Making Antimicrobial Stewardship a Priority: Integrating Evidence-based Practices and Guidelines to Improve Antimicrobial Use

Proceedings of a Midday Symposium and Live Webinar at the 51\textsuperscript{st} ASHP Midyear Clinical Meeting and Exhibition

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[www.cemidday.com](http://www.cemidday.com)

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Making Antimicrobial Stewardship a Priority: Integrating Evidence-based Practices and Guidelines to Improve Antimicrobial Use

Agenda

Welcome and Introductions
Kevin W. Garey, Pharm.D., M.S., FASHP

Overview of National Initiatives and New Guidelines that Affect Antimicrobial Stewardship Programs (ASPs)
Kevin W. Garey, Pharm.D., M.S., FASHP

Case studies in antimicrobial stewardship
All Faculty

Future Perspectives on ASPs
Edward J. Septimus, M.D., FiDSA, FACP, FSHEA

Faculty Discussion and Audience Questions
All Faculty

Faculty

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Professor and Chair
Department of Clinical Sciences and Administration
University of Houston College of Pharmacy
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Texas A&M Health Science Center College of Medicine
Houston, Texas
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- Kevin W. Garey, Pharm.D., M.S., FASHP, declares he received a research grant from Merck.
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Activity Overview

The National Action Plan for Combating Antibiotic-resistant Bacteria released by the White House in March 2015 highlighted the urgent need to slow the emergence of resistant bacteria and spread of resistant infections. Since that time, key collaborators within government and non-government organizations have responded with initiatives directly focused on improving antimicrobial stewardship programs (ASPs). These include new antibiotic stewardship guidelines jointly published by the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America, an Antibiotic Stewardship Playbook published by the National Quality Forum, and Core Elements of Hospital Antibiotic Stewardship Programs published by the Centers for Disease Control and Prevention. Pharmacists and physicians at the front lines of antimicrobial stewardship need to stay up to date on this fast evolving landscape and learn strategies to use best-practices to develop and establish ASP priorities and resources in their healthcare setting.

This educational activity will provide a state-of-the-art update on national initiatives that are directly influencing the role of ASPs. Using real-life examples, the faculty will discuss how to best use these resources to optimize ASPs and patient care. Examples will include case scenarios in managing patients with sepsis and Clostridium difficile.

Learning Objectives

At the conclusion of this application-based educational activity, participants should be able to

- Analyze National initiatives and Guidelines that are directly influencing the role of Antimicrobial Stewardship Programs (ASPs).
- Select specific clinical areas that ASPs are useful for combating antimicrobial resistance and decreasing the spread of resistant infections.
- Predict the future of antimicrobial stewardship and how national initiatives and standards will influence ASPs.
Continuing Education Accreditation

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Live Activity ACPE #: 0204-0000-16-468-L01-P

On-Demand Activity ACPE #: 0204-0000-16-468-H01-P

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The American Society of Health-System Pharmacists designates this enduring material for a maximum of 1.5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Additional Educational Opportunities about Antimicrobial Stewardship Coming in 2017

• Ask the Experts webinar – Faculty will explore issues raised by participant questions in today’s symposium (1 hour CE). Presented on April 19, 2017, 1:00 – 2:00 p.m. ET

For more information and to sign up to receive e-mail updates about this topic, visit www.cemiday.com
Faculty

Kevin W. Garey, Pharm.D., M.S., FASHP, Activity Chair
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Department of Clinical Sciences and Administration
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Kevin W. Garey, Pharm.D., M.S., FASHP is Professor at the University of Houston College of Pharmacy and Chair of the Department of Clinical Sciences and Administration at the University of Houston College of Pharmacy in Houston, Texas. Dr. Garey is an Adjunct Professor at the University of Texas School of Public Health and a Clinical Specialist and Researcher at Baylor St. Luke’s Medical Center in Houston, Texas. He received a Bachelor of Science in Pharmacy degree from Dalhousie University in Halifax, Nova Scotia, Canada, a Doctor of Pharmacy from the State University of New York in Buffalo, New York, and Master of Science in Biometry from the University of Texas School of Public Health in Austin, Texas. He completed a pharmacy practice residency at Bassett Healthcare, Cooperstown, NY and infectious disease specialty residency and fellowship training at the University of Illinois at Chicago College of Pharmacy in Chicago, Illinois.

Dr. Garey has numerous publications in infectious diseases topics and has presented extensively at national and international professional conferences. He has received numerous professional awards including the ASHP Drug Therapy Research Award, ASHP Best Practices Award in Health-System Pharmacy, the Society of Infectious Diseases Pharmacists Impact Paper in Infectious Diseases Pharmacotherapy Award and the University of Houston Faculty Leadership award. He is a Fellow of ASHP.

