

Antimicrobial Stewardship in the Emergency Department

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Disclosure

- We have no actual or potential conflict of interest in relation to this program or presentation.

Objectives

- Describe the role of healthcare providers for successful antimicrobial stewardship in the emergency department (ED)
- List interventions that could be implemented to impact antimicrobial stewardship in the ED
- Discuss challenges for implementing an antimicrobial stewardship program in the ED

Pretest Question 1

If there are no allergies, which treatment would you recommend for an uncomplicated UTI locally?

- A. ciprofloxacin
- B. trimethoprim-sulfamethoxazole
- C. nitrofurantoin
- D. piperacillin-tazobactam

Pretest Question 2

What are the challenges for implementing an antimicrobial stewardship program in the ED?

- A. Buy in from ED staff
- B. Support
- C. Resources
- D. All of the above

Pretest Question 3

Which of the following is not a benefit shown from a dedicated pharmacist-led ED culture follow-up?

- A. Decrease use of ED resources in the 96 hours after the visit
- B. Improvement in antibiotic selection following post-visit revisions
- C. Decrease in 30 day mortality
- D. Improvement in the appropriate antibiotic duration's post-visit revisions

Pretest Question 4

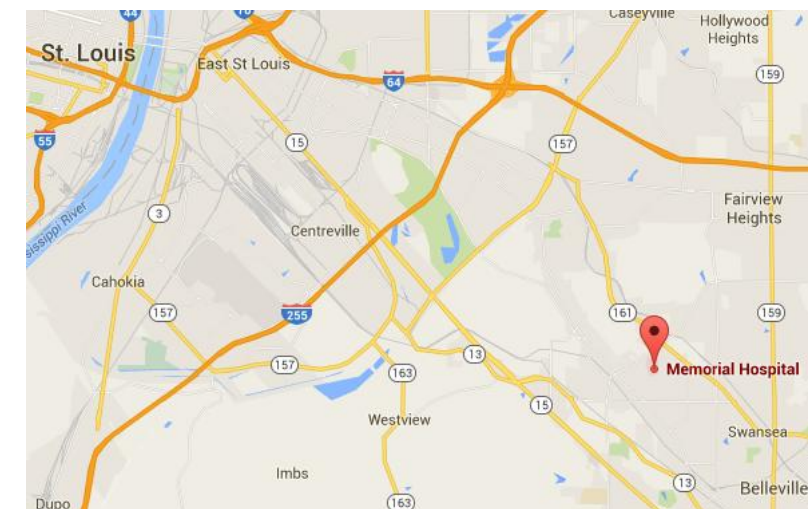
What are examples of health care providers successfully impacting antimicrobial stewardship in the ED?

- A. Clinical informatics building a clinical decision support tool to alert providers to avoid prescribing nitrofurantoin at ED discharge based upon age/serum creatinine
- B. ED providers utilizing hospital approved order sets and clinical pathways for selecting the most appropriate antimicrobial therapy which were updated by the antimicrobial stewardship team
- C. Microbiology laboratory personnel implementing a new PCR test for respiratory viruses/bacteria
- D. ED nursing staff gathering accurate antibiotic histories for patients failing outpatient antibiotic therapies
- E. All of the above

Memorial Hospital



- Community non-profit hospital
 - 216 bed capacity
 - Accredited Chest Pain Center
 - IDPH Stroke-Ready Hospital
 - Over 72,000 ED visits per year
 - > 10,000 pediatric ED visits/year
 - Magnet designation



