CONFLICT OF INTEREST DISCLOSURES

The views and opinions expressed in this series are those of the speakers and do not reflect the official policy or position of any agency of the US or NC government or UNC.

Our speakers have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:

- Dr. Kistler served as a consultant for Base10, Inc on their UTI embedded clinical support tool and received funding from Pfizer to study pneumococcal carriage.
- Dr. Willis has performed contracted research with: Pfizer (pediatric nirmatrelvir-ritonavir and maternal RSV vaccine), Novavax (pediatric COVID-19 vaccine), and Merck (monoclonal antibody for RSV prevention)
- Ms. Doughman owns individual Gilead stock.

The speakers do not intend to discuss an unapproved/investigative use of a commercial product/device in this series, and all COI have been mitigated.

These slides contain materials from a variety of colleagues, as well as the CDC, WHO, AHRQ, etc.
INTRODUCTIONS

Please put your name, hospital, and location in the chat!
CME AND CE CREDIT

- CME & CE for participants
  - Attendance and active participation per learning session
  - Click the link in the chat during the session to document your attendance
  - Complete surveys as requested
NC CLASP: YEAR TWO

In-depth discussion topics include:

- Optimal antibiotic therapy for common conditions
  - What’s in guidelines and why?
- Consequences of antibiotic overuse
- Penicillin Allergies
- Antibiotic overuse by setting:
  - Primary care, urgent care, ED
  - Dentistry
  - Rural vs urban vs suburban
- Implementing Stewardship
  - QI methodology
  - Coaching

11 learning sessions September 2023-May/June 2024

CE included: CME, RN, Pharmacist (ACPE)

Two in-person conferences
OUTLINE OF TODAY’S SESSION

- Review from last session
- Overview of harms caused by antibiotics in outpatient setting
  - *C. difficile* infections
  - Toxicity
  - Antibiotic resistance
- Breakout session: Antibiotic Harms
- Homework and Wrap-Up
REVIEW: SMART AIMS

- **Specific**
  - Have a clear goal in mind.
  - NOT: “Use fewer fluoroquinolones.”
  - “Reduce X by 25%.” “Increase Y by 50%.” “Achieve 90% compliance.”

- **Measurable**
  - Can’t be specific if you can’t measure it

- **Attainable**
  - Is there a strategy that’s likely to work?
  - Don’t set your goal too high

- **Relevant**
  - “If we achieve our aim, will our patients be safer/have better outcomes?”
  - Make sure your aim affects a lot of patients (or makes a big difference for a small number)

- **Time-bound**
  - Set a deadline
  - Work backward from there
HOMEWORK REVIEW

» Develop your target into a SMART Aim

» By [6/30/24], we will [reduce] [use of antibiotics for X] by [X%], compared to [baseline].

» How will you measure progress toward your goal?

» What will be the primary action you will take to achieve this goal?
Harm Caused by Antibiotics
ANTIMICROBIAL STEWARDSHIP GOALS

Public Health Significance
1. Prevent emergence of antimicrobial resistance
2. Prevent *C. difficile* infection
3. Prevent antibiotic-related toxicity
4. (Contain healthcare costs)
ANTIMICROBIAL STEWARDSHIP GOALS

Measuring Impact - System

1. \(C.\) difficile
2. Costs
3. Toxicity
4. Resistance
ANTIMICROBIAL STEWARDSHIP GOALS

Considering Impact - Patient

1. Cost
2. Toxicity
3. *C. difficile*
4. Resistance
MOTIVATION

- Preventing antimicrobial resistance (AMR) is the key long-term goal
- Linking individual actions to later AMR is extremely difficult
- More immediate risks and costs are likely more salient to the provider and patient
  - Acknowledging those potential harms and mitigating them can achieve multiple goals
C. DIFFICILE INFECTION

Steps to infection
1. Colonization with toxigenic C. difficile strain
   - Proton-pump inhibitors increase risk of colonization
2. Disruption of microbiome – usually antibiotics
   - Also opiates, chemotherapy

Antibiotics with greatest risk:
- Carbapenems, broad cephalosporins, clindamycin, fluoroquinolones
RISK FACTORS FOR C. DIFFICILE INFECTION

- Antibiotics!
  - Even surgical prophylaxis has a measurable effect
- Healthcare exposure (long-term care, acute care)
- Immunocompromised status
- Advanced age
- Other drugs: opiates, PPIs, chemotherapy
COMMUNITY-ACQUIRED *C. DIFFICILE* INFECTION

