

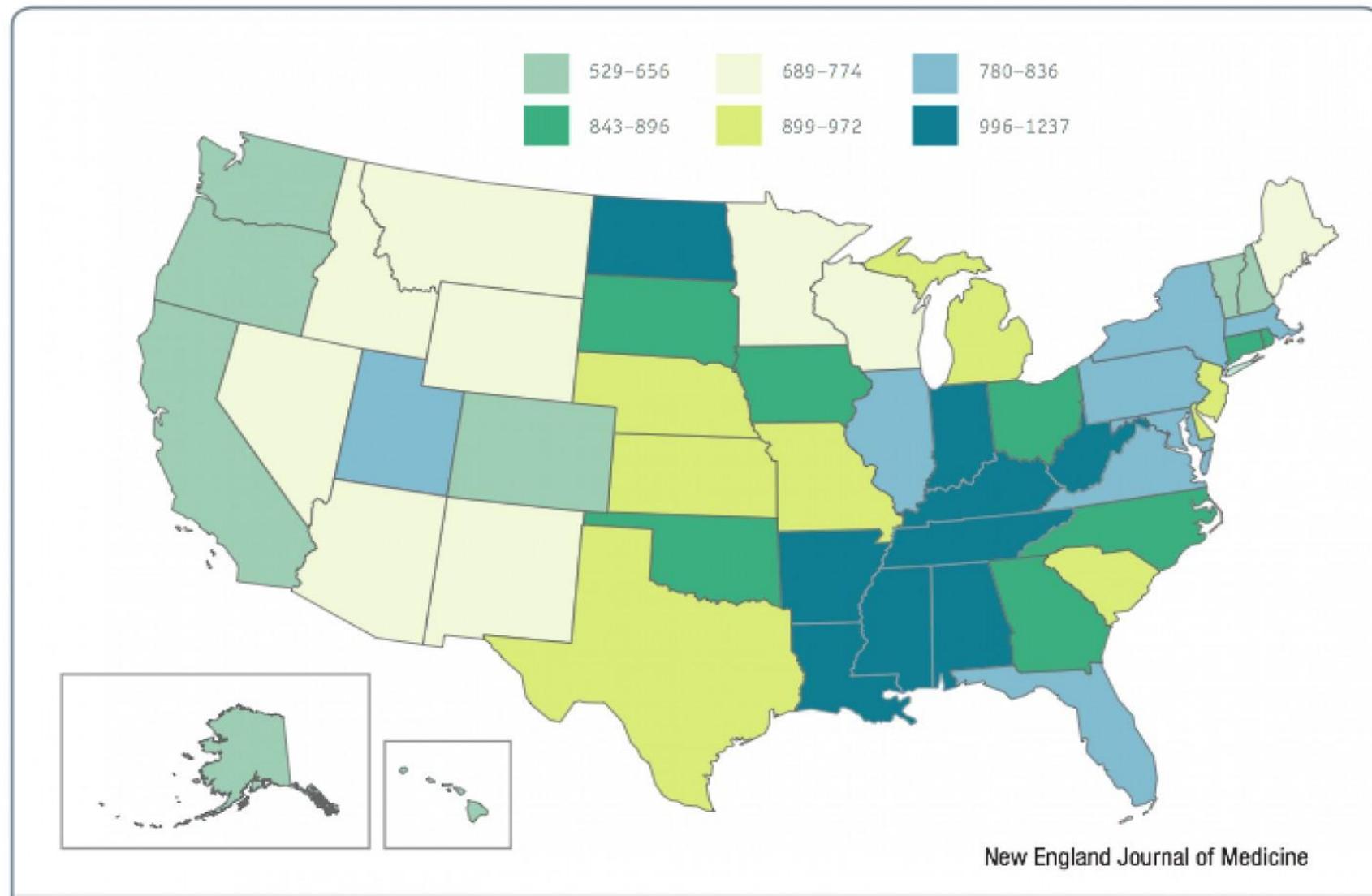
# Rational Antibiotic Use in the Management of Respiratory Tract [RTI] and Urinary Tract [UTI] Infections

