



# Best Practice in the Diagnosis and Treatment of ASB and UTI

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# Disclosures

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  - VA HSRD MERIT: 1I01HX002906-01A1

# Learning Objectives

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1. Differentiate uncomplicated from complicated urinary tract infection (UTI), and UTI from asymptomatic bacteriuria (ASB)
2. Review management practices for UTI versus ASB
3. Discuss antimicrobial and diagnostic stewardship strategies to improve the management of UTIs and decrease treatment of ASB

# Urinary Tract Infections (UTIs)

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- Inflammation & invasion of microorganism into the urothelium of the urinary tract
  - Urinary system = kidneys, ureters, bladder, and urethra
  - Causes a constellation of signs and symptoms, mostly referred to urinary tract
    - Non-specific symptoms make diagnosis of true infection difficult
    - Important to differentiate from contamination and colonization

# Epidemiology of UTIs

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- One of the most common infections both inpatient and outpatient
  - Lifetime incidence of 50% in adult female patients
  - Cystitis represents majority of cases (compared to pyelonephritis)
  - Prevalence increases with age
  - Underlying conditions increase risk (i.e., indwelling urinary catheters)

## Ambulatory

- 9 million visits/year

## Inpatient

- 100,000 hospitalizations/year

## Long-Term Care

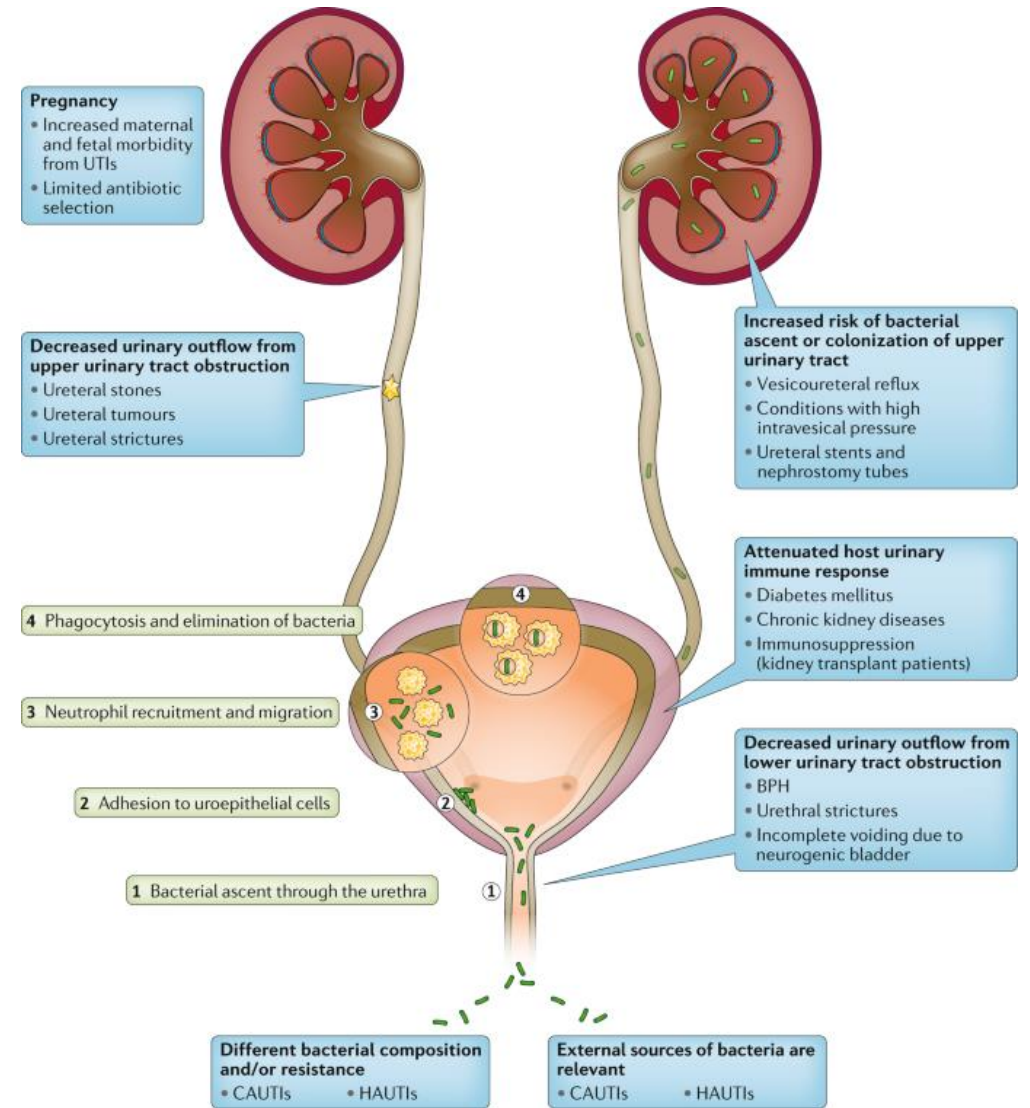
- Represent 50% of all antibiotic prescriptions

# Uncomplicated UTI Classifications

Classification	Definition
<b>Uncomplicated UTI</b>	A UTI with <b>no relevant functional or anatomical abnormalities</b> in the urinary tract, no relevant kidney function impairment, or risk of developing serious complications
<b>Acute uncomplicated cystitis</b>	A lower UTI in which the acute symptoms involve only the <b>lower urinary tract</b> (urgency, painful voiding (dysuria), and pain above the symphysis)
<b>Acute uncomplicated pyelonephritis</b>	An <b>upper UTI</b> with persistent symptoms including flank pain, flank tenderness, or fever (>38°C)
<b>Recurrent uncomplicated UTIs</b>	Occurrence of $\geq 2$ symptomatic episodes within 6months or $\geq 3$ symptomatic episodes within 12months

# Complicated UTIs

- **Structural or functional abnormality**
- Complicated (cUTI) have higher risk of treatment failure, require longer durations of antibiotics (and often broader spectrum)
- Would fail a typical course of antibiotics prescribed for uncomplicated UTI



# Treatment Uncomplicated UTIs

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- Treatment often empiric in nature
  - Urine cultures not frequently obtained in uncomplicated cystitis
  - Urine cultures common in:
    - Recurrent UTI
    - Upper UTI (acute uncomplicated pyelonephritis)
    - Those at risk for MDRs
- Risk factors for multidrug-resistant gram-negative urinary tract infections
  - Past isolation of a multidrug-resistant gram-negative urinary isolate
  - Inpatient (hospital, nursing home, long-term acute care facility)  antibiogram
  - Previous exposures to fluoroquinolone, trimethoprim-sulfamethoxazole, or broad-spectrum beta-lactam



# Treatment Uncomplicated UTIs

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- Lower UTI (cystitis) first line options:
  - TMP/SMX DS x 3 days
  - Nitrofurantoin x 5 days
  - Fosfomycin x 1 dose
- Upper UTI (pyelonephritis)
  - PO TMP/SMX, beta-lactam, fluoroquinolone x 7 - 10 days
  - If severe systemic symptoms (i.e. require hospitalization)
    - IV therapy for at least 24 hours then transition to PO options to complete 7-day course
    - IV Aminoglycoside
    - IV Ceftriaxone
    - IV Ciprofloxacin, levofloxacin