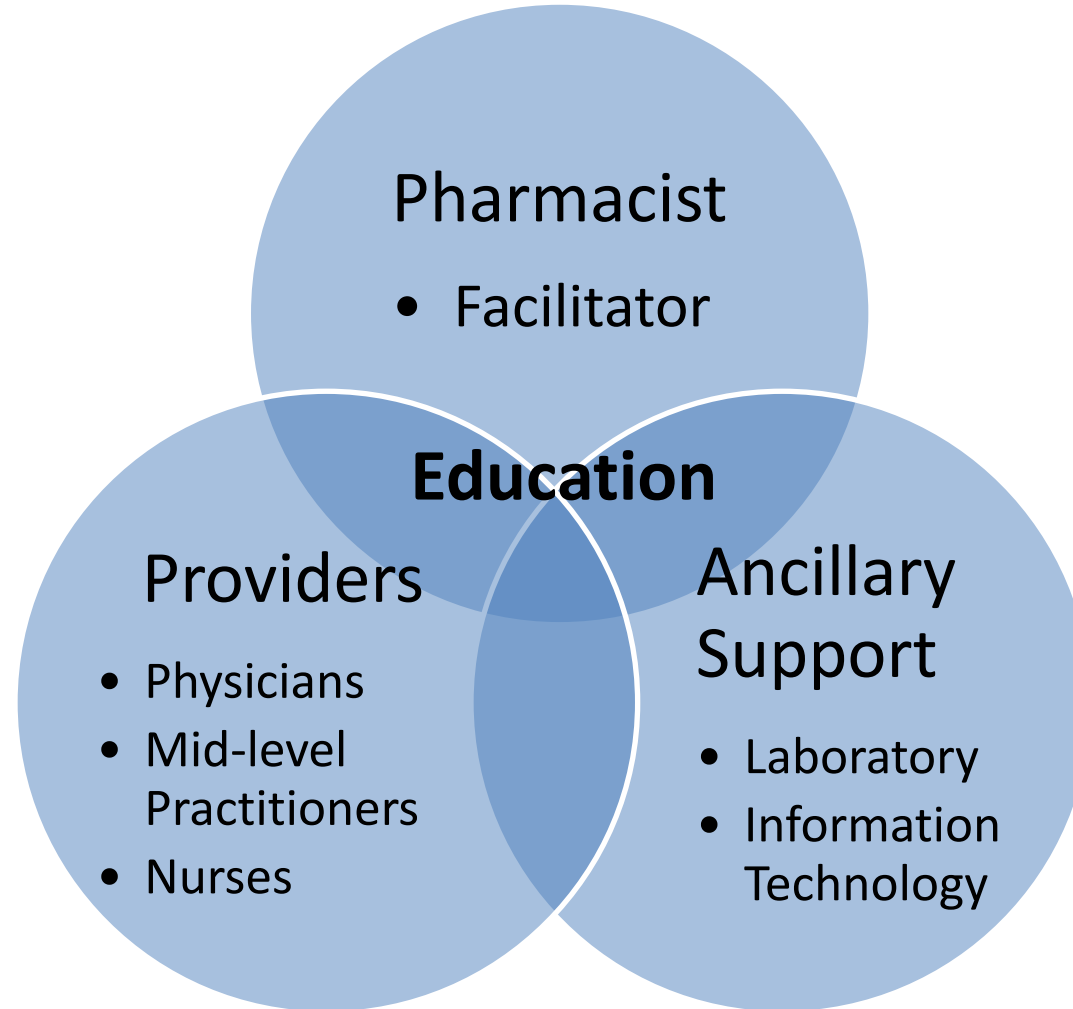
Core Elements for Antimicrobial Stewardship Programs (ASP)

- Leadership Commitment
- Accountability
- Drug Expertise
- Action
- Tracking
- Reporting
- Education

Inpatient ASP Support Team



Stewardship in the ED



ED Pharmacist Roles

- Promote appropriate antibiotic use
- Provide active feedback
- Continuous clinician education
- Perform pharmacotherapy consults
- Mitigate drug interactions & adverse effects
- Develop ED guidelines/protocols
- Culture follow-up & post-prescription review

ED Pharmacist Culture Follow-up #1

- 12 month pre/post retrospective study
 - Physician (n=2278) vs. pharmacist managed culture reviews (n=2361)
 - Single center teaching hospital
 - 18 hours of ED pharmacist coverage
- **Primary Endpoint:** unplanned readmission to ED w/in 96 h of discharge

ED Pharmacist Culture Follow-up #1

Reason for Unplanned Readmission to the Emergency Department

Reason	Physician-managed	Pharmacist-follow-up	P-value
Treatment Failure	85	21	<0.001
Noncompliance due to cost	63	18	<0.001
Noncompliance for any reason other than cost	172	67	<0.001
Allergy to medication	39	4	<0.001
Adverse drug reaction	60	50	0.08
Other	13	5	0.08
Total (% of cases)	432 (19%)	165 (7%)	<0.001

ED Pharmacist Culture Follow-up #2

- Retrospective observational study
- Discharged adult ED visits
- Single center
- Pre- and Post-Pharmacist review
 - Positive Cultures Reviewed: 411 (pre) vs. 459 (post)
- Appropriateness of revised regimen based upon IDSA/CDC guidelines and clinical guidelines

