“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.
Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

ADHS routinely seeks the input of highly qualified peer reviewers on the propriety, accuracy, completeness, and quality (including objectivity, utility, and integrity) of its materials. Although the specific application of peer review throughout the scientific process may vary, the overall goal is to obtain an objective evaluation of scientific information from its fellow scientists, consultants, and Committees.

Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.
Introduction to Slide Section

- **Preface:**
  Seven reasons to optimize antimicrobial therapy are discussed with focus on selection of antibiotic resistance, the lack of new drug development to combat bacterial resistance mechanisms, health and economic outcomes of bacterial resistance, the need to educate clinicians on optimal prescribing of antimicrobials, the increasing awareness of the impact of resistance by government, professional societies and the lay public.

- **Content:**
  Main presentation is 44 slides, with 8 back-up slides. With the subtitle slides excluded, this presentation can be completed within 45-60 minutes.

- **Suggestions for Presentation:**
  The intended audience includes prescribers, administrators, and other healthcare workers. This section serves to orient the audience to the challenges of suboptimal antimicrobial drug use, including adverse events and healthcare economics. It also outlines for administrators the threats of resistance and might be used to obtain support for an ASP.

- **Comments:**
  These slides could be combined with part 3 “Antimicrobial Stewardship: Making the Case” or part 10 “Barriers and Challenges”.

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### Reasons to Optimize Antibiotic Use

- Pathways to a Successful ASP
- Antimicrobial Stewardship: Making the Case
- ASPs: Nuts & Bolts
- Antimicrobial Stewardship: Measuring Antibiotic Utilization
- Antimicrobial Stewardship: Daily Activities
- Antimicrobial Stewardship: Computerized & Clinical Decision Support Services
- Microbiology: Cumulative Anti-biogram & Rapid Diagnostics
- Antimicrobial Stewardship Projects: Initiation & Advanced
- Antimicrobial Stewardship Barriers & Challenges: Structural & Functional
- Antibiotic Use in the Community
- Opportunities to Justify Continuing the ASP
- Antimicrobial Stewardship: Perspectives to Consider
- Summary
REASONS TO OPTIMIZE ANTIBIOTIC USE
Many Reasons to Improve Antibiotic Use

- Antibiotic resistance is a result of antibiotic overuse – nature’s perfect selection process in rapid action

- Antibiotic resistance impacts clinical outcomes and thereby it is also a patient safety issue

- Bacterial resistance impacts medical resources because most hospital-acquired infections (HAIs) are caused by drug-resistant bacteria

- Many hospital-acquired infections are not reimbursed by the Centers for Medicare and Medicaid (CMS)
  - Private insurers are following suit as “value-based purchasing” and “risk sharing models” become industry-wide
“The public will demand [the drug and]…then will begin an era…of abuses. The microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out which can be passed to other individuals and perhaps from there to others until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save. 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 organism. I hope the evil can be averted.”

REASONS TO OPTIMIZE ANTIBIOTIC USE:

1. SELECTION OF RESISTANT PATHOGENS
Associations Between Antibiotic Use and the Emergence of Resistance

- Changes in antimicrobial use are paralleled by changes in the prevalence of resistance

- Resistance is more common in health care-associated bacterial infections compared with community-acquired

- When compared with controls, patients harboring resistant organisms are more likely to have received prior antimicrobials

- Areas within hospitals (i.e. critical care units) that have the greatest rate of antimicrobial resistance also have the greatest rate of antimicrobial use

- Increasing the duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms
<table>
<thead>
<tr>
<th></th>
<th>Key Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>Enterococcus faecium (VRE)</td>
</tr>
<tr>
<td>S</td>
<td>Staphylococcus aureus (MRSA)</td>
</tr>
<tr>
<td>K</td>
<td>Klebsiella pneumoniae (ESBL-producing <em>E. coli</em> and <em>Klebsiella</em> species; <em>Klebsiella pneumoniae</em> carbapenem hydrolyzing beta-lactamases, KPC)</td>
</tr>
<tr>
<td>A</td>
<td>Acinetobacter baumannii</td>
</tr>
<tr>
<td>P</td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>E</td>
<td>Enterobacter species</td>
</tr>
</tbody>
</table>

- These 6 groups of bacteria currently cause the majority of hospital infections and effectively “escape” the effects of antibiotics.
- Some strains have become resistant to all antibiotics.
- Therapeutic options for these pathogens are so extremely limited that clinicians are forced to use older, and more toxic drugs, such as colistin.
- This list does not include important evolving pathogens, such as fungi, *Clostridium difficile*, metallo-beta-lactamase-producing Gram-negatives, colistin-resistant *A. baumannii*, and vancomycin-resistant *S. aureus* (VRSA).

Emergence of Resistance Can Be Rapid and Alarming: The Case of Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)\(^1,2\)

- First described in North Carolina in 1999
- CRKP has been identified in 24 states and is recovered routinely in certain hospitals in New York and New Jersey
- Analysis of 2007 data regarding health-care-associated infections reported to CDC indicated that 8% of all *Klebsiella* isolates were CRKP, compared with fewer than 1% in 2000 (CDC, unpublished data, 2008). The rise of KPCs was rapid between 2000 and 2010
- Facilitated by inability to detect isolates with low-level resistance by current breakpoints

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1  CDC.MMWR.March 20, 2009;58(10):256-60.

Endemicity/epidemics of KPCs in Puerto Rico by 2008 not shown in maps
The Selection of Bacteria Resistant to Powerful Antibiotics Occurs Rapidly

- Rise in ESBL-producing *Klebsiella pneumoniae* observed in 500-bed university-affiliated community hospital in Queens, NY
- Restriction of IV and PO cephalosporins (with 5 exceptions) in 1996
- Compared ESBL infection and colonization rates between 1995 and 1996
- Imipenem was used for the treatment of ESBL-producing *K.pneumoniae* infections

Results of cephalosporin restriction:
- 80% reduction in hospital-wide use of cephalosporins
- 141% increase in imipenem use
- 44% reduction in the incidence of ceftazidime-R *K.pneumoniae* overall
- 71% reduction within all ICUs

At the end of the restriction period, a concomitant 69% increase in the incidence of imipenem-resistant *Pseudomonas aeruginosa* occurred throughout the medical center

When you divide every 15 minutes, it is easy to overcome antibiotic pressure

Antibiotics and Bacterial Resistance: “Tragedy of the Commons”

- Antibiotics exist as a valuable resource for all
- Antibiotic therapy can cure an infection in a single person
- Overuse of the resource amongst a population leads to antibiotic resistance
- Antibiotic resistance restricts the value of the resource
- The resource becomes depleted as choices of antibiotics become limited
- No new novel antibiotics effective against MDROs
- Antibiotics exist no longer as a resource to treat infections
Predicted Issues in Gram-Negative Bacteria Resistance in the Next Decade

- Widespread occurrence of carbapenem resistance in hospitalized patients necessitating “routine” use of polymyxins or tigecycline
- Resistance to polymyxins and tigecycline commonplace in some hospitals
- Loss of improvement in intensive care unit survival rates due to impact of resistance in Gram-negative bacilli
- Calls for universal screening for multidrug-resistant gram-negative bacilli at hospital admission
- Increased acquisition of carbapenem-resistant organisms outside of hospitals
- Increased hospitalizations for community-onset urinary tract infections due to pathogens resistant to all orally administered antibiotics

Paterson D, Rogers B. Clin Infect Dis. 2010;51:1245-7
REASONS TO OPTIMIZE ANTIBIOTIC USE:

2. WHERE DID ANTIBIOTIC DEVELOPMENT GO?
Antibiotic Drug Development: Costly and Time-Consuming

- For new molecular entities which were antibiotics, approved by the FDA between 2003 to 2007, the clinical development phase (IND filing to NDA submission) was 6.0 years and the approval phase (NDA submission to approval) was 1.7 years.¹
- $100 million is spent for a phase III clinical trial program for each planned disease state indication.²
- At the time of discovery, the net present value of antibiotic to a drug company is MINUS $50 million. That compares to a positive $1 billion for a new musculoskeletal drug.²

² Spellberg B. APUA Newsletter. 2011;30(1)
Decline in the Number of New Antibacterial Agents Approved in the USA, 1983-2012

Number of Systemic Antibiotics Approved by the FDA in 5-Year Increments

Since 1983, the FDA has approved 62 to 142 New Drug Applications (NDAs) and 14 to 53 New Molecular Entities (NMEs) EACH YEAR.

In 2002, out of 89 new drugs, no new antibiotics were approved.

2 http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm
The Antibiotic Pipeline is Dry

- Only 2 new antibiotics have been approved since the Infectious Diseases Society of America’s (IDSA’s) 2009 pipeline status report, and the number of new antibiotics annually approved for marketing in the United States continues to decline.

- Since 2009, only 16 antibiotics for systemic infections were in development.

- Only seven of these have activity against key Gram-negative bacteria.
  - None of these agents was included in the 2009 list of antibacterial compounds in phase 2 or later development, and none addresses the entire spectrum of clinically relevant Gram-negative resistance.
  - None have activity against bacteria resistant to all current antibiotics.

REASONS TO OPTIMIZE ANTIBIOTIC USE:

3. ANTIBIOTIC USE IS SUBOPTIMAL
Total Outpatient Antibacterial Use in the United States and 27 European Countries in 2004

Comparative Use (DDD/1,000 inhabitants/day):
United States, 24.9; Europe, 19.0

DDD = defined daily dose. Methodology applied to IMS Health data, USA, 2004.
Excessive Use of Antibiotics

- Prospective observational study in a 650-bed university-affiliated hospital of adult non-ICU care inpatients; new antimicrobials examined over a 2-week period
- Results:
  - 1,941 days of antimicrobial therapy in 129 patients
  - 576 (30%) of 1,941 days of therapy were deemed unnecessary
  - Total average wholesale price (AWP) of all unnecessary antimicrobials prescribed for the study patients was $14,600, corresponding to an estimated yearly AWP of $350,400

Rates of Inappropriate Antibiotics in Patients with CAP or HCAP* by Pathogen Distribution

Administration of inappropriate initial antimicrobial treatment was statistically more common among HCAP patients (28.3% versus 13.0%; P < 0.001)

Of the 220 patients initially treated only with a CAP regimen (ceftriaxone plus azithromycin, or moxifloxacin), 49 (22.3%) initially received inappropriate antimicrobial treatment (CAP, 15 [13.6%] versus HCAP, 34 [30.9%]; P=0.002).

* HCAP = healthcare-associated pneumonia
# Asymptomatic Bacteruria (ASB): Frequently Treated Unnecessarily

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Lack of Adherence to Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalen et al, 2005</td>
<td>• Ottawa hospital&lt;br&gt;• 29 patients with catheter-associated ASB</td>
<td>52% prescribed antimicrobials inappropriately</td>
</tr>
<tr>
<td>Gandhi et al, 2009</td>
<td>• University of Michigan&lt;br&gt;• 49 patients with UTI diagnosed</td>
<td>32.6% did not meet criteria for UTI (most due to lack of symptoms)</td>
</tr>
<tr>
<td>Cope et al, 2009</td>
<td>• Houston VA&lt;br&gt;• 164 episodes of catheter-associated ASB</td>
<td>32% prescribed antimicrobials inappropriately</td>
</tr>
</tbody>
</table>

## Factors That Lead to Inappropriate Use of Antibiotics

<table>
<thead>
<tr>
<th>Internal</th>
<th>External</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of knowledge of infectious diseases, e.g., “more antibiotics are better”</td>
<td>Lack of time to educate patients and prescribers about when antibiotics are not indicated</td>
</tr>
<tr>
<td>“Double coverage is better for killing”</td>
<td>Lack of microbiologic data (and acquisition of it)</td>
</tr>
<tr>
<td>“Expanding” spectrum when consolidation is better</td>
<td>Fear of malpractice for not giving an antibiotic</td>
</tr>
<tr>
<td>Lack of knowledge about antibiotic spectrum of activity, e.g., “broader is easier (to prescribe) – one regimen for everything”</td>
<td>Misperception that antibiotics have only benefit and no harm</td>
</tr>
<tr>
<td>Lack of knowledge about dosing, e.g., “low dose for longer is better”</td>
<td>Pharmaceutical detailing - new does not always equal better</td>
</tr>
<tr>
<td>Lack of knowledge of antibiotic allergies and their implications</td>
<td>Critical access hospitals may not have availability of ID specialists</td>
</tr>
<tr>
<td>Lack of knowledge about when to give and stop antibiotics</td>
<td></td>
</tr>
</tbody>
</table>
“Doctor, Can You Answer This?”
Education Is Awareness

- How many patients last year grew vancomycin-resistant enterococci (VRE) from a non-urinary source at our hospital?
- Name 3 oral agents which target MRSA besides linezolid (Zyvox)
- Piperacillin-tazobactam (Zosyn) does not cover anaerobes: T or F?
- Resistance to ciprofloxacin in *E.coli* from the most recent antibiogram was _____%?
- *Clostridium difficile* infection is mostly due to prolonged antibiotic use with disruption of normal protective GI flora: T or F?
- Always treat asymptomatic bacteruria because it can lead to urosepsis: T or F?
- Can you effectively treat mild-to-moderate hospitalized community-acquired pneumonia (CAP) with less than 7 days therapy?
- What are the established drug regimens for treatment of community-acquired pneumonia?
- The attributable cost of a single CLA-BSI episode in 2009 at our hospital was $ ______________
- Vancomycin is as effective as cefazolin or nafcillin in treating an infection due to MSSA: T or F?
- The institution has specific recommendations for changing IV antibiotics to PO equivalents: T or F?
REASONS TO OPTIMIZE ANTIBIOTIC USE:

4. ANTIBIOTIC OVERUSE AND ENSUING RESISTANCE IMPACTS HEALTH & ECONOMIC OUTCOMES
Antibiotic Use, Costs, and Financial Outcomes

- Annually in the United States
  - 30% hospital admissions due to infection
  - 2 million people develop HAI
  - 30-50% hospitalized patients receive antibiotics
  - Yet up to 50% of antibiotic orders are unnecessary or inappropriate

- 30% of hospital pharmacy budget is composed of antimicrobials
- > $1.1 billion spent annually on unnecessary antibiotic prescriptions for respiratory infections in adults

- $15 million to treat 188 cases of ABX resistant infections
- Attributable costs (per episode)
  - MRSA: $9,275 to $13,901
  - VRE: $27,190
  - Resistant Enterobacter: $29,379

Reasons to Optimize Antibiotic Use: Clinical and Economic Consequences

- CDC recently provided conservative estimates that in the U.S., more than 2 million people are sickened every year with antibiotic-resistant infections, with at least 37,000 dying as a direct result with many more succumbing to other conditions complicated by an antibiotic-resistant infection or *C. difficile* infection.
- The total economic cost of antibiotic resistance to the U.S. economy is estimated as high as $20 billion in excess direct healthcare costs, with additional costs to society for lost productivity as high as $35 billion a year (2008 dollars).
- Up to 50% of all antibiotics prescribed are unnecessary or not optimally effective as prescribed.
- One of four core actions that will help fight these deadly infections includes **improving the use of antibiotics**.

CDC “Antibiotic Resistance Threats in the United States, 2013”
Available at: http://www.cdc.gov/drugresistance/threat-report-2013/
Impact of Inappropriate Initial Empiric Antibiotic Selection

- Studies have demonstrated that inappropriate initial therapy is an important independent determinant of mortality\(^1\)-\(^4\)
- Inappropriate initial antimicrobial therapy is defined as the use of an agent or agents to which the isolated pathogens are later determined to be non-susceptible\(^5\)

Drug resistance hinders selection of effective empiric therapy

Hospital and Societal Costs of Antimicrobial-Resistant Infections in a Chicago Teaching Hospital

• In a random sample of high-risk hospitalized adult patients (n=1,391) during calendar year 2000, 13.5% had an antimicrobial-resistant infection (ARI)
• Patients with an ARI (case) were propensity score-matched to patients without ARI (control); both community- and hospital-acquired infections were included
• ~70% of patients with an ARI were defined as having an HAI by CDC definition
• Medical costs (2008 dollars) were measured from the hospital perspective
  • Medical costs attributable to ARI ranged from $18,588 to $29,069 per patient
  • Excess duration of hospital stay was 6.4 to 12.7 days
  • Attributable mortality was 6.5%
• Lowering ARI rate from 13.5% to 10% was estimated to save ~$1 million per year in medical costs

Antibiotic Misuse Adversely Impacts Patients: *Clostridium difficile* Infection (CDI)

- CDI is problematic when three factors are aligned:
  - Coexisting co-morbidities, including advanced age, renal dysfunction, or immunosuppression
  - Disturbed intestinal microbiota as a result of antibiotic therapy
  - Exposure to vegetative cells or spores of *C. difficile*
- Antibiotic exposure is the single most important risk factor for the development of CDI
  - Antibiotic exposure increases risk of CDI by 7- to 10-fold for up to 30 days post-exposure and for up to 3-fold for the next 60 days\(^1\)
  - Up to 85% of patients with CDI have received an antibiotic in the 28 days prior to infection\(^2\)

---

**Clostridium difficile** Infection Inpatient Cases Increased Significantly Starting in 2001

### Incidence and Mortality

- Total incidence ~700K cases per year, including long-term acute care hospitals (LTACHs) and outpatient cases

- In 2009, there were 336,600 CDI-related hospital stays in the U.S., or 0.9% of all hospital stays

- Approximately 9.1% of CDI stays ended in death, compared with less than 2% for all other inpatients

- Since 2003, more severe cases of CDI with mortality rates as high as 17% have been identified at several US and Canadian hospitals

### Trends in Hospital Stays Associated with **Clostridium difficile** Infection (CDI), 1993-2009 (ICD-9-CM 008.45)

The number of hospital stays associated with CDI more than doubled from 2001 to 2005; hospital stays with CDI increased four-fold over this 16-year time period

---

3. Internal estimates based upon AMR/Arlington Medical Resources, Inc., and Decision Resources, Inc. 2009. Hospital Anti-Infectives Insight Series: *Clostridium Difficile*
Antibiotics Are Not Harmless: Antibiotic-Related Adverse Drug Reactions

- An estimated 142,505 visits (95% confidence interval [CI], 116,506–168,504 visits) annually were made to US emergency departments (EDs) for drug-related adverse events attributable to systemic antibiotics
- Antibiotics implicated in 19.3% of all ED visits for drug-related adverse events
- Most ED visits for antibiotic-associated adverse events were for allergic reactions (78.7% of visits; 95% CI, 75.3%–82.1% of visits)
  - Almost 50% of ED visits were associated with penicillins and cephalosporins
  - Sulfonamides associated with the highest rate of serious allergic reactions
  - 50% of all reactions were due to sulfonamides and clindamycin
  - Sulfonamides and fluoroquinolones were associated with the highest rate of neurological events
- Most prescriptions were for upper respiratory infections, chronic obstructive pulmonary disease (COPD), otitis media, and sinusitis

Antibiotic Resistance Can Be Considered an Adverse Event

ASHP definition of an adverse event:
• “Any unexpected, unintended, undesired, or excessive response to a drug that: 1) requires discontinuing the drug (therapeutic or diagnostic); 2) requires changing the drug therapy; 3) requires modifying the dose (except for minor dosage adjustments); 4) necessitates admission to a hospital; 5) prolongs stay in a health care facility; 6) necessitates supportive treatment; 7) significantly complicates diagnosis; 8) negatively affects prognosis; 9) results in temporary or permanent harm, disability, or death.”

FDA definition of a serious adverse event (related to drugs or devices)
• Events in which “the patient outcome is death, life-threatening (real risk of dying) condition, hospitalization (initial or prolonged), disability (significant, persistent, or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage.”

World Health Organization (WHO) definition of an adverse drug reaction:
• “Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.”
5. THE GOVERNMENT AND INSURERS DO NOT WANT TO PAY FOR THE CONSEQUENCES OF ANTIBIOTIC OVERUSE
CMS Proposes to Penalize Hospitals with Higher-Than-Expected Rates of Hospital-Acquired Conditions (HACs)

Starting October 2015, the HAC Reduction Program penalizes hospitals in the worst quartile (i.e., more HACs than 75% of other hospitals)

1% payment reduction based on a HAC measure set, which increases over time

For FY 2017 payment determination, these measures have been proposed

<table>
<thead>
<tr>
<th>AHRQ Patient Safety Indicators*</th>
<th>CDC Hospital-Acquired Infection (HAI) Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure ulcer rate</td>
<td>Central line-associated blood stream infection (CLABSI)</td>
</tr>
<tr>
<td>Foreign object left in body</td>
<td>Catheter-associated urinary tract infection (CAUTI)</td>
</tr>
<tr>
<td>Iatrogenic pneumothorax rate</td>
<td>Surgical site infection (SSI)</td>
</tr>
<tr>
<td>Postoperative physiologic and metabolic derangement rate</td>
<td>– SSI following colon surgery</td>
</tr>
<tr>
<td>Postoperative PE/DVT rate</td>
<td>– SSI following abdominal hysterectomy</td>
</tr>
<tr>
<td>Accidental puncture &amp; laceration rate</td>
<td>MRSA bacteremia</td>
</tr>
<tr>
<td></td>
<td>Clostridium difficile infection</td>
</tr>
</tbody>
</table>

While CMS has not yet announced the FY 2017 reporting periods for this program, a hospital’s performance in 2014 could impact payment in the future†

* CMS is also considering an alternative AHRQ composite measure. † Estimated based on proposed FY 2015 reporting periods, which are calendar years 2012-2013 for CDC HAI measures. CMS: Centers for Medicare and Medicaid Services. HAC: hospital-acquired condition. FY: fiscal year. AHRQ: Agency for Healthcare Quality and Research. CDC: Centers for Disease Control and Prevention. HAI: healthcare-associated infection.

CMS Surveyor Worksheet: Preparation for Metrics

- 3 new CMS Surveyor worksheets
- Adopted Oct 2011
- No penalties assessed
- Section 1.C. Systems to prevent transmission of MDROs and promote antibiotic stewardship, Surveillance

**Subsection 1.C.2.** Can the primary interview participants provide evidence that the hospital has developed and implemented policies and procedures aimed at preventing the development of, and preventing transmission of, MDROs?

- 1. C.2.a Facility has a multidisciplinary process in place to review antimicrobial utilization, local susceptibility patterns, and antimicrobial agents in the formulary and there is evidence that the process is followed.
- 1. C.2.b Systems are in place to prompt clinicians to use appropriate antimicrobial agents (e.g., computerized physician order entry, comments in microbiology susceptibility reports, notifications from clinical pharmacist, formulary restrictions, evidenced based guidelines and recommendations).
- 1. C.2.c Antibiotic orders include an indication for use.
- 1. C.2.d There is a mechanism in place to prompt clinicians to review antibiotic courses of therapy after 72 hours of treatment.
- 1. C.2.e The facility has a system in place to identify patients currently receiving intravenous antibiotics who might be eligible to receive oral antibiotic treatment.
National Patient Safety Goals: Reducing Hospital-Acquired Infections

- Focuses primarily on MRSA, VRE, CDI, MDR-GNB, but not inclusive
- National Patient Safety Goals – 3 new requirements
  - NPSG 07.03.01 addresses prevention of HAIs caused by multidrug-resistant organisms (MDROs)
  - NPSG 07.04.01 focuses on preventing catheter-related bloodstream infections
  - NPSG 07.05.01 addresses the prevention of surgical-site infections
- The new requirements focus on the development and implementation of evidence-based best practices, periodic risk assessment, measurement and monitoring of rates of infection, and the education of staff and patients.
- In addition, it is required that hospitals provide goal-related data to hospital leaders, governing bodies, physicians, medical staff, pharmacists, nursing staff, and other clinicians for appropriate action
- In 2009 hospitals will be scored on having met implementation requirements
- Starting January 1, 2010, health systems will be scored on all elements of the goals

Health and Human Services Developed Reduction Goals For Select Hospital Associated Infections (HAIs)

The following HAIs, data sources and five year reduction goals were identified\(^1\)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Source</th>
<th>National 5-year prevention target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream infections</td>
<td>NHSN</td>
<td>50% reduction</td>
</tr>
<tr>
<td>Adherence to central-line insertion practices</td>
<td>NHSN</td>
<td>100% adherence</td>
</tr>
<tr>
<td>\textit{Clostridium difficile} (hospitalizations)</td>
<td>HCUP</td>
<td>30% reduction</td>
</tr>
<tr>
<td>\textit{Clostridium difficile} infections</td>
<td>NHSN</td>
<td>30% reduction</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>NHSN</td>
<td>25% reduction</td>
</tr>
<tr>
<td>MRSA invasive infections (population)</td>
<td>EIP</td>
<td>50% reduction</td>
</tr>
<tr>
<td>MRSA bacteremia (hospital)</td>
<td>NHSN</td>
<td>25% reduction</td>
</tr>
<tr>
<td>Surgical site infections</td>
<td>NHSN</td>
<td>25% reduction</td>
</tr>
<tr>
<td>Surgical Care improvement project measures</td>
<td>SCIP</td>
<td>95% adherence</td>
</tr>
</tbody>
</table>

Steering committee\(^2\)

- Office of Healthcare Quality
- Agency for Healthcare Research and Quality
- Centers for Disease Control and Prevention
- Centers for Medicare and Medicaid Services
- National Institutes of Health
- Indian Health Service
- Health Resources and Services Administration
- Food and Drug Administration
- Office of the Assistant Secretary for Planning and Evaluation
- Office of the Assistant Secretary for Public Affairs
- Office of the National Coordinator for Health Information Technology
- U.S. Department of Defense
- U.S. Department of Veterans Affairs


REASONS TO OPTIMIZE ANTIBIOTIC USE:

6. PROFESSIONAL SOCIETIES ENDORSE ANTIMICROBIAL STEWARDSHIP
Professional Societies, Government, and Health Organizations Call for “More Action”

As the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship.

Timothy H. Dolitz,1 Robert C. Owens,2 John E. McGowan, Jr.3 Dale N. Gerding,4 Robert A. Weinstein,4
John P. Burke,5 W. Charles Huskins,3 David L. Paterson,6 Neil O. Fishman6 Christopher F. Carpenter,7 P. J. Brennan,8
Marianne Billeter9 and Thomas M. Hooper2

Clinical Infectious Diseases 2007;44:159–77
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1058-4838/2007/4402-0001$15.00

Developed through the ASHP Council on Pharmacy Practice and approved by the ASHP Board of Directors on April 17, 2009, and by the ASHP House of Delegates on June 16, 2009

The Joint Commission

2011 Hospital National Patient Safety Goals

IHI.org | A resource from the Institute for Healthcare Improvement
Reasons to Optimize Antibiotic Use: The Role of Antimicrobial Stewardship

FIGHTING BACK AGAINST ANTIBIOTIC RESISTANCE

Four Core Actions to Prevent Antibiotic Resistance

1. PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE
   Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safer food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2. TRACKING
   CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent these infections and prevent the resistant bacteria from spreading.

