Antibiotic Stewardship
Why We Must
How We Can

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Nothing to Disclose

Why We Have to Improve
Antibiotic Use

- Antibiotics are unlike any other drug, in that the use of the agent in one patient can compromise its efficacy in another.
- A lot of in-patient antibiotic prescriptions are unnecessary or sub-optimal.
- We are running out of antibiotics.
- We won't get new ones soon.
- Antibiotic overuse contributes to huge threats to the safety of our patients.
Antibiotic misuse adversely impacts patients - *C. difficile*

- Antibiotic exposure is the single most important risk factor for the development of *Clostridium difficile*.
  - Antibiotic exposure increases risk of CDAD by 7-10 fold for up to 30 days and 3 fold for the next 60 days. 1
  - Up to 85% of patients with CDAD have antibiotic exposure in the 28 days before infection. 2


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**Clostridium difficile Infections (CDIs) and Deaths Reach and Remain at Historic Highs**

- **CDI hospitalizations**
  - Increased 3-fold 2000-2009
  - 250,000 per year
- **Deaths linked to CDI**
  - 14,000 in 2007
- **$1 billion in medical costs**
  - CDIs in hospital patients only
- **Epidemic strain**
  - Causes more cases and severity
  - Strong link to quinolone exposure

  Hall AJ et al. Presentation at the 49th Annual IDSA Meeting;

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Antibiotic misuse adversely impacts patients - adverse events

- In 2008, there were 142,000 visits to emergency departments for adverse events attributed to antibiotics.
Antibiotic exposure increases the risks of resistance

<table>
<thead>
<tr>
<th>Pathogen and Antibiotic Exposure</th>
<th>Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbapenem Resistant Enterobacteriaceae and Carbapenems</td>
<td>15 fold 1</td>
</tr>
<tr>
<td>ESBL producing organisms and Cephalosporins</td>
<td>6-29 fold 3,4</td>
</tr>
</tbody>
</table>

Susceptibility Profile of Typical CRE

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Interpretation</th>
<th>Antimicrobial</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>I</td>
<td>Chloramphenicol</td>
<td>R</td>
</tr>
<tr>
<td>Amoxiclavine</td>
<td>R</td>
<td>Ciprofloxacin</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>R</td>
<td>Ertapenem</td>
<td>R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>R</td>
<td>Gentamicin</td>
<td>R</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>R</td>
<td>Imipenem</td>
<td>R</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>R</td>
<td>Meropenem</td>
<td>R</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>R</td>
<td>Piperacillin/Tazobactam</td>
<td>R</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>R</td>
<td>Teicoplanin</td>
<td>R</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Cefepime</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Cefalosporin</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>R</td>
<td>Tobramycin</td>
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<td>R</td>
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<tr>
<td>Cefepime</td>
<td>R</td>
<td>Tobramycin</td>
<td>R</td>
</tr>
</tbody>
</table>

Most Common Reasons for Unnecessary Days of Therapy

576 (30%) of 1941 days of antimicrobial therapy deemed unnecessary

- Duration of Therapy Longer than Necessary: 192 days
- Noninfectious or Nonbacterial Syndrome: 187 days
- Treatment of Colonization or Contamination: 94 days
Assessment of Treatment of UTI in 36 Hospitals

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No.</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated for UTI present on admission, without indwelling catheter</td>
<td>111</td>
<td>—</td>
</tr>
<tr>
<td>Urine culture was not ordered, although standard practice before treatment</td>
<td>18</td>
<td>(16.2)</td>
</tr>
<tr>
<td>Urine culture was positive, but no documented symptoms were present</td>
<td>23</td>
<td>(20.7)</td>
</tr>
<tr>
<td>Urine culture was negative, and no documented symptoms were present</td>
<td>3</td>
<td>(2.7 )</td>
</tr>
<tr>
<td><strong>No. of patients with potential for improvement in prescribing</strong></td>
<td>44</td>
<td>(39.6)</td>
</tr>
</tbody>
</table>

Assessment of Vancomycin Use in 36 Hospitals

<table>
<thead>
<tr>
<th>Patients treated with intravenous vancomycin</th>
<th>185</th>
<th>—</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diagnostic culture obtained around antibiotic initiation, although standard practice with most infections</td>
<td>17</td>
<td>(9.2 )</td>
</tr>
<tr>
<td>Diagnostic culture showed no Gram-positive bacterial growth, but patient still treated for long duration (&gt;3 days) (excludes presumed SSTI, which often can be culture negative)</td>
<td>40</td>
<td>(21.6)</td>
</tr>
<tr>
<td>Diagnostic culture grew only oxacillin-susceptible Staphylococcus aureus, but patient still treated for long duration (&gt;3 days) (likely missed opportunity to switch antibiotic based on culture result)</td>
<td>9</td>
<td>(4.9 )</td>
</tr>
<tr>
<td><strong>No. of patients with potential for improvement in prescribing</strong></td>
<td>66</td>
<td>(35.7)</td>
</tr>
</tbody>
</table>

The Pipeline is Dry

- Antibiotic development has contracted dramatically in recent years.
- Essentially no truly novel antibiotics on the horizon.
- Even with huge investments, it will likely be many years before we have new antibiotics.

