

# Antimicrobial Stewardship

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# Disclosures

- None
- No off label indications will be discussed

# Case

- 72 yo man with history of COPD
- H/o prior C. difficile colitis
- Intermittent sinus congestion and drainage over the past several months, started in the fall but persists
- Given 10 days of oral antibiotic 4 weeks prior

# Case

- Clinically stable until 2 days prior to presenting to emergency department had onset diarrhea, chills and malaise
- Admitted to ICU with septic shock
- Diffuse colitis on CT

# Goals

- Scope of the problem
- Elements of Antimicrobial Stewardship (AMS)
- Specific targeted conditions for intervention

# Antimicrobial Stewardship

- IDSA published initial guidelines in 1988
- IDSA & SHEA jointed issued updated guidelines in 1997
- Most recent guidelines 2007
- CDC Get Smart program started in 2012
- Maryland Antimicrobial Stewardship Initiative
- CMS/TJC requirement 2017

# Antimicrobial Stewardship

- Up to 50% of antibiotic use is inappropriate

# Antimicrobial Stewardship

- Increased antibiotic use leads to increased antibiotic resistance
- Increased antibiotic resistance leads to poorer patient outcomes

# Antibiotic Resistance

- 3 year study of patients admitted to BI-Deaconess Medical Center with resistant Enterobacter
- Case matched to patients with susceptible strains
- Outcomes reviewed

**Table 4. Outcomes for patients with emergence of third-generation cephalosporin-resistant *Enterobacter* species, according to multivariate analysis [33].**

Outcome	Patients with emergence of resistance	Patients without emergence of resistance	Value attributable to emergence of resistance	RR	<i>P</i>
Death, <sup>a</sup> % of patients	26	13	...	5.02	.01
LOS, <sup>b</sup> days	30	19	9	1.47 <sup>c</sup>	<.001
Hospital charges, <sup>d</sup> \$US	79,323	40,406	29,379	1.51 <sup>c</sup>	<.001

# Antibiotic Resistance

- 2 year study at U. Penn with infections due to *E. coli* or *K. pneumoniae* with ESBL production
- Case matched to patients with susceptible strains
- Outcomes reviewed

**Table 5. Outcomes for patients with infection due to extended-spectrum  $\beta$ -lactamase–producing *Escherichia coli* and *Klebsiella pneumoniae*, according to multivariate analysis [36].**

Outcome	Case patients (n = 33)	Control patients (n = 66)	RR (95% CI)	P
Death, <sup>a</sup> % of patients	15	9	...	...
LOS, <sup>b</sup> median days	11	7	1.73 (1.14–2.65)	.01
LOS, <sup>c</sup> median days	11	7	1.23 (0.81–1.87)	.34
Charge, <sup>c</sup> median US\$	66,590	22,231	1.71 (1.01–2.88)	.04

**NOTE.** LOS, length of hospital stay; RR, relative risk.

<sup>a</sup> OR, 1.91 (95% CI, 0.49–7.42); *P* = .35.

<sup>b</sup> Controlling for APACHE II score at the time of infection.

<sup>c</sup> Controlling for APACHE II score and LOS before infection.

# Outpatient Antimicrobial Stewardship

- National Action Plan for Combating Antibiotic-Resistant Bacteria
  - Goal to reduce inappropriate antibiotic use by 50% by 2020

# Outpatient Antimicrobial Stewardship

- 2010-2011 National Ambulatory Medical Care Survey
  - 184,032 visits
  - 12.6% visits resulted in antibiotic prescriptions
    - Sinusitis
    - Otitis media
    - Pharyngitis
  - For respiratory tract illness 221 prescriptions/1000 patient
    - 50% deemed clinically appropriate

