Antimicrobial Stewardship: A Public Health Priority

*CLSI Workshop*
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Objectives

• Describe rationale for antimicrobial use optimization and Antimicrobial Stewardship
• Discuss relevance of Antimicrobial Stewardship to public health
• Describe progress towards Antimicrobial Stewardship
  – US
  – Global
30-50% of antimicrobial use in acute care is either inappropriate or suboptimal

Rationale for Antimicrobial Use Optimization

• Antimicrobial resistance
• Patient safety
  – Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death
• Cost
  – Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy
## Cost of Antimicrobial-Resistant Infections (ARI)

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Patients with ARI</th>
<th>Patients without ARI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td>1391</td>
<td>188 (13.5)</td>
<td>1203 (86.5)</td>
</tr>
<tr>
<td><strong>APACHE II score</strong></td>
<td>42.1</td>
<td>54.8*</td>
<td>40.1*</td>
</tr>
<tr>
<td><strong>LOS (days)</strong></td>
<td>10.2</td>
<td>24.2*</td>
<td>8.0*</td>
</tr>
<tr>
<td><strong>HAI (n)</strong></td>
<td>260</td>
<td>135*</td>
<td>125*</td>
</tr>
<tr>
<td><strong>Cost per day ($)</strong></td>
<td>1651</td>
<td>2098*</td>
<td>1581*</td>
</tr>
<tr>
<td><strong>Total cost ($)</strong></td>
<td>19,267</td>
<td>58,029*</td>
<td>13,210*</td>
</tr>
<tr>
<td><strong>Death [n (%)]</strong></td>
<td>70</td>
<td>34 (18.1)*</td>
<td>36 (3.0)*</td>
</tr>
</tbody>
</table>

*P* < 0.001

Antibiotic Armageddon

Then

Now

New Antimicrobials

Resistance

We are here

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Timeline for Development of a New Antibiotic

- **Discovery**
- **Preclinical**
- **IND Filing**
- **Phase I**
- **Phase II**
- **Phase III**
- **FDA Review**
- **Product Launch**

Development time (years):

0 1 2 3 4 5 6 7 8 9 10
“...the only therapy area in which if I invent a new antibiotic...the new antibiotic is greeted with great applause and cheers, and then it’s not used very much. And from the economic standpoint of a developer, that means you’re not getting the return on the investment you’ve made, because you’ve spent $600 million [to] $1 billion to bring that new antibiotic to market.

– John Rex, MD, VP at AstraZeneca
Antibiotic Threats in the United States, 2013

• Foreword by Dr. Tom Frieden, MD, MPH, Director of CDC:
  • Antimicrobial resistance is one of our most serious public health threats.
  • The loss of effective antibiotics will undermine our ability to fight infectious diseases and manage infectious complications.

Antibiotic Threats in the United States 2013

• Four Core Actions to Prevent Antibiotic Resistance:
  – Preventing infections, preventing spread of resistance
    o Immunization, safe food preparation, handwashing, using antibiotics as directed
  – Tracking - risk factor analysis
  – Improving antibiotic prescribing/Antimicrobial Stewardship
    o To slow spread of resistant bacteria
  – Developing new drugs and diagnostic tests

Antimicrobial Stewardship

• Stewardship is the responsible overseeing and protection of something considered worth caring for and preserving
  – Antimicrobials are worth preserving
  – Not synonymous with restriction
Antimicrobial Stewardship Program (ASP)

- Promotes appropriate use of antimicrobials by selecting the appropriate agent, dose, duration and route of administration

- Objective:
  - Optimize the utilization of antimicrobial agents in order to:
    - Minimize acquired resistance
    - Improve patient outcomes and toxicity
    - Reduce treatment costs
Antimicrobial Stewardship: A Public Health Issue

• Public Health purpose:
  – Prevent disease
  – Promote health
  – Prolong life
• Antimicrobial Stewardship aligns with public health goals
What Can Public Health Agencies Do?