3. IMPROVING ANTIBIOTIC PRESCRIBING/STewardship
   Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4. DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS
   Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

http://www.cdc.gov/drugresistance/threat-report-2013/
REASONS TO OPTIMIZE ANTIBIOTIC USE:

7. PUBLIC MEDIA HAVE MADE CONSUMERS INTO SMART SHOPPERS WHO SEEK SAFE HEALTHCARE DELIVERY
Publically Available Information on Antibiotic Resistance: “A National Call to Action”
REASONS TO OPTIMIZE ANTIBIOTIC USE:

SUMMARY
Benefits of an Antimicrobial Stewardship Program: Beyond Pharmacy Costs (Univ Pennsylvania)

- Main target of program is to improve patient safety through active interventions and healthcare provider education

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HUP Program (n=96)</th>
<th>Usual Practice (n=95)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial appropriate</td>
<td>86 (90%)</td>
<td>30 (32%)</td>
<td>2.8 (2.1 – 3.8)</td>
</tr>
<tr>
<td>Cure</td>
<td>52/57 (91%)</td>
<td>34/62 (55%)</td>
<td>1.7 (1.3 – 2.1)</td>
</tr>
<tr>
<td>Failure</td>
<td>5 (5%)</td>
<td>29 (31%)</td>
<td>0.2 (0.1 – 0.4)</td>
</tr>
<tr>
<td>Clinical</td>
<td>0</td>
<td>10 (11%)</td>
<td>--</td>
</tr>
<tr>
<td>Microbiologic</td>
<td>0</td>
<td>8 (8%)</td>
<td>--</td>
</tr>
<tr>
<td>Superinfection</td>
<td>0</td>
<td>8 (8%)</td>
<td>--</td>
</tr>
<tr>
<td>Adverse drug effect</td>
<td>0</td>
<td>2 (2%)</td>
<td>--</td>
</tr>
<tr>
<td>Recurrent infection</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>--</td>
</tr>
<tr>
<td>Resistance</td>
<td>1 (1%)</td>
<td>9 (9%)</td>
<td>0.13 (0.02 – 1.0)</td>
</tr>
</tbody>
</table>

- Annual savings (600 interventions/month) amounted to $302,400 for antibiotic costs, $533,000 for infection-related costs, and $4.25 million in total hospital costs
- The majority of the cost savings were attributable to a decreased length of stay in the intensive care unit (ICU), although the total hospital length of stay in the study was unchanged

The Need for Antibiotic Stewardship is Now

- Many reasons to control antibiotic use in the hospital setting include:
  - Antibiotic overuse accelerates bacterial resistance ("collateral damage")
  - Effects of bacterial resistance on medical resources is high
  - Antibiotic resistance is a patient safety issue and is an adverse drug event
  - The “new reality” of hospital-acquired resistant bacterial infections includes penalties from Centers for Medicare and Medicaid (CMS) impacting reimbursement and state reporting mandates
  - Private insurers will follow suit; “value-based purchasing”

- The reality for the future includes:
  - More institutional outbreaks of multidrug-resistant organisms (MDROs), including *Clostridium difficile* infection
  - Few novel antimicrobial strategies to fight MDROs
  - Additional performance measures impacting ability to compete in the hospital marketplace – JCAHO, CMS, IHI, NCQA, CDC, HospitalCompare, NHSN

- Published guidelines and “success stories” employing stewardship strategies exist in great numbers which provide valuable templates
ADDITIONAL PRESENTATION SLIDES
“...the triumphs of the ‘wonder drugs’ have been adequately and repeatedly extolled in thousands of medical and lay publications, but the dangers and the harmful sequelae of their uses, and particularly their abuses, have not yet been given sufficient prominence.”

“The potentialities for the emergence of races of pathogenic bacteria that are resistant to the available antimicrobial agents by the continuous and widespread use of such agents has already been adequately demonstrated....”

“Despite over 70 years of clinical antibiotic use, bacteria continue to outperform clinicians by developing increasing levels of resistance to both old and new antibiotics. Just as bacteria continue to adapt, clinicians must continue to adapt their practice”

“Given both the frequency of inappropriate antimicrobial use and the association between antimicrobial use and the emergence of resistance, ASPs may help reduce the selective pressure responsible for the emergence and propagation of antimicrobial-resistant pathogens. However, implementation of antimicrobial stewardship programs requires support from hospital leadership, including significant initial financial investments. Studies support the safety, effectiveness, and financial benefits of such programs....”

The Antibiotic Pipeline is Dry

- In the IDSA policy report (July 2004) entitled “Bad Bugs, No Drugs: As Antibiotic R&D Stagnates, a Public Health Crisis Brews,” multiple legislative, regulatory, and funding solutions were suggested.

- To address the problem of the dwindling antibiotic pipeline, IDSA launched the “10 × ’20 Initiative” in 2010 calling for development and regulatory approval of 10 novel, efficacious, and safe systemically administered antibiotics by 2020.

Many Scientific Policy Groups Have Expressed Concern for Increasing Antibiotic Resistance

- Infectious Diseases Society of America (IDSA) and “Bad Bugs, No Drugs” policy report (July, 2004)
  - Expressed concern for the decreasing activity in new antibiotic development
  - Identified several problematic bacterial pathogens, including *Acinetobacter baumannii*, ESBL-producing *Enterobacteriaceae*, MRSA, *Pseudomonas aeruginosa*, and vancomycin-resistant *Enterococcus faecium*
  - Antimicrobial Availability Task Force (AATF) pursues solutions to the lack of drug research and development as a political action committee for IDSA

- Society for Healthcare Epidemiology of America (SHEA) launches Antimicrobial Stewardship initiative

- Centers for Disease Control and Prevention (CDC) launches “Get Smart for Healthcare” campaign
  - Includes state Antimicrobial Stewardship Programs (ASPs), training and educational materials, slide sets, HAI prevention tools, gap analyses, champion statements, business plans, certification program links (Society of Infectious Diseases Pharmacists, SIDP; Making a Difference in Infectious Diseases, MAD-ID), drug utilization study forms, antibiotic order sheets, best practice websites
  - CDC launches National Antimicrobial Use Benchmarking program via NHSN Antibiotic Use and Resistance module (2011)

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1 Infectious Diseases Society of America. *Bad Bugs, No Drugs*. July 2004. Available at: www.idsociety.org
2 Talbot GH et al. *Clin Infect Dis* 2006;42:657-68
3 http://www.shea-online.org/news/stewardship.cfm
4 http://www.cdc.gov/getsmart/healthcare/improve-efforts/resources/index.html#ASTrO
5 http://www.cdc.gov/nhsn/psc_ma.html
The Burden of Antimicrobial Resistance

- Bacterial resistance limits the choice of antibiotics which might be effective, often relying on newer and more expensive antibiotics to treat infections
- Infections due to antibiotic-resistant pathogens have negative clinical and economic consequences compared to infections due to antibiotic-susceptible pathogens

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Methicillin-susceptible S aureus(^1) ((n = 165))</th>
<th>Methicillin-resistant S aureus(^1) ((n = 121))</th>
<th>Imipenem-susceptible P aeruginosa(^2) ((n = 719))</th>
<th>Imipenem-resistant P aeruginosa(^2) ((n = 135))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>6.7%</td>
<td>20.7(^a)%</td>
<td>16.7%</td>
<td>31.1(^b)%</td>
</tr>
<tr>
<td>Median Hospital Charges</td>
<td>$52,791</td>
<td>$92,363(^a)</td>
<td>$48,381</td>
<td>$81,330(^c)</td>
</tr>
</tbody>
</table>

\(^a\) p < 0.001
\(^b\) Relative risk, 1.86; 95% CI, 1.38-2.51; \(^c\) p < 0.001

- As bacterial resistance increases, the accurate selection of appropriate empiric therapy decreases
- Studies have demonstrated that inappropriate initial therapy is an important independent determinant of mortality

The Impact of Healthcare-Associated Infections (HAIs) in the USA

• The Centers for Disease Control and Prevention (CDC) estimates that 1.7 million patients contract healthcare-associated infections every year and nearly 99,000 of them die 1,3,4
  • HAIs are estimated to be one of the top 10 causes of death in the US
• The annual direct medical costs of HAIs to hospitals range from $28.4 to $33.8 billion 2,3,4
  • A study of 1.7 million hospitalized patients discharged from 77 hospitals found that the additional cost of treating a HAI averaged $8,832
• In Pennsylvania, 23,287 (1.2%) hospital-admitted patients contracted at least one HAI during their stay5
  • Mortality: 9.4% (HAI) vs 1.8% (no HAI)
  • Avg LOS: 21.6 days (HAI) vs 4.9 days (no HAI)
  • Estimated Medicare payments: $20,471 (HAI) vs $6,615 (no HAI)
  • Readmission within 30 days (infection/complication): 29.8% (HAI) vs 6.2% (no HAI)

2 Scott, RD. The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention, 2009. Division of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, 2009.
3 GAO Report; April 16, 2008; GAO-08-283; HHS Action Plan to Prevent HAIs; released Jan 6, 2009
4 http://www.ihi.org/IHI/Programs/Campaign/Campaign.htm?TabId=2#InterventionMaterials
# Payment Policies for Nosocomial Infections

<table>
<thead>
<tr>
<th>Payer</th>
<th>Catheter-associated urinary tract infections</th>
<th>Vascular catheter-associated infections</th>
<th>Surgical Site Infections</th>
<th>After elective orthopedic procedures and bariatric surgery for obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIGNA</td>
<td>No payment</td>
<td>No payment</td>
<td>No payment</td>
<td>Payment</td>
</tr>
<tr>
<td>Wellpoint</td>
<td>No payment</td>
<td>No payment</td>
<td>No payment</td>
<td>Payment</td>
</tr>
</tbody>
</table>

Other payers are beginning to take steps that would eliminate hospital payments for 28 “never events” endorsed by the National Quality Forum (NQF). Although nosocomial infections are not included in the initial NQF list of these “never events” they may be added in the future.

“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

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Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.
Preface:
Defining antimicrobial stewardship is paramount in setting the stage for the stewardship program – its goals and objectives. Basic structure and function is one of the earliest steps to developing an ASP by identifying the necessary team members, direction of the ASP, core strategies, and adaptability of functional models. The basic structure of the ASP should be established to provide direction but requires significant discussions with stakeholders and prescribers. These slides provide such a framework for such discussions.

Content:
13 slides which can be presented within 30 minutes. Note that significant discussion time may be needed to elaborate on several valuable issues.

Suggestions for Presentation:
Pharmacists and pharmacy directors, infectious disease physicians, and ASP champions compose the primary audience.

Comments:
It is important to identify the “right reasons” for creating an ASP. Share ideas and identify institutional needs during meetings with medical departments, nursing, microbiology, epidemiology, and pharmacy. Everyone will have something to contribute and gain.
PATHWAYS TO A SUCCESSFUL ANTIMICROBIAL STEWARDSHIP PROGRAM
Antimicrobial Stewardship: A Definition

Processes designed to optimize the appropriate use of antimicrobials by ensuring that every patient receives...

...an antibiotic only when one is needed, with

The right agent
The right dose
The right route
For the right duration ...

... in order to optimize clinical outcomes and minimize unintended consequences of antimicrobial use
Why Does Antimicrobial Stewardship Matter?

• 200-300 million antibiotic courses are prescribed annually
  • 45% are for outpatient use

• 25-40% of hospitalized patients receive antibiotics
  • At least 30% are unnecessary or sub-optimal
  • 5% of hospitalized patients experience an adverse drug reaction directly related to antibiotic use

• More than $1.1 billion is spent annually on unnecessary adult antibiotic prescriptions for upper respiratory tract infections
  • 50-80% of outpatient antibiotic use is inappropriate

• Antibiotics are unlike any other drug – use of the agent in one patient can compromise efficacy in another
Antibiotic Stewardship: Why Do It?

The Wrong Reasons ..............
- To save money or because my CFO thought it would be a good idea.
- Because we (Administration) can’t control the physicians’ prescribing but we think Pharmacy can.
- I enter a lot of orders for antibiotics.
- There just seems to be a lot of antibiotic overuse.
- Antibiotic resistance is bad.
- In my experience these antibiotics work just fine.

The Right Answers (Examples)
- To improve the quality of care in our institution.
- To create a multi-disciplinary program that will encourage appropriate antimicrobial use in our institution.
- Antibiotic utilization has increased by 17% in the last year, and our goal is to reduce this number to 5% growth for FY11.
- Based on a review of 100 general medicine and surgical patients who received ≥ 3 antibiotics, only 30% of patients had therapy de-escalated after culture and susceptibility reports were returned, so our goal is to improve this to 60% by year-end.

Courtesy of Drs Kavita Trivedi (CDPH) and Kristi Kuper (Cardinal Health); delivered April 13, 2011 as a seminar to acute care hospitals in CA preparing for ASP mandate.
Developing an Antimicrobial Stewardship Program: The Core Team and Supporting Stakeholders

- Develop a culture change which embraces prudent antibiotic use
- Identify and gain solid commitment from members of the ASP
- Administrative support is essential
- ASP operates under auspices of the CMO and QA/Safety
- A commanding Chief Medical Officer, Medical Executive Committee, and Pharmacy and Therapeutics Committee enhance the success of an ASP
- Patient safety is linked to antibiotic resistance – make them believe it

### Support Team
- Infection Control
- Quality Assurance/Patient Safety
- Information Technology
- Microbiology
- Hospital Epidemiologist

### Core Team
- Infectious Disease Physician
- Clinical Pharmacist with ID Training

### Collaborative Team
- Med Executive & Pharmacy and Therapeutics Committees
- Hospital Administration & Pharmacy Director
Successful ASPs Need Effective Partnering With Many Other Clinicians

<table>
<thead>
<tr>
<th>Microbiology &amp; Laboratory</th>
<th>Nursing</th>
<th>Infection Prevention</th>
<th>Medical Staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid testing and</td>
<td>IV-to-PO transition therapies</td>
<td>Review CDI and MDRO cases for antibiotic use</td>
<td>CPOE educational screens</td>
</tr>
<tr>
<td>notification; MRSA v.</td>
<td></td>
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<tr>
<td>MSSA BSI</td>
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<td></td>
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</tr>
<tr>
<td>Procalcitonin results</td>
<td>Identification of “true” allergy</td>
<td>NPSG 7.0’s for MDRO</td>
<td>Antibiotic plans in chart</td>
</tr>
<tr>
<td>Blood culture contamination</td>
<td>Education and support for prolonged infusions</td>
<td>HAIs treated optimally</td>
<td>Evidence-based treatment guidelines</td>
</tr>
<tr>
<td>Antibiogram development &amp;</td>
<td>Rapid initiation of empiric antibiotics</td>
<td>Maintenance of sterile injectables</td>
<td>Therapeutic interchange</td>
</tr>
<tr>
<td>education</td>
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<tr>
<td>Empiric antibiotic</td>
<td>Reminders to physicians: “did he/she see the</td>
<td>Cleaning of equipment and rooms known to facilitate</td>
<td>Restricted or non-formulary antibiotics</td>
</tr>
<tr>
<td>prescribing guidelines</td>
<td>C&amp;S report?”</td>
<td>transmission of pathogens</td>
<td></td>
</tr>
<tr>
<td>Selective reporting rules</td>
<td>SCIP guidelines; time to antibiotic</td>
<td>Differentiate colonization from infection</td>
<td>Optimize clinical and economic outcomes</td>
</tr>
<tr>
<td>on AST</td>
<td>administration</td>
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</tbody>
</table>
Who Can Direct the Antibiotic Stewardship Program?

- Small institutions may not have ID-trained physicians and pharmacists, and many may not have ID physicians with adequate time to contribute to an ASP program.

- Basic requirements of a “potential champion” for the ASP:
  - Interest in stewardship, patient safety, and performance improvement
  - Basic knowledge of antibiotics
  - Dedicated time and commitment
  - Activities are scalable to both time commitments and comfort levels

- Alternatives to ID-trained physicians:
  - Consider hospitalist, microbiology director, or intensivist

- Alternatives to ID-trained pharmacist
  - Pharmacist with advanced training (critical care, etc)
Definition: Judicious use of antimicrobials in order to improve patients outcomes, control resistance and decrease healthcare expense

Achieved through:

- Education
  - Stewardship training; Grand Rounds
  - Institution-specific empiric therapy guidelines

- Guidelines
  - CAP, HAP, VAP, IAI, SCIP (surgical prophylaxis), UTI, SSTI/DFI, FN
  - Renal dosing, PK/PD, monitoring serum concentrations of vancomycin, aminoglycosides, and anti-fungals

- Order Sets
  - Early conversion to PO

- Dose Optimization
  - De-escalation of therapy; appropriate duration of therapy; infection markers

- IV to PO

- Streamlining
  - Intervention tracking; develop tools

Core Strategies Include a Large Number of Tactics
Flow diagrams assist in labor and time-motion studies, but may be too complex or resource-intensive for current healthcare systems.

Recommendation: Stay basic and have well-defined objectives to direct the ASP activities.

The New ASP Model:
Adaptable to All Institutional Settings

Comprehensive program led by ID physician or physician champion, plus clinical pharmacist

Individual interventions based on goals of institution, with assistance from interested individuals

Simple initial strategies:
- Simple audit (review of orders) of specific drugs
- Pharmacy order entry system (e.g. antibiotic indication)
- Develop evidenced-based guidelines for 3-4 agents (see IDSA guidelines)
- Educate medical staff (2-minute “elevator speech”)
- All pharmacists can apply guidelines and approve drugs
- Post-prescription review on days 2-3 with physician champion
- IV-to-PO conversion is a good demonstration project
- SCIP guidelines and other performance outcomes and measures

Function Trumps Structure
How Can I Justify My ASP Pharmacist FTEs? Program at a Small Community Hospital

- 120-bed community hospital studied in 2000
- Antibiotic support team (AST) – ID physician, clinical pharmacist, members of infection control and microbiology
  - ID MD devoted 8-12 hours per week on AST
- Concurrent chart review 3 days per week targeting patients receiving multiple, prolonged, or high-cost antimicrobial therapy
- Results:
  - 488 recommendations; 69% accepted
  - Antibiotic costs reduced 19%, $18.21/pt-day to $14.77/pt-day
  - Total estimated savings of $177,000 in 2000, only one year later after ASP inception and implementation

Yes…Function Trumps Structure!

LaRocca A. Clin Infect Dis. 2003;37:742-3 (letter)
Assess Your Needs To Implement a Successful Antimicrobial Stewardship Program

Take inventory of your resources

Meet with anybody who will talk to you

Gather baseline data

Write a proposal

Get approval or acknowledgment of your plan by key stakeholders

Pilot your intervention

"Is it only me?"

"They don't understand!"

"The docs will never go for this"

"They don’t understand!"

"The docs will never go for this"

Moral support

Moral support

Personal relationships

Personal relationships

What are the problems? Cost, resistance, too many broad-spectrum agents, etc?

What are the problems? Cost, resistance, too many broad-spectrum agents, etc?

Disease management issues

Disease management issues

Lack of evidenced-based practice?

Lack of evidenced-based practice?

Behaviors of prescribers

Behaviors of prescribers

Goals & objectives

Goals & objectives

Benchmarks?

Benchmarks?

Formal business model

Formal business model

ASP physician role and compensation

ASP physician role and compensation

Consequences of not addressing the problems

Consequences of not addressing the problems

Review goals & objectives of program

Review goals & objectives of program

What are the clear deliverables?

What are the clear deliverables?

Financial support?

Financial support?

Receptiveness to change; “what if I do this?”

Receptiveness to change; “what if I do this?”

Go slow

Go slow

Focus on low-hanging fruit

Focus on low-hanging fruit

Document interventions & roadblocks

Document interventions & roadblocks

Identify the true best performers

Identify the true best performers

Advertise services of ASP

Advertise services of ASP

Continue to build support

Continue to build support
“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

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Introduction to Slide Section

• **Preface:**
  So how do you convince hospital administration to fund an ASP, provide compensation to a physician champion, tell prescribers that their antimicrobial orders will be monitored, and reorganize pharmacist functions to devote sufficient time for achieving the proposed goals and objectives of the ASP?

• **Content:**
  28 slides; 3 back-up slides.

• **Suggestions for Presentation:**
  Due to the nature of this section many users will find this material educational rather than for presentation to a large audience. However, the clinical examples presented can be used to make a case for support and implementation of an ASP.

• **Comments:**
  There are 10 examples which can be used the “make the case”. Importantly, not all of these examples provide a cost benefit back to the pharmacy budget but rather focus on patient outcomes. The “bigger picture” is consistent with providing optimal patient care and using antimicrobials wisely. Several examples of accountabilities are provided in slide #3 which can be included as either short-term or long-term objectives. Costs could be calculated for many of these potential interventions. But do not overpromise! Business planning is also introduced.
ANTIMICROBIAL STEWARDSHIP: MAKING THE CASE
Formulary Management Versus Patient-Centric Program: Can Both Be Accomplished Simultaneously?

- Pre-prescription review may restrict expensive agents through enforcement of empiric antibiotic guidelines based on the antibiogram
- Post-prescription review may focus on expensive agents or commonly overused antibiotics
  - Study of over-used antibiotics, albeit lower cost, such as vancomycin
  - Study of specific disease states, such as bacteremia, asymptomatic bacteriuria, or community-acquired pneumonia
  - Assesses antibiotic when C&S results are most commonly available
  - Allows for assessment of IV-to-PO conversion and other de-escalation opportunities
- Disease-specific objectives can be challenging but are aligned more closely with clinical outcomes
  - Studying the effect of an ASP on the improvement of clinical outcomes requires a focus on key objectives
- Focus on formulary management as the sole objective limits the ASP to controlling drug costs, and clinical outcomes may be largely ignored
  - A patient-centric ASP uses evidence-based guidelines to improve clinical outcomes and manage drug costs
Accountabilities of the Antimicrobial Stewardship Team: Elements For a Business Model (Examples)

- Decrease antibiotic budget by 20% each year for 2 consecutive years
- Increase physician and pharmacist knowledge about bacterial resistance and appropriate antibiotic use as assessed by annual survey and examination
- Specific intervention goals of the ASP (i.e., over first 2 years)
  - Decrease duration of IV ABX therapy by 30%
  - Increase IV-to-PO sequential therapy by 50%
  - Create pathways/guidelines for 80% of all infection-related hospitalizations
  - Decrease re-admission rates for community-acquired pneumonia by 50%
  - Decrease number of patients receiving ≥ 3 ABXs by 50%
  - Eliminate duplicative therapy with selected broad-spectrum agents
  - Increase appropriate antibiotic therapy for BSIs within 24 hrs of +BC to 100%
  - Increase de-escalation (C&S results) by 80% for targeted antibiotics
  - Decrease vancomycin use > 3 days by 30%
  - Eliminate vancomycin therapy for blood culture contamination

But …. don’t promise what you can’t deliver
Don’t Promise What You Cannot Deliver

- Decreased bacterial resistance
  - Limited evidence from single-centered studies frequently with inadequate study periods
  - Resistance may improve for one class of agents but worsen for another – is this progress?
  - Do not promise this, but it may be an outcome of ASP activities
  - No studies have defined what degree of decreased antibiotic pressure will result in decreased resistance with any specific MDRO
  - Use of complex time series analysis requires trends over many years
- Decreased *Clostridium difficile* infection
  - Difficult to achieve with antibiotic stewardship alone
  - Requires intensive changes in environmental decontamination, patient isolation procedures, and hand hygiene
- Cost-savings which are unlikely
  - Read literature on ASPs to find institutions which are similar – how much did they save and how were their ASPs managed
  - Go slow, target low-hanging fruit, and focus on interventions which will likely produce a substantial cost-savings
The Cost of HAIs Is Significant, But Lower HAI Rates Is Not a Promise To Be Made

- The Centers for Disease Control and Prevention (CDC) estimates that 1.7 million patients contract healthcare-associated infections every year and nearly 99,000 of them die
  - HAIs are estimated to be one of the top 10 causes of death in the US
- The annual direct medical costs of HAIs to hospitals range from $28.4 to $33.8 billion
  - A study of 1.7 million hospitalized patients discharged from 77 hospitals found that the additional cost of treating a HAI averaged $8,832
- In Pennsylvania, 23,287 (1.2%) hospital-admitted patients contracted at least one HAI during their stay
  - Mortality: 9.4% (HAI) vs 1.8% (no HAI)
  - Average LOS: 21.6 days (HAI) vs 4.9 days (no HAI)
  - Estimated Medicare payments: $20,471 (HAI) vs $6,615 (no HAI)
  - Readmission within 30 days (infection/complication): 29.8% (HAI) vs 6.2% (no HAI)

While every effort should be made to decrease HAIs, ASPs may directly impact rates of *C. difficile* infection and surgical site infections

2 Scott, RD. The direct medical costs of healthcare-associated infections in U.S. hospitals and the benefits of prevention, 2009. Division of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, 2009.
3 GAO Report; April 16, 2008; GAO-08-283; HHS Action Plan to Prevent HAIs; released Jan 6, 2009 .
4 http://www.ihi.org/IHI/Programs/Campaign/Campaign.htm?TabId=2#InterventionMaterials
Approximated Cost-Savings Can Be Estimated For Your Business Model – Look For Opportunities

- IV-to-PO switch
  - If the average change in decreasing duration of therapy of 5 common IV antibiotics through conversion to orals is 3 days, and the ASP could intervene on 70% of these regimens, how many days of therapy could be saved?

- Pharmacodynamic dose optimization, e.g., dosing of IV beta-lactams (for susceptible pathogens)
  - Cefepime 2 grams IV Q8H → 1 gram IV Q6H
  - Piperacillin-tazobactam 4.5 grams IV Q6H (doses over 20 mins) converted to piperacillin-tazobactam 4.5 grams IV Q8H (doses over 4 hours)

- Discontinue duplicate therapy
  - How often is metronidazole combined with piperacillin-tazobactam or a carbapenem? Perform an audit, then estimate costs of discontinued metronidazole.

- Pathogen-directed therapy based on results of C&S
  - What is baseline de-escalation rate within 48 hours following availability of C&S results? What cost-savings could be associated with a 30% improvement (increase in de-escalation)?