Dr. Garey's research interests involve clinical and translational research involving healthcare-associated infections including post-surgical infections, candidemia, and Clostridium difficile infection.
Making Antimicrobial Stewardship a Priority: Integrating Evidence-based Practices and Guidelines to Improve Antimicrobial Use

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Edward J. Septimus, M.D., FACP, FIDSA, FSHEA, is Medical Director, Infection Prevention and Epidemiology at Hospital Corporation of America (HCA) and Professor of Internal Medicine at Texas A&M Health Science Center College of Medicine in Houston, Texas. He is also Professor, Distinguished Senior Fellow, at the George Mason University School of Public Health.

Dr. Septimus received his Bachelor of Science from The Ohio State University and his Doctor of Medicine degree from Baylor College of Medicine in Houston. He completed his postgraduate training in internal medicine and infectious diseases at Baylor College of Medicine in Houston and is board certified in both internal medicine and infectious diseases. He is fellow of the American College of Physicians, Infectious Diseases Society of America (IDSA), and Society for Healthcare Epidemiology of America (SHEA).

His practice interests include patient safety, infection prevention, antimicrobial stewardship and resistance, public health including vaccine preventable diseases, sepsis, medical informatics, clinical integration, and human factors engineering. Dr. Septimus has lectured nationally and internationally on surviving sepsis, reduction of healthcare-associated infections, antimicrobial stewardship, influenza, methicillin-resistant Staphylococcus aureus (MRSA), the economic case for quality, and employee health. He is Past President of the Texas Infectious Diseases Society and has served on the Board of Directors of the IDSA. He is on the IDSA Antimicrobial Resistance Committee, the SHEA Antimicrobial Stewardship Committee, and the IDSA Quality Measurement Committee. In 2011 he was appointed to the Healthcare-Associated Infections/Preventable Adverse Events Advisory Panel for the Texas Department of State Health Services. Dr. Septimus is also a member of the FDA Anti-Infective Drug Advisory Group and is co-chair of the National Quality Forum (NQF) Patient Safety Steering Committee.

Dr. Septimus has published over 100 peer-reviewed articles and book chapters. He was the first recipient of the IDSA Annual Clinician Award, received the John S. Dunn Sr. Outstanding Teacher Award in 2010, 2011, 2013 and 2014, and received the Clinical Excellence Award from HealthTrust in 2013.
CE IN THE MIDDAY
Making Antimicrobial Stewardship a Priority: Integrating Evidence-based Practices and Guidelines to Improve Antimicrobial Use

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Learning Objectives

• Analyze National initiatives and Guidelines that are directly influencing the role of Antimicrobial Stewardship Programs (ASPs).
• Select specific clinical areas that ASPs are useful for combating antimicrobial resistance and decreasing the spread of resistant infections.
• Predict the future of antimicrobial stewardship and how national initiatives and standards will influence ASPs.

Do you ever wonder how anything ever gets done in the U.S.?

• President’s Executive Order and National Strategy (Sep 2014)
• PCAST Report to the President (Sep 2014)
• National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) (Mar 2015)

Tools for Stewardship Change (U.S.)

White House (Executive Branch)

Dept of Health and Human Services

Centers for Disease Control and Prevention (CDC)
• Best Practice Documents for Public Health
• Core Elements
• Mechanism to monitor disease (NHIN)
• Antibiotic Utilization (AU) module

Centers for Medicare & Medicaid Services (CMS)
• Administers Medicare and Medicaid (i.e., pay for stuff)
• Conditions of participation
• Core measures (what hospitals have to do)

Non-governmental organizations (NGOs):
National Quality Forum (NQF): Develops standards (that may become core measures)
The Joint Commission (TJC): Accredits hospitals (make sure they are following core measures)
Scientific societies (IDSA): Publishes guidelines (that may form the basis for core measures)

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- Strengthen antibiotic stewardship in inpatient, outpatient, and long-term care settings
  - Alignment with CDC Core Elements
  - Compliance with Conditions of Participation and The Joint Commission (TJC) accreditation requirements
- Implement annual reporting of antibiotic use in inpatient and outpatient settings and identify variation at geographic, provider, and patient levels
- Establish and improve antibiotic stewardship programs across all healthcare settings
- Reduce inappropriate antibiotic use by 50% in outpatient settings and 20% in inpatient settings
- Establish State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states


CDC Core Elements of Hospital Antibiotic Stewardship Programs

- Leadership commitment from administration
- Accountability: Single leader responsible for outcomes
- Drug expertise: Single pharmacy leader
- Action: Implementing at least one action
- Tracking: Monitoring antibiotic use and resistance
- Reporting: Regular reporting information
- Education: Educating clinicians


