

5 Common Errors in Antimicrobial Prescribing (Hospitalized Patients)

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Presenter Disclosure

- Relationships with commercial interests:
 - Grants/Research Support: Merck
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 - Consulting Fees: N/A
 - Other: N/A

Case #1

- 68 yo man admitted with low-grade fever, chest pain and purulent sternal wound discharge 3 weeks post CABG
- Wound probes to bone, c/s (+) methicillin susceptible *S. aureus*
- CV surgeon contacted, trial of IV Cloxacillin is recommended

What is the prescribing error?

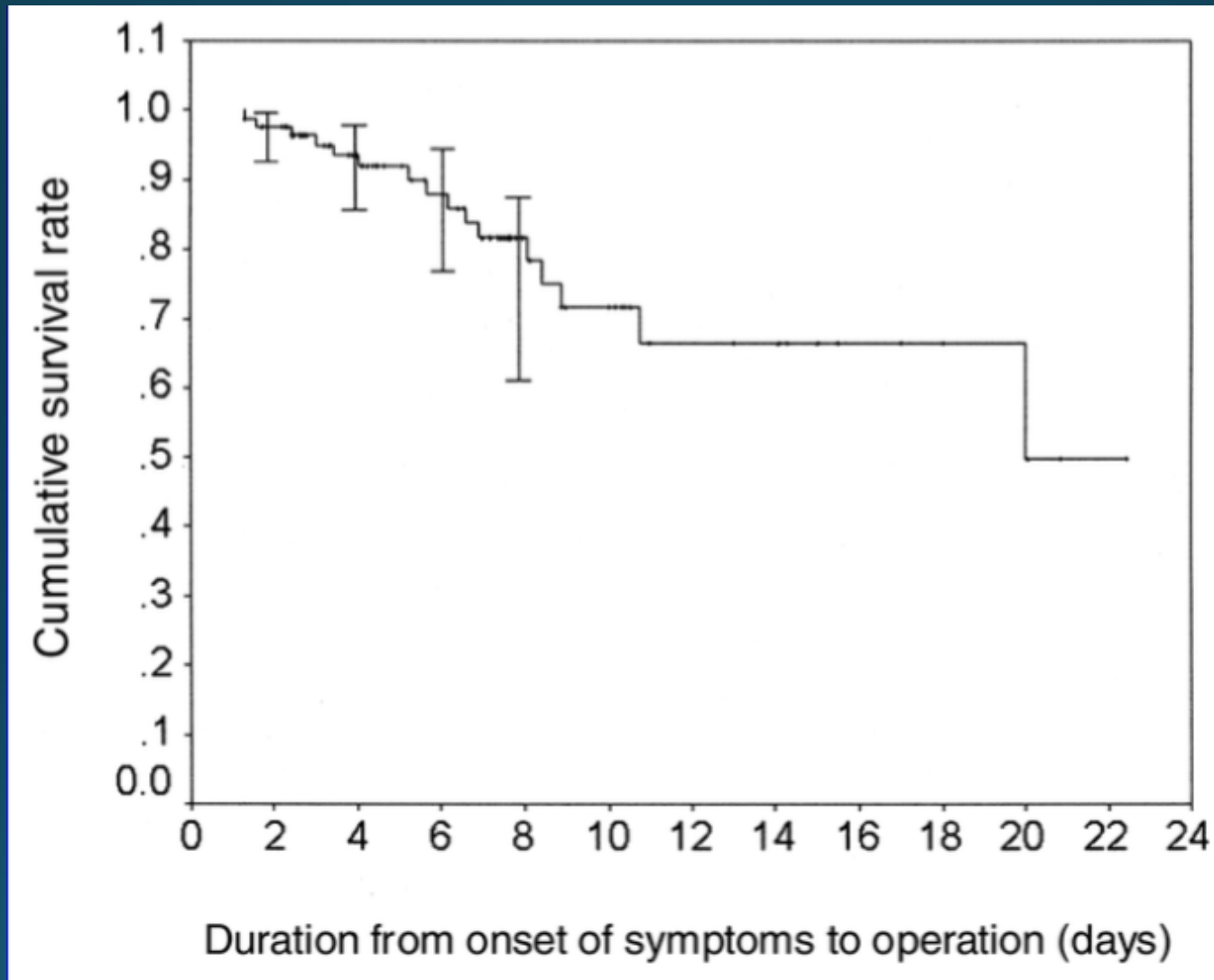


Source Control

Table 3. Mortality differences after relaparotomy for persisting abdominal sepsis according to the preoperative APACHE II score.