• Awareness

• Resources / Education

• Convene effective partnerships

• Surveillance / Evaluation
10 Essential Public Health Services

Source: CDC
Role of Public Health in Antimicrobial Stewardship

- Monitor and detect antimicrobial susceptibility patterns and antimicrobial utilization trends
- Diagnose and investigate concerning patterns and trends in antimicrobial susceptibility
- Inform, educate, and empower patients, healthcare providers, and state survey agencies on appropriate antimicrobial use
- Partner with community organizations in promoting Antimicrobial Stewardship strategies across regions
Role of Public Health in Antimicrobial Stewardship

• Identify best practices and policies in Antimicrobial Stewardship and share them widely
• Advocate for legislation to improve patient safety and protect the public’s health by limiting development of resistant infections
• Link healthcare facilities with each other to enhance Antimicrobial Stewardship across regions
Role of Public Health in Antimicrobial Stewardship

• Assure competent ASPs in healthcare facilities
• Evaluate and improve ASPs in healthcare facilities
• Research innovative solutions to barriers in Antimicrobial Stewardship implementation
Antimicrobial Stewardship is a Public Health Priority

- Appropriate antimicrobial use is important for healthcare quality and safety
- Public health agencies play a key role in uptake, guidance, and surveillance
- Successful approaches must fit context
  - Balance specific expectations with adaptable interventions
  - Visible results beyond individual activities are needed for sustainability
Antimicrobial Stewardship
Progress in the United States
• Dr. Tom Frieden: CDC recommends every hospital adopt an ASP with seven core elements

• Dr. John Combes (VP of American Hospital Association):
  – In support of CDC recommendation
Core Elements:
- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

### CDC Checklist for Core Elements for Hospital ASP

#### Leadership support

<table>
<thead>
<tr>
<th>Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
</tbody>
</table>

#### Accountability

<table>
<thead>
<tr>
<th>Is there a physician leader responsible for program outcomes of stewardship activities at your facility?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
</tbody>
</table>

#### Drug Expertise

<table>
<thead>
<tr>
<th>Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
</tbody>
</table>

#### Key support for the antibiotic stewardship program

**Does any of the staff below work with the stewardship leaders to improve antibiotic use?**

<table>
<thead>
<tr>
<th>Clinicians</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection Prevention and Healthcare Epidemiology</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Quality Improvement</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Microbiology (Laboratory)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Information Technology (IT)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nursing</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

#### Actions to support optimal antibiotic use

<table>
<thead>
<tr>
<th>Does your facility have a policy that requires prescribers to document in the medical record or during order entry a dose, duration, and indication for all antibiotic prescriptions?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
<tr>
<td>Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to assist with antibiotic selection for common clinical conditions?</td>
</tr>
<tr>
<td>B</td>
</tr>
</tbody>
</table>

#### Specific interventions to improve antibiotic use

**Are the following actions to improve antibiotic prescribing conducted in your facility?**

<table>
<thead>
<tr>
<th>Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics 48 hours after the initial orders (e.g., antibiotic time out)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
</tr>
<tr>
<td>Do specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing (i.e., pre-authorization) at your facility?</td>
</tr>
<tr>
<td>D</td>
</tr>
<tr>
<td>Does a physician or pharmacist review courses of therapy for specified antibiotic agents (i.e., prospective audit with feedback) at your facility?</td>
</tr>
<tr>
<td>E</td>
</tr>
</tbody>
</table>

#### Business-driven interventions

**Are the following actions implemented in your facility?**

<table>
<thead>
<tr>
<th>Automatic changes from intravenous to oral antibiotic therapy in appropriate situations?</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
</tr>
<tr>
<td>Dose adjustments in cases of organ dysfunction?</td>
</tr>
<tr>
<td>G</td>
</tr>
<tr>
<td>Dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?</td>
</tr>
<tr>
<td>H</td>
</tr>
<tr>
<td>Automatic alerts in situations where therapy might be unnecessarily duplicative?</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>Time-sensitive automatic stop orders for specified antibiotic prescriptions?</td>
</tr>
<tr>
<td>J</td>
</tr>
</tbody>
</table>

#### Diagnosis and infections specific interventions

**Does your facility have specific interventions in place to ensure optimal use of antibiotics to treat the following common infections?**

