

# Antimicrobial Stewardship for All: What You Need to Know

**Marc H. Scheetz, Pharm.D., M.Sc.**   **Heather M. Draper, Pharm.D., BCPS**

Associate Professor of Pharmacy Practice  
Midwestern University Chicago  
College of Pharmacy  
Downers Grove, Illinois  
Infectious Diseases Pharmacist  
Northwestern Memorial Hospital, Chicago, Illinois

Clinical Specialist, Emergency Medicine  
Mercy Health Saint Mary's  
Grand Rapids, Michigan





# Disclosure

- **Marc Scheetz:**
  - **Merck: Grant/Research Support**
  - **Premier: Speaker's Bureau**



# Objectives

- Discuss emerging issues in antimicrobial resistance among pathogens commonly causing infectious diseases and the implications for antimicrobial drug use in healthcare facilities.
- Describe and develop methods for surveillance of antimicrobial resistance in healthcare facilities.
- Explain the components of an effective antimicrobial stewardship program.
- Apply appropriate metrics for evaluating antimicrobial consumption in healthcare facilities.
- Develop methods for monitoring trends and identifying opportunities for improvement in antimicrobial use within a healthcare facility.

# Antimicrobial Stewardship for All – What You Need to Know

**Heather M. Draper, Pharm.D., BCPS**

Clinical Specialist, Emergency Medicine

Mercy Health Saint Mary's

Grand Rapids, Michigan



# *Emerging Issues in Antimicrobial Resistance*





*“...It is **not difficult to make microbes resistant** to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant... “*

*—Sir Alexander Fleming  
Nobel Prize Lecture, 1945*



**“...The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out....In such a case the thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organisms. I hope this evil can be averted.”**

**—Sir Alexander Fleming  
New York Times  
June 26, 1945**



***“A good gulp of whiskey at bedtime –  
it’s not very scientific, but it helps.”***

**—Sir Alexander Fleming,  
when questioned about the common cold**



# EXTRA! EXTRA! “New” Superbug Isolated in U.S. Patient!

The screenshot shows the CDC website header with the logo and tagline "Centers for Disease Control and Prevention, CDC 24/7: Saving Lives, Protecting People™". A search bar is visible in the top right. Below the header is a green navigation bar for "Emergency Preparedness and Response". A sidebar on the left lists "Health Alert Network", "HAN Jurisdictions", "HAN Message Types", and "Sign Up for HAN Updates". The main content area shows a breadcrumb trail: "Resources for Emergency Health Professionals > Health Alert Network > HAN Archive > 2016 > HAN00390". The headline reads: "Alert to U.S. Healthcare Facilities: First *mcr-1* Gene in *E. coli* Bacteria found in a Human in the United States".

The screenshot shows the Fox News Health website. The header includes the Fox News logo and "Health" category. Navigation tabs include "Health Home", "Men's Health", "Women's Health", "Children's Health", "Alternative Medicine", "Diabetes", and "Heart Health". The article headline is "Researchers find second 'superbug' gene in US patient". It is dated "Published June 27, 2016" and attributed to "Reuters". Social media sharing icons for Facebook (60), Twitter (29), and Email (3) are present. A large image of pink, rod-shaped bacteria is shown at the bottom of the article.

The screenshot shows the MedlinePlus website. The header includes the MedlinePlus logo and tagline "Trusted Health Information for You". A search bar is in the top right. Navigation tabs include "Health Topics", "Drugs & Supplements", and "Videos & Tools". The article headline is "U.S. Officials Confirm Superbug Resistant to All Antibiotics". It is dated "Friday, May 27, 2016" and written by "Margaret Farley Steele". The article text states: "FRIDAY, May 27, 2016 (HealthDay News) -- U.S. researchers have identified the nation's first patient with an infection resistant to all existing antibiotics. Scientists have warned for years the day could come when 'superbugs' resisted all last-resort antibiotics. This new case, involving a 49-year-old Pennsylvania woman, suggests that day may soon be here." A "Related MedlinePlus Health Topics" box lists "Antibiotic Resistance".

<http://emergency.cdc.gov/han/han00390.asp>  
<http://www.foxnews.com/health/2016/06/27/researchers-find-second-superbug-gene-in-us-patient.html>  
[https://www.nlm.nih.gov/medlineplus/news/fullstory\\_159074.html](https://www.nlm.nih.gov/medlineplus/news/fullstory_159074.html)



# mcr-1 “Superbugs”

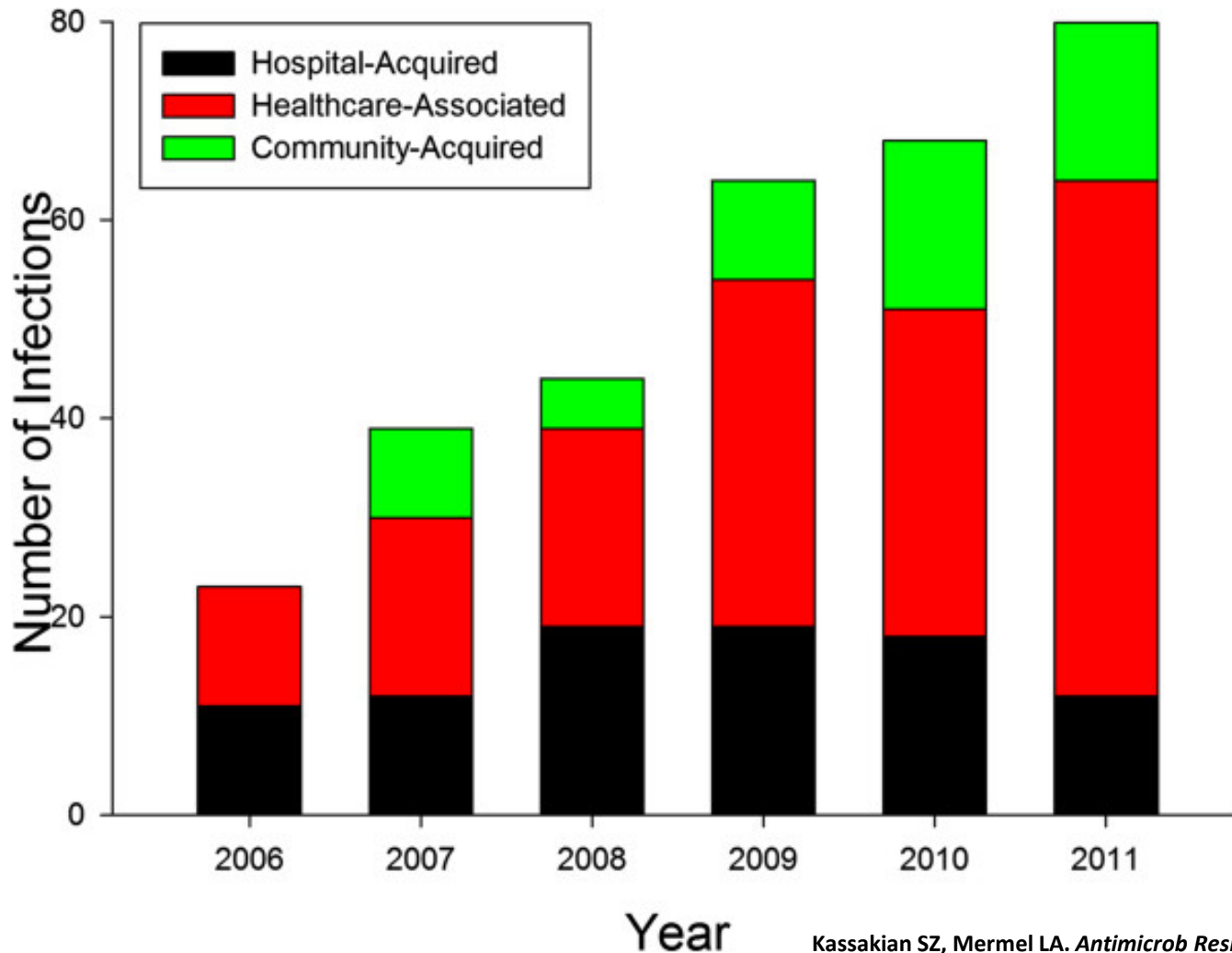
- Plasmid-mediated colistin resistance (mcr-1) found in  $\approx 1\%$  of hospitalized patients in China
- Historical isolates with mcr-1 gene from the 1980s in *Enterobacteriaceae*
- mcr-1 gene has been identified in humans, food animals, and environmental samples in 20 countries



# Multidrug-Resistant Bacteria

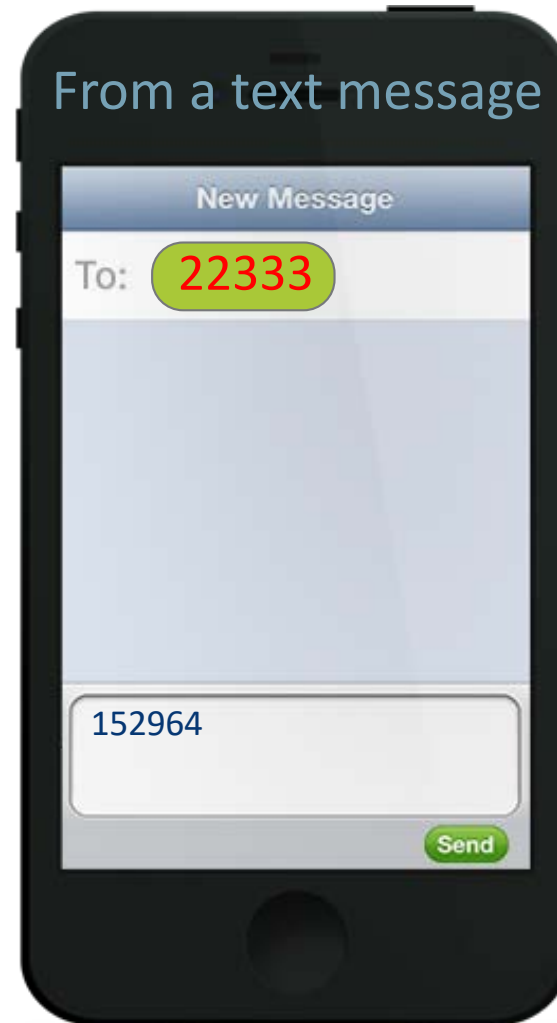
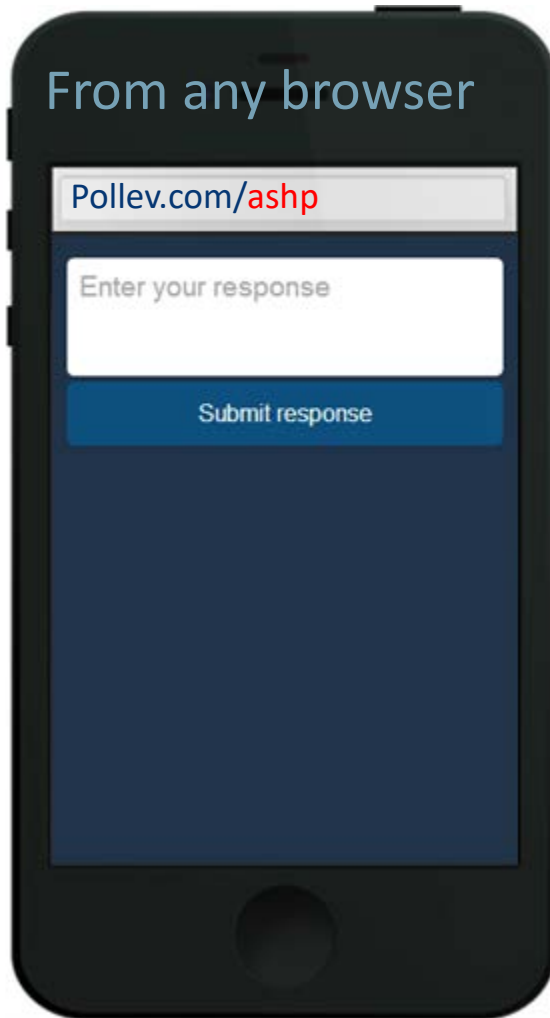
- Multidrug-resistant bacteria no longer only a “hospital” problem
- Case in point: extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*
  - 18% community-acquired
  - 53% healthcare-associated
  - 29% hospital-acquired

# Origin of Infection due to ESBL-Producing Bacteria



# Time for a Poll

How to vote via the web or text messaging



# How to vote via text message

How's my presentation so far?

Respond at [PollEv.com/ashp](http://PollEv.com/ashp) Text a **KEYWORD** to 22333



# How to vote via the web

How's my presentation so far?

Respond at [PollEv.com/ashp](http://PollEv.com/ashp) Text a **KEYWORD** to 22333

It's amazing. **152964**

It's incredibly amazing! **152965**

It's aw-right. **152968**

0%





**Question #1: Which one of the following currently represents the largest threat related to antimicrobial resistance, according to the Centers for Disease Control and Prevention?**

- A** *Neisseria gonorrhoeae*
- B** *Staphylococcus aureus*
- C** *Escherichia coli*
- D** *Streptococcus pneumoniae*



# Question #1

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)

# Emerging Antimicrobial Resistance: Pathogens of Concern

## Concerning Threats

- Vancomycin-Resistant *Staphylococcus aureus*
- Erythromycin-Resistant Group A *Streptococcus*
- Clindamycin-Resistant Group B *Streptococcus*

## Serious Threats\*

- Multidrug-Resistant *Acinetobacter*
- Fluconazole-Resistant *Candida*
- ESBL-producing *Enterobacteriaceae*
- Methicillin-Resistant *Staphylococcus aureus*
- Drug-Resistant *Streptococcus pneumoniae*

# Emerging Antimicrobial Resistance: Pathogens of Concern

## Urgent Threats

- *Clostridium difficile*
- Carbapenem-resistant *Enterobacteriaceae*
- *Neisseria gonorrhoeae*



# World Health Organization Antimicrobial-Resistant Pathogens of Concern

Pathogen	Antimicrobial Resistance
<i>Escherichia coli</i>	cephalosporins, fluoroquinolones
<i>Klebsiella pneumoniae</i>	cephalosporins, carbapenems
<i>Staphylococcus aureus</i>	methicillin
<i>Streptococcus pneumoniae</i>	penicillin
Non-typhoidal <i>Salmonella</i>	fluoroquinolones
<i>Shigella</i> species	fluoroquinolones
<i>Neisseria gonorrhoeae</i>	↓ susceptibility to cephalosporins

# Mechanisms of Resistance

*“Strong and ubiquitous **selection pressure** has seemingly been accompanied by **a shift from ‘natural’ resistance**, such as inducible chromosomal enzymes, membrane impermeability, and drug efflux, **to the modern paradigm of mobile gene pools** that largely determine **the epidemiology of modern antibiotic resistance.**”*



**Question #1: Which one of the following currently represents the largest threat related to antimicrobial resistance, according to the Centers for Disease Control and Prevention?**

- A** *Neisseria gonorrhoeae*
- B** *Staphylococcus aureus*
- C** *Escherichia coli*
- D** *Streptococcus pneumoniae*

# Mechanisms of Resistance

- **Target modification or mimicry**
  - Porin modification
  - Seen in fluoroquinolone and  $\beta$ -lactam resistance
- **Altered drug entry or expulsion/efflux**
- **Drug modification (destruction or modification)**
  - $\beta$ -lactamases
  - Methylases (e.g., aminoglycosides)

# Mechanisms of Resistance

- Resistance can transfer from one genus of bacteria to another
  - Via mobile gene pools
  - e.g.,  $\beta$ -lactamases between *Escherichia coli* and *Klebsiella pneumoniae*
  - Vancomycin resistance *vanA* gene cluster from *Enterococcus* (VRE) to *Staphylococcus aureus* (VRSA)
- Resistance can transfer from the environment to humans





# Mechanisms of Resistance

- **Horizontal transfer may vary depending on location and the environment of bacteria**
  - **Environmental: transduction by bacteriophages**
  - **Gastrointestinal tract: transformation or conjugation plasmids**



***“...there is an urgent, immediate need for new agents with activity against these panresistant organisms. There is no evidence that this need will be met in the foreseeable future.”***



# Question #2: A decrease in which one of the following outcomes is associated with antimicrobial resistance?

- A** Healthcare costs
- B** Hospital length of stay
- C** Mortality
- D** Clinical cure rate

# Question #2

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)



# The Toll of Drug Resistance

- Increased rate of treatment failure
- Extended length of hospital stay
- Increased need for isolation precautions
- Increased mortality
- Increased costs both during hospitalization and after discharge



# Implications for Healthcare

- **Patient placement and discharge planning may require home infusion and/or long-term care stays**
- **Judicious use of antibiotics, particularly broad-spectrum agents, is needed**
- **Efforts must be targeted to decrease resistance**

# Implications for Healthcare

- Will minimum inhibitory concentration (MIC) reporting be “enough”?
- Increasing need for rapid diagnostic tests
  - Penicillin-Binding Protein 2 (PBP2) for *Staphylococcus aureus*
- More sophisticated diagnostic tools will be needed
  - Matrix-Assisted Laser Desorption/Ionization Time-of-Flight mass spectrometry (MALDI-TOF)



# Question #2: A decrease in which one of the following outcomes is associated with antimicrobial resistance?

- A** Healthcare costs
- B** Hospital length of stay
- C** Mortality
- D** Clinical cure rate



# *Surveillance of Antimicrobial Resistance*





# Question #3: The most effective surveillance efforts focus on antimicrobial resistance trends in which of the following?