ED Pharmacist Culture Follow-up #2

- Level 1: Bug-drug mismatch
- Level 2: Incorrect duration for diagnosis
- Level 3: Potential for home med adverse interaction w/o adjustment
- Level 4: Lack of dose adjustment
- Level 5: Revised regimen conflicts w/ documented allergies

ED Pharmacist Culture Follow-up #2

Comparison of Inappropriate post-visit revisions in discharged adult ED visits*

	Pre-Pharmacist	Post-Pharmacist	P-value
Positive Culture Needing Revisions w/ 1 or more inappropriate levels	34/73 (46.6%)	11/75 (14.7%)	N/A
Level 1: Incorrect antibiotic agent based upon culture & susceptibility	14 (19.2%)	1 (1.3%)	P<0.003
Level 2: Incorrect antibiotic regimen duration*	20 (27.4%)	9 (12%)	P<0.02
Level 3: Potential for abx/home med interaction w/o adjustment	1 (1.4%)	1 (1.3%)	P=0.99
Level 4: Lack of dose adjustment	4 (5.5%)	0 (0%)	P=0.04
Level 5: Regimen conflict w/ documented allergy history	0 (0%)	0 (0%)	N/A

ED Pharmacist Culture Review

- Pharmacist managed culture follow-up
 - Decrease unplanned readmission
 - Decrease number of inappropriate regimens
 - Improve antibiotic selection, dosing, duration
 - Decrease median time to culture review and patient/Primary Care Provider notification
- Challenges

Post-prescription Review

- Review of outpatient prescriptions prior to discharge
 - Antibiotic selection
 - Adverse drug event recognition/interception
- Focus review on certain patient populations
 - Culture negative
 - Multiple antibiotics
 - Prolonged therapy duration

Clinical Decision Support

- IT system delivers patient data to providers
- Utilizes real-time patient data
 - Weight, height, laboratory testing, culture data, serology, etc
- Guides providers to use certain antibiotic therapies
 - Example: avoiding nitrofurantoin for UTI treatment in patients with low renal function

Pneumonia Patient Case

- 43yom presents to ED w/ dyspnea from a group home. Previously discharged w/in 2 months
- T101.4 P98 BP132/81 RR24 O2 Sat 91% RA
- Chest x-ray: RLL infiltrates and opacities
- ED Diagnosis: Healthcare-associated pneumonia
- Started on vancomycin + cefepime; Admitted.
- MRSA surveillance culture: negative
- WBC 11.5 (43% lymphocytes, 52% neutrophil)

Pneumonia Patient Case

What would you recommend to the treating physician?

- A. Continue current antibiotics and start oseltamivir therapy for influenza
 - B. Discontinue both antibiotics and start oseltamivir therapy
 - C. Discontinue vancomycin and start oseltamivir therapy
 - D. Continue current antibiotics and await infectious diseases consult recommendations
- What if more information were available?

Pneumonia Patient Case

- 43yom w/ dyspnea from group home
- WBC 11.5 (43% lymphocytes, 52% neutrophil)
 - MRSA nasal surveillance (-) → d/c vancomycin
 - Influenza A PCR positive
 - Initiate respiratory isolation & oseltamivir 75 mg PO BID
 - Procalcitonin level 2.38
 - Underlying bacterial PNA? → Continue cefepime and follow Procalcitonin trends

Rapid Diagnostic Testing

- Procalcitonin (PCT) Level
 - Diagnostic biomarker for bacterial infections
 - Best for respiratory tract infections and sepsis
 - Not useful for localized infections: cellulitis or endocarditis
 - PCT Levels <0.05 normal, $>0.25-0.5$ elevated, > 2 critical high
 - Caution: low volume states, severe pancreatitis, multiple trauma, major surgery, burns
 - Can shorten antibiotic duration dramatically
- Urinary antigen test
- Polymerase Chain Reaction (PCR)

Rapid Diagnostic Testing

- **Multiplex PCR Panels**, Results within 1 hour
- **Respiratory Panel**, 20 viruses and bacteria

Viruses:

- Adenovirus
- Coronavirus HKU1
- Coronavirus NL63
- Coronavirus 229E
- Coronavirus OC43
- Human Metapneumovirus
- Human Rhinovirus/Enterovirus
- Influenza A
- Influenza A/H1
- Influenza A/H1-2009
- Influenza A/H3
- Influenza B
- Parainfluenza Virus 1
- Parainfluenza Virus 2
- Parainfluenza Virus 3
- Parainfluenza Virus 4
- Respiratory Syncytial Virus