- Assess potential to change antibiotic prescription habits
  - Acute uncomplicated cystitis, e.g., shorter duration and use of preferred agents

## Several Resources of ASP Business Plans

- Page 4 of 5 of CDC template for an ASP business plan

### Outcome Measurements

The success of this proposal depends on the regular monitoring and evaluation of the outcomes of interest, namely the impact of these activities on antibiotic use, antibiotic resistance, and cost savings. An annual report will be provided summarizing these outcome measurements.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Potential Cost Savings</th>
<th>Clinical and Microbiologic Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic Approvals</td>
<td></td>
<td>• Improved appropriateness of antibiotic suggestions(^6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Improved infection cure rate(^5)</td>
</tr>
<tr>
<td>Post-prescribing Review</td>
<td>$ 103,000</td>
<td>• Decrease in antibiotic-related adverse drug events(^7)</td>
</tr>
<tr>
<td>• IV to PO Conversions</td>
<td>$ 242,000</td>
<td>• Decrease in median length of stay by up to 3 days(^5,7,8)</td>
</tr>
<tr>
<td>• Decrease Antibiotic Duration</td>
<td></td>
<td>• Decrease in antibiotic resistance(^2,9,10)</td>
</tr>
<tr>
<td>• Duplicate Therapy</td>
<td></td>
<td>• Decrease in inappropriate antibiotic utilization(^5)</td>
</tr>
<tr>
<td>• Pharmacokinetics</td>
<td></td>
<td>• Decrease in antibiotic resistance(^9)</td>
</tr>
<tr>
<td>• De-escalation/ Streamlining</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surveillance of Antibiotic Resistance and Utilization</td>
<td></td>
<td>• Decrease in antibiotic resistance(^9)</td>
</tr>
<tr>
<td></td>
<td>$ 345,000 *</td>
<td></td>
</tr>
<tr>
<td>Total potential measurable cost savings</td>
<td>$ 345,000 *</td>
<td></td>
</tr>
<tr>
<td>2 Additional FTE’s (ID Clinical Pharmacy Specialists)</td>
<td>$ 180,000 **</td>
<td></td>
</tr>
<tr>
<td><strong>NET POTENTIAL MEASURABLE COST SAVINGS</strong></td>
<td><strong>$ 165,000</strong></td>
<td></td>
</tr>
</tbody>
</table>

* additional cost savings can be achieved by LOS reductions, safety, resistance, and patient outcomes over time

** excludes benefits

Business Plan Elements for ASP Justification:
Specifics Are Important and Negotiable

- The longitudinal evaluation to quantify cost-savings is influential because the data is collected from and pertains to the specific health care facility
  - Obtain data on the rate of a specific infection, propose a change in management, study the potential effects of instituting the change, apply cost-savings (calculated by multiplying the amount of decrease in the infection rate by the published cost of each occurrence of the infection)

- A presentation to administration to negotiate an ASP should consist of:

| Internal preparation (what are the direct needs of the ASP) | • Identify, list, and understand the costs, organized into present costs, costs of inaction, and costs of definitive action
| | • Structure a best alternative to negotiating an agreement (BATNA)
| | • Establish a global fee for ID physician role based on proposed hours/week |

| External preparation (what are the needs of the hospital) | • Evaluate past obstructions
| | • What is the hospital’s BATNA
| | • Establish fair market value (FMV) |

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,1 Robert C. Owens,2 John E. McGowan, Jr.,3 Dale N. Gerding,4 Robert A. Weinstein,5 John P. Burke,6 W. Charles Huskins,7 David L. Paterson,8 Neil O. Fishman,9 Christopher F. Carpenter,10 P. J. Brennan,9 Marianne Billeter,11 and Thomas M. Hooton12

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“Effective antimicrobial stewardship programs can be financially self-supporting and improve patient care. Comprehensive programs have consistently demonstrated a decrease in antimicrobial use (22%–36%), with annual savings of $200,000–$900,000 in both larger academic hospitals and smaller community hospitals”
# Impact of Antibiotic Stewardship Programs

<table>
<thead>
<tr>
<th>Hospital Size</th>
<th>Participation by Clinicians</th>
<th>Antimicrobial Cost Savings</th>
<th>Drug Resistance &amp; Infectious Diseases Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>174 beds</td>
<td>ID MD: x, Clin RX: x, Micro: x</td>
<td>Annual cost reduction: $200,000-$250,000</td>
<td>Reduced rate of nosocomial <em>Clostridium difficile</em> and MDR-Enterobacteriaceae</td>
</tr>
<tr>
<td>250 beds</td>
<td>ID MD: x, Clin RX: x, Micro: x, Data Analyst: x</td>
<td>Cost-savings during 18 month study: $913,236</td>
<td>Decreased resistance rates</td>
</tr>
<tr>
<td>650 beds</td>
<td>ID MD: x, Clin RX: x, Micro: x</td>
<td>Net savings for 1 year: $189,318</td>
<td>Reduced rate of VRE colonization and bloodstream infections</td>
</tr>
<tr>
<td>120 beds</td>
<td>ID MD: x, Clin RX: x, Micro: x</td>
<td>19% decrease ABX costs/pt; annual cost reduction: $177,000</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Example #1: Guideline-Concordant Therapy in Community-Acquired Pneumonia (CAP) Improves Outcomes

- 1,649 patients, ≥ 65 years of age, hospitalized with CAP (2001-2007); 43 centers; 12 countries
- Initial empiric therapy for CAP was evaluated for guideline compliance according to the 2007 IDSA/ATS guidelines (59% adherent, 41% non-adherent)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Adherent</th>
<th>Non-Adherent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical stability by 7 days*</td>
<td>71% (95% CI, 68%-74%)</td>
<td>57% (95% CI, 53%-61%)</td>
</tr>
<tr>
<td>Median length of stay*</td>
<td>8 days (IQR, 5-15 days)</td>
<td>10 days (IQR, 6-24 days)</td>
</tr>
<tr>
<td>In-hospital mortality*</td>
<td>8% (95% CI, 7%-10%)</td>
<td>17% (95% CI, 14%-21%)</td>
</tr>
</tbody>
</table>

*P<0.01

An ASP structured to strengthen compliance with treatment guidelines may impact patient outcomes and length of stay

Example #2: ASP Plus Automated Pharmacy Technology Improve Antimicrobial Appropriateness for CAP

- A multidisciplinary committee sought to optimize initial selection of antibiotics for adult CAP as a CMS performance measure.
- A large urban multi-campus academic medical center developed several tools in the emergency department:
  - Algorithm for ED providers identifying appropriate antibiotic selections.
  - Development of a CAP Toolkit consisting of appropriate antibiotics and dosing regimens bundled with the treatment algorithm.
  - Preloading an automated ED medication dispensing and management system.
- Appropriate antibiotic selection for CAP was studied in 2 EDs, comparing rates prior to intervention in 2008 to post-intervention in 2011:
  - In the pilot ED, appropriate antibiotic selection for CAP improved from 54.9% to 93.4% (P=0.001).
  - In the second ED, appropriate antibiotic prescribing regimens for CAP improved from 64.6% to 91.3% (P=0.004).

The combination of interdisciplinary teamwork, antibiotic stewardship, education, and information technology was associated with replicable and sustained prescribing improvements.

Example #3: Impact of Antimicrobial Stewardship Programs, University of Kentucky (1998-2002)

- Members and institution size:
  - ID physician, ID pharmacist
  - 473 beds
- Interventions:
  - Recommendations regarding antibiotic selection
  - De-escalation of antibiotic therapy on day 3
- Outcomes:
  - Dramatic reduction in antimicrobial expenditures
  - Stabilization of *Pseudomonas aeruginosa* susceptibility

NOTE: This study trended inflation rates to simulate rise in antimicrobial expenditures if the ASP was non-existent

Example #4: Impact of Antimicrobial Stewardship Programs, Maine Medical Center (2001-2004) 1,2

- Members and institution
  - ID physician and ID pharmacist
- Interventions
  - Concurrent chart review 3 days per week
  - Targeted patients receiving multiple, prolonged, or high-cost therapies
- Outcomes:
  - At 3 months, antibiotic charges decreased ($1,287, intervention group; $1,674 in control group; p < 0.04)
  - At 3 years, monthly antibiotic expenditures had decreased approximately $25,000

---

Example #5: Program at a Small Community Hospital

- 120-bed community hospital studied in 2000
- Antibiotic support team (AST) – ID MD, PharmD, members of infection control and microbiology
  - ID MD devoted 8-12 hours per week on AST
- Concurrent chart review 3 days per week targeting patients receiving multiple, prolonged, or high-cost antimicrobial therapy
- Results:
  - 488 recommendations; 69% accepted
  - Antibiotic costs reduced 19%; $18.21/pt-day to $14.77/pt-day
  - Total estimated savings of $177,000 in 2000 (vs. 1999)

LaRocca A. Clin Infect Dis. 2003;37:742-3 (letter)
Example #6: Program at a Large Community Hospital

- In a 530-bed community hospital, an ASP team comprised 2 ID physicians and 3 ICU pharmacists
- Prospective audit of new antibiotic starts and weekly use of 8 targeted antimicrobials*; outcomes were compared in the 1-year pre-ASP and 1-year post-ASP periods
- Results:
  - A total of 510 antimicrobial orders were reviewed, of which 323 (63%) were appropriate, 94 (18%) prompted de-escalation, 61 (12%) were denied, and 27 (5%) led to formal consultation with an ID physician
  - There was a 25.4% decrease in defined daily doses of the targeted antimicrobials
  - The ASP was associated with ~50% reduction in the odds of developing *C. difficile* infection (OR 0.46, 95% CI, 0.25-0.82)
  - The ASP was not associated with decreased 30-day mortality after discharge or readmission rate
  - The antimicrobial cost per patient-day decreased by 13.3%, from $10.16 to $8.81, translating to a decreased antimicrobial budget of 15.2%, or $228,911.

* Targeted antimicrobials included aztreonam, caspofungin, daptomycin, ertapenem, linezolid, meropenem, tigecycline, and voriconazole

Example #7: Telemedicine in a Setting of Limited Resources

- 141-bed rural community hospital
- Antibiotics with potential for overuse and misuse were identified
  - Linezolid, vancomycin, daptomycin, piperacillin/tazobactam, imipenem, and ertapenem
- Stewardship planners included Chief Medical Officer (CMO), Director of Pharmacy, a clinical microbiologist, and infection prevention
- “Mole whackers” included 5 pharmacists (1 with clinical training), 2 PGY1 pharmacy residents, CMO (once weekly)
- Program included teleconferencing capability with a remotely located ID physician contracted by the institution (once weekly)
- Hospital used a drug formulary, but had no prior authorization program or computerized physician order entry; back-end IT was limited

Example #7: Telemedicine in a Setting of Limited Resources (cont’d)

- Interventions included audit and feedback:
  - Pharmacist review of new antimicrobial orders
  - Medication orders triaged for immediate intervention via written form of weekly discussion with CMO
  - Complex cases were elevated to remote weekly discussions with ID physician using telemedicine
- Simultaneously, education was performed using CME sessions for medical staff and ID-focused hospital newsletters, including stewardship certification of the ASP staff
- Outcomes (pre/post):
  - Average number of ASP interventions increased from 2/week to 25/week
  - Streamlining of empiric antibiotic regimens increased from 44% to ~80%
  - Antibiotic purchases decreased from $13,000/1,000 patient-days to $6,300/1,000 patient-days
  - Rates of *C. difficile* infection declined from 8.2 cases/10,000 patient-days to 3.1 cases/10,000 patient-days

Example #8: Antimicrobial Stewardship in a Long-Term Acute Care Hospital (LTACH)

- 60-bed LTACH (defined as high-acuity patients requiring long-term care (mean, > 25 days)
- High antimicrobial utilization similar to ICUs: 993 DDD/1,000 patient-days
- Resources:
  - Program planners included ID physician and Director of Pharmacy
  - “Mole whackers” included a pharmacist (no specialty training) and an ID physician (1 hour/week)
  - Limited IT support (no EMR or CPOE)
  - No formulary restrictions or prior authorization

Example #8: Antimicrobial Stewardship in a Long-Term Acute Care Hospital (LTACH) (cont’d)

- **Interventions:**
  - Pharmacist identified patients for review for a one-hour weekly meeting with ID physician
  - Pharmacist provided recommendations via a non-permanent chart note

- **Outcomes (pre/post)**
  - Total antimicrobial use decreased 21%, from 993 DDD/1,000PD to 786 DDD/1,000PD
    - Carbapenems decreased 39%
    - Fluoroquinolones decreased 42%
    - Linezolid decreased 58%
    - Metronidazole decreased 31%
  - Antimicrobial costs/patient-day decreased 28% ($29/PD to $20.8/PD)
  - Rate of *C. difficile* infection increased but was not statistically significant (5.1 cases/10,000 pt-days to 11.3 cases/10,000 pt-days, P=0.14)

Example #9: Antimicrobial Stewardship in a Long-Term Care Facility; Keeping a ‘LID’ on Antibiotic Use

- An infectious disease consultation service (LID) was introduced to provide on-site consultations to residents of a 160-bed Veterans Affairs LTCF
- Systemic antimicrobial use and positive *C. difficile* tests were for the 36 months before and the 18 months after initiation of LID
- Results:
  - Total systemic antibiotic administration decreased by 30% (P<0.001), with significant reductions in both oral (32%; P<0.001) and intravenous (25%; P=0.008) agents
  - The greatest reductions were observed for tetracyclines (64%; P<0.001), clindamycin (61%; P<0.001), trimethoprim/sulfamethoxazole (38%; P<0.001), fluoroquinolones (38%; P<0.001), and beta-lactam/beta-lactamase inhibitor combinations (28%; P<0.001)
  - The rate of positive *C. difficile* tests at the LTCF declined in the post-intervention period relative to the pre-intervention rates (P=0.04)

Implementation of an LTCF ID service led to a significant reduction in total antimicrobial use

Example #10: Temporal Effects of a Restrictive Antibiotic Policy

- A restrictive antibiotic policy banned routine use of ceftriaxone and ciprofloxacin following an educational program.
- Monthly consumption of 9 antibiotics (DDD/1000 pt-bed days) measured 9 months before until 16 months after policy introduction.
- Hospital-acquired *C. difficile*, MRSA and ESBL-producing coliforms were monitored (case/month/1000 pt-bed days).
- Results (between first and final 6 months):
  - Average monthly consumption of ceftriaxone and ciprofloxacin decreased 95% and 73%, respectively.
  - *C. difficile* was reduced by 77%, MRSA by 25%, and ESBL-producing coliforms by 17%.
  - An audit 3 years after the policy showed sustained reduction in *C. difficile*, MRSA, and ESBL-producing coliform rates.

ASP activities have occasionally reported a decrease in bacterial resistance, but this is difficult to achieve and is likely multifactorial; however, the effect of antimicrobial stewardship on *C. difficile* infection rates is well-documented but also relies on many factors.

The Pitch for Antimicrobial Stewardship Programs: Hospital Administration

- The basic approach
  - If done right, an intervention will save money, improve outcomes, and increase provider satisfaction
  - Identify active issues in your facility
  - Meet with stakeholders (“C” suite), department heads, and other prescribers to assess their needs
  - Are there opportunities for reduction in LOS?
- Emphasize “low-hanging fruit” initially – results can be observed in the short-term and allow sufficient time to study what issues constitute “high-hanging fruit”
  - Estimate cost-savings on expensive agents (e.g., linezolid, daptomycin, echinocandins, carbapenems, aztreonam, tigecycline) but not necessarily the workhorse antibiotic
  - Include cost-savings from antibiotic redundancy and improved contracting
  - IV-to-PO switch, especially fluoroquinolones, voriconazole and linezolid
The Pitch for Antimicrobial Stewardship Programs: Hospital Administration (cont’d)

- Use evidence from other institutions (reduced antibiotic budget, reduction in \textit{C. difficile} infection, improved patient-level outcomes, decreased ICU or total LOS, improved antibiotic use, safety)
- Be synchronous with the goals of hospital administration; what are administrators interested in – what are their issues?
  - Decrease and control costs
  - Improve regulatory compliance (IPPS, core measures)
  - Remain competitive with surrounding institutions, including public reporting and patient surveys
  - Optimize patient safety, especially if it decreases costs
- Can bacterial resistance be decreased?? Not in the short-term, so do not promise upfront (use to justify ASP later, if this is observed – take credit for it)
- Pick a clinical syndrome with evidence-based management guidelines as a second phase, unless you are confident that a clinical change can occur within the first phase
Stewardship Case for Pharmacy Administration

- Review antibiotic formulary and what is on the shelves – look for redundant agents and “clear the shelves”; implement therapeutic substitution
  - Assess the need for multiple echinocandins
  - Does Pharmacy need to stock both ceftazidime and cefepime?
- Work with purchasing agent – are there contracting opportunities?
- Batching of intravenous antimicrobials, such as caspofungin and daptomycin
- Analyze pharmacy workflow in compounding agents
- Study the root causes of delayed administration of antimicrobials
- Assess the availability of antimicrobials in automated dispensing machines
  - Can some agents be packaged differently with instructions for reconstitution?
  - Should certain items be packaged with treatment guidelines, such as a “CAP kit”
- Improve regulatory compliance and performance measures, such as SCIP

Winning over hospital administration means winning over Pharmacy Directors too, but there are additional activities which are Pharmacy-department specific

The Pitch for Antimicrobial Stewardship Programs: Prescribers

- Address what prescribers need:
  - Optimize patient safety – difficult to argue against
  - Regulatory compliance, such as surgery; sometimes compelling
  - Potential to reduce resistance
  - What reports and interactions do they need? Data monitoring and transparency
- Do not emphasize control of costs – you do not want to be perceived as the “antibiotic cop”
- Communication skills are essential
  - The ASP is not telling them what to do; it is trying to make their lives easier!! (Antibiotic selection and management are actually very complex activities!)
  - Anecdotes can be compelling, especially if they are from institutional experiences
- Education can be a carrot – what reports and interactions do they need?
  - “Do you know about the most recent endocarditis prophylaxis guidelines? Let me give you a quick summary.”
The Pitch for Antimicrobial Stewardship Programs: Prescribers (cont’d)

- Antimicrobial stewardship will help them take better care of patients:
  - Guide therapy for complex patients and resistant infections
  - De-escalation of antibiotics optimize therapy
  - Guide dosing in patients with renal/hepatic dysfunction
  - IV to PO switch for earlier discharge
  - Decrease unintended consequences of antimicrobial use, e.g., *Clostridium difficile* infections
  - Prevent adverse events, e.g., drug-drug and drug-disease interactions
  - Guide drug selection in patients with multiple allergies
  - Improve drug compliance and education at discharge
  - Improve transition of care

- Recruit thought leaders in different specialties to support and reiterate your message
  - The peer champion perspective is powerful
  - Nurses work well in the right setting since they are the direct caregiver
ADDITIONAL SLIDES
Example: Guideline-Concordant Therapy in CAP

- 54,619 patients (non-ICU) hospitalized for CAP at 113 community hospitals
- 65% received initial guideline-concordant therapy

<table>
<thead>
<tr>
<th>Measure</th>
<th>Guideline-Concordant Therapy (vs Non-Concordant Therapy)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>Odds ratio =0.70</td>
<td>95% CI, 0.63-0.77</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Odds ratio =0.83</td>
<td>95% CI, 0.72-0.96</td>
</tr>
<tr>
<td>Renal failure</td>
<td>Odds ratio =0.79</td>
<td>95% CI, 0.67-0.94</td>
</tr>
<tr>
<td>Length of stay</td>
<td>Decreased 0.6 days</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Duration of IV therapy</td>
<td>Decreased 0.6 days</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

An ASP structured to strengthen compliance with treatment guidelines may impact patient outcomes and length of stay

Example: Reduction in Broad-Spectrum Antimicrobial Use

- A 4-year program in a 731-bed tertiary-care teaching hospital
- Review of charts 48 hours after prescribing broad-spectrum antibiotics (antibacterials + anti-fungals)
- Recommendation (written) to streamline or D/C
  - Automatic implementation of recommendation if no response within 24 hours by attending/resident
- Results (changes to regimens after 3rd day):
  - 92% complete or partial acceptance of recommendation
  - 27% reduction in broad-spectrum antibiotics
  - 20% decrease in monthly costs ($340,591 in 2000 to $274,030 in 2003)
  - Interventions did not alter antibiotic susceptibility rates over 4 years of program

**Example: A Controlled Trial of a Critical Pathway for Treatment of Community-Acquired Pneumonia**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Critical Pathway</th>
<th>Conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS, median</td>
<td>5.0 days</td>
<td>6.7 days</td>
</tr>
<tr>
<td>LOS, average</td>
<td>8.2 days</td>
<td>9.6 days</td>
</tr>
<tr>
<td>Duration IV antibiotics, mean</td>
<td>4.6 days</td>
<td>6.3 days</td>
</tr>
<tr>
<td>% Patients receiving monotx</td>
<td>64%</td>
<td>27%</td>
</tr>
<tr>
<td>BDPM (# bed days per patient managed)</td>
<td>4.4 days</td>
<td>6.1 days</td>
</tr>
<tr>
<td>Reduction in CAP admission rate</td>
<td>18%</td>
<td>---</td>
</tr>
</tbody>
</table>

19 Canadian centers; 1,743 CAP patients during 7-month 1998 study period

Critical pathway (9 centers) = clinical prediction rule for admission decision (Fine score) + levofloxacin therapy (500mg IV/PO x 10 days) + practice guidelines (criteria-based practice guidelines for IV to PO switch and discharge, assessment by study RN, chart notes recommending IV to PO switch and hospital discharge)

Reduction of BDPM by 1.7 days = $1,700 (U.S.) saved per patient treated

Critical pathway and conventional sites showed similar QOL scores and adverse clinical outcomes (ICU admission, mortality, readmissions, complications, any adverse outcome)

“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.
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All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

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By now all clinicians should understand why antimicrobial stewardship should be part of the mindset of prescribers. Unfortunately, the “Nuts and Bolts” are frequently unclear or not even discussed in the stewardship literature leaving programs to adopt examples from published studies. These slides may help direct young ASPs to get off the ground.

20 slides; 1 back-up slide. Because these slides constitute the crux of an ASP and are technical in nature, one hour should be allotted for presentation.

This section naturally follows “Pathways to a Successful Program”. But once your “case has been adopted” the real nuts and bolts need to be discussed with your stakeholders and ASP participants.

The repetition between some slides have been included depending upon audience or presentation style. However, the basic messages of sequential phases and steps of the ASP are most important to review. Documentation is emphasized as the means to collect data on interventions and outcomes. The mandate of stewardship in California, as well as potential federal mandates for ASPs, are discussed.
ANTIMICROBIAL STEWARDSHIP PROGRAMS: THE NUTS AND BOLTS
Perspective #1:
Four Phases … in Sequence

Philosophy of ABX Stewardship

- Goals and objectives of ASP
- Business model (written & slides); cost of resistance
- Staff models for internal discussion; “how to do this?”
- List of challenges with associated solutions

Acceptance by Hospital System

- Identify champions
- Job responsibilities, functions, anticipated outcomes
- General and daily activities – a framework to discuss
- Identify and meet with all stakeholders; specific agendas

Implementation

- Measure antibiotic use and resistance
- List of projects, by year; divided into levels of difficulty
- Roll out to Pharmacy Department staff
- Specific interventions within classes (low-hanging fruit)
- Documentation requirements
- Education of staff (Pharmacy, IPAC, Micro, CMO/Med Staff)

Sustain Stewardship Program;
Continuous Education, Feedback & Quality Improvement

- Attention to antibiogram and trends
- List of high (higher) hanging fruit; projects; feedback
- Continuous documentation of benefits; assign value to improvement of care
- Strengthen ASP functions in the business model
- Report on progress to departments; feedback
## An Alternative Perspective:
### Twelve Steps to Implementing an ASP

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Assess motivations for an ASP</td>
<td>7</td>
<td>Define how progress is to be measured; what constitutes success?</td>
</tr>
<tr>
<td>2</td>
<td>Identify physician champion; form core group (physician-pharmacy)</td>
<td>8</td>
<td>Establish an implementation plan; identify phases</td>
</tr>
<tr>
<td>3</td>
<td>Gain administration support (includes P&amp;T, Med Exec, Departments); business model and physician compensation plan developed</td>
<td>9</td>
<td>Identify resources (education of pharmacists, tools, training, medical meetings, networking, society membership, software)</td>
</tr>
<tr>
<td>4</td>
<td>Identify which of the defined problems/issues will be addressed by the ASP</td>
<td>10</td>
<td>Establish frequency of monitoring and documentation; daily activities and hierarchy of notifications</td>
</tr>
<tr>
<td>5</td>
<td>Assess barriers to success (level of education, work flow)</td>
<td>11</td>
<td>Establish mechanism and schedule for reporting of results (to whom?; with what?)</td>
</tr>
<tr>
<td>6</td>
<td>Identify Team members, roles, responsibilities, and accountabilities; meeting frequency</td>
<td>12</td>
<td>Market the program (internal and external; insurers/contract groups)</td>
</tr>
</tbody>
</table>
Baseline Data Collection

- Antimicrobial Consumption – multiple methods
  - Hospital purchase costs
  - Antibiotic costs per patient day
  - Daily defined doses (DDD)/1000 pt days
  - Days of therapy (DOT)
  - Length of therapy (LOT)
  - Days of IV and Oral therapy
- Antibiotic prescribing issues
  - Ask around; focus groups
- Antimicrobial Susceptibility Report (antibiogram)
- Length of stay – total and ICU LOS
- Healthcare-associated infections
- Physician survey
- Performance measures – areas for improvement?
  - % Patients on > 3 days targeted antibiotics
  - % Patients on ≥ 3 antimicrobial agents

Baseline data collection relies on ASP goals and objectives
## Sequence of ASP Projects: First Steps, First Year

<table>
<thead>
<tr>
<th>First steps</th>
<th>Develop First-Year Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Get all Team members together</td>
<td>• Identify “low-hanging fruit” for first-year plans</td>
</tr>
<tr>
<td>• Introduce program to all stakeholders</td>
<td>• Duplication of therapy</td>
</tr>
<tr>
<td>• Meet with ID and pharmacy staffs</td>
<td>• Unnecessary combination therapy</td>
</tr>
<tr>
<td>• Know strengths of information systems</td>
<td>• Vancomycin use system-wide</td>
</tr>
<tr>
<td></td>
<td>• Choose one broad-spectrum agent or class to study use</td>
</tr>
<tr>
<td></td>
<td>• IV-to-PO sequential therapy</td>
</tr>
<tr>
<td></td>
<td>• Disease-specific performances: CAP in the ED and HAP in the ICU</td>
</tr>
<tr>
<td></td>
<td>• Lectures and Grand Rounds with ID physician</td>
</tr>
</tbody>
</table>
Sequence of ASP Projects: Second Year

Second Year Plans

- System-wide education of clinicians
- Duration of therapy
- Vaccination rates
- Guideline development
- Clinician feedback (“report cards”)
- Drug information questions and monographs
- Bacterial resistance demographics – beyond the antibiogram; redesign antibiogram
- Resistance trending
- Information technology – CPOE
- Automatic stop orders
- Audit appropriateness of dose reduction based on renal function
- Nosocomial multidrug-resistant organism infection investigations (with infection prevention and control)
Process Measures for Evaluating ASP Success: Progress Should Reflect Goals and Program Intensity

Develop TEAM and hold regular meetings to focus on improvements
Design interventions based on benchmarks, guidelines, best practice
Discuss process, expectations, and responsibilities for each intervention
Implement interventions through education and DIRECT prescriber contact (1-to-1 or department level)

TRACK ANTIBIOTIC UTILIZATION
Track compliance with selected interventions
Track MDRO outbreaks
Track changes in antibiogram susceptibilities

TRACK PATIENT OUTCOMES (i.e., improved clinical response, length-of-stay, decreased mortality, avoidance of healthcare costs)

Continue to exercise quality improvement
Report to department heads, stakeholders, CMO, P&T, Med Ed, CQI and QA
Meet with IT and CFO
Ask clinicians what they need