We can then use the core elements as a checklist for all future projects

<table>
<thead>
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<th>Do we have this (yes / no)?</th>
<th>Who is responsible?</th>
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<tr>
<td>Education</td>
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</table>

Policy Changes at NHSN

- Creation of a regional public health network for resistance testing and antibiotic use
- Routine reporting of antibiotic use and resistance data to NHSN by 95% of Medicare-eligible hospitals, DOD, and VA healthcare facilities
- Enhance reporting infrastructure and provide incentives
  - Require reporting to NHSN as part of CMS inpatient quality report (IQR)
  - Publish results on Hospital Compare website
- Add electronic reporting of antibiotic use and resistance data to Stage 3 Meaningful Use for EHR systems
- CDC and partners will submit an antibiotic utilization (AU) electronic clinical quality NHSN-reporting measure to NQF and CMS

DOD=Department of Defense; VA=Veterans Affairs; EHR=electronic health record
**NHSN AU Module**

**Basic Metric is the 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

**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

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**National Quality Forum**

Google: National Quality Forum and Antibiotic Stewardship Playbook


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**Antibiotic Stewardship Playbook**

National Quality Partners Playbook: Antibiotic Stewardship in Acute Care

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**The Joint Commission**

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**..and last but not least, new guidelines!**


[http://cid.oxfordjournals.org/content/62/10/e51.full.pdf+html](http://cid.oxfordjournals.org/content/62/10/e51.full.pdf+html)
Stewardship guidelines provide evidence-based answers to a number of questions (n=27)

- Q5-28: Interventions
- Q9-13: Optimization of therapy
- Q14-20: Microbiology and Laboratory Diagnostics
- Q21-27: Measurement

- It is amazing to me the power of the guidelines to influence change (at least in the U.S.)
- These updated guidelines provide positive support for almost any facet of stewardship
- Pretty much anything you want to do now has guideline support!

Which of the following is MOST important to increase your ability to provide ASPs at your practice site?

a. CDC Core Elements for Hospital Antibiotic Stewardship
b. CDC NHSN AU Module
c. NQF Antibiotic Stewardship Playbook
d. The Joint Commission Standards for ASP
e. IDSA-SHEA Guidelines for implementing an ASP

Case # 1

This is a 54 year-old female readmitted to the hospital for probable deep sternal SSI. Three weeks earlier she underwent a CAB surgery, MV repair, and an AVR. She received “appropriate” surgical antibiotic prophylaxis. She has type 2 diabetes mellitus.

On readmission she was febrile (102°F), BP 90/60 mmHg, HP-120 bpm; lungs decreased breath sounds on left, no rubs, had purulence from lower sternum. The white blood count was 18,000 cells/mm³ with 15% bands, lactate 3.1 mEq/L, Scr 2.1 mg/dL, blood cultures were drawn.

SII: Surgical site infection; CAB: Coronary artery bypass; M/V: Mechanical valve; A/V: Aortic valve replacement
Case #1 continued

• ID was called into the emergency department (ED)
• Gram stain was performed which showed

Which of the following antibiotics would be best to start empirically in this patient?

a. Daptomycin  
b. Cefazolin  
c. Vancomycin  
d. Ceftaroline

Case #1 continued

• Vancomycin was started
• At 12 hours blood cultures were positive for gram-positive cocci in clusters
• Culture from sternum was identified at *Staphylococcus aureus* the next morning with sensitivities pending
• Patient was taken to surgery for sternal debridement
• TEE indicated a vegetation on her AV

Scenario #1 Traditional Method

**Suspected Infection**

• Fluid or Tissue Sample
• Gram Stain
  – Bacteria present? If so, Gram-negative or positive?
  – Results in minutes
• Sample incubated in culture media
  – Usually 24 hours for growth
• Biochemical testing to determine the organism
  – Minutes to 24 hours
• Susceptibility testing
  – Another 24-48 hours
  – At 48 hours susceptibilities revealed methicillin-susceptible *S. aureus* (MSSA)

Scenario #2 Rapid Molecular Methods

• Technologies available
  – Polymerase chain reaction (PCR)
  – Multiplex PCR
  – Nanoparticle Probe Technology
  – Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS)
  – From blood culture MALDI confirmed *S. aureus* and PCR indicated this was a MSSA within 4 hours of + blood culture. **Total time 16 hours vs. 48 hours by traditional methods**

Rapid Identification of Positive Blood Cultures (N=118)