Bacteria:

- *Bordetella pertussis*
- *Chlamydomphila pneumoniae*
- *Mycoplasma pneumoniae*

Rapid Diagnostic Testing

- Other multiplex PCR panels available
- Limited hands-on time
- Gastrointestinal
 - 22 pathogens (bacteria, parasites, viruses)
- Blood
 - 24 bacteria, yeasts, and 3 resistance genes
- Cerebrospinal Fluid
 - 14 bacteria, viruses, and yeasts

Treatment Durations

- Shortening treatment durations
 - Goal:
 - Sustaining efficacy while minimizing collateral damage
 - Strategies
 - Education
 - Protocols
- Compare site data versus guideline recommendations

Dose Optimization

- Based upon individual characteristics
 - Weight, renal function, site of infection, minimum inhibitory concentrations
 - Pharmacokinetics/pharmacodynamics
- Alternative dosing strategies
 - Extended infusion beta-lactams
- Loading dosages in ED
- Appropriate initial dosing

Streamlining/De-escalation

- Narrow coverage as soon as possible
- Limited opportunity in ED
- Rapid diagnostics can help
- Restricting unnecessary empiric coverage
 - Avoiding gram negative and anaerobic activity for cellulitis

ED Specific Antibigram

- Inpatient vs. outpatient data
- Cumulative institution results over-estimate local resistance patterns in community
- Logistical challenges
- Limited data

Disease Specific Issues

- Skin and Soft Tissue Infections
 - ED prescribing challenges
 - Incision & drainage +/- antibiotics
- Urinary Tract Infections
 - Resistance and empiric selection
 - Fluroquinolone/Bactrim resistance
 - Urinalysis (UA) interpretation
 - Appropriate UA/Culture & susceptibility ordering

ED Stewardship Barriers

- Stressful environment
- Time
- High turnover
- Trust/Relationships
- Resources
- Support

Impact of an Antimicrobial Stewardship Intervention on Treatment of Urinary Tract Infections in the Emergency Department

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Southern Illinois University Edwardsville

PGY-2 Infectious Diseases Residency Director

HSHS St. John's Hospital - Springfield, Illinois

HSHS St. John's Hospital

- Regional teaching hospital
 - 439 acute care beds
 - Level I trauma center
 - 65,000 emergency department (ED) visits annually
 - Major cardiovascular and surgery center
 - Children's hospital & level III neonatal intensive care
 - Clinical pharmacy services and inter-professional rounding



Patient Case

- 29 year female presents to the ED complaining of urinary frequency, urgency and dysuria
- No fever or pain at the costovertebral angle
- Labs are within normal limits
- Physician diagnoses an uncomplicated urinary tract infection (UTI)
- Which treatment is most appropriate?