*IDSA UTI guidelines are from 2011!  
Updates to be published 2023*

# Fluoroquinolones and UTI

- FDA BlackBox Warning in 2016 recommends against use in uncomplicated UTIs
  - Resistance increasingly common
  - Collateral damage very common
  - Risk of adverse events high
- Still represent 40% of prescriptions for uncomplicated UTI
- Rule of thumb: if other agents are an option use them

## FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together

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The FDA has issued new information about this safety issue, see the FDA Drug Safety Communication issued [July 26, 2016](#)

### Safety Announcement

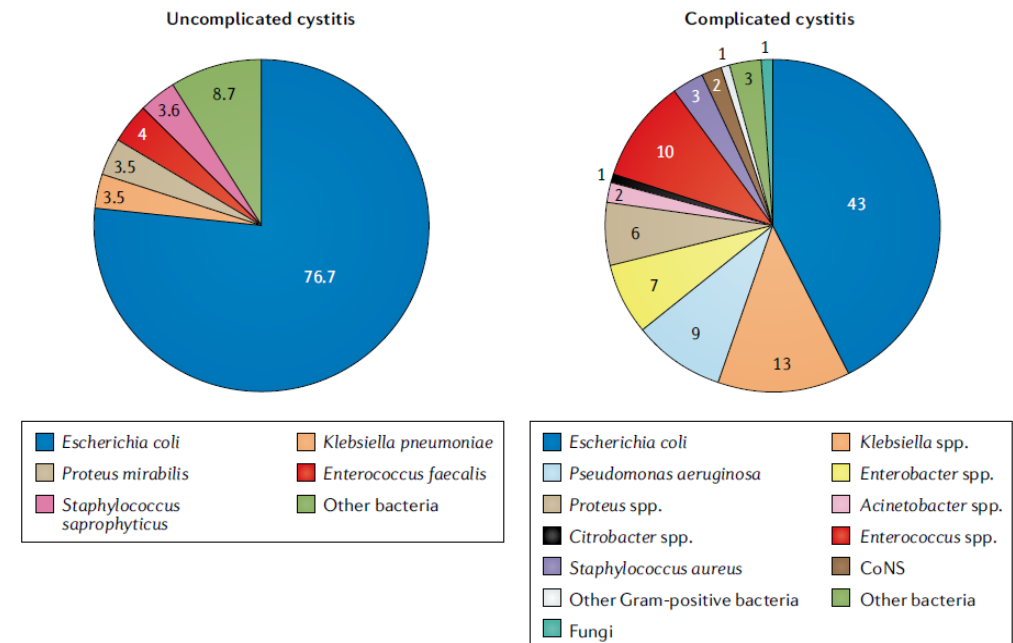
**[ 05-12-2016 ]** The U.S. Food and Drug Administration is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment 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, we are requiring the drug labels and Medication Guides for all fluoroquinolone antibacterial drugs to be updated to reflect this new safety information. We are continuing to investigate safety issues with fluoroquinolones and will update the public with additional information if it becomes available.

# Treatment of Complicated UTI

- Microbiology more diverse and antibiotic resistance more common
- To optimize empiric treatment, review local antibiograms, patient past antibiotic exposure and resistant organisms
  - i.e. avoid TMP/SMX if previous courses
- Urine cultures essential to direct therapy decisions
- *New IDSA guidelines in progress!!*



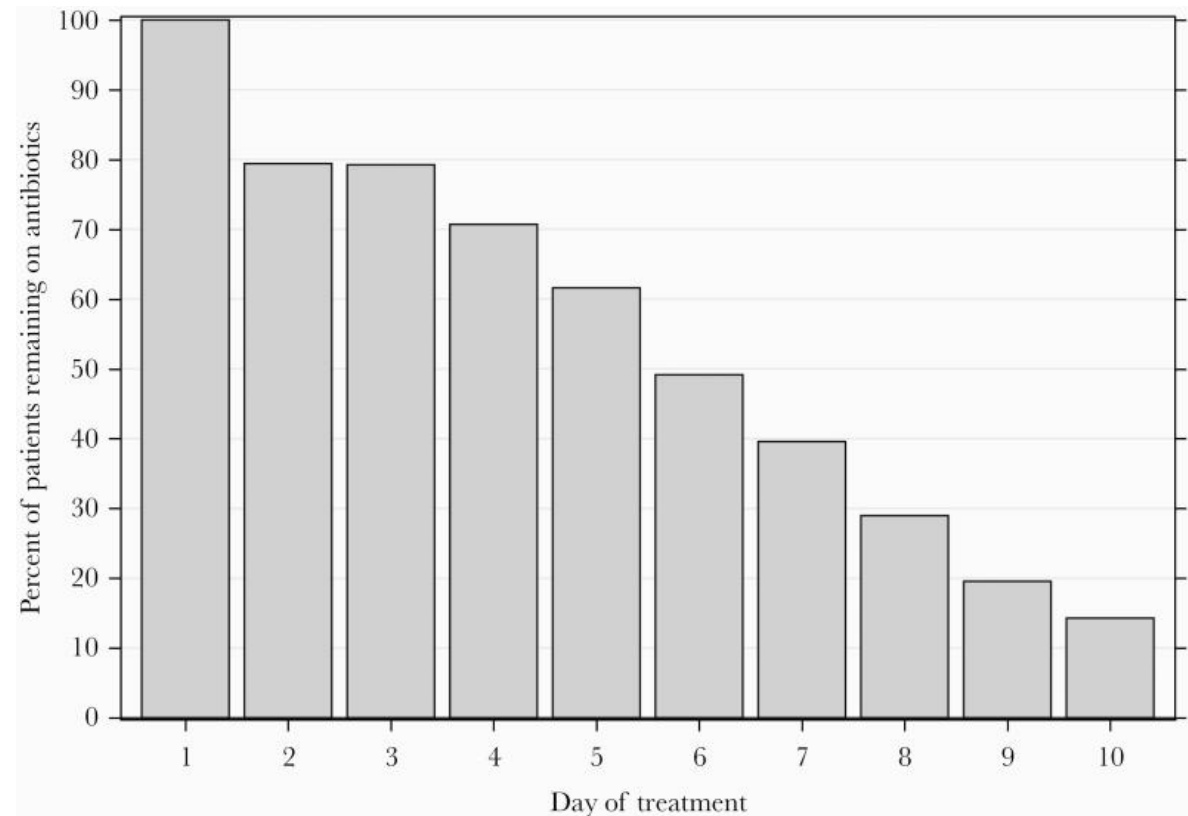
# Asymptomatic Bacteriuria (ASB)