<table>
<thead>
<tr>
<th>Panel</th>
<th>Targets</th>
<th>Accuracy Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adкровь ADX Panel, Biofire Diagnostics, Salt Lake City, Utah</td>
<td>Detects 29 bacterial targets, 3 resistance genes, and 5 yeast targets</td>
<td>93-92</td>
</tr>
<tr>
<td>Verigene BC-GP and BC-GN RUO, Nanosphere, Inc., Northbrook,</td>
<td>BC-GP test has 12 bacterial targets and 3 resistance markers</td>
<td>90-96</td>
</tr>
<tr>
<td></td>
<td>BC-GN RUO test has 6 bacterial targets and 6 resistance markers</td>
<td>94-98</td>
</tr>
</tbody>
</table>

Which of the following antibiotic therapies should be used now for this patient?

a. Continue vancomycin
b. Switch from vancomycin to cefazolin
c. Switch from vancomycin to nafcillin
d. Switch from vancomycin to linezolid

**Case #2**

- MM is a 71-year-old Hispanic female admitted for asthma and possible pneumonia in February. Her temperature was 99°F, BP 120/70 mmHg, HR 140 bpm and she was in rapid atrial fibrillation. Bilateral wheezing. WBC was 13,000 cells/mm³, Scr 1.2 mg/dL, lactate 1.9 mEq/L. Influenza EIA for A&B were negative. She was treated with bronchodilators and corticosteroids. Her CXR showed haziness at right base. She was admitted to the ICU. On exam she was wheezing, had a grade II/VI murmur. She was started on aztreonam and moxifloxacin (allergic to β-lactams) plus furosemide.

**Case #2 continued**

- Day 2-MRSA nasal screen was negative, blood cultures showed no growth, urinary pneumococcal antigen negative, sputum “normal flora”, ↑ WBC 29,000 cells/mm³. At the end of day 2, patient required intubation. The covering intensivist changed her antibiotics to vancomycin, ciprofloxacin, and gentamicin. Her CXR was repeated (see next slide). You are rounding the next morning and are asked for your input.
Which of the following would you do? (Choose all that apply)
   a. Continue same treatment and wait for final cultures
   b. Repeat culture
   c. Order viral studies
   d. Discontinue vancomycin
   e. Discontinue ciprofloxacin

Case #2 continued
- Intensivist ordered a multiplex respiratory PCR, which was + for influenza A
- Manual differential on WBC was 90% neutrophils with 2% bands
- All antibiotics were discontinued
- Oseltamivir was ordered
- Key point-EIA for influenza: Sensitivity/Specificity 50-70%/90-95%
- Corticosteroids cause demarginating and increase WBC with mature neutrophils

Reflections on how ASP tools helped me with this case
- CDC Core elements for Hospital Antibiotic Stewardship
- CDC NHSN AU Module
- NQF Antibiotic Stewardship Playbook
- The Joint Commission Standards for ASP
- IDSA-SHEA Guidelines

Case #3
- BT is a 51-year Hispanic female admitted to the hospital for subjective fever, chills, weakness, polyuria without dysuria, and lower abdominal discomfort. Patient has diabetes but did not obtain her last refill for metformin. She was triaged at 1600
- Lab-WBC 23,000 cells/mm³, 24% bands, platelets 26,000/mm³, SCr 1.3 mg/dL, BG 614 mg/dL, alb 1.9 g/dL, U/A +glu and ket, prot, WBC 5-7 cell/mm³, few bacteria; lactate 3.5 mEq/L, alk phos 191 units/L, ALT 32 units/L. PT/PTT normal. Lab was available at 1830
- CXR clear, blood cultures drawn

Sepsis: Defining a Disease Continuum

See enlargement, p. 21
What about New Definitions (SEP-3)?

- **Sepsis:** NO
  - Infection plus two or more sequential organ failure assessment points (qSOFA)
    - systolic hypotension of 100 mm Hg or below **YES**
    - tachypnea of at least 22 breaths/min **NO**
    - altered mental state **NO**
- **Septic shock** NO
  - Fluid-unresponsive hypotension
  - administration of vasopressors or vasoactive medication to maintain mean arterial blood pressure of 65 mm Hg or higher after adequate fluid resuscitation
  - high lactate (more than 2 mmol/L)

Case #3 continued - And Now the Rest of the Story

- An IV was started at 1800
- Insulin and fluids were given a 500-ml bolus followed by lactated Ringer’s at 125mL/hour
- At 1900 the patient was transferred to the telemetry unit
- At 0330 the next day 1 gram of ceftriaxone was given
- At 0800 her BG was down to 312 mg/dl, her lactate was 3 mEq/L, and her platelet count had decreased to 23,000 cells/mm³, SCr was down to 0.7 mg/dl, WBC decreased to 12,600 cells/mm³; PCT 26
- 1100 microbiology reports + blood cultures for gram-negative rods
- 1130 patient returns from CT scan
- Afebrile

Did the care provided in case #3 meet the SEP-1 CMS standard?

