Antimicrobial/Medication Stewardship and Prevention of *C. difficile* Infection

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Physician Lead, Infection Prevention and Control and Antimicrobial Stewardship

Lakeridge Health

Disclosures

- Occasional speaking honoraria
- Some slides are repeated from previous presentations…
  - (And so I apologize for recycling jokes…)

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Objectives

- Understand rationale for ASP
- Review evidence for ASP in CDI prevention
- Review other medications that should be used prudently
- Understand ways YOU can be an antimicrobial steward

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Antimicrobial Stewardship: Definition

"Coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration."

Policy Statement on Antimicrobial Stewardship by SHEA, IDSA, PIDS.
ICHE 2012; 33: 322-327

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Antimicrobial Stewardship: Bottom Line

- Right drug
- Right dose
- Right time
- Right duration
- ….only when needed

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Why Do We Need Antimicrobial Stewardship?

Evolution of Antimicrobial Prescriptions

- 2000 B.C.
  - "Here, eat this root."
- 1000 A.D.
  - "This is not healthy. Here, say this prayer."
- 1850 A.D
  - "That prayer is superstition. Drink this potion."
- 1940 A.D
  - "That potion is poison. Here, take this penicillin. It is a miracle drug."
- 1985 A.D.
  - "Penicillin is worthless. Here, take this new, bigger, better antibiotic."
- 2012 A.D
  - "Those antibiotics don't work anymore. Here, eat this root."

Neil Fishman. SHEA Fellows' Course 2011.

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Antibiotic Utilization

- 30-50% of all hospitalized patients receive antibiotics
  - 70% of all ICU patients
- 30-50% of antimicrobial use is either unnecessary or inappropriate

Reimann, D'Ambola. JAMA 1968.
Hecker MT et al. Arch Int Med. 2003; 163:972-978.

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Antibiotic Utilization

- Overuse of antibiotics…
  - Increases adverse drug events
    - 5% of hospitalized patients who receive antibiotics experience an adverse event
  - Causes emergence of resistant bacteria
  - Contributes to rising cost of care
  - Resistant bacteria result in increase morbidity and mortality

Hoffman, et al. Am J Health Syst Pharm 2007;64:258-314.
Hidron et al Infect Control Hosp Epidemiol 2008;996-1011.

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WORLD ECONOMIC FORUM

COMMITTED TO IMPROVING THE STATE OF THE WORLD

Insight Report

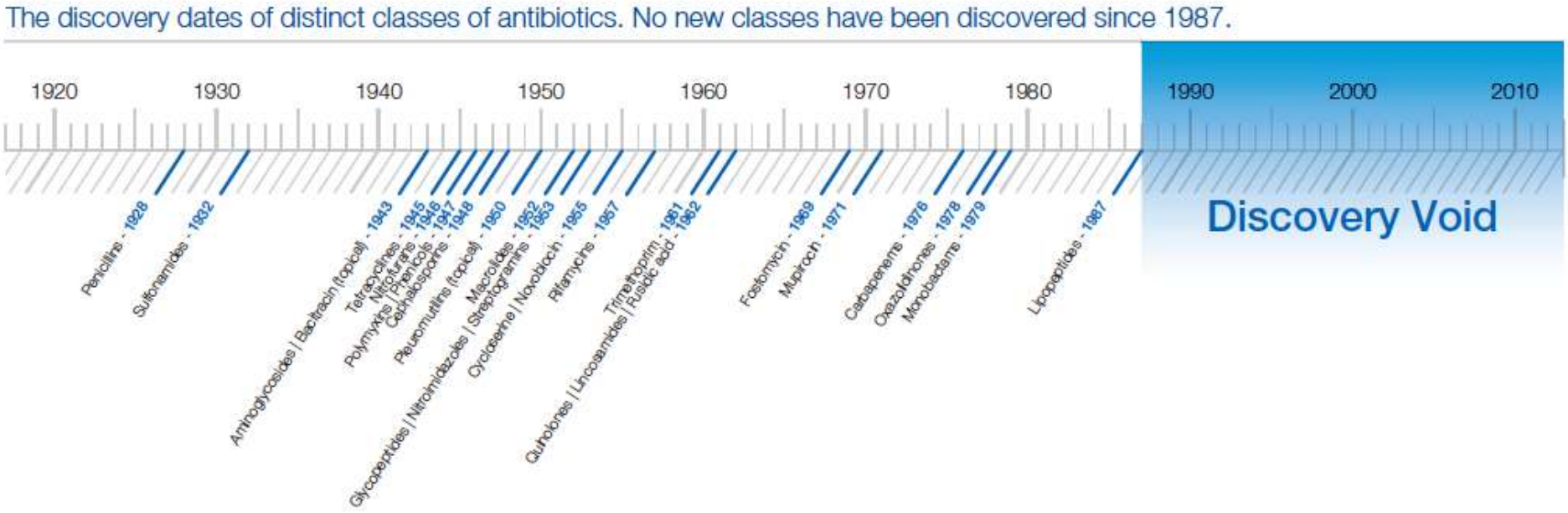
Global Risks 2013
Eighth Edition

The Dangers of Hubris on Human Health

The Dangers of Hubris on Human Health

"While viruses may capture more headlines, **arguably the greatest risk of hubris to human health comes in the form of *antibiotic-resistant bacteria*.** We live in a bacterial world where we will never be able to stay ahead of the mutation curve. A test of our resilience is how far behind the curve we allow ourselves to fall. "

Dramatic Drop in Development and Approval of Antimicrobial Agents



The Human Microbiome

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Antimicrobial Stewardship: Bigger Picture

ACCREDITATION CANADA
AGRÉMENT CANADA

Driving Quality Health Services
Force motrice de la qualité des services de santé

An Overview of Accreditation Canada's Antimicrobial Stewardship ROP

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Antimicrobial Stewardship: Bigger Picture

Public Health Ontario
PARTNERS FOR HEALTH

Santé publique Ontario
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SHARE

Antimicrobial Stewardship Program (ASP)

PHO, in partnership with the Ontario Hospital Association, is developing an antimicrobial stewardship program (ASP) in Ontario. As of January 2013, all acute care hospitals undergoing accreditation must have an ASP in place in accordance with Accreditation Canada's Required Organizational Practices. There are any number of ways to initiate and sustain a stewardship program. How will you build your program? Share your story.

For more information email: asp@oahpp.ca.

Building a Stewardship Program

- Initiating and sustaining an ASP
- Metrics and Evaluation

More »

ASP in Action

- Hospitals share their ASP stories

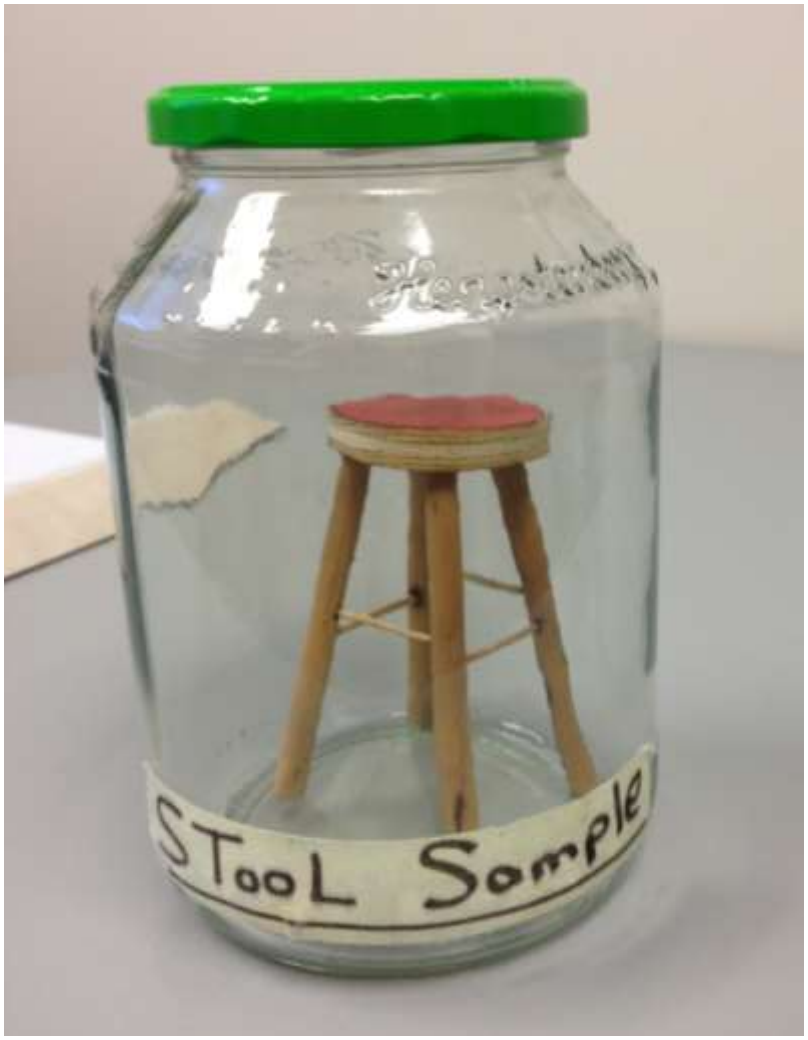
More »

About ASP

- Goals and Principles
- Advisory Committee

More »

Now the good stuff: *C. difficile*



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C. difficile

- Antibiotic exposure is the single most important risk factor for the development of *C. difficile* infection
- ~85% of patients with CDI have antibiotic exposure in the 28 days before infection
- Crude CDI LOS 34 days vs. 8 days no CDI
  - HA-CDI increases median LOS ~6 days

Chang et al Infect Control Hosp Epidemiol 2007;28:926-931.
Forster et al CMAJ 2011

Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

Vanessa Stevens,[1,3,4] Ghinwa Dumyati,[2] Lynn S. Fine,[2] Susan G. Fisher,[3] and Edwin van Wijngaarden[3]

- Retrospective cohort study
- 10,154 hospitalizations; 241 cases of CDI
- Dose-dependent increases in risk of CDI with cumulative antibiotic exposure
- Highest risk antibiotics: FQs, clinda, B-lac/BLI

Stevens et al. CID 2011

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Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

Vanessa Stevens,[1,3,4] Ghinwa Dumyati,[2] Lynn S. Fine,[2] Susan G. Fisher,[3] and Edwin van Wijngaarden[3]

- **Defined daily doses** (HR vs. DDD <3)

DDD	Crude HR	Adjust HR
3-7.79	1	1
7.8-21	3*	3*
>21	5*	5*

Stevens et al. CID 2011

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Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

Vanessa Stevens,[1,3,4] Ghinwa Dumyati,[2] Lynn S. Fine,[2] Susan G. Fisher,[3] and Edwin van Wijngaarden[3]

- **Antibiotic days** (HR vs. days <4)

Abx days	Crude HR	Adjust HR
4-7	1.5	1.5
8-18	3*	3*
>18	10*	8*

Stevens et al. CID 2011

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Cumulative Antibiotic Exposures Over Time and the Risk of *Clostridium difficile* Infection

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- **Number of antibiotics** (HR vs. 1 antibiotic)

# Abx	Crude HR	Adjust HR
2	3*	3*
3-4	4*	3*
>5	12*	10*

Stevens et al. CID 2011

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What about other medications?