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- IDSA Definition
  - Presence of bacteria in the urine  $\geq 10^5$  colony forming units per milliliter (CFU/mL) in the absence of signs and symptoms of a UTI
- Incidence varies with patient population, increases with age
  - Young, healthy females: 5 – 10 %
  - Elderly: 15% community dwelling but upwards of 60% in long-term care
  - Patients with indwelling catheters: if chronic near 100% chance
- Rarely need to treat ASB but there are exceptions
  - Does not predict development of UTI; does not cause complications
  - Major exceptions: ASB in pregnancy, endoscopic urological procedure

# ASB is a Major Driver of Inappropriate Antibiotics

- Cohort of 43 hospitals, adults with ASB
- Urine cultures ordered in ED (80%)
- Three quarters (74.4%, 1830 of 2461) of adult patients with ASB treated for UTI
- Median treatment duration of 6 days (IQR, 3–9 days)
  - More than 75% stay on antibiotics for greater than 3 days
- Unnecessary treatment associated with prolonged hospitalization and development of CDI



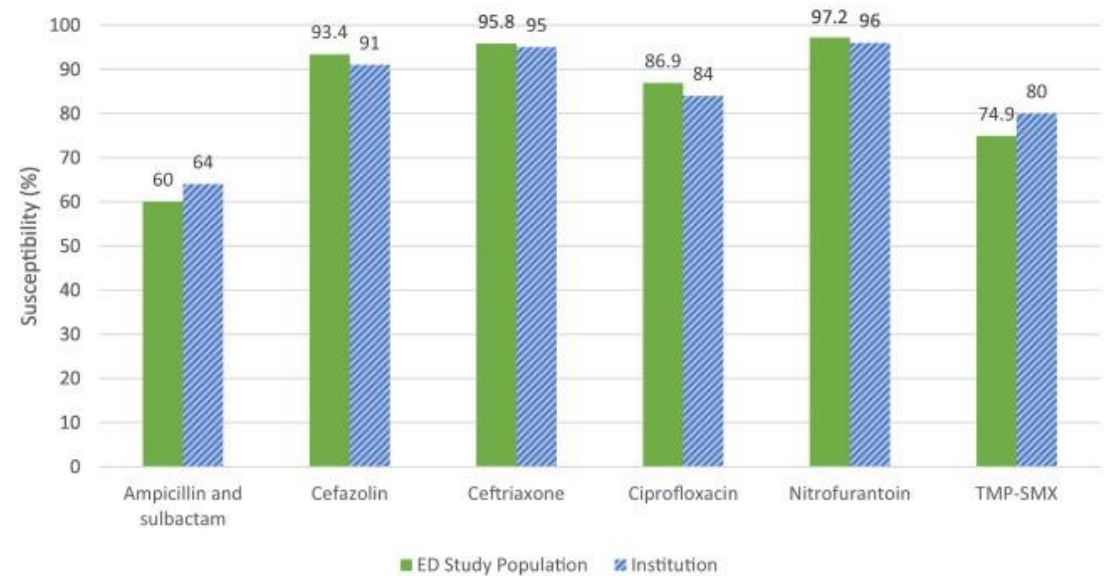
# ASB is a Major Driver of Inappropriate Antibiotics

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- Patients started on UTI treatment in the ED, more likely to:
  - Have spinal cord injury (OR = 5.71)
  - Have indwelling urinary catheter (OR = 1.55)
  - Present with AMS (OR = 2.51)
  - Present with change in urine color/malodourous urine (OR = 1.93)
  - Have abnormal UA (OR = 9.42)
- In patients started on UTI treatment once admitted, more likely to:
  - Present with AMS (OR = 1.96)
  - Have a positive UA (OR = 3.3.6)
  - Have a positive urine culture with > 100,000 cfu/mL (OR = 2.85)

# Antibiotic Resistance is on the Rise

- Especially true for urinary sources!
  - Ambulatory/ED resistance to common oral agents increasing
  - TMP/SMX resistance approaching or exceeding 20% in *E. coli* urinary isolates
  - Risk factors for TMP/SMX resistance
    - Recurrent UTI
    - TMP-SMX use within 90 days
    - Genitourinary abnormalities (cUTI)
  - ESBL phenotype increased by 30% since 2011



# Antimicrobial and Diagnostic Stewardship for UTIs



# Challenges in the Diagnosis of UTI

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- Differentiating ASB from is UTI challenging
  - ~70% of urine cultures ordered without clinical indication
- Withholding treatment is *more* challenging
  - ~70% of ASB receive antibiotic therapy

# The Five Ds of Antibiotic Stewardship for Urinary Tract Infections

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## DIAGNOSIS

Challenges in differentiating ASB from UTI

## DRUG

Right empiric antibiotic based on resistance patterns

## DOSE

Dosage appropriate based on patient conditions

## DURATION

Embracing “shorter is better” mentality

## DE-ESCALATION

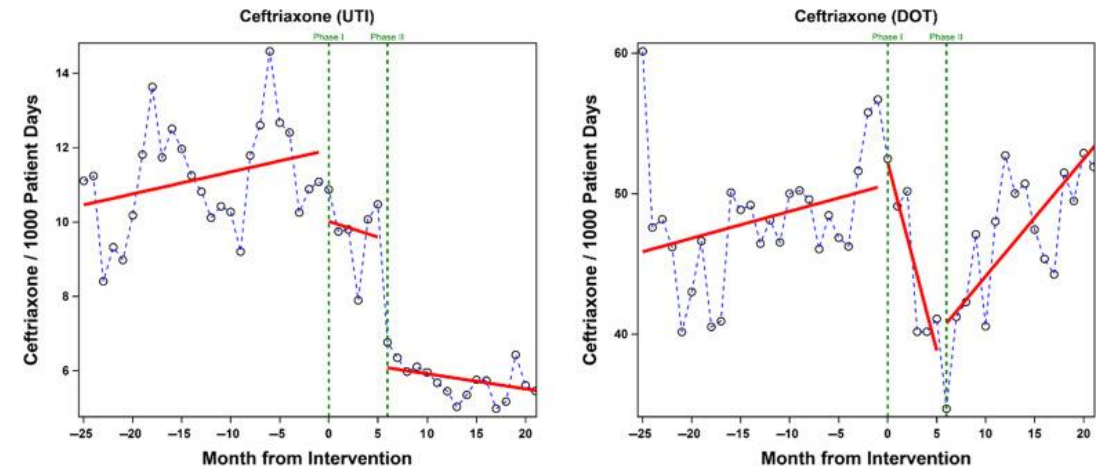
Based on susceptibility results or negative cultures

# Antibiotic Stewardship Strategies

Strategy	Description	Challenges
<b>Local guidelines &amp; provider education</b>	Multifaceted intervention to increase provider awareness of diagnosis/prescribing appropriateness	Poorly defined implementation strategies for outpatient settings
<b>Urinary antibiograms</b>	Stratify local antibiograms by patient location (e.g., ED) and infection site	Limited samples & resources this challenging
<b>Computerized clinical decision support (CCDS)</b>	Embedded decision aids in EMR to default to appropriate dose/duration	Time intensive to create; workarounds possible
<b>Post-prescription review</b>	Review results of urine culture to recommend narrowing or stopping antibiotics	Labor-intensive, delays in results beyond prescription duration