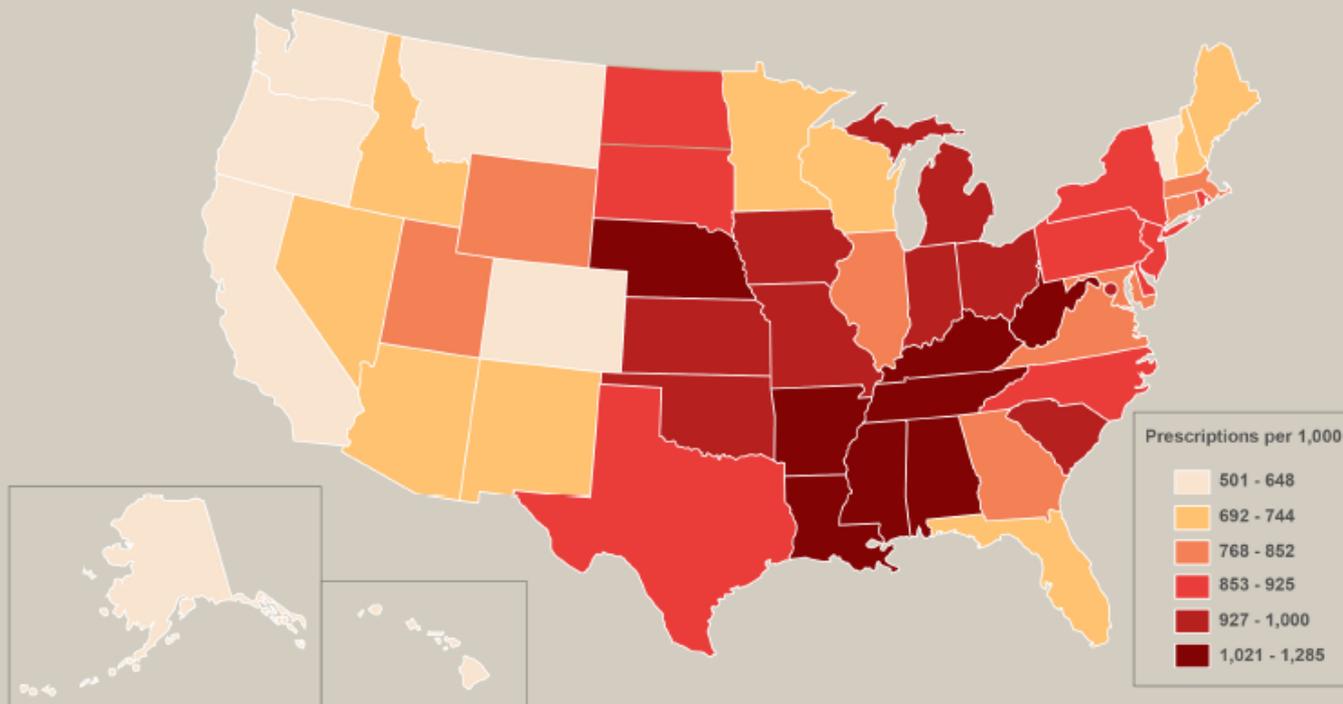
Table 1. Sampled Visits and Ambulatory Care Visits With Antibiotics Prescribed by Age Group and Diagnosis From the US NAMCS/NHAMCS, 2010-2011

Diagnosis <sup>a</sup>	Age Group, y							
	0-19		20-64		≥65		All Ages	
	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)	Unweighted No. Sampled Visits	Weighted Visits With Antibiotics Prescribed, % (95% CI)
Sinusitis	549	84.7 (79.1-89.0)	1492	70.9 (66.4-75.0)	256	53.8 (44.4-62.9)	2297	72.2 (68.2-75.9)
Suppurative otitis media	2083	82.0 (78.2-85.3)	415	69.0 (59.1-77.4)	50	<sup>b</sup>	2548	79.5 (76.0-82.7)
Pharyngitis	1580	56.2 (49.8-62.4)	1107	72.4 (66.8-77.4)	65	<sup>b</sup>	2752	62.2 (57.2-67.0)
Skin, cutaneous, and mucosal infections	1053	48.7 (42.8-54.7)	2591	53.5 (50.0-57.0)	536	39.8 (31.6-48.5)	4180	50.0 (46.9-53.1)
Other skin, cutaneous, and mucosal conditions	4631	11.3 (9.4-13.4)	8828	11.0 (9.1-13.2)	4654	6.5 (4.4-9.5)	18 113	9.6 (8.0-11.5)
Urinary tract infections	554	73.2 (63.9-80.9)	1821	75.0 (69.4-80.0)	627	65.2 (56.8-72.8)	3002	72.2 (67.7-76.3)
Viral upper respiratory tract infection	2083	21.2 (16.9-26.3)	931	43.0 (36.7-49.5)	200	39.4 (27.2-53.1)	3214	29.6 (25.7-33.8)
Bronchitis or bronchiolitis <sup>c</sup>	491	55.2 (45.3-64.8)	821	72.4 (60.1-82.1)	193	60.9 (45.9-74.0)	1505	64.5 (56.6-71.6)

# Outpatient Antibiotic Use

- 506 antibiotic prescriptions per 1000 persons in ambulatory settings 2010-2011
- Approx 154 million antibiotic prescriptions in the US during 2010-2011
- 2014 data 835 antibiotic prescriptions per 1000 persons
- 2014 Sweden 328 antibiotic prescriptions per 1000 persons

## Community Antibiotic Prescriptions per 1,000 Population by State - 2014



Data source: QuintilesIMS Xponent, 2014

CS-17-28789-A

**Figure 1.** Antibiotic prescriptions per 1000 persons by state (sextiles) for all ages — United States, 2014.



This project was made possible through a partnership with the CDC Foundation. Support for this project was provided by The Pew Charitable Trusts.