APACHE II score	Relaparotomy ≤ 48 hr (%)	Relaparotomy > 48 hr (%)	Significance (<i>p</i>)
≤ 10	0	25	0.09
11–15	0	33	0.02
16–20	0	78	0.002
21–25	57	100	0.02
≥ 26	79	94	0.2
Overall	28	77	0.0001

Influence of Source Control on Survival Necrotizing Fasciitis



Prescribing Error #1

ANTIMICROBIAL THERAPY IS NEVER A SUBSTITUTE FOR SOURCE CONTROL

COMMON PRINCIPLES OF SOURCE CONTROL

- Abscesses > 3cm require drainage
- Osteomyelitis is incurable unless sequestrum removed
- Debride devitalized tissue
- Extract Infected prosthetic devices
- Relieve obstruction (ex.ureteric stones in urosepsis, common duct stones in biliary sepsis)

Case #2

- DK 84 yo with alcoholic cirrhosis, 8 drinks/day
- Admitted Dec 31st with pneumonia
- CRB-65 score = 2
- Rx Cefuroxime 1.5 gm IV Q8H + Doxycycline 100 mg po BID x 12 days
- ID consult requested to determine treatment duration

What is the prescribing error?



IV to PO Conversion

General Criteria:

The Patient:

- ___ is tolerating food, enteral feeds and/or other oral medications **AND**
- ___ is not showing evidence of malabsorption (e.g. diarrhea/vomiting)

Antimicrobial Criteria

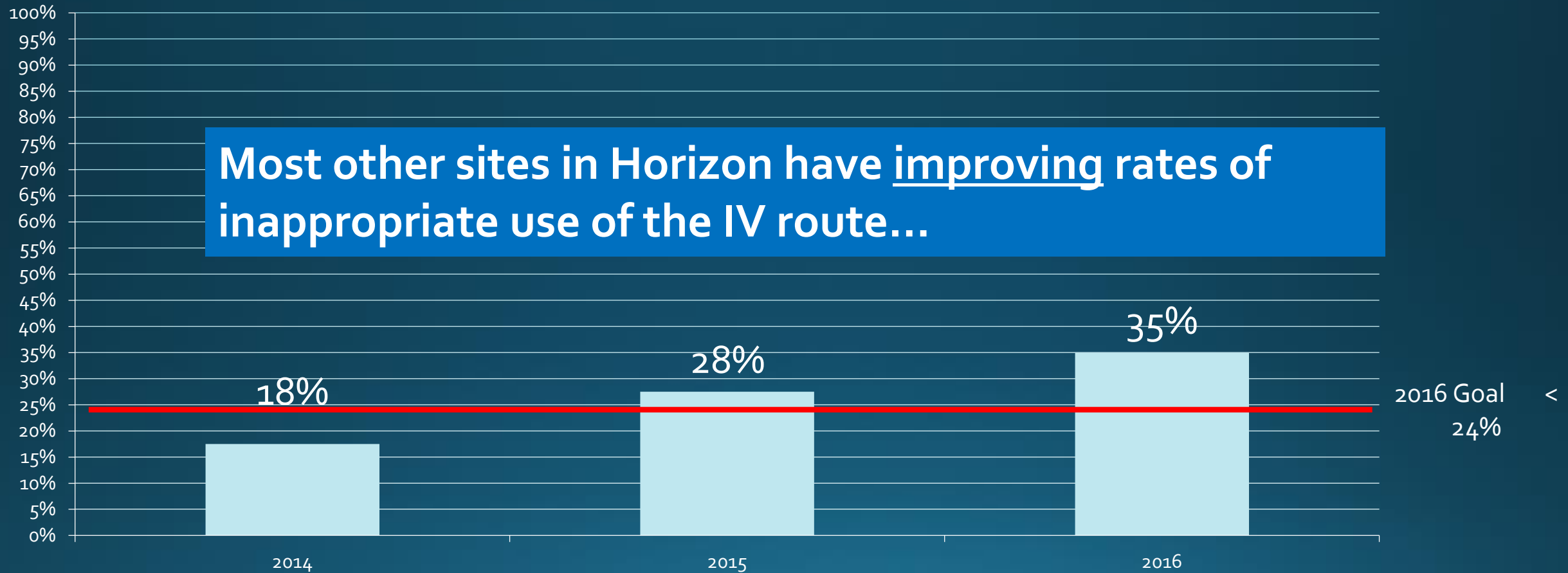
The Patient:

