complete a Return On Investment before asking

## Question 2

Rapid diagnostics are critical to antibiotic stewardship.

A. True

B. False

# Creating the Program

- Step 1 – Form a team
  - ✓ Identify members and responsibilities
  - ✓ Involve as many professions as possible
    - Pharmacists, physicians, nurses, microbiologists, epidemiologists
  - ✓ Troubleshooting
    - Professionals not available (i.e. no ID physician, outside lab, unwillingness)
      - Many hospitals use smaller teams with best available expertise; additional training may be necessary
      - Pharmacy can positively impact antibiotic consumption without ID support

# Creating the Program

- Step 2 – Create a policy
  - ✓ Defines team members and reporting structure
  - ✓ Identifies strategies to be used
    - Prospective audit and feedback
    - Criteria-based therapy
  - ✓ Establishes metrics
  - ✓ Troubleshooting
    - Lack of support
      - Involving the entire hospital improves global support
      - Metrics help identify outliers and abuse
      - Infectious Diseases practitioners should also adhere to criteria as an example
        - » May be the primary override that is peer reviewed through committee

# A Word About Metrics

## *Utilization*

- \$ per PAPD – dollars per pharmacy adjusted patient day
  - ✓ Presented as aggregate as well as for individual agents
  - ✓ Based on purchases – normalizes over time
- DOT per 1000 PD – days of therapy per 1000 patient days
  - ✓ Day of therapy - each day that an antibiotic is given to a patient
- DDD per 1000 PD – defined daily dose per 1000 patient days
  - ✓ may be monitored but has limitations for individual hospitals or systems

# A Word About Metrics

## *Clinical*

- *C. difficile* per AA – rate of *Clostridium difficile* Associated Disease (CDAD) per adjusted admission (AA)
  - ✓ antibiotic overuse is directly correlated to CDAD
- LOS – length of stay
  - ✓ may also monitor ICU length of stay and ventilator days
- Adverse events – from antibiotics
- Mortality



# A Word About Metrics

## *Resistance*

- Antibiograms – include trending
- Resistance rates – rates of VRE, MRSA, ESBL, etc.

## *Program*

- Criteria-Based Antibiotics Adherence
  - ✓ may be broken down by prescriber
- Intervention Acceptance Rate
  - ✓ may be broken down by prescriber
- IV to PO
  - ✓ ratio of accepted conversions over possible conversions

# Creating the Program

- Step 3 – Education
  - ✓ Identify a lead stewardship pharmacist – intense training program
  - ✓ Educate all pharmacists in stewardship basics
  - ✓ Administrator education
  - ✓ Physician newsletters and section meeting presentations
  - ✓ Nursing education and infection control
  - ✓ NOTE: education is an ongoing process; update regularly
- ✓ Troubleshooting
  - Lack of local expertise
    - Utilize national education providers
    - Resources from Centers for Disease Control and Infect Dis Society of America

# Creating the Program

- Step 4 – Optimize technology
  - ✓ Alerts for targeted antimicrobials
  - ✓ Order sets
  - ✓ Criteria process
  - ✓ Laboratory reports
  
- ✓ Troubleshooting
  - Time and backlogs
    - Allow adequate time – plenty customization needed
    - Document process for future use
  - Overrides
    - Use peer review process

# Creating the Program

- Step 5 – Set a date and activate
  - ✓ May complete several earlier steps simultaneously
  - ✓ May still intervene before formal process in place
  - ✓ Lots of advertising before official start
  
- ✓ Troubleshooting
  - First antibiotic denial
    - May lead to anger and rejection of the program
    - Typically subsides after 90 days

# Review

- All healthcare facilities should develop an antibiotics stewardship program to limit the impact of resistance
- Choose components that are most likely to impact antibiotic consumption
- Build and adjust the program continuously
- Regulatory requirements strongly encourage program development

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