# Goals of Antimicrobial Stewardship

- Decrease resistance
- Decrease inappropriate antibiotic use
- Decrease costs

# What is Antibiotic Stewardship?

- Definition of Stewardship: “the careful and responsible management of something entrusted to one’s care”
- Limiting inappropriate use
  - *“The most important decision is not what antibiotics to use, but whether to use antibiotics at all.”*
- Optimizing antibiotic therapy
  - The Right Antibiotic at
  - The Right Dose for
  - The Right Duration
- Minimizing adverse events
  - Resistance
  - Adverse Effects
  - Cost

# AMS Strategies

- Education
- De-escalation of therapy
- Dose optimization
- IV to PO conversion
- Guidelines/order sets/clinical pathways

# Antimicrobial Stewardship

- Right Antibiotic
- Right Dose
- Right Duration

# Antimicrobial Stewardship

- Right Antibiotic
  - Does patient need antibiotics
  - Guidelines for specific conditions
    - Uncomplicated cystitis
    - Acute bacterial rhinosinusitis
    - Pharyngitis
    - Skin and soft tissue infections

# Antimicrobial Stewardship

- Right Dose
  - Optimal antibiotic dosing is often smaller more frequent doses

# Antimicrobial Stewardship

- Right Duration
  - Uncomplicated cystitis: 3 days
  - Pneumonia: 5 days
  - Group A Streptococcal pharyngitis: 10 days
  - Cellulitis: 5 days

# SpeakUp™: Antibiotics

## When do you really need an antibiotic?

Antibiotics are powerful drugs for fighting infections. They don't work for every sickness. This chart shows when you may be given an antibiotic.

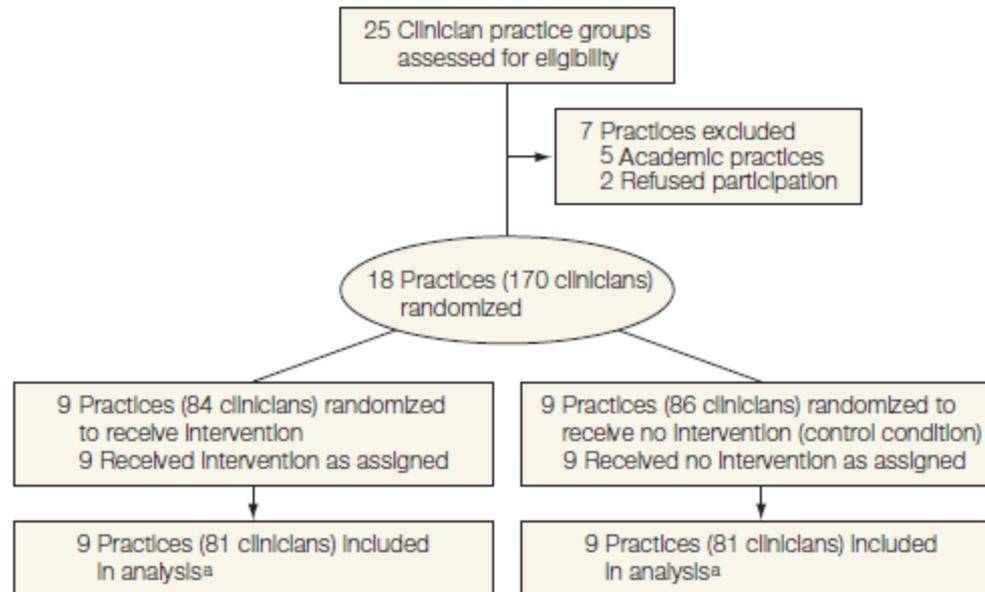
Illness	Virus	Bacteria	Should you expect an antibiotic?
Bronchitis (in healthy children and adults)	✓	✓	May be recommended
Cold or runny nose	✓		No
Ear infection	✓	✓	May be recommended
Flu	✓		No
Fluid in the middle ear	✓		No
Sinus infection	✓	✓	May be recommended
Sore throat (except strep)	✓		No
Strep throat		✓	Yes
Urinary tract infection		✓	Yes