- ___ is clinically improving (normal mental status; improved clinical signs and symptoms; normalizing WBC count; etc...) **AND**
- ___ is hemodynamically stable (pulse rate less than 100 beats/min; respiratory rate less than 24 breaths/min; systolic blood pressure greater than 90 mmHg; oxygen saturation greater than or equal to 90% on room air or at baseline) **AND**
- ___ has been afebrile for at least 48 hours (temperature less than 37.8°C) **AND**
- ___ does not have *Staphylococcus aureus* bacteremia

- Most hospitalized patients can be switched to PO after 3 days
- No need to observe stable patients overnight after IV to PO switch (Nathan et al *Am J Med* 2006;119:512)

Proportion of Hospitalized Patients With Inappropriate Use Of IV Antimicrobial on Day #3

The Moncton Hospital



Prescribing Error #2

The Majority of Patients With Community Acquired Infection Can Undergo IV to Oral Step-Down by Day #3

Benefits of early step-down

- Facilitates discharge
- Reduces complications
 - Infections, phlebitis, thromboembolism
- Facilitates early and/or more frequent ambulation
- Reduces the risk of falls
- Reduces costs
 - Drug acquisition cost, pharmacy preparation, nursing administration

Case #3

- 53 yo woman presents to ER with 1 day Hx of fever and rapidly ascending pain, edema and erythema right leg.
- History of penicillin allergy
- Prescribed IV Clindamycin and admitted to hospital

What is the prescribing error?



Prescribing Error #3

Cefazolin is The Drug of Choice For Moderate Erysipelas And Cellulitis

Benefits of Cefazolin in Moderate Erysipelas/Cellulitis

- Covers >95% of implicated microbes
- Reduces complications
 - Low risk *C. difficile*
 - Low risk phlebitis
 - Safe even in severe penicillin allergy (Type 1 Hypersensitivity)
- Reduces costs
 - Can give as once daily outpatient parenteral therapy by combining with 1 gram oral probenacid
 - Inexpensive
 - Step-down to Cefadroxil 500 mg PO BID x 1 week

Case #4

- 83 yo woman on family medicine ward
- Attending nurse notes cloudy, foul-smelling urine and sends sample for urinalysis/culture
- On call physician called at 1715 hrs because urine c/s (+) *E. coli*
- Ciprofloxacin 500 mg po bid x3 days prescribed

What is the prescribing error?

Canadian Urological Association

Five Things Physicians and Patients Should Question

Released October 29, 2014

www.choosingwiselycanada.org/

4 Don't use antimicrobials to treat asymptomatic bacteriuria in the elderly.

Studies suggest that asymptomatic bacteriuria in the elderly does not carry significant risk of morbidity if left untreated. Antimicrobial treatment studies for asymptomatic bacteriuria in older adults demonstrate no benefits and show increased adverse antimicrobial effects. Consensus criteria has been developed to characterize the specific clinical symptoms that, when associated with bacteriuria, define urinary tract infection. Screening for and treatment of asymptomatic bacteriuria is recommended before urologic procedures for which mucosal bleeding is anticipated.

Withholding Inpatient Urine C/S Results Reduces Unnecessary Antimicrobial Prescribing in Non-catheterized Patients

'The majority of positive urine cultures from inpatients without an indwelling urinary catheter represent asymptomatic bacteriuria. If you strongly suspect that your patient has developed a urinary tract infection, please call the microbiology laboratory.'