<table>
<thead>
<tr>
<th>Community-acquired pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
</tr>
<tr>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>L</td>
</tr>
<tr>
<td>Skin and soft tissue infections</td>
</tr>
<tr>
<td>M</td>
</tr>
<tr>
<td>Surgical prophylaxis</td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Empiric treatment of Methicillin-resistant Staphylococcus aureus (MRSA)</td>
</tr>
<tr>
<td>O</td>
</tr>
<tr>
<td>Non-C. Difficile infection (CDI) antibiotics in new cases of CDI</td>
</tr>
<tr>
<td>P</td>
</tr>
</tbody>
</table>

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http://www.cdc.gov/getsmart/healthcare/implementation/checklist.html

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CDC Checklist for Core Elements for Hospital ASP

<table>
<thead>
<tr>
<th>Process measures</th>
<th>Measure performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?</td>
<td>Yes</td>
</tr>
<tr>
<td>B. Does your stewardship program monitor adherence to facility-specific treatment recommendations?</td>
<td>Yes</td>
</tr>
<tr>
<td>C. Does your stewardship program monitor compliance with one of more of the specific interventions in place?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic use and outcome measures</th>
<th>Measure performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>D. Does your facility track rates of <em>C. difficile</em> infection?</td>
<td>Yes</td>
</tr>
<tr>
<td>E. Does your facility produce an antibiogram (cumulative antibiotic susceptibility report)?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Does your facility monitor antibiotic use (consumption) at the unit and/or facility wide level by one of the following metrics:

<table>
<thead>
<tr>
<th>Measure performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>F. By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?</td>
</tr>
<tr>
<td>G. By number of grams of antibiotics used (Defined Daily Dose, DDD)?</td>
</tr>
<tr>
<td>H. By direct expenditure for antibiotics (purchasing costs)?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reporting information to staff on improving antibiotic use and resistance</th>
<th>Measure performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Does you stewardship program share facility-specific reports on antibiotic use with prescribers?</td>
<td>Yes</td>
</tr>
<tr>
<td>B. Has a current antibiogram been distributed to prescribers at your facility?</td>
<td>Yes</td>
</tr>
<tr>
<td>C. Do prescribers ever receive direct, personalized communication about how they can improve their antibiotic prescribing?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education</th>
<th>Measure performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Does your stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescribing?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
ASP Guidelines

• Guidelines for the Development of an Institutional ASP - developed by professional societies (IDSA/SHEA)
  – *CID* 2007
  – Team, elements of an ASP including strategies and measurement, research priorities and future directions
SHEA/IDSA/PIDS ASP Policy Statement

• Publication date: April 2012 *Infection Control Hospital Epidemiology*

• Recommend CMS require all healthcare institutions (inpatient and outpatient settings) develop ASPs
  – According to IDSA/SHEA guidelines
  – Creation of a multidisciplinary team
  – Closed/restricted antimicrobial formulary
  – Institutional guidelines for common infectious syndromes

• Recommend CMS require healthcare institutions develop ASPs
  – Implement interventions to improve antimicrobial use to:
    o Reduce redundant treatment regimens, reduce treatment of non-bacterial syndromes, narrow spectrum for culture-confirmed organisms
  – Periodic distribution of facility-specific antibiograms
  – Processes to measure and monitor antimicrobial use at each institution

• Education must be provided to clinicians and clinicians in-training
New ASP Guideline

• Joint IDSA/SHEA Guideline on grading the ASP evidence
  – To be presented at ID Week 2014

• White paper developed by SHEA on core competencies of ASPs
www.stewardship-education.org

- Joint website of professional societies including IDSA, SHEA, PIDS, SIDP, ASHP, NFID
- Up-to-date information on education, policy and research
- One educational offering: https://www.coursera.org/course/antimicrobial
  - Free Stanford University online CME
  - >20,000 participants
President Obama’s Council of Advisors and Technology

• Assembled antimicrobial resistance working group in December 2013
• Recommendations on Antimicrobial Stewardship in human medicine, use of antibiotics in agriculture, international surveillance, developing new antimicrobials and diagnostics, future research
  – Forthcoming
Antimicrobial Stewardship Progress Internationally
Antimicrobial resistance is a threat to global health security endangering prevention and treatment of infections.