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Acid Suppression and CDI Risk

"The hippies knew… acid is good, man."

- Dr. Mark Crislip (edgydoc.com)

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Host and Pathogen Factors for *Clostridium difficile* Infection and Colonization

N ENGL J MED 365;18 NEJM.ORG NOVEMBER 3, 2011

Vivian G. Loo, M.D., Anne-Marie Bourgault, M.D., Louise Poirier, M.D., François Lamothe, M.D., Sophie Michaud, M.D., M.P.H., Nathalie Turgeon, M.D., Baldwin Toye, M.D., Axelle Beaudoin, M.Sc., Eric H. Frost, Ph.D., Rodica Gilca, M.D., Ph.D., Paul Brassard, M.D., Nandini Dendukuri, Ph.D., Claire Béliveau, M.D., Matthew Oughton, M.D., Ivan Brukner, Ph.D., and Andre Dascal, M.D.

Table 2. Odds Ratios for Health Care–Associated *Clostridium difficile* Infection and Colonization According to Various Patient and Pathogen Characteristics.*

Variable	Odds Ratio (95% CI)	
	Health Care–Associated *C. difficile* Infection	Health Care–Associated *C. difficile* Colonization
Antibiotic	5.25 (2.15–12.82)	1.04 (0.61–1.78)
Chemotherapy	1.33 (0.49–3.65)	2.37 (1.09–5.14)
Proton-pump inhibitor	2.64 (1.71–4.09)	1.71 (1.15–2.53)
H_2 blocker	0.98 (0.55–1.73)	2.14 (1.24–3.70)
Glucocorticoid	0.97 (0.48–1.97)	1.33 (0.72–2.45)
NSAID	0.85 (0.55–1.30)	1.21 (0.79–1.84)

Proton Pump Inhibitors and Risk for Recurrent *Clostridium difficile* Infection

Arch Intern Med. 2010;170(9):772-778

Amy Linsky, MD; Kalpana Gupta, MD, MPH; Elizabeth V. Lawler, DSc; Jennifer R. Fonda, MA; John A. Hermos, MD

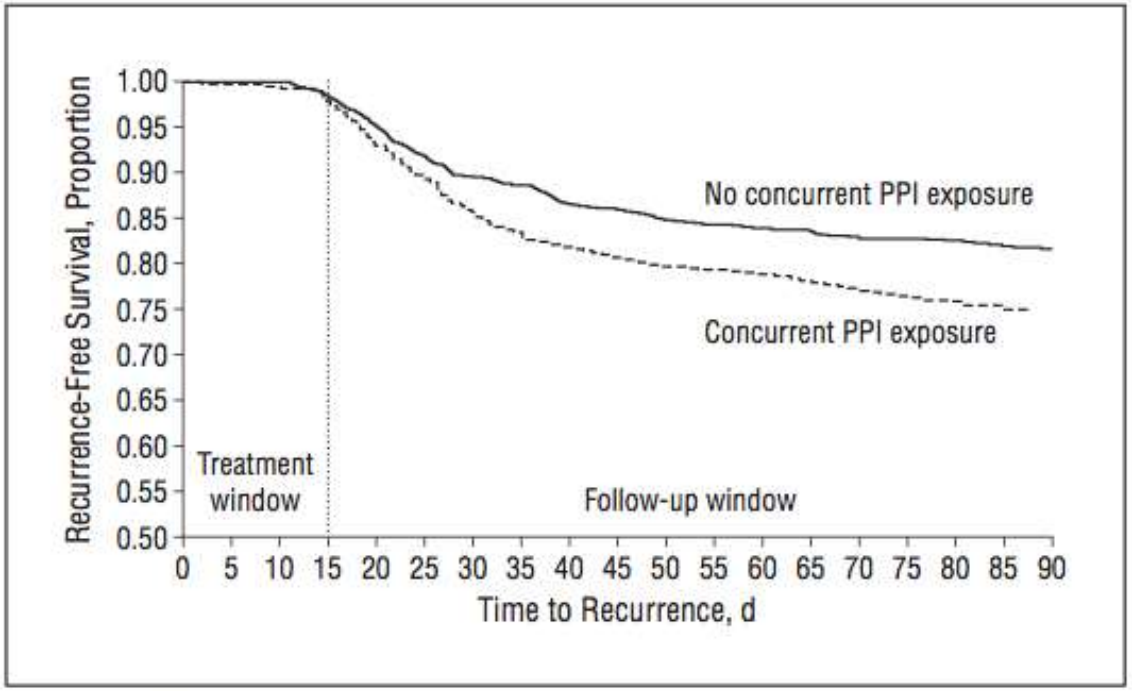

Figure 2. Recurrence-free survival in those exposed vs unexposed to proton pump inhibitors (PPIs) during treatment for incident *Clostridium difficile* infection. Time to recurrence started from the incident toxin finding or the start of antibiotic treatment (≤3 days after the diagnosis).

- **PPI use associated with a 42% increased risk of recurrence**

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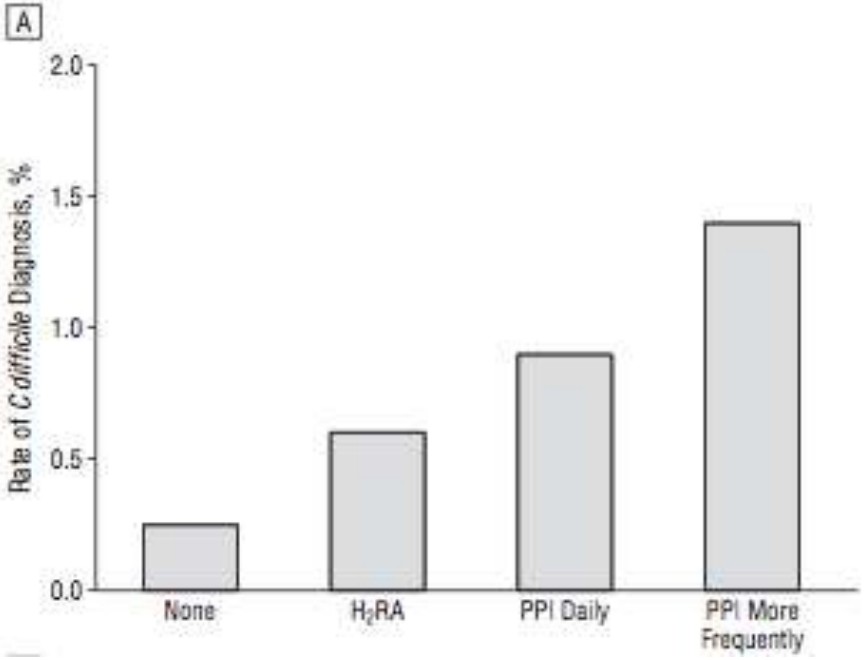
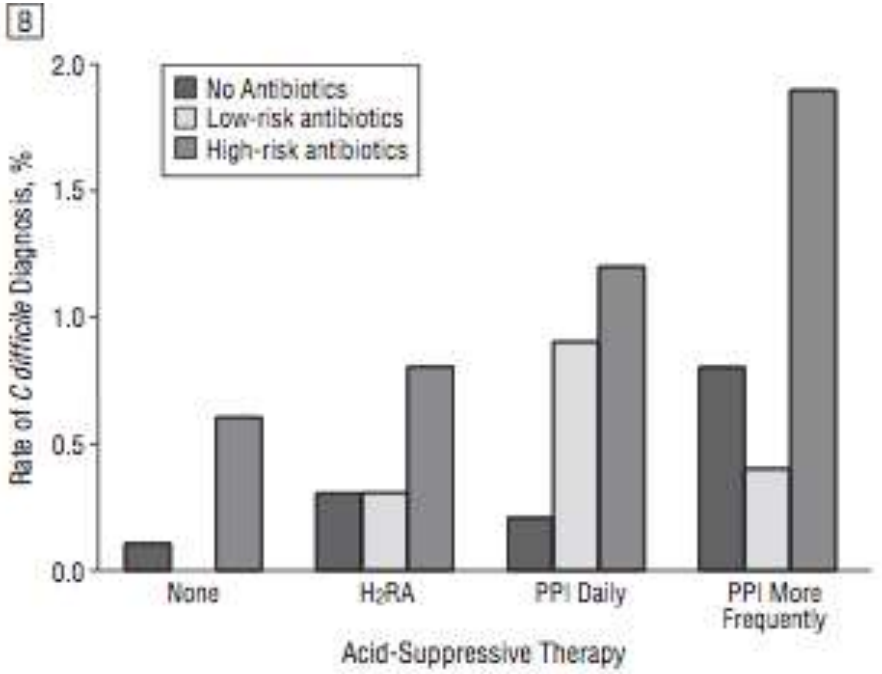
Iatrogenic Gastric Acid Suppression and the Risk of Nosocomial *Clostridium difficile* Infection

Michael D. Howell, MD, MPH; Victor Novack, MD, PhD; Philip Grgurich, PharmD; Diane Soulliard, PharmD; Lena Novack, PhD; Michael Pencina, PhD; Daniel Talmor, MD, MPH

Arch Intern Med. 2010;170(9):784-790





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RESEARCH ARTICLE Open Access

Depression, antidepressant medications, and risk of *Clostridium difficile* infection

Mary A M Rogers[1*], M Todd Greene[1], Vincent B Young[1], Sanjay Saint[1,2], Kenneth M Langa[1,2], John Y Kao[1] and David M Aronoff[1]

- Study 1: Population based study of older adults in US.
- Study 2: Case-control study of hospitalized adults testing positive for CDI
- Depression increases odds of CDI
- Fluoxetine and mirtazapine associated with increased risk of CDI

Rogers *et al. BMC Medicine* 2013, **11**:121
http://www.biomedcentral.com/1741-7015/11/121

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The effects of statins on the clinical outcomes of *Clostridium difficile* infection in hospitalised patients