- 134/151 (89%) positive urine cultures identified in asymptomatic patients
- 15/31 (48%) Rx pre-intervention vs 4/33 (12%) Rx post-intervention
- ARR=36%(95% CI 15-57%: P= .002) NNT=2.7
- Lab called for 5/37 (14%) cultures
- 4 UTI's identified, all given appropriate empiric Rx
- No symptoms or sepsis in the untreated group

Moncton UTI Bundle

UTI Bundle: Suppression of lab reporting of positive cultures; pharmacy prospective audit & feedback; physician and nurse education.

	Pre-Intervention (276)	Post-Intervention (268)	P-value
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- **ARR = 52.3%**
 - **NNT = 2**
 - **i.e. for every 2 urine cultures with results suppressed and pharmacy follow-up you will prevent 1 case of inappropriate treatment of asymptomatic bacteriuria**
- **781 to 138 days of avoidable antimicrobial therapy**

Sepsis at 72 hours	0/276	1/268 (0.4%)	0.49
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Prescribing Error #4

Do not Treat Asymptomatic Bacteriuria (Except during Pregnancy or Prior to Urologic Procedures)

- Treatment of asymptomatic bacteriuria associated with no benefit and significant harms (Nicolle et al. Clin Infect Dis 2005:643-654)
- Foul smelling or cloudy urine does not indicate UTI (UTI is a clinical diagnosis based upon the presence of dysuria, frequency and urgency)
- Up to 90% of urine specimens submitted in hospitalized patients represent asymptomatic bacteriuria
- Quinolone no longer recommended as empiric therapy (E. coli resistance approximately 20% in those with Hx recurrent UTI)

Case #5

- 70 yo woman presents to ER with crampy abdominal pain and constipation
- Focal LLQ abdominal tenderness with no guarding or rebound
- WBC=11, normal creatinine, sigmoid thickening/mesenteric stranding on CT
- Discharged home on Ciprofloxacin 500 mg bid + Metronidazole 500 mg bid

What is the prescribing error?

Antimicrobial Therapy for Intra-Abdominal Infections

(NB Provincial Health Authorities Anti-Infective Stewardship Committee, November 2015)

Origin/Severity of Intra-Abdominal Infection	Probable Pathogens	Preferred Empiric Regimens	Alternative Empiric Regimens	Comments
<p>Community Acquired Infection, Mild to Moderate severity:</p> <ul style="list-style-type: none"> i.e. gastroduodenal perforation, cholangitis^a, cholecystitis^a, appendicitis, diverticulitis^b, primary (spontaneous) bacterial peritonitis With no evidence of systemic toxicity (APACHE II score less than 15) 	<p>Core: Enterobacteriaceae (i.e. <i>E.coli</i>, <i>Klebsiella spp.</i>, <i>Proteus spp.</i>, <i>Enterobacter spp.</i>) Anaerobes (i.e. <i>B. fragilis</i>, <i>Clostridium spp.</i> etc...), <i>Streptococcus spp.</i>, ± <i>Enterococcus spp.</i> (see below if isolated)</p>	<p>ceFAZolin 2 g IV q8h^{g,*} + metroNIDAZOLE 500 mg IV/PO q12h^{a,b}</p> <p>Intravenous-to-Oral Conversion^c: amoxicillin/clavulanate 875/125 mg po q12h^{h,*}</p>	<p>CefOXitin 2 g IV q6h^{h,*}</p> <p>OR</p> <p>gentamicin 5 – 7 mg/kg IV q24h* + metroNIDAZOLE 500 mg IV/PO q12h</p> <p>OR</p> <p>ciprofloxacin 400 mg IV OR 500 mg PO q12h* + metroNIDAZOLE 500 mg IV/PO q12h</p>	<p>Duration of Therapy, dependent on clinical picture:</p> <ul style="list-style-type: none"> 5 – 7 days usually sufficient if optimal source control obtained If intra-abdominal abscess: antimicrobial therapy may be prolonged, with duration dependant on resolution (up to 4 to 6 weeks) Day of intervention (drainage, surgery, etc.) considered as day 1 of therapy
<p>Community Acquired Infection, Severe:</p> <ul style="list-style-type: none"> As above with APACHE II score greater than or equal to 15, signs of systemic toxicity, greater than 70 years old, immunocompromised, secondary peritonitis, cancer, poor nutritional status or incomplete or delayed source control 	<p>Core</p>	<p>cefTRIAxone 2 g IV q24h^g + metroNIDAZOLE 500 mg IV/PO q12h</p> <p>Intravenous-to-Oral Conversion^c: As for mild to moderate above</p>	<p>piperacillin/tazobactam 3.375 g IV q6h^{d,e,h,*}</p> <p>OR</p> <p>ampicillin 2 g IV q6h^{h,*} + gentamicin 5 – 7 mg/kg IV q24h* + metroNIDAZOLE 500 mg IV q12h</p> <p>OR</p> <p>ciprofloxacin 400 mg IV q12h* + metroNIDAZOLE 500 mg IV q12h</p>	<p>Stop antimicrobial within 24 hours if:</p> <ul style="list-style-type: none"> acute stomach, duodenum &/or proximal jejunum perforation if no acid-reducing therapy or malignancy and source control achieved OR penetrating bowel trauma repaired within 12 hours OR intraoperative contamination of a surgical field from enteric contents OR acute appendicitis without perforation, abscess or local peritonitis OR patients undergoing cholecystectomy for acute cholecystitis unless evidence of infection outside wall of the gallbladder (ex. perforation)
<p>Healthcare Associated</p> <ul style="list-style-type: none"> Hospitalized greater than 48 hours at time of onset, recent prolonged hospitalization, post-operative infection, long term care, rehab, dialysis, nursing home, recent antibiotics 	<p>Core Plus: <i>Pseudomonas</i>, Multidrug Resistant (MDR) Gram-negative bacteria, MRSA (see below if isolated)</p>	<p>piperacillin/tazobactam 3.375 g IV q6h^{d,e,h,*}</p>	<p>imipenem-cilastin 500 mg IV q6h^{e,g,*} (preferred if suspected MDR Gram-negative)</p> <p>OR</p> <p>ciprofloxacin 400 mg IV q12h* + metroNIDAZOLE 500 mg IV q12h + vancomycin 15 mg /kg IV q12h^{f,*}</p>	