# Urinary Antibiograms

- Susceptibilities of urine cultures often differ by site of infection and setting of acquisition
- Site-specific antibiograms help improve empiric prescribing patterns



*Urinary antibiogram combined followed by EMR nudge to prescribe narrow antibiotic therapy in the setting of AMS audit and feedback*

# Provider Education & Feedback

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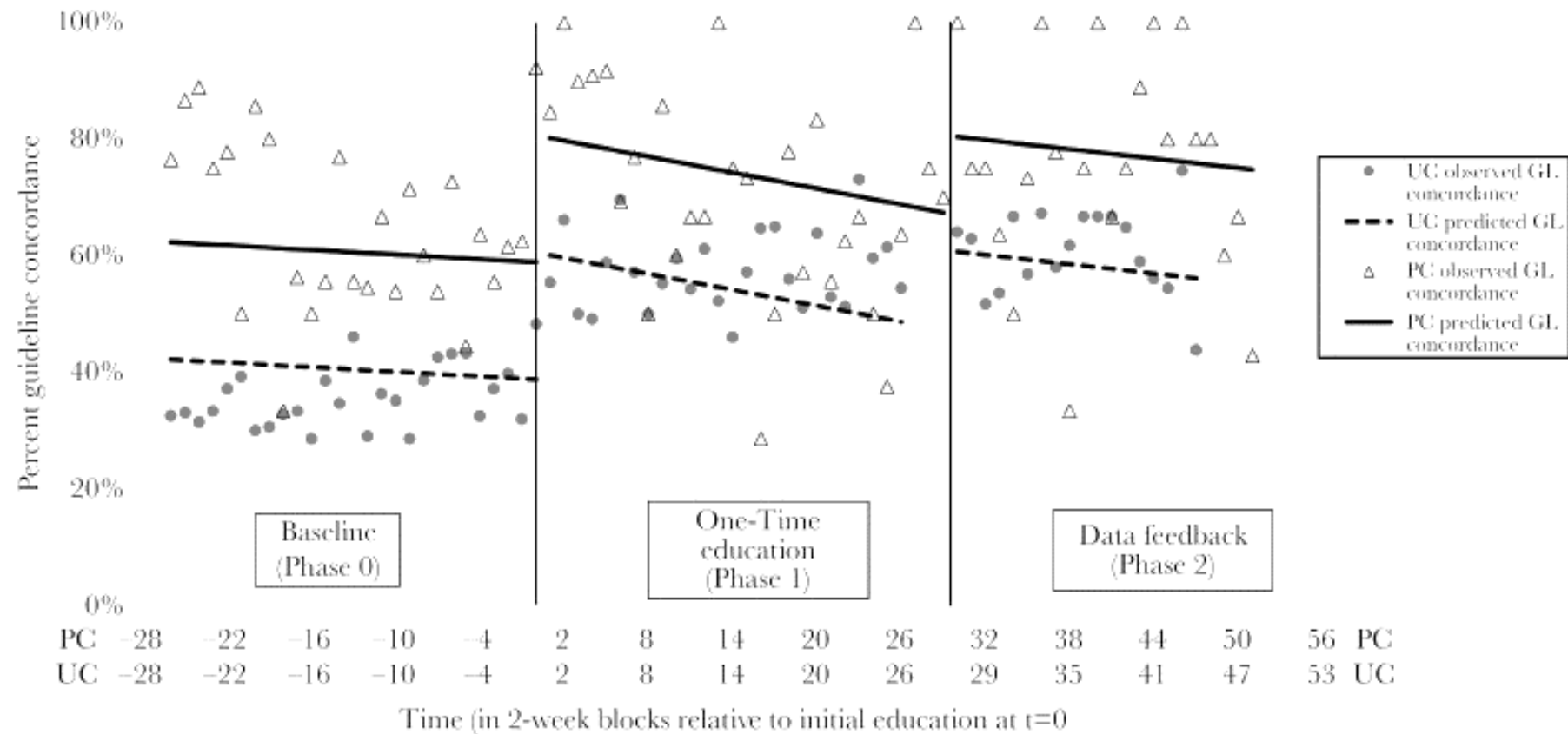
## **Phase 1:** Development site-specific UTI guidelines and antibiograms

- Empiric antibiotic recommendations based on local susceptibility patterns and consensus guidelines
- Educational sessions on guidelines for appropriate diagnosis, antibiotic selection, and duration of therapy

## **Phase 2:** Clinic- and provider-specific feedback

- Repeat educational sessions
- Routine data feedback emails and in-person feedback sessions