a. Yes
b. No

SEP-1 CMS Compliance

**Early Management Bundle: Severe Sepsis/Septic Shock**

- **Numerator:** Patients who receive ALL of the following:
  - Received within 3 hours of presentation of severe sepsis
    - Initial lactate level **YES**
    - Broad-spectrum or other antibiotics administered **NO**
    - Blood cultures drawn prior to antibiotics **YES**
  - And received within 6 hours of presentation of severe sepsis:
    - Repeat lactate level only if initial lactate level is elevated **YES**
    - But not in 6 hours
  - And only if septic shock present or lactate ≥4 mEq/L DNA
  - Resuscitation with 30 ml/kg crystalloid fluids

**SEP 3 and SEP-1**

- **Time is tissue!**
  - Continue early recognition and implementation of the Sepsis Bundle
- Further testing and validation needed
  - CMS
  - NOF
  - qSOFA
- **Unintended consequences**
  - Clinicians under pressure from SEP-1 may feel obligated to give all patients with possible sepsis broad-spectrum antibiotics and fluids regardless of probability of sepsis
  - SEP-1 may cause confusion between clinicians using the new definition (SEP 3) and quality teams using old definitions for SEP-1
SEP-1 Deficiency

- Lack of de-escalation evaluation as part of the measure despite the recommendation in the Surviving Sepsis Campaign


Reflections on how ASP tools helped me with this case

- CDC Core elements for Hospital Antibiotic Stewardship
- CDC NHSN AU Module
- NQF Antibiotic Stewardship Playbook
- The Joint Commission Standards for ASP
- IDSA-SHEA Guidelines

Bottom Line

- Clinical judgment an essential path to acquiring the reflective ability and knowledge to understand the condition and needs of the patient
- Requires intellectual and professional maturity, the ability to pay attention, to reason and summarize data

Margot Phaneuf, RN

A stewardship pharmacist’s dilemma: What therapy to choose for CDI treatment?

Metronidazole is inferior to vancomycin
Vancomycin is inferior to fidaxomicin

The eternal problem of the stewardship pharmacist (cost vs. value)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Efficacy</th>
<th>Safety</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>Terrible (at clinical cure and preventing recurrence)</td>
<td>Irreversible neurotoxicity and VRE</td>
<td>-</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Terrible (at preventing recurrence)</td>
<td>VRE</td>
<td>-</td>
</tr>
<tr>
<td>Fidaxomicin</td>
<td>Good (especially preventing recurrence)</td>
<td>None</td>
<td>-</td>
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</tbody>
</table>

VRE=vancomycin resistant enterococci

Let’s do one more case seeing how we can use these stewardship tools

67 year old white male with a prior history of C. difficile infection one month prior to admission
Stool for C. difficile toxin is positive
Start therapy
Metronidazole
Vancomycin
Fidaxomicin

See enlargement, p. 22
Let's assume you want a policy where patients with first recurrence of CDI get fidaxomicin

<table>
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<tr>
<td>Leadership commit</td>
<td>No</td>
<td>Need to convince pharmacy director (and CFO) to increase drug budget</td>
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<tr>
<td>Accountability</td>
<td>Yes</td>
<td>ID MD will use (overuse) this if given the green light</td>
</tr>
<tr>
<td>Drug expertise</td>
<td>Yes</td>
<td>C-diff toxin positive, first recurrence fidaxomicin</td>
</tr>
<tr>
<td>Action</td>
<td>Yes</td>
<td>I can get monthly expenditures and C-diff recurrence rates</td>
</tr>
<tr>
<td>Tracking</td>
<td>Yes</td>
<td>I will report to ASP</td>
</tr>
<tr>
<td>Reporting</td>
<td>Yes</td>
<td>Yes (and I won't forget to do this since I have a checklist)</td>
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**Pitch to Leadership (simple)**

- **C. difficile** recurrence is bad
- Fidaxomicin will reduce these recurrences
- Will any of the stewardship tools help
  - The Joint commission: No
  - NHSN AU Module: I think *C. diff* is now a reportable condition, let’s check
  - IDSA-SHEA Guidelines: Any mention of *C. diff* I can use as ammo?

Let’s assume you want a policy where patients with first recurrence of CDI get fidaxomicin

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Using the CDC core elements checklist can tell you where your problems exist

You have a leadership problem!!

