North Carolina SPICE
Statewide Program for Infection Control & Epidemiology

NC CLASP OUTPATIENT STEWARDSHIP
YEAR 2, SESSION 2

Commonly Used Outpatient Antibiotics

September 27, 2023

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. 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)
- 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, clinic, and location in the chat!

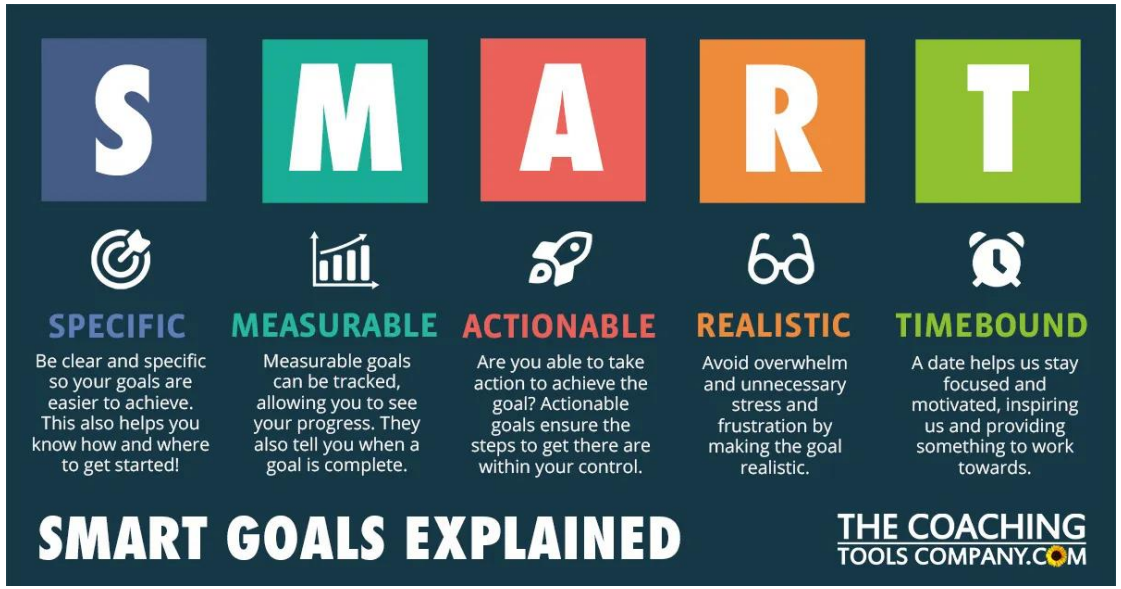
CME AND CE CREDIT

- 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

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?



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

QUICK REVIEW: ANTIBIOTIC-RELATED HARMS

- *C. difficile* infection
- Antimicrobial resistance
- Antibiotic-related toxicities

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

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10% Reduction in:	Would reduce CA-CDI by:
Penicillins	12.1%
Clindamycin	7.6%
Cephalosporins	7.5%
Fluoroquinolones	4.8%
All antibiotic prescribing	**16.8%**

Highest-risk Antibiotics:

- Carbapenems
- **Broad cephalosporins**
- **Clindamycin**
- **Fluoroquinolones**

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

Major Antibiotic-Associated AEs (Short list)

- IgE-mediated allergic reactions
  - Urticaria, wheezing → 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

BREAKOUT SESSION

- Are there antibiotics that you think are overused in your clinic setting? Which ones?

- If you needed expertise on antibiotic selection, what resources are available? Is this a gap in your practice?