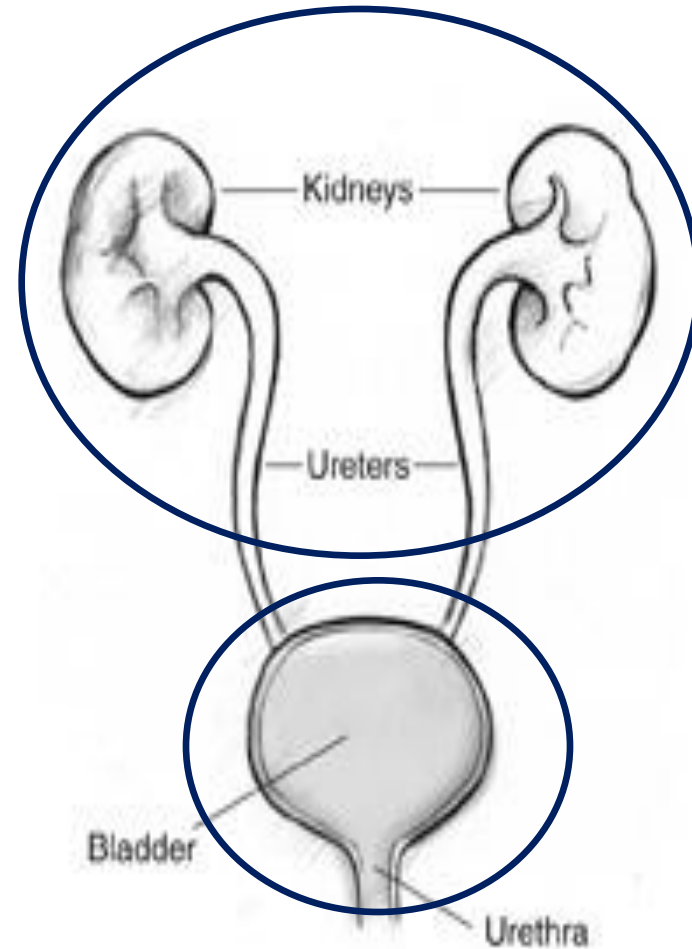
Uncomplicated UTI

If there are no known drug allergies, which treatment would you recommend for this patient?

- A. ciprofloxacin
- B. trimethoprim-sulfamethoxazole
- C. nitrofurantoin
- D. piperacillin-tazobactam

Urinary Tract Infections (UTIs)

- 10.5 million outpatient visits annually
- Most common diagnosis in ED for women
- Wide-range of symptoms and severity



Foxman B. Infect Dis Clin N Am 2014:1-13.
Gupta K, et al. Clin Infect Dis 2011: e103-120.
<http://diabetes.niddk.nih.gov>

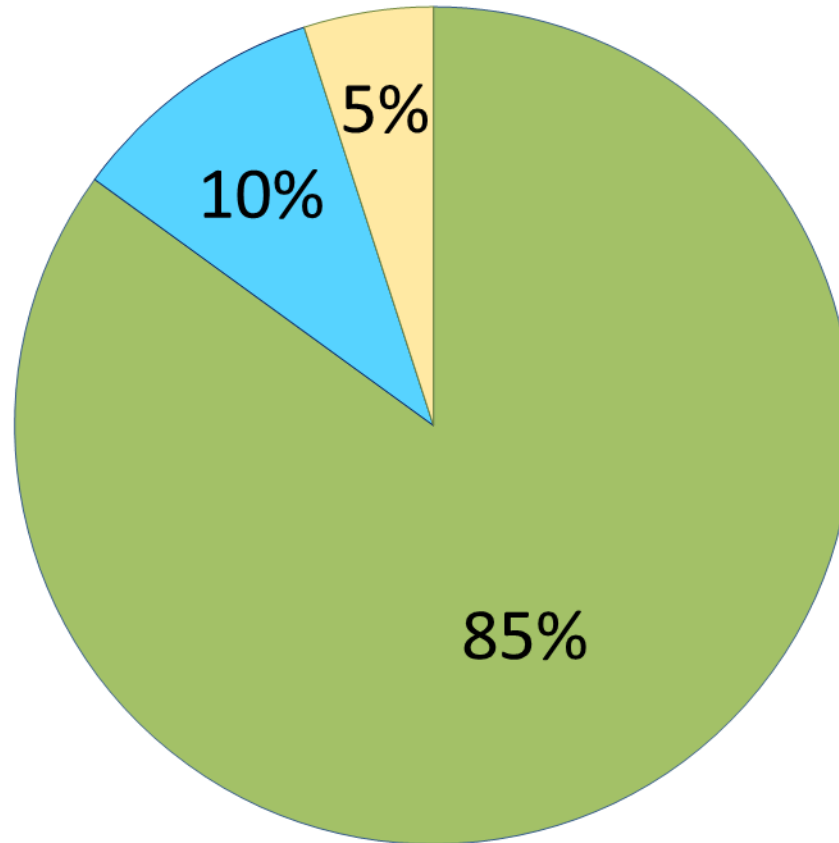
Urinary Tract Infections

Classification	Definition
Uncomplicated	Premenopausal, non-pregnant women with no known urologic abnormalities or comorbidities
Complicated	Catheterization; functional or anatomical abnormalities of the urinary tract

Gupta K, et al. Clin Infect Dis 2011: e103-120.