- A** The ICU of an individual institution
- B** All patient care areas in an individual institution
- C** All inpatient floors in a multi-hospital health system
- D** All emergency departments within the State of Nevada

# Question #3

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)



# Surveillance of Antimicrobial Resistance

- Surveillance efforts will [ideally] encompass local, regional, national, and international populations
- Local surveillance
  - Broken down by location – i.e., ICU vs. hospital vs. emergency department
  - Collectively as a “community”
- Surveillance should [ideally] include both clinical and microbiological information as well as antimicrobial use patterns



# Surveillance of Antimicrobial Resistance

- Findings should be used to guide treatment decisions
- Findings should be used to track effectiveness of interventions over time



# Question #3: The most effective surveillance efforts focus on antimicrobial resistance trends in which of the following?

- A** The ICU of an individual institution
- B** All patient care areas in an individual institution
- C** All inpatient floors in a multi-hospital health system
- D** All emergency departments within the State of Nevada



# Goals for Surveillance Efforts

- **Specific:** well-defined questions, produces generalizable results
- **Measurable:** validated tests, standardized methodology
- **Assessable:** outcomes can be identified and evaluated
- **Realistic:** timetable sensible, achievable
- **Targeted:** address relevant issue, clearly defined outcomes



# Application and Outcomes of Surveillance Efforts

- Improve empiric antimicrobial prescribing
- Guide antimicrobial policies and utilization
- Education
- Monitor the use of antimicrobial drugs and susceptibility of pathogens





# Application and Outcomes of Surveillance Efforts

- Direct infection control efforts
- Reduce the spread of resistant organisms
- Identify resistance patterns as they emerge
- Monitor changes in resistance patterns



# Question #4: Which one of the following culture reports would be most appropriate to request for constructing an antibiogram?

- A** Without stratification by location
- B** Stratified by ICU and non-ICU locations
- C** Stratified by ICU, inpatient, and community locations
- D** Stratified by inpatient care areas (e.g., floors)

# Question #4

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)



# Oldie But Goodie: The Antibioqram

**Mercy Health Saint Mary's  
INPATIENT  
ANTIBIOGRAM  
January – December 2015**

Produced by Inpatient Pharmacy  
and Microbiology Departments

	Penicillin	Oxacillin	Vancomycin	Clindamycin	Tetracycline	Azithromycin	Ampicillin	Ampicillin – Sulbactam	Cefazolin	Cefuroxime	Ceftriaxone	Cefepime	Gentamicin	Tobramycin	Amikacin	Aztreonam	Sulfamethoxazole – trimethoprim	Meropenem	Nitrofurantoin	Ciprofloxacin	Levofloxacin	Piperacillin - tazobactam	# Isolates		
<i>Staphylococcus aureus</i>		58	100	63	92			58	58				96				97						599		
<i>Staphylococcus epidermidis</i>		34	100										84										50		
<i>Enterococcus species</i> <sup>3,4</sup>	88		90				88						75						96			76	469		
<i>Streptococcus pneumoniae</i>	100 <sup>1</sup>		100		74	61 <sup>7</sup>	100				100 <sup>2</sup>						77					100 <sup>5</sup>	43		
<i>Acinetobacter baumannii</i> <sup>6</sup>							80					50					68	90			64		22		
<i>Citrobacter freundii</i> <sup>8</sup>												100					89	100			98		84	44	
<i>Citrobacter koseri</i> <sup>8</sup>												100					100	100			100		100	18	
<i>Escherichia coli</i>							52	58	92			94	95				94	100	96	79			95	934	
<i>Enterobacter aerogenes</i> <sup>8</sup>											75	98					100	100	77	97	100		94	97	32
<i>Enterobacter cloacae</i> <sup>8</sup>											78	98					97	100	80	88	99		95	88	138
<i>Haemophilus influenzae</i>					53	100	58	100				98	100				62				100			67	
<i>Klebsiella pneumoniae</i>								79	85			90	91				94	100	90	89	99	41	92	91	314
<i>Klebsiella oxytoca</i>								69	96			98	100				100	100	98	100	100	78	100	96	50
<i>Proteus mirabilis</i>							79	85	93			97	97				91	100	97	75	100		61	100	129
<i>Pseudomonas aeruginosa</i>												90					96	97			87		78	81	338
<i>Serratia marcescens</i> <sup>8</sup>											100	100	100				93	100	100	96	100		100		27
<i>Stenotrophomonas maltophilia</i>																	86						88		45

1) 49% sensitive for meningitis      2) 74% sensitive for meningitis      3) 48 non-urine isolates *E. faecium* (83% were VRE)      4) 36 non-urine isolates *E. faecalis* (11% were VRE)  
 5) 750 mg or Moxifloxacin 400 mg      6) Tigecycline: 76%      7) Erythromycin tested

8) This organism is known to harbor inducible AmpC beta lactamases and may develop resistance during prolonged therapy with third generation cephalosporins such as ceftriaxone and cefotaxime.

# Antibiogram: Application to Practice

**Mercy Health Saint Mary's  
INPATIENT  
ANTIBIOGRAM  
January – December 2015**

Produced by Inpatient Pharmacy and Microbiology Departments

Penicillin	Oxacillin	Vancomycin	Clindamycin	Tetracycline	Azithromycin	Ampicillin	Ampicillin – Sulbactam	Cefazolin	Cefuroxime	Ceftriaxone	Cefepime	Gentamicin	Tobramycin	Amikacin	Aztreonam	Sulfamethoxazole – trimethoprim	Meropenem	Nitrofurantoin	Ciprofloxacin	Levofloxacin	Piperacillin – tazobactam	# Isolates
------------	-----------	------------	-------------	--------------	--------------	------------	------------------------	-----------	------------	-------------	----------	------------	------------	----------	-----------	---------------------------------	-----------	----------------	---------------	--------------	---------------------------	------------

**Mercy Health Saint Mary's  
H2CC - ICU  
ANTIBIOGRAM  
January – December 2015**

Produced by Inpatient Pharmacy and Microbiology Departments

Penicillin	Oxacillin	Vancomycin	Clindamycin	Tetracycline	Azithromycin	Ampicillin	Ampicillin – Sulbactam	Cefazolin	Ceftriaxone	Cefepime	Gentamicin	Tobramycin	Amikacin	Aztreonam	Sulfamethoxazole – trimethoprim	Meropenem	Nitrofurantoin	Ciprofloxacin	Levofloxacin	Piperacillin – tazobactam	# Isolates
------------	-----------	------------	-------------	--------------	--------------	------------	------------------------	-----------	-------------	----------	------------	------------	----------	-----------	---------------------------------	-----------	----------------	---------------	--------------	---------------------------	------------

**Mercy Health Saint Mary's  
Emergency Department  
ANTIBIOGRAM  
January – December 2015**

Produced by Inpatient Pharmacy and Microbiology Departments

	Oxacillin	Vancomycin	Clindamycin	Tetracycline	Azithromycin	Amoxicillin	Amoxicillin – clavulanate	Piperacillin – tazobactam	Cefazolin	Cefuroxime	Ceftriaxone	Cefepime	Tobramycin	Sulfamethoxazole – trimethoprim	Nitrofurantoin	Ciprofloxacin	Levofloxacin	# Isolates
<i>Staphylococcus aureus</i>	60	100	82	95										96				179
<i>Enterococcus species</i>		99				98									98	86		136
<i>Streptococcus pneumoniae</i> <sup>1,2</sup>				76	63	100					100 <sup>3</sup>						99	45 <sup>2</sup>
<i>Acinetobacter baumannii</i> <sup>1</sup>												80	100	100		100		5
<i>Citrobacter species</i> <sup>1,4,7</sup>								92			92	100	100	96		96		26
<i>Escherichia coli</i>						53	60	95	96	97	97	98	95	76	95	88		921
<i>Enterobacter species</i> <sup>5,7</sup>								80			86	97	94	80		94		35
<i>Klebsiella pneumoniae</i>							92	97	99	99	99	100	100	97	40	99		144
<i>Klebsiella oxytoca</i> <sup>1</sup>							33	93	80	100	100	100	100	93	60	100		15
<i>Proteus mirabilis</i>						82	97	100	98	100	100	100	89	85		88		65
<i>Pseudomonas aeruginosa</i>								91				93	95			80		44

- 1) 49% sensitive for
- 5) 750 mg or Moxifl
- 8) This organism is l

- 1) 57% sensitive for menit
- 5) 750 mg or Moxifloxaci
- 7) This organism is knowr

\*\*Note – Only

- 1) Less than 30 isolates tested
- 2) Only 2 *S. pneumoniae* isolates from ER (inpatient isolates added to total)
- 3) 76% sensitive for meningitis
- 4) *C. freundii* and *C. koseri*
- 5) *E. aerogenes* and *E. cloacea*
- 6) Levofloxacin 750 mg or Moxifloxacin 400 mg
- 7) This organism is known to harbor inducible AmpC beta lactamases and may develop resistance during prolonged therapy with third generation cephalosporins



# Antibiogram: Application to Practice

## Mercy Health Saint Mary's INPATIENT ANTIBIOGRAM January – December 2015

Produced by Inpatient Pharmacy  
and Microbiology Departments

	Penicillin	Oxacillin	Vancomycin	Clindamycin	Tetracycline	Azithromycin	Ampicillin	Ampicillin – Sulbactam	Cefazolin	Cefuroxime	Ceftriaxone	Cefepime	Gentamicin	Tobramycin	Amikacin	Aztreonam	Sulfamethoxazole – trimethoprim	Meropenem	Netilmicin	Ciprofloxacin	Levofloxacin	Piperacillin - tazobactam	# Isolates
<i>Staphylococcus aureus</i>		58	100	63	92			58	58				96				97						599
<i>Staphylococcus epidermidis</i>		34	100										84										50
<i>Enterococcus species</i> <sup>3,4</sup>	88		90				88						75						96		76		469
<i>Streptococcus pneumoniae</i>	100 <sup>1</sup>		100		74	61 <sup>7</sup>	100				100 <sup>2</sup>						77				100 <sup>5</sup>		43
<i>Acinetobacter baumannii</i> <sup>6</sup>							80					50		81			68	90			64		22
<i>Citrobacter freundii</i> <sup>8</sup>											100			100	100	86	89	100		98		84	44
<i>Citrobacter koseri</i> <sup>8</sup>											100			100	100	100	100	100		100		100	18
<i>Escherichia coli</i>							52	58	92		94	95		94	100	94	76	100	96	79		95	934
<i>Enterobacter aerogenes</i> <sup>8</sup>											75	98		100	100	77	97	100		94		97	32
<i>Enterobacter cloacae</i> <sup>8</sup>											78	98		97	100	80	88	99		95		88	138
<i>Haemophilus influenzae</i>					53	100	58	100		98	100						62			100			67
<i>Klebsiella pneumoniae</i>							79	85			90	91		94	100	90	89	99	41	92		91	314
<i>Klebsiella oxytoca</i>							69	96			98	100		100	100	98	100	100	78	100		96	50
<i>Proteus mirabilis</i>							79	85	93		97	97		91	100	97	75	100		61		100	129
<i>Pseudomonas aeruginosa</i>											90			96	97			87		78		81	338
<i>Serratia marcescens</i> <sup>8</sup>											100	100	100	93	100	100	96	100		100			27
<i>Stenotrophomonas maltophilia</i>																	86				88		45

1) 49% sensitive for meningitis

2) 74% sensitive for meningitis

3) 48 non-urine isolates *E. faecium* (83% were VRE)

4) 36 non-urine isolates *E. faecalis* (11% were VRE)

5) 750 mg or Moxifloxacin 400 mg

6) Tigecycline: 76%

7) Erythromycin tested

8) This organism is known to harbor inducible AmpC beta lactamases and may develop resistance during prolonged therapy with third generation cephalosporins such as ceftriaxone and cefotaxime.

# Antibiogram Trends: Application to Practice

Inpatient—Fluoroquinolones	2015	2016
<i>Escherichia coli</i>	80% ↑(4%)	79% ↔
<i>Proteus mirabilis</i>	66% ↑(12%)	61% ↔
<i>Pseudomonas</i>	84% ↑(17%)	78% ↓(6%)
<i>Streptococcus pneumoniae</i>	100% ↑*	100% ↔

\*100% susceptibility for the first time in 5 years

Critical Care Unit—Fluoroquinolones	2015	2016
<i>Escherichia coli</i>	83% ↑(15%)	79% ↔
<i>Proteus mirabilis</i>	61% ↑(26%)	50% ↓(11%)
<i>Klebsiella pneumoniae</i>	98% ↑(8%)	100% ↔
<i>Pseudomonas</i>	90% ↑(33%)	75% ↓(15%)
<i>Streptococcus pneumoniae</i>	100% ↑*	95%†

\*100% susceptibility for the first time in 5 years †1 resistant isolate





# Question #4: Which one of the following culture reports would be most appropriate to request for constructing an antibiogram?

- A** Without stratification by location
- B** Stratified by ICU and non-ICU locations
- C** **Stratified by ICU, inpatient, and community locations**
- D** Stratified by inpatient care areas (e.g., floors)



# Targeted Surveillance for High Risk Populations or Procedures

- Hospital setting: surgical prophylaxis/site infections, healthcare-associated infections
- Community setting: respiratory and urinary tract infections
- Everyone: *Clostridium difficile* infections



# Targeted Surveillance for High Risk Antimicrobial Therapies

- Hospital setting: e.g., carbapenems
- Community setting: e.g., 3<sup>rd</sup>-generation cephalosporins
- Everyone: fluoroquinolones



# Rapid Pathogen Identification: Immediate Surveillance

- Polymerase chain reaction (PCR)-based detection technology
- Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry
- Microarrays
- Microfluidics
- Cell lysis-based approach
- Whole-genome sequencing



# Role of Clinical Decision Support Software in Surveillance

- Surveillance may be possible with integrated, advanced clinical decision support software
- May allow for decision making at the patient level and more rapid identification of worrisome trends on a real-time basis

# *Components of an Effective Antimicrobial Stewardship Program*





# Antimicrobial Stewardship Programs (ASPs)

- **What we know about ASPs: improved clinical outcomes**
- **We “want” to have an impact on antimicrobial prescribing...but now we are going to “have to”**
- **Components defined by guidelines and now regulatory bodies**



***“The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as Clostridium difficile), and the emergence of resistance.”***



# Who Cares About ASPs?

- **The White House**
- **Centers for Disease Control and Prevention (CDC)**
- **Centers for Medicare & Medicaid Services (CMS)**
- **The Joint Commission**
- **U.S. Food and Drug Administration (FDA)**



# White House National Action Plan for Combating Antibiotic-Resistant Bacteria

- In March 2015, the White House released a National Action Plan for Combating Antibiotic-Resistant Bacteria
- Several objectives were outlined, including the need for antimicrobial stewardship programs in all healthcare settings
- A reduction in inappropriate antibiotic use by 50% in outpatient settings and 20% in inpatient settings is expected



# CMS Proposed Standards for Infection Prevention and Control and Antibiotic Stewardship Programs (§482.42)

- Proposed requirements would stipulate that the following goals are met:
  1. Coordinate among all components of the hospital responsible for antibiotic use and factors that lead to antimicrobial resistance
  2. Document the evidence-based use of antibiotics
  3. Demonstrate improvements in proper antibiotic use, such as reductions in *Clostridium difficile* infections and antibiotic resistance



# The Joint Commission Antimicrobial Stewardship Standard for Hospitals

- Standard goes into effect on January 1, 2017
- Recommends core elements as described in the CDC Core Elements of Hospital Antibiotic Stewardship Programs



# U.S. Food and Drug Administration

- FDA advises restricting use of fluoroquinolones for uncomplicated infections
- FDA Guidance for Industry (GFI) #213
  - Initially recommended phasing out “medically important” antibiotics in feed animals
  - December 2016: will be illegal to use “medically important” antibiotics in food or water for production purposes in feed animals

U.S. Food and Drug Administration. FDA drug safety communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. July 26, 2016. <http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm>.