Information available on the Centers for Disease Control and Prevention website

# Does It Work

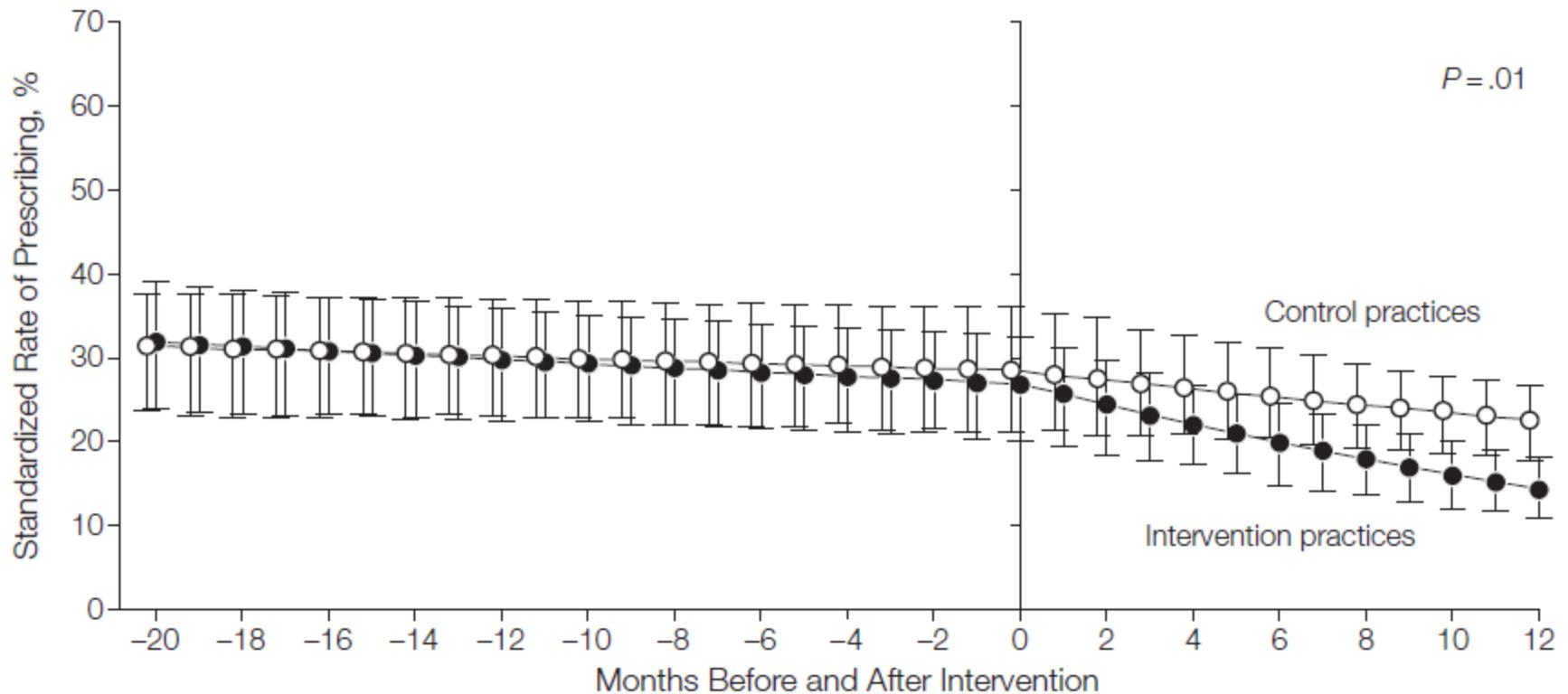
- Trial involving large primary care network with 16 sites participating
- Split into intervention group and usual practice
  - Intervention group had clinical education session on antimicrobial stewardship and 1 year personalized follow up with audits of prescribing practices and feedback
  - Usual practice group no intervention