Next, I’m off to Hospital Compare to look at my rates

![Medicare.gov Hospital Compare](image)

**Last, let’s go back to those impossible to read ASP guideline questions**

Q5: Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?
Answer: Using an antibiotic that prevents recurrent C diff should be good here

Q20: Which Overall Measures Best Reflect the Impact of ASPs and Their Interventions?
Answer: CDI mentioned

See enlargement, p. 22
Pitch to Leadership (simple and improving)

- Our C. diff rates are terrible
- The ASP guidelines target C. diff
- C. difficile recurrence is bad and drives readmission rates
- Fidaxomicin will reduce these recurrences and reduce rates
- I am getting more confident on my pitch to leadership but still need help!
  - Off to the NQF Antibiotic Stewardship Playbook

NQF Antibiotic Stewardship Playbook

- Scanning through resources on how to conduct gap analyses and build business models for your intervention
- Multiple statements suggest PubMed search to support intervention

PubMed search term: Fidaxomicin and economics

Patients who received oral vancomycin (n=46) or fidaxomicin (n=49) for the treatment of CDI via a protocol that encouraged fidaxomicin for select patients.

- CDI-related readmissions: Fidaxo: 20.4%; Vanco: 41.3%

Drug acquisition costs

- Vancomycin
- Fidaxomicin

500,000
400,000
300,000
200,000
100,000
50,000
0

$33,333 $62,112 $454,800 $195,200

Drug acquisition costs

Hospital readmission costs

- Vancomycin (183 days)
- Fidaxomicin (67 days)

Even better: You find an article that supports your first line treatment for recurrent CDI recommendation

UK, 2012-13: seven hospitals incorporate fidaxomicin into clinical protocols. Letters below indicate individual hospitals

- Before Fidaxo
- After Fidaxo

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Routine use of fidaxomicin associated with decreased readmission

UK, 2012-13: seven hospitals incorporate fidaxomicin into clinical protocols. Letters below indicate individual hospitals. Mortality rates decreased from 18.2% and 17.3% to 3.1% and 3.1% in hospitals A and B, respectively (p<0.05, each).

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Readmission within 30 days or primary CDI Before Fidaxo After fidaxo

P<0.05

- Our C. diff rates are terrible
- The ASP guidelines target C. diff
- C. difficile recurrence is bad and drives rates
- Fidaxomicin will reduce these recurrences and reduce rates
- ...and I have evidence that readmission rates may also decrease!

See enlargement, p. 24

Policy Accepted: Patients with first recurrence CDI get fidaxomicin

<table>
<thead>
<tr>
<th>CDC core element</th>
<th>Do we have this (yes / no)?</th>
<th>Who / what do I need?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leadership commitment</td>
<td>Yes</td>
<td>CFO promoted me to pharmacy director and increased my drug budget</td>
</tr>
<tr>
<td>Accountability</td>
<td>Yes</td>
<td>ID MD will use (override) this if given the green light</td>
</tr>
<tr>
<td>Drug expertise</td>
<td>Yes</td>
<td>Me!</td>
</tr>
<tr>
<td>Action</td>
<td>Yes</td>
<td>C diff toxin positive, first recurrence: fidaxomicin</td>
</tr>
<tr>
<td>Tracking</td>
<td>Yes</td>
<td>I can get monthly expenditures and C. diff recurrence rates</td>
</tr>
<tr>
<td>Reporting</td>
<td>Yes</td>
<td>I will report to ASP</td>
</tr>
<tr>
<td>Education</td>
<td>Yes</td>
<td>Yes (and I won’t forget to do this, since I have a checklist)</td>
</tr>
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With all these tools (and problems) what is the future of ASP?

Stewardship “Bundle”

- Duration of antibiotic therapy
- 48-72 hour “Time out”
- Microbiologic stewardship
- Rapid molecular diagnostics
- IV to PO switch
- Biomarkers-Procalcitonin
- Peer comparisons: Dashboard (audit and feedback)
- Prevention: SSI, CLABSI, CAUTI, VAE
- Immunizations

CLABSI=central line-associated blood stream infections; CAUTI=catheter-associated urinary tract infections; VAE=ventilator associated events

Future

- Rapid diagnostics
- Whole genome sequences
- Microbiome research
- Use of big data and precision machine learning to improve antimicrobial prescribing
- Use of mobile devices
- TJC and new CMS conditions for participation
- Public reporting of SAAR

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Which of these changes in your practice are you likely to make after today's presentation?

- Share and review the current national policies on ASPs with colleagues and leaders of the ASP programs in my healthcare practice setting.
- Review current policies and procedures for implementing ASPs in my practice setting.
- Review ASPs that are currently instituted in my practice setting.
- Review and use national ASP tools into the ASPs in my healthcare practice setting.
- Convene a meeting with colleagues to discuss new and innovative ways to incorporate future ASPs in my practice site.
- Implement one new ASP initiative at my practice site.

Key Takeaways

- Major policy efforts are directed towards antimicrobial stewardship
  - Take advantage of these tools; they are really helpful
- Antimicrobial stewardship is an everyday event in every patient
  - The principles of ASP can be used in almost every patient we see
- The future of ASP is strong
  - Effective ASPs are the optimal way to slow down or stop overuse of antimicrobials and resistance.
Stewardship guidelines provide evidence-based answers to a number of questions (n=27)

I. Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?