U.S. Food and Drug Administration. Phasing Out Certain Antibiotic Use in Farm Animals. February 25, 2015. <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm378100.htm>.

U.S. Food and Drug Administration. New animal drugs and new animal drug combination products administered in or on medicated feed or drinking water of food-producing animals: recommendations for drug sponsors for voluntarily aligning product use conditions with GFI #209. December 2013.

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf>.



# Outcomes Associated with ASPs

- Decreased antimicrobial use (particularly broad-spectrum agents)
- Decreased inappropriate prescribing
- Improved adherence to treatment guidelines
- Improved patient outcomes
  - Decreased treatment failure
  - Increased clinical cure rates



# Outcomes Associated with ASPs

- Decreased *Clostridium difficile* infection
- Decreased hospital length of stay
- Decreased costs
- Decreased antimicrobial resistance...?



# CDC Core Elements of Hospital Antibiotic Stewardship Programs

- **Leadership Commitment**: allow for dedicated time, resources, and participation
- **Accountability**: assign a stewardship program leader responsible for program outcomes
- **Drug Expertise**: identify a pharmacist leader
- **Action**: implement at least one recommended action/intervention





# CDC Core Elements of Hospital Antibiotic Stewardship Programs

- **Tracking**: monitor prescribing and resistance patterns
- **Reporting**: regular reporting on antibiotic use, resistance, and outcome measures
- **Education**: educate clinicians about resistance and optimal prescribing

## Checklist for Core Elements of Hospital Antibiotic Stewardship Programs

The following checklist is a companion to *Core Elements of Hospital Antibiotic Stewardship Programs*. This checklist should be used to systematically assess key elements and actions to ensure optimal antibiotic prescribing and limit overuse and misuse of antibiotics in hospitals. CDC recommends that all hospitals implement an Antibiotic Stewardship Program.

Facilities using this checklist should involve one or more knowledgeable staff to determine if the following principles and actions to improve antibiotic use are in place. The elements in this checklist have been shown in previous studies to be helpful in improving antibiotic use though not all of the elements might be feasible in all hospitals.

LEADERSHIP SUPPORT	ESTABLISHED AT FACILITY
A. Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	<input type="checkbox"/> Yes <input type="checkbox"/> No
B. Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	<input type="checkbox"/> Yes <input type="checkbox"/> No
ACCOUNTABILITY	
A. Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	<input type="checkbox"/> Yes <input type="checkbox"/> No
DRUG EXPERTISE	
A. Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?	<input type="checkbox"/> Yes <input type="checkbox"/> No
KEY SUPPORT FOR THE ANTIBIOTIC STEWARDSHIP PROGRAM	
<i>Does any of the staff below work with the stewardship leaders to improve antibiotic use?</i>	
B. Clinicians	<input type="checkbox"/> Yes <input type="checkbox"/> No
C. Infection Prevention and Healthcare Epidemiology	<input type="checkbox"/> Yes <input type="checkbox"/> No
D. Quality Improvement	<input type="checkbox"/> Yes <input type="checkbox"/> No
E. Microbiology (Laboratory)	<input type="checkbox"/> Yes <input type="checkbox"/> No
F. Information Technology (IT)	<input type="checkbox"/> Yes <input type="checkbox"/> No
G. Nursing	<input type="checkbox"/> Yes <input type="checkbox"/> No



# **IDSA/SHEA\* Guidelines for...Antimicrobial Stewardship: Team Members**

- **Essential: Infectious diseases physician, pharmacist, hospital administration, medical staff leadership, local providers**
  
- **Optimal: clinical microbiologist, infection control specialist, information system specialist, hospital epidemiologist**



# Question #5: Which one of the following is considered a core strategy for an antimicrobial stewardship program?

- A** Formulary restriction and preauthorization
- B** Education
- C** Guidelines and clinical pathways
- D** Antimicrobial cycling

# Question #5

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)



# IDSA/SHEA\* Guidelines for...Antimicrobial Stewardship: Core Strategies

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization



# IDSA/SHEA Guidelines for...Antimicrobial Stewardship: Supplemental Strategies

- Education
- Guidelines and clinical pathways
- Antimicrobial order forms



# **IDSA/SHEA Guidelines for...Antimicrobial Stewardship: Supplemental Strategies**

- **Streamlining or de-escalation of therapy**
- **Dose optimization**
- **Parenteral-to-oral conversion**
- **Computer surveillance and clinical decision support**





# IDSA/SHEA Guidelines for...Antimicrobial Stewardship: Supplemental Strategies

- Antimicrobial cycling—**NOT RECOMMENDED**
- Combination therapy—**NOT RECOMMENDED**



# Question #5: Which one of the following is considered a core strategy for an antimicrobial stewardship program?

- A** Formulary restriction and preauthorization
- B** Education
- C** Guidelines and clinical pathways
- D** Antimicrobial cycling

# Antimicrobial Consumption Metrics in the Hospital Setting.

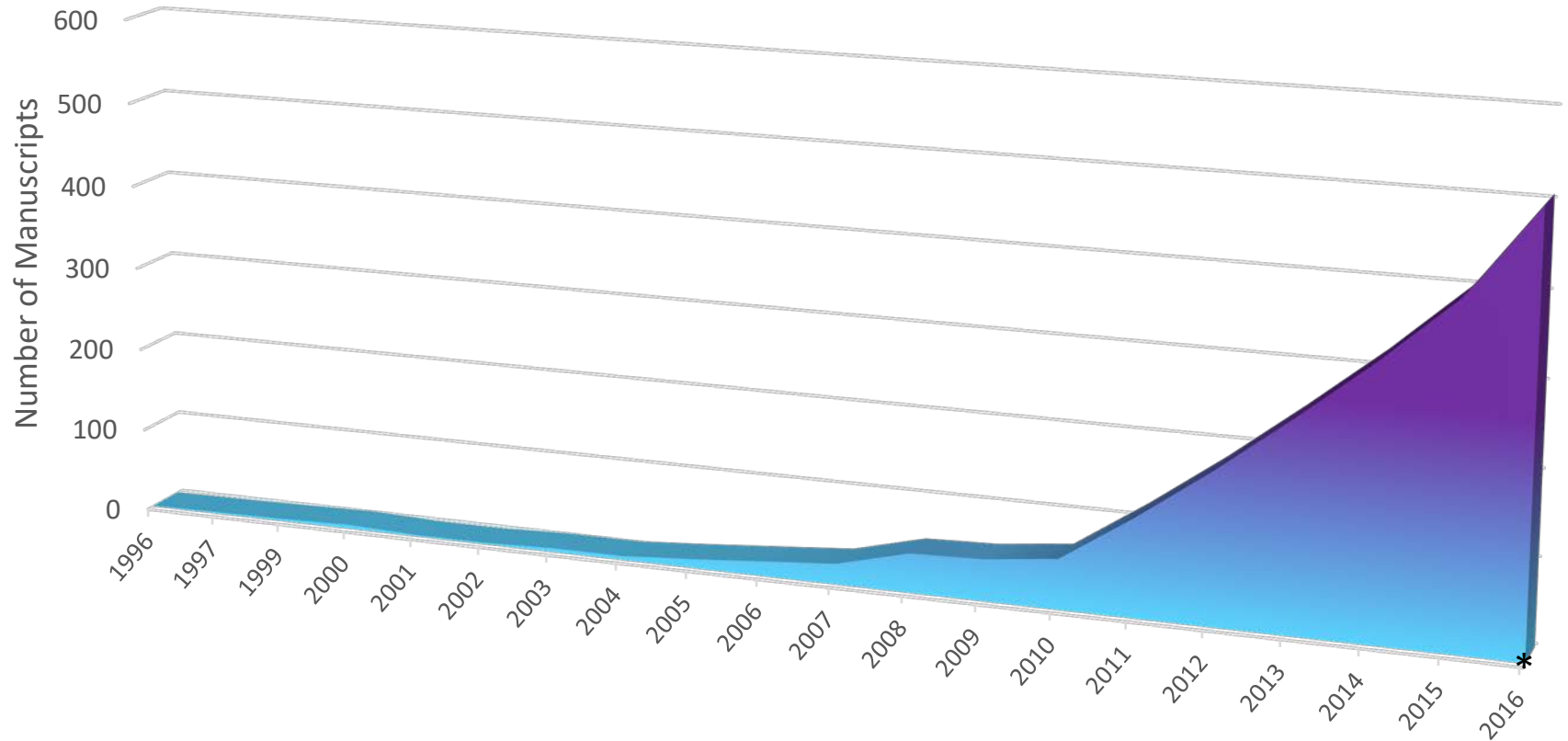
## Marc H. Scheetz, Pharm.D., MSc

Associate Professor of Pharmacy Practice  
Midwestern University Chicago College of Pharmacy  
Downers Grove, Illinois  
Infectious Diseases Pharmacist  
Northwestern Memorial Hospital, Chicago, Illinois





# Antimicrobial Stewardship Manuscripts



Manuscripts identified in PubMed using key words “antimicrobial stewardship”, search completed 5/9/16 (Scheetz)

\*2016 data projected based on rate of manuscript publication through 5/9/16



# What is Antimicrobial Stewardship?

- “...**antimicrobial-use regulation** employing sophisticated epidemiologic methods, molecular biological organism typing, and precise resistance mechanism analysis will be required to determine the **best methods** to prevent and control this problem and ensure our optimal antimicrobial-use **"stewardship."** Consideration of the long-term effects of antimicrobial selection, dosage, and duration of treatment on resistance development should be a part of every antimicrobial treatment decision.”



# Policy Statement of SHEA, IDSA, and PIDS

1. *Antimicrobial stewardship* programs should be **required** through regulatory mechanisms.
2. *Antimicrobial stewardship* should be **MONITORED** in ambulatory healthcare settings.
3. **Education** about antimicrobial resistance and antimicrobial stewardship must be accomplished.
4. **Antimicrobial use DATA** should be collected and readily available for both **inpatient and outpatient settings**.
5. **Research** on *antimicrobial stewardship* is needed.

Slightly less prominent...

“ Team members should include... a **pharmacist**”

“Antimicrobial stewardship is a **patient safety issue and a public health issue....**”



# 2016. A Seat at the Table

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society of Healthcare Epidemiology of America. [Barlam TF et al. 2016; 62:e51-77. Clin Infect Dis. \(2016\)](#)

“In addition to members of IDSA and the SHEA, representatives from diverse geographic areas, pediatric and adult practitioners, and a wide breadth of specialties representing major medical societies were included among the panel’s membership (American College of Emergency Physicians [ACEP], **American Society of Health-System Pharmacists [ASHP]**, American Society for Microbiology [ASM], PIDS, Society for Academic Emergency Medicine [SAEM], **Society of Infectious Diseases Pharmacists [SIDP]**, and the Surgical Infection Society [SIS]).”



“This guideline does not specifically address the structure of an ASP, which has been well outlined in a previous guideline [8] and in the CDC’s Core Elements of Hospital Antibiotic Stewardship Programs and Core Elements of Antibiotic Stewardship for Nursing Homes [7, 9]. ***These documents emphasize the importance of physician and pharmacist leadership for an ASP***, the need for infectious diseases expertise, and the role of measurement and feedback as critical components of ASPs.”





# What Should Stewardship Programs be Measuring?

- Resistance >> yes, complex.
- Outcomes >> yes, complex.
- Cost >> until we are “under the auspices of quality...” and probably even then.
- **ATB Use >> the driver of the above outcomes!!!**



Question #6: What is the best measure of antimicrobial consumption according to the 2016 IDSA/SHEA guideline?

- A** Defined Daily Doses (DDD<sub>s</sub>)
- B** Purchased Grams of Antibiotics (PGA)
- C** Days of Therapy (DOT<sub>s</sub>)
- D** Renally-adjusted Days of Therapy (raDOT<sub>s</sub>)

# Question #6

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)

Question #6: What is the best measure of antimicrobial consumption according to the 2016 IDSA/SHEA guideline?

- A** Defined Daily Doses (DDD<sub>s</sub>)
- B** Purchased Grams of Antibiotics (PGA)
- C** **Days of Therapy (DOT<sub>s</sub>)**
- D** Renally-adjusted Days of Therapy (raDOT<sub>s</sub>)



American Pharmacists Association™  
Improving medication use. Advancing patient care.

**ashp**  
Certification  
Resources

... straight from the horse's mouth.

## Measurement.

### XX. Which Overall Measures Best Reflect the Impact of ASPs and their Interventions?

#### *Recommendation*

21. We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD) (*weak recommendation, low quality evidence*).

### XXI. What is the Best Measure of Expenditure on Antibiotics to Assess the Impact of ASPs and Interventions?

#### *Recommendation*

22. We recommend measuring antibiotic costs based on prescriptions or administrations instead of purchasing data (*good practice recommendation*).



American Pharmacists Association™  
Improving medication use. Advancing patient care.



# Tracking and Analyzing: Antibiotic Consumption



# Antibiotic Use, by the Numbers/Numerators

- Antibiotic use should be quantified to compare with:
  - Self
  - Others
- Defined Daily Doses (DDD)s
  - <http://www.whocc.no/atcddd/>
  - Can be calculated from purchasing data
- Days of Therapy (DOTs)
  - More accurate... barcoding<sup>1</sup>
- NHSN-AUR (National Healthcare Safety Network-Antibiotic Use and Resistance Module) (Antibiotic Days)

Schirmer P, et al. Infect Control Hosp Epidemiol. 2012 Apr;33(4):409-11.

World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2016. [http://www.whocc.no/atc\\_ddd\\_index](http://www.whocc.no/atc_ddd_index)

National Healthcare Safety Network. Antimicrobial use and resistance (AUR) module. January 2016. <http://www.cdc.gov/nhsn/pdfs/training/aur/aur-training.pdf>



# Step 1. Comparing to self

- You are often your own best control!
- A denominator is probably helpful for temporal changes (census shifts, new programs, etc)
  - Standardize to patient day(s)
- Stratifications can be useful
  - Use in intensive care vs. general floors, etc.
- NOTE: Refrain from analyzing trends in variables that you cannot impact!!!!



# Step 1. Comparing to Self

- A denominator is necessary.
  - DDD per 1000 patient days
  - Duration of therapy (DOTs) per 1000 patient days
  - Cost per patient day
- Internal validity first: control for changes in hospital/program size across time
- External validity: control for variables likely to affect use/cost (e.g., patient severity of illness, patient disease state)



# NHSN AUR Module

- Aggregated monthly, with summaries
  - Inpatient units singly & combined (FacWideIN)
- Numerator: Antimicrobial days (Days of Therapy Administered)
  - 89 antimicrobials (antibacterial, antifungal, and anti-influenza agents)
  - Stratification by route of administration:
    - IV/IM/Oral/Respiratory
- Denominators:
  - Days Present: number of days spent in specific unit or facility
  - Admissions: number of patients admitted to the facility



American Pharmacists Association™  
Improving medication use. Advancing patient care.



So What is the Difference between all  
of these Antibiotic-Use Metrics?