**Figure 1.** Selection and Randomization of Practice Groups



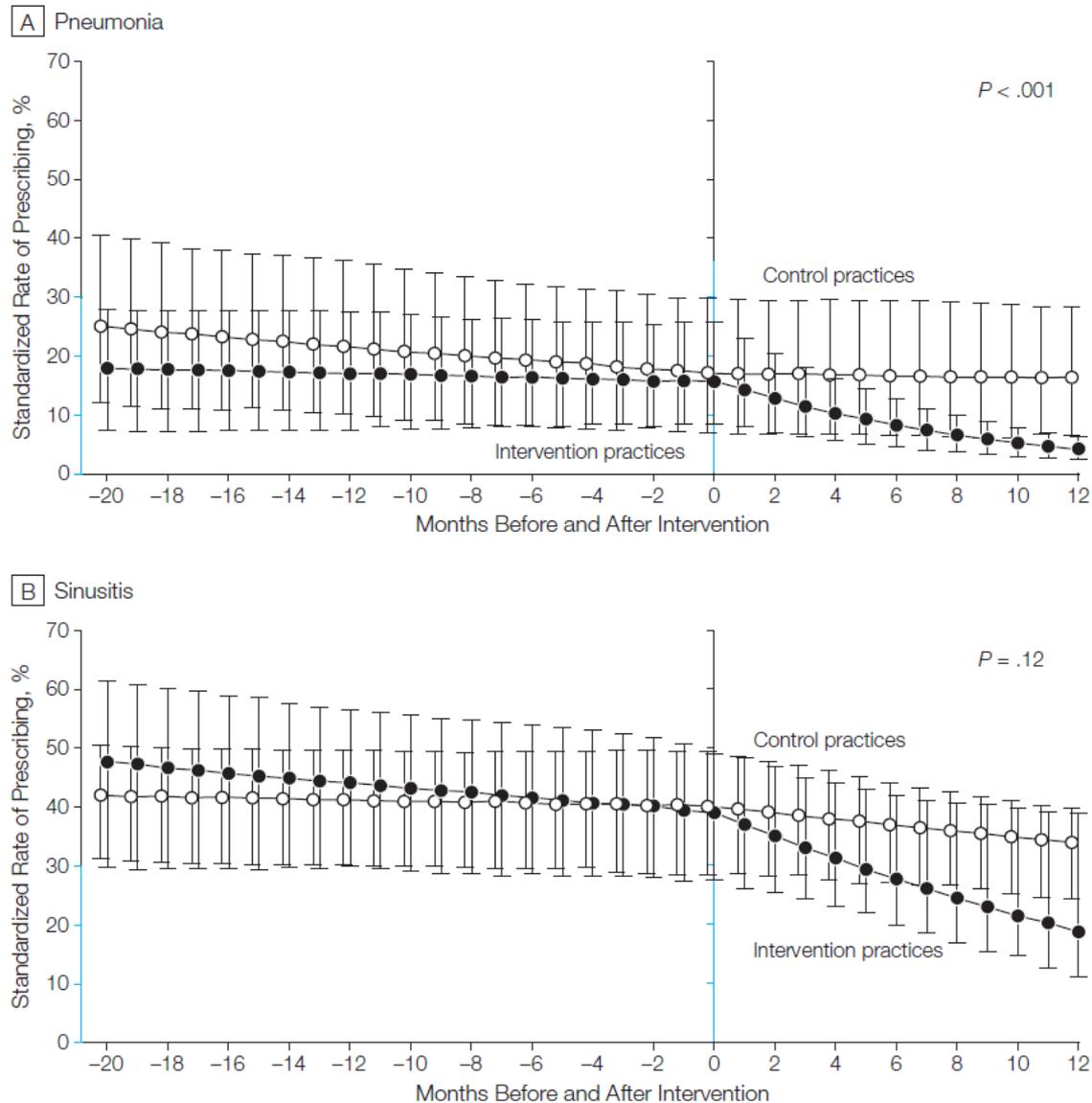
<sup>a</sup>Three clinicians in the intervention group and 5 in the control group did not attend acute-care encounters during the study period.

**Figure 2.** Standardized Rates of Broad-Spectrum Antibiotic Prescribing at Acute Care Office Visits Over Time



The estimate of interest (and associated  $P$  value) is the treatment  $\times$  time interaction term, representing the relative changes in trajectories before and during the intervention. Error bars indicate 95% CIs.

**Figure 3.** Standardized Rates of Broad-Spectrum Antibiotic Prescribing at Acute Care Office Visits by Specific Acute Respiratory Tract Infection



# Case

- 67 yo woman with no significant PMH
- Presented with several days dysuria and urgency
- UA was notable for +LE and pyuria (20-50 WBC/hpf) and culture grew E. coli
- Treated with TMP/SMX for 3 days with resolution of symptoms
- Repeat culture revealed E. coli

# Asymptomatic Bacteriuria

# Definition

- Asymptomatic bacteriuria (ASB) is the isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person without symptoms or signs referable to urinary tract infection
- Patients with ASB do not have urinary symptoms of: dysuria, increased urgency, increased frequency, suprapubic tenderness, costovertebral angle pain/tenderness

# Complications of treatment of ASB

- Increased use of antibiotics
- Increased antibiotic resistance
- Increased *C. difficile* infections
- Increased adverse drug reactions
- Increased testing of urine cultures and hospital resources
- Potential increased length of stay in hospital
- Overestimation of UTIs (and catheter-associated UTIs) in the hospital

**Overall: Screening men and non-pregnant women for ASB is ineffective in improving clinical outcomes. There is no impact on mortality when treating ASB.**

# Colonization: high prevalence of ASB in selected populations

Population	Prevalence
Healthy pre-menopausal women	1-5%
Pregnant women	2-10%
Post-menopausal women (50-70 y/o)	3-9%
Elderly women in the community	11-16%
Elderly men in the community	4-19%
Diabetic women	9-27%
Diabetic Men	1-11%
HD patients	28%
Female long-term care residents	25-50%
Male long-term care residents	15-40%
Patients with short-term urinary catheters	9-23%
Patients with long-term urinary catheters	100%

# Evaluation of the UA

- Urine WBC
  - Pyuria alone is not an indication of treatment. It requires symptoms
  - Pyuria can be seen in patients with catheter use, STDs, renal tuberculosis, interstitial nephritis, and/or ASB.
  - However, the absence of pyuria may rule out a UTI.
- Urine LE & urine nitrites
  - The presence of LE suggests WBC will be present and nitrites suggest that gram-negative organisms are present, yet neither of these findings is diagnostic of a UTI

