RIGHT FROM THE START: STEWARDSHIP INTERVENTIONS TO OPTIMIZE EMPIRIC ANTIMICROBIAL THERAPY FOR INPATIENTS

March 13, 2024
NC CLASP Hospital Stewardship
Year 2
INTRODUCTIONS

Please put your name, hospital, and location in the chat!
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.
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

Six one-hour learning sessions
September 2023-June 2024

CE included: CME, RN, Pharmacist (ACPE)

Two in-person conferences

Discussion topics include:

- Stewardship interventional tools
- Small hospital strategies
- Diagnostic stewardship/ collaborating with the Clinical Microbiology lab
- Stewardship in skin/skin structure infections
- **Impacting empiric therapy decisions**
- Handling antibiotic allergies

- Regional in-person sessions: February, April, July: Stewardship in transitions of care
- May 22, 2024: Full day, in-person conference

Is there another topic you’d like to discuss in these sessions?
### CORE ELEMENT #4: ACTION
“IMPLEMENT INTERVENTIONS.... TO IMPROVE ANTIBIOTIC USE”

<table>
<thead>
<tr>
<th>Patient-specific</th>
<th>System wide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective audit and feedback*</td>
<td>Facility-specific treatment guidelines*</td>
</tr>
<tr>
<td>-Bug-drug mismatch/de-escalation</td>
<td>Promote routine individual antibiotic process review i.e. “time out”</td>
</tr>
<tr>
<td>-Drug specific monitoring</td>
<td>Clinical decision support systems</td>
</tr>
<tr>
<td>-Disease-specific monitoring</td>
<td>Cumulative susceptibility report (antibiogram)</td>
</tr>
<tr>
<td>-Optimize route of administration</td>
<td>Drug / Disease state treatment review</td>
</tr>
<tr>
<td>-Duration of therapy</td>
<td>Formulary Management, shortage management</td>
</tr>
<tr>
<td>Optimize antimicrobials for next level of care</td>
<td>Antimicrobial dosing recs</td>
</tr>
<tr>
<td><strong>Preauthorization of certain drugs/classes</strong>*</td>
<td>Micro lab output optimization strategies, diagnostic stewardship</td>
</tr>
</tbody>
</table>

Examples, list not all-inclusive
* CDC “priority” interventions
83 year old male patient with history of BPH, hypertension, CAD with stent 12 years ago. Last antibiotic course (oral cefpodoxime) was 4 years ago for a presumed UTI. NKA. Admitted to floor bed from home via ED with complaints of fever, feeling “woozy”, lower abdominal pain, difficulty urinating. T: 101.9F, BP: 110/55, HR 113, RR 14, SpO2 99% on room air. Mental status intact. Large urine output after bladder catheterization. BP responded to fluid challenge. WBC: 16.7, 86% PMN, 6.1 band forms. CMP unremarkable. Urinalysis, urine and blood cultures pending. Urology consulted.

Treatment initiated: Meropenem and Vancomycin

What intervention systems would your AS program have used to help this patient?

Which of these are “proactive” relative to the prescription of treatment?

Which ones are “reactive?”
Stewardship interventions to optimize empiric therapy

EMPIRIC ANTIMICROBIAL THERAPY
THE INFECTION TREATMENT PROCESS

Moment 1: Does my patient have an infection that requires antibiotics?

Moment 2: Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should be initiated?

Moment 3: Can I stop antibiotics? Can I narrow therapy? Can I change from IV to oral therapy?

Moment 4: What duration of antibiotic therapy is needed for my patient’s diagnosis?

AHRQ Pub No 17 (20)-0028-EF, Nov 2019
HOW CAN AN ANTIMICROBIAL STEWARDSHIP PROGRAM HELP OPTIMIZE EMPIRIC THERAPY DECISIONS?