Etiology - Uncomplicated Cystitis

■ *E. coli* ■ *S. saprophyticus* ■ Other



Practice Guidelines

- Uncomplicated cystitis and pyelonephritis in women
 - Infectious Diseases Society of America and European Society for Microbiology and Infectious Diseases
 - Focus on collateral damage and resistance
- Guidance for Catheter-associated UTI and Asymptomatic Bacteriuria also available

Antimicrobial Stewardship in the ED

- Education
- Institution-specific recommendations and clinical pathways
- ED pharmacist
- Post-prescription review
 - Culture follow-up
- Antibigram development

Study Aims

- To determine if education and feedback to ED providers changes the empiric treatment of acute uncomplicated cystitis and pyelonephritis
- To assess the agreement between empiric antibiotics and isolated pathogen susceptibilities

Methods

- Inclusion criteria
 - ≥ 12 years of age
 - Discharged home from the ED
- Compared before and after education
- Four month periods
- Endpoints
 - Adherence to recommendations
 - Discharge antibiotic susceptibility to the isolated pathogen

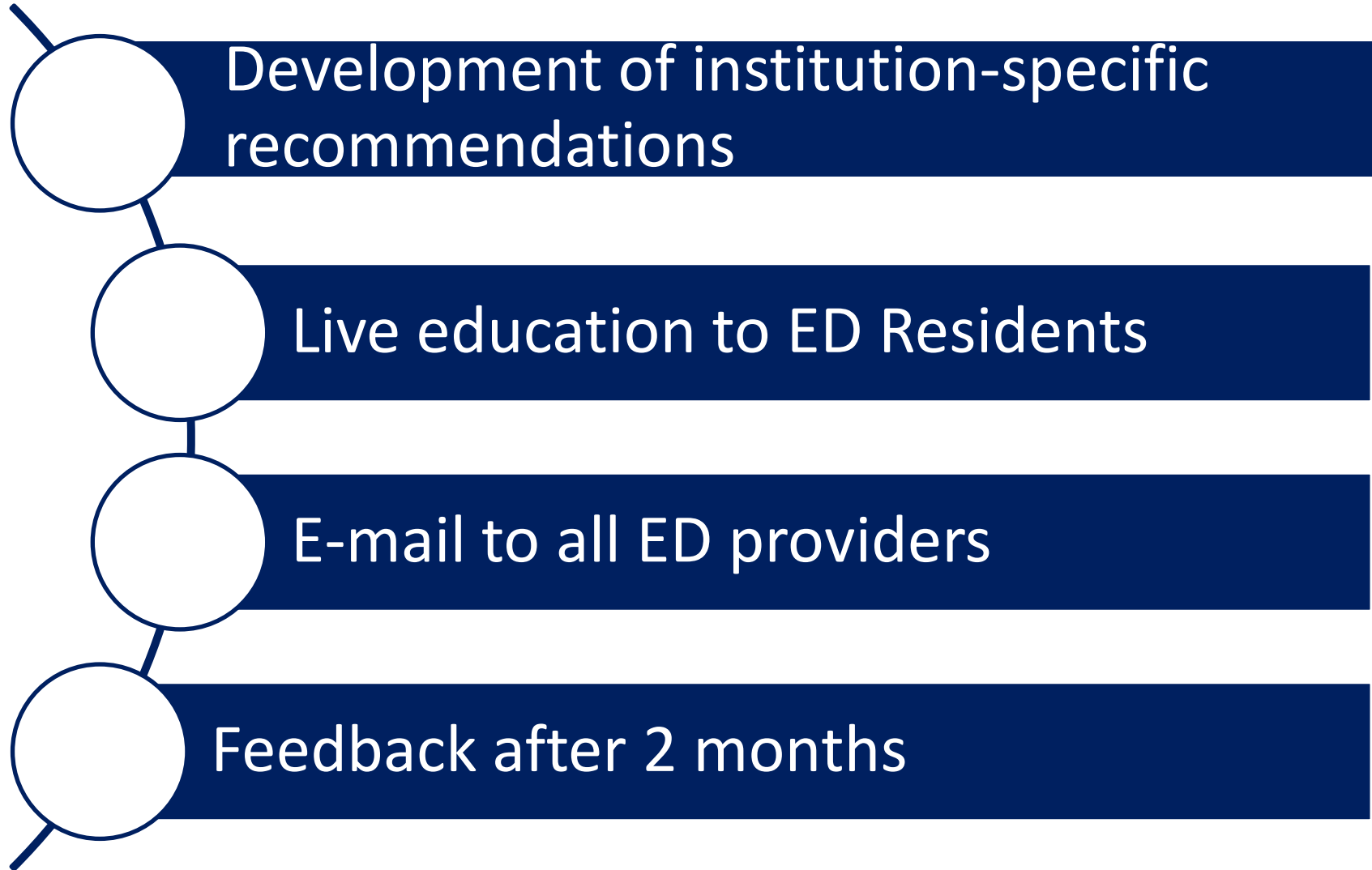
Statistical Plan

- Sample: 260 patients
- Effect size: 20%
- Power: 90%
- Alpha: 0.05
- Nominal data: Chi-square test
- Continuous data: Student's t-test