# Evaluation of the UA

- Urine squamous epithelial cells  $> 2/\text{hpf}$ 
  - A positive result suggests that the specimen is contaminated and results of the urinalysis should be ignored
- $\geq 3$  bacterial species in urine culture
  - Presence of  $\geq 3$  bacterial species suggest that the specimen is contaminated and results of the urine culture should be ignored

# Who to Treat

Patient Population	Evidence
Pregnant women	More likely to experience premature delivery and to have infants of low birth weight. Increased risk of developing pyelonephritis.
Before Transurethral Resection of the Prostate (TURP)	High risk of post-procedure bacteremia and sepsis
Traumatic genitourinary procedures for which mucosal bleeding is anticipated	High risk of post-procedure bacteremia and sepsis

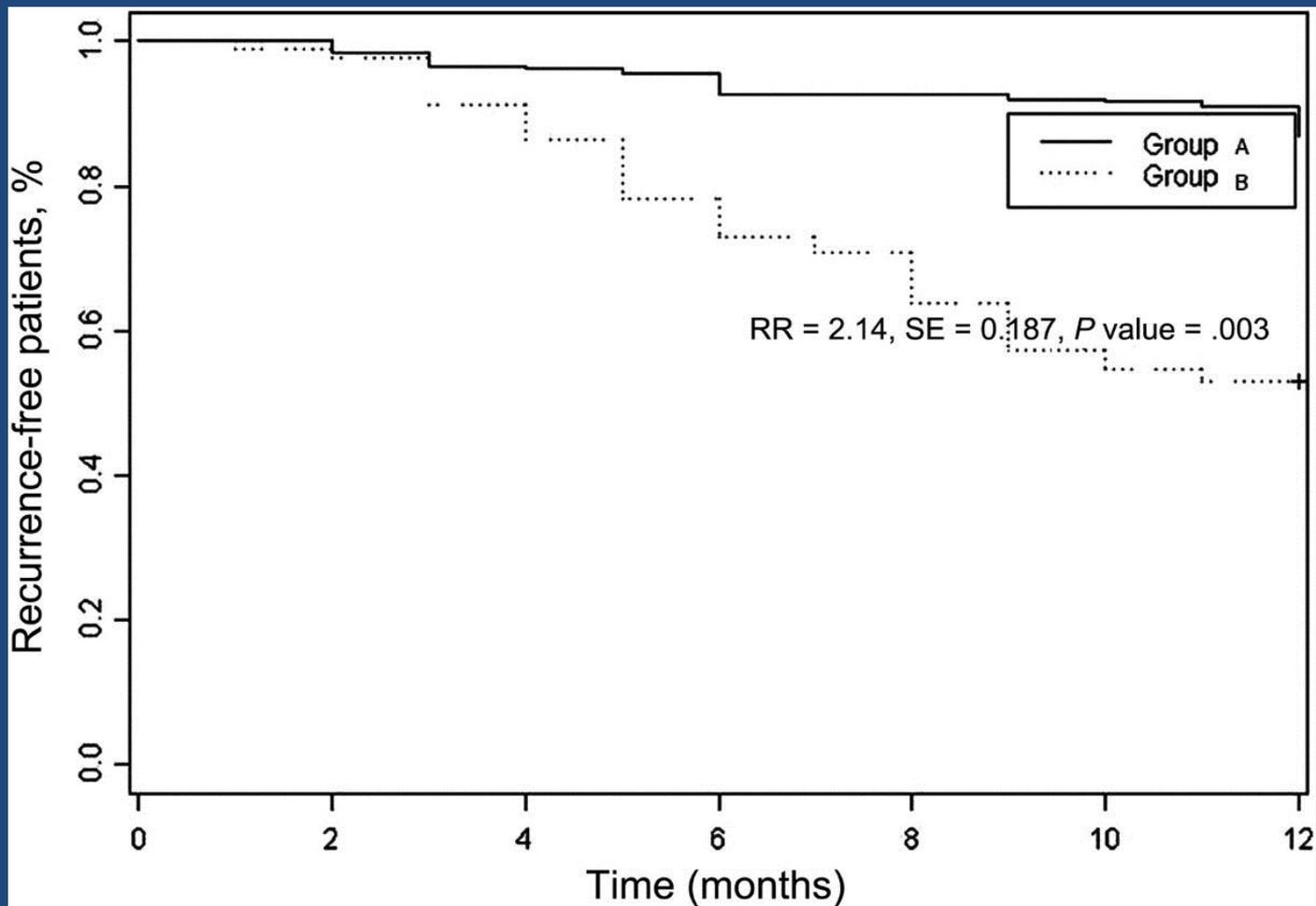
# Who Not to Treat

Patient Population	Evidence
Premenopausal, non-pregnant women	May increase risk of UTI and pyelonephritis, but not HTN, CKD, GU cancer, or mortality. If treated, may increase risk of resistance.
Diabetic women	No difference in rates of symptomatic UTI, mortality, or progression of diabetes. Treatment did not decrease number of hospitalizations for UTI. If treated, increases risk of ADR.
Older persons living in the community	No change in mortality
Elderly, institutionalized subjects	No changes in mortality or chronic genitourinary symptoms. Increases ADR and resistance.
Persons with spinal cord injury	High levels of reinfection and resistance
Catheterized patients while the catheter remains in situ	When treated, often immediate recurrence and increased risk of resistance