- Local Susceptibility Trends
- Local Treatment Guidelines
- Pre-Authorization program
Stewardship interventions to optimize empiric therapy

THE CUMULATIVE SUSCEPTIBILITY REPORT
OR “ANTIBIOGRAM”
# Memorial Medical Center

## 1 January - 31 December 2020 Antibiogram

### Percent Susceptible

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of Strains</th>
<th>Amikacin</th>
<th>Ampicillin</th>
<th>Cefazolin (systemic)</th>
<th>Cefazolin (urine)</th>
<th>Cefepime</th>
<th>Ceftriaxone</th>
<th>Ceftazidime</th>
<th>Ciprofloxacin</th>
<th>Ertapenem</th>
<th>Gentiamicin</th>
<th>Meropenem</th>
<th>Piperacillin-tazobactam</th>
<th>Trimethoprim-sulfamethoxazole</th>
<th>Tobramycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>32</td>
<td>60</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>33</td>
<td>34</td>
<td>42</td>
<td>41</td>
<td>R</td>
<td>57</td>
<td>60</td>
<td>46</td>
<td>48</td>
<td>59</td>
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<tr>
<td><em>Citrobacter freundii</em></td>
<td>49</td>
<td>100</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>81</td>
<td>72</td>
<td>67</td>
<td>90</td>
<td>98</td>
<td>96</td>
<td>99</td>
<td>83</td>
<td>67</td>
<td>97</td>
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<tr>
<td><em>Enterobacter cloacae</em></td>
<td>76</td>
<td>99</td>
<td>99</td>
<td>35</td>
<td>68</td>
<td>87</td>
<td>92</td>
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<td>99</td>
<td>91</td>
<td>94</td>
<td>73</td>
<td>92</td>
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<tr>
<td><em>Escherichia coli</em></td>
<td>1433</td>
<td>99</td>
<td>35</td>
<td>68</td>
<td>87</td>
<td>92</td>
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<td>72</td>
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<td>99</td>
<td>99</td>
<td>94</td>
<td>73</td>
<td>92</td>
</tr>
<tr>
<td><em>Klebsiella (formerly Enterobacter) aerogenes</em></td>
<td>31</td>
<td>100</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>81</td>
<td>68</td>
<td>60</td>
<td>92</td>
<td>99</td>
<td>91</td>
<td>99</td>
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<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>543</td>
<td>99</td>
<td>R</td>
<td>72</td>
<td>89</td>
<td>93</td>
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<td>95</td>
<td>86</td>
<td>81</td>
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<tr>
<td><em>Morganella morganii</em></td>
<td>44</td>
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<td>R</td>
<td>R</td>
<td>R</td>
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<td><em>Proteus mirabilis</em></td>
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<td>87</td>
<td>80</td>
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<td>99</td>
<td>99</td>
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<td>90</td>
<td>100</td>
<td>70</td>
<td>73</td>
<td>93</td>
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<tr>
<td><em>Pseudomonas aeruginosa</em></td>
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<td>97</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>88</td>
<td>R</td>
<td>86</td>
<td>75</td>
<td>R</td>
<td>80</td>
<td>80</td>
<td>85</td>
<td>R</td>
<td>83</td>
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<td><em>Salmonella spp.</em></td>
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<td>88</td>
<td>-</td>
<td>-</td>
<td>98</td>
<td>97</td>
<td>97</td>
<td>90</td>
<td>100</td>
<td>-</td>
<td>91</td>
<td>86</td>
<td>-</td>
<td>-</td>
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<tr>
<td><em>Serratia marcescens</em></td>
<td>50</td>
<td>100</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>95</td>
<td>87</td>
<td>80</td>
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<td>99</td>
<td>94</td>
<td>99</td>
<td>94</td>
<td>91</td>
<td>89</td>
</tr>
<tr>
<td><em>Shigella spp.</em></td>
<td>33</td>
<td>-</td>
<td>64</td>
<td>-</td>
<td>-</td>
<td>98</td>
<td>98</td>
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<td>-</td>
<td>100</td>
<td>91</td>
<td>69</td>
<td>-</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>72</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>-</td>
<td>R</td>
<td>63</td>
<td>6</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>-</td>
<td>98</td>
<td>R</td>
</tr>
</tbody>
</table>

**Abbreviation:** R, intrinsic resistance.

**Symbol:** -, drug not tested or drug not indicated.

*The percent susceptible for each organism/antimicrobial agent combination was generated by including the first isolate of that organism encountered in a given patient.*

*The percent susceptible applies to the treatment of patients with infections other than uncomplicated urinary tract infections (UTIs).*

*Cefazolin (systemic) refers to application of susceptibility breakpoint minimal inhibitory concentration (MIC) ≤ 2 µg/mL and applies to the treatment of* *complicated infections.*