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# Disclosures

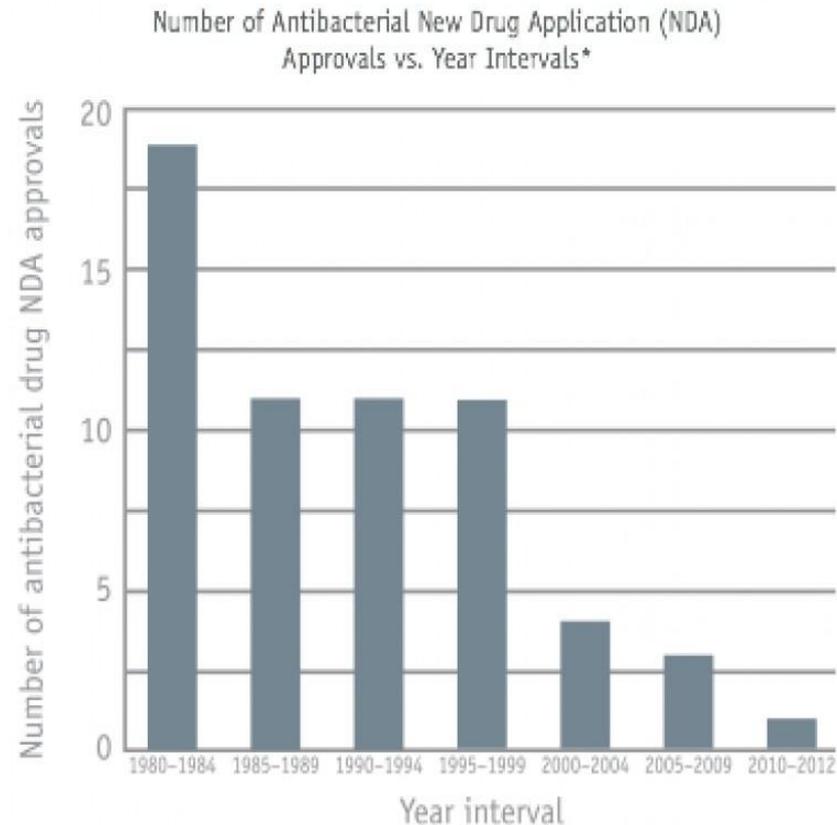
- Advisory Board member: Gilead Pharmaceuticals

## Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010



## Tomorrow's Antibiotics: The Drug Pipeline

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.



\*Intervals from 1980-2009 are 5-year intervals, 2010-2012 is a 3-year interval. Drugs are limited to systemic agents. Data courtesy of FDA's Center for Drug Evaluation and Research (CDER).

# Objectives

- **Describe and discuss Upper and Lower RTIs, and diagnostic approaches.**
- **Review rational use on antibacterial agents for RTIs.**
- **Describe and discuss asymptomatic bacteriuria vs simple UTIs vs complicated UTIs, and diagnostic approaches.**
- **Review rational use of antibacterial agents for UTIs.**

# Definitions

- Upper RTI: Common cold [viral], Pharyngitis\*, Croup [Acute laryngotracheobronchitis], Acute laryngitis\*, Otitis externa / media\* / Mastoiditis, Acute sinusitis\*, Epiglottitis
- Lower RTI: **Acute bronchitis** \* [mainly viral], Acute exacerbations of COPD, Bronchiolitis, **Acute pneumonia** [ bacterial / CAP / ABP ], Empyema, Lung abscess, Chronic pneumonia, Cystic fibrosis

# Microbial etiology

- Acute bronchitis

- Influenza A/B\*
- Rhinoviruses
- Coronaviruses
- Adenoviruses
- Respiratory Syncytial Virus
- Human metapneumovirus
- Parainfluenzavirus
- Measles virus

[ <10% bacterial ]