Question #7: True or False: Days of Therapy (DOTs) can be predicted from Defined Daily Doses (DDD)

**A** True

**B** False

# Question #7

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)

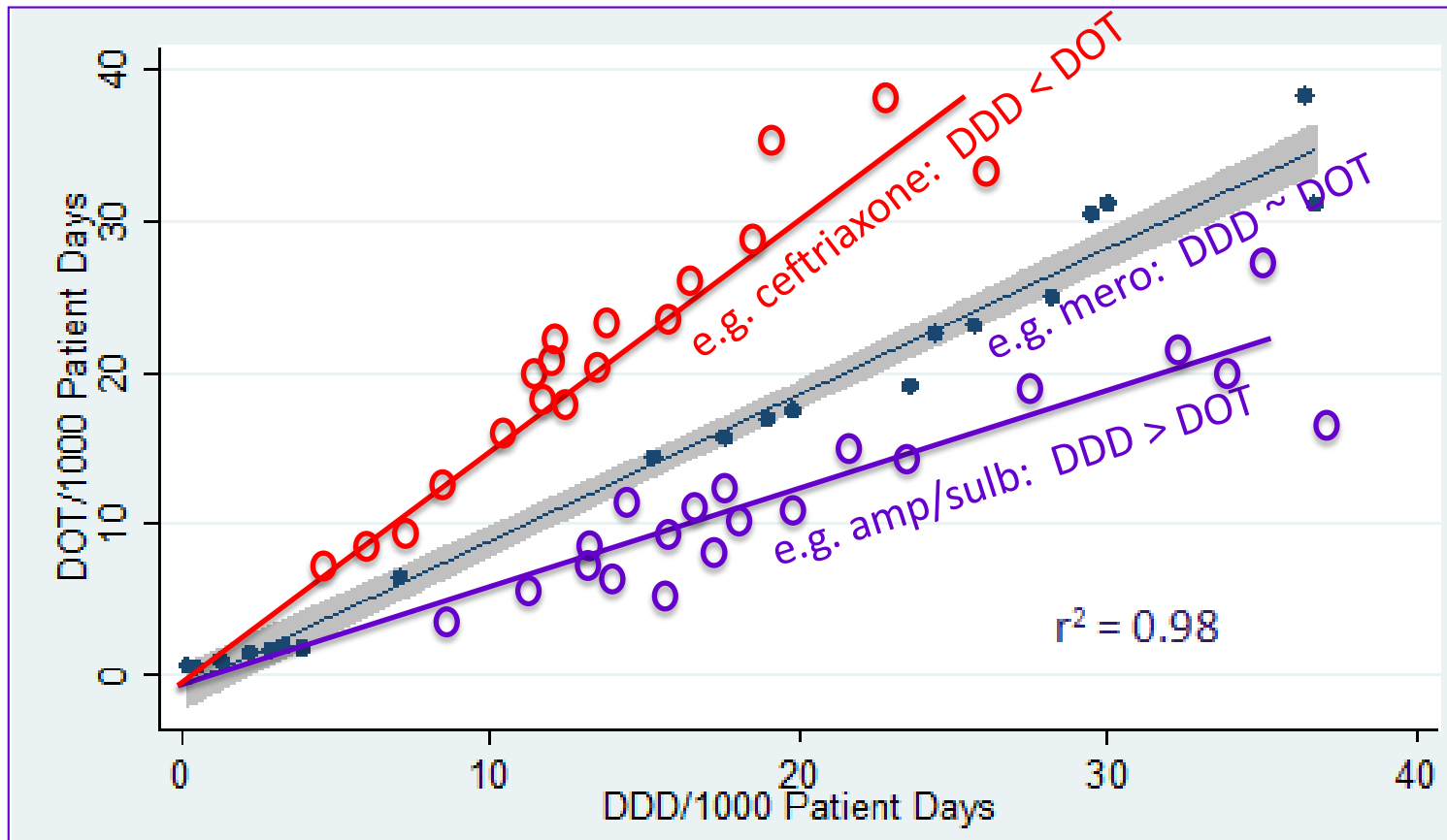


Question #7: True or False: Days of Therapy (DOTs) can be predicted from Defined Daily Doses (DDD)

**A True**

**B False**

# DDDs do not always equal DOTs



# DDDs do not always equal DOTs

- ... but agreement between DDD and DOT is generally good (i.e.,  $r^2$  is high).<sup>1</sup>
  - Pick one method and stick with it.
- Likely reasons that DDD > DOT<sup>2</sup>
  - WHO classification is high compared to practice.<sup>1</sup>
    - e.g. ceftriaxone WHO DDD = 2 g per day; many give 1 g per day
  - Not all “ordered” doses are given.
- Likely reasons that DDD < DOT<sup>1</sup>
  - Renal function adjustments not captured
    - e.g. Vancomycin DDD = 2 g per day; patients with renal failure may receive 2 g per week.
  - WHO classification is low compared to practice.
    - e.g. Ampicillin/Sulbactam DDD = 2 g per day; many are giving much more than this





# NHSN: AUR module

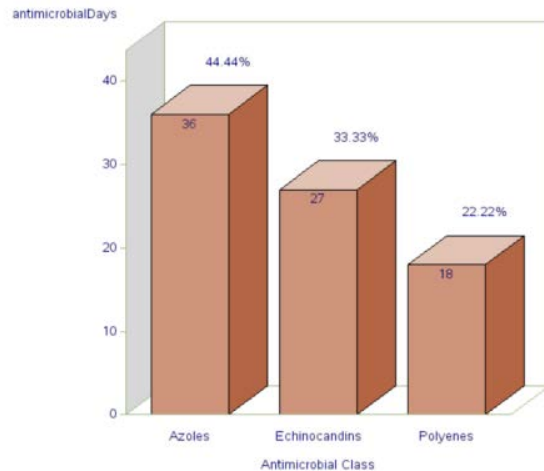


## Surveillance for Antimicrobial Use and Antimicrobial Resistance Options



### National Healthcare Safety Network (NHSN)

**National Healthcare Safety Network**  
Bar Chart - All Data - Proportion of Antimicrobial Days per Antifungal Class by Location  
As of: December 17, 2015 at 12:38 PM  
Date Range: SUMMARYAU summaryYr 2014 to 2014  
Location=ICU-A



Data contained in this report were last generated on December 3, 2015 at 3:39 PM.

## Resources for NHSN Users Already Enrolled

### Training

- [Introduction to the NHSN Antimicrobial Use and Resistance \(AUR\) Module \(updated January 2016\)](#) [PDF - 571 KB]
- **New!** Antibiotic Stewardship - March 2016 [Video - 36 min]
  - [YouTube link - Antibiotic Stewardship](#)
  - [CDC Streaming Video - Antibiotic Stewardship](#)
  - [Slide set - Antibiotic Stewardship](#) [PDF - 1 MB]
- **New!** Analysis of Antibiotic Resistance Data - March 2016 [Video - 48 min]
  - [YouTube link - Analysis of Antibiotic Resistance Data](#)
  - [CDC Streaming Video - Analysis of Antibiotic Resistance Data](#)
  - [Slide set - Analysis of Antibiotic Resistance Data](#) [PDF - 1 MB]
- **New!** Antimicrobial Use and Resistance Module Protocol - March 2016 [Video - 36 min]
  - [YouTube link - Antimicrobial Use and Resistance Module Protocol](#)
  - [CDC Streaming Video - Antimicrobial Use and Resistance Module Protocol](#)
  - [Slide set - Antimicrobial Use & Resistance Module Protocol](#) [PDF - 780 KB]
- **New!** Standardized Antibiotic Administration Ratio - March 2016 [Video - 24 min]
  - [YouTube link - Standardized Antibiotic Administration Ratio](#)
  - [CDC Streaming Video - Standardized Antibiotic Administration Ratio](#)
  - [Slide set - Standardized Antimicrobial Administration Ratio](#) [PDF - 956 KB]

# What are the Differences with ADs and DOTs

- NHSN ADs are based on eMAR and/or BCMA administrations
  - If a patient is scheduled to receive vancomycin thrice weekly because of renal dysfunction, there will be 3 ADs for a week of therapy.
  - The same patient can be counted as 7 DOTs based on calendar days of antibiotic therapy.
- Does the floor shift below you? I.e. what about denominators?
  - It depends... NHSN uses Days Present.
  - *“days present is calculated as the number of patients who were present for any portion of each day of a calendar month for a patient care location”<sup>1</sup>*

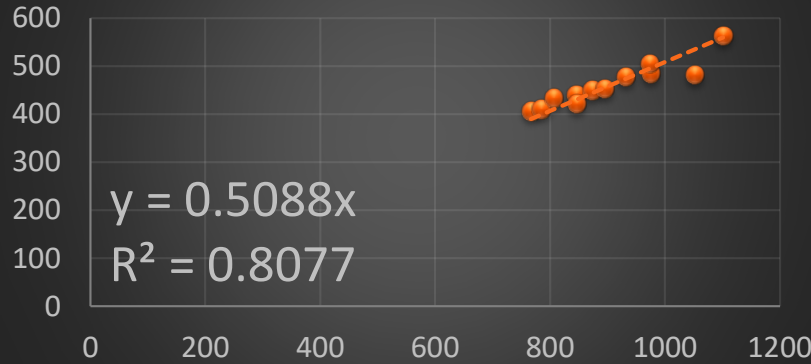
# What are the Differences with ADs and DOTs

- NHSN ADs are based on eMAR and/or BCMA administrations
  - If a patient is scheduled to receive vancomycin thrice weekly because of renal dysfunction, there will be 3 ADs for a week of therapy.
  - The same patient can be counted as 7 DOTs based on calendar days of antibiotic therapy.
- Does the floor shift below you? I.e. what about denominators?
  - It depends... NHSN uses Days Present.
  - *“days present is calculated as the number of patients who were present for any portion of each day of a calendar month for a patient care location”<sup>1</sup>*

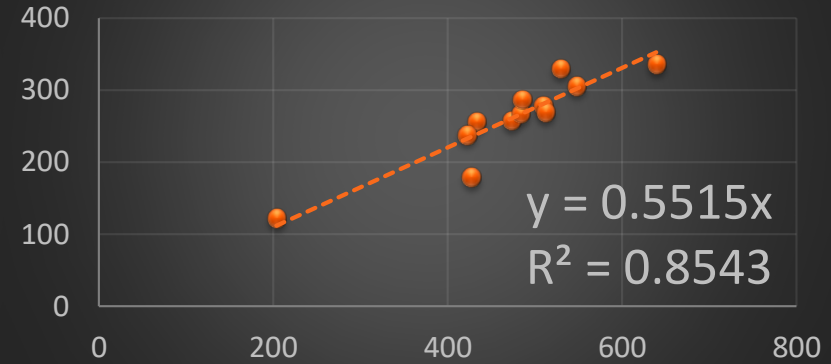
# NHSN Methods vs. DOT methods

DOT/1000 Pt Days

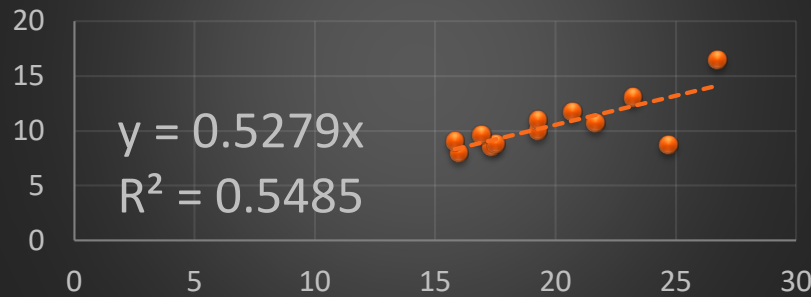
## Piperacillin-Tazobactam



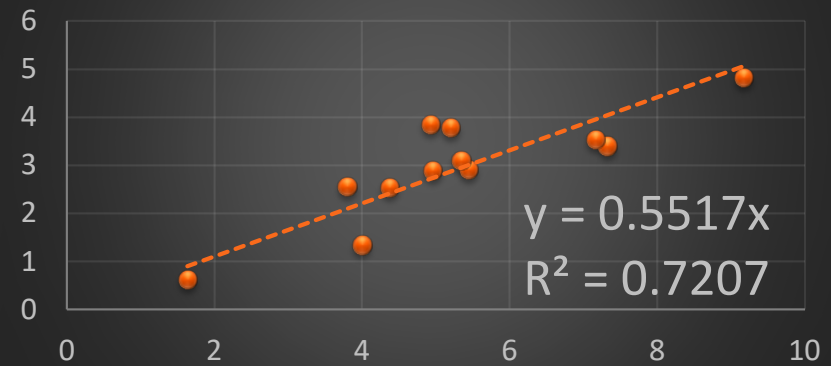
## Cefepime



## Imipenem and Meropenem

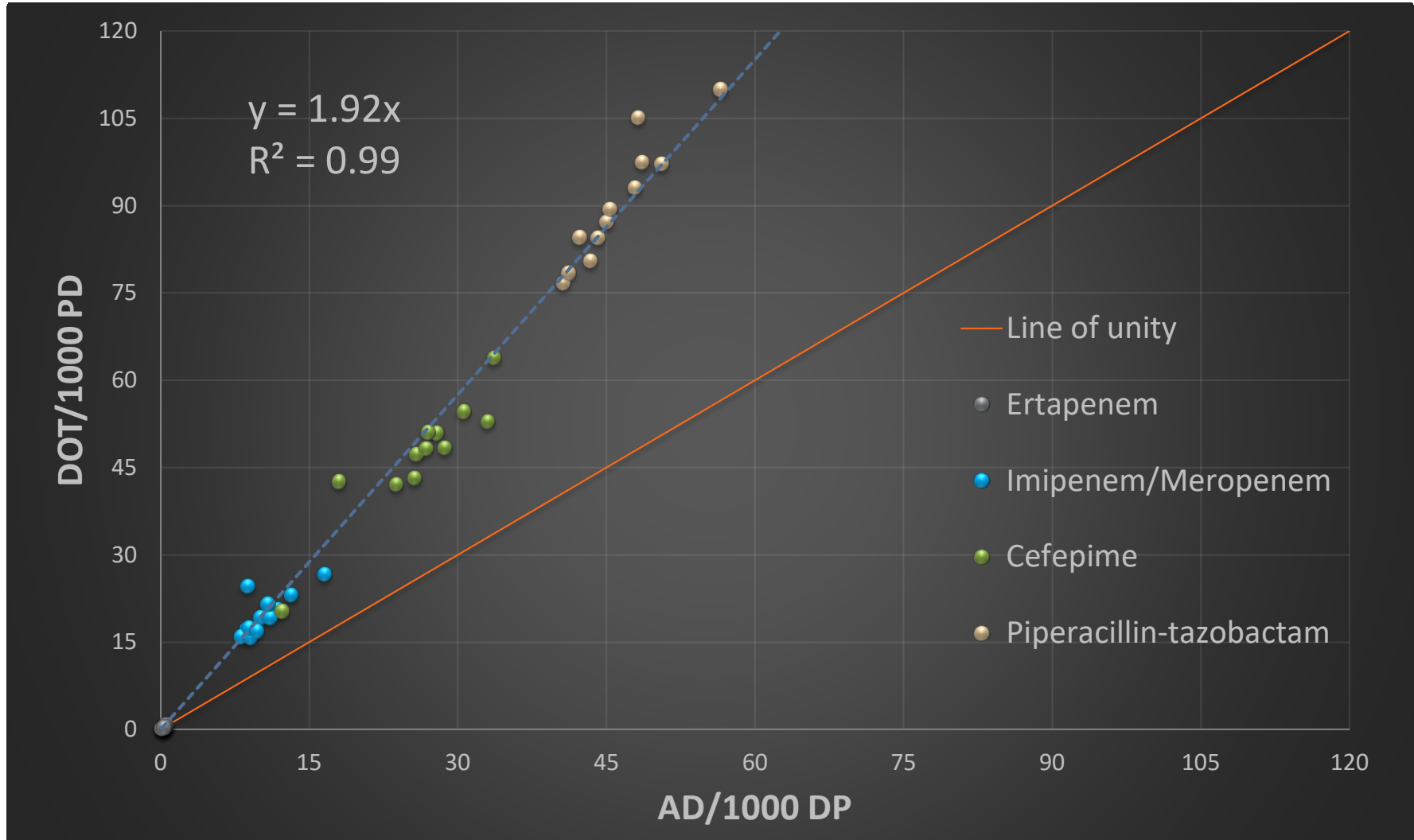


## Ertapenem



AD/1000 Days Present

# NHSN Methods vs. DOT methods





American Pharmacists Association™  
Improving medication use. Advancing patient care.



It matters less where you start with metrics... but more *that* you start tracking.



# Internal tracking

- You are often your own best control!
- A denominator is necessary to standardize and control for census shifts, new programs, etc.
  - Standardize to patient days (e.g., 1,000 patient days).
- Stratifications can be useful
  - Use in MICU vs. general floors, etc.
- NOTE: Refrain from reporting trends in variables that you cannot impact!!!!