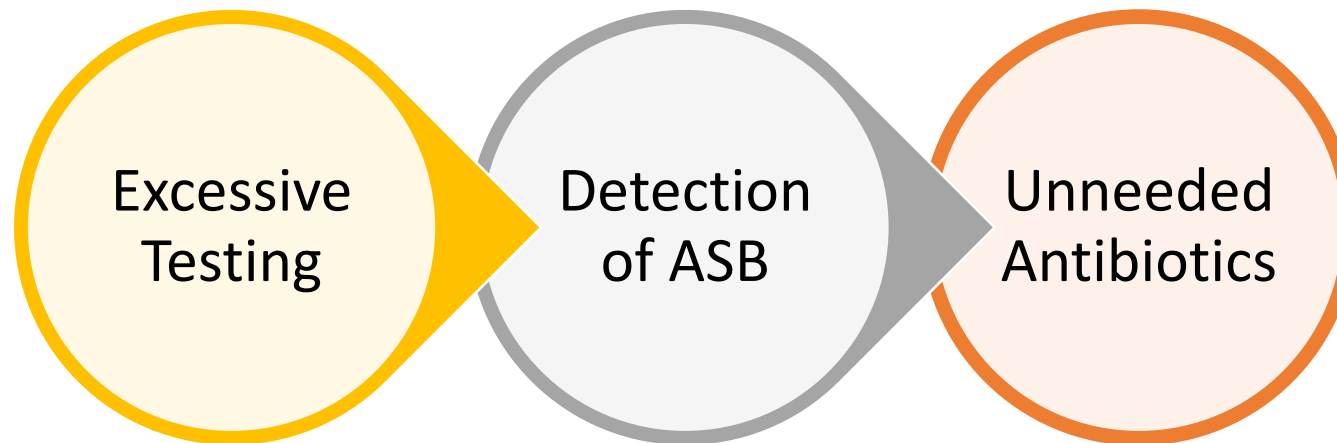
# Provider Education & Feedback



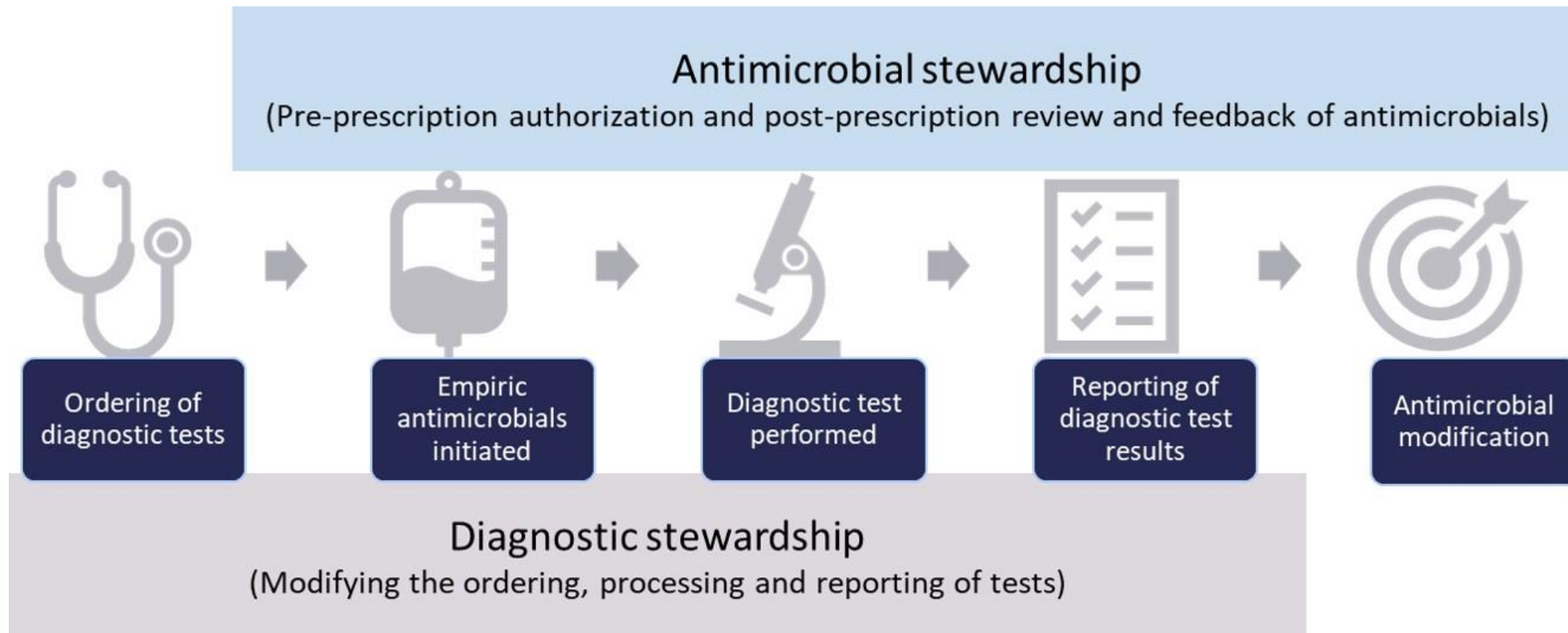
# Antimicrobial Stewardship is Not Enough

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- Traditional AMS interventions occur after diagnosis
  - UA and urine culture have already been ordered
- Diagnostic stewardship works synergistically, and upstream, of AMS interventions



# What is Diagnostic Stewardship?



Provide the right test, for the right patient, prompting the *right action*



# Diagnostic Stewardship for UTIs

Strategy	Description	Challenges
<b>Provider education</b>	Education on process and policies, ordering urine culture only in symptomatic patients	Time-consuming, may not change behaviors
<b>Clinical indications</b>	Must select from list of evidence-based symptoms prior to ordering urine culture	Work-arounds possible
<b>Clinical decision support</b>	Incorporate evidence-based guidance into EMR to guide urine culture and/or antibiotic ordering	Time consuming to implement; need health IT resources
<b>Conditional reflex urine culturing</b>	Limit processing of urine cultures based on pre-defined criteria (i.e. WBC on UA)	May still yield positive cultures in patients with ASB
<b>Cascade reporting</b>	Restrict reporting of more broad-spectrum antibiotics in urine culture results	Extra work for providers when needed; can be ignored
<b>Modified reporting</b>	Report minimal results or interpretation of results in the EMR	Easily ignored

# Best Practices for Diagnostic Stewardship

## Urine Culture Ordering

<b>Appropriate Practices</b>	<ol style="list-style-type: none"> <li>1. Require documentation of signs or symptoms of UTI to obtain a urine culture</li> <li>2. Replace stand-alone urine culture orders with conditional reflex urine cultures*+</li> <li>3. Implement best practice alerts to discourage ordering urine cultures in the absence of signs or symptoms of UTI*</li> <li>4. Automatically cancel repeat urine cultures within 5 days of a positive culture (during the same hospital admission)</li> </ol>
<b>Inappropriate Practices</b>	<ol style="list-style-type: none"> <li>1. Include urine cultures in standard order sets for: <ul style="list-style-type: none"> <li>• ED evaluation</li> <li>• Hospital admission</li> <li>• Inpatient pre-op</li> <li>• Assessment of altered mental status</li> <li>• Assessment of falls in long-term care</li> </ul> </li> <li>2. Order urine cultures in response to change in urine characteristics (i.e. smell, appearance)</li> </ol>

*Conditional urine cultures are defined as cultures, although ordered by the clinician, that are only performed after specific criteria are met on urinalysis (i.e. WBC > 10 per hpf)*

*\* Except for patients undergoing urological procedures*

*+ Disagreement around use in urinary catheters and the ER setting*

# Education – Kicking CAUTI

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- Quasi-experimental quality improvement study implementing provider audit and feedback on screening and treatment of ASB
  - Reduce unnecessary urine cultures (diagnostic stewardship)
  - Reduce unnecessary antibiotic use (antibiotic stewardship)
- Evaluate impact as well as sustainability



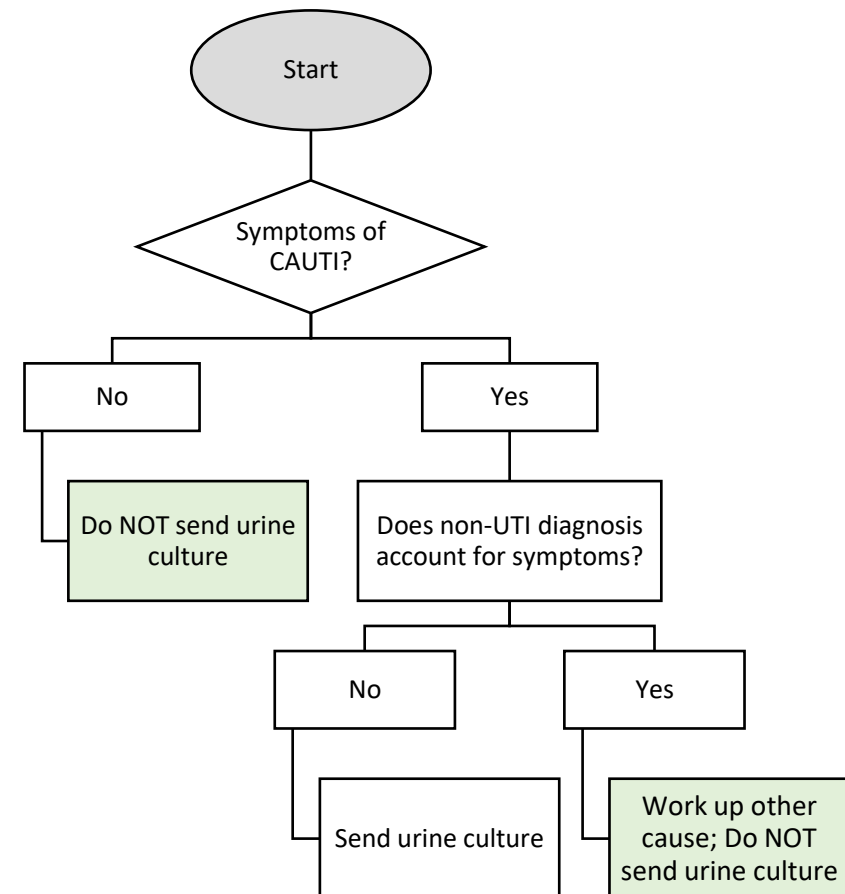
**Kicking UTI**  
The No Knee-Jerk  
Antibiotics Campaign