*Cefazolin (urine) refers to application of urinary susceptibility breakpoint MIC ≤ 16 µg/mL (using a cefazolin dosage regimen of 1 g intravenously [IV] every 12 hours) and can be used to predict susceptibility for oral cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalixin, and loracarbef when used for therapy of uncomplicated UTIs due to* *E. coli, K. pneumoniae, and P. mirabilis.* Cefazolin as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, these drugs should be tested individually if needed for therapy.
SAMPLE MENU OF ANTIBIOGRAM SUBSET OPTIONS
500 BED ACUTE CARE HOSPITAL
JANUARY 1- DECEMBER 31, 20XX

All lab isolates (n= 4443)
All In-patients  (2250)
In-patient urine (426)
All Outpatients  (2193)
Outpatient urine  (1603)

All ICU patients (1651)
Heme-Onc patients (106)
Surgical service patients (168)
Pediatrics (225)
USES OF THE CUMULATIVE ANTIMICROBIAL SUSCEPTIBILITY REPORT

- Helping prescribers select effective therapy when culture results are pending
- Informing and updating local guidelines for empirical treatment of common infection syndromes
- Updating periprocedural or perioperative prophylaxis recommendations
- Providing a rationale for antimicrobial formulary selection
- Surveying local resistance and benchmarking, identifying targets for stewardship interventions and best practices
- Providing the context for new drug susceptibility testing results.

Key References
- CLSI document M-39, 5th ed, 2022,
- Also NC CLASP session January 2024
DISSEMINATING ANTIBIOGRAM DATA FOR CLINICAL USE

➤ Getting the data to the prescribers of empiric therapy is vital
  ➤ On the web, newsletter, pocket card, linked in order-entry screens, Phone App?
  ➤ Confidentiality is an issue

➤ Slice the data as many ways as they will allow, cognizant of the lower limit of 30 isolates/time period

➤ Know the strengths and limitations of your dataset
  ➤ which data were used
  ➤ Procedures used to prepare

➤ Share with various user groups for their applications
ANTIBIOGRAM LIMITATIONS AND PRECAUTIONS

- Sample size
  - Infrequent organisms
  - Getting specific by patient population and site

- Starts with an organism, *not* a diagnosis
  - You have to know which organisms cause the syndrome and how frequently

- Doesn’t differentiate positive cultures and true infections
  - Trach colonizers, etc.

- Patient’s history often more important
  - Prior organisms, infection risk factors, antibiotic exposure, healthcare exposure
<table>
<thead>
<tr>
<th>Number of antibiogram charts</th>
<th>Dissemination of antibiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single chart for hospital</td>
<td>Posted on hospital website</td>
</tr>
<tr>
<td>Inpatients</td>
<td>Newsletter</td>
</tr>
<tr>
<td>Outpatients</td>
<td>Phone App</td>
</tr>
<tr>
<td>ICU</td>
<td>Pocket card</td>
</tr>
<tr>
<td>Urine</td>
<td>Link to order entry screen</td>
</tr>
<tr>
<td>Any service-specific antibiogram</td>
<td>Other</td>
</tr>
</tbody>
</table>
Stewardship interventions to optimize empiric therapy

CONDITION-SPECIFIC LOCAL TREATMENT GUIDELINES
## BENEFITS OF CONDITION-SPECIFIC LOCAL GUIDELINES

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce variance in decision-making</td>
<td>Sepsis, febrile neutropenia: Speed is priority</td>
</tr>
<tr>
<td>Can optimize empiric antimicrobial therapy</td>
<td>Any condition</td>
</tr>
<tr>
<td>Limit inadequate microbiologic diagnosis</td>
<td>Bone biopsies for deep decubitus ulcer</td>
</tr>
<tr>
<td>Diagnostic Stewardship</td>
<td>Overuse of ETT aspirate cultures in ICU</td>
</tr>
<tr>
<td>Difficulty coordinating subspecialists</td>
<td>Diabetic foot infections</td>
</tr>
<tr>
<td>Stewardship of high-value drugs</td>
<td>\textit{C difficile} therapies</td>
</tr>
<tr>
<td>Targeting antibiotic details and duration</td>
<td>Any condition!</td>
</tr>
</tbody>
</table>
PRIORITIZING DISEASE STATE GUIDELINES

- Frequently encountered conditions:
  - Involve relative broad-spectrum antibiotics
  - Diagnostic Criteria complex or vague
  - Unjustified variance in prescribing or diagnostics ordered
  - General guideline documents available from reputable source (IDSA, ATS, etc)

- Pneumonia (HAP, CAP)
- Urinary Tract Infection
- Skin/skin structure infection
- Febrile neutropenia
- Diabetic foot infection
HABITS OF LOOKUP: GUIDELINE COMPETITORS