# Trend your Data.

- A picture is worth a thousand words/*statistics*.
- At least 3 time points before/after (assuming for homogenous data) are necessary to determine the secular trend (i.e., non-periodic trend).<sup>1</sup>

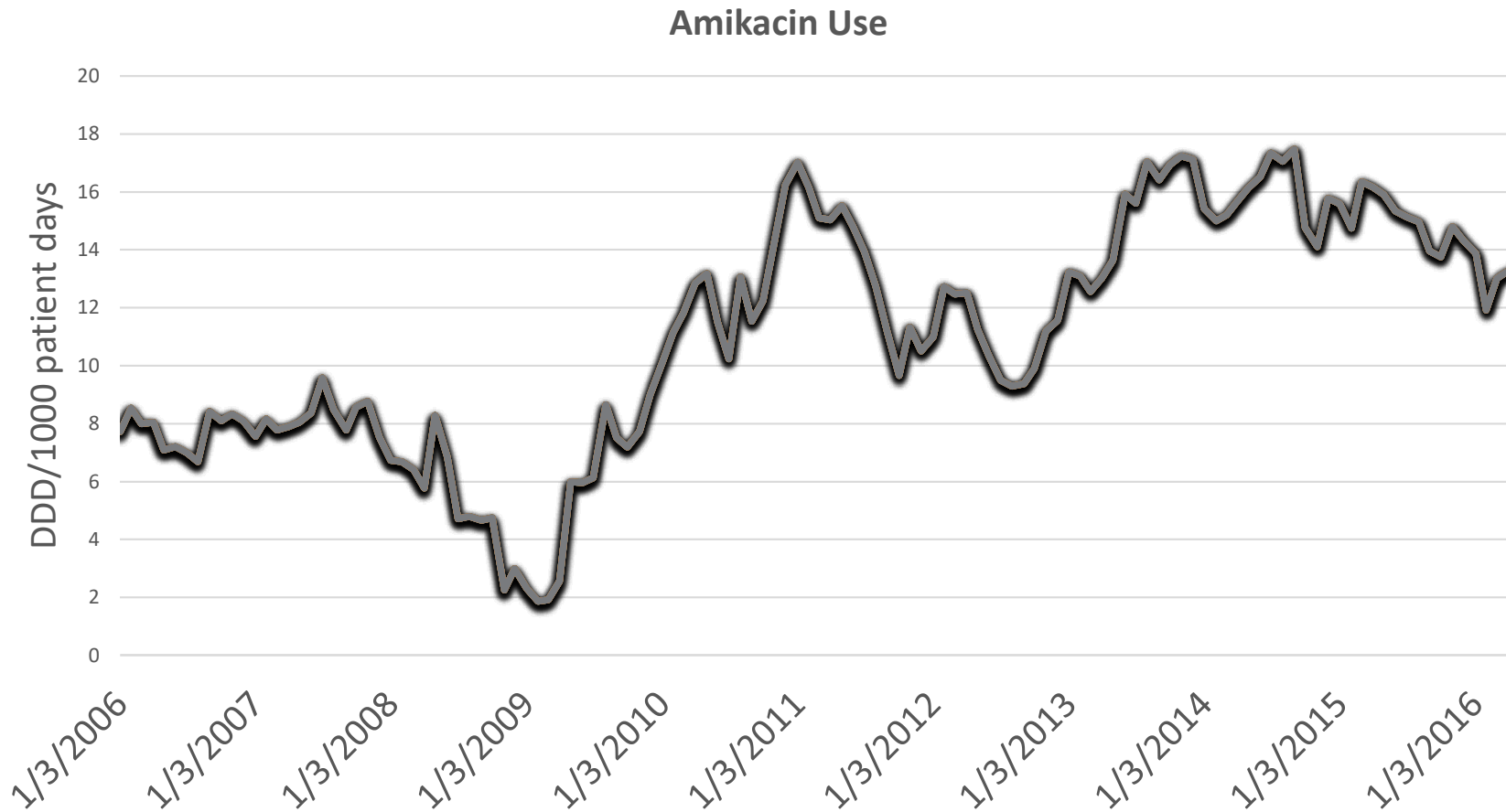
1. Including Interrupted Time Series (ITS) Designs in a EPOC Review.

<http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/inttime.pdf> accessed 10/28/16





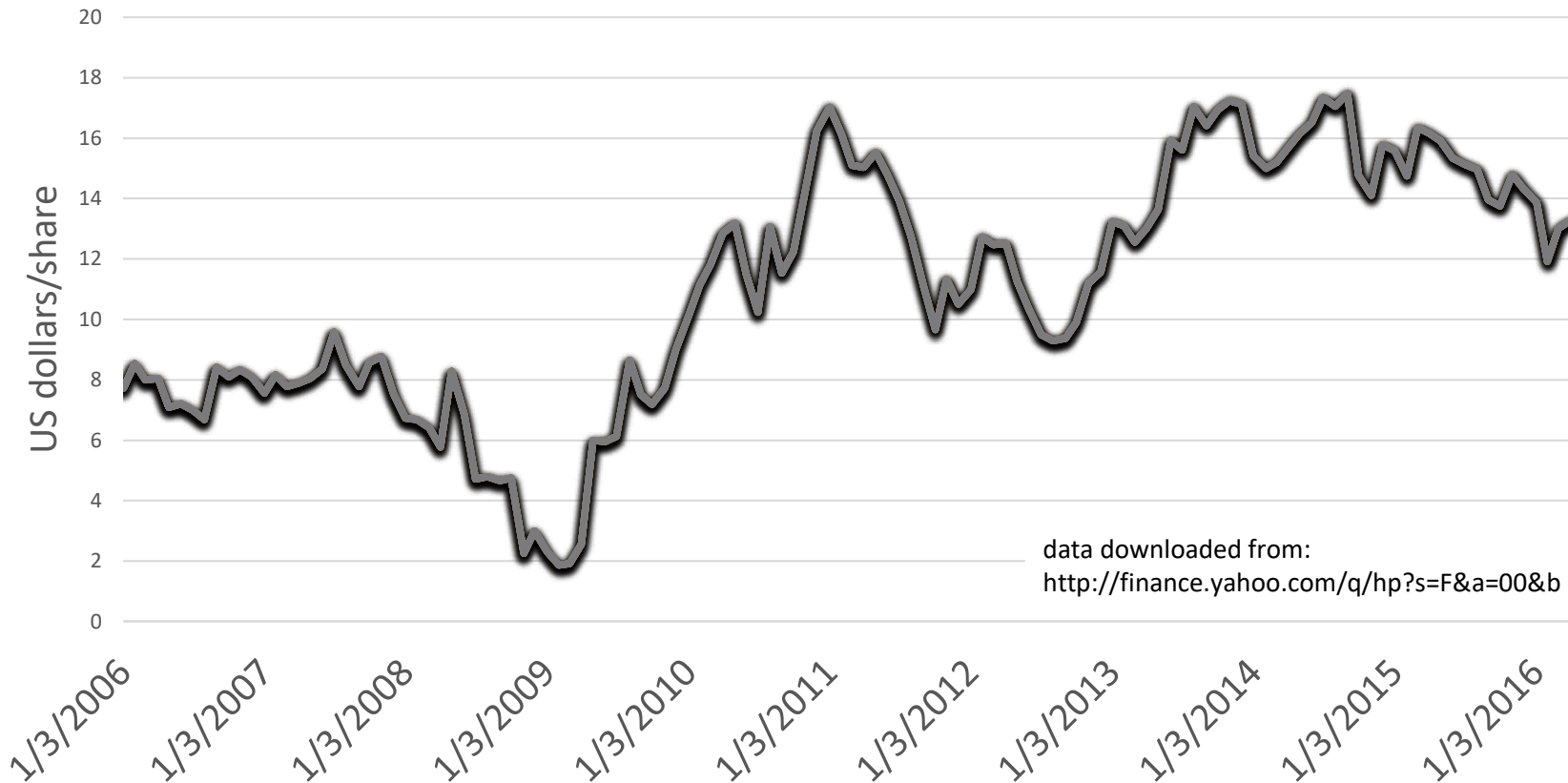
# Amikacin Use





# I lied. These are stock data.

Ford stock price



data downloaded from:  
<http://finance.yahoo.com/q/hp?s=F&a=00&b>



American Pharmacists Association™  
Improving medication use. Advancing patient care.

**ashp**  
Certification  
Resources

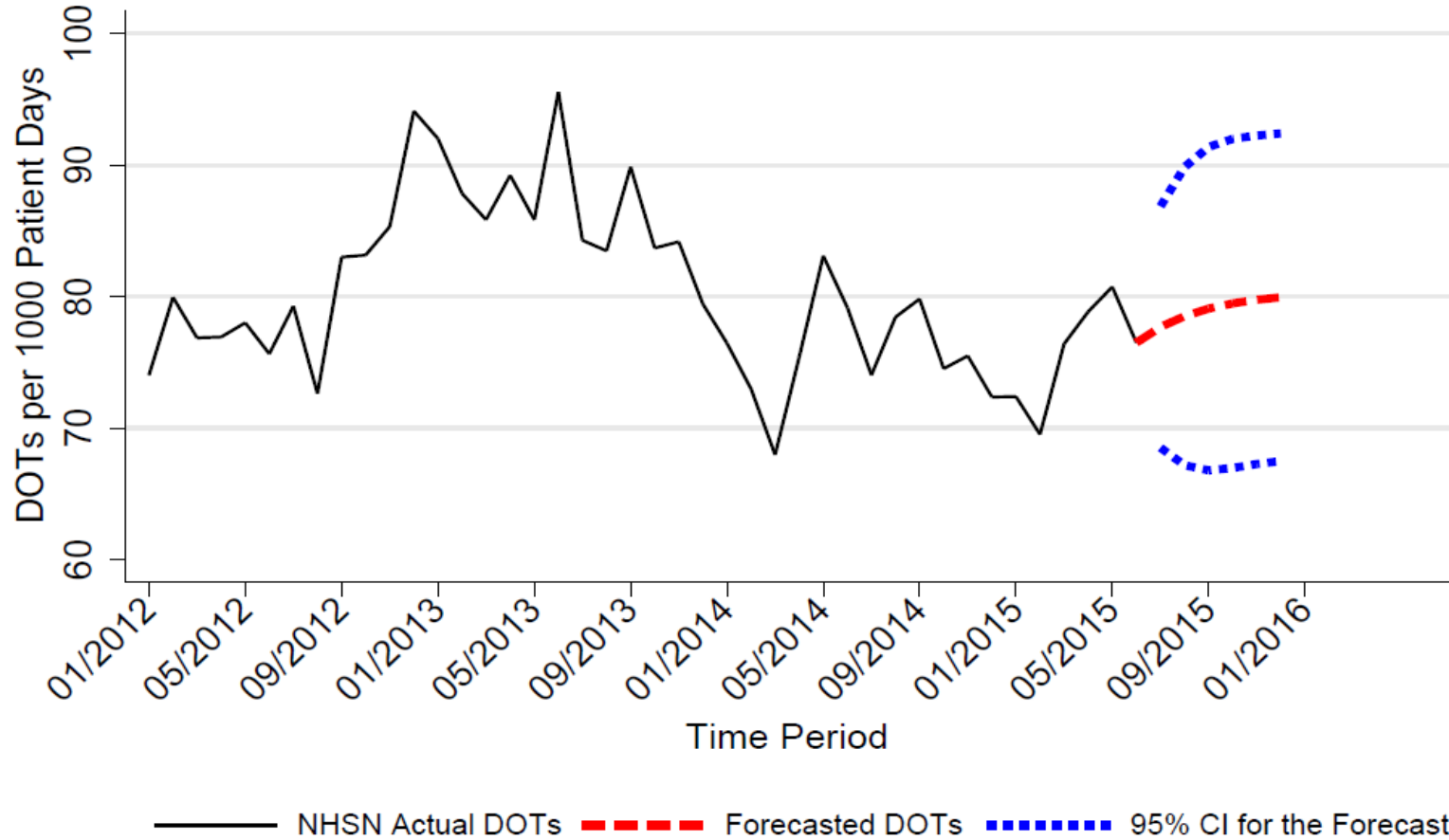
# Predicting the Future is Hard.