# Education – Kicking CAUTI

## Case-based audit and feedback

- Address two points in chain of events
  - Decision to *order* urine culture
  - Decision to *treat* positive urine culture
- Train clinicians on algorithm
- Select cases with teaching points AFTER positive urine culture
- Goal = overcome provider barriers to evidence-based care

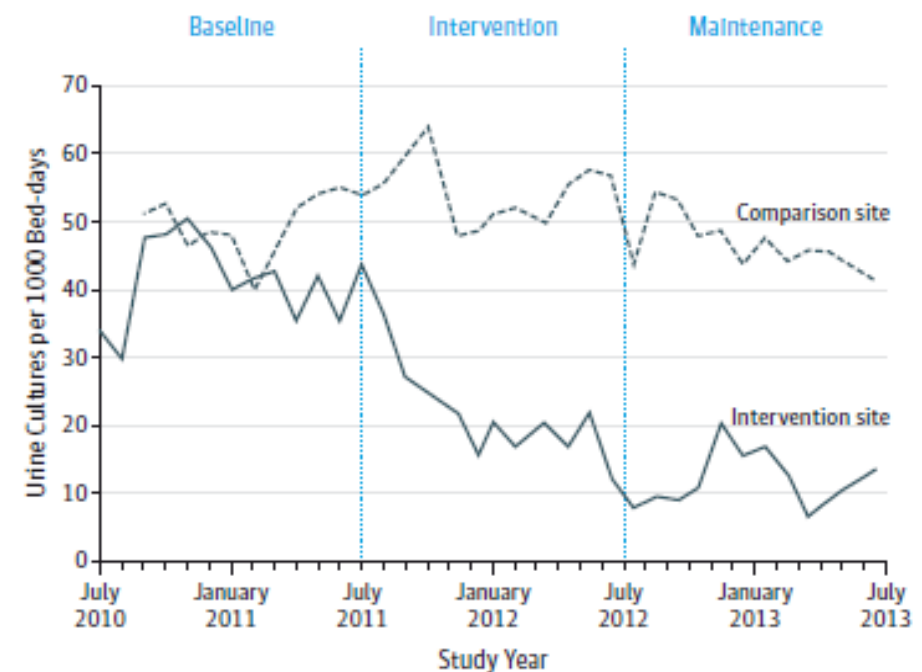
## Actional Algorithm



# Education – Kicking CAUTI

- Intervention Site
  - Urine culture orders decreased
  - 41.2/1,000 bed-days to 23.3/1,000 bed-days
- Control Site
  - Urine culture orders remained the same
- Antimicrobial Use
  - ASB over-treatment decreased
  - IRR, 0.35; 95% CI, 0.22-0.55,  $P < .001$
  - *Intervention site only*

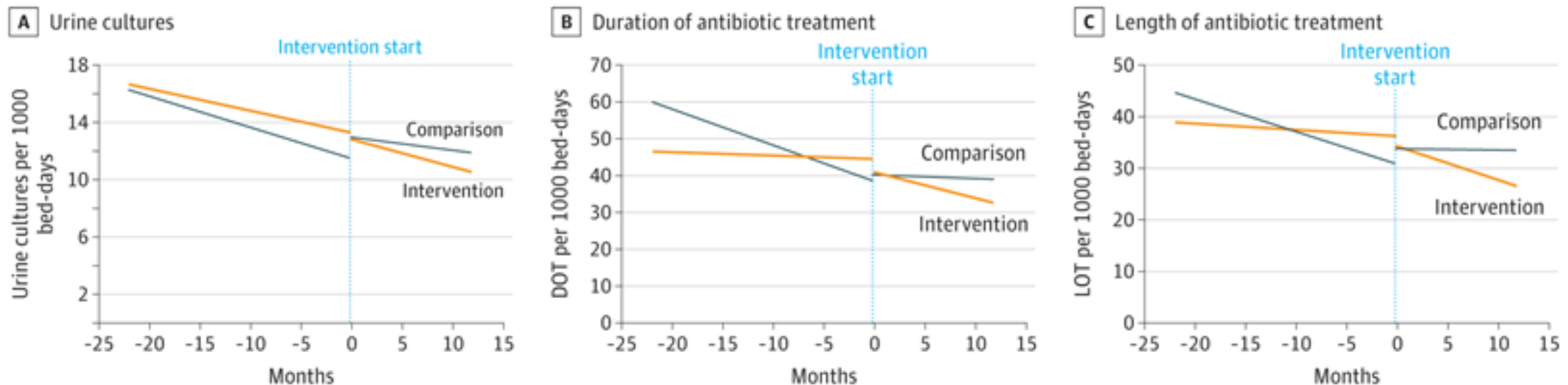
Figure. Monthly Rates of Urine Culture Orders per 1000 Bed-days



Shown are the intervention vs comparison sites across the 3 study periods ( $P < .001$ ).