FLUOROQUINOLONES - Risk of Disabling and Persistent Serious Adverse Reactions

Starting date: January 23, 2017
Posting date: January 23, 2017
Type of communication: Dear Healthcare Professional Letter
Subcategory: Drugs
Source of recall: Health Canada
Issue: Important Safety Information
Audience: Healthcare Professionals, General Public
Identification number: RA-61900

[Report a Concern](#)

- [Issue](#)
- [Who is affected](#)
- [Report health or safety concerns](#)
- [Related AWRs](#)

Audience

Healthcare professionals

Key messages

- Rare cases of disabling and persistent serious adverse reactions including tendinopathy, peripheral neuropathy, and central nervous system disorders have been reported to Health Canada for fluoroquinolones when used systemically (i.e. taken by mouth or by injection).**
- Healthcare professionals are reminded to:**
 - Consider the potential for disabling and persistent serious adverse events when choosing to prescribe a fluoroquinolone.**
 - Avoid fluoroquinolones in patients who have previously experienced serious adverse reactions associated with them.**
 - Stop fluoroquinolone treatment if a patient reports any serious adverse reaction. Patients should be switched to an alternative treatment with a non-fluoroquinolone antibacterial drug, if needed, to complete the treatment course.**
- Health Canada is currently working with manufacturers to strengthen the prescribing information for these drugs.**

Prescribing Error #5

Avoid Ciprofloxacin + Metronidazole Therapy for Intra-Abdominal Infection

- Quinolones not listed as first-line therapy for intra-abdominal infection in New Brunswick Antimicrobial Stewardship Guidelines
 - Poor activity against gram (+) cocci
 - 20% of *E. coli* quinolone resistant
 - ↑ *C. difficile* risk
 - Recent Health Canada and FDA warnings regarding serious adverse events

Summary

1. Antimicrobial therapy is never a substitute for source control
2. The majority of patients with community acquired infections can step-down to oral therapy after day #3
3. Cefazolin is the drug of choice for moderate erysipelas or cellulitis
4. Do not treat asymptomatic bacteriuria
5. Avoid ciprofloxacin + metronidazole therapy for intra-abdominal infection