# Treatment of Asymptomatic Bacteriuria

- Study collected urine samples from asymptomatic women
- If urologic organisms identified patients either
  - Received no treat (Group A)
  - Treatment for the identified organism (Group B)
- Monitored incidence of UTI for the following 12 months

# Treatment of Asymptomatic Bacteriuria



# Case

- 48 yo man presents with 7 days of URI sx
- Initially sore throat with rhinitis and rhinorrhea
- Those sx have improved but now c/o of “sinus pressure” and ongoing nasal discharge
- Sx have improved but are still present at day 7

# Sinusitis

# Sinusitis

- Rhinosinusitis
  - Acute Rhinosinusitis
    - Acute bacterial rhinosinusitis
  - Chronic Rhinosinusitis
- 12% of population diagnosed in a given year
- 11% of all primary-care visits
- Approx 80% of visits result in antibiotic prescription

# Sinusitis

- 90% or greater ARS is viral in nature
- Guidelines exist to aid determination of ABRS from VRS (Viral Rhinosinusitis)
  - Symptoms persists beyond 10 days from onset without some improvement (not resolution)

# Sinusitis

- VRS: Symptomatic management – nasal steroids, saline irrigation, analgesics
- ABRS: Symptomatic management and Amoxicillin 5-10 days
- Chronic rhinosinusitis: Evaluation for mechanical factors and symptomatic management

# Case

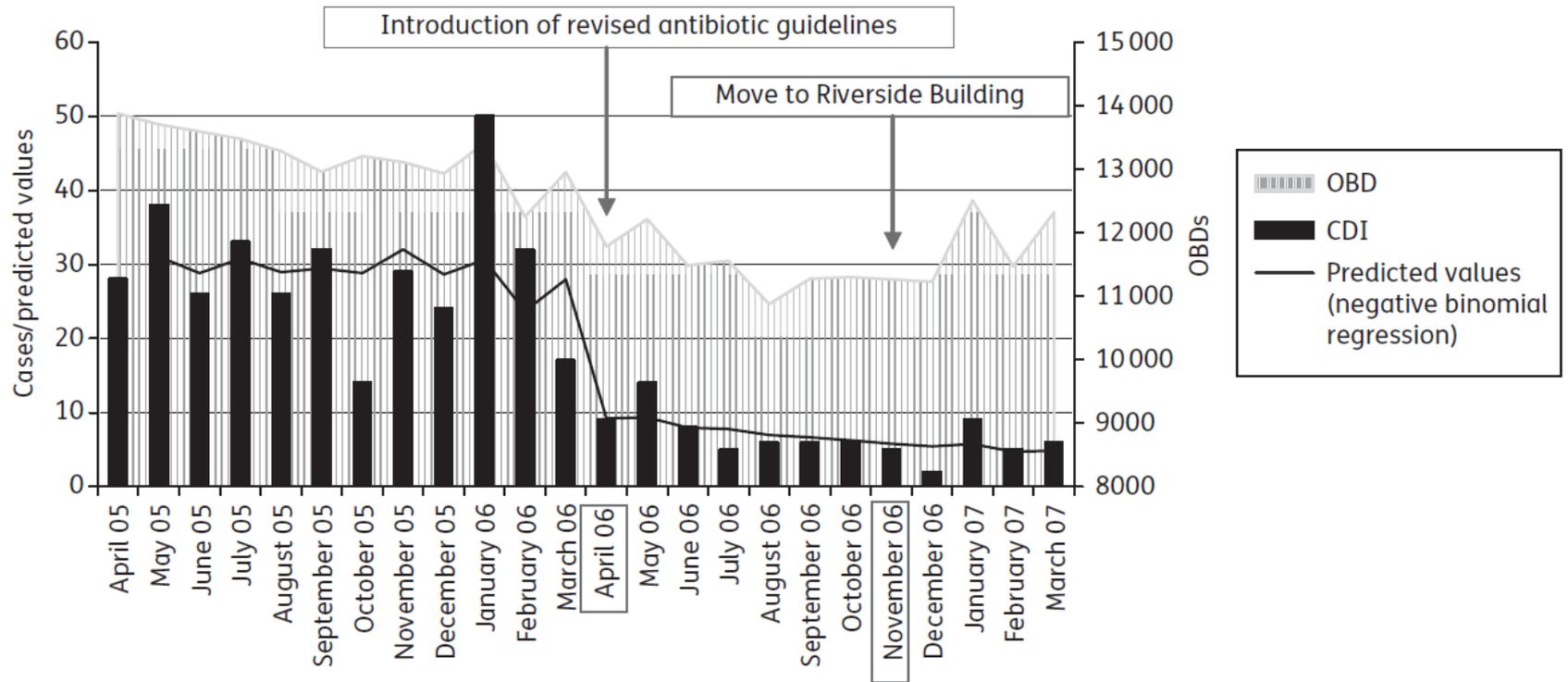
- 32 yo woman presents with several days of sore throat with some odynophagia
- No fevers but has some nasal congestion
- On exam tonsils are erythematous and enlarged
- Rapid Strep Ag test is negative