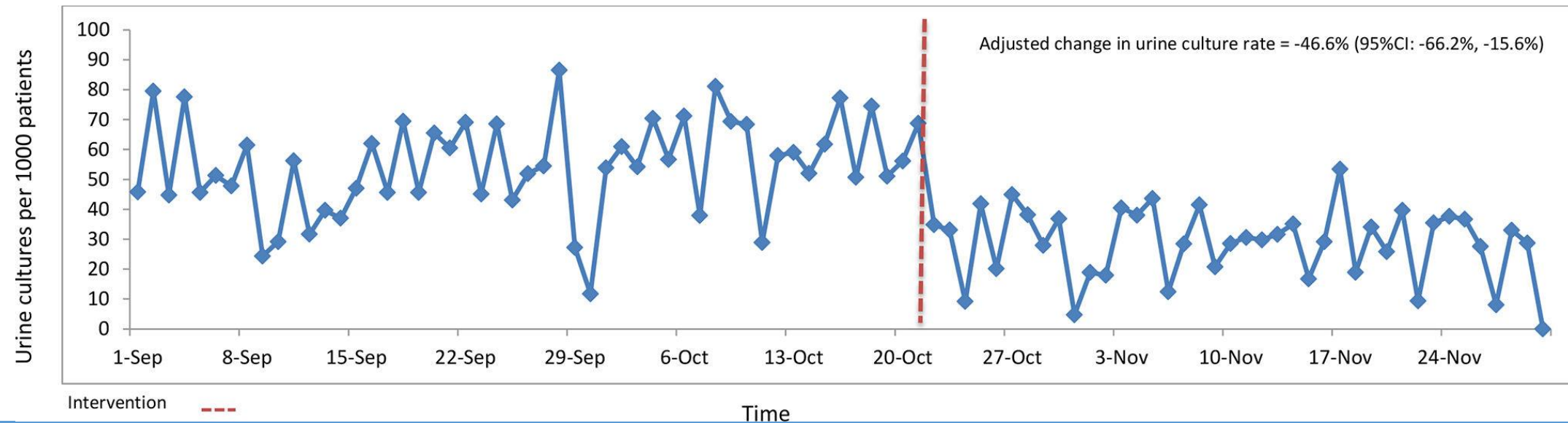
# Less is More for ASB Project

- Scaling up of Kicking CAUTI across geographically district Vas
  - Evidence-based clinically actional algorithm
  - Case-based education to train clinicians to use the algorithm
  - Assisted by local site champion(s) (infectious diseases physician and/or pharmacist)



# Order Set Design Changes

- Removal of urine cultures from “frequently ordered” in order sets
  - Pre-/post study of ED orders for UA/UC
  - Daily culture rate per 1,000 ED visits down 46.6%
  - Similar reduction found for hospitalized patients



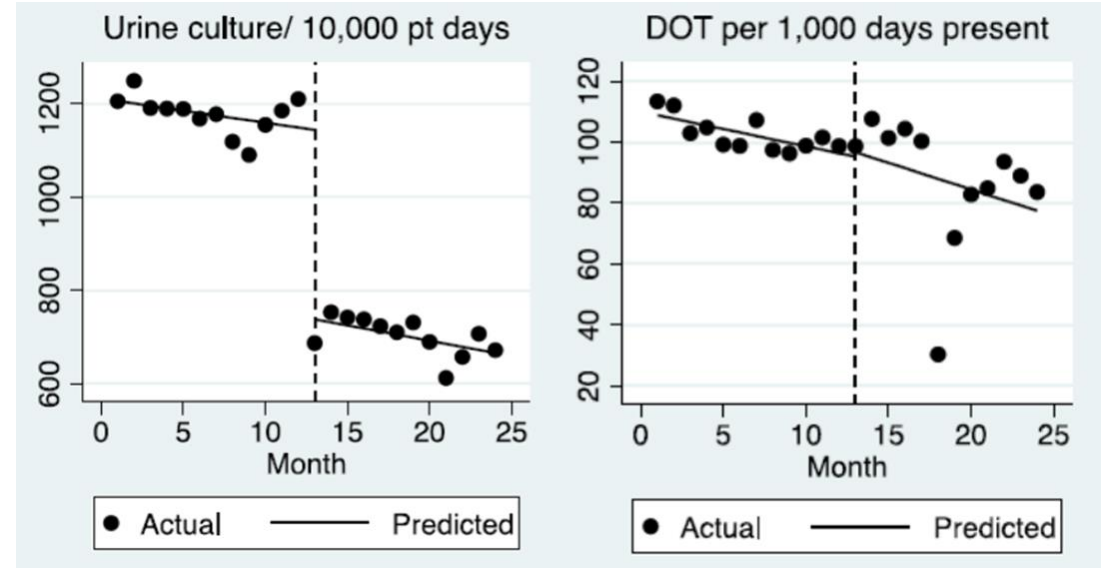
# Appropriate Clinical Indications for Urine Culture Ordering

Patients without Urinary Catheters		
<p><b>Appropriate</b></p> <p>Dysuria, suprapubic pain, flank pain, Costovertebral angle (CVA) tenderness, or septic shock</p>	<p><b>Uncertain</b></p> <p>Fever or systemic leukocytosis with no other known cause</p>	<p><b>Inappropriate</b></p> <p>Altered mental status, or change in urine characteristics (color, sediment, smell)</p>
Patients with Urinary Catheters		
<p><b>Appropriate</b></p> <p>Dysuria, suprapubic pain flank pain, Costovertebral angle (CVA) tenderness, or septic shock</p>	<p><b>Uncertain</b></p> <p>Fever, systemic leukocytosis with no other known cause, or delirium*</p>	<p><b>Inappropriate</b></p> <p>Change in urine characteristics (color, sediment, smell)</p>



# Urine Culture Clinical Decision Support

- Multi-center: adult inpatient & outpatient sites
- Addition of order set in the EMR
  - Added: Type of urine study
  - Changed: UA with reflex to culture
  - UA with reflex to culture **requires** clinical indications



**Urine Cultures**  
**40%**



**UTI Abx DOTs**  
**15%**



**Appropriateness**  
**42% to 57%**

# Best Practices for Diagnostic Stewardship

## Urine Culture Processing

<b>Appropriate Practices</b>	<ol style="list-style-type: none"> <li>1. Use elevated urine WBC count as a criterion to reflex to urine culture when a clinician orders a urine culture (all settings)</li> <li>2. Require documentation of collection site method (i.e. clean catch) prior to processing urine cultures</li> </ol>
<b>Inappropriate Practices</b>	<ol style="list-style-type: none"> <li>1. Automatically reflex routine urinalyses to urine cultures for abnormal findings when a urine culture was not specifically requested by the ordering clinician</li> </ol>

*Guidance is for all healthcare settings unless specifically noted*

*These recommendations apply to symptomatic patients only. Patients that do not have symptoms of urinary tract infection should not be cultured.*

# Conditional Urine Reflex Culturing

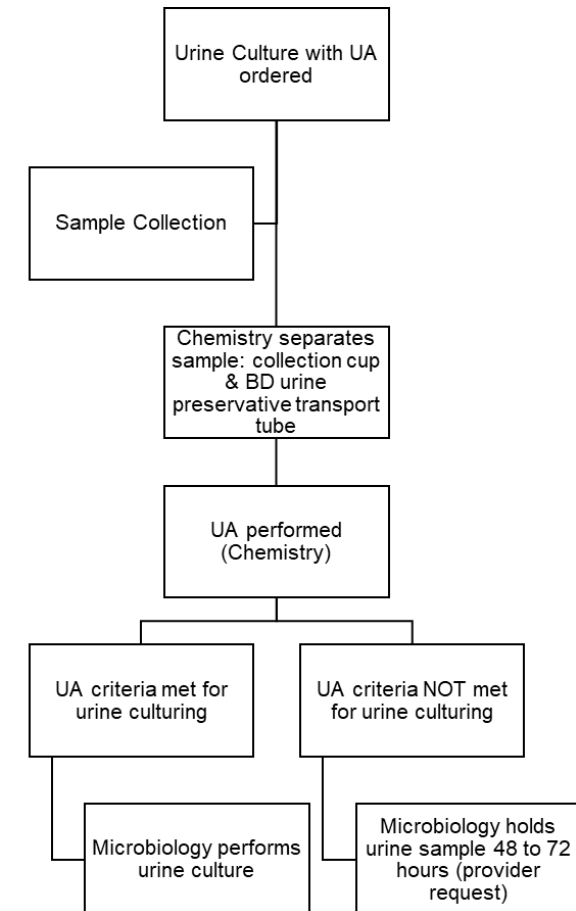
Urine cultures often ordered without appropriate indications