CATEGORIZATION:
• IV-to-PO
• Dose optimization
• Discontinue (lack of infection)
• Discontinue (duration; infection resolved)
• D/C unnecessary combination
• De-escalate
• Change to guideline antibiotics

PER MONTH:
# interventions
# hrs spent in ASP
Reports, ASP meetings
Educational activities
% Interventions accepted

Planning & implementation
Benchmarking & trending
Documentation
Education & feedback
Measure Something

- What to measure depends on objectives of the program, data available, and the audience
- Demonstrate effectiveness of the antibiotic stewardship program
  - Improved patient outcomes
  - Improved patient safety
  - Decreased antimicrobial use
- Study your institution’s antibiogram – assess the need for a “deeper dive” into patient demographics (refer to Antibiogram Toolkit)
- Internal benchmarking and trending
- External benchmarking
  - Multi-hospital systems
  - Quality improvement measures

Everything measured has the potential of becoming a report with actionable items
## Valuable Metrics for the ASP

<table>
<thead>
<tr>
<th>Purpose</th>
<th>Metric</th>
<th>Examples</th>
</tr>
</thead>
</table>
| Workload statistics   | Daily activities          | • Hours on patient care rounds  
• Prescriber education  
• Projects, such as antibiogram development  
• Antibiotic utilization review (AUR) committee, nursing, infection prevention, department meetings  
• Pharmacy residents and fellows; mentoring  
• Number and type of interventions  
• Formulary reviews; P&T Committee  
• Meetings with sales representatives, etc |
| Antibiotic use        | Monthly or quarterly      | • Normalize antibiotic use data (e.g., per 1,000 patient bed days)  
• DDD, DOT, LOT  
• Costs |
| Specific initiatives  | Improve clinical outcomes; prevent resistance; performance measures | • Surgical antibiotic prophylaxis (% improvement)  
• Avoiding treatment of asymptomatic bacteriuria (pre/post intervention)  
• Other audits |
Documentation is Mandatory to Justify Continued Approval for ASP Operations – Monthly or Quarterly

• Basic activities:
  • Hours spent performing ASP functions
  • Review of ASP activities
  • Educational activities

• Categorization of interventions:
  • IV-to-PO
  • Dose optimization
  • Discontinuation (all antibiotics)
  • D/C unnecessary combination
  • De-escalate antibiotic
  • Change to guideline antibiotic(s)
  • Cancel laboratories (e.g., therapeutic drug monitoring)

• Significant achievements, milestones, or communications
  • Reflect on ASP goals and objectives
  • Ongoing projects – list them

• Number of interventions
  • Submitted to clinician
  • Acceptance rate (%) of interventions
  • Trending specific classes of interventions

• Antibiotic utilization

• Specific activities
  • ASP meeting time
  • Antibiogram development
  • Development of resources
  • Tracking outcomes
  • Chart review
  • Patient rounds
  • P&T committee, Pharmacy department

• Direct education
  • Department meetings, presentations
  • 1-to-1 meetings with prescribers
  • Develop tools to facilitate “message”
  • Other educational opportunities
Documenting Outcomes is Where the Value’s ("Money’s") At! Emerge From the Silos

<table>
<thead>
<tr>
<th>ACTIVITIES</th>
<th>OUTCOMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Intervene on allergies</td>
<td>• Safety</td>
</tr>
<tr>
<td>• Dose-adjustment</td>
<td>• Toxicity</td>
</tr>
<tr>
<td>• Disease-state measurement</td>
<td>• Compliance core measures</td>
</tr>
<tr>
<td>• Infection prevention</td>
<td>• Care bundles</td>
</tr>
<tr>
<td>• Optimize therapy</td>
<td>• LOS (total, ICU)</td>
</tr>
<tr>
<td>• Decrease broad-spectrum</td>
<td>• Superinfections</td>
</tr>
<tr>
<td>• Optimal dose &amp; combinations</td>
<td>• Cure “resistant” infections</td>
</tr>
<tr>
<td>• Optimize therapy</td>
<td>• Infection-related mortality</td>
</tr>
<tr>
<td>• Decrease duration of therapy</td>
<td>• HAI incidence (eg, CDI, SSTIs)</td>
</tr>
<tr>
<td>• Evaluate discharge ABXs</td>
<td>• Prevent 30-day readmissions</td>
</tr>
</tbody>
</table>

Activities translate into clinical outcomes – document both!
Track Functionality and Measure Outcomes: Examples of Metrics

- Examine potential links between ASP activities and changes on bacterial susceptibilities, hospital-acquired infection rates (especially *C. difficile* infection), and other infection-related quality indicators.
- Institutional data on antibiotic use and infection rates can be compared with benchmark data from local hospitals, CDC, and published literature.
- Prescriber surveys may establish baseline “perceptions”, suggest educational activities for development, and can assess impact of ASP using post-education surveys.¹
- Improvements in antibiotic prescribing, such as decreasing use of fluoroquinolones and selected cephalosporins.²
- Appropriate dosing of certain antibiotics with high potential for toxicity, such as aminoglycosides, voriconazole, polymyxins, and vancomycin.
- Interventions regarding antibiotic allergies, such as improving access to appropriate beta-lactams via penicillin skin testing.³
- Decreasing redundancy of anaerobic antibiotic coverage.⁴

Document ASP activities which demonstrate a favorable impact on clinical outcomes, antimicrobial resistance, and health care costs

California Legislative Mandates Regarding Antimicrobial Stewardship Programs

- Acute care hospitals in California are encouraged to implement ASPs.
- The emphasis on the judicious use of antimicrobials within California hospitals was established by California Health and Safety Code 1288.8, which states the following:
  - "(a) By January 1, 2008, the department shall take all of the following actions to protect against HAI in general acute care hospitals statewide:
    - (3) Require that general acute care hospitals develop a process for evaluating the judicious use of antibiotics, the results of which shall be monitored jointly by appropriate representatives and committees involved in quality improvement activities."

- In order to provide acute care hospitals (ACHs) with further guidance, the California Healthcare Associated Infections Advisory Committee proposed a 3-tier definition for what constitutes an ASP.
- The purpose of the 3-tier definition is to provide ACHs with an understanding of what is considered a basic program while encouraging implementation of additional strategies to achieve and intermediate or advanced status.

http://www.cdph.ca.gov/services/boards/Pages/AntibioticStewardshipSubcommittee.aspx (accessed 11/14/2013)
1 California Senate Bill 739. Approved and filed on September 28, 2006
California Legislative Mandates Regarding ASPs: Three-Tiered Definition for ASPs and Expectations

**Basic tier hospital:**
- Hospital antimicrobial stewardship policy/procedure
- Physician-supervised multidisciplinary antimicrobial stewardship committee, subcommittee, or workgroup
- Program support from a physician or pharmacist who has attended specific training on antimicrobial stewardship (e.g., CE training program offered by the CDC and SHEA or other recognized professional organization, or post-graduate training with concentration in antimicrobial stewardship)
- Reporting of ASP activities to hospital committees involved in quality improvement activities

**Intermediate tier hospital:**
- Annual antibiogram developed using CLSI guidelines with distribution to/education of the medical staff
- Institutional guidelines for the management of common infection syndromes (e.g., order sets, clinical pathways, empiric antimicrobial therapy guide, etc.)
- Monitoring of usage patterns of antibiotics determined to be of importance to the resistance ecology of the facility, using defined daily dosing (DDD) or days of therapy (DOT)
- Regular education of hospital staff/committees about antimicrobial stewardship

**Advanced tier hospital:**
- Antimicrobial formulary that is reviewed annually with changes made based on local antibiogram
- Prospective audit with intervention/feedback
- Formulary restriction with preauthorization

http://www.cdph.ca.gov/services/boards/Pages/AntibioticStewardshipSubcommittee.aspx (accessed 11/14/2013; from meeting minutes of “ASP Preface and Definition, 11-07-2013”)
CMS Surveyor Worksheet: Preparation for Metrics

- 3 new CMS Surveyor worksheets
- Adopted Oct 2011
- No penalties assessed
- Section 1.C. Systems to prevent transmission of MDROs and promote antibiotic stewardship, Surveillance
- Subsection 1.C.2. Can the primary interview participants provide evidence that the hospital has developed and implemented policies and procedures aimed at preventing the development of, and preventing transmission of, MDROs?

  - 1. C.2.a Facility has a multidisciplinary process in place to review antimicrobial utilization, local susceptibility patterns, and antimicrobial agents in the formulary and there is evidence that the process is followed.
  - 1. C.2.b Systems are in place to prompt clinicians to use appropriate antimicrobial agents (e.g., computerized physician order entry, comments in microbiology susceptibility reports, notifications from clinical pharmacist, formulary restrictions, evidenced based guidelines and recommendations).
  - 1. C.2.c Antibiotic orders include an indication for use.
  - 1. C.2.d There is a mechanism in place to prompt clinicians to review antibiotic courses of therapy after 72 hours of treatment.
  - 1. C.2.e The facility has a system in place to identify patients currently receiving intravenous antibiotics who might be eligible to receive oral antibiotic treatment.
Development of National Quality Measures for Antibiotic Use in the USA

- **Process**
  - CDC solicited input on potential measures from a variety of key stakeholders
  - CDC developed a few candidate measures
  - These measures are currently being piloted as part of a new Center for Medicare and Medicaid Services inpatient infection control worksheet

- **Issues**
  - How will the measures be assessed? Chart review? Are reviewers able to assess complex ID cases?
  - The Joint Commission (TJC) uses the Tracer Method, but would this work for antibiotic stewardship metrics?
  - What would be an acceptable level of compliance with the measures?
  - How do these measures apply to patients in pediatric hospitals and adults in long-term acute care hospitals and skilled nursing facilities?
Monitoring Your Antibiotic Stewardship Program: Five Basic Rules

• Do not panic – it will take time to see results, but know how you plan to justify your program ahead of time

• Communicate your program – take advantage of department meetings with nurses and physicians; develop a business card to provide clinicians

• Choose metrics to report – there are many
  • Antibiotics by cost, utilization (DDD, DOT), or indication; trend over time
  • Antibiotics by duration or culture and sensitivity results (prospective review)
  • Program objectives and initiatives
  • Patient demographics, such as hospital unit or admitting service
  • CMS performance measures; IDSA guidelines
  • Adverse drug events

• Track interventions and activities, including acceptance of ASP recommendations

• Be creative
  • Are you already doing things that could count as stewardship?
  • Learn about data streams within your institution
  • Find your champions – talk to everyone who will listen
  • Celebrate and advertise your successes
  • Be flexible – not everything will work and things will change, but that is job security
Take Home Message

• Start small and look for the “low-hanging fruit” ¹
  • IV-to-PO conversions, batching intravenous antimicrobials, therapeutic substitutions, and formulary restriction (with prior authorization based on criteria and education with feedback) or other prospective audit review and interventions

• Goals must be measurable and achievable
• Develop protocols, policies, and other services, but be sure they can be approved and implemented
• Educate face-to-face as preferred method; enhance clinical interfaces
• Develop an intervention program based on a model of actionable feedback²
  • Real-time feedback with easily accessible and concise reports or well-attended group presentations
  • Individualized or focus group feedback; concept of shared responsibility amongst prescribers
  • Create a nonpunitive atmosphere in which prescribing practices would not be used to assess job performance, or at least maintain confidentiality
  • Customize feedback based on differences in antibiotic decision-making patterns and limited clinical data; formulate more solid treatment pathways using interdisciplinary committee review

• Document ASPs interventions to prove its success
• Expand program whenever possible

² Patel S et al. Interdisc Perspect Infect Dis. Volume 2012, Article ID 150367, 6 pages
Tips Review

• Recruit an ID physician, or physician with interest and passion for antimicrobial stewardship (if no ID physician available)
• Get buy-in from providers before starting the program
• Start small
  • Concentrate on use of 1 drug/drug class or syndrome instead of comprehensive antimicrobial stewardship; start targeted rather than broad-based
  • Don’t start with your workhorse antibiotic
• Develop tools for daily ASP activities
  • Guidelines, therapeutic recommendations, and clinical pathways
  • Standard order forms
  • Some activities may need P&T approval, e.g., IV-to-PO automatic switch
• Develop communication tools to communicate messages to prescribers
• Consider antimicrobial stewardship training/certification for clinical pharmacists (many ID certification programs available, e.g., MAD-ID and SIDP)
• Use available free online resources on stewardship but study primary literature
• Partner with IT for clinical decision support tools in order sets
  • Dosing calculators
  • Pop-up screens/ drop-down menus
ADDITIONAL SLIDES
It Has to be a Well-Orchestrated Effort

• Ask yourself: “why do I want to develop, improve, and/or participate in antibiotic stewardship?”
• Develop your goals and objectives for the ASP based on institution-specific area for improvement; function as a quality assurance and patient safety initiative; identify expected outcomes of the ASP
• Support and collaboration of hospital administration, medical staff leadership, and local providers; get your “buy-in”
• Recruit physician leader, usually infectious disease
• Develop a business model based on institution-specific data, but this may require prior audits and interviews
• Determine appropriate initial stewardship strategies for the institution
• Collaborate and obtain adequate authority to perform activities
• Coordinate activities between key stakeholders (e.g. Infectious Diseases, Pharmacy, Infection Control and Microbiology)
• Recruit more leaders and find your champions
• Begin collecting antimicrobial consumption and antibiogram data
• Develop and execute a daily plan

“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

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Preface:
Measuring antimicrobial use is essential in any ASP. However, even today, many technologies are not amenable to providing accurate data. Targeted antimicrobials as well as overall use should be considered for tracking utilization. Defined daily doses are frequently discussed but other measures of antimicrobial use are also useful. The measures used should reflect the program’s goals but also should permit benchmarking. Appropriate adjustment for census and patient location are mandatory.

Content:
12 slides

Suggestions for Presentation:
This slide section may be used for education, self-study, or presentation to the stewardship committee and pharmacy director. The ASP should study each potential measure and decide how each plays a role in tracking usage while assessing the time and labor involved in collecting such data.

Comments:
Measures of antimicrobial use are frequently equated to bacterial resistance. However, proving biologic causality between use and resistance is elusive since institutional resistance, as revealed on antibiograms, is composed of several influences including antimicrobial use in the community and long-term care institutions.
ANTIMICROBIAL STEWARDSHIP: MEASURING ANTIBIOTIC UTILIZATION
Measuring Antimicrobial Use

- Surveillance of antimicrobial use allows targeting of areas with high or increased use of specific agents
  - Perform at least annually
  - Stratify by antibiotic agent
  - Create data for hospital units, medical service, or specific providers
- Normalize antibiotic use data (measure rate of use) to account for fluctuations in length of stay and patient census
  - Per 1,000 patient days
    - Normalizes antibiotic use for decreased length of stay and census
    - Avoids a “perceived decrease” in antibiotic use unless antibiotic use is adjusted by an appropriate denominator
  - Per admission or discharge
    - Affected by patients in observation status, which may not be regarded as admissions
- Assess changes in antibiotic use after interventions
  - Important to look at all classes of antibiotics – are providers just substituting one agent for another? (Example: ertapenem + tobramycin in place of meropenem for empiric coverage of *Pseudomonas* plus ESBLs when meropenem but not ertapenem is restricted)
Measuring Antibiotic Use: Data Sources

- Data measurement depends on purpose
  - Assessment of individual hospital costs and consumption
  - Comparison with similar institutions
  - Resistance to antimicrobial agents

<table>
<thead>
<tr>
<th>Source</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
</table>
| Cost-based methodologies, such as hospital purchase data | • Easy data to obtain  
  • Grams purchased over time can be converted to other units of measure, e.g., DDDs | • Loses accuracy as price fluctuates, such as generic entries, price contracting  
  • Stock may be sitting on shelf  
  • Month-to-month stock turnover  
  • Size of inventory |
| Pharmacy dispensing data                         | • Surrogate for what is actually administered                             | • Incorrect billing  
  • Credit of returned doses                                                   |
| Antibiotic administration data                   | • Most accurate data  
  • Bar coding at point of care is better than charting on MAR               | • Most difficult to obtain                                                   |
Basics of Antibiotic Use Metrics: DDD vs PDOT

- Defined daily dose (DDD)
  - The usual adult daily dose defined by the World Health Organization (WHO)
  - Problems: does not consider renal dose adjustment; WHO has changed DDD for some drugs; does not consider number of patients exposed to drug
  - Adjusted for hospital census, i.e., per 1,000 patient days (pt-days)
  - Example:
    - Vancomycin, 1.0 DDD = 2 grams
    - A patient who receives 1 gm BID = 1.0 DDD; 5 days of treatment = 5.0 DDDs

- Patient days of therapy (PDOT)
  - 1.0 DOT is the administration of at least one dose of a single agent on a given day
  - Problems: it is unclear number of patients who receive the drug
  - Insensitive to renal function and dosage; simply one day of exposure
  - Can be adjusted for hospital census, i.e., per 1,000 patient days (pt-days)
  - Example:
    - One patient receives vancomycin 1 gram Q12H x 5 days = 5 PDOTs
    - Another patient receives vancomycin 1 gram Q24H x 5 days = 5 PDOTs
Basics of Antibiotic Use Metrics: DDD vs DOT

• Defined daily dose (DDD)
  • The **usual adult daily dose** defined by the World Health organization (WHO)
  • Example:
    • Vancomycin, 1.0 DDD = 2 grams (1 gm BID or 2 grams daily)
    • A patient who receives 1 gm BID x 5 days = 5.0 DDDs
    • A patient who receives 500 mg BID x 5 days = 1 gm x 5 days = 5 gms (divided by 2 gms usual adult daily dose) = 2.5 DDDs
    • A hospital “uses” 1,000 gm of vancomycin (e.g. purchases, dispenses, or administers) in the first quarter of the year for 4,500 patient days, then: (1000 gm/2 gm/4,500 patient days) x 1,000 = 111 DDD/1,000 patient days

• Days of therapy (DOT)
  • 1.0 DOT represents the administration of a single agent on a given day regardless of the number of doses administered or dosage strength; in essence, 1.0 DOT is the administration of at least **one dose of a single agent** on a given day
  • Example:
    • A patient receives vancomycin 1 gram Q12H x 5 days = 5 DOTs
    • Another patient receives vancomycin 1 gram Q24H x 5 days = 5 DOTs
    • One patient receives ceftriaxone 1 gm Q24H x 5 days and azithromycin 500 mg Q24H x 5 days = 10 DOTs (each drug is counted separately)

# Measuring Antibiotic Use: DDD versus DOT

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defined daily dose (DDD)</td>
<td>• Standardized comparisons among hospitals or countries</td>
<td>• DDD may not represent appropriate dose for the specific infection being treated</td>
</tr>
<tr>
<td></td>
<td>• Can be used where limited access to computerized pharmacy data exists (does not require order level data)</td>
<td>• Poor estimate in pediatrics</td>
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<tr>
<td></td>
<td></td>
<td>• Underestimates usage for drugs that are renally adjusted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Is not sensitive to drugs commonly used for surgical prophylaxis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Approved DDD may change as new dosages are approved</td>
</tr>
<tr>
<td>Days of therapy (DOT)</td>
<td>• Can be used in pediatrics</td>
<td>• Overemphasizes appropriate multi-drug regimens</td>
</tr>
<tr>
<td></td>
<td>• Not influenced by discrepancies of prescribed daily dose or assigned DDD</td>
<td>• Does not resolve all renal dosing issues, e.g., vancomycin Q3 days in severe renal dysfunction (1 DOT every 3 days, what is duration of exposure?)</td>
</tr>
<tr>
<td></td>
<td>• Not influenced by changes in the recommended DDD</td>
<td>• Difficult to measure, even with computerized pharmacy records</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Time-consuming</td>
</tr>
</tbody>
</table>
A Potential Useful New Measure: Length of Therapy (LOT)

- Can be used to complement days of therapy (DOT)
- Hospitals that use more combination therapy will have higher DOTs than those that use monotherapy, but LOT should be the same
  - Ciprofloxacin + metronidazole x 5 days = 10 DOTs, 5 LOTs
  - Ertapenem x 5 days = 5 DOTs, 5 LOTs
- DOT ÷ LOT – measures the number of antimicrobial agents administered per patient per day
- Mean DOT or LOT per discharge or DOT or LOT per 1,000 patient-days provide a more complete picture of antimicrobial use when applied to different medical services within the hospital
- When the DOT or LOT values per 1,000 patient-days are risk-adjusted by case-mix index (CMI) inter-hospital comparisons can be made (cautiously)
Benchmarking Antimicrobial Use: Current Issues

- The most appropriate metric for measuring antibacterial drug use for benchmarking purposes remains a matter of considerable debate.
- Benchmarking may identify outliers, both high and low, so that best practice strategies can be identified and implemented to improve patient care.
  - Risk adjustment is used to control for interhospital differences in case mix that otherwise confound comparisons, such as case mix index (CMI), bed size, academic vs community hospital, and transplant services.
  - Benchmarking can be done through reporting to the National Healthcare Safety Network – Antimicrobial Use and Resistance module (NHSN AUR module) or the University HealthSystem Consortium (UHC).

Are There Antibiotic Use Metric Data Available For The USA?

- Use of 50 antibacterial drugs administered to adults discharged from 130 US hospitals between August 1, 2002 and July 31, 2003
- Of 1,795,504 patients, 59.8% received at least 1 dose of an antibacterial drug
- The mean (± SD) of total antibacterial drug use measured by the number of DDDs per 1000 patient-days and the number of DOTs per 1000 patient-days were not significantly different, although the correlation was poor

<table>
<thead>
<tr>
<th>Parenteral Agent</th>
<th>No. of hospitals</th>
<th>Mean DDDs/1,000 pt-days (± SD)</th>
<th>Mean DOTs/1,000 pt-days (± SD)</th>
<th>Mean administered daily dose, g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>130</td>
<td>80.3 ± 35.4</td>
<td>94.3 ± 27.7</td>
<td>2.46</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>123</td>
<td>18.0 ± 22.1</td>
<td>13.5 ± 16.3</td>
<td>0.72</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>123</td>
<td>75.6 ± 57.5</td>
<td>74.9 ± 55.8</td>
<td>0.51</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>130</td>
<td>44.9 ± 28.2</td>
<td>62.9 ± 35.9</td>
<td>1.46</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>130</td>
<td>46.1 ± 39.0</td>
<td>52.7 ± 26.6</td>
<td>1.63</td>
</tr>
<tr>
<td>Pip-tazobactam</td>
<td>127</td>
<td>30.3 ± 20.3</td>
<td>42.7 ± 28.5</td>
<td>10.1</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>126</td>
<td>28.1 ± 14.3</td>
<td>32.8 ± 15.4</td>
<td>1.32</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>130</td>
<td>20.8 ± 17.1</td>
<td>18.0 ± 14.8</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Is Antimicrobial Use Data Correlated With Bacterial Resistance?

- Measurement of fluoroquinolone (FQ) use in 17 U.S. hospitals during 2000
- Fluoroquinolone use (DDD/1,000 pt-days) correlated with %MRSA, but not FQ-resistant *E. coli*
- Questions:
  - Why does a 4-fold difference in hospital FQ use density produce similar rates of MRSA within the range of 30% to 45% (blue oval)?
  - Why does hospital FQ use not translate into changes in resistance?
  - How do patient demographics relate to antibiotic resistance, beyond antibiotic exposure?
  - Is resistance being imported into the hospital?

*Mathematical Correlations Between Antibiotic Use and Bacterial Resistance May Not Infer Biological Causality When Other Important Demographic Factors Are Not Considered*

Measuring Antimicrobial Use: Summary and Considerations

- Measure something: DDD, DOT, LOT
- Normalize data to account for fluctuations in patient volume
- Trend data over time
- Trend specific agents
  - Usually for the whole institution but may be useful to trend by unit or service
- Antibiotic use per indication or per syndrome
- Review antimicrobial use at group or individual prescriber level
- Consider service-specific reports
  - Intensive care unit
  - Solid organ transplant
  - Bone marrow transplant
- Consider reporting antifungal and antiviral agents separately
- Consider reporting antimicrobial use for benchmarking (e.g. NHSN AUR)
“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

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“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

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Preface:
Deciding upon an antimicrobial formulary strategy, such as pre-authorization versus prospective audit-review-feedback will depend upon the ASP’s philosophy, desired intensity of antimicrobial order review, and the available workforce and level of education. Various strategies and tactics are discussed as parts of low-hanging fruit (initial) and high-hanging fruit (advanced) programs. Seven potential intervention categories (for documentation) are studied.

Content:
15 slides including 3 back-up slides. This slide section provides a valuable starting point for defining the daily activities of the ASP pharmacist and other members of the team. Please allow one hour for presentation and discussion.

Suggestions for Presentation:
ASP team members and pharmacists are important audiences.