- Discipline-specific guidelines
- Guidelines from one’s training
- Up-to-Date, or other web-based resource
- Smart phone apps
- Popular quick references
- Some clinicians prefer a printed pocket guide
IMPROVING GUIDELINE UPTAKE

- Engage end-users and stakeholders in development
- Incorporate local susceptibility data
- Use multiple methods to get guidelines as close to point-of-prescription as possible
- Study common conditions to know which most need guidance
- Educate on rationale, how to access

- Pocket cards
- Best Practice Advisories
- Links on order entry screens
- Disease-specific EMR order sets
- Include time-saving steps (e.g., provisional treatment duration recs, discharge Rx options)
- Smart Phone App
QUESTIONS? GUIDELINES

Who contributes to your institution’s local guidelines?

- We have yet to develop local guidelines
- Infectious Disease team
- Pharmacists
- Hospitalists
- Surgeons
- Other

How do you communicate/disseminate your institution’s guidelines?

- On Hospital website
- In EMR order sets
- Best practice advisories BPA (“Pop-ups”)
- Smart phone App
- Printed form
- Other
Stewardship interventions to optimize empiric therapy

RESTRICTION / PRE-AUTHORIZATION OF SPECIFIC ANTIBIOTICS
PRE-AUTHORIZATION OF CERTAIN DRUGS/CLASSES

- A system that requires case-by-case approval by a stewardship clinician prior to utilization of certain antimicrobials

- Which antibiotics should be restricted?
  - Difficult to use properly, safely
  - Reserved for resistant pathogens
  - Higher cost/benefit compared to other options

- Set up:
  - Which antimicrobials?
  - Who will grant approval?
  - Mechanism to acquire approval?
  - 24/7? Other time window…. 
PRE-APPROVAL MODELS

MECHANISM

- ID consult. Antibiotic restricted to ID recs
- Real-time, point of initial prescription approval
  - e.g. dedicated pager, “approver on call”
- Second signature on order
- Approver team
  - ID trained MD
  - ID trained PharmD
  - Other delegate

TIME-FRAME

- No dispensing until approval
  - Makes the staff pharmacist a gatekeeper
- 18-24 hours of drug permitted with follow-up approval mechanism for continued therapy
- Some programs run for part of the day. (e.g. 7am -11pm)
"Hybrid"

- Initial 24 hour supply dispensed pursuant to drug-specific order set.
- Concurrent Review by AS team
- Second order by ID prescribed required for use > 24 hours

One-on-One early review

- Antimicrobial dispensed as ordered
- Email or call to AS practitioner (ID physician)
- AS practitioner contacts prescriber to discuss case 1:1 with initial prescriber within 24+ hours
CAVEATS AND EXAMPLES

- Must avoid delays in therapy
  - Monitor for this

- Providers can feel a loss of autonomy
  - Approvers need to promote individual patient care, NOT policing prescribing
  - Should get to the place where most requests for restricted agent are approved

- Success can depend on skills of approver
  - One-on-one educational opportunity
  - Can increase visibility and approachability of AS clinicians

- Manipulation of any system happens

- Useful for rapid response in shortage situations

Pre-Auth agents
- Carbapenems
- Beta-lactamase inhibitor combos
- Anti-Staph beta lactams
- Lipoglycopeptides
- Antifungals
- C difficile agents

Shortage management
- IV acyclovir
- Amp sulbactam
Stewardship interventions to optimize empiric therapy

OTHER MODALITIES TO OPTIMIZE EMPIRIC RX
OTHER MODALITIES WITH IMPACT ON EMPIRIC RX

- Requiring diagnosis to accompany antibiotic orders
- Prior MRSA nasal screening to limit application of empiric anti-MRSA agents
- Formulary and associated management policies
- Embedding guideline links and best-practice alerts (BPAs) in Order Entry algorithms.
- Application of rapid, near real-time molecular diagnostics
- Time-out to re-think diagnostics and empiric regimen – as well as for de-escalation
BREAK OUT

- Share your experience with a pre-authorization intervention

- How did you start it?

- What barriers and challenges has it posed?

- If you have no pre-approval structure, what barriers do you anticipate?
Questions?
Comments?
Discussion?
Antibiotic Stewardship Conference

5.22.24 | 9 am - 4 pm
Enterprise Conference Center
Winston-Salem NC

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/