- Mycoplasma pneumoniae
- Chlamydia pneumoniae
- Bordetella pertussis\*

- Acute bacterial pneumonia

- Streptococcus pneumoniae\*
- Hemophilus influenzae
- Mycoplasma pneumoniae
- Chlamydia pneumoniae
- Legionella pneumophila
- Staphylococcus aureus
- Enteric GNRs

- HCAP / HAP / VAP

- Pseudomonas aeruginosa
- MRSA
- Multi-drug resistant organisms

# Diagnosis

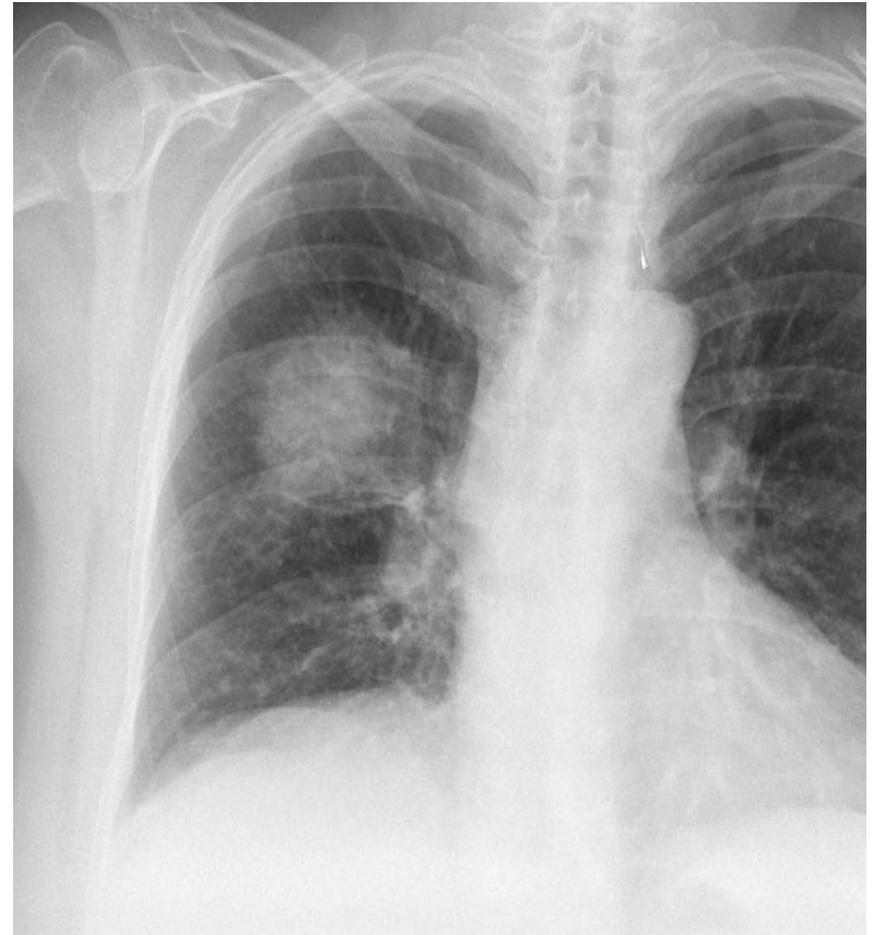
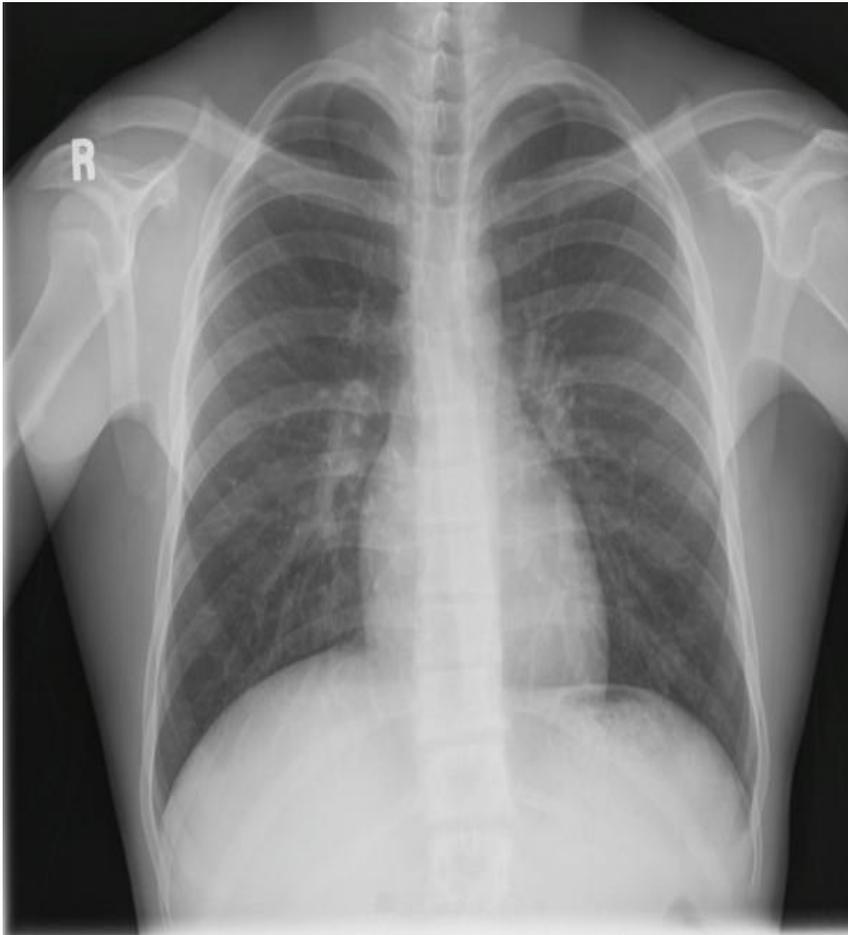
- **Acute bronchitis**