Comments:
A brief history of institutional activities is discussed, but the initial daily activities may be more dependent on defining opportunities, such as patient rounds, high-admission physicians, or specific prescribing issues. However, as the ASP evolves additional activities as well as projects should become obvious.
ANTIMICROBIAL STEWARDSHIP: DAILY ACTIVITIES
Applying Antibiotic Stewardship Principles to Everyday Practice

- Antibiotic stewardship includes the following key principles:
  - Selection of the most appropriate antimicrobial treatment
  - Optimization of drug selection, dosing and duration of therapy needed to cure infection and reduce emergence of resistance
  - Improvement of patient safety through reducing the risk of toxicity, adverse effects, and hospital-acquired infections

- Core Strategies:
  - Pre-authorization/formulary restriction
  - Prospective review and feedback

- Other Strategies: Education, guidelines, order sets, dose optimization, IV to PO switch, streamlining of therapy, information technology

- Institutional comprehensive programs incorporate multiple strategies and gain cooperation among different professionals in health care

CDC and the Driver Diagram

IHI and CDC partnership to organize theories and ideas needed for improvement

Antibiotic Stewardship Driver Diagram

- **Primary Drivers**
  - Timely and appropriate initiation of antibiotics
  - Appropriate administration and de-escalation
  - Data monitoring, transparency, and stewardship infrastructure
  - Availability of expertise at the point of care

- **Secondary Drivers**
  - Promptly identify patients who require antibiotics
  - Obtain cultures prior to starting antibiotics
  - Do not give antibiotics with overlapping activity or combinations not supported by evidence or guidelines
  - Determine and verify antibiotic allergies and tailor therapy accordingly
  - Consider local antibiotic susceptibility patterns in selecting therapy
  - Start treatment promptly
  - Specify expected duration of therapy based on evidence and national and hospital guidelines
  - Make antibiotics patient is receiving and start dates visible at point of care
  - Give antibiotics at the right dose and interval
  - Stop or de-escalate therapy promptly based on the culture and sensitivity results
  - Reconcile and adjust antibiotics at all transitions and changes in patient’s condition
  - Monitor for toxicity reliably and adjust agent and dose promptly
  - Monitor, feedback, and make visible data regarding antibiotic utilization, antibiotic resistance, ADEs, C. difficile, cost, and adherence to the organization’s recommended culturing and prescribing practices
  - Develop and make available expertise in antibiotic use
  - Ensure expertise is available at the point of care

Leadership and Culture

Hospitals with established or developing ASPs demonstrated use of two core stewardship strategies:

- Prospective monitoring of prescribing and appropriateness after the first dose of a targeted antibiotic (66%)
- Preauthorization/restriction (38%)
- Other strategies: time-sensitive automatic stop orders with reevaluation (40%); use of local antibiograms (95%); and tracking resistance patterns (76%)

52% of respondents stated their hospital did not have an antibiotic stewardship program, although most of these hospitals performed supplemental strategies of stewardship to a similar extent as hospitals with established ASPs:

- Closed formularies (73% vs 80%), education of prescribers (69% vs 77%), guidelines/clinical pathways (60% vs 69%), automatic substitutions (72% vs 72%), automatic dose adjustments by pharmacy (49% vs 49%), and IV-to-PO conversion protocols for pharmacy (41% vs 46%), respectively

Hospitals with an established ASP differed from those without an ASP:

- Proactive pharmacy-driven streamlining and/or de-escalation (42% vs 26%) and dose optimization (56% vs 45%)
## Approaches to Core Stewardship Strategy: Formulary Restriction and Preauthorization

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Personnel</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Restrict dispensing of targeted antimicrobials to approved indications | Antimicrobial committee to create guidelines  
| Formulary adherence                             | Approval personnel (physicians, ID fellows, clinical pharmacist)            | Most direct control over antimicrobial use – immediate and significant reductions in use and cost       | Perceived loss of autonomy for prescribers; confrontational                                               |
| Automatic switches within class                 |                                                | Individual educational opportunities                                         | Need for all-hours consult; labor-intensive;                                                           |
|                                                |                                                | Compliance rates not determined by contacting physician                    | Potential delay in therapy                                                                             |
|                                                |                                                | More guidelines mean more interventions                                     | Non-targeted antimicrobials not reviewed                                                                |
|                                                |                                                | Most responsive measure to nosocomial outbreak of infection                  | May simply shift use from one agent to another (“squeezing the balloon”)                               |
|                                                |                                                | Can serve as ID hotline for general advice                                  | Intense monitoring of overall trends in use                                                             |

## Approaches to Core Stewardship Strategy: Prospective Audit, Intervention and Feedback

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Personnel</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Prospective and daily review of antimicrobials for appropriateness</td>
<td>▪ Antimicrobial committee to create guidelines</td>
<td>▪ Post-prescription intervention by clinician given authority (or AST)</td>
<td>▪ Compliance is voluntary and may be as low as 20%</td>
</tr>
<tr>
<td>▪ Contact prescribers to recommend alternative therapy</td>
<td>▪ Personnel available for regimen review (usually clinical pharmacists)</td>
<td>▪ Avoids loss of autonomy for prescribers</td>
<td>▪ Delayed antimicrobial stewardship</td>
</tr>
<tr>
<td>▪ Focus on other activities, e.g., IV-to-PO switch, de-escalation, disease state management and outcomes</td>
<td></td>
<td>▪ Direct individual educational opportunities and feedback</td>
<td>▪ Additional staffing and/or responsibility at each facility</td>
</tr>
</tbody>
</table>

## Seven Potential Interventions

<table>
<thead>
<tr>
<th>INTERVENTION and DOCUMENTATION CLASS</th>
<th>COMMENTS and EXAMPLES</th>
</tr>
</thead>
</table>
| **IV-to-PO sequential therapy**     | • Many agents have oral formulations or similar oral equivalents  
                                        • It involves a target IV antibiotic list and simple guidelines for assessing patient clinical and GI status  
                                        **EXAMPLES**: fluoroquinolones, clindamycin, ampicillin/sulbactam, linezolid, metronidazole, fluconazole, voriconazole, etc. |
| **Dose optimization (PK/PD principles)** | • Adjusting doses for renally-eliminated antibiotics  
                                        • Addresses under-utilized strategies for pharmacodynamic applications (extended infusions, etc)  
                                        **EXAMPLES**: Maximum doses of beta-lactams and fluoroquinolones, and extended interval aminoglycosides, in severe disease |
| **Elimination of duplicative therapy** | • Consult with ID on frequent combinations observed; prepare guidelines for intervention (e.g., automatic D/C)  
                                        **EXAMPLES**: 3rd generation cephalosporin + amikacin for *E.coli* (both agents demonstrate susceptibility; no ESBL); beta-lactam/beta-lactamase inhibitor + metronidazole for anaerobes; respiratory FQ + clarithromycin for community-acquired pneumonia |
## Seven Potential Interventions (cont’d)

<table>
<thead>
<tr>
<th>INTERVENTION and DOCUMENTATION CLASS</th>
<th>COMMENTS and EXAMPLES</th>
</tr>
</thead>
</table>
| Institutional guideline-specific therapy | • Develop and implement once approved by P&T Committee  
EXAMPLE: Empiric antibiotic treatment of sepsis using hospital antibiogram data; treatment of specific infections where targeted antibiotics are commonly used (e.g. diabetic foot infection) |
| Discontinuation of therapy based on lack of infectious process | • Evaluate empiric antibiotic regimens on hospital day #2 or #3 for differential diagnosis – determine if infection has been ruled out  
• Physicians document daily antibiotic plan |
| De-escalation (based on C&S on HD #2-3; patient improving on current therapy) | • D/C vancomycin if cultures are negative for resistant gram positive bacteria  
• Follow C&S reports to de-escalate antibiotics to narrower spectrum agents  
• EXAMPLE: Pneumococcal pneumonia therapy changed to amoxicillin PO if fully susceptible to penicillin |
| Discontinuation based on clinical resolution of infection | • For CAP, discontinue therapy after ≥5 d of treatment if afebrile x 24 hrs and no more than 1 symptom remains indicative of initial infection  
• Uncomplicated UTI generally resolves with only 3 days of trimethoprim-sulfamethoxazole or fluoroquinolone |
**Example: Antibiotic Order Form**

**ADULT ANTIMICROBIAL ORDER FORM**

USE THIS FORM TO ORDER ALL ANTINFECTIVE AGENTS FOR TREATMENT

| Allergies: □ Penicillin □ Cephalosporins □ Sulfonamides □ Other: __________________________ |
| Age: _______ years | Height: _______ inches | Weight: _______ lb/Kg | Serum Creatinine: _______ mg/ml |

All Antibiotic Orders have an Automatic 7 Day Stop Unless Specified. Surgical prophylaxis is initiated in OR. Continuation of prophylactic antimicrobial therapy, if required at all, MUST be written on the surgical prophylaxis form (obtained from intranet → go to clinical links/ antimicrobial management) or post operative order sets.

Indication: □ Empiric / awaiting culture results □ Documented / culture proven

Sites: □ Abdominal □ Bone and Joint □ Genitourinary □ Upper Respiratory □ Lower Respiratory □ CNS □ Skin & Soft Tissue (including surgical wounds) □ Other: _______

Pathogen: □ Anaerobes □ Gram Negative Rods □ Streptococcus □ Pseudomonas □ Viral □ Fungal □ Staphylococcus □ Other: _______

THE FOLLOWING AGENTS REQUIRE APPROVAL OF THE ANTIMICROBIAL TEAM OR THE ID CONSULTANTS:

**ANTIMICROBIAL TEAM BEEPER 2847**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cefepime</th>
<th>Fluconazole IV</th>
<th>Imipenem</th>
<th>Moxifloxacin IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>Amphotericin products</td>
<td>Ciprofloxacin IV</td>
<td>Fluocytosine</td>
<td>Itraconazole P.O.</td>
</tr>
<tr>
<td>Azithromycin IV</td>
<td>Daptomycin</td>
<td>Foscarnet</td>
<td>Linezolid IV/P.O.</td>
<td>Vancomycin P.O.</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Ertapenem</td>
<td>Ganciclovir IV</td>
<td>Micaflugin</td>
<td>Voriconazole IV/P.O.</td>
</tr>
<tr>
<td>Caspofungin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RESTRICTED AGENTS APPROVED BY ID ATTENDING OR FELLOW:

Select antimicrobial agent and check dose if available. Drugs that are in BOLD below require dosage adjustment in renal insufficiency. Consult pharmacy for dosing.

If Initial therapy, please indicate here □ STAT
What to Implement and Measure: Low-Hanging vs High-Hanging Fruit

EARLY and SUSTAINED:
(measure basic performances based on initial objectives)
- Decrease antibiotic use (DDD, DOT, or grams utilized adjusted for census)
- Decrease unnecessary combinations (e.g., pip/tazo + metronidazole)
- Decrease vancomycin use
- Increase IV-to-PO conversion (decrease ratio of IV days/PO days)
- Increase compliance with de-escalation when cultures are available
- Improve dose-optimization (not just dose reduction)
- Discuss improvements to antibiogram design

LATER:
(as costs plateau, and initial programs become “auto-pilot”):
- Develop evidence-based guidelines, tailored to institutional data (disease-state)
- Improve appropriateness of empiric therapy
- Discontinue therapy when appropriate
- Institute antibiogram education
- Optimize serum concentration monitoring policies
## Approaches to Core Stewardship Strategy: Additional Tactics

### Automatic Stop Orders

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Personnel</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automatic stop is part of initial antibiotic order</td>
<td>Approved by Antibiotic Utilization Review (AUR), P&amp;T, and Medical Executive</td>
<td>Decreased antibiotic use and costs, Prescriber needs to justify extended duration, Can be disease-specific when evidenced-based</td>
<td>Must be closely monitored, All prescribers must be aware of policy, Difficult to implement if CPOE</td>
</tr>
<tr>
<td>Strong and experienced ASP</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Development of Clinical Practice Guidelines & Protocols

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Personnel</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation of best practices</td>
<td>Approved by AUR, P&amp;T, and probably Medical Executive</td>
<td>Dictates therapy without direct intervention, Educates while enforcing evidenced-based therapies</td>
<td>Long development phase, Approval by multiple departments, Need to offer alternative regimens</td>
</tr>
<tr>
<td>Strong and experienced ASP</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Other Activities: Restricting Target Antibiotics to Reduce Selection of Drug-Resistant Bacteria and *C. difficile*

<table>
<thead>
<tr>
<th>Antimicrobials Associated with Emergence of Resistance in Gram-Negatives</th>
<th>High-Risk Antimicrobials Associated with <em>Clostridium difficile</em> Infection (^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroquinolones (example: <em>E. coli</em>)</td>
<td>Fluoroquinolones</td>
</tr>
<tr>
<td>Third-generation cephalosporins (example: ESBLs)</td>
<td>2(^{nd}), 3(^{rd})-, or 4(^{th})-generation cephalosporins</td>
</tr>
<tr>
<td>Carbapenems (example: KPC)</td>
<td>Carbapenems, clindamycin</td>
</tr>
</tbody>
</table>

Addressing use of selected antimicrobials may decrease selection of some ESBL- and carbapenemase-producing Gram-negative bacilli while also potentially decreasing *C. difficile*

Could be an initial stewardship step in an outbreak situation

---

Impact of the Use of High-Risk Antibiotics on the Course of an Epidemic of *C. difficile*

- Quebec hospital with epidemic hypervirulent NAP1/027 *C. difficile* strain
- Enhanced infection control procedures did not alter CDI incidence ($P=0.63$)
- Implementation of an antibiotic stewardship program decreased both total antibiotic consumption (23%) and targeted antibiotic consumption (54%)
- Targeted drugs: cephalosporins, macrolides, clindamycin, ciprofloxacin
Daily Activities: Summary

- Create a reliable and basic daily or weekly on-service plan, allowing time for projects, education, and meetings (e.g., P&T)
  - Example: ICU rounds AM, wound care or transplantation service rounds late morning, lunch with the ASP physician champion/ID physician, educational presentation midday, prospective review of targeted antimicrobials in the afternoon, meeting the ASP ID physician late afternoon (as available), and projects in between
- Ensure that daily activities have high “pay-off potential” determined by the number of intervention opportunities or change of practice
  - ICU rounds are likely to encounter antibiotic use in almost every patient with many consultants for a single patient (“cooks in the kitchen”)
  - Development of CAP guidelines and educational meetings
- Take advantage of complex situations which offer multiple points of intervention
  - Example: Patient A is started on 3 antibiotics, an antiviral, and 2 anti-fungals; de-escalation, consolidation, pathogen-directed therapy, renal dose adjustment, and IV-to-PO conversion may lead to several interventions over 3-5 days
- Every potential intervention or meaningful interaction should be captured through documentation in a well-designed and thorough monthly/quarterly report – “no time to be modest”
ADDITIONAL SLIDES
Adequate Opportunities to Exercise Stewardship: “The 5 D’s” and Interventions

Select Accurate Empiric Drug Therapy
- Education using antibiograms
- Consensus Guidelines & clinical pathways; clinical decision support tools
- Antibiotic order forms
- Appropriate consideration of combination therapy

Select Dose
- Education using PK/PD concepts
- Consensus Guidelines & clinical pathways; clinical decision support tools
- Antibiotic order forms, especially for prolonged infusions
- Use adequate dose/duration to cure infection & reduce toxicity

De-escalate
- Education
- Discontinue combinations if not indicated by C&S
- Pathogen-directed therapy based on C&S results
- IV-to-PO therapy

Adequate Duration
- Education
- Consensus Guidelines & clinical pathways for some infections
- Antibiotic order forms with automatic stop orders
- Clinical decision support tools and computer prompts
- Use adequate dose/duration to cure infection & reduce toxicity

Decreased Potential for Emergence of Resistance
Selected Activities of Antimicrobial Stewardship

- Education
- De-escalation Protocols
- Appropriate Duration
- Drug Selection and Dose Optimization
- Parenteral to Oral Conversion
- Guidelines/Clinical Pathways
Focus and Intervention: Another Means of Aligning ASP Objectives and Tactics

Broad Focus

- Hospital guidelines for empiric antibiotic use
- Community-acquired pneumonia order set

Targeted Focus

- Audit and feedback of all antibiotic orders
- Audit and feedback of specific antibiotics

Broad Intervention

Targeted Intervention
“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

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Preface:
Manual antimicrobial utilization calculations and adjustment by census and patient location is laborious and frequently inaccurate. Several vendors provide software to assist in targeting potential interventions, documentation, and presentation or creation of reports. However, some EMR systems already provide ASP metrics. Time not spent in creating daily reports, identifying interventions, or collecting patient-related data provides more time for education, project development, and acting on interventions.

Content:
10 slides for self-study and assessment of technology resources currently or potentially available. How to assess the need to purchase new software specifically designed for ASPs is also discussed.

Suggestions for Presentation:
“What are the means to collect data and identifying antimicrobial prescribing interventions?” This is an important question because time needed for data collection is inversely proportional to the number of daily interventions. CDSS needs to be discussed early in the ASP development.

Comments:
CDSS becomes part of the business planning and daily activities.
ANTIMICROBIAL STEWARDSHIP: COMPUTERIZED AND CLINICAL DECISION SUPPORT SERVICES (CDSS)
Computer Decision Support Systems (CDSS): Programmable Dashboards

- Programming current computer systems may assist in targeting antibiotic prescribing activities, but are difficult to develop as “home-made” software.

<table>
<thead>
<tr>
<th>Twelve Potential Identifiers to Consider for “Real-Time” Stewardship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core measure compliance (CAP)</td>
</tr>
<tr>
<td>Creatinine clearance and targeted antibiotics</td>
</tr>
<tr>
<td>Identify antibiotics as IV-to-PO candidates</td>
</tr>
<tr>
<td>Restricted antibiotic lists</td>
</tr>
<tr>
<td>Vancomycin ≥ 3 days with negative cultures</td>
</tr>
<tr>
<td>Duplicative therapy</td>
</tr>
</tbody>
</table>

- Several third-party software vendors are geared toward stewardship and may be run in parallel with EMRs, such as Epic and Cerner\(^1\).
- Several commercial third-party vendors focused toward antimicrobial stewardship are available but at an appreciable cost (range, $100,000 to $500,000 per year – depending on institution size)\(^1\).

---

Computer-Assisted Strategies

- Software programs interface with several databases
  - Electronic medical record (EMR) or health record (EHR)
  - Electronic medication administration record (eMAR)
  - Laboratory and radiology reporting systems
- Software programs augment the stewardship program in many ways
  - Identify high-use antimicrobial agents
  - Track disease demographics within an institution (e.g., % patients admitted for pneumonia)
  - Identify target patients that prioritize stewardship review or may be at risk for emergence of MDROs (e.g., patient scoring to identify “high-risk” patients)
  - Consolidate patient-specific information (e.g., patients on vancomycin whose renal functions are rapidly changing
  - Documentation and assessment of outcomes of specific antibiotic regimens
  - Incorporate treatment guidelines, order sets, and “best practice alerts (BPAs)"
  - Communicate and record ASP recommendations and interventions
  - Allergy information and maximum dose checking
  - 96-hour stop dates

Computerized Decision Support Services (CDSS): A Solution to Our Problems?

Problems with traditional interventions:
- Antimicrobial decision-making is complex
  - Drug-drug, drug-food interactions
  - Allergies and contraindications
- Multiple variables to consider
  - Clinical suspicion of infection and empiric therapy
  - Common pathogen(s)
  - Antibiogram data
- Incomplete patient-specific information
  - Individual patient characteristics
  - Prior cultures
  - Organ system issues
- Timeliness, integration, and synchronicity between point of care and decision support
- Population and institutional considerations
- Guidelines and regulations

Features of CDSS likely to increase clinician uptake:
- Primary determinant of user satisfaction is speed
- Integrate CDSS with clinical workflow
- Easy to use; avoids arduous data entry
- Simple and evidence-based recommendations
- Documentation of reasons to override recommendations
- Impacts are monitored; provide performance feedback
- Provides incentives to use CDSS
- Aligns guideline developers and users
- Adaptable to local users and data
- Accompany CDSS with conventional education

Example: Community-Acquired Pneumonia, Risk for Infection with *Pseudomonas*, Non-ICU

![Medications Table]

<table>
<thead>
<tr>
<th>Medications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Acquired CMS Regimen 4a with Pseudomonal Risk</td>
<td>Select Levofl oxacin as a first agent</td>
</tr>
<tr>
<td>LEVOfl oxacin</td>
<td>750 mg, INJ PREMIX, IVPB, Daily, Brand Name: Levaquin</td>
</tr>
<tr>
<td>Select one of the following as a second agent</td>
<td></td>
</tr>
<tr>
<td>piperacillin-tazobactam (Zosyn)</td>
<td>4.5 g, INTERMIT, IVPB, Q6H</td>
</tr>
<tr>
<td>cefepime</td>
<td>2 g, INTERMIT, IVPB, Q12H, Brand Name: Maxipime</td>
</tr>
<tr>
<td>meropenem</td>
<td>500 mg, INTERMIT, IVPB, Q6H, Brand Name: Merrem</td>
</tr>
<tr>
<td>imipenem-cilastatin (Primaxin (IV))</td>
<td>500 mg, INJ, IVPB, Q6H</td>
</tr>
<tr>
<td>If MRSA suspected, add one of the following to CMS Regimen 4a above</td>
<td></td>
</tr>
<tr>
<td>vancomycin</td>
<td>15 mg/kg, INJ PREMIX, IVPB, Q12H</td>
</tr>
<tr>
<td>Consult Pharmacy. (Consult Pharmacokinetics Duration of Therapy.)</td>
<td>Drug Name: vancomycin, Indication (pharmacy): pneumonia, 1 Each, MISC,...</td>
</tr>
<tr>
<td>Vancomycin Allergic/Intolerant:</td>
<td></td>
</tr>
<tr>
<td>linezolid</td>
<td>600 mg, INJ PREMIX, IVPB, Q12H, Brand Name: Zyvox</td>
</tr>
</tbody>
</table>

Courtesy: Dr Teresa Seville, MD; Mayo Clinic Hospital, Phoenix AZ, October 2013
Example: Implementation of a Clinical Decision Support System and Use of Computerized Alerts

• Quasi-experimental pre-/post-intervention study
  • Absence of reliable identification of patients with potential ASP interventions; no prospective audit or intervention/feedback (pre-implementation, Sept 2007-Feb 2008)
  • Introduction of a computerized system in Oct 2008 (TheraDoc, Hospira Inc) led to a system of prospective audit with intervention and feedback
  • Post-implementation study period Sept 2009-Feb 2010
• 8 types of alerts generated by electronic surveillance: influenza and pneumococcal vaccination, polyantibacterials, redundant anaerobic agents, drug-bug mismatch, vancomycin for coagulase-negative staphylococci, vancomycin for MSSA, and lack of positive cultures
• Post-implementation actionable alerts = 2,054 (24% of all alerts generated electronically); non-vaccination actionable alerts = 707
• Results: 88% (250/284) of interventions were accepted
• Alert type with highest number of actionable alerts was ‘no positive cultures’ (374 of 1,096 alerts, 34%)
• Significant time spent reviewing alerts, making interventions on actionable alerts, and documentation (2-5 hours/day)

Example: Computer-Assisted Surveillance for Redundant Antibiotic Combinations

- Pharmacist-based intervention at a 600-bed public teaching hospital
- Study included 1,189 inpatients receiving at least 2 antibiotics during a 23-day surveillance (1 month)
  - 137 episodes (11.5%) of inappropriate combinations
  - 98% compliance in changing regimens
- Cost savings $10,800, decreased 584 days of therapy of redundant drug
  - $83 cost savings per episode
  - Total pharmacist time $2,880 (0.33 hr per case)
- Annualized cost savings $48,000 (includes labor of ID pharmacist)

Example: The Impact of a Computerized Physician Order Entry Program Targeting Linezolid Use

- Prospective evaluation of linezolid use in a 214-bed nonacademic community hospital–based hospital following addition of an ID physician to the program
- Subsequent addition of a customized CPOE-ASP order entry template with linezolid decision algorithm based on FDA-approved indications
  - Alternative therapies were provided
- Monitor linezolid use during a 32-month period (Jan 2008 to Sept 2010)
- Results:
  - Baseline linezolid use (7 months) averaged 44 DDD/1,000 PTD
  - Decrease to mean of 7 DDD/1,000 PTD and sustained over 16-months following CPOE implementation and ID physician involvement (P<0.001 from baseline)
  - The proportion of non-appropriate linezolid use decreased from 77% (26 of 34 orders) to 11% (1 of 13 orders; P<0.003)
  - No changes in LOS, census, patient case mix
  - No effect on LOS for skin and soft tissue infections nor incidence of VRE
  - Overall cost of linezolid over 16 months after CPOE-ASP implementation resulted in a cost savings of more than $638,000, compared to 16 months prior to CPOE-ASP implementation (annualized, cost savings approximately $479,000 yearly)

The Role of Electronic Medical Records and Technology: Summary

- Begin planning early; institution-specific IT programming may take several months.
- Identify early institution-specific templates from vendor menus, so the ASP Team must decide on a desirable set of prompts which address the current antimicrobial prescribing deficiencies and objectives of the ASP program.
- Work with other departments to resolve issues of competition and prioritization of programming requests and project builds.
- Network with other ASP practitioners to gain their experience with EMR and third-party software vendors; be familiar with shortcomings, timelines, interface and compatibility issues, and future product updates.
- Evaluate the vendor’s technical support capabilities and response time.
- Work with contracting departments to identify upfront costs, annual fees, and costs of updates.
- None of the currently available programs can measure the impact of ASPs, so your documentation will need to be translated into deliverables.
- Systems should have reporting options consistent with NHSN’s AUR module.
“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.
Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

ADHS routinely seeks the input of highly qualified peer reviewers on the propriety, accuracy, completeness, and quality (including objectivity, utility, and integrity) of its materials. Although the specific application of peer review throughout the scientific process may vary, the overall goal is to obtain an objective evaluation of scientific information from its fellow scientists, consultants, and Committees.

Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.
Introduction to Slide Section

- **Preface:**
The microbiologist could be your new best friend early in the ASP development and implementation process. A strong relationship can assist in development of the antibiogram, implementation of rapid diagnostics, selection of antimicrobials on susceptibility panels, and susceptibility reporting policies. The clinical laboratory can assist in capturing data, such as turnaround time for diagnostics and notification processes to prescribers and pharmacy.

- **Content:**
15 slides with 1 additional slide.

- **Suggestions for Presentation:**
Appropriate audience would be microbiologists, including their directors, and the ASP committee. The presentation could be given in 30 minutes with time for questions and discussion. Alternatively, this is part of the self-learning modules for antimicrobial stewardship.

- **Comments:**
Also, refer to the antibiogram toolkit made available on the ADHS website. Clinical examples from the literature are provided for discussion. Newer technologies are reviewed including procalcitonin.
MICROBIOLOGY LABORATORY, THE CUMULATIVE ANTIBIOGRAM, AND RAPID DIAGNOSTICS

[ALSO, REFER TO THE ANTIBIOGRAM TOOLKIT PROVIDED BY THE HEALTHCARE-ASSOCIATED INFECTIONS PROGRAM ON THIS WEBSITE]
The Clinical Microbiologist: ASPs New Best Friend

- Microbiologists are an essential team member of the antibiotic stewardship team
- Incorporate antibiogram data into point of decision antibiotic prescribing
- Create real-time alerts of key pathogens
  - Resistant Gram-negative bacteria [(e.g., extended spectrum B-lactamase (ESBL)+, carbapenem resistant Enterobacteriaceae (CRE)], daptomycin-nonsusceptible MRSA, INH-resistant or MDR-TB, fluconazole-resistant *Candida albicans*
- Collaborate in the selection of testing panels aligned with the antibiotic formulary
- Add notes to culture reports when appropriate
  - Explanation of susceptibility reports for ESBLs and KPCs
  - Suggestions of when to consult the ID service
- Education of prescribers when specimens are not appropriate for culture
  - Saliva (vs sputum), urine specimens with low bacterial counts on microscopy, skin swabs (vs deep tissue, curettage, sterile sites)
- Facilitate saving isolates for additional testing and research
  - Unusual resistance patterns or rare pathogens
  - Molecular analyses
Example of Selective Reporting on Culture and Sensitivity Result

<table>
<thead>
<tr>
<th>GNB Susceptibility Card Results</th>
<th>Susceptibility Interpretation</th>
<th>What You Report (if urine culture)</th>
<th>What You Report (if blood culture)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aztreonam</td>
<td>S</td>
<td>X</td>
<td>X(^a)</td>
</tr>
<tr>
<td>Cefepime</td>
<td>S</td>
<td>X(^b)</td>
<td>X(^c)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>S</td>
<td>X(^b)</td>
<td>X(^c)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>S</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pip/tazobactam</td>
<td>S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>S</td>
<td>X(^d,e)</td>
<td></td>
</tr>
</tbody>
</table>

Footnotes:

a. Report “only use if severe allergy to penicillin is documented”

b. Institution’s drug dosing guidelines may suggest lower dose, e.g., cefepime 1gm IV Q12H, or ciprofloxacin 250mg PO/200 IV Q12H to 500mg PO/400mg IV Q12H, x 5 days

c. For more serious infections, pathology note may suggest cefepime 1gm IV Q6H or 2gm IV Q8H, or ciprofloxacin 400mg IV Q8H if normal renal function

d. Note may suggest combination with an anti-pseudomonal beta-lactam

e. Serum peak/MIC ratio is generally optimal for tobramycin, e.g., Cpmax/MIC > 8 even if isolate is S to gent and tobra

Example above assumes the institution does not stock ceftazidime or levofloxacin although these agents may be part of the testing card; monomicrobial infection; nitrofurantoin not represented in this example
Effect of Antimicrobial Stewardship on Resistance is Difficult to Evaluate

- Changes in resistance observed from sequential antibiogram data cannot be easily linked to effects of antimicrobial stewardship on prescribing
- Antibiograms are generally inadequately designed to reflect changes in resistance patterns as a result of changes in hospital antibiotic use
  - Antibiograms include data on bacterial isolates from patients with infections, but also include those that represent colonization
  - Antibiogram reporting policies (i.e., duplicate reporting) may change making analyses over time difficult
  - Bacterial isolates in hospitalized patients may represent community-onset infections (cultures obtained in ED or <48 hours following admission) or may reflect antibiotic exposures at other facilities or as an outpatient (“importation” of resistance)
  - Hospital-wide antibiograms may be less useful for areas with higher prevalence of drug resistance (e.g., ICU)
  - Antibiograms do not accurately assess specific interventions at a specific time period
  - Antibiograms cannot detect emergence of MDRO phenotypes
- Antibiograms include “first isolate” whose susceptibility may not reflect previous antibiotic exposure; tracking “last isolate” may better reflect the impact of antibiotics

Effect of Antimicrobial Stewardship on Resistance is Difficult to Evaluate (cont’d)

- Resistance has two dimensions: population-based and patient-specific (ASP interventions may affect the latter without showing a change in the former)
  - Antibiograms pool the same isolates obtained from the entire hospital population
  - Antibiograms may fail to study patient-specific groups, such as pediatric cystic fibrosis, neuro ICU vs surgical ICU, *Pseudomonas aeruginosa* from respiratory isolates versus urinary tract isolates, etc.
  - Beneficial effects of an ASP in facilitating appropriate antimicrobial use may be diluted by the larger population inclusive in an antibiogram
- The existing literature has several limitations
  - Most studies are quasi-experimental and study short pre-/post-intervention periods
  - Studies on hospital-onset *C. difficile* rates may not account for the influence of other factors, such as improved environmental cleaning or change in isolation policies
  - Interrupted time-series analysis can help demonstrate the effectiveness of an ASP in reducing resistance, but this tool is complex and requires a large amount of data; yet it has the best chance to provide findings which support a favorable impact of ASP interventions on bacterial resistance

Antimicrobial resistance is multifactorial; antimicrobial exposure is only one of many possible reasons for the emergence or spread of drug-resistant organisms

Does Antibiotic Switching Result in Decreased Resistance?