- ~1/3 of cases are community-associated (CA-CDI)
  - Majority of CDI cases in children and young adults are CA-CDI
- ~7% of CA-CDI cases recur
- Mortality: 0.7%
  - Vs ~9% for HA-CDI

*Clostridioides difficile*** is related to antibiotic use and antibiotic resistance:

- **223,900** cases
- **12,800** deaths


Association Between Outpatient Antibiotic Prescribing Practices and Community-Associated Clostridium difficile Infection

Raymund Dantes,1 Yi Mu,1 Lauri A. Hicks,1 Jessica Cohen,1,2 Wendy Bamberg,3 Zintars G. Baldavs,4 Ghinwa Dumyani,5 Monica M. Farley,5,7 Stacy Holzbauer,8 James Meek,5 Erin Phipps,10 Lucy Wilson,11,12 Lisa G. Winston,11,14 L. Clifford McDonald,1 and Fernanda C. Loasa1

<table>
<thead>
<tr>
<th>10% Reduction in:</th>
<th>Would reduce CA-CDI by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillins</td>
<td>12.1%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>7.6%</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>7.5%</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>4.8%</td>
</tr>
<tr>
<td>All antibiotic prescribing</td>
<td>16.8%</td>
</tr>
</tbody>
</table>
ANTIBIOTIC RESISTANCE
RISK FACTORS FOR ANTIBIOTIC RESISTANCE

- **Antibiotic exposure**
  - Especially recent and/or long-term antibiotic exposure (e.g., UTI prophylaxis)
  - Usually difficult to link this directly

- **Healthcare exposure**

- **Household contact with at-risk individuals**

- **Travel to certain international regions**

- **Immunocompromised status**

- **Conditions causing frequent antibiotic exposure:**
  - E.g., recurrent UTIs due to urologic conditions, tracheostomy dependence
Antibiotic Resistance of *Escherichia coli* in United States

![Graph showing the percentage of resistant invasive isolates from 1999 to 2014 for Cephalosporins (3rd gen) and Fluoroquinolones. The graph indicates an increase in resistance over time.](https://example.com/antibiotic-resistance-graph)

- **Cephalosporins (3rd gen)**
- **Fluoroquinolones**

Center for Disease Dynamics, Economics & Policy (cddep.org)
ANTIBIOTIC-RELATED TOXICITY
US Emergency Department Visits for Outpatient Adverse Drug Events, 2013-2014

Shehab, et al., *JAMA* 2016

- ED-based surveillance, sampling nationwide
- Antimicrobials caused ~16% of ED visits for adverse drug events (ADEs)
  - #2, between anticoagulant/antiplatelet drugs and diabetes drugs
- 7% of cases required inpatient admission (14.5% of quinolone-related events)
Of all ED visits for adverse drug events, antibiotics accounted for:
- 56.4% of visits in children < 6
- 31.8% of visits in children 6-19

In children, 6 of the top 7 drugs causing an ED visit were antibiotics (ibuprofen #3)
Major Antibiotic-Associated AEs (Short list)

- IgE-mediated allergic reactions
  - Urticaria, wheezing $\rightarrow$ anaphylaxis
  - Most common with penicillins, then sulfonamides
- Stevens-Johnson Syndrome/TEN
  - TMP-SMX most commonly
- QT Prolongation
  - Macrolides, fluoroquinolones
- Fluoroquinolones:
  - Various neurologic effects, tendinopathy, aortic aneurysm
ANTIBIOTICS ARE UNIQUE

- Most outpatient antibiotics are:
  - Safe
  - Cheap
  - Effective (when indicated)

BUT...

- When else do we prescribe medicines for conditions we’re not even sure the patient has?
BREAKOUT SESSION

- What immediate harms have you seen with antibiotic prescribing?

- When discussing avoidance of unnecessary antibiotics, what messages resonate best with patients? Providers?
  - Side effects? Antimicrobial resistance? C-diff? Other ideas?
HOMEWORK

- If you already have a SMART Aim:
  - What data will you need to achieve your SMART Aim? Can you get that data?

- If you do not have a SMART Aim, make one!
  - For example: “By [6/30/24], we will [reduce] [use of antibiotics for X] by [X%], compared to [baseline].”
  - How will you measure progress toward your goal?
  - What will be the primary action you will take to achieve this goal?
Antibiotic Stewardship Conference

11.15.23 | 9 am - 4 pm
The Friday Conference Center
Chapel Hill, NC

More information at spice.unc.edu/ncclasp/
All the information from today’s session will be on our website https://spice.unc.edu/ncclasp/
RESOURCES

- CDC Antimicrobial Resistance Threat Report, 2019:

- SMART Aims
  - CDC Guide with template