THREE WAYS TO OVERUSE ANTIBIOTICS

1. Prescribing antibiotics when none are indicated

2. Using an antibiotic that is too broad for the infection (or otherwise suboptimal)

3. Using an excessive duration

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COMMONLY USED OUTPATIENT ANTIBIOTICS

BACTERIAL CAUSES OF COMMON INFECTIONS

- Pharyngitis: Group A Strep
  - Most episodes are viral!
- Acute otitis media, sinusitis, and community-acquired pneumonia:
  - Pneumococcus >> *H. influenzae* and *Moraxella catarrhalis*
  - Atypical pneumonia: *Mycoplasma pneumoniae*
- COPD Exacerbations: viruses most common
  - *H. influenzae*, *M. catarrhalis*, Pneumococcus

BACTERIAL CAUSES OF COMMON INFECTIONS

- Urinary tract infection:
  - *E. coli* >> other Gram-negative rods, *Enterococcus*
- Skin and soft-tissue infection:
  - Abscess: *S. aureus* >> Group A Strep
  - Cellulitis: Group A Strep > *S. aureus*
- Dental infections:
  - Oral anaerobes

BETA-LACTAM ANTIBIOTICS

- Penicillins, cephalosporins
- Tend to accumulate well at sites of infection:
  - Respiratory tract
  - Urinary tract (most in very high concentrations)
- Toxicity is pretty minimal
  - Diarrhea is fairly common
  - Allergy is the most common major issue
- Most are inexpensive, available in liquid, usually taste OK to good

AMOXICILLIN

Dosing/PK	Good levels with BID dosing
Toxicity	Minimal. Allergy is main concern
C-diff risk	Low
Guideline recommendations	First-line for: • Pediatric acute otitis media • Pediatric acute bacterial sinusitis (or amox-clav) • Streptococcal pharyngitis • Pediatric CAP, Adult CAP (if healthy)
Notes	Should be most commonly prescribed antibiotic, especially in pediatrics

~100% (Always active)
90-99% (Almost always active)
50-89% (Resistance more frequent)
<50% (Usually or always inactive)

Pneumococcus	*H. flu, Moraxella*	Atypicals
Group A Strep		Oral anaerobes
MSSA		MRSA
E. coli, K. pneumoniae		*Pseudomonas*

AMOXICILLIN-CLAVULANATE

Dosing/PK	Good levels with BID dosing
Toxicity	Diarrhea is common. Penicillin allergy
C-diff risk	Low-moderate
Guideline recommendations	First-line for: • Acute bacterial sinusitis • Adult CAP (if risk factors, with atypical coverage) • COPD exacerbation • Bite wound prophylaxis or treatment • Dental infections Second-line for: • Pediatric otitis media
Notes	Adds H-flu/Moraxella and anaerobic coverage to amox. Should be very commonly prescribed

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CEPHALEXIN (1ST GEN)

Dosing/PK	Short half-life: TID or QID dosing for most infections (BID for strep throat)
Toxicity	Quite well-tolerated
C-diff risk	Low
Guideline recommendations	First-line for: • Cellulitis and erysipelas • Abscesses with low risk for MRSA Also great for: nonsevere UTI Second-line for: • Streptococcal pharyngitis
Notes	High urinary concentrations allows treatment of most UTI due to *E. coli* and other Gram-negative enterics. No H-flu or *Moraxella* activity.

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CEFDINIR

Dosing/PK	Adequate levels with BID dosing. Daily dosing may be inadequate for pneumococcus. Only 10-20% urinary excretion.
Toxicity	Occasional diarrhea. Turns stools red.
C-diff risk	Moderate
Guideline recommendations	First-line for: nothing Second-line for: • Amox or amox-clav indications with penicillin allergy • UTI
Notes	Commonly overprescribed due to convenience. Poorer activity against pneumococcus than amoxicillin. **Cefpodoxime** is very similar, with BID dosing.

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NON-BETA-LACTAMS

AZITHROMYCIN

Dosing/PK	Long half-life → 5-day course. Poorly absorbed, minimal urinary excretion.
Toxicity	• Some N/V/D (weakly promotile) • QT prolongation: rare cardiovascular events • Hepatotoxicity (rare)
C-diff risk	Very low
Guideline recommendations	First-line for: • Adult CAP with risk factors – with amox-clav • COPD exacerbation • Pertussis Also good for: bacterial diarrhea Third-line for: streptococcal pharyngitis
Notes	Typically used for atypical coverage. For respiratory infections, fairly weak on its own. Pretty good for bacterial diarrhea.