- Two-year study to examine the effect of restricting cephalosporins to control an ESBL-producing *Klebsiella* outbreak
- Cephalosporins were allowed only for surgical prophylaxis, bacterial meningitis, spontaneous bacterial peritonitis, and gonococcal disease
- Results:
  - “Squeezing the balloon” should be avoided; essentially trading one antibiotic resistance problem for another
  - There is insufficient data to recommend antibiotic switching or cycling to decrease drug resistance per IDSA/SHEA guidelines

<table>
<thead>
<tr>
<th>The Good News</th>
<th>The Bad News</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% reduction in cephalosporin use</td>
<td>141% increase in imipenem use</td>
</tr>
<tr>
<td>44% reduction in ceftazidime-resistant <em>Klebsiella pneumoniae</em></td>
<td>69% increase in imipenem-resistant <em>Pseudomonas aeruginosa</em></td>
</tr>
</tbody>
</table>

- Modeling of resistance transmission suggests diversity of antibiotics have the greatest potential to decrease resistance

Example: The Effect of an Antimicrobial Formulary Change on Hospital Resistance Patterns

- Reduce the use of ceftazidime and cefotaxime and replace with cefepime
- Two 6-month periods before and after the formulary change
- 5 selected MDRO phenotypes were studied
- Results between two 6-month periods:
  - Ceftazidime use decreased from 9600 grams to 99 grams; cefotaxime use decreased from 6314 grams to 732 grams (combined decrease 89%)
  - Cefepime increased from 0 gram to 5396 grams (64% decrease over combined use of other 2 cephalosporins)
  - Infections due to ceftazidime-R *K.pneumoniae* decreased from 13% to 3%, piperacillin-R *P.aeruginosa* decreased from 22% to 14%, and ceftazidime-R *P.aeruginosa* decreased from 25% to 15% (p < 0.05 for all)
  - Infections from MRSA dropped insignificantly and VRE infections increased significantly

Rapid Diagnostic Testing and Antimicrobial Stewardship: The Advantage of Early Knowledge

- Time required for bacterial identification and susceptibility testing have critical impact on guiding therapy, and coupled with timely communication, can result in increased appropriateness of therapy

- Several commercial assays are available for the rapid identification of *Staphylococcus* species, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Clostridium difficile*, and *Candida* species

- Detection times are measured in hours, typically 1-2 hours
  - Using traditional techniques, the average time required for a microbiology laboratory to deliver antimicrobial susceptibility testing results to a clinician is 40 hours

- Commercial methods include PNA-FISH, PCR, MALDI-TOF, and rapid antigen detection

1 Goff D, Jankowski D, Tenover F. Pharmacotherapy. 2012;32(8):677-87
Rapid Diagnostic Testing Integrated into ASPs May Deliver Favorable Outcomes

- Rapid differentiation of *S. aureus* and coagulase-negative staphylococci in positive blood cultures
  - PNA-FISH vs traditional methods: reduction in median length of stay from 6 to 4 days (p<0.05), a trend toward less vancomycin use from 6.78 DDD to 4.9 DDD in patients not in the ICU, and a decrease in hospital costs of $4005/patient
  - Rapid PCR vs historical control: a 1.7-day decrease in time to optimal antimicrobial therapy for MSSA bacteremia (p=0.002), a decrease in length of stay of 6.2 days (p=0.07), and a decrease in mean hospital cost by $21,387/episode of S. aureus bacteremia (p=0.02) when an infectious disease
- PNA-FISH, *C. albicans* versus non-albicans *Candida* in fungemia
  - Savings of $1,837/patient treated, mostly with decreased caspofungin use

Example: An ASP’s Impact with Polymerase Chain Reaction MRSA/S. aureus Blood Culture Test

- Evaluated clinical and economic outcomes of a rapid polymerase chain reaction (rPCR) methicillin-resistant S. aureus/S. aureus blood culture test
- Single-center (pre-rPCR vs post-rPCR) study compared inpatients with S. aureus bacteremia
- An ID pharmacist was contacted with results of the rPCR; effective antibiotics and an infectious diseases consult were recommended
- Clinical and economic outcomes in 156 patients:
  - Mean time to switch from empiric vancomycin to cefazolin or nafcillin in patients with MSSA bacteremia was 1.7 days shorter post-rPCR (P=0.002); and mean time to switch from vancomycin to daptomycin in patients with MRSA bacteremia was 5.5 days shorter post-rPCR (P=0.15)
  - Mean time to ID consult decreased (9 days pre-rPCR to 3 days post-rPCR; P=0.25)
  - In the post-rPCR MSSA and MRSA groups, the mean LOS was 6.2 days shorter (21.5 to 15.3 days; P=0.07)
  - The total mean hospital costs were $21,387 less ($69,737 to $48,350; P=0.02)
  - Mean ICU costs decreased by $9,930 (P=0.03)
  - Mean pharmacy costs were decreased by $2,918 (p=0.08)

Example: Polymerase Chain Reaction (PCR) Used in an ASP Intervention for Coagulase-Negative Staphylococci

- Evaluate the impact of interventions by an ASP team on the duration of anti-staphylococcal antibiotic therapy, hospital LOS, and related costs
- Quasi-experimental pre- and post-intervention study (53 inpatients; 31 pre-intervention and 22 post-intervention) in patients with positive blood cultures for coagulase-negative staphylococci (CoNS) identified by PCR
- Intervention made when blood culture result was determined to be a contaminant
- Excluded patients <18yo or >89yo, neutropenia, incomplete records, and duplicate or mixed blood cultures
- Results (pre- vs post-intervention periods):
  - Antistaphylococcal antibiotics discontinued 32 hrs sooner from time of PCR (median 57.7 vs 25.7 hrs; p=0.005)
  - Total antibiotic exposure decreased 43.5 hrs (97.6 vs 54.1 hrs; p=0.011)
  - Infection-related LOS decreased 4.5 days (10 vs 5.5 days; p=0.018)
  - Infection-related costs decreased $8338 ($28,973 vs $20,635; p=0.144)
  - The pharmacist initiated vancomycin in 7 (21.9%) patients with CoNS bloodstream infections

Even Newer Technologies Being Analyzed For Opportunities in ASPs

• Matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI-TOF MS) uses a new technology to identify bacteria and yeast from agar plate colonies
  • The time from putting the target plate into the instrument to final result is fast, within a few minutes.

• Matrix-assisted laser desorption and ionization time-of-flight mass spectrometry (MALDI-TOF MS) coupled with ASP and rapid antimicrobial susceptibility testing.
  • The mean hospital length of stay in the preintervention group survivors (n=100) was 11.9 versus 9.3 days in the intervention group (n=101; P=0.01).
  • Mean hospital costs per patient were $45,709 in the preintervention group and $26,162 in the intervention group (P=0.009).

Is It Time for Procalcitonin (PCT) – A Biomarker of Systemic Inflammation Used in Diagnosing Bacterial Infections?

• Schuetz et al concluded in a review that inclusion of PCT data in clinical algorithms improves individualized decision-making regarding use of antibiotics in patients in critical care for respiratory tract infections and sepsis¹

• A recent report from AHRQ stated that procalcitonin guidance reduces antibiotic use when used to discontinue antibiotics in adult ICU patients and to initiate or discontinue antibiotics in patients with respiratory tract infections²
  • Future research should compare procalcitonin guidance with antibiotic stewardship programs and to implementation of guidelines
  • Outcomes of high interest for future research are the consequences of reduction in antibiotic use for antibiotic resistance and for adverse events of antibiotic therapy.

• A meta-analysis by Li et al concluded that PCT-guided antibiotic therapy in patients with respiratory tract infections appears to reduce antibiotic use without affecting overall mortality or length of stay in the hospital³

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Summary: Value Your Microbiologists

- The clinical microbiology laboratory plays a critical role in the timely identification of microbial pathogens, performance of susceptibility testing, identification and molecular epidemiologic investigation of local outbreaks of infection, and resistance surveillance
  - These roles are in flux: changing breakpoints in Gram-negative bacteria, advances in molecular diagnostics and rapid testing, improved computer surveillance, and use of biomarkers to potentially avoid the need for extended courses of broad-spectrum empirical therapy
- The ASP includes the clinical microbiologist as an integral member of the AST to assist in the prudent use of antimicrobials and direct appropriate therapy based on local guidelines
  - Development and publication of the antibiogram
  - Prioritization of tested antimicrobials
  - Selective reporting of susceptibility profiles (e.g., not routinely reporting susceptibility of *S. aureus* to rifampin to prevent inadvertent monotherapy with rifampin)
  - Clonal characterization of resistant and outbreak strains (resistant strains which are diverse may be approached with antimicrobial interventions)

Dellit T et al. Clin Infect Dis. 2007;44:159-77
ADDITIONAL SLIDES
## Comparative Susceptibility Reporting Tracks Resistance in the U.S. and Globally

<table>
<thead>
<tr>
<th>Surveillance Study</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABC</strong></td>
<td>Annual susceptibility data for Group A/B streptococci, MRSA, <em>N.meningitidis</em>, <em>S.pneumoniae</em>, <em>H.influenzae</em></td>
</tr>
<tr>
<td><strong>Aware</strong></td>
<td>Ceftaroline global susceptibilities for Gram-positive and Gram-negative pathogens encountered in pneumonia</td>
</tr>
<tr>
<td><strong>EARSS</strong></td>
<td>Participation by dozens of countries in Europe; hospital and community</td>
</tr>
<tr>
<td><strong>MYSTIC and OPTAMA (PK-PD)</strong></td>
<td>Many publications</td>
</tr>
<tr>
<td><strong>SENTRY</strong></td>
<td>Global reports</td>
</tr>
<tr>
<td><strong>TEST</strong></td>
<td>Studies in staphylococci, Gram-negatives, and anaerobes</td>
</tr>
<tr>
<td><strong>TRUST</strong></td>
<td>Originally <em>S.pneumoniae</em> susceptibilities; included gram-negatives later; not many publications</td>
</tr>
<tr>
<td><strong>ZAAPS and LEADER (USA)</strong></td>
<td>Linezolid susceptibilities against large collections of Gram-positive pathogens</td>
</tr>
</tbody>
</table>

- Large national or global susceptibility testing programs provide insight into methodologies, resistance patterns by site of infection, and MIC distributions (in relation to breakpoints)
- May provide comparative data, MIC distributions (generally, not in Vitek/MicroScan), novel resistance mechanisms
- Sponsors are generally committed to report annual surveillance data for 5 years following FDA approval; many continue past this according to commercial interests
“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

A Note To Our Readers and Slide Presenters

The objectives of the Subcommittee on Antimicrobial Stewardship Programs are directed at education, presentation, and identification of resources for clinicians to create toolkits of strategies that will assist clinicians with understanding, implementing, measuring, and maintaining antimicrobial stewardship programs.

The slide compendium was developed by the Subcommittee on Antimicrobial Stewardship Programs (ASP) of the Arizona Healthcare-Associated Infection (HAI) Advisory Committee in 2012-2013.

ASP is a multidisciplinary committee representing various healthcare disciplines working to define and provide guidance for establishing and maintaining an antimicrobial stewardship programs within acute care and long-term care institutions and in the community.

Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.
Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

ADHS routinely seeks the input of highly qualified peer reviewers on the propriety, accuracy, completeness, and quality (including objectivity, utility, and integrity) of its materials. Although the specific application of peer review throughout the scientific process may vary, the overall goal is to obtain an objective evaluation of scientific information from its fellow scientists, consultants, and Committees.

Please credit ADHS for development of its slides and other tools. Please provide a link to the ADHS website when these material are used.
**Introduction to Slide Section**

- **Preface:**
  Developing a schedule for ASP projects depends strongly on the needs of the institution. However, this needs to be balanced against those projects which are simpler ("low-hanging fruit") versus more difficult projects ("high-hanging fruit") which require a greater knowledge of data collection capabilities and data analysis. The latter should be considered once the ASP is well-established and has tackled issues such as IV-to-PO sequential therapy.

- **Content:**
  37 slides with 2 additional slides.

- **Suggestions for Presentation:**
  Identification of projects requires significant time to discuss with the ASP committee, physicians, department heads, and pharmacy. The presentation will require at least 1 hour with another hour of discussion. Planning for the first and following years requires evaluation of all potential projects and incorporation of these into a timeline as well as identifying potential clinical and financial outcomes.

- **Comments:**
  These slides are the real “nuts and bolts” which determine daily activities and support of the ASP’s objectives. The slides should be carefully reviewed prior to presentation.

---

<table>
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<th>Reasons to Optimize Antibiotic Use</th>
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<tbody>
<tr>
<td>Pathways to a Successful ASP</td>
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<td>Antimicrobial Stewardship: Making the Case</td>
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<td>ASPs: Nuts &amp; Bolts</td>
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<td>Antimicrobial Stewardship: Measuring</td>
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<td>Antimicrobial Stewardship: Computerized &amp; Clinical Decision Support Services</td>
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<td>Microbiology: Cumulative Antibiogram &amp; Rapid Diagnostics</td>
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<td>Antimicrobial Stewardship Projects: Initiation &amp; Advanced</td>
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<td>Antimicrobial Stewardship Barriers &amp; Challenges: Structural &amp; Functional</td>
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<td>Antibiotic Use in the Community</td>
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<td>Opportunities to Justify Continuing the ASP</td>
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<td>Antimicrobial Stewardship: Perspectives to Consider</td>
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<tr>
<td>Summary</td>
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</tbody>
</table>
ANTIMICROBIAL STEWARDSHIP PROJECTS: INITIATION AND ADVANCED
Identify Areas for Improvement: Baseline Data Collection Examples

- What is the prevalence of inappropriate antibiotic use? Examples:
  - Treatment of asymptomatic bacteriuria
  - Dual anaerobe therapy, such as metronidazole prescribed with piperacillin/tazobactam, ampicillin/sulbactam, or carbapenems
  - Broad spectrum antibiotics for infections due to organisms with effective narrower spectrum agents per susceptibility report
- What is the lag time between culture & sensitivity results and effective antibiotic therapy?
- How often are positive blood cultures not covered with appropriate agents in timely manner?
- For patients who are converted to PO antibiotics, what % are converted back to IV?
- Do you have data on % patients who receive antibiotics for > 3days?
- Does the antibiogram eliminate duplicate agents?
- What is the frequency of prescribers stating an antibiotic plan in the chart?
- What is the prescriptive compliance for institutional guidelines regarding use of broad-spectrum antibiotics?
- What is the frequency of non-compliance with TJC/CMS core measures for CAP treatment?
Identify Areas for Improvement: Possible Projects

- IV-to-PO switch - the most basic stewardship function
- Ensure all antibiotic orders carry an indication
- Improve SCIP performance measures
- Reassess all antibiotic therapies at 72 hours
- There is a daily antibiotic plan, or recognition of current antibiotics
- Improve empiric antibiotic therapy in the ICU patient
  - Early appropriate therapy decreases ICU LOS, costs, and mortality
  - Develop the “ICU antibiogram” or even a “VAP antibiogram”
  - Conduct a retrospective audit on appropriate empiric (<72 hours) therapy
- “Bug-drug mismatch” – get the daily culture report
- Asymptomatic bacteriuria – discourage antibiotic use; educate clinicians
- Sepsis campaign – get cultures before antibiotics are administered if possible
- Check daily blood culture reports for significant pathogen not treated or potential contamination
  - If contamination is highly suspected work towards discontinuation of antibiotics
Educational Opportunities

• Pharmacy staff
  • Scheduled inservices to reinforce antibiotic use guidelines within the institution (and why!)
  • Includes beta-lactam selection, when to use fluoroquinolones, criteria for IV-to-PO transition therapy, MRSA treatment options, empiric versus targeted therapy, and disease-based reviews (e.g., CAP vs HCAP, candidemia)

• Prescriber education
  • Goal is to maintain collegial relationship while quietly changing prescribing patterns
  • Educational seminars, daily rounds, conferences
  • Develop a toolbook with prescriber input
  • Face-to-face interactions with single prescribers
  • Don’t forget NPs and PAs
Educational Opportunities (cont’d)

• Nursing
  • Appropriate reasons for cultures (e.g. urine cultures in patients with catheters, no chronic wound swabs)

• Microbiology
  • Antibiogram templates which may improve prescriber education
  • Consider combined ID-microbiology rounds (works well in academic centers with ID fellows)
  • Feedback on patient outcomes related to reporting susceptibilities and rapid testing diagnostics

• Infection prevention
  • Relate epidemiology and patient tracking with antimicrobial prescribing
  • Turnaround time between prescriber alerts (issued by laboratory) and isolation (if appropriate) and therapy – work with laboratory and computer systems
Example: Providing Usage Feedback to Prescribers is Education to Improve Antimicrobial Use

- 110-bed VA facility
- 2,807 antibiotic courses evaluated for compliance with institutional guidelines
- Compared to historical controls (prior to ASP audit and feedback)
- ASP recommendations were made direct-to-prescriber in several categories:
  - Unjustified use of an antimicrobial
  - Inappropriate dose
  - Availability of a more effective drug
  - Availability of a less toxic drug
  - Availability of a drug with narrower spectrum
  - Switch from IV to PO therapy
  - Duration of therapy can be shortened
- Audits were performed with feedback and consisted of the following:
  - Weekly reports on compliance with guidelines and ASP recommendation acceptance (internal medicine, surgery)
  - Quarterly department-specific reports (department heads, P&T, infection control, CQI)
  - Monthly reports on ID topics

Framework for Studying Disease States: Looking for Improvements in Outcomes

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Application to Skin and Soft Tissue Infection</th>
</tr>
</thead>
</table>
| Baseline assessment                               | • Retrospective audit of specific SSTI (cellulitis, surgical site infection, abscess, etc)  
|                                                   | • What needs improvement – meet with IDs       |
| Identify specific and measurable outcomes         | • What information needs to be collected?      
|                                                   | • Resources – IT, pharmacy computer, CDSS      |
| Involve key stakeholders                          | • Internal med, hospitalist, ED, ID, CMO, surgery |
| Design the intervention with team input           | • Current state of practice versus what needs to be achieved  
|                                                   | • How to get there with the intervention       |
| Implement a new multi-faceted approach to disease state | • Guideline development and presentation to P&T  
|                                                   | • Education of stakeholders and department heads |
| Evaluate interim results, such as safety and effectiveness of new approach | • Prospective; collect data over shorter period  
|                                                   | • Interim study post-intervention – what has been achieved  
|                                                   | • Reports                                      |
| Modify the intervention as needed                 | • Revise guidelines, as needed                 
|                                                   | • P&T, re-educate; highlight changes           |
Don’t Forget Stewardship Opportunities with Treatment of Fungal Infections

- Formulary echinocandin choice; therapeutic interchange opportunities
- IV-to-PO conversion of fluconazole
- IV-to-PO conversion of voriconazole
- Ensure acidic gastric environment for absorption of some agents
- Switch to fluconazole from other anti-fungals for *Candida albicans*, as appropriate
  - Identification of *C.albicans*
  - Rapid identification, e.g., PNA-FSH
- Susceptibilities of *C.albicans* and selected non-albicans *Candida spp*
- Comprehensive care bundle on the management of candidemia
  - Compliance with candidemia care bundle was significantly higher in the AST group versus the control group (78.0% vs 40.5%, p=0.0016); significantly improved rates of ophthalmologic examination (97.6% vs 75.7%, p=0.0108), selection of appropriate antifungal therapy (100% vs 86.5%, p=0.0488), and compliance with appropriate therapy duration (97.6% vs 67.7%, p=0.0012)\(^1\)
- Therapeutic drug monitoring, i.e., voriconazole and posaconazole, due to PK variability, variable absorption (food and gastric pH effects)

ANTIMICROBIAL STEWARDSHIP PROJECTS: LOW-HANGING FRUIT
Drug Optimization Program: IV-to-PO and Dosing

- All patients who receive targeted IV and PO antibiotics are monitored for opportunities to change the route or dose depending upon the clinical picture.
- Optimization can be protocol-driven but requires sound clinical judgment.
- Monitoring patient responses avoids the single observation point in time.
  - How many patients converted from IV to PO agent are changed back to the IV antibiotic within 72 hours? (Report these results with outcomes analysis).
- Correction of under-dosed regimens (as important as over-dosed regimens).
  - Do patients need increased dosing? Example: MSSA bacteremia in a patient on nafcillin 2 grams IV Q8H.
- Pharmacodynamic modeling considers site of infection, pathogen-specific MIC, and looks for opportunity to employ prolonged/extended infusions.
  - Loading doses in obesity and high volume of distribution.
  - Rapid clearance due to sepsis.
  - Dosing in special disease states: CHF, cystic fibrosis, cirrhosis, burn patients.
- Renal dose adjustments of renally-cleared antimicrobials.
Example: IV-to-PO Conversion Form and Criteria

IV to PO Conversion Order Form/Worksheet

Height: __________  Weight: __________

Allergies: _____________________________

(Date/Time: __________)

Pharmacy recommends:

D/C (enter drug, dose, and route)

Start (enter drug, dose, and route)

This change will take place on ______ at ______

Pharmacist’s signature:

______________________________

Criteria for Conversion to PO:

___ Tolerating other drugs by oral route

___ Being fed enterally (at minimum a clear liquid diet), i.e. a functioning GIT

___ Patient does NOT have persistent N/V, ileus, gastric outlet obstruction, active GI bleed, loss of consciousness, NPO orders that applies to all meds

If an antibiotic: (in addition to above)

___ Resolution of fever for 24 hours

___ CBC improving, preferably < 15K in absence of steroids

___ Patient does NOT have meningitis, endocarditis, septicemia, neutropenia, osteomyelitis, or MRSA

___ Hemodynamically stable
Example: Package Labeling, RN Education, and Timing of Administration

- Co-administration of an oral fluoroquinolone with divalent/trivalent cation-containing (DTCC) compounds inhibits fluoroquinolone (FQ) absorption
- Case-control study with 46 inpatients (receiving an oral FQ and a DTCC within 2 hours)
- Patients with a resistant isolate had been exposed to nearly twice as many days of fluoroquinolone-DTCCs co-administration (P=0.04).
- Efforts should be directed at modifying hospital policies for dosing oral fluoroquinolones and DTCCs to prevent co-administration

Example: A Simple Community-Acquired Pneumonia (CAP) Audit

- 17 agents used to treat 176 unique episodes of CAP
- 96 patients received 3 or more antibiotics
- Included several cases of use of piperacillin-tazobactam, cefotetan, fluconazole, and carbapenems for at least 3 days
- 21 cases were treated with cefazolin (no patient had concomitant SSTIs)
- No positive culture results for *Pseudomonas aeruginosa*
- All but 5 patients had at least one blood culture performed within 24 hours of admission

Potential questions to optimize treatment of CAP:
- Number and costs of antibiotics consistent with core measures and IDSA guidelines?
- What are drug and total costs associated with these admissions?
- What was the range, mean, and median length of stay for these patients?

Business model calculations:
- Cost differences between audited antibiotics versus compliance with guidelines?
- What cost-savings for appropriate blood cultures and decreased LOS by 1 day?
- If ADRs to inappropriate antibiotics, could these have been prevented?