**BACK  
TO  
THE FUTURE**



# Forecasting

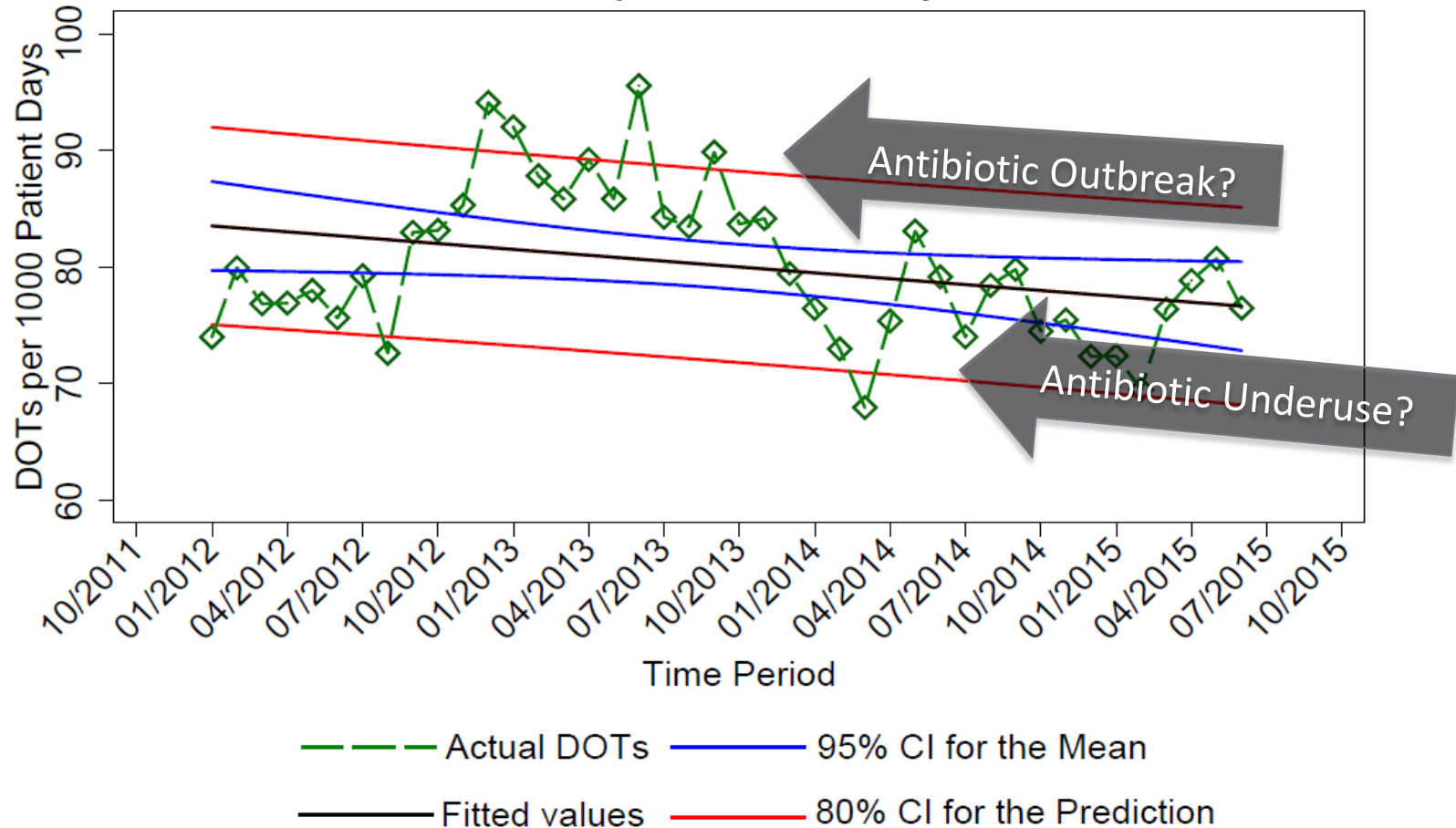
## Facility Wide Vancomycin Use



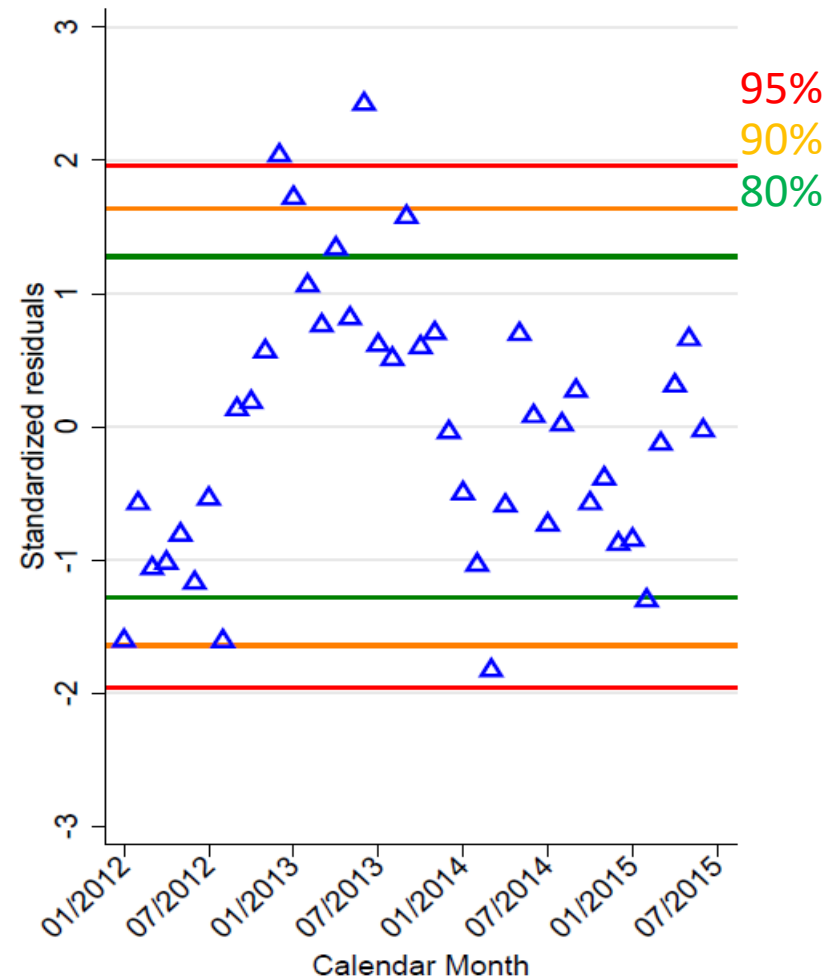
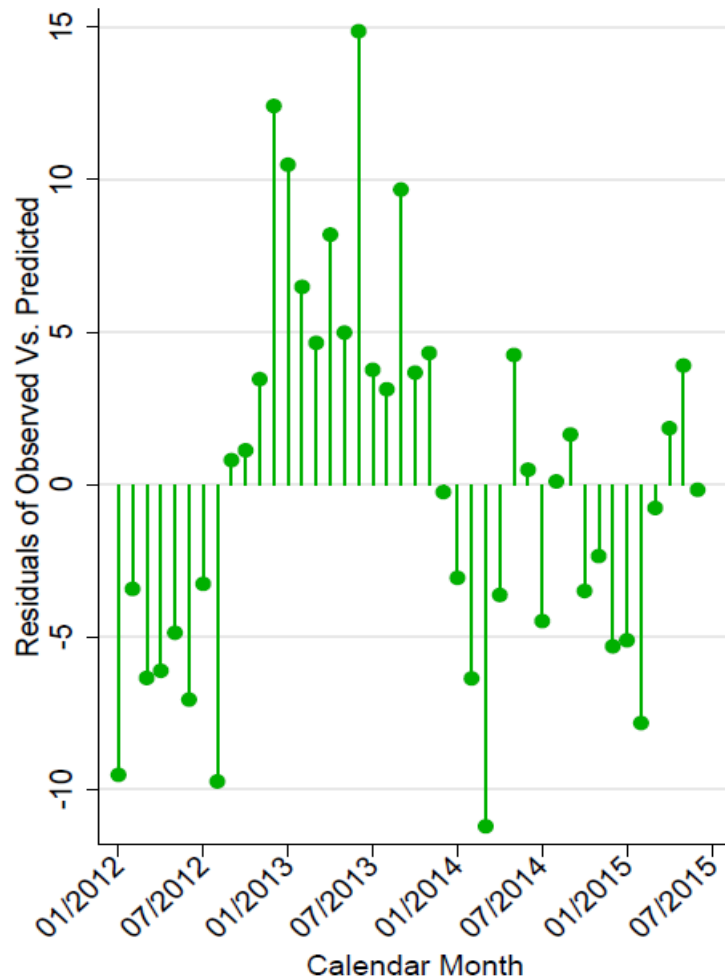
Scheetz et al. Unpublished because the reviewers didn't like it.

# Simple Regressive Methods

## Whole Hospital, Vancomycin Use



# Vancomycin, Whole Hospital





American Pharmacists Association™  
Improving medication use. Advancing patient care.



It gets more complex.



# Question 8: Which statement about seasonality in hospital antibiotic use is correct?

- A** There usually is not seasonal variation.
- B** There is seasonal variation, but it is not predictable.
- C** There is seasonal variation, and it is predictable.



# Question #8

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
*or*

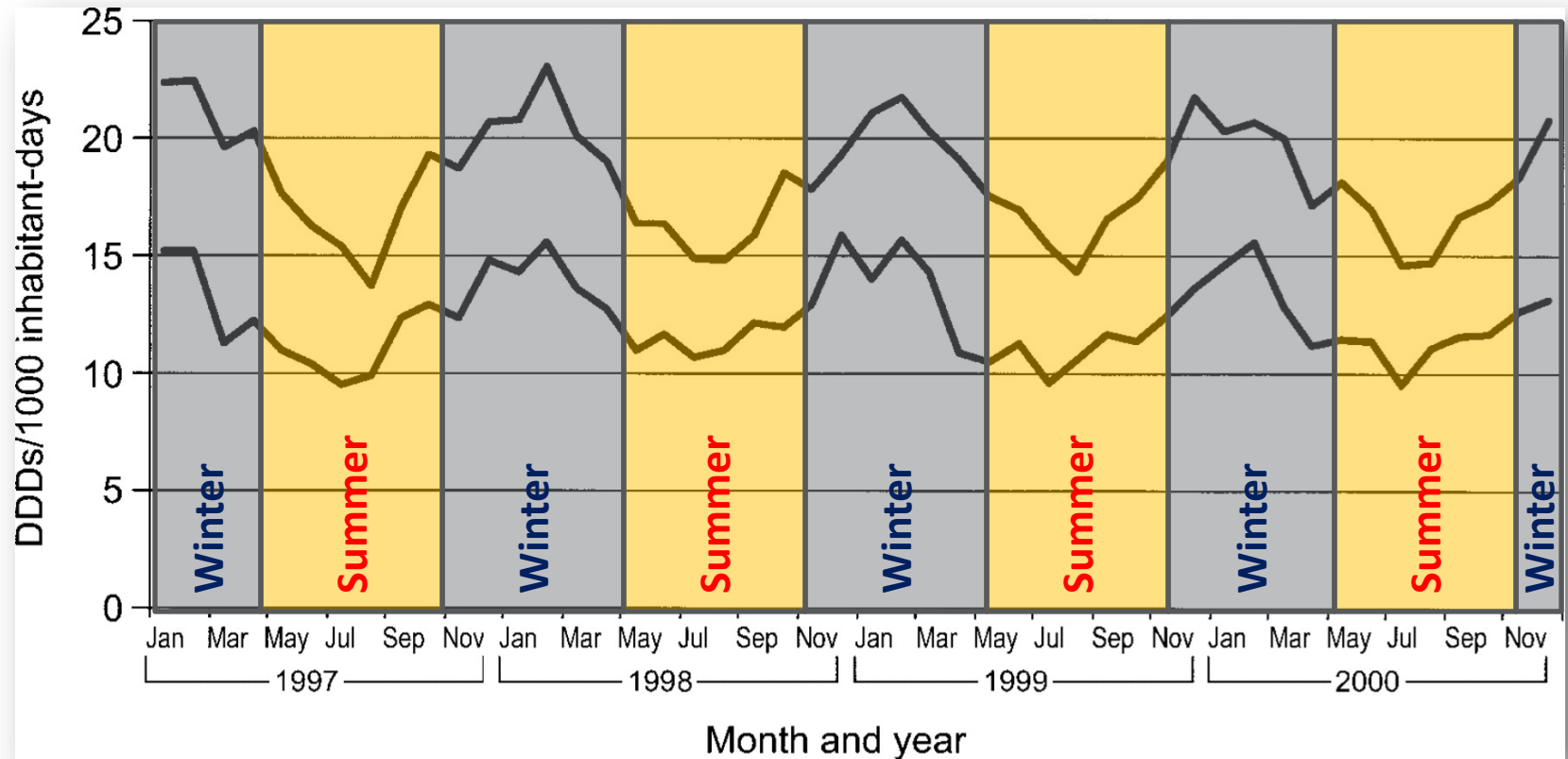
[Open poll in your web browser](#)



# Question 8: Which statement about seasonality in hospital antibiotic use is correct?

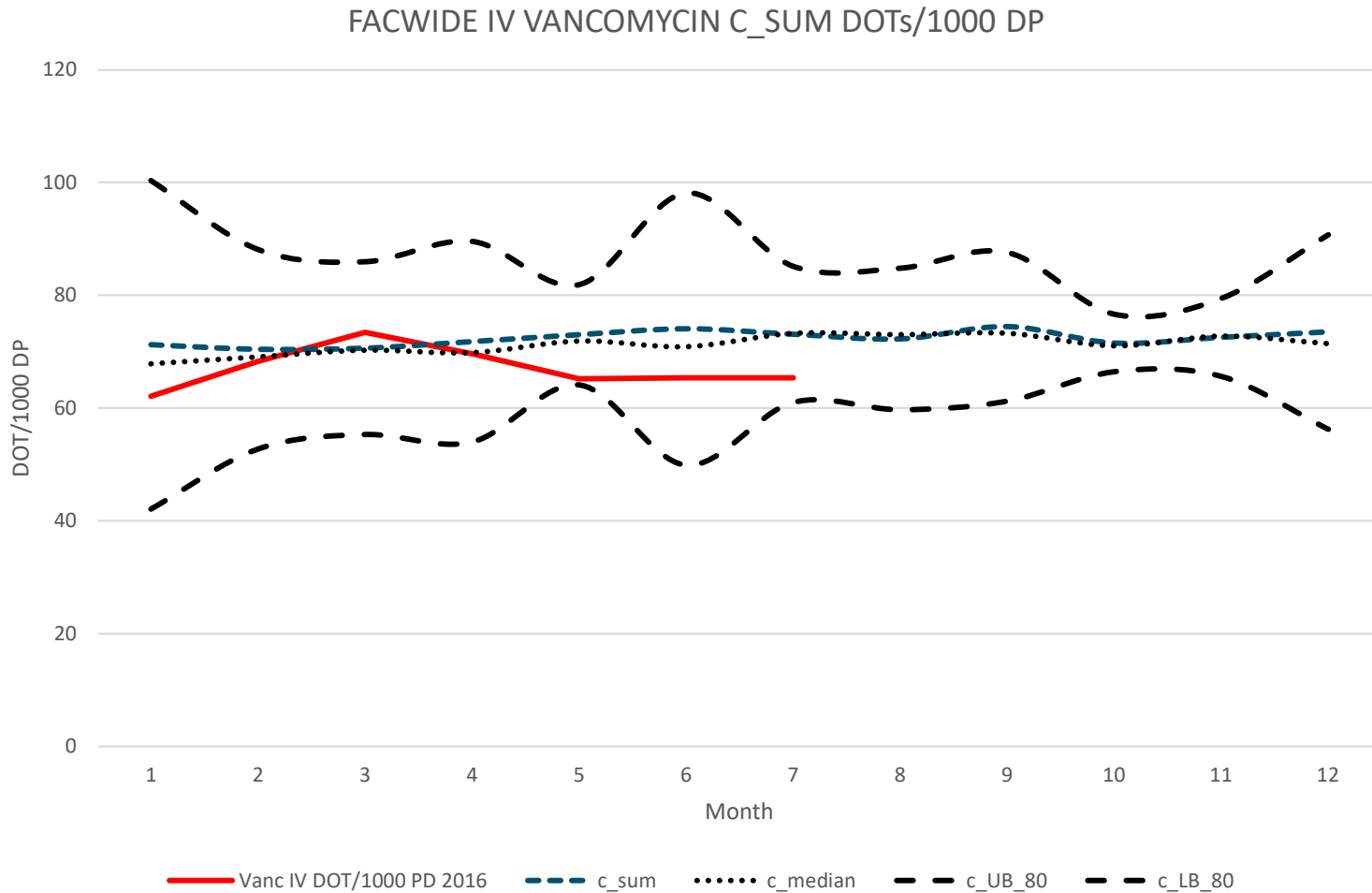
- A** There usually is not seasonal variation.
- B** There is seasonal variation, but it is not predictable.
- C** There is seasonal variation, and it is predictable.

## Seasonal Variation in Antibiotic Consumption in British Columbia (top) and Denmark (bottom), 1997–2000.





# Monthly Variability in Vancomycin



Slide courtesy of Dr. Jim Rhodes.

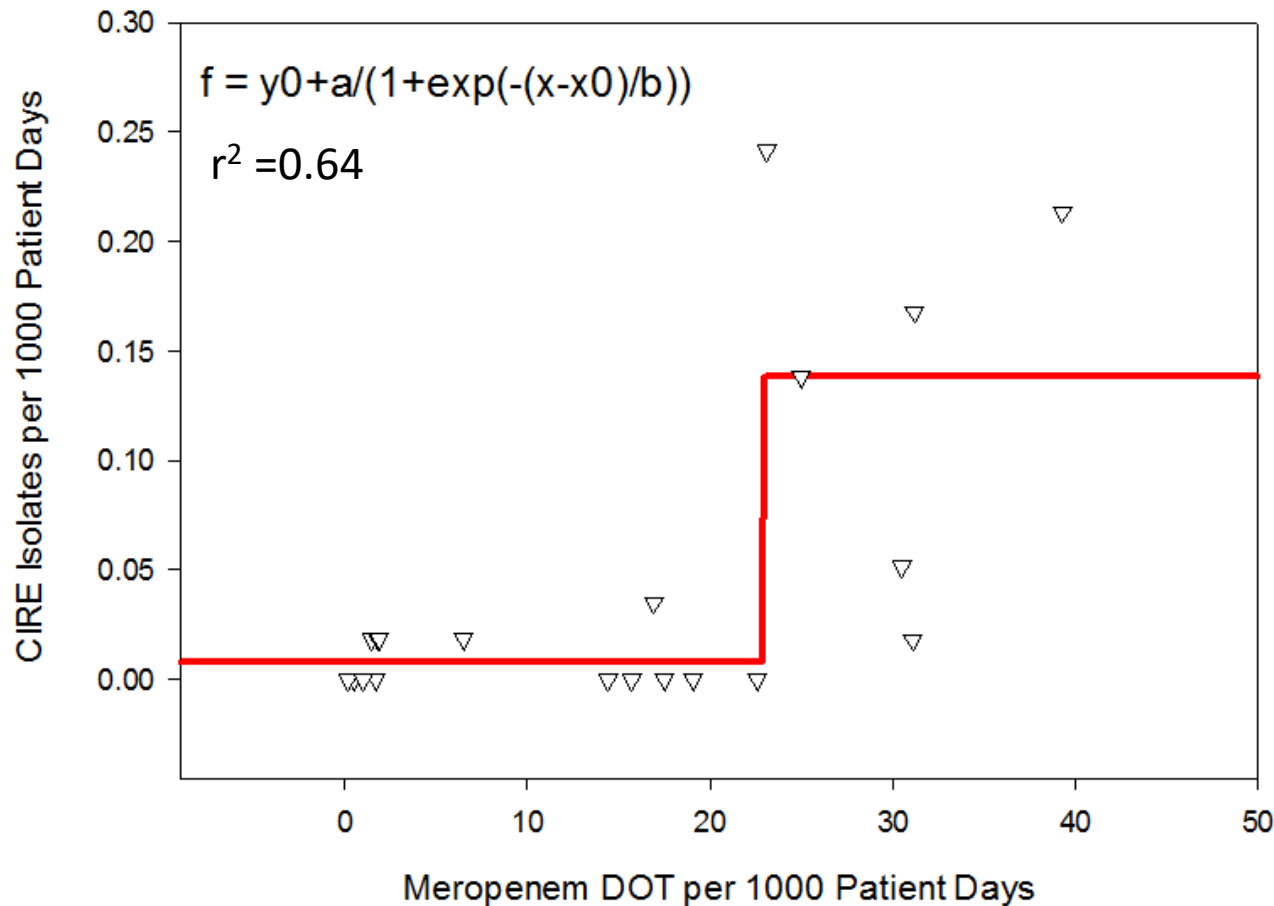


American Pharmacists Association™  
Improving medication use. Advancing patient care.