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CLINDAMYCIN

Dosing/PK	TID dosing required. Excellent GI absorption. No urinary excretion. Suspension is famously "unpalatable."
Toxicity	• GI intolerance and diarrhea common • Esophagitis
C-diff risk	High
Guideline recommendations	Beta-lactam alternative for: • Dental infections • Streptococcal pharyngitis Can also be used for: • Skin and soft-tissue infections (but increasing *S. aureus* resistance)
Notes	Rising resistance in *S. aureus* limits empiric use.

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TRIMETHOPRIM-SULFAMETHOXAZOLE

Dosing/PK	BID dosing, good absorption, excellent distribution, good urine levels. Adjust if GFR <30.
Toxicity	• Rare/severe: Stevens-Johnson, neutropenia, anaphylaxis • Hyperkalemia, esp if renal dysfunction
C-diff risk	Low
Guideline recommendations	Good choice for: • Purulent skin and soft-tissue infection • UTI Many odd uses: *Pneumocystis*, *Stenotrophomonas*, *Burkholderia*, *Nocardia*
Notes	Still excellent for *S aureus*, including MRSA

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DOXYCYCLINE

Dosing/PK	BID dosing. 20% urinary excretion – not recommended for UTI
Toxicity	Common: pill esophagitis/gastritis (take with plenty of water) Teeth staining in children is rare with doxy May be teratogenic (rare with doxy)
C-diff risk	Low
Guideline recommendations	First-line for: -RMSF, Ehrlichiosis, Lyme -Chlamydia Second-line for: -Community-acquired pneumonia -Acute bacterial sinusitis -SSTI (usually + GAS coverage) -Syphilis
Notes	Effective for minor staphylococcal infections. Crucial for rickettsia. Various other indications. Gram-negative coverage unclear.