European Centre for Disease Prevention and Control/European Medicines Agency Joint Technical Report
Stewardship To Reduce \textit{C. difficile} Infection

- Stewardship program formed at a community hospital to address high \textit{C. difficile} rates.
- Focused on post-prescription review of broad spectrum agents (but not quinolones)
- 25.4\% decrease in targeted antibiotics
  - 216 DDD/1000 patient days to 161.
- More than three fold reduction in \textit{C. difficile} infections (3.7\% to 0.9\%).

\textit{Am J Infect Control} 2013;41:145

Targeted antibiotic consumption and nosocomial \textit{C. difficile} disease

\textit{Tertiary care hospital; Quebec, 2003-2006}


Antibiotic Stewardship to Combat \textit{C. difficile}

- 2014 meta-analysis on the impact of stewardship on \textit{C. difficile} included 16 studies.
- Stewardship programs were significantly protective against \textit{C. difficile}
  - Pooled risk ratio 0.48; 95\% CI: 0.38, 0.62
- Restrictive interventions were most effective.
- Protection especially strong in geriatric settings.

Impact of Reductions in Antibiotic Prescribing on C. difficile in England

![Graph showing the impact of reductions in antibiotic prescribing on C. difficile in England.](https://example.com/graph)

https://www.hpa.org.uk/web/HPAweb&Page&HPAwebAutoListName/Page/1179745282388

P. aeruginosa susceptibilities before and after implementation of antibiotic restrictions (CID 1997;25:230)

![Bar graph showing P. aeruginosa susceptibilities before and after antibiotic restrictions.](https://example.com/bar_graph)


Stewardship optimizes patient safety: decreased patient-level resistance

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Cipro</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>3 days</td>
<td>10 days</td>
</tr>
<tr>
<td>LOS ICU</td>
<td>9 days</td>
<td>15 days</td>
</tr>
</tbody>
</table>

Antibiotic resistance/superinfection

14% vs 38%

Study terminated early because attending physicians began to treat standard care group with 3 days of therapy.
Total costs of parenteral antibiotics at 14 hospitals

Antimicrobial Costs after Stewardship Program Ends

Clinical outcomes better with antimicrobial management program

Clinical outcomes better with antimicrobial management program

Appropriate Cure Failure

AMP = Antibiotic Management Program

UP = Usual Practice

**What is “Antibiotic Stewardship”**

- Ensuring that every patient gets:
  - An antibiotic only when one is needed
  - The right agent
  - At the right dose
  - For the right duration

**Goals of Stewardship**

- The primary goal of antibiotic stewardship is improving patient safety.
- Reducing antibiotic use and saving money are NOT the primary goals of antibiotic stewardship.
- They simply happen to be desirable side effects.

**Changing the Way We Think About Antibiotic Stewardship**

- A lesson learned from experience with infection control.
- Infection prevention works best when it’s viewed as everyone’s responsibility with healthcare epidemiology and infection control as a resource to help.
- Stewardship should be the same- it’s not something someone does “to you” or “for you.”
Antibiotic Stewardship and Infection Control

• Both require changes in provider behavior.
• Both struggle to engage providers.
• Both hampered by some limitations of the evidence base.
  – Essentially all stewardship studies are single center
• Both have a number of proven interventions that are not being fully implemented.

Advantages for Infection Control

• Objective (ok, relatively) outcomes to monitor-infection rates.
• Easy to interpret the outcome measure- lower is better.
• Slowly growing evidence base from large, multi-center trials (STAR-ICU, REDUCE MRSA)
• It’s required.

Infection Control Requirements

• An infection control program is part of Center for Medicare and Medicaid Services (CMS) Conditions of Participation for acute care hospitals.
• Infection control requirements in long term care as well.
• Many (and growing) reporting requirements for healthcare associated infections with payment implications.
Infection Control Advantages

- All acute care hospitals have an infection control program that get financial support from the facility.
  - Some better supported than others.
- There is a large group of highly trained experts around the country (and world) who focus on preventing infections.
  - You are present in almost every hospital.