- Dry or productive cough for 3 weeks or less, mostly wintertime, low-grade fevers
- Initially with rhinitis, nasal congestion, malaise, sore throat
- Occasionally with wheezing
- < 7% with abnormal CXR
- WBC or CRP do not reliably discriminate viral from bacterial infections
- Serum Procalcitonin is not elevated with viral infection
- **Molecular diagnostics [PCR]**

- **Acute pneumonia**

- Cough, sputum production, dyspnea, chest pain, fever, fatigue, sweats, headache, nausea, myalgia, abdominal pain, occasional diarrhea
- Typically abnormal CXR
- Sputum gram stain / culture
- Blood cultures [HCAP, HAP, VAP, immunocompromised]
- **Serum procalcitonin** [and CRP] are usually elevated with bacterial infection
- Serum Ab [Mycoplasma] and Urine Ag [Legionella] tests
- Molecular diagnostics [PCR]

# Chest Radiography



# Management considerations

- Acute bacterial pneumonia pathogens differ from those associated with HCAP, HAP, VAP and Aspiration pneumonia
- Viral pneumonias cannot be reliably distinguished from bacterial pneumonia based on physical examination, WBC or CXR
- Despite exhaustive effort, an etiology for CAP is achieved only ~ 50% of the time
- Older series indicated 25% mortality, while modern series show about 10-15% mortality from pneumococcal bacteremia [so vaccinate!]

# Rational antibiotic use in RTIs

- Acute bronchitis is a viral infection 90% of the time, and can be treated symptomatically
- Empiric antibiotic choices include macrolides, fluoroquinolones, beta-lactams [PCN, Ceph], vancomycin doxycycline, and clindamycin – but treatment hinges on the clinical situation [IDSA/ATS guidelines]
- CAP can typically be treated for 5 - 10 days
- Prior treatment with fluoroquinolones, cephalosporins or clindamycin can predispose to *Clostridium difficile* infection
- Infections untreatable with antibiotics can sometimes be treated surgically