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FLUOROQUINOLONES

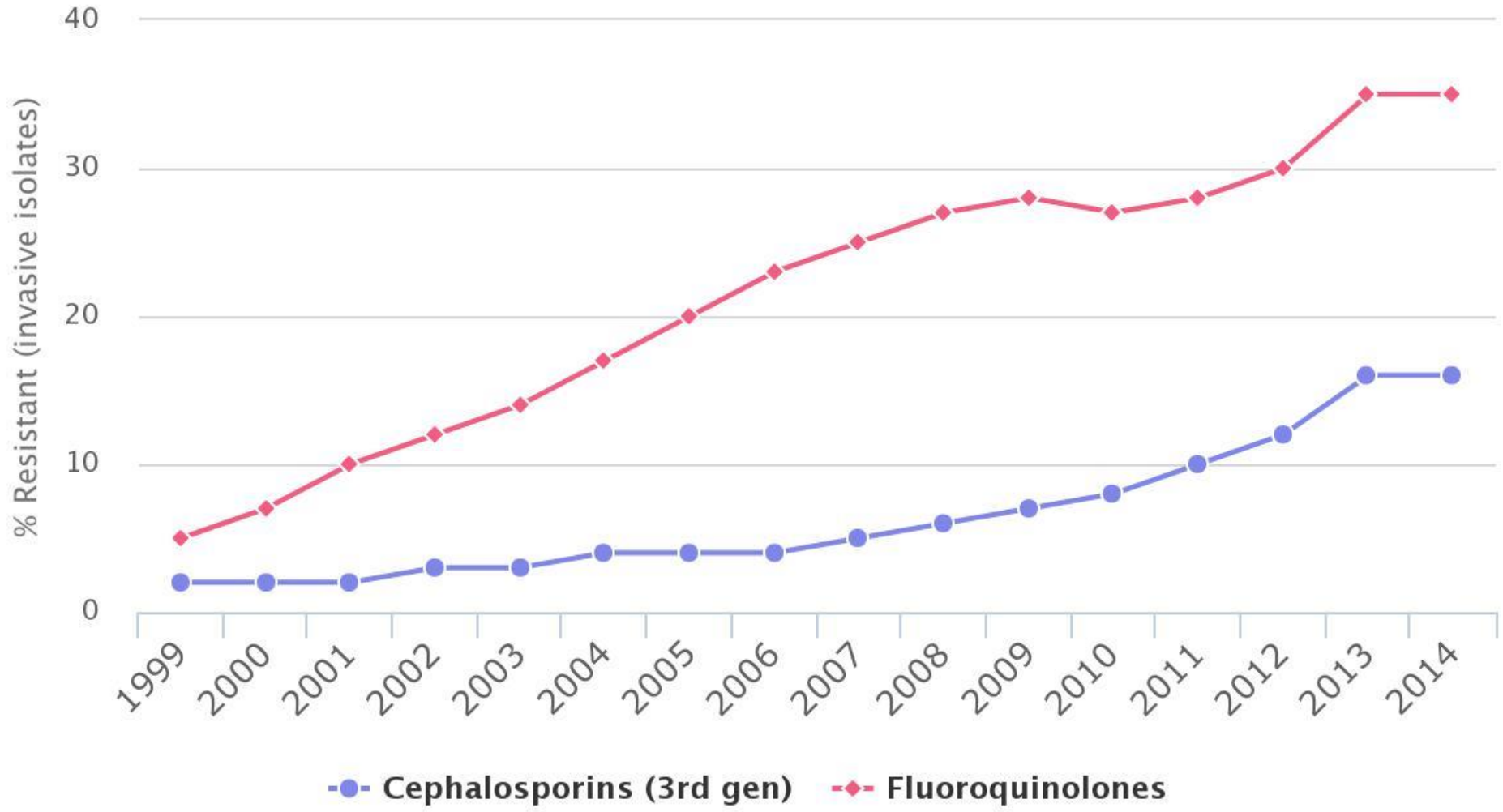
Advantages

- Excellent oral bioavailability and good half-life
- Favorable schedules:
  - Ciprofloxacin BID, levofloxacin daily
- Adverse effects uncommon
- Good distribution, great for urine

Disadvantages

- Rapid development of resistance
  - Typically via target mutation
  - *S. aureus* can develop resistance on therapy → AVOID
- High risk for *C. difficile*
- Toxicity is rare but can be severe:
  - QT prolongation
  - Aortic aneurysm or dissection
  - Tendinopathy, tendon rupture
  - Neurologic adverse effects – seizures, hallucinations, delirium, peripheral neuropathy

Antibiotic Resistance of *Escherichia coli* in United States



Center for Disease Dynamics, Economics & Policy (cddep.org)

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CIPROFLOXACIN

Dosing/PK	BID dosing, good absorption, good urine levels.
Toxicity	Several important toxicities (see above)
C-diff risk	**High**
Guideline recommendations	Good choice for: • UTI, especially pyelonephritis • Intra-abdominal infections • Wounds with *Pseudomonas* risk (aquatic, etc)
Notes	Increasing antibiotic resistance over time. Minimal Gram-positive activity.

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LEVOFLOXACIN

Dosing/PK	Daily dosing (over age 5), ~100% absorption
Toxicity	Several important toxicities (see above)
C-diff risk	**High**
Guideline recommendations	Third-line for: -Community-acquired pneumonia -Acute bacterial sinusitis (Beta-lactam based therapy preferred!)
Notes	Does most of what ciprofloxacin does, slightly less Gram-negative activity. Much better Gram-positive activity with good activity against respiratory pathogens. **Moxifloxacin** similar, better anaerobic activity but less Gram-negative activity.

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FUTURE SESSIONS

- Commonly encountered outpatient conditions
  - Which ones would you like to see highlighted? Please put them in the chat
  - Will review microbiology, guideline-recommended antibiotics and alternatives, dosing and duration
- Penicillin allergy and other special circumstances
- Goal: Provide you with the knowledge to make the best possible antibiotic choices, and to help colleagues do the same!