Challenges for Antibiotic Stewardship

- Some outcomes are subjective and very hard to assess: infection cure rates.
- Some outcomes are easier to assess, but very multi-factorial: *C. difficile* rates, resistance.
- Some outcomes can be hard to interpret: antibiotic use: is lower always better? How much is too much or too little?
- Some outcomes are irrelevant to providers: costs.

Challenges for Antibiotic Stewardship

- Very limited evidence base.
  - Only one multi-center stewardship intervention trial that I know of.
- A lot of the single center studies have antibiotic costs as the primary outcome.
Challenges for Antibiotic Stewardship

• Currently, only the state of California has a requirement that hospitals have an antibiotic stewardship program.
• No federal requirements and no accreditation standards.
• Fewer than half of hospitals have programs. — Those programs are constantly under pressure to “show value”
• Very limited pool of stewardship experts.

Re-Thinking the Model

• The goal of the stewardship program is not to dictate antibiotic choices.
• It’s to ensure that there are systems and support to help every provider use antibiotics optimally.
• For this to work, every provider has to play a role in stewardship.

Changing the Way We Think About Antibiotic Stewardship

• We need other groups to assume leadership roles in stewardship:
  – Hospitalists- pneumonia, urinary tract infections, skin and soft tissue infections
  – Intensivists- antibiotic use in critical care
  – Surgeons- surgical prophylaxis and surgical site infections
• We also need to find more ways for stewardship programs to partner with infection control.
Supporting Stewardship

- Experience with preventing infections in hospitals also demonstrates that the efforts of front line providers are more effective when they are supported by a program with specific expertise.
- For antibiotic use, this is an antibiotic stewardship program.

Recommendations for Antibiotic Stewardship Programs

- The proven benefits of antibiotic stewardship programs has led to formal recommendations for their implementation:
  - “CDC recommends that all hospitals implement an antibiotic stewardship program.”
  - American Hospital Association also recommends antibiotic stewardship programs as a “Top 5” intervention for hospitals.

How Do We Make It Happen?

- Hospitals don’t all look the same, and neither do stewardship programs.
- There must be flexibility in how programs are implemented.
- But, there are certain key elements that have been strongly associated with success.
Core Elements for Antibiotic Stewardship Programs

- Leadership commitment from administration
- Single leader responsible for outcomes
- Single pharmacy leader
- Antibiotic use tracking
- Regular reporting on antibiotic use and resistance
- Educating providers on use and resistance
- Specific improvement interventions

Leadership Commitment

- There should be a formal expression of support for the stewardship program from the facility administration.
- Leadership must ensure that staff have time to implement the stewardship program.
- Financial support helps—alot. But is not always imperative.

Program Leadership

- There should be a designated leader of the antibiotic stewardship program.
- Physicians have proven very effective in this role.
  - Prescribing is a medical staff function
- Pharmacy leadership is also critical.
- Leadership by committee is not as effective.
Antibiotic Use Tracking

• Important to monitor antibiotic use to:
  – Find potential opportunities for improvement
  – Assess the effectiveness of stewardship efforts
• Also helpful to monitor process and outcome measures for antibiotic use
  – How often are treatment recommendations followed?
  – How much antibiotics are we using and where?
  – What are C. difficile rates?

Reporting and Education

• Stewardship programs need to feed data back to the hospital on:
  • Antibiotic use - process and outcome measures
  • C. difficile
  • Issues with resistance

Interventions to Improve Use

• Ultimately, specific interventions to improve the use of antibiotics are where the rubber meets the road for stewardship programs.
Key Moments for Antibiotic Stewardship

- There are certain moments when interventions are likely to be both well received by providers and helpful in improving patient outcomes.
- We should identify and take advantage of them.

**Key Moments for Antibiotic Stewardship**

- Patients with *C. difficile*
- Patients with positive blood cultures
- Patients being given IV antibiotics at discharge
- Patients on unnecessarily duplicative therapy.
- Patients being treated for:
  - Community acquired pneumonia (CAP)
  - Urinary tract infection (UTI)
  - Skin and soft tissue infections
- Patients who have gotten 3 days of therapy.

Measuring Antibiotic Use

- Measurement of antibiotic use remains one of the major challenges in stewardship.
  - You can’t improve something you can’t measure
- This is a challenge both at the facility level and at the regional and national level.
Addressing the Challenge
- As CDC began considering options for ways to improve the measurement of antibiotic use, we wanted something that would be useful to individual facilities wanting to assess the impact of stewardship intervention and would provide a bigger picture on antibiotic use.
- The Antibiotic Use Module of the National Healthcare Safety Network was the result.