Underlying driving concern is the impact of resistance on health and the potential for an unwanted post-antibiotic era.

- Factors go beyond the health sector demanding a global response.

http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf?ua=1
Encourage member states:

- To increase political awareness, engagement and leadership to accelerate efforts to secure access to effective antimicrobials and use them responsibly
- To improve, among all relevant stakeholders, awareness of:
  - Threat posed by antimicrobial resistance
  - Need for responsible use of antibiotics
  - Importance of infection prevention and control measures

World Health Assembly May 2014
Resolution

• Encourage member states:
  – To support research and development to:
    o Combat antimicrobial resistance and promote responsible use of antimicrobial medicines
    o Develop practical and feasible approaches for extending the lifespan of antimicrobial medicines
    o Encourage the development of novel diagnostics and antimicrobial medicines

Conclusions
Antimicrobial Resistance and Stewardship

• Antimicrobial resistance is a recognized public health threat

• Public health organizations - in US and internationally are focused on Antimicrobial Stewardship
  – CDC, WHO

• CDC recommends every US hospital adopt an ASP
Antimicrobial Stewardship is a Public Health Priority

• Antimicrobial resistance is a complex problem driven by many interconnected factors
  – Single, isolated interventions have little impact
  – Coordinated action is required to minimize emergence and spread of antimicrobial resistance

• How can CLSI and the microbiology community promote Antimicrobial Stewardship?
Join SHEA Today - www.shea-online.org

Select Member Benefits:

• Subscription to *Infection Control and Hospital Epidemiology* (ICHE).

• Monthly e-newsletter

• Member rates for meetings

• Engagement in guideline, policy and research development

• And more!

Questions? Email info@shea-online.org
Questions/Comments

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World Alliance Against Antibiotic Resistance (WAAAR)

- Nonprofit organization
- 700+ individuals from 55 different countries representing key stakeholders (MDs, veterinarians, pharmacists, evolutionary biologists, ecologists, environmentalists) including patients’ advocacy groups.
- Receives support from >100 professional groups throughout the world
WAAAR

• Primary goal is to raise awareness about the urgency and magnitude of the threat and to promote an international dialogue foreffective responses.
  – Target antibiotic prescribers, politicians and policy-makers, patient safety and advocacy groups, pharmaceutical industry, international health organizations, and the general population.

• Individual actions, no matter how well intended, are doomed to failure unless there is an international dialogue, a common sense of purpose, and broad consensus on how best to proceed.
WAAAR Declaration June 23, 2014

Calls for Ten Actions:

1) Promote awareness of all stakeholders including public on threat of antimicrobial resistance

2) Organized financed approach to containment of antimicrobial resistance in each country

3) Continuous access to antibiotics of assured quality in all countries

4) Integrated surveillance of antibiotic resistance and antibiotic use
WAAAR Declaration June 23, 2014

Calls for Ten Actions:

5) Use of diagnostic tests

6) Antibiotic Stewardship - prudent, controlled and monitored approaches to the use of antibiotics
   – In humans
   – In animals
   – Progressive elimination of “over-the-counter” access to antibiotics for humans or animals
WAAAR Advocates for the Following Ten Actions:

6) Antibiotic stewardship - prudent, controlled and monitored approaches to the use of antibiotics
   - Ban use of antibiotics as growth promotion in food animals, and exceptional use in prophylaxis.
   - Rational use of metaphylaxis and of animal treatment
   - Limitation of the use of critically important antibiotics in humans and animals (eg, carbapenems)
WAAAR Advocates for the Following Ten Actions:

7) Educational efforts to change
8) Containment of bacterial infection and prevention of transmission
9) Increased support towards basic and applied research and development of new antibiotics
10) Request for UNESCO to include the "concept of antibiotic" in the list of the intangible cultural heritage
   - Non-renewable and endangered resource