II. Are Is Didactic Education a Useful Antibiotic Stewardship Intervention for Reducing Inappropriate Antibiotic Use?

III. Should ASPs Develop and Implement Facility-Specific Clinical Practice Guidelines for Common Infectious Diseases Syndromes to Improve Antibiotic Utilization and Patient Outcomes?

IV. Should ASPs Implement Interventions to Improve Antibiotic Use and Clinical Outcomes That Target Patients With Specific Infectious Diseases Syndromes?

V. Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?


VII. Should Computerized Clinical Decision Support Systems Integrated into the Electronic Health Record at the Time of Prescribing be Incorporated as Part of ASPs to Improve Antibiotic Prescribing?

VIII. Should ASPs Implement Strategies That Promote Cycling or Mixing in Antibiotic Selection to Reduce Antibiotic Resistance?

IX. In Hospitalized Patients Requiring Intravenous (IV) Antibiotics, Does a Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program Lead to Improved Clinical Outcomes and Reduced Costs?

X. In Hospitalized Patients, Should ASPs Advocate for Alternative Dosing Strategies Based on PK/PK/Pharmacodynamic Principles to Improve Outcomes and Decrease Costs for Broad-Spectrum β-Lactams and Vancomycin?

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?

XII. In Patients With a Reported History of β-Lactam Allergy, Should ASPs Facilitate Initiatives to Implement Allergy Assessments With the Goal of Improved Use of First-Line Antibiotics?

XIII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration?

XIV. Should ASPs Work With the Microbiology Laboratory to Develop Stratified Antibiotics, Compared With Nonstratified Antibiotics?

XV. Should ASPs Work With the Microbiology Laboratory to Perform Selective or Cascade Reporting of Antibiotic Susceptibility Test Results?

XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

XVII. Should ASPs Advocate for Rapid Diagnostic Testing on Blood Specimens to Optimize Antibiotic Therapy and Improve Clinical Outcomes?

XVIII. In Adults in Intensive Care Units (ICUs) With Suspected Infection, Should ASPs Advocate Procalcitonin (PCT) Testing as an Intervention to Decrease Antibiotic Use?

XIX. In Patients With Hematologic Malignancy, Should ASPs Advocate for Incorporation of Novel Use-Based Fungal Markers in Interventions to Optimize Antifungal Use?

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

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

XXII. What Measures Best Reflect the Impact of Interventions to Improve Antibiotic Use and Clinical Outcomes in Patients With Specific Infectious Diseases Syndromes?

XXIII. Should ASPs Develop Facility-Specific Clinical Guidelines for Management of Fever and Neutropenia (FNH) in Hematology-Oncology Patients to Reduce Unnecessary Antibiotic Use and Improve Outcomes?

XXIV. In Immunocompromised Patients Receiving Antifungal Therapy, do Interventions by ASPs Improve Utilization and Outcomes?

XXV. In Residents of Skilled Nursing Homes and Skilled Nursing Facilities, do Antibiotic Stewardship Strategies Decrease Unnecessary Use of Antibiotics and Improve Clinical Outcomes?

XXVI. In Neonatal Intensive Care Units (NICUs), do Antibiotic Stewardship Interventions Reduce Inappropriate Antibiotic Use and/or Resistance?

XXVII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy in Terminally Ill Patients?

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**Sepsis: Defining a Disease Continuum**

**SIRS (Systemic Inflammatory Response Syndrome)**
- **Adult Criteria**
  - A clinical response arising from a nonspecific insult, including ≥ 2 of the following:
  - Temperature: > 38.3°C or < 36°C
  - Heart Rate: > 90 beats/min
  - Respiration: > 20/min
  - WBC count: > 12,000/mm³, or < 4,000/mm³, or > 10% immature neutrophils

**Severe Sepsis**
- **SIRS** + New onset organ dysfunction
- **Septic Shock** = refractory hypotension after 30ml/kg IVFs or lactate > 4mmol/L

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A stewardship pharmacist’s dilemma: What therapy to choose for CDI treatment?

Metronidazole is inferior to vancomycin

Vancomycin is inferior to fidaxomicin

PubMed search term: Fidaxomicin and economics

Patients who received oral vancomycin (n=46) or fidaxomicin (n=49) for the treatment of CDI via a protocol that encouraged fidaxomicin for select patients.