# Pulling the trigger on antibiotic Rx

- Treat the symptoms [or defer an antibiotic prescription] if the syndrome is likely to be viral
- See if a rapid diagnostic test [PCT, Multiplex PCR, CXR, POC testing] is available
- Pathogen identification and susceptibility test results allows for de-escalation of therapy [inpt.]
- Spectrum coverage, host factors, collateral damage, and costs factor into choosing an agent(s)
- Consultation with ID is recommended if **bacterial resistance** and **patient allergies** severely limits antibiotic choices

# Definitions / Urinary Tract Infections

- Asymptomatic bacteriuria [ASB]: Presence of **significant bacteriuria** with no symptoms referable to the urinary tract
  - F:  $\geq 100\text{K}$  CFU/ml of the same organism in 2 consecutive voided specimens, or 1 fresh catheter sample
  - M:  $\geq 100\text{K}$  CFU/ml in 1 voided specimen, or fresh catheter sample
- Simple UTI: [**~cystitis**, ~pyelonephritis] Ascending infection in younger females, typically due to E coli [rarely yeast],  $\geq 1000$  CFU/ml with symptoms

# Complicated UTI [~Nosocomial]

- Typically associated with indwelling catheters (97%), anatomical or functional abnormalities, surgery or instrumentation
- Nosocomial: Acquired in any institutional setting providing health care
- CA-UTI:  $\geq 1000$  CFU/ml in symptomatic pt
- Symptoms: Fever/rigors, altered mentation, flank pain, CVA tenderness, pelvic discomfort, new or worsening incontinence / malaise / lethargy
- SCI patients: Increased spasticity, autonomic dysreflexia, sense of unease

# Epidemiology of CA-UTI

- Accounts for 40% of nosocomial infections in US hospitals annually
- The incidence of bacteriuria in indwelling catheter systems with a closed drainage system is 3 - 8% / day
- Serial urine cultures growing the same isolate implies a focal nidus of infection, while different isolates implies contamination or incorrect collection technique
- CA-bacteriuria comprises a large reservoir of antibiotic-resistant organisms, and is a frequent target of inappropriate antimicrobial therapy

# Diagnosis / Nosocomial UTI

- Urinalysis [Dipstick and Microscopic]: Typically all that's needed to diagnose uncomplicated UTI [cystitis] in the outpatient setting
- CA-UTI: Symptoms [no other recognized cause], Urine culture  $\geq 100\text{K}$  CFU/ml, or UCx with 1K-100K CFU/ml and (+) dipstick [Nitrite(+), LE(+)], pyuria or bacteria seen on Gram stain
- Urine cultures can be helpful in looking for patterns of infection, and susceptibility testing