Linking consumption to resistance...  
even more difficult

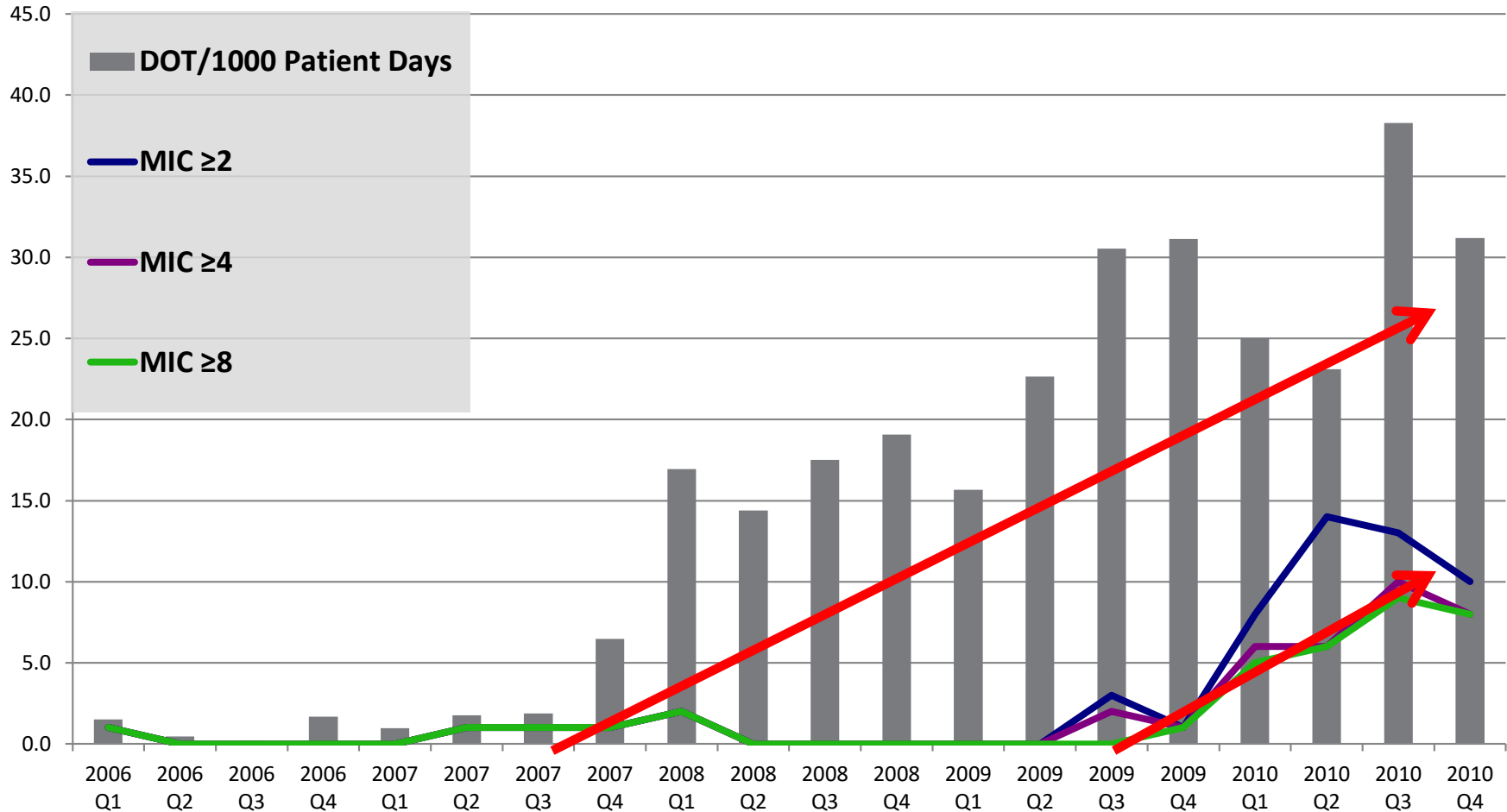
# Visual Interpretation can be Adequate.



Sigmoid-4 Parameter Model Describes Meropenem Carbapenem Intermediate or Resistant Enterobacteriaceae relationship. Adapted from: McLaughlin, Scheetz, et al. Antimicrob Agents Chemother. 2013 Oct; 57(10): 5131–5133.

# Co-trending Consumption and Resistance

## Meropenem DOT/1000 Patient Days and CRE Isolates

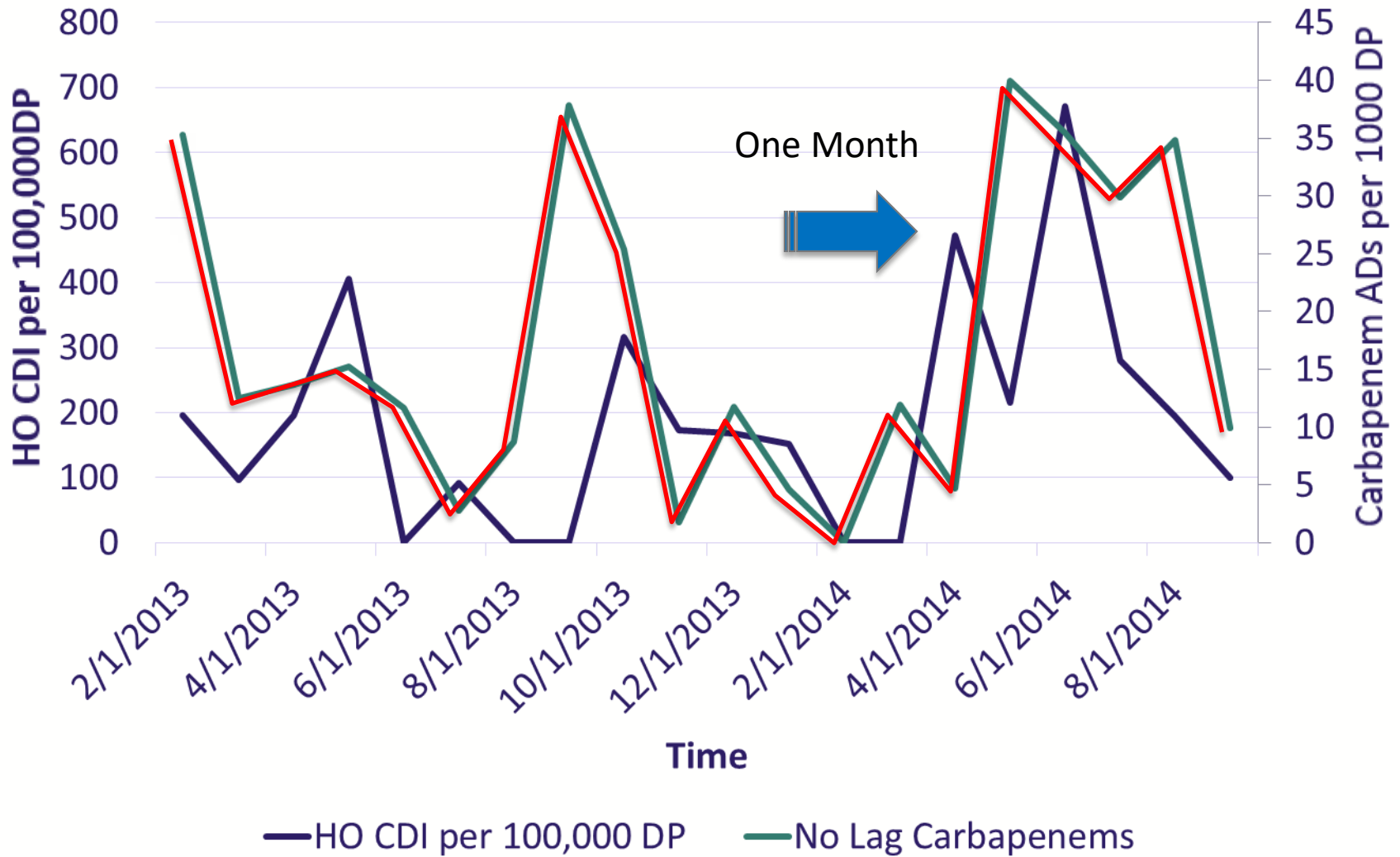


MIC= minimum inhibitory concentration in mg/L  
CRE=carbapenem resistant Enterobacteriaceae

Griffith M, et al. Interscience Conference on Antimicrobial Agents and Chemotherapy . Poster Presentation K-1419/308.

### Two Comparisons:

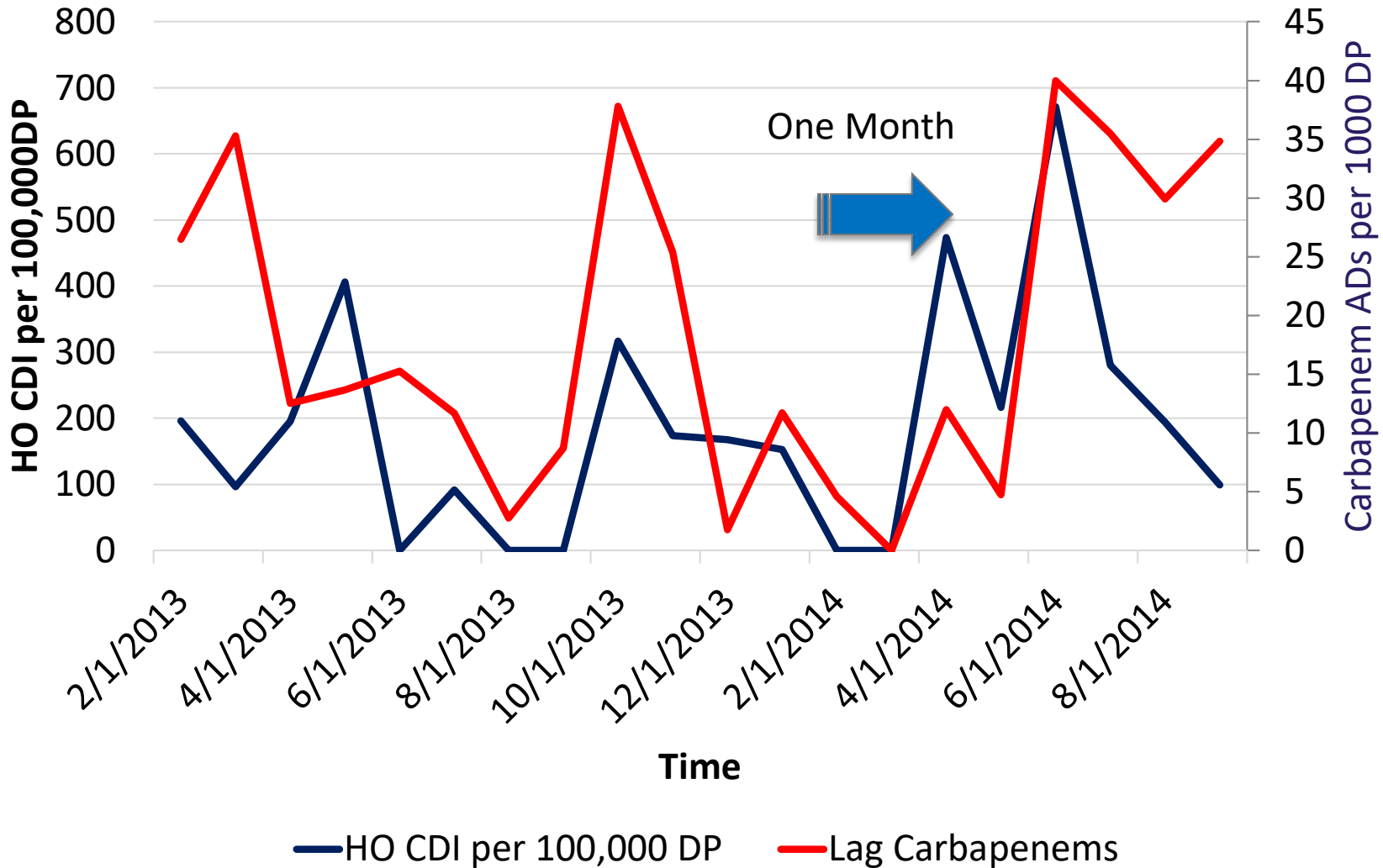
- 1. Effect of antibiotic in February 2013 → on CDI in February 2013
- 2. Effect of antibiotic in February 2013 → on CDI in March 2013



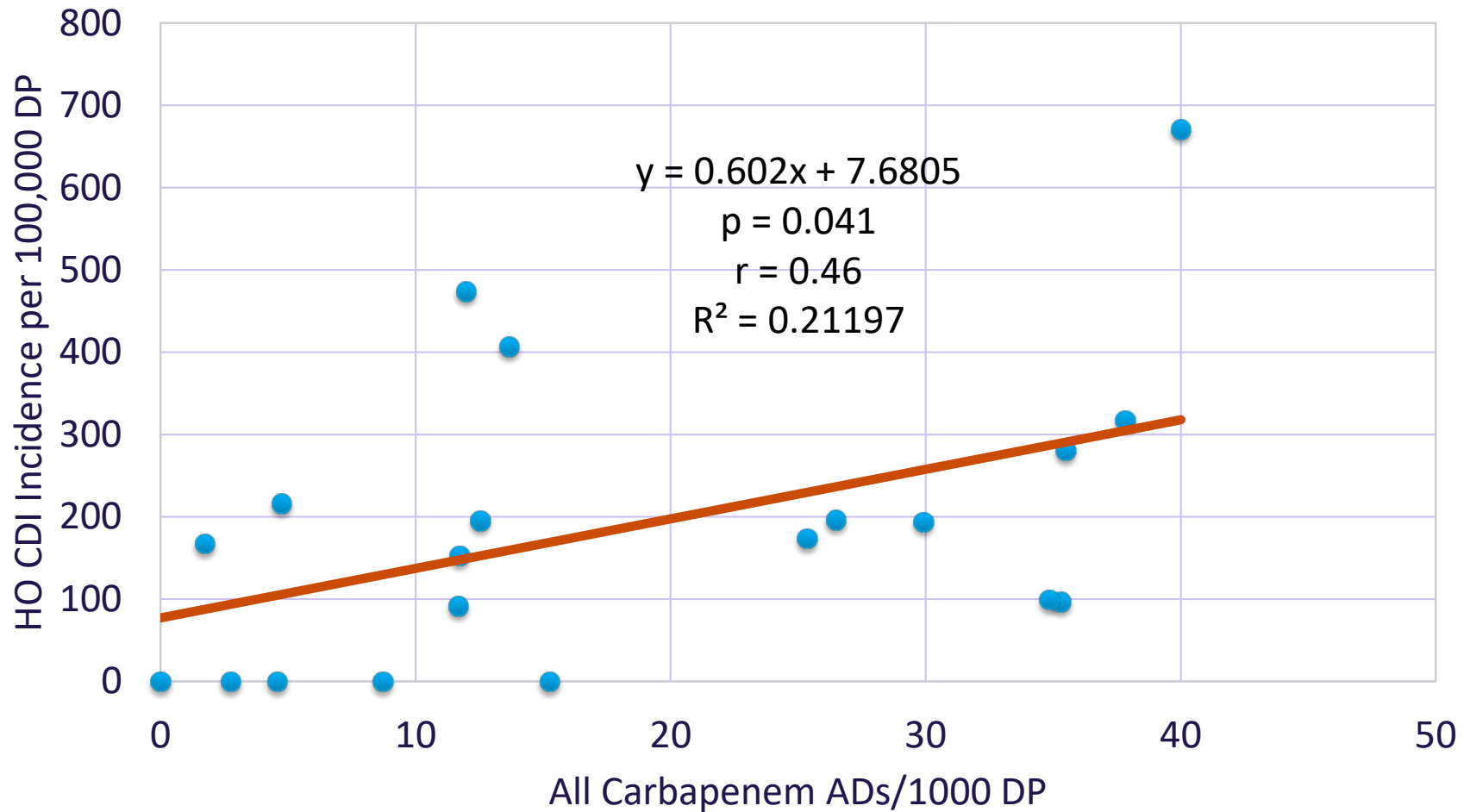


## Two Comparisons:

1. Effect of antibiotic in February 2013 → on CDI in February 2013
2. Effect of antibiotic in February 2013 → on CDI in March 2013



# Cancer Ward: One-Month Lag, Correlation between Carbapenem ADs and HO CDI Incidence, January 2013 - September 2014



# Comparing to Others. External Benchmarking

- Again, a denominator is necessary.
  - DDDs per 1000 patient days
  - DOTs per 1000 patient days
  - Cost per patient day
- Internal validity first: control for changes in hospital/program size across time
- External validity: control for variables likely to affect use/cost (e.g., patient severity of illness, patient disease state)
- Be aware that it is very difficult to compare yourself with other hospitals at this time.
  - A study by Pakyz et al. demonstrated that the only variable that predicted broad-spectrum antimicrobial use in a multi-hospital study was total duration of antibiotic use.<sup>1</sup>



## Standardized Antimicrobial Administration Ratio (SAAR)

SAAR is an Observed-to-Expected (O-to-E) ratio

- ❑ **Observed antibacterial use** – Days of therapy reported by a healthcare facility for a specified category of antimicrobial agents in a specified patient care location or group of locations
- ❑ **Predicted/Expected antibacterial use** – Days of therapy predicted on the basis of nationally aggregated AU data for a healthcare facility's use of a specified category of antimicrobial agents in a specified patient care location or group of locations

The SAAR metric is constructed by using an indirect standardization method for comparing observed to expected days of therapy. Detailed information on the SAAR can be found in the NHSN AUR Module Protocol: <http://www.cdc.gov/nhsn/pdfs/pscmanual/11pscaurcurrent.pdf>.