# Pharyngitis

# Pharyngitis

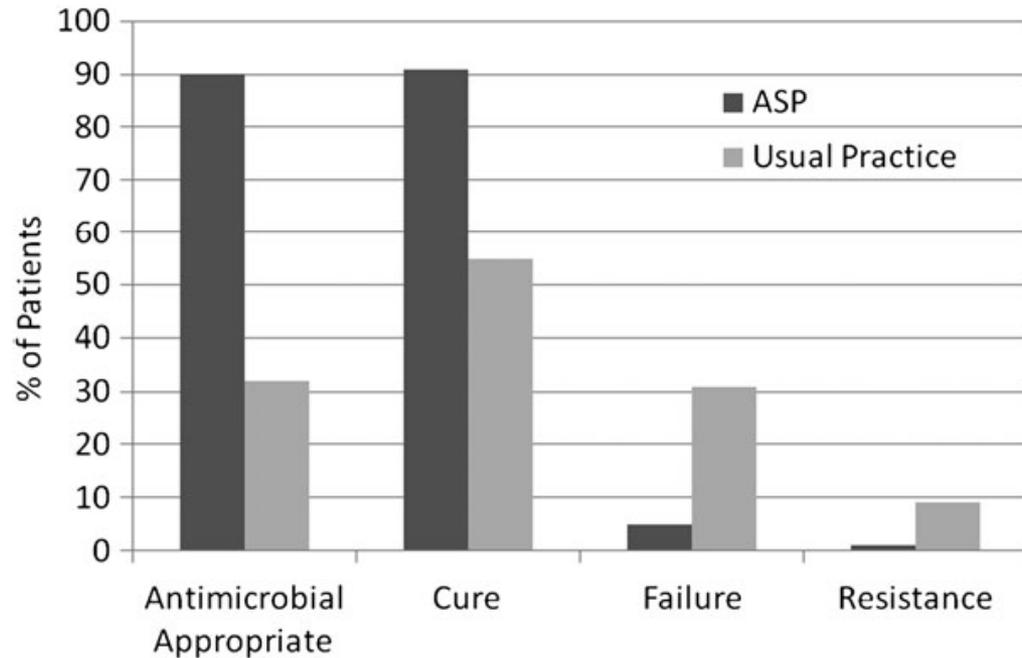
- Can be difficult to distinguish between viral and Streptococcal pharyngitis
- Overtly viral symptoms include rhinorrhea, rhinitis, hoarseness, oral ulcers and cough
- Do not test with viral symptoms and treatment is symptomatic
- Rapid testing or culture should be performed
- In adults a negative rapid test is sufficient
- Treatment if positive

# C. difficile Colitis



**Figure 2.** Monthly count data for new cases of CDI and the number of OBDs before and after the introduction of revised antibiotic guidelines.

# Other Benefits of Antimicrobial Stewardship



**Figure 1.** Clinical outcomes in a randomized controlled trial comparing the Hospital of the University of Pennsylvania's antimicrobial stewardship program (ASP) to usual practice [12].

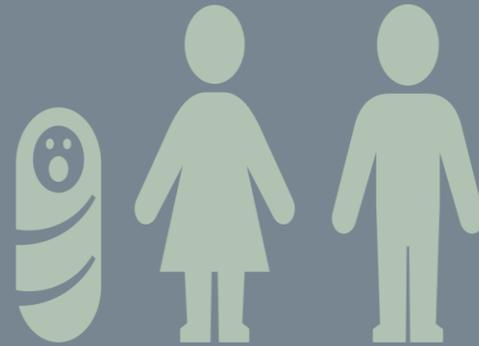
# Antibiotics Are Not Benign



ANTIBIOTICS ARE RESPONSIBLE  
FOR ALMOST

**1** OUT OF **5**

EMERGENCY DEPARTMENT VISITS  
FOR ADVERSE DRUG EVENTS



ANTIBIOTICS ARE THE  
MOST COMMON CAUSE OF  
EMERGENCY DEPARTMENT VISITS  
FOR ADVERSE DRUG EVENTS  
IN CHILDREN UNDER  
18 YEARS OF AGE.