HOMEWORK

- After reviewing commonly used outpatient antibiotics, are there any that you think might be overused in your clinic setting? Or overused in your community? Which ones and for which situations?

SAVE THE DATE

Antibiotic Stewardship Conference

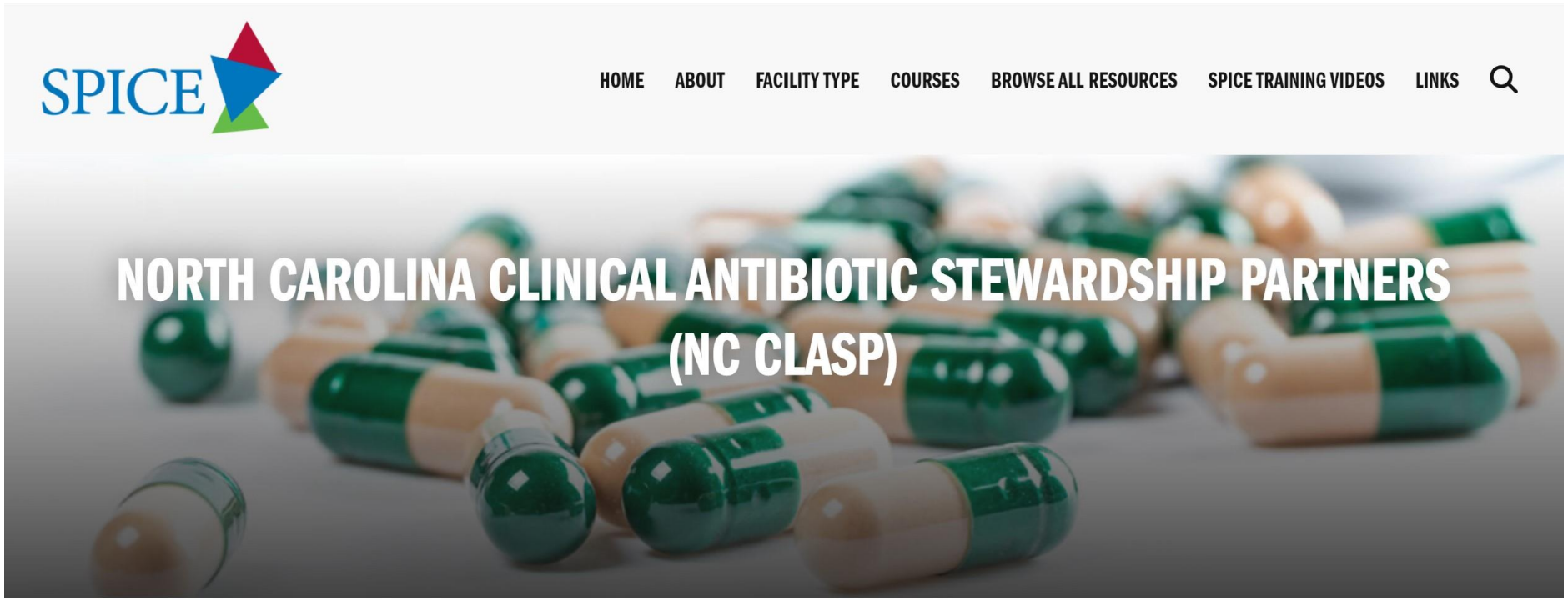
11.15.23 | 9 am - 4 pm
The Friday Conference Center
Chapel Hill, NC

North Carolina Clinical Antibiotic Stewardship Partners

More information at spice.unc.edu/ncclasp/

THE NORTH CAROLINA CLINICAL ANTIBIOTIC STEWARDSHIP PARTNERS (NC CLASP)

- All the information from today's session will be on our website https://spice.unc.edu/ncclasp/



RESOURCES

- New York State Antibiotic Prescribing Guide
  - Compendium of diagnostic and treatment guidelines for common outpatient conditions
- CDC Treatment Recommendations
  - Summarizes professional society guidelines, management of penicillin allergy