# Treatment issues

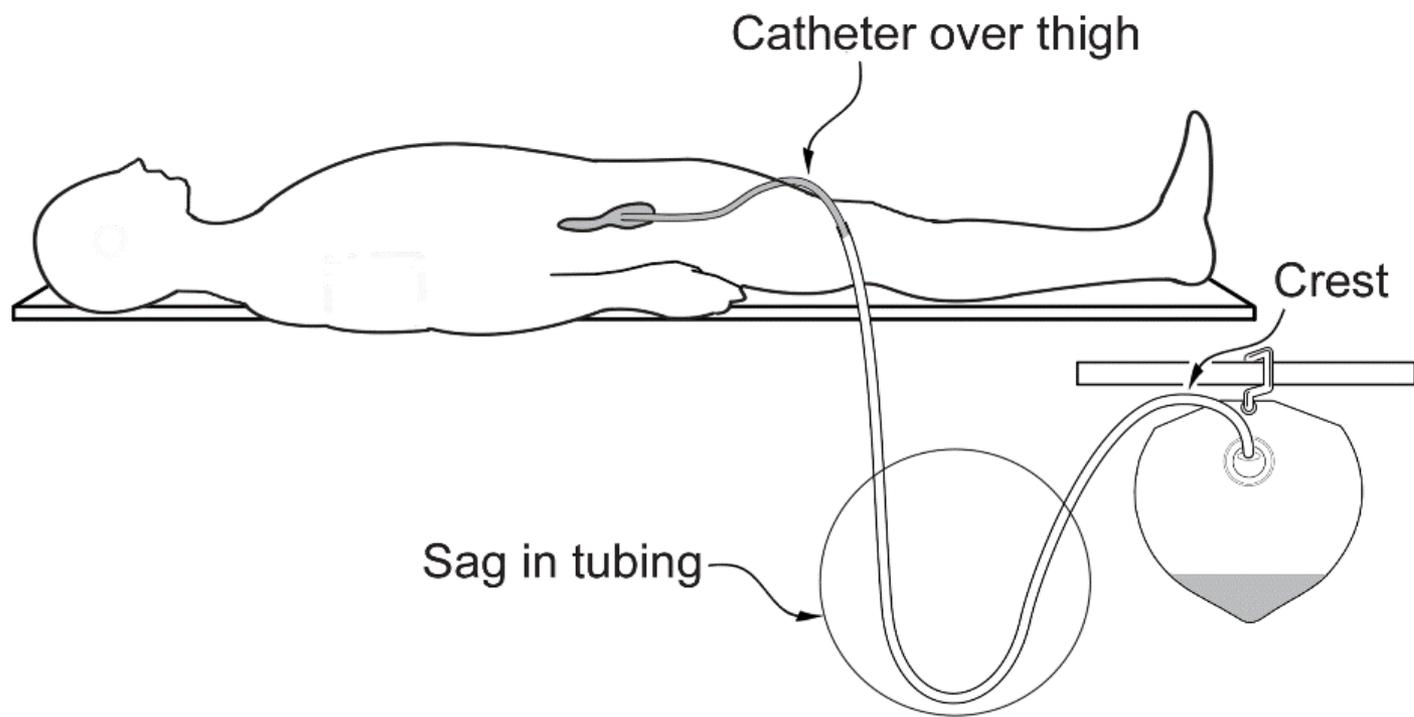
- Problems arise when the organism is multi-drug resistant, or the patient has numerous drug allergies or adverse reactions
- Treatment can often be for 1-5 days for cystitis, but may be closer to 5-10 days for complicated UTIs
- Removal [or replacement] of the catheter helps reduce the bioburden [biofilm]
- Recurrent UTIs merit work up for anatomical or functional problems
- Oral agents are tried first, but IV agents may be needed for difficult cases

# Antibiotic agents for UTI

- Oral: Ciprofloxacin, Levofloxacin, penicillins, cephalosporins, SXT / TMP/SMZ / Bactrim, Nitrofurantoin [only if the GFR  $\geq$  50 mls/min], fosfomycin
- IV: Extended-spectrum penicillins [Zosyn], cephalosporins, aztreonam, carbapenems, aminoglycosides, fluoroquinolones, linezolid
- ? bladder irrigation
- ? antibiotic - impregnated or antibiotic - coated catheters

# Accepted Prevention Strategies

- Reduce exposure to catheterization at the outset
- Try alternative catheter methods [condom, supra-pubic, intermittent] rather than Foley
- Closed catheter drainage system, and positioning
- Use of multiple infection control techniques and strategies simultaneously [“bundling”]
- Methenamine hippurate [Hiprex] / mandelate [Mandelamine] are bladder antiseptics that may be helpful in patients without an indwelling catheter, do not have a neurogenic bladder, and a GFR  $\geq 50$  mls/min



# Marginal Prevention Strategies

- Enhanced meatal care
- Cranberry products: No published data in catheterized adults without neurogenic bladder
- Bladder irrigation with saline or antibiotics
- Antimicrobial dugs in the drainage bag
- Prophylactic antibiotics at the time of catheter removal or replacement
- ? Routine catheter change
- Mannosides
- Bacterial interference

# Antibiotic Stewardship

- Optimizing antibiotic selection for a given syndrome, taking into account pathogen, as well as host factors, and their interaction
- Avoiding empiric approaches, and striving for a microbiologic diagnosis
- Look for clinical decision support tools online or with your EMR [eg. VirtuWell / HPMG]
- De-escalate regimens as soon as possible
- Emphasize non-antibiotic approaches to prophylaxis [infection control, vaccination, etc]