NHSN Antibiotic Use Module
- Launched in 2012.
- Allows facilities to electronically submit data on antibiotic use to NHSN through their hospital pharmacy computer system.
  - House-wide and unit specific use

Flexibility of the AU Module
- The data can be used:
  - By facilities to monitor interventions on single units or facility wide
  - To collect aggregate information on antibiotic use at a regional and national level
  - Eventually, to create antibiotic use benchmarks.
Example Use of Data for a Hospital (AU Analysis Output Options):
Line List Rate Tables, by Location

<table>
<thead>
<tr>
<th>Location</th>
<th>ABX Days</th>
<th>Sur</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MICU</td>
<td>4000</td>
<td>1000</td>
<td>Excessive</td>
</tr>
<tr>
<td>SICU</td>
<td>2000</td>
<td>2000</td>
<td>Consistent</td>
</tr>
<tr>
<td>Medical Ward</td>
<td>3000</td>
<td>4000</td>
<td>Lower Use</td>
</tr>
<tr>
<td>Surgical Ward</td>
<td>1000</td>
<td>3000</td>
<td>Much Lower</td>
</tr>
<tr>
<td>Hospital</td>
<td>170,250</td>
<td>171,000</td>
<td>Consistent</td>
</tr>
</tbody>
</table>

Example Data Only; SUR is a ratio of actual usage patterns compared to expected patterns given the patient population defined by the location (e.g., MICU, SICU, etc)

Challenges with the AU Module
- Data submission is totally electronic.
- Electronic submission requires that a facility have both electronic medication administration system AND a pharmacy system that can send data to NHSN.
- This is the future, but we’re not there yet.
Antibiotic Use Benchmarking

- Infection rate benchmarking has proved very helpful in driving improvements.
  - No one wants to be worse than their peers
- We’d like to do the same for antibiotic use.
  - “Standardized Use Ratio”
- NHSN AU module will allow that, but we have a lot to work on risk adjustment (and we need a lot more facilities to enroll)

Assessing “Appropriate” Antibiotic Use

- If our ultimate goal is to improve antibiotic use, we need some way to measure that.
- It can be very hard to determine if antibiotic use is “appropriate” or not.
  - Mostly done as part of research studies where they have ID clinicians review charts.
- We want something that would be more broadly applicable.

Assessing Appropriate Antibiotic Use

- CDC assembled a group of experts to develop and refine some forms that could be used by any clinician to assess the appropriateness of antibiotic use.
- Focused on a few conditions:
  - Community acquired pneumonia
  - Urinary tract infection
  - Use of agents for resistant gram positives
  - General antibiotic use
Assessing Appropriate Antibiotic Use

- Forms are available on the Get Smart for Healthcare website.
- They can be modified to meet the needs of your facility.
- Modified versions of the forms were used for the national pilot assessment of appropriate use reported in the MMWR Vital Signs on antibiotic stewardship (March 4, 2014).

Antibiotic Stewardship Requirements

- There is considerable and growing support for antibiotic stewardship to be present in every US hospital:
  - CDC and the American Hospital Association have both called for this.
- There is also growing support for antibiotic stewardship to become a federal requirement through Conditions of Participation.

Be Careful What You Wish For

- Prescriptive mandates have benefits and drawbacks.
- You get universal compliance—but is this compliance just on paper?
- Would a mandate lead facilities to do the minimum to comply and end up hurting some really strong programs?
- How do you monitor success?
- What about other unintended consequences?
Solutions to These Challenges

• We can train hospital surveyors on what to look for to make sure that stewardship efforts are most effective in actually improving use.
  – CA has growing experience with this.
• We need to monitor antibiotic use and also come up with ways to look at treatment outcomes to look for potential adverse consequences.

Antibiotic Stewardship and Infection Control

• Are logical partners and already closely linked in most hospitals.
• We need to advance this partnership.
• APIC and SHEA have identified several key opportunities for collaboration.

Opportunities for Partnership

• Identifying MDROs and monitoring trends.
• Supporting efforts to prevent the spread of MDROs and C. difficile (hand hygiene).
• Analyzing and reporting surveillance data.
• Education
• Developing treatment algorithms and other protocols to improve antibiotic use.
But How? And Is That All?

- I think there’s more we can do to enhance the partnership between infection control and antibiotic stewardship.
- We need to work to develop more concrete actions and ones that are strongly synergistic.
- I think we can and David Calfee look forward to discussing this with you at 3pm today during the antibiotic stewardship “Ask the Expert” session.(Room 210 C&D).

Some is not a number
Soon is not a time

- All hospitals should have an antibiotic stewardship program.
- All providers must engage in antibiotic stewardship efforts.
- Antibiotic stewardship and infection control are perfect partners.
- We need to develop even more, and more specific, ways to work together.
- We need to do it now.