Adapted from: MUE/DUE CAP, 1995; courtesy Mark Redell
Perioperative Antibiotic Prophylaxis: Interventions and SCIP 2013

- Goals
  - Minimize surgical site infection (SSI) rates
  - Decrease variability
  - Compliance with SCIP measures
  - Follow national guidelines and best practices
  - Consider local epidemiology
- Surgical Care Improvement Project (SCIP) ¹
  - SCIP-Inf-1: Prophylactic antibiotic received within 1 hr prior to surgical incision (2 hrs for vancomycin)
  - SCIP-Inf-2: Prophylactic antibiotic selection for surgical patients according to procedure type
  - SCIP-Inf-3: Prophylactic antibiotics discontinued within 24 hours after surgery end time (48 hours for cardiac)
- Opportunities for antibiotic stewardship include education on recently published guidelines²; changes from previous recommendations

1 SCIP guidelines are available at: http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures.aspx
Examples of ASP Projects Involving SCIP Measures

<table>
<thead>
<tr>
<th>Project Addressing Specific Performance</th>
<th>Reason to Optimize Performance</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug selection/dosing</td>
<td>• Decrease SSI rate</td>
<td>• Order forms</td>
</tr>
<tr>
<td>• Based on type surgical procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Weight-adjusted dosing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>• Lack of evidence to show durations &gt; 24-48 hours decreases SSI</td>
<td>• Order forms with automatic stop orders</td>
</tr>
<tr>
<td>• &lt; 24 hours for most procedures</td>
<td>• Emergence /selection of resistance</td>
<td></td>
</tr>
<tr>
<td>• Historical acceptance for 48 hours in CV surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>• Compliance with guidelines; regulatory</td>
<td>• Post OR guidelines, SCIP measures</td>
</tr>
<tr>
<td>• Written material</td>
<td></td>
<td>• Outpatient surgery antibiotic prophylaxis order form</td>
</tr>
<tr>
<td>• Inservices to nursing, anesthesiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special circumstances</td>
<td>• Increased SSI rate</td>
<td>• Audible and visual automated reminder systems</td>
</tr>
<tr>
<td>• Re-dosing for prolonged procedures</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ANTIMICROBIAL STEWARDSHIP PROJECTS:
HIGH-HANGING FRUIT AND TAKING YOUR PROGRAM TO THE NEXT LEVEL
Examples of Higher-hanging Fruit: Optimizing Antibiotic Selection

- In suspected or proven HCAP, vancomycin was discontinued in 88 of 91 patients with negative nasal and throat swabs for MRSA when adequate lower respiratory tract cultures were not available and clinical pulmonary infection scores were <6\(^1\)

- Large urban multi-campus academic medical center addressed appropriate antibiotic selection in the ED (2008 to 2011; quasi-experimental before-after study)\(^2\)
  - Interventions: algorithm for antibiotic selection, “CAP Kit”, and pre-loading an automated ED medication dispensing and management system
  - Appropriate antibiotic selection increased from 55% to 65% to >90% in 2 Eds (P=0.004)

---

Optimizing Patient Outcomes in Ventilator-associated pneumonia (VAP): Use of a Clinical Pathway to Improve Empiric Antibiotic Therapy

- Appropriate antibiotic therapy improved (71.6% vs 48.6%; P=0.007)
- Infection-related mortality was reduced by 69% (8.5% vs 21.6%; P=0.029)
- Mean infection-related length-of-stay decreased (11.7 ± 8.1 vs 26.1 ± 18.5; P<0.001)
- Fewer superinfections overall and by MDR pathogens
- A number of patients with nonsusceptible *P. aeruginosa* were successfully treated

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Historical control group (n=73)</th>
<th>Clinical pathway group (n=93)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>COST VAP ($)</td>
<td>Mean ± SD 95,150 ± 84,260</td>
<td>44,435 ± 29,995</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) 75,698 (38,449 – 137,922)</td>
<td>35,841 (22,288 – 56,351)</td>
<td></td>
</tr>
<tr>
<td>COST POSTVAP ($)</td>
<td>Mean ± SD 108,955 ± 88,842</td>
<td>85,730 ± 55,437</td>
<td>0.077</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) 95,479 (47,979 – 156,556)</td>
<td>76,443 (41,640 – 115,010)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Range 11,465 – 635,963</td>
<td>10,334 – 283,332</td>
<td></td>
</tr>
<tr>
<td>Antibiotic cost ($)</td>
<td>Mean ± SD 934 ± 1533</td>
<td>766 ± 755</td>
<td>0.450</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) 482 (222 – 985)</td>
<td>535 (261 – 998)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Range 12 – 10,572</td>
<td>85 – 5,125</td>
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</tbody>
</table>

Stewardship Based on Infection Severity Score: Decreased Antibiotic Duration and Patient-Level Resistance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experimental Group (n=39)</th>
<th>Standard Therapy Group (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic continuation &gt; 3 days</td>
<td>28% (11/39)</td>
<td>97% (38/39)</td>
</tr>
<tr>
<td>Duration of antibiotics, days, mean (range)</td>
<td>3 (3)</td>
<td>9.8 (4-20)</td>
</tr>
<tr>
<td>Total antibiotic costs (mean/pt)</td>
<td>$6,482 ($259)</td>
<td>$16,004 ($640)</td>
</tr>
<tr>
<td>Length of ICU stay, days (mean/median)</td>
<td>9.4 / 4</td>
<td>14.7 / 9</td>
</tr>
<tr>
<td>Antimicrobial resistance and/or superinfections</td>
<td>14% (5/37)</td>
<td>38% (14/37)</td>
</tr>
</tbody>
</table>

Study was terminated early because attending physicians began to treat standard care group with 3 days of therapy

CPIS = clinical pulmonary infection score (temperature, peripheral WBC count, tracheal secretions, oxygenation, progression of pulmonary infiltrate, culture of tracheal aspirate; score >6 is suggestive of pneumonia

De-escalation: Streamlining Therapy to Narrowest Spectrum Agent Based on Culture Results

- **Serious infection suspected**
  - Begin empiric antibiotic treatment with a combination of agents targeting the most likely pathogens based on local data
  - **Pathogen identified?**
    - **Yes**
      - De-escalate antibiotics based on results of clinical microbiology data
      - Significant clinical improvement after 48-96 hours of antibiotic treatment?
        - **Yes**
          - Search for superinfection, abscess formation, noninfectious causes of symptoms, inadequate tissue penetration of antibiotics
        - **No**
          - Continue initial treatment
          - Reassess within appropriate time frame
    - **No**
      - Continue initial treatment
      - Reassess within appropriate time frame
  - **No**
    - Discontinue antibiotics after 7-14 days based on site of infection and clinical response

### Escalation and De-Escalation Patterns in the Treatment of VAP (n=390 patients)

<table>
<thead>
<tr>
<th>Number of Drugs</th>
<th>Increase</th>
<th>No change</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>15</td>
<td>39</td>
</tr>
<tr>
<td><strong>No Net Change</strong></td>
<td>13</td>
<td>242</td>
<td>34</td>
</tr>
<tr>
<td><strong>De-Escalation</strong></td>
<td>12</td>
<td>19</td>
<td>17</td>
</tr>
</tbody>
</table>

- **Spectrum of Activity**
  - Decrease
  - No change
  - Increase

- **De-Escalation** (22%)
- **No Net Change** (67%)
- **Escalation** (11%)

Kollef MH, et al. *CHEST* 2006;129:1210-8
Evaluate Antibiotic Combinations to Reduce Redundant Therapy

- **Rationale**
  - Beyond “getting it right” empiric coverage, lack of evidence for the most part
  - May increase the probability of AEs and/or resistance and increase cost
- **Pharmacist-based intervention at a 600-bed public teaching hospital**
  - Screening of 1,189 inpatients receiving ≥2 antibiotics during a 23-day surveillance via computer-assisted tool
  - 192 episodes with 137 (71%) deemed inappropriate combinations
  - MD errors in prescribing in 77/137 episodes, primarily redundant coverage for gram-positive or anaerobic organisms
  - Changing regimens decreased 584 days of therapy of redundant drug
  - Clinical and microbiologic outcomes with monotherapy were significantly better than with combination and associated with less AEs
  - Cost savings realized despite the cost of a pharmacist
  - No benefit seen in combination therapy for *P aeruginosa* 

Evaluate Antibiotic Therapy at Defined Time Periods for Stewardship Opportunity: Example in the ICU

- Prospective, controlled interrupted time series in a single tertiary care center with 3 intensive care units
- Formal review of all critical care patients on their third or tenth day of broad-spectrum antibiotic therapy was conducted, and suggestions for antimicrobial optimization were communicated to the critical care team

Results

- The mean monthly broad-spectrum antibiotic use decreased from 644 days of therapy per 1,000 patient-days in the pre-intervention period to 503 days of therapy per 1,000 patient-days in the post-intervention period (P<0.0001)
- The incidence of nosocomial C. difficile infections decreased from 11 to 6 cases in the study intensive care units, whereas the incidence increased from 87 to 116 cases in the control wards (P=0.04)
- Overall gram-negative susceptibility to meropenem increased in the critical care units
- ICU length of stay and mortality did not change

Institution of a formal prospective audit and feedback program appears to be a safe and effective means to improve broad-spectrum antimicrobial use in critical care

Severe Sepsis/Septic Shock: The Value of Appropriate Antibiotics

- The survival rates after appropriate and inappropriate initial antimicrobial therapy were 52.0% and 10.3%, respectively (OR, 9.45; 95% CI 7.74 to 11.54, p<0.0001)
- The association remained robust following adjustment for many clinical factors

There was a significant association at the <1 hr time point for mortality with early goal-directed therapy (EGDT) which included appropriate antibiotics

Study provides both a severe sepsis pathway and a severe sepsis antibiogram

Shorter Antibiotic Courses Matter

• Goals of reducing antibiotic durations of therapy\(^1\):
  • Decreased selection of resistant pathogens
  • Decreased *Clostridium difficile* infection
  • Decreased antibiotic-related organ toxicity
  • Decreased hospital costs
  • Improved compliance with outpatient antibiotic regimens
  • Potential earlier removal of an IV catheter

• How were current treatment durations determined?
  • Trial and error
  • Well-defined endpoints, e.g., mortality, persistent bacteremia, recurrence
  • Historical data, often very old, which established early “standards”
  • Limited or absent randomized clinical trials – mostly observational studies, clinical experience, and expert opinion
  • Lack of perceived harm with longer courses

\(^1\) File T. J Hosp Med. 2012 (suppl);7:S22-S33.
Guidelines Support Treatment of Many Infections With Shorter Courses of Therapy: CAP/HAP

- Community-acquired pneumonia (CAP), adults\(^1,2\)
  - Patients with CAP should be treated for a minimum of 5 days, should be afebrile for 48–72 h, and should have no more than 1 CAP-associated sign of clinical instability before discontinuation of therapy
  - Longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was complicated by extrapulmonary infection, such as meningitis or endocarditis
  - In infants and children >3 months of age, while treatment courses of 10 days have been best studied, shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis
- Hospital-acquired, healthcare-associated, and ventilator-associated pneumonia in adults\(^3\)
  - A shorter duration of antibiotic therapy (7 to 8 days) is recommended for patients with uncomplicated HAP, VAP, or HCAP who have received initially appropriate therapy and have had a good clinical response, with no evidence of infection with non-fermenting gram-negative bacilli

Short-Course (SC) versus Extended-Course (EC) Therapy for Mild-to-Moderate CAP

- Systematically review randomized controlled trials comparing SC (≤ 7 days) and EC (> 7 days) antibiotic regimens for mild-to-moderate CAP
  - 15 randomized clinical studies of monotherapy; 2,796 patients
  - 4 drug classes – FQs, beta-lactams, macrolides, ketolides
- Findings:
  - Overall, there was no difference in the risk of clinical failure between the SC and EC regimens (0.89, 95% CI, 0.78-1.02)
  - There were no differences in the risk of mortality (0.81, 95% CI, 0.46-1.43) or bacteriologic eradication (1.11, 95% CI, 0.76-1.62)
  - In subgroup analyses, there was a trend toward favorable clinical efficacy for the SC regimens in all antibiotic classes (range of relative risk, 0.88-0.94)

Duration of Therapy in VAP: 8 Days versus 15 Days

- Largest trial to compare outcomes of appropriate initial antibiotic therapy with short-course (8-day; n=197) versus standard course (15-day; n=204) regimens in a well-defined group of ICU patients with quantitatively-confirmed VAP.
- Outcomes of 8-day versus 15-day, measured 28 days after VAP onset:
  - No excess mortality (18.8% vs 17.2%; 90% CI -3.7% to + 6.9%)
  - No increase in recurrent infections (28.9% vs 26.0%, 90% CI -3.2 to +9.1%)
  - On day 60, no difference in mechanical ventilation-free days, organ failure-free days, length of ICU stay, or mortality rates
  - Higher pulmonary infection-recurrence rate in 8-day group (40.6% vs 25.4%, 90% CI 3.9% - 26.6%) for gram-negative non-fermenting bacilli
  - MDR pathogens emerged less frequently in the 8-day group patients who had recurrent infection (42.1% vs 62.0%; p=0.04)

If the patient responds rapidly, and the isolated pathogen is susceptible to the initial regimen, therapy may be halted early (7-10 days)

Chastre J et al. JAMA 2003;290:2588-98
Guidelines Support Treatment of Many Infections With Shorter Courses of Therapy: UTIs

• Diagnosis and treatment of asymptomatic bacteriuria in adults\(^1\)
  • Treat with appropriate antimicrobials: pregnancy (x3-7d); prior to TURP or other urologic procedures associated with bleeding; asymptomatic women with catheter-associated bacteriuria that persists 48hrs after indwelling catheter removal (optional); possibly other conditions, such as neutropenia and post-renal transplant

• Antimicrobial treatment of acute uncomplicated cystitis and pyelonephritis in women\(^2\)
  • Uncomplicated cystitis: nitrofurantoin (100mg BID) x 5d; TMP/SMX (1DS BID) x 3d; fosfomycin (3gm once); or FQ x 3d; beta-lactams x 7d
  • Pyelonephritis: ciprofloxacin (500mg BID or 1gm ER QD) x 7d; aminoglycoside (preceded by optional ceftriaxone 1gm IV/IM x 1) x 7d total; TMP/SMX (1 DS BID) x 14d; or levofloxacin (750mg QD) x 5d


TMP/SMX = trimethoprim/sulfamethoxazole; DS = double-strength tab, 160mg/800mg; FQ = fluoroquinolone
Guidelines Support Treatment of Many Infections With Shorter Courses of Therapy: UTIs (cont’d)

• Diagnosis, prevention, and treatment of catheter-associated UTIs in adults¹
  • Provides recommendations when not to use antimicrobials, such as prophylaxis
  • Treatment x 7d for patients with CA-UTI who have prompt resolution of symptoms, and 10-14d of treatment for those with a delayed response, regardless of whether the patient remains catheterized or not; levofloxacin x 5d may be considered in patients with CA-UTI who are not severely ill
  • A 3d antimicrobial regimen may be considered for women ≤65 yrs who develop CA-UTI without upper urinary tract symptoms after an indwelling catheter has been removed

Guidelines Support Treatment of Many Infections With Shorter Courses of Therapy: IAIs

- Complicated intra-abdominal infections (IAIs) in adults
  - Antimicrobial therapy of established infection should be limited to 4–7 days, unless it is difficult to achieve adequate source control
  - For acute stomach and proximal jejunum perforations, in the absence of acid-reducing therapy or malignancy and when source control is achieved within 24 h, prophylactic antibiotic therapy directed at aerobic gram-positive cocci for 24h is adequate
  - Bowel injuries attributable to penetrating, blunt, or iatrogenic trauma that are repaired within 12 h and any other intraoperative contamination of the operative field by enteric contents should be treated with antibiotics for 24h
  - Acute appendicitis without evidence of perforation, abscess, or local peritonitis requires only prophylactic administration of narrow spectrum regimens active against aerobic and facultative and obligate anaerobes; treatment should be discontinued within 24 h
  - The administration of prophylactic antibiotics to patients with severe necrotizing pancreatitis prior to the diagnosis of infection is not recommended
- Additional comment on pharmacokinetic considerations
  - Empiric therapy of patients with complicated intra-abdominal infection requires the use of antibiotics at optimal doses to ensure maximum efficacy and minimal toxicity and to reduce antimicrobial resistance

Skin and Soft-Tissue Infections Requiring Hospitalization: Opportunities for Antibiotic Stewardship

- Single institution academic medical center; 322 consecutive adult patients hospitalized during 2007
- Cellulitis, 20%; cutaneous abscess, 32%; SSTI with complicating factors, 48%
- Culture-positive results in 150 patients
  - 145 (97%) were *S. aureus* or streptococci
- Antibiotic selection and duration was excessive in culture-positive infections
  - Broad aerobic gram-negative activity, 61% - 80%
  - Anaerobic activity, 73% - 83%
  - Only one-third of patients received therapy targeted only at gram-positive organisms
  - Median duration of therapy was 13-14 days amongst 3 infection types
- Guideline implemented in 2009 led to several improvements:
  - Microbiologic cultures decreased 80%
  - Median duration of therapy decreased from 13 days to 10 days
  - Decrease in use of broad aerobic gram-negative antibiotics (66% to 36%; P<0.001), antipseudomonal antibiotics (28% to 18%; P=0.02), or broad anaerobic activity (76% to 49%; P<0.001)

Optimizing Antibiotic Dosing Using Pharmacokinetic (PK) and Pharmacodynamic (PD) Principles

- FDA recommendations for antibiotic dosing in renal dysfunction are based on achieving similar AUC based on otherwise normal healthy volunteers of normal weight
  - Usually unpublished data ("on file")
  - AUCs may not be an appropriate pharmacodynamic target
  - Since CrCL ranges can vary by 2- to 3-fold, beware of cutting doses in half
- FDA dosing recommendations are based on Cockcroft-Gault estimations (not on calculation of eGFR/MDRD) and use actual serum creatinine values
- Most FDA dosing recommendations are inaccurate in certain patient populations (obesity, low body weight, fluid overload, sepsis)
- Pharmacodynamics, as studied in hospitalized patients with infections, along with consideration of MICs, provides more accurate information on dosing antimicrobials
  - Once-daily dosing aminoglycosides
  - Prolonged infusion of short half-life (≤ 2 hrs) beta-lactams
Pharmacodynamic Properties of Beta-Lactams That May Influence Clinical Success

- For beta-lactams, time free drug concentration is above MIC (fT>MIC) is the key pharmacodynamic variable
- Antimicrobial effect is estimated using % of dosing interval in which the free drug serum concentration exceeds the MIC (%fT > MIC)

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Stasis end point</th>
<th>Max kill end point*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbapenems</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Penicillins</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>40</td>
<td>60 - 70</td>
</tr>
</tbody>
</table>

*Generally considered a 3-log reduction in colony forming units.

Drusano GL. Clin Infect Dis. 2003;36 (suppl 1):S42-50
Prolonged Infusions of Beta-Lactams with Short Half-Lives Optimize PK-PD

- Dose escalation either by administering higher doses (or administering a dose more frequently; data not shown) achieves only small increments in efficacy because there is little increase in the time during which the drug concentration exceeds the MIC (fT>MIC)

- An extended infusion time for a carbapenem increases the time the drug concentration exceeds the MIC compared with a shorter infusion time

Optimizing Clinical Outcomes Using Prolonged Infusions of Beta-Lactams

- Single-center cohort study of patients who received piperacillin-tazobactam (PTZ) therapy for susceptible *P. aeruginosa* infection (n=194 patients)\(^1\)
- Changed practice from intermittent infusions of PTZ (3.375 g IV for 30 min every 4-6 h) to extended infusions of PTZ (3.375 g intravenously for 4 h every 8 h)
  - Among patients with APACHE II scores ≥17, 14-day mortality rate was significantly lower among patients who received extended-infusion therapy than among patients who received intermittent-infusion therapy (12.2% vs. 31.6%, respectively; P=0.04)
  - Median duration of hospital stay after collection of samples for culture was significantly shorter for patients who received extended-infusion therapy than for patients who received intermittent-infusion therapy (21 days vs. 38 days; P=0.02).
- Using meropenem 2 gm Q8H or cefepime 2gm Q8H, both as 3-hr infusions, plus a clinical pathway, Nicasio et al demonstrated significant improvements in VAP patients\(^2,3\)
  - Lower total costs associated with treatment of VAP and post-VAP hospitalization

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ADDITIONAL SLIDES
Hospitalized Patient Demographics: Potential Projects Focusing on Outcomes

- How frequently is metronidazole prescribed with pip/tazo, amp/sulb, carbapenems?
- Does the antibiogram eliminate duplicates?
- Is there an ability to classify isolates on the antibiogram as community-acquired vs hospital-acquired (i.e., present-on-admission)?
- Are you familiar with the medical staff’s understanding of antibiotics and their use?
- Do you know the contribution of HAIs to unexpected deaths in your institution?
- Do you know the cost associated with a 1% change in hand hygiene compliance?
- Is there data to account for non-compliance with JCAHO/CMS core measures for CAP?
- For patients with HAIs, what is the time to appropriate therapy?
- What is the frequency of prescribers stating an antibiotic plan in the chart?
- If MRSA screening is performed, how often is vancomycin prescribed following results?
- What is the prescriptive compliance for institutional guidelines regarding use of broad-spectrum beta-lactams?
- Have intensivists studied the duration of ventilator assistance in patients with VAP?
- For patients who are converted to PO antibiotics, what % are converted back to IV?
- Do you have data on % patients who receive antibiotics for > 3days?
- Have you tracked the rise of MDRO pathogens (e.g., ESKAPEs) in hospitalized patients?
Prolonged Infusions of Beta-Lactam Antibiotics: Implications for Antimicrobial Stewardship¹

- The optimal dosage and administration of antibiotics are essential to combat antibiotic resistance
- While many factors combine to play a role in favorable clinical outcomes, the absence of an appropriate dose and administration strategy of beta-lactams appropriate for the MIC of the pathogen, might lead to failure
- The literature contains many instances of “resistant pathogens” being successfully treated using prolonged infusions of higher dose regimens (but not necessarily “heroic” doses)
- Literature which suggests that clinical outcomes are not improved using prolonged infusions of beta-lactams often include the majority of infections due to pathogens with very low MICs, UTIs, and mild infections in non-immunocompromised patients
- Breakpoints have been lowered for many pathogens as a result of pharmacodynamics and target attainment
  - Piperacillin-tazobactam, *P. aeruginosa*
  - Carbapenems, Enterobacteriaceae (specifically to address KPCs)
  - Cephalosporins, ESBL-producing Enterobacteriaceae

Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

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Preface:
Parts 10 and 11 include discussion of barriers. This slide section deals with the structure and function of the ASP – resources, knowledge of antimicrobials, and a culture reluctant to accept or continue the ASP. A brief history of identifying barriers is provided (references by Pope and Trivedi). However, several scenarios which may become barriers are discussed as well as the need for effective and accurate communication.

Content:
10 slides with 1 additional slide

Suggestions for Presentation:
The section may be best applied as self-learning, or preparation for the barriers which will come.

Comments:
Slide section 12 may be an adjunct to this section.
ANTIMICROBIAL STEWARDSHIP BARRIERS AND CHALLENGES: STRUCTURAL & FUNCTIONAL
Common Barriers

- Lack of resources
  - Staffing: Pharmacist and/or physician champion availability
    - ID staff willingness to participate may be due to
      - Lack of time
      - Lack of compensation for stewardship activities
      - Fear of antagonizing colleagues and decrease in referrals
  - Funding
  - IT resources
- Clinical/Knowledge Base
  - Consistency between stewardship and ID recommendations
  - Lack of appreciation for the development of drug resistance
- Culture
  - Antimicrobial stewardship is not a priority
  - Perceived loss of prescriber autonomy
  - Opposition to change from administration and/or prescribers
Current Antibiotic Stewardship Programs: Barriers to Effective ASPs

- Two month electronic survey (2008) sent to US hospital practitioners
- 357 responses
- Hospitals without ASPs identified several barriers (178 respondents):
  - Personnel shortages (55%)
  - Financial considerations (36%)
  - Higher-priority clinical initiatives (34%)
  - Opposition from prescribers (27%)
  - Resistance from administration (14%)
  - Other barriers (19%)

However, in this survey, only 26% of hospital ASP programs monitored clinical outcomes, such as mortality and length of stay; rather, focus was on direct drug expenditures and pharmacy savings.

Barriers: A Survey of California Hospitals

- Web-based survey of general acute care hospitals in California
- 233 of 422 hospitals (53%) responded
- 50% of hospitals reported a current ASP and 30% were in planning stages
- 20% of hospitals reported no planned ASP and described barriers
- Of 135 responding hospitals, 22% reported that Senate Bill 739 influenced initiation of an ASP

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Percent Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staffing constraints</td>
<td>47%</td>
</tr>
<tr>
<td>Lack of funding</td>
<td>42%</td>
</tr>
<tr>
<td>Lack of initiation of formal proposal</td>
<td>42%</td>
</tr>
<tr>
<td>ASP is not a priority</td>
<td>24%</td>
</tr>
<tr>
<td>No administrative support</td>
<td>18%</td>
</tr>
<tr>
<td>No medical staff support</td>
<td>18%</td>
</tr>
</tbody>
</table>

Barriers…Perceived and Real: Infectious Diseases Pharmacist

• Dilemma
  • The number of “ID-trained” clinical pharmacists doesn’t match the demand, nor do the number of training programs
  • Requiring completion of a post-graduate ID training program to administer stewardship would be an impediment at present

• Possible solutions:
  • Financial and administrative support for in-house and external programs and training
  • Programs developed by professional organizations
  • “Tool kits” to direct baseline activities and enhance existing ones
  • Best practice sharing (e.g. round tables, web-based)
  • Partner with other clinical pharmacy specialist colleagues and/or staff pharmacist to accomplish any or all components

Possible delays in “appropriate” therapy\(^1\)
  - Lack of “dedicated approver” may increase response time to approval
  - Empirically prescribe “unrestricted” antibiotics to circumvent but may be “inappropriate”
  - Overall increase in time from decision to treat \(\rightarrow\) medication administered
  - Requires process to be monitored

Possible Solutions
  - Monitor the process for delays
  - Antibiotic order forms incorporating restriction criteria

Transmittal of Information: The Importance of Accurate Information

- Prior approval systems may be used in ASPs, requiring that approval be obtained from ASP practitioners before certain antimicrobials can be used.
- The effectiveness of a prior approval system depends on the accuracy of the patient data communicated from the primary service.
  - Inaccurate communications were defined as clinically significant discrepancies between communication data elements abstracted from the form documenting the call to the ASP and data in the medical record, with the medical record as the gold standard.
  - Clinically significant discrepancies were those likely to influence antimicrobial prescribing.
- Inaccurate communication of patient data during telephoned interactions requesting approval from ASP practitioners were common.
  - Overall 39% of calls contained an inaccuracy in at least 1 type of patient data.
  - Most frequent inaccuracies included current antibiotics (12.9%) and microbiological data (11.9%).

Clinically significant differences in information provided on the call which was inaccurate is likely to affect antimicrobial(s) prescribed.

Unintended Consequences of Restrictive Formularies

- If ASP operations is restricted to certain on-service hours, prescribers may wait until off-hours to order restricted antibiotics\(^1\)
  - Possible solution: Monitor prescriptions and adjust ASP strategy if needed
- Restrictive formularies may encourage creativity when prescribers want to circumvent restrictions
  - Example: If meropenem is restricted, coverage of ESBLs plus *P. aeruginosa* may result in prescribing a combination of two formulary antibiotics, such as ertapenem plus tobramycin
  - Possible solution: Review antibiotic use and educate providers
- Creates animosity between ASP and senior prescribers who may value decision-making autonomy rather than giving up this traditional structure\(^2\)
  - Possible solution: Consider making senior prescribers part of a ASP clinical workgroup

---
Challenge: When Cultures Do Not Help

Chart shows whether, in 135 patients who received piperacillin-tazobactam for at least 72 hours and in whom treatment was determined to be appropriate, treatment was altered on the basis of microbiologic culture results. Study was conducted at 4 hospitals affiliated with Emory University, 2003-2005.

In 65% of the cases, cultures were not helpful in streamlining treatment.

- Therapy altered based on cultures or cultures supported use: 65%
- Therapy NOT altered despite culture results that support optimization of therapy: 8%
- Cultures obtained but no growth or “normal flora”: 56%
- No cultures obtained: 11%
- Cultures obtained after antibiotics: 33%

Possible solution: Use guidelines and local antibiogram to streamline treatment.