S. W. Park*, A. R. Choi*, H. J. Lee*, H. Chung*, J. C. Park*, S. K. Shin*, S. K. Lee*, Y. C. Lee*, J. E. Kim† & H. Lee*

- Overall response to metronidazole 91.9%
- Successful treatment associated with:
  - Absence of PPIs (OR 0.69)
  - Exposure to statins (OR 1.45)
- Recurrence associated with:
  - No statin exposure (3% vs. 7.3%)

Aliment Pharmacol Ther 2013; **38**: 619–627

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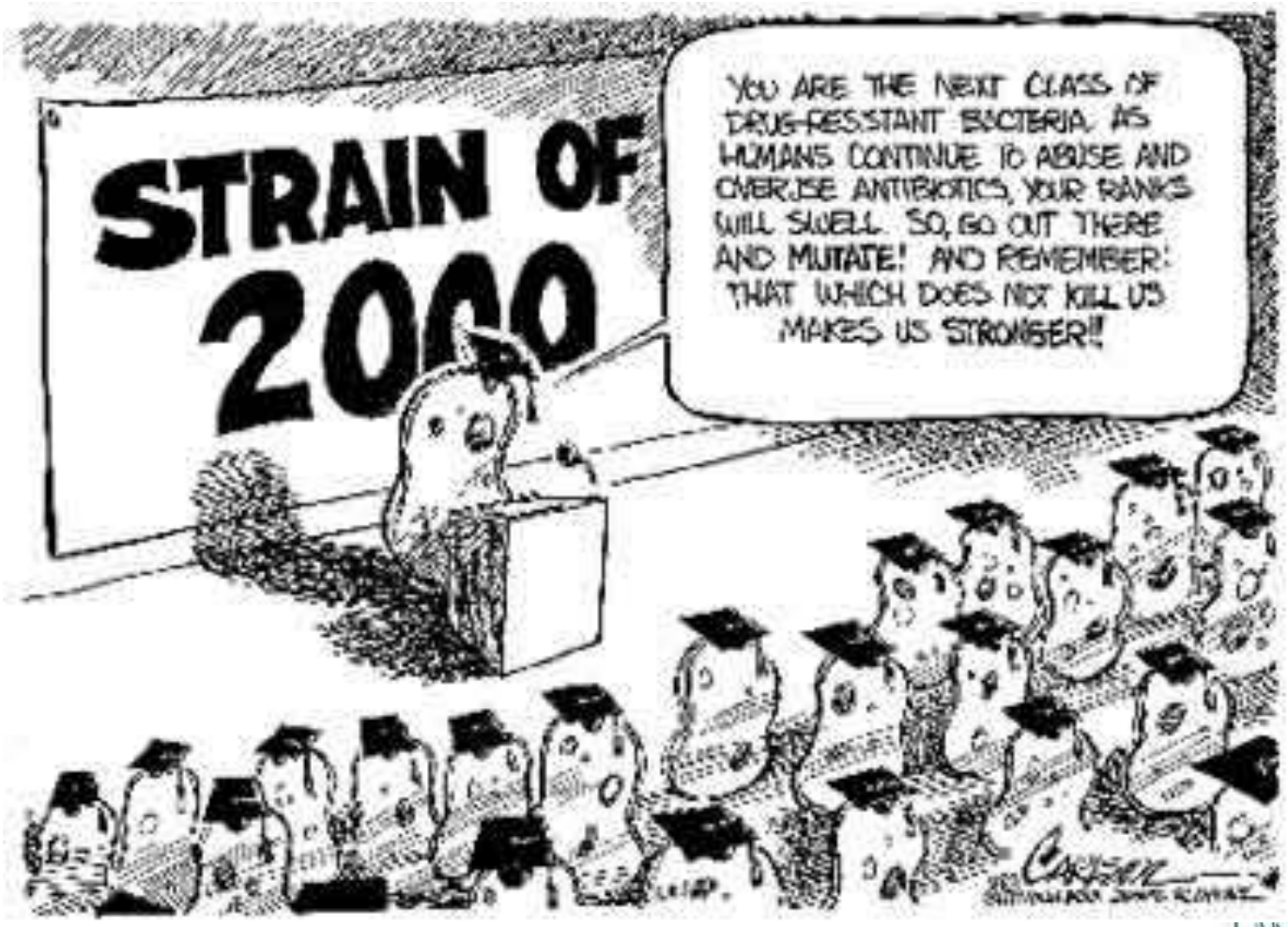
Do Antimicrobial Stewardship Programs Make a Difference?



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Evidence for ASP in CDI Prevention

- Change in fluoroquinolones associated with decreased CDI (Gaynes et al. CID 2004; Kellen et al. ICHE 2009)
- Overall decrease in antibiotic use associated with decreased CDI (Valiquette et al. CID 2007; Nuila et al. ICHE 2008)
- Decreased use of broad-spectrum cephalosporins associated with decreased CDI (McNulty et al. JAC 1997; Khan et al. J Hosp Infect 2003; Thomas et al. CID 2005)
- Reduced use of clindamycin associated with decreased CDI (Brown et al. ICHE 1990; Pear et al. Ann Int Med 1994; Climo et al. Ann Int Med 1998)

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ASP: Evidence

Study, year, study	Location	Type of ASP Introduced	Outcomes
Elligsen 2012 Interrupted Time Series Analysis	University teaching hospital, Toronto, ON	Audit and feedback in Critical Care Units from: -3rd gen cephalosporins -β-lactam/β-lactamase inhibitors -Carbapenems -Fluoroquinolones -Vancomycin	-Days of therapy -AROs -*C. difficile* -Length of stay -ICU mortality

Elligsen M, et al. Audit and feedback to reduce broad-spectrum antibiotic use among Intensive Care Unit Patients: A controlled interrupted time series analysis. ICHE 2012 33: 354-361

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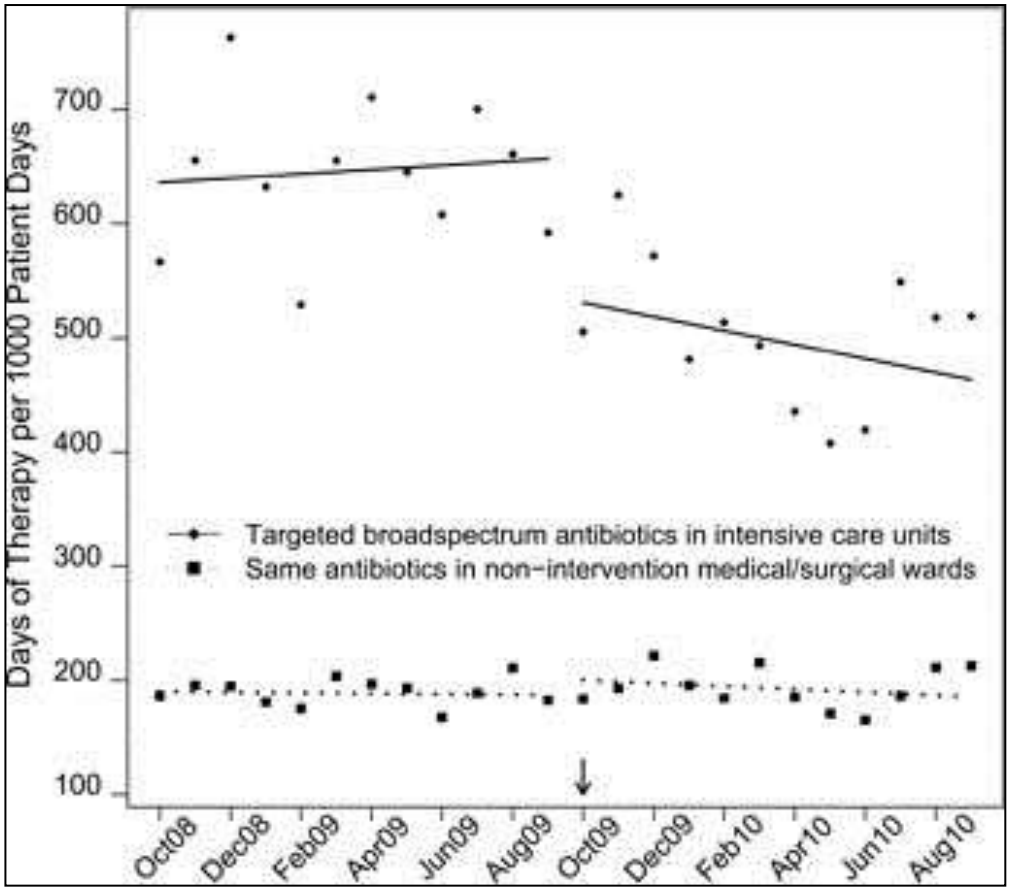
ASP: Evidence

Monthly use of broad-spectrum antibiotics in critical care patients and control medical and surgical ward patients



Elligsen M, et al. Audit and feedback to reduce broad-spectrum antibiotic use among Intensive Care Unit Patients: A controlled interrupted time series analysis. ICHE 2012 33: 354-361

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ASP: Evidence

- Nosocomial C. difficile decreased 31%
  - 16 cases pre-intervention to 11 cases post-intervention
- Non-intervention (non-ICU) wards had a 33% increase in cases
  - 87 cases to 116 cases during the same time periods

Elligsen M, et al. Audit and feedback to reduce broad-spectrum antibiotic use among Intensive Care Unit Patients: A controlled interrupted time series analysis. ICHE 2012 33: 354-361

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ASP: Evidence

Study, year, design	Location	Type of ASP Introduced	Outcomes
Valiquette et al 2007 Before/after Study	Secondary/ tertiary care hospital, Quebec, Canada	Audit and feedback: -2nd gen cephalosporins -3rd gen cephalosporins -ciprofloxacin -clindamycin -macrolides	-Total antimicrobial use -Targeted antimicrobial use -*C. difficile* rates

Valiquette et al. Impact of a reduction in use of high-risk antibiotics on the course of an epidemic NAP1/027 strain. CID 2007; 45: S112-S121

Ohl C, et al. Antimicrobial stewardship programs in community hospitals:. CID 2011; 53 (suppl 1): S23-S28