Methods

- Individual chart reviews
- Pyelonephritis definition
 - Flank pain
 - Fever
 - Elevated systemic white blood cell count
- IRB approval obtained

Education



Local Resistance Patterns

	Susceptibility Rates for <i>E. coli</i> (%)			
	Nitrofurantoin (urine only)	Ciprofloxacin	TMP- SMX	Cefazolin
Emergency Department	99	80	75	96

TMP-SMX = Trimethoprim-sulfamethoxazole

Treatment Recommendations

- Acute uncomplicated cystitis
 - 1st choice
 - Nitrofurantoin monohydrate/macrocrystals
100 mg every 12 hours for 5 days
 - Only for patients with CrCl >60 ml/min
 - 2nd choice
 - Cephalexin 500 mg every 12 hours for 7 days
 - (Fosfomycin 3g single dose, non-formulary)

Treatment Recommendations

- 3rd choice

- TMP-SMX 160/800 mg one tablet every 12 hours for 3 days

- If poor renal function and allergic to beta-lactam drugs

- 4th choice

- Ciprofloxacin 250 mg every 12 hours for 3 days

- If poor renal function and allergic to both beta-lactam and sulfa drugs

FDA Safety Communication

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health



May 12, 2016

Fluoroquinolone Antibacterial Drugs: Drug Safety Communication - FDA Advises Restricting Use for Certain Uncomplicated Infections

[Posted 05/12/2016]

AUDIENCE: Internal Medicine, Family Practice, Pharmacy, Patient

ISSUE: FDA is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

An FDA safety review has shown that fluoroquinolones when used systemically (i.e. tablets, capsules, and injectable) are associated with disabling and potentially permanent serious side effects that can occur together. These side effects can involve the tendons, muscles, joints, nerves, and central nervous system.

As a result, FDA is requiring the drug labels and Medication Guides for all fluoroquinolone antibacterial drugs to be updated to reflect this new safety information. FDA is continuing to investigate safety issues with fluoroquinolones and will update the public with additional information if it becomes available.

See the [FDA Drug Safety Communication \(/Drugs/DrugSafety/ucm500143.htm\)](https://www.fda.gov/Drugs/DrugSafety/ucm500143.htm) for a list of currently available FDA approved fluoroquinolones for systemic use.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm500665.htm>

Results - Cystitis

Patient Characteristic	Pre-education n=106	Post-education n=134	P-value
Mean age, years	32	29	0.11
Discharge antibiotic (%)	NTF = 13 (12)	NTF = 106 (79)	< 0.001
	FQ = 35 (33)	FQ = 19 (14)	0.005
	TMP-SMX = 56 (53)	TMP-SMX = 7 (5)	< 0.001
		Cephalexin = 2 (1.5)	0.21
Antibiotic duration, mean days (\pm SD)	TMP-SMX = 7.1 (3.0)	TMP-SMX = 7.7 (2.56)	0.63
	FQ = 6.3 (2.37)	FQ = 7.6 (2.31)	0.054
	NTF = 7.5 (1.50)	NTF = 7.1 (2.20)	0.47

NTF= Nitrofurantoin , FQ=Fluoroquinolones, TMP-SMX=Trimethoprim-sulfamethoxazole

Results - Cystitis

Guideline Adherence Criteria	Pre-education n=106	Post-education n=134	P-value
	n (%)	n (%)	
Discharge antibiotic	17 (16)	110 (82)	<0.001
Discharge antibiotic dose	87 (82)	123 (92)	0.02
Discharge antibiotic frequency	105 (99)	130 (97)	0.27
Discharge antibiotic duration	22 (21)	33 (25)	0.48
Cystitis institution-specific recommendation adherence	3 (3)	30 (22)	<0.001

Cystitis Cultures

Characteristic	Pre-education n=106	Post-education n=134	P-value
Cultures performed (%)	58 (55)	95 (71)	0.02
Positive cultures (%)	34 (59)	54 (57)	0.83
Pathogen (%)			
<i>Escherichia coli</i>	25 (74)	36 (67)	0.50
<i>Proteus mirabilis</i>	3 (9)	2 (4)	0.31
Group B Streptococcus	2 (6)	7 (13)	0.29
<i>Staphylococcus saprophyticus</i>	1 (3)	1 (2)	0.74
Agreement between empiric antibiotic and isolated pathogen susceptibility (%)	25 (74)	48 (89)	0.05