Urine cultures ordered are **ONLY** performed based on pre-defined criteria on urinalysis (UA)

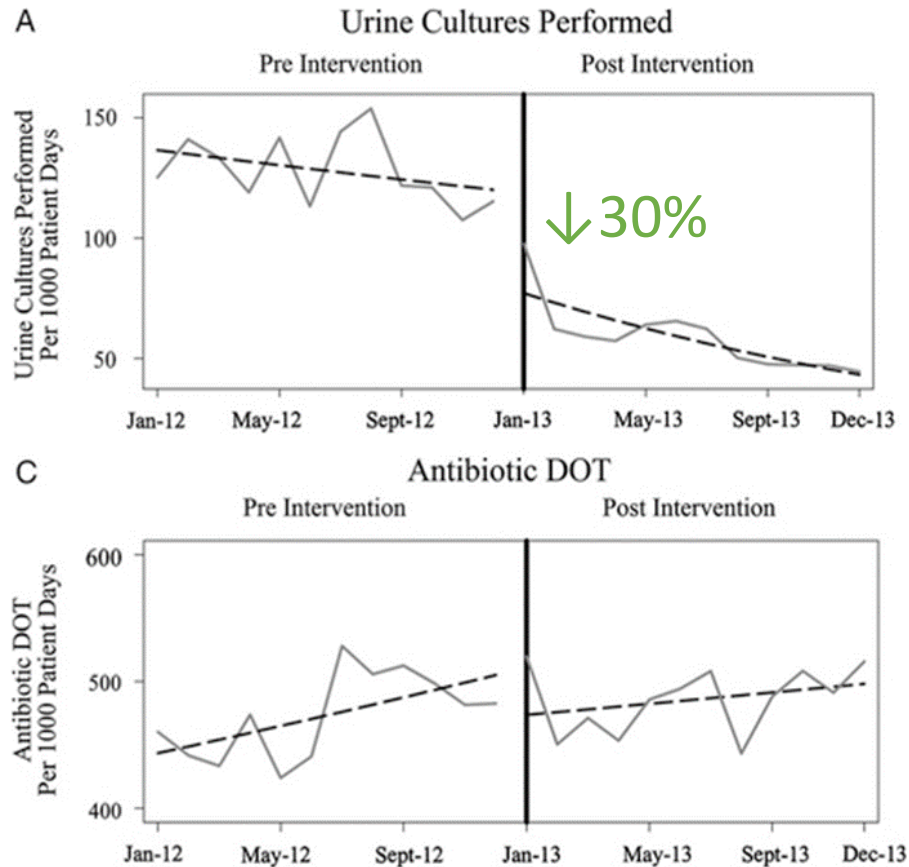
- NOT automatic reflex to urine culture when UA is ordered

Expert agreement: Elevated urine WBC as a criterion to reflex to urine culture

- Minimum 10 WBC per hpf



# Conditional Reflex Urine Culturing



- Single-centered pre/-post-study implementing conditional urine culture testing (WBC > 10/hpf) in ICUs
- Population-level analysis
  - Urine cultures performed decreased 30% ( $P < .001$ )
  - Positive urine cultures decreased 28% ( $P < .001$ )
  - No change in overall antibiotic use (DOTs)
- Patient-level analysis
  - New antibiotics in response to culture decreased (41% vs 23%,  $P = .002$ )

# Decreased Culturing Doesn't Guarantee Decreased Antibiotics

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- Single-center study with reflex culturing → if any UA criteria met, report of **POSITIVE** placed in EMR
  - Reflex UA positive had more UTI antibiotics
    - 14.1% vs 2.5%,  $P < 0.01$
  - Reflex UA positive more quickly prescribed UTI antibiotics
    - 3 hours vs 7 hours,  $P = 0.02$
- *How you implement just as important as what you implement*

# Best Practices for Diagnostic Stewardship

## Urine Culture Reporting

<b>Appropriate Practices</b>	<ol style="list-style-type: none"> <li>1. In urine culture reports, to:             <ul style="list-style-type: none"> <li>• Inform clinicians that even high colony counts (i.e.&gt; 100,000 CFU) may not represent true infection in the absence of symptoms or signs<sup>‡</sup></li> <li>• Nudge clinicians to not treat asymptomatic bacteriuria<sup>‡</sup></li> <li>• Nudge clinicians to not to treat mixed flora<sup>‡</sup></li> <li>• Differentiate typical uropathogens versus contaminants<sup>‡</sup></li> </ul> </li> <li>2. Withhold urine culture results (including organism identification and antibiotic susceptibilities) when there are more than two unique bacterial strains identified in culture</li> <li>3. Preferentially report only IDSA-recommended antibiotics if organism is susceptible</li> <li>4. Withhold fluoroquinolone susceptibilities unless there is resistance to preferred oral antibiotics</li> </ol>
<b>Inappropriate Practices</b>	<ol style="list-style-type: none"> <li>1. Nudge clinicians not to treat if there are less than 100,000 CFU of bacteria</li> <li>2. Withhold information about urine culture organism identification or antibiotic susceptibilities unless the clinician contacts the clinical microbiology laboratory</li> </ol>

Guidance is for all healthcare settings unless specifically noted. These recommendations apply to symptomatic patients only. Patients that do not have symptoms of urinary tract infection should not be cultured.

<sup>‡</sup>Due to expert disagreement, this recommendation does not extend to those undergoing a urological procedure

# Nudges & Framing Overview

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## NUDGES

Behavioral interventions to guide decision making through choice architecture

### FRAMING

Presenting choices to highlight positive or negative aspects of a decision, changing their relative attractiveness

### CASCADE REPORTING

Report narrow spectrum agents only when possible, report more if resistant

### SELECTIVE REPORTING

Restrict reporting of agents based on pre-defined criteria (i.e. intrinsic resistance, high ADE)

# Modified Reporting

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## Report Comment

“This POSITIVE urine culture may represent asymptomatic bacteriuria or urinary tract infection. If urinary tract infection is suspected clinically, please call the microbiology laboratory ... for identification and susceptibility results.”

- Randomized trial of lab reporting intervention to decrease treatment of ASB
- Modified reporting arm had significantly less unnecessary antibiotic therapy
  - 80% vs 52.7%,  $P = 0.002$
- Number needed to benefit = 3.7



# Conclusions

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- Clinically challenging to differentiate UTI from ASB, making best management practices difficult to implement
- Inappropriate antibiotics for ASB are prevalent and lead to increased antibiotic resistance and patient harm
- Antimicrobial stewardship *combined* with diagnostic stewardship initiatives decrease misdiagnosis of UTI and improve antibiotic use



# Best Practice in the Diagnosis and Treatment of ASB and UTI

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