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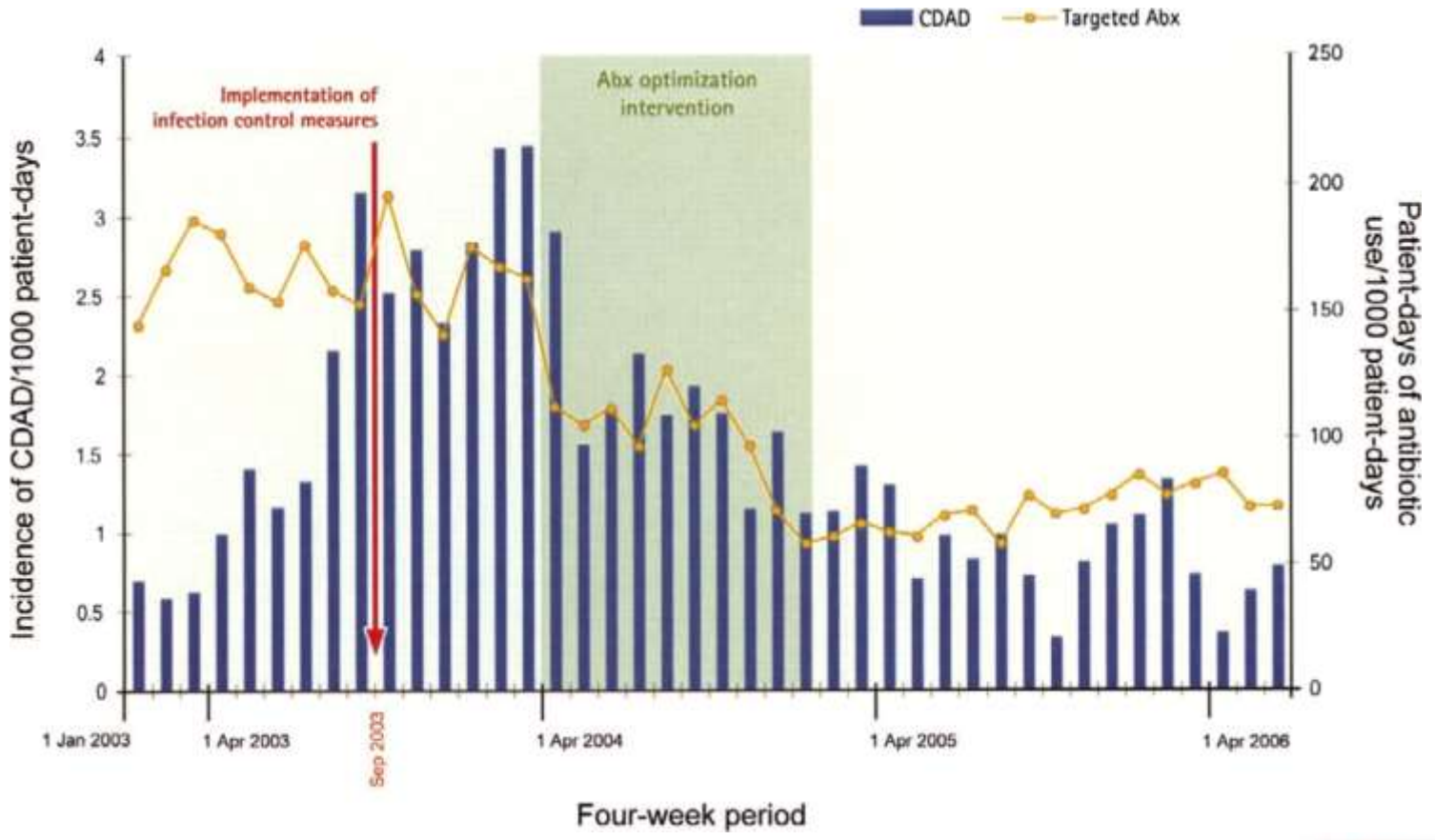
ASP: Evidence

Targeted antibiotic consumption and nosocomial *C. difficile* incidence per 1000 patient-days of hospitalization



Valiquette et al. Impact of a reduction in use of high-risk antibiotics on the course of an epidemic NAP1/027 strain. CID 2007; 45: S112-S121

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ASP: Evidence

Study, year, design	Location	Type of ASP Introduced	Outcomes
Schabas et al.	Small Community Hospital, Campbellford	• Restriction of fluoroquinolone use	*Clostridium difficile* infection

Schabas et al Can J Infect Dis Med Microbiol 23(2): Summer 2012

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ASP: Evidence

- Restriction and prior authorization of FQs
- 71% of CDI cases had prior FQ exposure
- Pre-implementation: 55 cases in 15 months
- After implementation: 1 case in 24 months

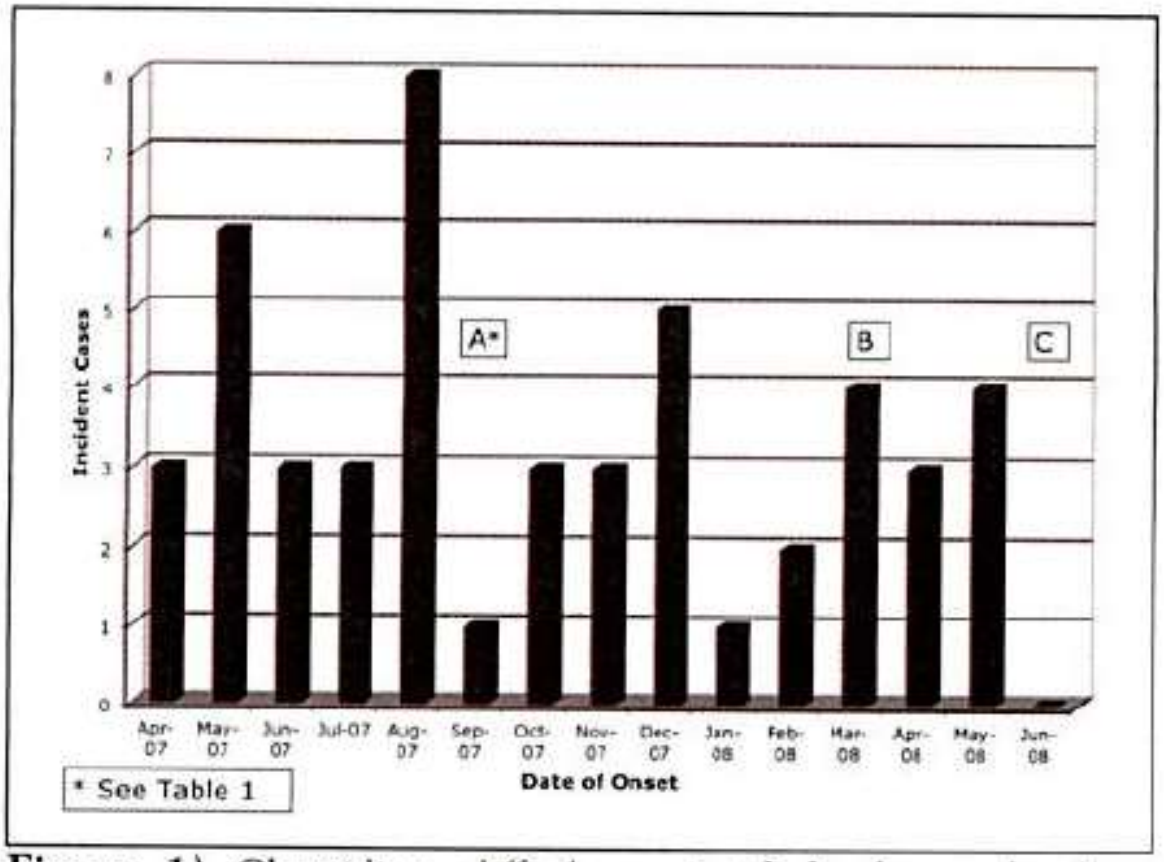

Figure 1) Clostridium difficile-*associated diarrhea outbreak at Campbellford Memorial Hospital (Trent Hills, Ontario) April 2007 to May 2008*

Schabas et al Can J Infect Dis Med Microbiol 23(2): Summer 2012

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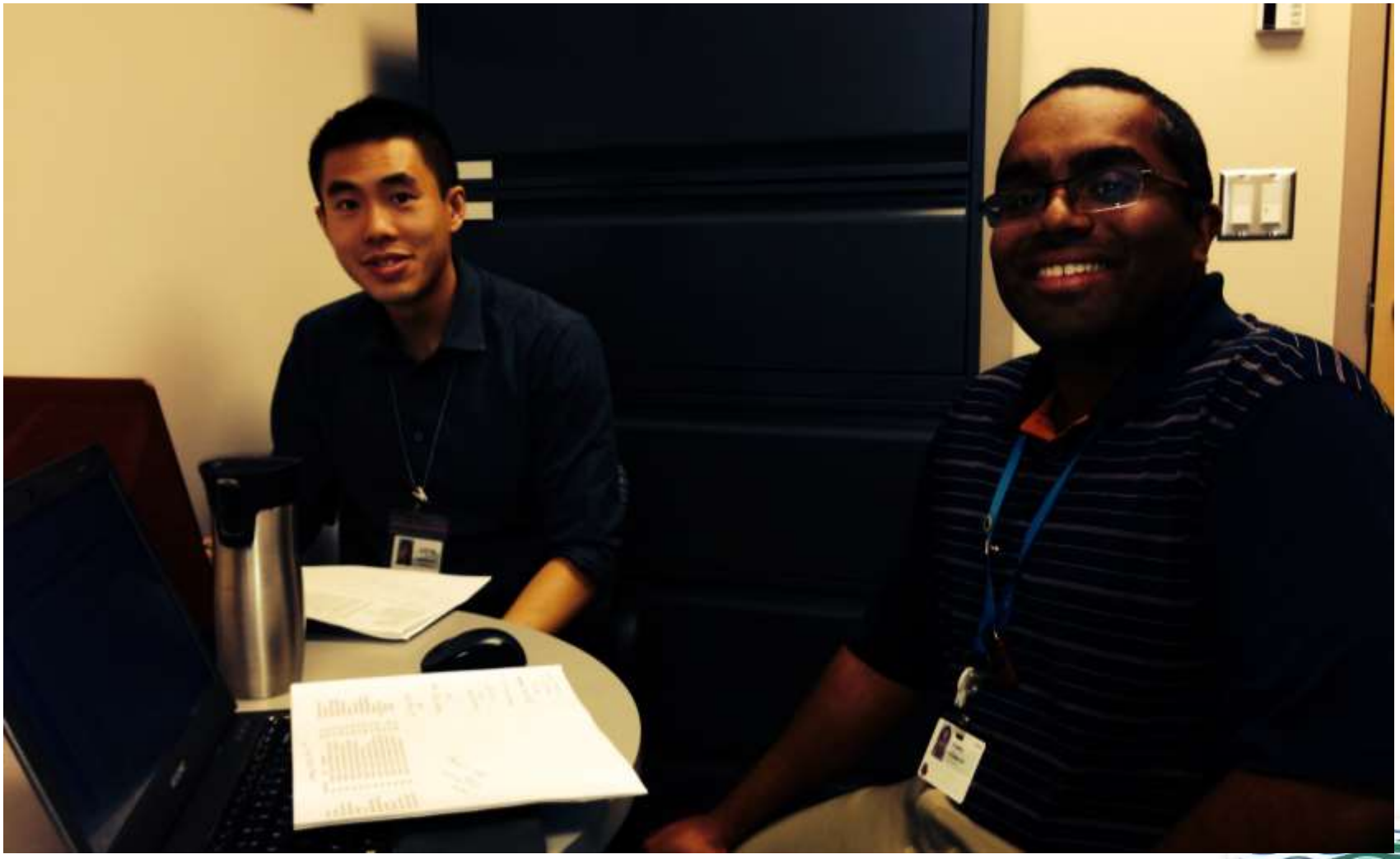
ASP: Lakeridge Health