ADDITIONAL SLIDES
Common Barriers to Antibiotic Stewardship

- Stewardship program barriers
  - Physician autonomy
  - Prescriber lack of appreciation of resistance development
  - Individual patient versus ecological perspective
  - Restriction policies are onerous
  - Can be difficult to encourage streamlining
  - Gatekeeper mentality
  - Need to sustain efforts
  - Consistency among stewardship and ID practitioner recommendations

- ID staff involvement
  - ID staff may not want to assume additional responsibility
  - Disputes regarding “fair and equitable” compensation
    - In a recent EIN survey, only 18% of 502 respondents received any remuneration
  - Fear of antagonizing colleagues in other specialties leading to decreased consultation
  - Perceived “conflict of interest”

EIN = Emerging Infections Network
Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.

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Introduction to Slide Section

- **Preface:**
  One of the most common barriers and challenges is dealing with antimicrobial prescribing in the community. Since a significant amount of bacterial resistance is imported this barrier often feels out of the control of the ASP.

- **Content:**
  6 slides, but note there is more subject matter published in the European literature. Fortunately, this is a rapidly growing topic of discussion and many projects in antimicrobial stewardship in the community setting have been initiated.

- **Suggestions for Presentation:**
  Internists and family medicine prescribers can benefit from introduction to the CDC’s Get Smart campaign. These slides could be used with a number of slides in other parts of the slide toolkit.

- **Comments:**
  Several materials are available on the CDC website and these could be copied and distributed as part of an educational plan to optimize antibiotic use in the community, or even at hospital discharge.
ANTIMICROBIAL STEWARDSHIP BARRIERS AND CHALLENGES:

ANTIBIOTIC USE IN THE COMMUNITY
GET SMART: Know When Antibiotics Work

- CDC launched a national campaign for appropriate antibiotic use in the community in 1995, renamed in 2003 as GET SMART: KNOW WHEN ANTIBIOTICS WORK, in conjunction with the launch of a national media campaign.
- Campaign aims to reduce the rate of antibiotic resistance by:
  - Promoting adherence to appropriate prescribing guidelines
  - Decreasing demand for antibiotics for viral upper respiratory infections in young children
  - Increasing adherence to prescribed antibiotics for upper respiratory infections
- GET SMART campaign targets the 5 respiratory conditions which encompass the majority of antibiotic over-prescribing: otitis media, sinusitis, pharyngitis, bronchitis, and the common cold
- The target audiences include patients, providers, and parents of young children
- The campaign organized its first annual GET SMART about antibiotics week in 2008

http://www.cdc.gov/getsmt/campaign-materials/about-campaign.html
http://www.cdc.gov/getsmt/campaign-materials/week/promotional-media.html
GET SMART For Healthcare

- Complementary program to community-based GET SMART campaign
- Focused on improving antimicrobial use in inpatient healthcare settings such as acute-care facilities and long-term care through the implementation of antimicrobial (or antibiotic) stewardship programs
- ASPs ensure that hospitalized patients receive the right antibiotic, at the right dose, at the right time, and for the right duration
- Antibiotic overuse contributes to the growing problems of *Clostridium difficile* infection and antibiotic resistance in healthcare facilities
- Goals:
  - Improving antibiotic use through stewardship interventions and programs improves patient outcomes, reduces antimicrobial resistance, and saves money.
  - Interventions to improve antibiotic use can be implemented in any healthcare setting—from the smallest to the largest.
  - Improving antibiotic use is a medication-safety and patient-safety issue.

http://www.cdc.gov/getsmtah/healthcare/inpatient-stewardship.html
Outpatient Antimicrobial Stewardship and Primary Care Pediatricians: Effect of Intervention

Cluster randomized trial of outpatient antimicrobial stewardship (pre-post)
Study period Oct 2008 – June 2011
Excluded children with chronic medical conditions, antibiotic allergies, and prior antibiotic use
18 pediatric primary care practices (162 clinicians) in PA and NJ
Intervention included one 1-hour on-site clinician education session (June 2010) followed by 1 year of personalized, quarterly audit and feedback of prescribing for bacterial and viral acute respiratory tract infections or usual practice
Outcome and measures included rates of broad-spectrum (off-guideline) antibiotic prescribing for 1 year after the intervention (versus control group)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Relative Decrease Observed Between Groups</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention Group</td>
<td>Control Group</td>
</tr>
<tr>
<td>Broad-spectrum ABX prescribing</td>
<td>26.8% → 14.3%</td>
<td>28.4% → 22.6%</td>
</tr>
<tr>
<td>Off-guideline prescribing for children with pneumonia</td>
<td>15.7% → 4.2%</td>
<td>17.1% → 16.3%</td>
</tr>
<tr>
<td>Off-guideline prescribing for children with acute sinusitis</td>
<td>38.9% → 18.8%</td>
<td>40.0% → 33.9%</td>
</tr>
</tbody>
</table>

“Commandments” For Appropriate Antibiotic Use in the Outpatient Setting: Sound Familiar?

1. Use antibiotics only when needed; teach the patient how to manage symptoms of non-bacterial infections
2. Select the adequate antibiotic; precise targeting is better than shotgun therapy
3. Consider pharmacokinetics and pharmacodynamics when selecting an antibiotic; use the shortest antibiotic course that has proven clinical efficacy
4. Encourage patient compliance
5. Use antibiotic combinations only in specific situations
6. Follow only evidence-based guidelines; beware those sponsored by drug companies
7. Rely (rationally) upon the clinical microbiology lab
8. Prescribe antibiotics empirically but intelligently; know local susceptibility trends and also surveillance limitations

Antimicrobial Stewardship:
Arizona Partnerships Working to Improve the Use of Antimicrobials in the Hospital and Community

Part 12

“Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

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<tbody>
<tr>
<td>Pathways to a Successful ASP</td>
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<tr>
<td>Antimicrobial Stewardship: Making the Case</td>
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<tr>
<td>ASPs: Nuts &amp; Bolts</td>
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<td>Antimicrobial Stewardship: Measuring Antibiotic Utilization</td>
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<td>Antimicrobial Stewardship: Daily Activities</td>
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<td>Antimicrobial Stewardship: Computerized &amp; Clinical Decision Support Services</td>
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<td>Microbiology: Cumulative Anti-gram &amp; Rapid Diagnostics</td>
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<tr>
<td>Antimicrobial Stewardship Projects: Initiation &amp; Advanced</td>
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<tr>
<td>Antimicrobial Stewardship Barriers &amp; Challenges: Structural &amp; Functional</td>
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<td>Antibiotic Use in the Community</td>
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<td>Opportunities to Justify Continuing the ASP</td>
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<tr>
<td>ANTImicrobial Stewardship: Perspectives to Consider</td>
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</table>

- **Preface:**
  Administrators provide support for the ASP, but they request outcomes data in return. Length of stay can be an important marker for the success of the ASP as well as reduction in the antimicrobial costs of the pharmacy budget. On the other side there is the cost of dismantling the ASP as the example provided disproved the wisdom of such action.

- **Content:**
  5 slides with 3 additional slides.

- **Suggestions for Presentation:**
  Self-learning slide module to provide ideas about surviving the ASP venture. These slides follow part 3 – “Making the Case”.

- **Comments:**
  The additional slides present the data from the article by Standiford et al in another light. But it is essential reading and this has likely been repeated many times yet outcomes never published. A final idea might be to adjust annual cost-saving to the increase in inflation. An ASP which has reached a plateau in real dollar savings for that budget period has actually saved expenses through a 3% inflation rate over several years.
ANTIMICROBIAL STEWARDSHIP
BARRIERS AND CHALLENGES:
OPPORTUNITIES TO JUSTIFY CONTINUING THE ASP
Antibiotic Stewardship Can Decrease LOS

- Oklahoma City VA\(^1\)
  - ID pharmacist
  - Mean hospital LOS decreased from 13.3 days to 10.8 days (P<0.01)
- Pittsburgh VA\(^2\)
  - Critical care unit, ID physicians and intensivists
  - Algorithm development
  - Mean ICU LOS 9 days vs 15 days (P=0.04)
- Six hospitals across the UK\(^3\)
  - Evaluation audit tool assessed all patients on antibiotic treatments on acute care wards
  - Early discontinuation, conversion from IV-to-PO, and placement of selected patients in an outpatient parenteral antibiotic therapy program saved 481 inpatient bed-days amongst 1,356 patients reviewed

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The Cost of Discontinuing an ASP

- ASP was implemented at the Univ Maryland Med Cntr (July 2001); continued for 7 years
- The ASP was terminated; the resources were used to increase ID consults (ASP was considered heavily resourced)
- Utilization costs decreased from $44,181 per 1,000 patient-days at baseline (prior to FY 2001) to $23,933 (a 45.8% decrease) by the end of the program (FY 2008)
- There was a reduction of ~$3 million within the first 3 years
- After the program was discontinued at the end of FY 2008, antimicrobial costs increased from $23,933 to $31,653 per 1,000 patient-days, a 32.3% increase within 2 years

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>FY 2008 ($)</th>
<th>FY 2009 ($)</th>
<th>Change</th>
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<tr>
<td>TOTAL (of above)</td>
<td>1,916,964</td>
<td>2,642,146</td>
<td>+ 52%</td>
</tr>
</tbody>
</table>

Discontinuation of an ASP resulted in increased antimicrobial costs of 32.3%, or $2 million, over 2 years

Key Points in Overcoming Barriers and Challenges: Anticipate Challenges, Be Persistent, Incentivize Team

- ASP start-up does not require significant financial resources – only time and motivation
- Acceptance requires use of objective data to develop interventions with stakeholders
- Leave nothing to chance: Think through components of a potential intervention to maximize success
- Organize a multi-disciplinary team – Engage respected members of the institution and hospital leadership early
- Engage a large number of target providers
  - Use peer champions to disseminate and deliver messages to colleagues
  - Use real-time cases to promote guideline utilization
  - Start with face-to-face meetings
- Audit and provide feedback of ASP metrics to drive change in provider behavior
- Automation – use IT when possible but interventions do not need to be IT-driven to be successful
- Be willing to compromise
- Stay focused on goals; overly broad interventions may fail
ADDITIONAL SLIDES
Discontinuation of the Antibiotic Stewardship Program: Hard Lessons

• An antimicrobial stewardship program was fully implemented at the University of Maryland Medical Center in July 2001 (beginning of fiscal year [FY] 2002)
  • Antimicrobial monitoring team (AMT) = an infectious diseases–trained clinical pharmacist and a part-time infectious diseases physician
  • AMT provided real-time monitoring of antimicrobial orders and active intervention and education when necessary

• Outcomes of the 7 year program:
  • Utilization costs decreased from $44,181 per 1,000 patient-days at baseline prior to the full implementation of the program (FY 2001) to $23,933 (a 45.8% decrease) by the end of the program (FY 2008)
  • There was a reduction of approximately $3 million within the first 3 years, much of which was the result of a decrease in the use of antifungal agents in the cancer center

Discontinuation of the Antibiotic Stewardship Program: Hard Lessons (cont’d)

- The AMT was terminated in order to use the resources to increase infectious diseases consults throughout the medical center as an alternative mode of stewardship.
- After the program was discontinued at the end of FY 2008, antimicrobial costs increased from $23,933 to $31,653 per 1,000 patient-days, a 32.3% increase within 2 years that is equivalent to a $2 million increase for the medical center.
The Cost of Discontinuing an ASP

- After the program was discontinued at the end of FY 2008, antimicrobial costs increased from $23,933 to $31,653 per 1,000 patient-days.
- These increased antibiotic utilization costs were observed for a variety of drug classes.
- Discontinuation of the ASP at the University of Maryland Medical Center resulted in increased antimicrobial costs of 32.3%, or $2 million, over 2 years.

### Increase in Costs of 5 Selected Antimicrobials One Year Following Discontinuation of an ASP

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Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

- Glenn Tillotson; Clin Infect Dis. 2010;51:752

“…we hold closely the principles that antibiotics are a gift to us from prior generations and that we have a moral obligation to ensure that this global treasure is available for our children and future generations.”

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Their work was guided by the best available evidence at the time although the subject matter encompassed thousands of references. Accordingly, the Subcommittee selectively used examples from the published literature to provide guidance and evidenced-based criteria regarding antimicrobial stewardship. The slide compendium reflects consensus on criteria which the HAI Advisory Committee deems to represent prudent practice.
Disclaimers

All scientific and technical material included in the slide compendium applied rigorous scientific standards and peer review by the Subcommittee on Antimicrobial Stewardship Programs to ensure the accuracy and reliability of the data. The Subcommittee reviewed hundreds of published studies for the purposes of defining antimicrobial stewardship for Arizonan clinicians. The Arizona Department of Health Services (ADHS) and members of its subcommittees assume no responsibility for the opinions and interpretations of the data from published studies selected for inclusion in the slide compendium.

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Introduction to Slide Section

- **Preface:**
The perspectives of the ASP pharmacist have been discussed in previous slide parts. However, it is valuable to consider perspectives and needs of others in the ASP – hospital administrator and other “C” suite personnel such as the CMO, pharmacy director, and the ASP physician. The obvious recipient of ASP activities is the patient. The patients’ perspectives, as consumers of healthcare, must be recognized and integrated into the focus of ASP activities – the well-being of patients.

- **Content:**
7 slides; 2 supplemental slides

- **Suggestions for Presentation:**
This slide section is best used in conjunction with “Barriers and Challenges”, “Nuts and Bolts”, and “Making the Case”. Understanding the needs of other members of the ASP will be valuable in structuring activities and setting expectations and timelines.

- **Comments:**
Slides could be added to this slide section appropriate to your audience which addresses perspectives of healthcare workers in epidemiology, infection prevention, microbiology, environmental services, employee health, and IT.
ANTIMICROBIAL STEWARDSHIP: PERSPECTIVES TO CONSIDER
Expectations of the Patient

• Consumers consider HAIs and bacterial resistance unacceptable from a societal and personal perspective
  • Sources of litigation have been published
  • Patient dissatisfaction on hospital surveys
  • Patients beginning to “shop for the cleaner hospital”
• Antibiotic resistant infections are more difficult to manage clinically\(^1\)
  • Therapy may include long-term IV antibiotics
• Continued patient exposure to broad-spectrum antibiotics guarantees one consequence – bacterial resistance
  • Bacterial resistance has implications for the single patient (as source of new MDROs) and downstream effects (patients in nearby beds, future patients, and HCWs)\(^2\)
• Bacterial resistance, and HAIs, are not the “cost of doing business”

Expectations of the Hospital Administrator

- Effective antimicrobial stewardship programs are financially self-supporting\(^1\)
- Comprehensive programs have consistently demonstrated a decrease in antimicrobial use (22% to 36%), with annual savings of $200,000 to $900,000 in both larger academic hospitals and smaller community hospitals\(^1\)
- Additional financial advantages affecting total hospital costs and quality may be expected, such as improved safety of antibiotic use, lower HAI rates, and shorter length-of-stay\(^1\)
- Dozens of different programs have been published
  - Small and large hospitals
  - Community and academic medical centers
  - Variety of strategies
- Administrative (hospital and medical department) support is mandatory to establish the infrastructure to measure antimicrobial use and to track use on an ongoing basis, and to determine authority, compensation, and expected outcomes for the program\(^1\)

Expectations of the Pharmacy Director

- Change in staffing is frequently required to initiate an ASP\textsuperscript{1}, and may include a request for hiring additional staff.
- Assessment of infectious diseases knowledge may be required if the ASP functions are to be shared amongst the Pharmacy staff.
  - Recommendations for training and certification for pharmacists practicing infectious diseases pharmacotherapy recently published\textsuperscript{2}.
- Accountability measures need to be developed for “ID Pharmacist” functions.
- Expectations on reductions in direct antibiotic purchases need to be established, but should conform to the phase-in timeline of the ASP program.
- Cost reductions in antibiotic spend will eventually achieve a plateau, and may be affected by market entry of new agents.
  - However, trend lines can partly justify the anticipated antibiotic costs per year in the absence of an ASP.
- National Patient Safety Goals (NPSGs) for 2009-2010 phase in several antibiotic stewardship activities which will be mandated, measurable, and/or documented in 2010\textsuperscript{3}.

\textsuperscript{1} Dellit T, et al. *Clin Infect Dis* 2007;44:159-177.
\textsuperscript{3} Accessible at: http://www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/09_hap_npsgs.htm
Expectations of the Chief Medical Officer

- The CMO serves as a champion for the program and supports the ASP philosophy to the medical staff.
- Intervention with specific prescribers, P&T Committee, and Med Exec Committee, may be necessary for the success of the program and as issues arise between medical staff and Pharmacy.
- The day-to-day role and compensation of the ID physician partaking in ASP.
- The CMO should discuss how antibiotic stewardship practices can be translated into accreditation standards within the institution:
  - Daily documentation of the antibiotic plan can be used to quantify accountability, and can be easily performed by retrospective or prospective chart review.
  - Antibiotic report cards have been discussed as a means of prescriber profiling.
  - Assessing the role of evidence-based medicine in clinical pathway and guidelines development.

Expectations of the ASP Physician

- Business planning and presentations to “C” suite personnel: justification and sustaining the ASP
- Compensation for time out of office, loss of revenue, and stress on partners
- Expectations from Pharmacy: clinical expertise, consistent program hours, ability of pharmacists to accurately and appropriately interface with physicians
- Responsibility for other oversight: infection prevention/epidemiology, microbiology, ASP educational programs, P&T Committee, CMO, etc
- Defining their authoritative role as core member of the ASP
- Perceptions by medical staff
  - Balancing consults with informal review of antibiotic prescribing
  - Potential conflicts of interest
- Need to serve as role models for antibiotic use

ADDITIONAL SLIDES
## Understand Viewpoints of Shareholders: Appreciate Diversity of Viewpoints and Concerns

<table>
<thead>
<tr>
<th>Consumer of Healthcare</th>
<th>Administrator</th>
<th>Pharmacy Director</th>
<th>Chief Medical Officer</th>
<th>Infectious Diseases Physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Societal perspective on resistance</td>
<td>Antimicrobial stewardship programs are financially self-supporting</td>
<td>Additional staffing may be necessary to devote dedicated Pharmacist to core team</td>
<td>Dedicate resources to support AST</td>
<td>Compensation (time out of office, revenue, stress on partners)</td>
</tr>
<tr>
<td>Bacterial resistance is generated primarily in healthcare settings</td>
<td>Comprehensive programs have demonstrated a decrease in antimicrobial use (22% to 36%) with annual savings of $200,000 to $900,000</td>
<td>Assessment of infectious diseases knowledge of Pharmacy staff to support program</td>
<td>Serve as a champion</td>
<td>Working with Pharmacy (expertise), eg, hours for review</td>
</tr>
<tr>
<td>Litigation and unfavorable hospital surveys</td>
<td>Additional financial advantages include improved safety, lower HAI rates, and shorter length-of-stay</td>
<td>Accountability measures need to be developed</td>
<td>Leads the culture change in how antibiotics are used by medical staff</td>
<td>Role in ASP (authority)</td>
</tr>
<tr>
<td>Antibiotic resistant infections are more difficult to manage</td>
<td>Infrastructure and compensation to support a multidisciplinary program</td>
<td>Expectations on reductions in direct antibiotic purchases</td>
<td>Determine how antibiotic stewardship practices are translated into accreditation standards within the institution</td>
<td>Perceptions by medical staff; balancing private practice consults with informal review of antibiotic prescribing</td>
</tr>
<tr>
<td>Bacterial resistance has downstream effects</td>
<td></td>
<td>Phase-in timeline of the AST program</td>
<td>Improved clinical outcomes can be used to generate a “best practices center”</td>
<td>Conflicts of interest (actually, there are none)</td>
</tr>
<tr>
<td>HAIs, usually due to MDR pathogens, are not the “cost of doing business”</td>
<td></td>
<td></td>
<td></td>
<td>Serve as role models for antibiotic use</td>
</tr>
</tbody>
</table>
The Pharmacists Role in Antimicrobial Stewardship and Infection Prevention: A White Paper (ASHP)

- The American Society of Health-System Pharmacists (ASHP) believes that pharmacists have a responsibility to take prominent roles in antimicrobial stewardship programs and participate in the infection prevention and control programs of health systems.

- This responsibility arises, in part, from pharmacists’ understanding of and influence over antimicrobial use within the health system.

- ASHP believes that the pharmacist’s ability to effectively participate in antimicrobial stewardship and infection prevention and control efforts can be realized through clinical endeavors focused on proper antimicrobial utilization and membership on multidisciplinary work groups and committees within the health system.

- These efforts should contribute to the appropriate use of antimicrobials, ultimately resulting in successful therapeutic outcomes for patients with infectious diseases, and reduce the risk of infections for other patients and health care workers.
Antibacterials – indeed, anti-infectives as a whole – are unique in that misuse of these agents can have a negative effect on society at large. Misuse of antibacterials has led to the development of bacterial resistance, whereas misuse of a cardiovascular drug harms only the one patient, not causing a societal consequence.”

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Introduction to Slide Section

- **Preface:**
  A pathway to success requires a ‘culture change’ when applied to antimicrobial stewardship. Rather than summarizing ASPs another approach has been used in this “Summary” – getting everyone onboard to believe that disruptions to the current practices of using antimicrobials is a good thing and benefits everyone including patients.

- **Content:**
  7 slides and two additional slides

- **Suggestions for Presentation:**
  The “Summary” slide part can be used in many other sections. The focus is to emphasize the paradigm shift represented by antimicrobial stewardship. ‘Managing change’ is an important concept as the activities of the ASP equate to ‘benevolent disruptive innovation’.

- **Comments:**
  The slides might be used to gain trust, add direction, and strengthen cohesion amongst healthcare workers and hospital administration for the ASP.
SUMMARY
Kotter’s Steps\textsuperscript{1}: Managing Change

- **Step 1: Create a sense of urgency**
  - Focus on patient safety and cost with hospital leaders
    - Local data regarding resistance and *C. difficile* infection
    - National recommendations and regulations
    - Current and potential examples of cost-savings

- **Step 2: Form a powerful guiding coalition**
  - Team of leaders who represent key stakeholders
  - Team member characteristics: position of power, expertise, credibility, leadership

- **Step 3: Create a compelling vision for change**
  - Potential vision statement: “Helping patients receive the right antibiotics when they need them”

- **Step 4: Communicate the vision effectively**
  - Communicate to all levels, including senior leadership, department heads, unit directors, prescribers
  - Communicate regularly

\textsuperscript{1} Kotter J. Harvard Business Review. 1995 (Mar-Apr):59-67
\textsuperscript{2} Morris A et al Healthcare Quarterly. 2010;13:64-70
Kotter’s Steps: Managing Change (cont’d)

- **Step 5:** Empower others to act on the vision
  - Work with units or teams to develop mutually acceptable approaches
  - Empower non-traditional decision-makers, such as pharmacists and nurses

- **Step 6:** Plan for and create short-term wins
  - Pick the low-hanging fruit, i.e., surgical prophylaxis and reduction in vancomycin use
  - Recognize the Team and the front-line staff as critical in making the changes

- **Step 7:** Consolidate improvements and create still more change
  - Continue project-based interventions
  - Avoid only performing reviews of antibiotic use – extend to outcomes

- **Step 8:** Institutionalize new approaches
  - Ensure there is institutional understanding of the positive results
  - Strive to have prescribers themselves be stewards of antimicrobials

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2 Morris A et al Healthcare Quarterly. 2010;13:64-70
Summary of Antimicrobial Stewardship:
Structure Your Initiatives and Anticipate Barriers

- One size does not fit all
- Perform a baseline assessment of assets, deficits; gather pilot data
- Address any deficits that will impede the basic program and fix first
- Pre-determine barriers and differentiate the real from the misunderstood
- Pro-actively address the valid obstacles
- Prioritize available resources as well as additional resources needed
- Choose reasonable, sequential initiatives that are practical and beneficial to the institution and will lead to a logical progression of next steps
- Bring in specialists but realize everyone has a stake in the program and ultimately in the patient
- Involve providers, encourage them, educate them, report back to them (good and bad)
- Cost-reduction of the antimicrobial budget is not a primary justification for antimicrobial stewardship, but cost-savings will be realized from ASP activities
- Create a campaign towards antibiotic stewardship; market the program
Appropriate Expectations:
Maintain a Positive and Constructive Attitude

- Antimicrobial stewardship program development includes many complex activities which will require appropriate discourse, education, and sometimes compromise.
- Focus will change as the program progresses through various stages, but maintain direction towards satisfying the mutually agreed-upon ASP goals.
- Refrain from “changing the world” in one year or immediately after every initiative – some changes will occur quickly and others over many months or years.
- Unexpected roadblocks will occur which impact the trajectory of the program and projects, or influence even the simplest ASP initiatives – some of these will be out of your control.
- Attempt to anticipate these challenges through advanced planning and participate in working groups to understand the perspectives of clinicians in their departments.
- Revel in the impact you have on improving patient outcomes.
Pathways to Success Summary: Antimicrobial Management in Hospitals Means A “Culture Change”

• Programs can be successful but accountability of prescribers should be established – GET EVERYONE ON THE SAME PAGE
  • Antibiotic resistance poses health risks for patients and HCWs
  • Adopt a philosophy of accountability for antibiotic resistance
  • Create a campaign towards antibiotic stewardship
  • Everyone has a stake in the program
• Hospital administration and Med Exec should endorse the ASP
  • Provide commitment to the “new culture” and improve patient outcomes
  • Adequate resources committed to achieve cost savings and improved patient outcomes
• Face-to-face education and medical staff feedback should be ongoing
• Patient safety and quality care are interwoven into antibiotic resistance dilemmas, and the antibiotic stewardship team should operate under their auspices
• Create an optimal environment for acceptance of change and learning
ADDITIONAL SLIDES
Antibiotic Stewardship: Lessons Learned

- Several strategies, including prescriber education, formulary restriction, prior approval, streamlining, empiric treatment based on antibiogram data, and computer-assisted programs have been proposed to improve antibiotic use.

- Although rigorous clinical data in support of these strategies are lacking, the most effective means of improving antimicrobial stewardship will most likely involve a comprehensive program that incorporates multiple strategies and collaboration among various specialties within a given healthcare institution.

Figure adapted from: MacDougall C et al.. Clin Microbiol Rev. 2005;18(4):638-56.
Assess Organizational Capacity for Change (OCC): Adapt To New Opportunities and Create New Capabilities

- Trustworthy leadership
  The ability of administration to earn the trust of the rest of the organization and to show the members of the organization the way to meet its collective goals

- Trusting followers
  The ability of the organization’s members to constructively dissent and/or enthusiastically follow a new path advocated by its leaders

- Capable champions
  The ability of an organization to empower change leaders to evolve and emerge

- Involved management
  The ability of managers to effectively link components of the organization

- Innovative culture
  The ability to establish norms of innovation and encourage innovative activity

- Accountable culture
  The ability to carefully steward resources and successfully meet deadlines

- Systems communications and systems thinking
  The ability to communicate vertically, horizontally, and with customers; the ability to focus on root causes and recognize the interdependencies within and outside the organizational boundaries