Treatment Recommendations

- Acute Uncomplicated Pyelonephritis
 - Give 1 dose of a long acting parenteral agent
 - Ceftriaxone 1 g or
 - Gentamicin/tobramycin 5 mg/kg
 - With fluoroquinolones since *E. coli* resistance >10%
 - Always with TMP-SMX or β -lactam

Treatment Recommendations

- Oral prescription if being discharged
 - 1st choice:
 - Ciprofloxacin 500 mg every 12 hours for 7 days
 - 2nd choice:
 - TMP-SMX 160/800 mg every 12 hours for 14 days
 - 3rd choice:
 - Cephalexin 500 mg every 6 hours for 14 days

Results - Pyelonephritis

Patient Characteristic	Pre-education n=68	Post-education n=24	P-value
Mean age, years	34.3	31	0.29
Discharge antibiotic (%)	FQ = 32 (47) TMP-SMX = 29 (43) NTF = 7 (10)	FQ = 17 (70) TMP-SMX = 1 (4) NTF = 5 (20) Cephalexin = 1 (4)	0.04 < 0.001 0.19
Antibiotic duration, mean days (±SD)	FQ = 8.6 (3.01) TMP-SMX = 6.9 (2.71) NTF = 8.9 (2.67)	FQ = 8.6 (2.18) TMP-SMX = 7 NTF = 6.2 (1.1)	0.91 0.96 0.06

FQ=Fluoroquinolones, TMP-SMX=Trimethoprim-sulfamethoxazole, NTF= Nitrofurantoin

Results - Pyelonephritis

Guideline Adherence Criteria	Pre-education n=68	Post-education n=24	P-value
	n (%)	n (%)	
Empiric long-acting parenteral	6 (9)	3 (12.5)	0.60
Discharge antibiotic	61 (90)	19 (79)	0.19
Discharge antibiotic dose	55 (81)	19 (79)	0.86
Discharge antibiotic frequency	62 (91)	19 (79)	0.12
Discharge antibiotic duration	6 (8.8)	10 (42)	0.0003
Pyelonephritis institution-specific recommendation adherence	1 (2)	3 (12.5)	0.02

Discussion

- Baseline adherence to guidelines low
- Increased nitrofurantoin use
 - Pyelonephritis?
- No effect on duration of treatment
- Urine cultures
- Improved empiric prescribing based on isolated pathogens

Limitations

- Single center study
- Limited time frame
- Prospective design, but retrospective analysis
- Relied on chart documentation
 - Coding and list extraction
- Small number with pyelonephritis

Summary

- Institution-specific recommendations and education based on local susceptibility do impact prescribing
- Improved agreement between empiric therapy and isolated pathogen susceptibilities in cystitis
- Continued need for antimicrobial stewardship

Future directions

- Evaluate readmissions
- Additional education/feedback
 - Duration of therapy
 - Long-acting parenteral agents
- Inpatient treatment recommendations
- Expand to other infectious diseases

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Original Contribution

Impact of an antimicrobial stewardship intervention on urinary tract infection treatment in the ED^{☆,☆☆,★}



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ABSTRACT

Study objective: The study objective is to assess changes in treatment of uncomplicated urinary tract infections (UTIs) after implementation of recommendations based on national guidelines and local resistance rates.

Methods: This preintervention and postintervention study included patients discharged home from the emergency department (ED) with an uncomplicated UTI at a 439-bed teaching hospital. Emergency department prescribers were educated on how local antimicrobial resistance rates impact UTI practice guidelines. Empiric treatment according to recommendations was assessed as the primary outcome. Agreement between chosen therapy and isolated pathogen susceptibility was compared before and after education. Reevaluation in the ED or hospital admission within 30 days for a UTI was also evaluated.

Conclusion

- ED offers unique opportunities for ASP efforts
 - Inpatient and outpatient setting
 - Stressful environment with high turnover
- Pharmacists are key pieces in facilitating ASP
 - Prescribers, nurses, lab and IT integral to success
 - Clinical pathways, rapid testing and decision support are useful tools
- Utilize available resources/technology to guide antimicrobial use in your ED

Post Test Question 1 – Patient case

If there are no allergies, which treatment would you recommend for an uncomplicated UTI locally?

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Key References

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