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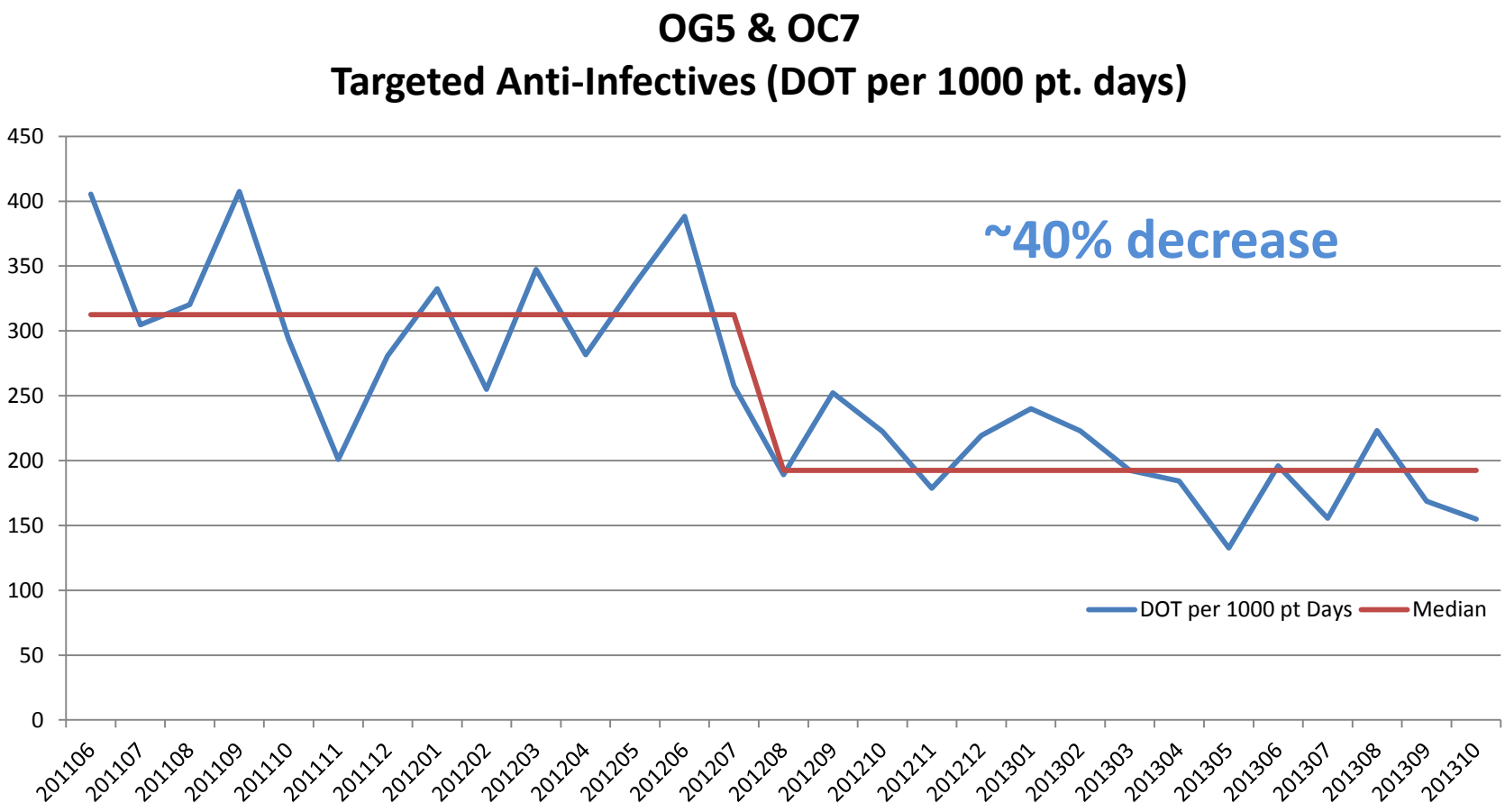
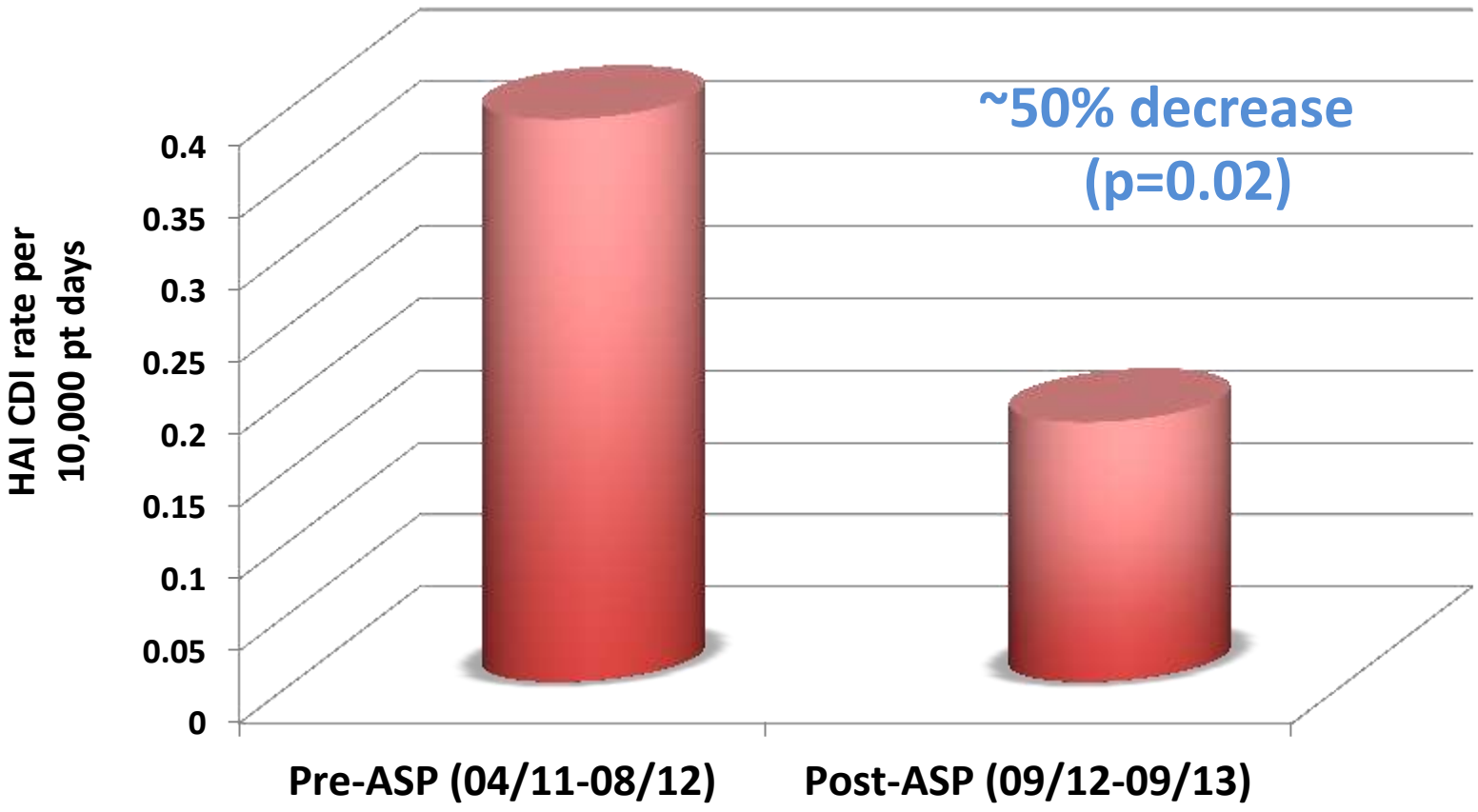
ASP: Lakeridge Health



ASP: Lakeridge Health



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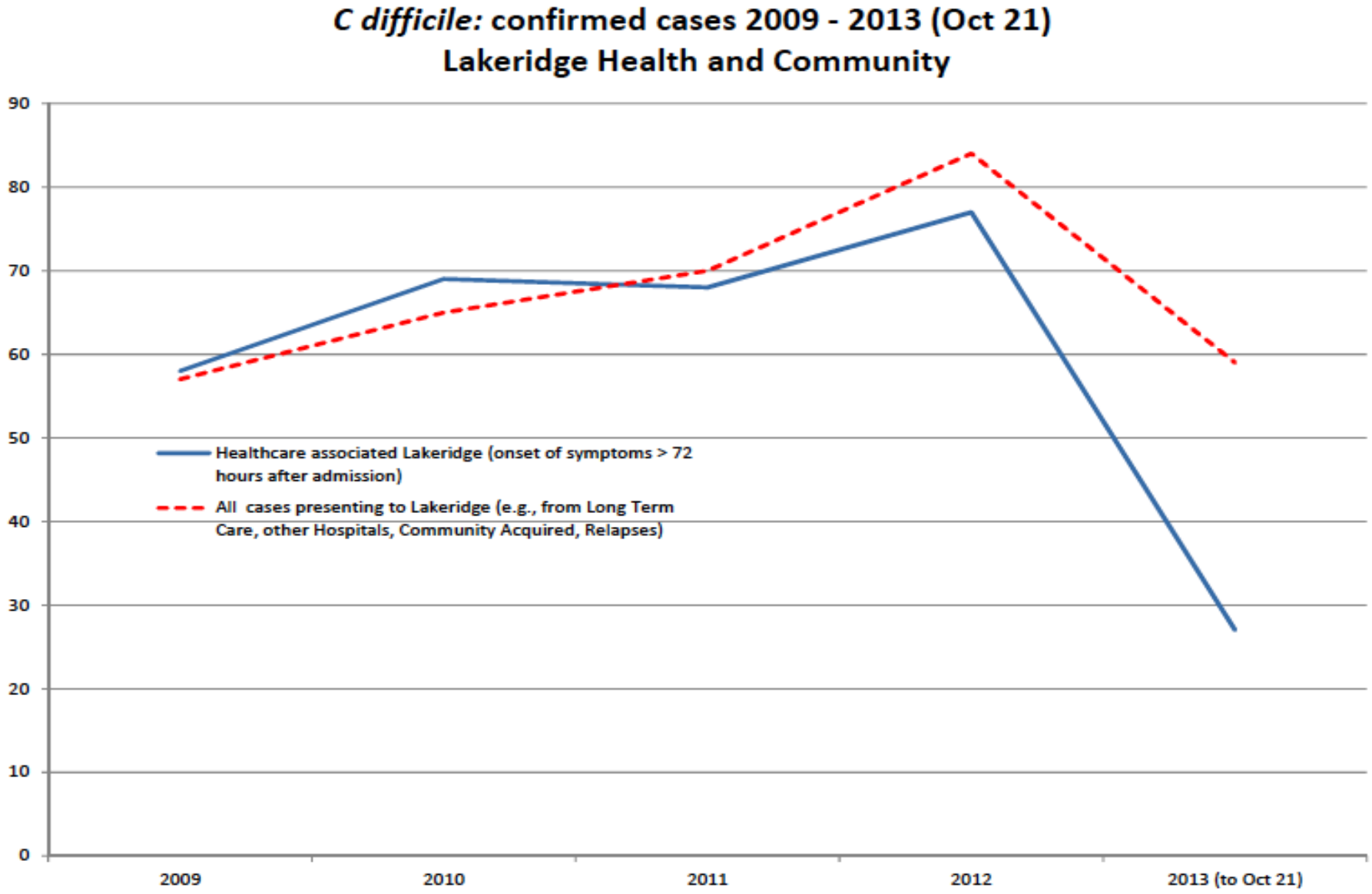
ASP: Lakeridge Health