## Interpreting SAAR values

The SAAR is a ratio. The calculated SAAR value is always greater than 0, and a value of 1.0 suggests equivalency between observed and predicted antimicrobial use.

- ❑ A high SAAR (above 1.0) that achieves statistical significance (i.e., different from 1.0) may indicate excessive antimicrobial use.
- ❑ A SAAR that is not statistically different from 1.0 indicates antimicrobial use is equivalent to the referent population's antimicrobial use.
- ❑ A low SAAR (below 1.0) that achieves statistical significance (i.e., different from 1.0) may indicate antimicrobial under use.

**Note:** A SAAR alone is not a definitive measure of the appropriateness or judiciousness of antimicrobial use, and any SAAR may warrant further investigation. For example, a SAAR above 1.0 that does not achieve statistical significance may be associated with meaningful excess of antimicrobial use and further investigation may be needed. Also, a SAAR that is statistically different from 1.0 does not mean that further investigation will be productive.



## SAAR Calculations Cover 5 Antibiotic Agent Categories

High value targets for antimicrobial stewardship programs:

1. **Broad spectrum agents predominantly used for hospital-onset/multi-drug resistant bacteria** – aminoglycosides, some cephalosporins, penicillin B-lactam/b-lactamase inhibitor combinations, and other agents
2. **Broad spectrum agents predominantly used for community-acquired infection** – ertapenem, some cephalosporins, and some fluoroquinolones
3. **Anti-MRSA agents** – ceftaroline, dalbavancin, daptomycin, linezolid, oritavancin, quinupristin/dalfopristin, tedizolid, telavancin, and vancomycin
4. **Agents predominantly used for surgical site infection prophylaxis** – cefazolin, cefotetan, cefoxitin, cefuroxime

High level indicators for antimicrobial stewardship programs:

5. **All antibiotic agents** – All agents included in NHSN AUR protocol



American Pharmacists Association™  
Improving medication use. Advancing patient care.



# Other Manifestations of Consumption

Tracking and Analyzing Costs...  
because you probably “have to”

Question 9: A dollar bill, today, is worth:



- A** More today than it will be in 1 year
- B** Less today than it will be in 1 year
- C** The same today as it will be in 1 year
- D** At least 4 pulls on the quarter slot machines



# Question #9

Your poll will show here

1

Install the app from  
[pollev.com/app](https://pollev.com/app)

2

Make sure you are in  
Slide Show mode

Still not working? Get help at [pollev.com/app/help](https://pollev.com/app/help)  
or

[Open poll in your web browser](#)

Question 9: A dollar bill, today, is worth:



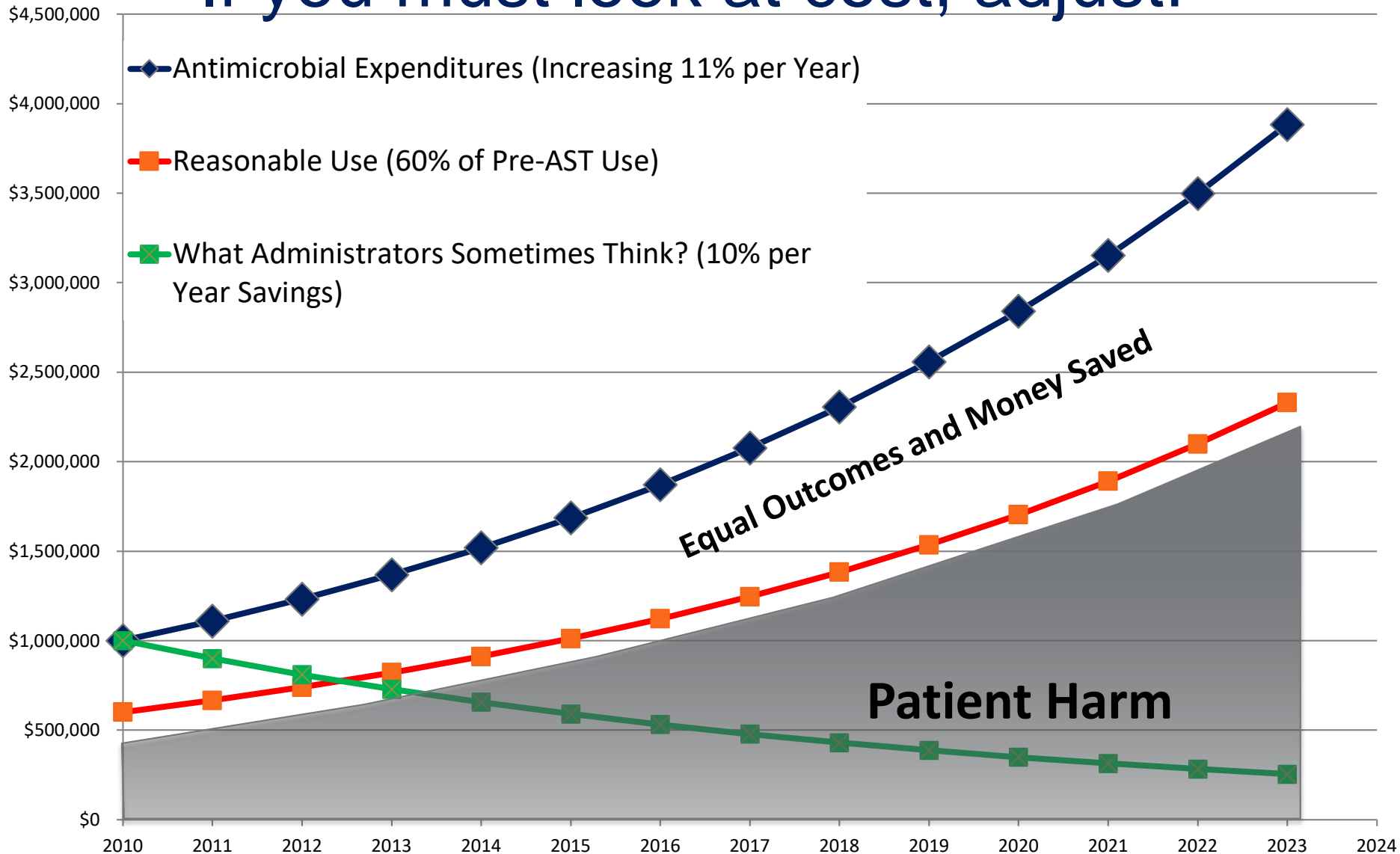
- A** More today than it will be in 1 year
- B** Less today than it will be in 1 year
- C** The same today as it will be in 1 year
- D** At least 4 pulls on the quarter slot machines

# You CANNOT escape COST!

## What can you do?

- Due to compounding of market price increases, yearly drug cost increases can often be logarithmic.
- This must be understood by administration.
- Failing to account for increasing drug costs will doom your ASP in short order.
  
- An example
  - Assume a fixed rate of 11% per year increase in drug costs.
  - Predict what a reasonable reduction in Antibiotic Costs would be from your ASP.

# If you must look at cost, adjust!





# Key Takeaways

- Who to compare with:
  - Self? Absolutely!
  - Others? Yes, but realize that this is more difficult.
- What to measure
  - Antibiotic use/consumption? (yes!!)
  - Antibiotic cost? (yes, but carefully)

# A call to action

“There is perhaps never been a more critical juncture for antimicrobial stewardship. There is growing interest from key stakeholders-clinicians, healthcare administrators, and policy makers-and a growing body of evidence demonstrating the benefits of stewardship. We now need to harness the interest and the science to move forward toward making stewardship programs and integral part of healthcare facilities.”



Modified from:  
<http://en.wikipedia.org/wiki/File:Unclesamwantyou.jpg#filelinks>



# Key Takeaways

- **Key Takeaway #1: Antimicrobial drug resistance is reaching a critical level. It results in increased hospitalizations, treatment failures, mortality, and costs. Efforts to curb antimicrobial resistance are greatly needed.**
- **Key Takeaway #2: The pharmacist is a key member of the antimicrobial stewardship team and should pursue a leadership role in stewardship efforts.**
- **Key Takeaway #3: The CDC and IDSA/SHEA guidelines provide guidance and recommendations for establishing an antimicrobial stewardship program, including program components and strategies.**



American Pharmacists Association™  
Improving medication use. Advancing patient care.

APhA



# Questions?





# References

- Liu YY, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis* 2016; 16: 161-8.
- Centers for Disease Control and Prevention Emergency Preparedness and Response Website. Alert to U.S. healthcare facilities: first *mcr-1* gene in *E. coli* bacteria found in a human in the United States. <http://emergency.cdc.gov/han/han00390.asp>. Accessed July 9, 2016.
- Wenzel RP, Bearman G, Edmond MB. Screening for MRSA: a flawed hospital infection control intervention. *Infect Control Hosp Epidemiol* 2008; 29: 1012-8.
- Kassakian SZ, Mermel LA. Changing epidemiology of infections due to extended spectrum beta-lactamase producing bacteria. *Antimicrob Resist Infect Control* 2014; 3: 9.



# References

- Centers for Disease Control and Prevention Antibiotic/Antimicrobial Resistance Webpage. Biggest Threats. [http://www.cdc.gov/drugresistance/biggest\\_threats.html](http://www.cdc.gov/drugresistance/biggest_threats.html). Accessed July 9, 2016.
- World Health Organization. Antimicrobial resistance: global report on surveillance – 2014 summary. [http://apps.who.int/iris/bitstream/10665/112647/1/WHO\\_HSE\\_PED\\_AIP\\_2014.2\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/112647/1/WHO_HSE_PED_AIP_2014.2_eng.pdf?ua=1). Accessed July 9, 2016.
- Iredell J, Brown J, Tagg K. Antibiotic resistance in Enterobacteriaceae: mechanisms and clinical implications. *BMJ* 2016; 352: h6420.
- Holmes AH, Moore LSP, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* 2016; 387: 176-87.



# References

- Munita JM, Bayer AS, Arias CA. Evolving resistance among gram-positive pathogens. *Clin Infect Dis* 2015; 61 (Suppl 2): S48-57.
- Finley RL, Collignon P, Joakim Larsson DG, et al. The scourge of antibiotic resistance: the important role of the environment. *Clin Infect Dis* 2013; 57: 704-10.
- Boucher HW, Talbot GH, Bradley JS. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 48: 1-12.
- Lode HM. Clinical impact of antibiotic-resistant gram-positive pathogens. *Clin Microbiol Infect* 2009; 15: 212–217.
- Tleyjeh IM, Tlaygeh HM, Hajel R, Montori VM, Baddour LM. The impact of penicillin resistance on short-term mortality in hospitalized adults with pneumococcal pneumonia: a systematic review and meta-analysis. *Clin Infect Dis* 2006; 42:778–97.

# References

- **Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y.** The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005; 26: 166-174.
- **World Health Organization.** Surveillance standards for antimicrobial resistance. 2002. [http://apps.who.int/iris/bitstream/10665/67426/1/WHO\\_CDS\\_CSR\\_DRS\\_2001.5.pdf](http://apps.who.int/iris/bitstream/10665/67426/1/WHO_CDS_CSR_DRS_2001.5.pdf).
- **Bax R, Bywater R, Cognaglia G, et al.** Surveillance of antimicrobial resistance—what, how, and whither. *Clin Microbiol Infect* 2001; 7: 316-325.
- **Masterson RG.** Surveillance studies: how can they help the management of infection? *J Antimicrob Chemother* 2000; 46 Suppl B: 53-58.



# References

- Pulido MR, García-Quintanilla M, Martín-Peña R, Cisneros JM, McConnell MJ. Progress on the development of rapid methods for antimicrobial susceptibility testing. *J Antimicrob Chemother* 2013; 68: 2710-2717.
- Lee TB, Montgomery OG, Marx J, Olmsted RN, Scheckler WE. Recommended practices for surveillance: Association for Professionals in Infection Control and Epidemiology (APIC), Inc. *Am J Infect Control* 2007; 35: 427-40.
- Pestotnik SL. Expert clinical decision support systems to enhance antimicrobial stewardship programs: insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 2005; 25: 1115-25.
- Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44: 159-77.



# References

- **The White House. National action plan for combating antibiotic-resistant bacteria. March 2015. [https://www.whitehouse.gov/sites/default/files/docs/national\\_action\\_plan\\_for\\_combating\\_antibiotic-resistant\\_bacteria.pdf](https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf).**
- **U.S. Department of Health and Human Services Centers for Medicare & Medicaid Services. Hospital and Critical Access Hospital (CAH) changes to promote innovation, flexibility, and improvement in patient care. <https://www.gpo.gov/fdsys/pkg/FR-2016-06-16/pdf/2016-13925.pdf>. Accessed July 9, 2016.**
- **The Joint Commission Website. Prepublication requirements: new antimicrobial stewardship standard. [https://www.jointcommission.org/assets/1/6/HAP-CAH\\_Antimicrobial\\_Prepub.pdf](https://www.jointcommission.org/assets/1/6/HAP-CAH_Antimicrobial_Prepub.pdf). Accessed July 9, 2016.**



# References

- U.S. Food and Drug Administration. FDA drug safety communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. July 26, 2016. <http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm>.
- U.S. Food and Drug Administration. Phasing Out Certain Antibiotic Use in Farm Animals. February 25, 2015. <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm378100.htm>.
- U.S. Food and Drug Administration. New animal drugs and new animal drug combination products administered in or on medicated feed or drinking water of food-producing animals: recommendations for drug sponsors for voluntarily aligning product use conditions with GFI #209. December 2013. <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf>.



# References

- Ohi CA, Ashley SD. Antimicrobial stewardship programs in community hospitals: the evidence base and case studies. *Clin Infect Dis* 2011; 53 (Suppl 1): s23-28.
- Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* 2003; 24: 699–706.
- Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs. 2014.  
<http://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf>.





# References

- Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44: 159-77.
- Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; 62(10): e51-77.



# Recommended Resources

- **Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44: 159-77.**
- **Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; 62(10): e51-77.**



# Recommended Resources

- The White House National Action Plan for Combating Antibiotic-Resistant Bacteria:  
[https://www.whitehouse.gov/sites/default/files/docs/national\\_action\\_plan\\_for\\_combating\\_antibiotic-resistant\\_bacteria.pdf](https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf)
- The Joint Commission Antimicrobial Stewardship Standard:  
[https://www.jointcommission.org/assets/1/6/New\\_Antimicrobial\\_Stewardship\\_Standard.pdf](https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf)
- CMS Proposed Rule on Infection Control and Antibiotic Stewardship Programs:  
[https://www.federalregister.gov/articles/2016/06/16/2016-13925/medicare-and-medicaid-programs-hospital-and-critical-access-hospital-cah-changes-to-promote#h-22.](https://www.federalregister.gov/articles/2016/06/16/2016-13925/medicare-and-medicaid-programs-hospital-and-critical-access-hospital-cah-changes-to-promote#h-22)



# Recommended Resources

- **ASHP Resource Center:**  
<http://www.ashp.org/menu/PracticePolicy/ResourceCenters/Inpatient-Care-Practitioners/Antimicrobial-Stewardship>
- **CDC Get Smart for Healthcare:**  
<http://www.cdc.gov/getsmart/healthcare/index.html>
- **CDC Antimicrobial Stewardship Resources:**  
<http://www.cdc.gov/getsmart/healthcare/>



# Recommended Resources

- **IDSA Promoting Antimicrobial Stewardship in Human Medicine:**  
[http://www.idsociety.org/Stewardship\\_Policy/](http://www.idsociety.org/Stewardship_Policy/)
- **American Hospital Association's Antimicrobial Stewardship User Guide:**  
<http://www.ahaphysicianforum.org/resources/appropriate-use/antimicrobial/>



# Recommended Resources

- **ASHP Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control:**  
**<https://www.ashp.org/DocLibrary/BestPractices/SpecificStAntimicrob.aspx>**
- **Pulido MR, García-Quintanilla M, Martín-Peña R, Cisneros JM, McConnell MJ. Progress on the development of rapid methods for antimicrobial susceptibility testing. *J Antimicrob Chemother* 2013; 68: 2710-2717.**