CDI-related readmissions: Fidaxo: 20.4%; Vanco: 41.3%

Drug acquisition costs

- Vancomycin: $6,333
- Fidaxomicin: $62,112
- Vancomycin (183 days): $454,800
- Fidaxomicin (87 days): $196,200

Hospital readmission costs


Even better: You find an article that supports your first line treatment for recurrent CDI recommendation

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90-day hospital recurrence rate

- Before Fidaxo
- After fidaxo

- First line, all episodes
- First line, R-CDI
- Select episodes only

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Assessment Test

This assessment test has been provided as a study aid only. Follow the prompts at the end of the presentation to claim credit. Credit must be claimed within 60 days of completing the activity.

1. Which document discusses a national strategy for addressing antibiotic resistance?
   a. PCAST Report to the President.
   b. President’s Executive Order and National Strategy.
   d. There is no document that discusses a national strategy for addressing antibiotic resistance.

2. Proposed policy changes listed in the National Action Plan for Combating Antibiotic-Resistant Bacteria include all of the following EXCEPT:
   a. Implement annual reporting of antibiotic use in inpatient and outpatient settings and identify variation at geographic, provider, and patient levels.
   b. Establish and improve antibiotic stewardship programs across all healthcare settings.
   c. Reduce inappropriate antibiotic use by 20% in outpatient settings and 50% in inpatient settings.
   d. Establish State Antibiotic Resistance (AR) Prevention (Protect) Programs in all 50 states.

3. What is the most widely used healthcare-associated infection tracking system?
   a. CDC’s National Healthcare Safety Network.
   b. CDC’s Core Elements of Hospital Antibiotic Stewardship Programs.

4. Case: MA is a 54 year-old female readmitted to the hospital for probable deep sternal SSI. Three weeks earlier she underwent a CAB surgery, MV repair, and an AVR. She received “appropriate” surgical antibiotic prophylaxis. She has type 2 diabetes mellitus.

   On readmission, she was febrile (102°F), BP 90/60 mmHg, HP-120 bpm; lungs decreased breath sounds on left, no rubs, had purulence from lower sternum. The white blood count was 18,000 cells/mm3 with 15% bands, lactate 3.1 mEq/L, SCr 2.1 mg/dL, blood cultures were drawn.

   ID was called into the emergency department (ED). Gram stain was performed which showed gram positive cocci in clusters.
Making Antimicrobial Stewardship a Priority: Integrating Evidence-based Practices and Guidelines to Improve Antimicrobial Use

Which of the following antibiotics would be best to start empirically in this patient?

a. Daptomycin.
b. Cefazolin.
c. Vancomycin.
d. Ceftaroline.

5. Case continued: MA was started on vancomycin therapy.
   • At 12 hours blood cultures were positive for gram-positive cocci in clusters
   • Culture from sternum was identified at *Staphylococcus aureus* the next morning with sensitivities pending
   • Patient was taken to surgery for sternal debridement
   • TEE indicated a vegetation on her AV
   • Susceptibility testing was performed and at 48 hours susceptibilities revealed methicillin-susceptible *S. aureus* (MSSA)

Which of the following antibiotic therapies should be used now for this patient?
   a. Continue vancomycin.
b. Switch from vancomycin to cefazolin or nafcillin.
c. Switch from vancomycin to linezolid.
d. Discontinue all antibiotics and re-culture.

6. • BT is a 51-year Hispanic female admitted to the hospital for subjective fever, chills, weakness, polyuria without dysuria, and lower abdominal discomfort. Patient has diabetes but did not obtain her last refill for metformin. She was triaged at 1600
   • Nontoxic PE: T-99.2°F, BP 95/60 mmHg, HR 120 bpm, RR 16/min; lift-sided abdominal pain to deep palpation only, no rebound or CVA tenderness-BS+
   • Lab: WBC 23,000 cells/mm³, 24% bands, platelets 26,000/mm³, SCr 1.3 mg/dL; BG 614 mg/dL, alb 1.9 g/dL, U/A +glu and ket, prot, WBC 5-7 cell/mm³, few bacteria; lactate 3.5 mEq/L, alk phos 191 units/L, ALT 32 units/L. PT/PTT normal. Lab was available at 1830
   • CXR clear, blood cultures drawn
   • An IV was started at 1800
   • Insulin and fluids were given a 500-mL bolus followed by lactated Ringer’s at 125mL/hour
   • At 1900 the patient was transferred to the telemetry unit
   • At 0330 the next day 1 gram of ceftriaxone was given
   • At 0800 her BG was down to 312 mg/dL, her lactate was 3 mEq/L, and her platelet count had decreased to 23,000 cells/mm³, SCr was down to 0.7 mg/dL, WBC decreased to 12,600 cells/mm³; PCT 26
   • 1100 microbiology reports + blood cultures for gram-negative rods
   • 1130 patient returns from CT scan
   • Afebrile
Did the care provided in this case meet the SEP-1 CMS standard?

a. Yes.

b. No.