What Constitutes an Antimicrobial Stewardship Program?

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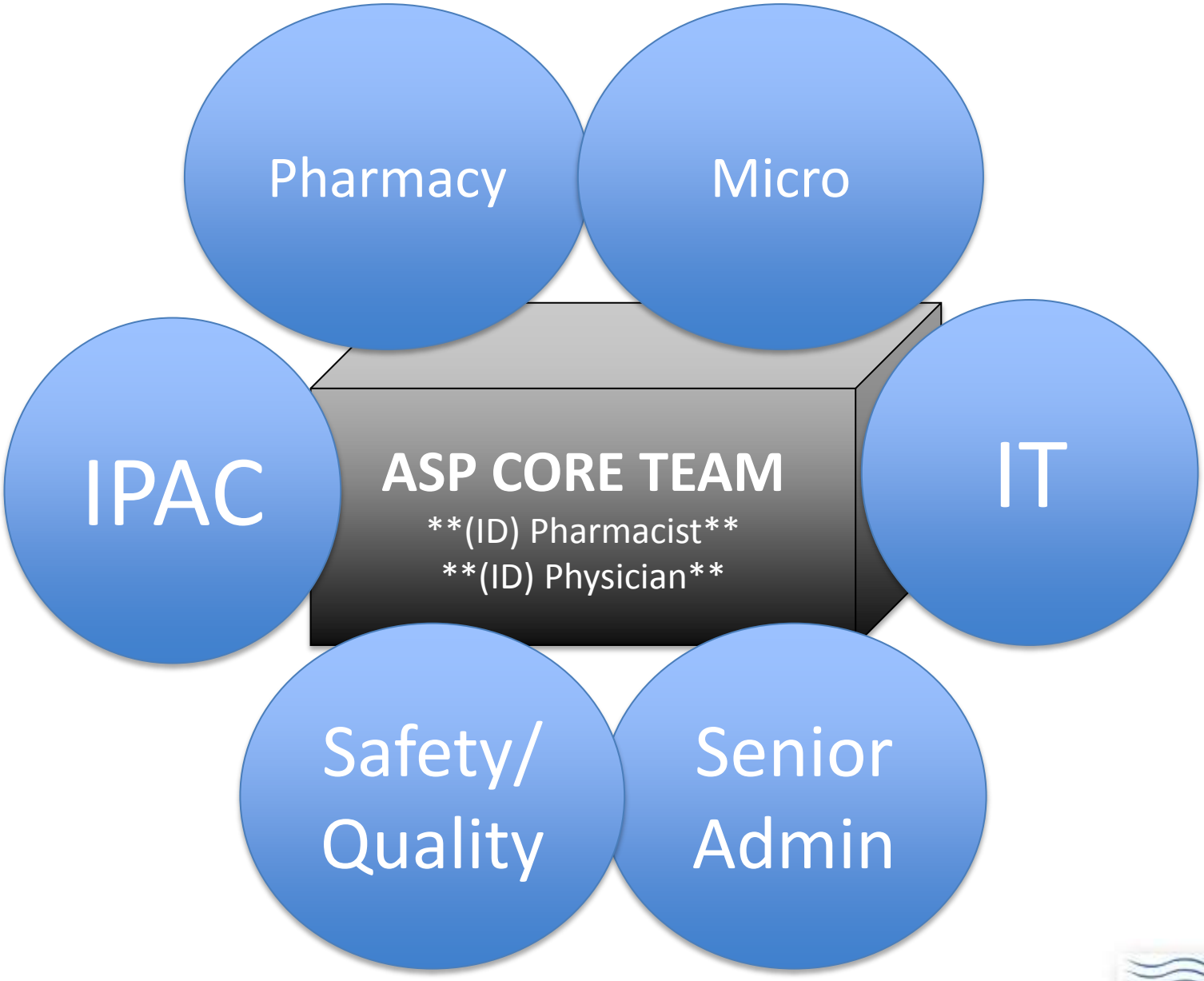
Pharmacy
Micro
IPAC
ASP CORE TEAM
(ID) Pharmacist
(ID) Physician
IT
Safety/ Quality
Senior Admin

ASP Goals

- Improve individual patient outcomes
  - Best treatment for their infection
  - Decrease HAI w/ ARO (especially C. diff)
  - Minimize adverse drug reactions
- Improve “local” antibiotic resistance profile
- Do the above in a cost effective way

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LH ASP Activities

Antimicrobial Usage	IPAC/Quality	ID Management
Audit-Feedback	CAUTI Prevention	CDI treatment
IV→PO stepdown	Probiotics/PPI	Pre-printed Orders
Formulary Restriction	CLI/VAP Prevention	Optimized dosing
Education	Blood Culture Contamination	AE Monitoring

Specific ASP Strategies

- Prospective audit and feedback
  - Streamlining/de-escalation of therapy
  - Dose optimization
  - Minimum effective duration
  - Drug allergy/interaction review
  - Targets:
    - Specific drugs
    - Duration
    - Bug/drug mismatch
  - ***Education/discussion/raise awareness***

IDSA/SHEA Guidelines for Development of an Institutional Program to Enhance Antimicrobial Stewardship. CID 2007; 44: 159-177

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Prospective Audit-Feedback

THE NEW YORKER

ANNALS OF MEDICINE

SLOW IDEAS

Some innovations spread fast. How do you speed the ones that don't?

BY ATUL GAWANDE

JULY 29, 2013

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LH ASP

- Daily audit-feedback: Critical Care
  - Since November 1, 2011
- Weekly audit-feedback: LH-Whitby Rehab
  - March 1, 2012
- Daily audit-feedback: Medicine wards (OG5, OC7)
  - Since August 27, 2012
- Daily audit-feedback: Medicine wards (OG9, OC6)
  - Since September 1, 2013

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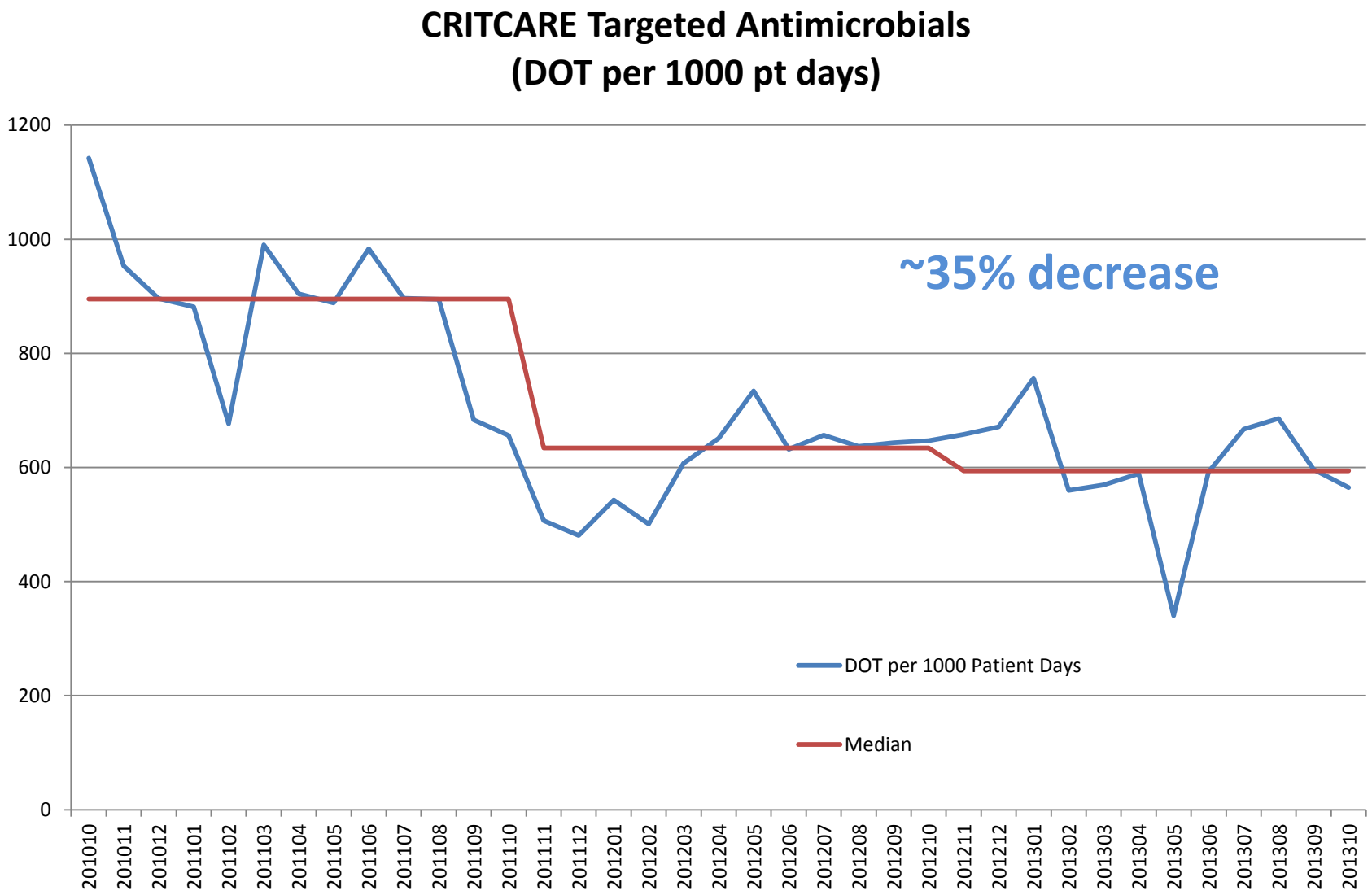
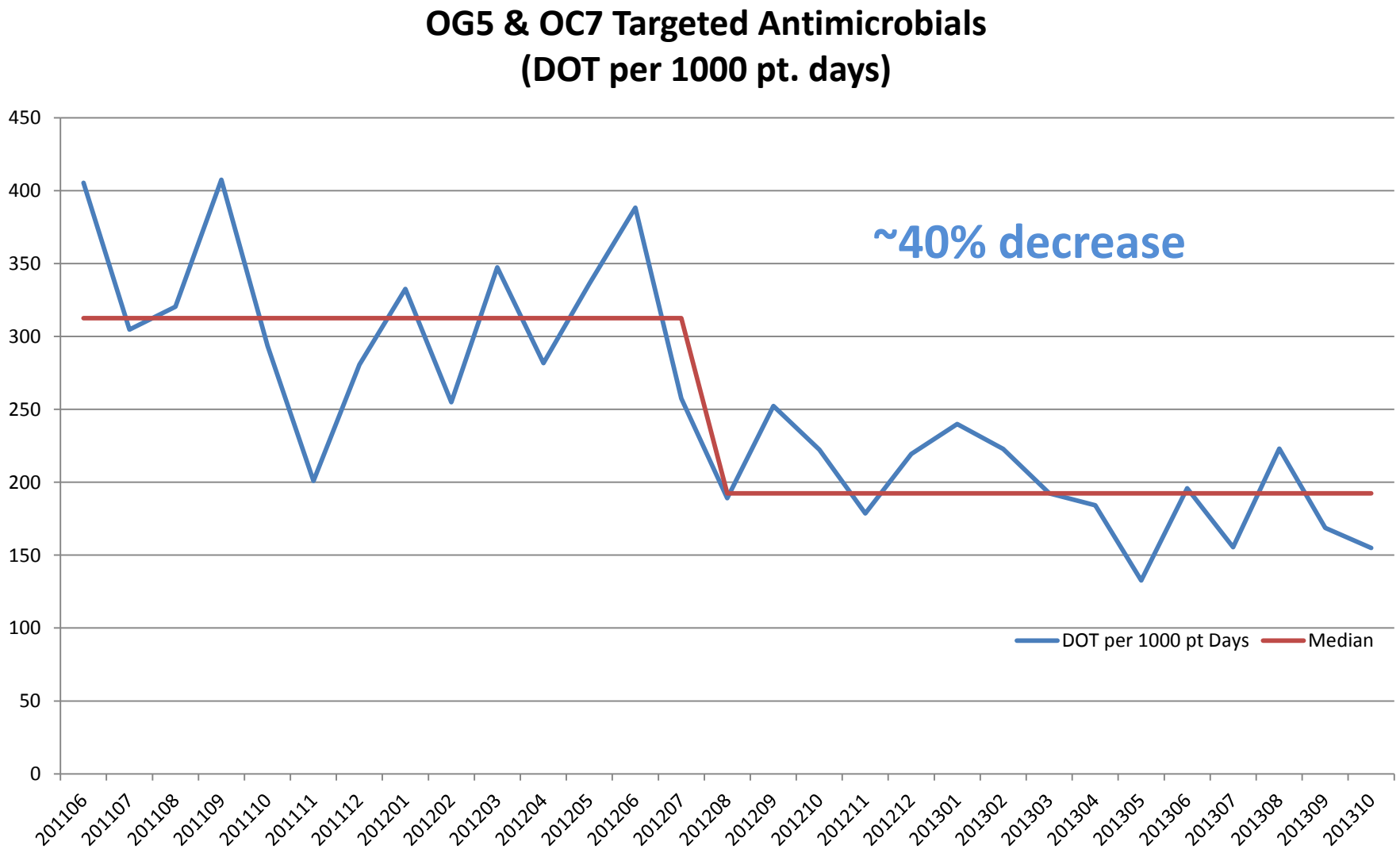
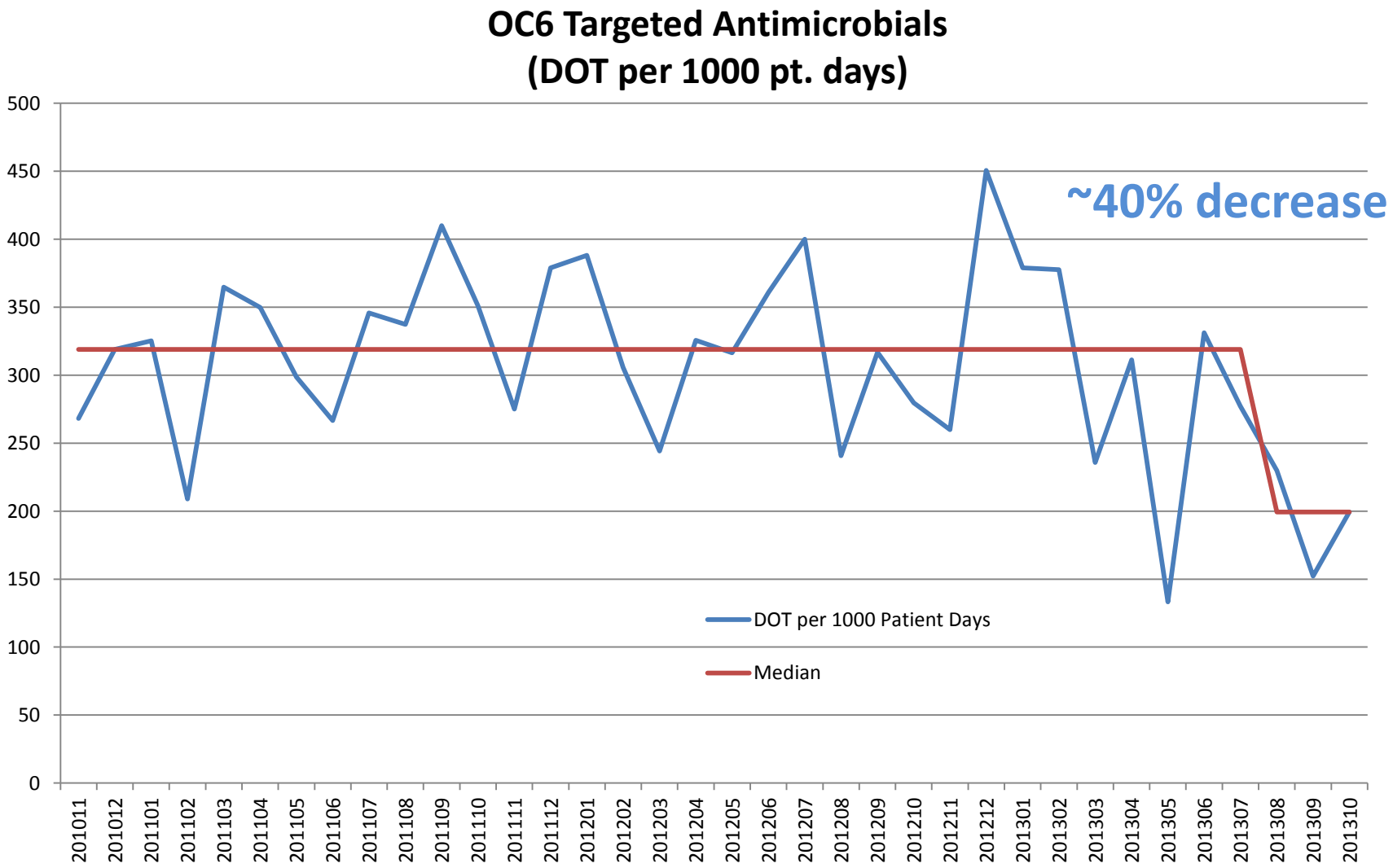
CrCU Targeted Antibiotics



ASP: Lakeridge Health



OC6 Targeted Antibiotics



How to Be an Antibiotic Steward…

"Be sure to keep taking the medication until it's all finished – even if you begin to look better."

LAKERIDGE HEALTH

Lesson 1:
Don’t Do Something; Just Sit There

HARD CASES | JUNE 10, 2013, 4:51 PM | 103 Comments

The New York Times

Don't Do Something; Just Sit There

By ABIGAIL ZUGER, M.D.

"The art of doing nothing is learning to help by not doing or advising," he wrote. "The evaluation is the treatment."

Our Obsession with Dental Antibiotic Prophylaxis and an E-mail from Mom

Paul Sax • March 30th, 2012
Categories: Health Care, Patient Care

It's broadly misconceived by dentists and orthopedists alike that the risk of antibiotics is lower than the risk of "seeding" an artificial joint or plate by the dental work.
Clearly *wrong*.
But that doesn't stop them. And it's because surgeons are much more worried about passive errors (not doing something) than they are about harming someone with an active error (medication side effect).
They're surgeons, after all. Maddening.
Paul

Paul E. Sax, MD

Effects of Clinical Pathways for Common Outpatient Infections on Antibiotic Prescribing

Timothy C. Jenkins, MD,[a,b,e,f] Amy Irwin, DNP, RN,[a] Letoynia Coombs, EdD,[g] Lauren DeAlleaume, MD,[c,g] Stephen E. Ross, MD,[e] Jeanne Rozwadowski, MD, MPH,[c,e] Brian Webster, MD,[h] L. Miriam Dickinson, PhD,[g] Allison L. Sabel, MD, PhD, MPH,[d,i] Thomas D. MacKenzie, MD, MSPH,[c,d,e] David R. West, PhD,[e,g] Connie S. Price, MD[a,b,e,f]

[a]Department of Medicine, [b]Division of Infectious Diseases, [c]Department of Community Health Services, [d]Department of Patient Safety and Quality, Denver Health Medical Center, Denver, Colo; [e]Department of Medicine, [f]Division of Infectious Diseases, [g]Department of Family Medicine, University of Colorado Denver, Aurora; [h]Wilmington Health, Wilmington, NC; [i]Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora.

Table 4 Antibiotic Prescriptions for Non-pneumonia Acute Respiratory Infections*

	Study Group			Control Group		
	Baseline Period N = 15,114	Intervention Period N = 7897	*P*	Baseline Period N = 7650	Intervention Period N = 4052	*P*
Antibiotic prescribed for acute respiratory infection	6460 (42.7)	2991 (37.9)	<.0001	3045 (39.8)	1569 (38.7)	.25
Upper respiratory infection	1135 (21.6)	468 (15.6)		371 (12.8)	182 (14.2)	
Acute bronchitis	1773 (60.5)	737 (54.9)		625 (57.2)	289 (51.1)	
Pharyngitis	715 (29.9)	426 (31.5)		565 (40.6)	364 (37.3)	
Acute rhinosinusitis	2242 (66.5)	1060 (65.9)		999 (70.2)	524 (65.8)	
Acute otitis media	595 (50.6)	300 (51.2)		485 (57.5)	210 (48.5)	

Effects of Clinical Pathways for Common Outpatient Infections on Antibiotic Prescribing

Timothy C. Jenkins, MD,[a,b,e,f] Amy Irwin, DNP, RN,[a] Letoynia Coombs, EdD,[g] Lauren DeAlleaume, MD,[c,g] Stephen E. Ross, MD,[e] Jeanne Rozwadowski, MD, MPH,[c,e] Brian Webster, MD,[h] L. Miriam Dickinson, PhD,[g] Allison L. Sabel, MD, PhD, MPH,[d,i] Thomas D. MacKenzie, MD, MSPH,[c,d,e] David R. West, PhD,[e,g] Connie S. Price, MD[a,b,e,f]

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Table 5 Broad-Spectrum Antibiotic Prescriptions for All Clinical Pathway Conditions*

	Study Group			Control Group		
	Baseline Period N = 21,351	Intervention Period N = 11,619	*P*	Baseline Period N = 10,017	Intervention Period N = 5403	*P*
Broad-spectrum antibiotic prescribed	5645 (26.4)	2630 (22.6)	<.0001	2004 (20.0)	1047 (19.4)	.35
Upper respiratory infection	771 (14.7)	272 (9.0)		216 (7.5)	116 (9.1)	
Acute bronchitis	1333 (45.5)	524 (39.1)		506 (46.3)	228 (40.3)	
Pharyngitis	337 (14.1)	153 (11.3)		150 (10.8)	96 (9.8)	
Acute rhinosinusitis	1429 (42.4)	646 (40.2)		506 (35.5)	274 (34.4)	
Acute otitis media	333 (28.3)	171 (29.2)		152 (18.0)	77 (17.8)	
Urinary tract infection	963 (29.2)	641 (32.7)		280 (24.3)	119 (19.2)	
Skin and soft tissue infection	283 (13.3)	143 (10.6)		101 (11.9)	70 (13.5)	
Pneumonia	196 (24.2)	80 (19.1)		93 (25.5)	67 (31.8)	

UTI/ASB

- **Do not send** urine samples unless patients have definite signs or symptoms of UTI
- **Remove** (or don't insert) the urinary catheter

Urinary Tract Infections

Does the Smell Really Tell?

Urine odor may be misleading in detecting urinary tract infections in elderly nursing home residents.

Susan J. Midthun, MS, RN, Ruth Paur, MS, MT (ASCP), and Glenda Lindseth, PhD, RN, FADA

LAKERIDGE HEALTH

Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic

A Prospective Study of 1497 Catheterized Patients

Paul A. Tambyah, MBBS; Dennis G. Maki, MD

Background: Catheter-associated urinary tract infection (CAUTI) is the most common nosocomial infection, accounting for more than 1 million cases each year in US hospitals and nursing homes.

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regarding symptoms. To more precisely define the role of CAUTI in patients' symptoms, a subset of 1034 patients, 89 of whom developed CAUTI with more than 10^3 colony-forming units per milliliter, who did not have another potentially confounding site of infection besides the urinary tract, was analyzed.

Outcome Measures: Presence of fever, symptoms commonly associated with community-acquired urinary tract infection, and peripheral leukocytosis.

Results: There were 235 new cases of nosocomial CAUTI during the study period. More than 90% of the infected patients were asymptomatic; only 123 infections (52%)

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Conclusions: Whereas CAUTIs are a major reservoir of antibiotic-resistant organisms in the hospital, they are rarely symptomatic and infrequently cause bloodstream infection. Symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CAUTI.

Arch Intern Med. 2000;160:678-682

"Only 1 of the 235 episodes of CAUTI (0.4%) ... Was associated with secondary bloodstream infection"

Bacteremia and Mortality with Urinary Catheter–Associated Bacteriuria

Quratulain F. Kizilbash, MD, MPH;[1,2] Nancy J. Petersen, PhD;[2,3,4] Guoqing J. Chen, MD, MPH, PhD;[2,3,4] Aanand D. Naik, MD;[2,3,5] Barbara W. Trautner, MD, PhD[1,2,3]

"Three episodes of (308 patients with) bacteriuria developed bacteremia (0.7%)."

"CAUTI rather than CAABU was associated with bacteremia, but neither predicted mortality."

"Use of antimicrobials was not associated with bacteremia or mortality."

Infect Control Hosp Epidemiol 2013;34(11):1153-1159

UTI

- **Do not treat** asymptomatic bacteriuria
  - Except pregnancy, pre-TURP
  - Beware of blaming behavioural symptoms alone on cystitis
    - They probably had bacteriuria when feeling fine as well
- Negative urinalysis has high NLR
- Positive urinalysis has low PLR

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Lesson 2:
Minimize Harm

Community-associated *Clostridium difficile* infection and antibiotics: a meta-analysis

Abhishek Deshpande[1]*†, Vinay Pasupuleti[1]†, Priyaleela Thota[1], Chaitanya Pant[2], David D. K. Rolston[3], Thomas J. Sferra[4], Adrian V. Hernandez[5] and Curtis J. Donskey[1,6]

Antibiotic	OR of CDI
clindamycin	20
fluoroquinolones	6
cephalosporins	5
penicillins	3
macrolides	3
SMZ/TMP	2
tetracyclines	1

J Antimicrob Chemother
doi:10.1093/jac/dkt129

LAKERIDGE HEALTH

Does Doxycycline Protect Against Development of *Clostridium difficile* Infection?

Sarah B. Doernberg,[1] Lisa G. Winston,[1] Daniel H. Deck,[2] and Henry F. Chambers[1]

- 2734 hospitalizations
- 5.6 per 10,000 pt. days if received ceftriaxone
- 1.6 per 10,000 pt. days if ceftriaxone/doxycycline
- 8.11 per 10,000 pt days if ceftriaxone without doxycycline

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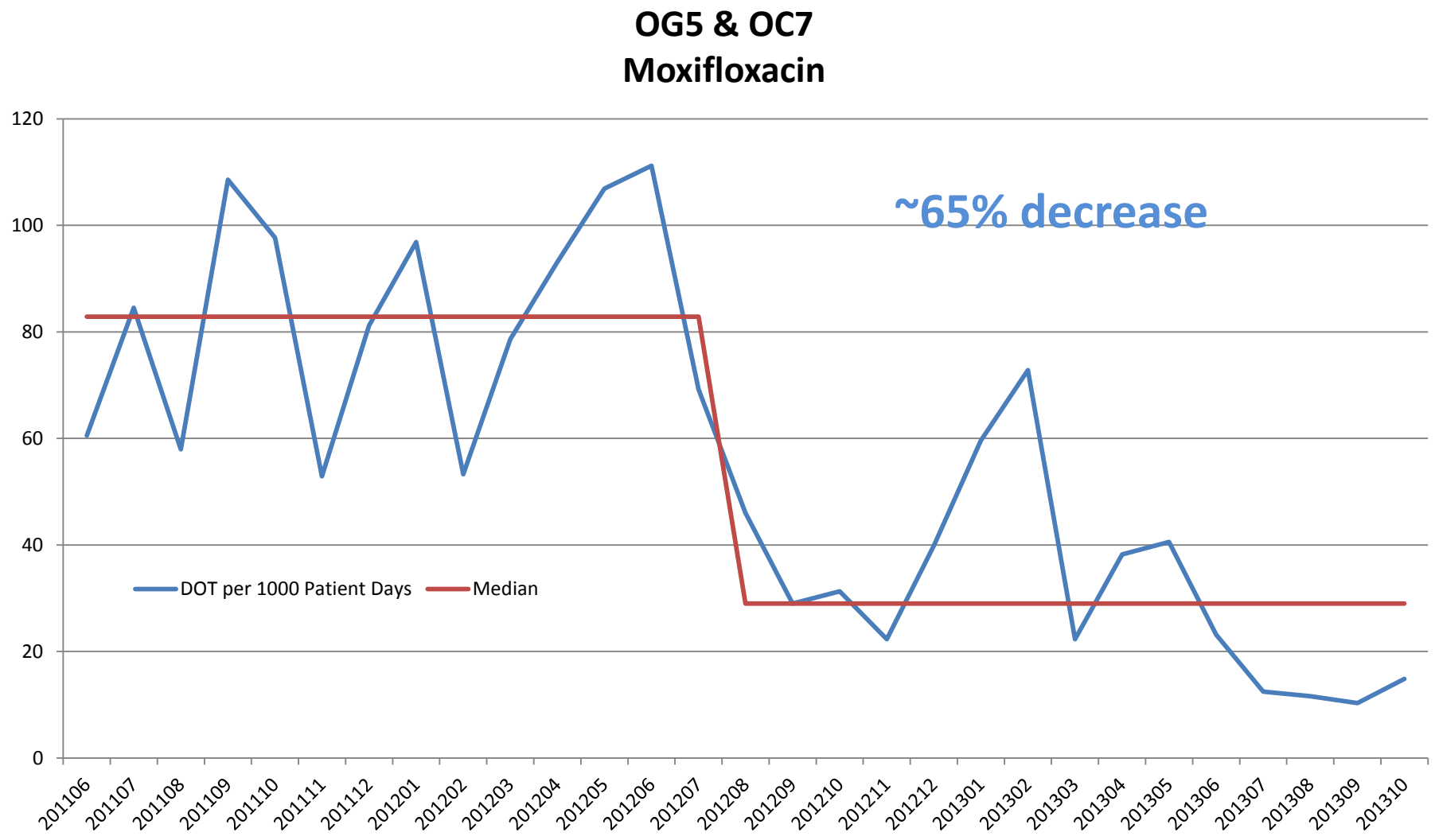
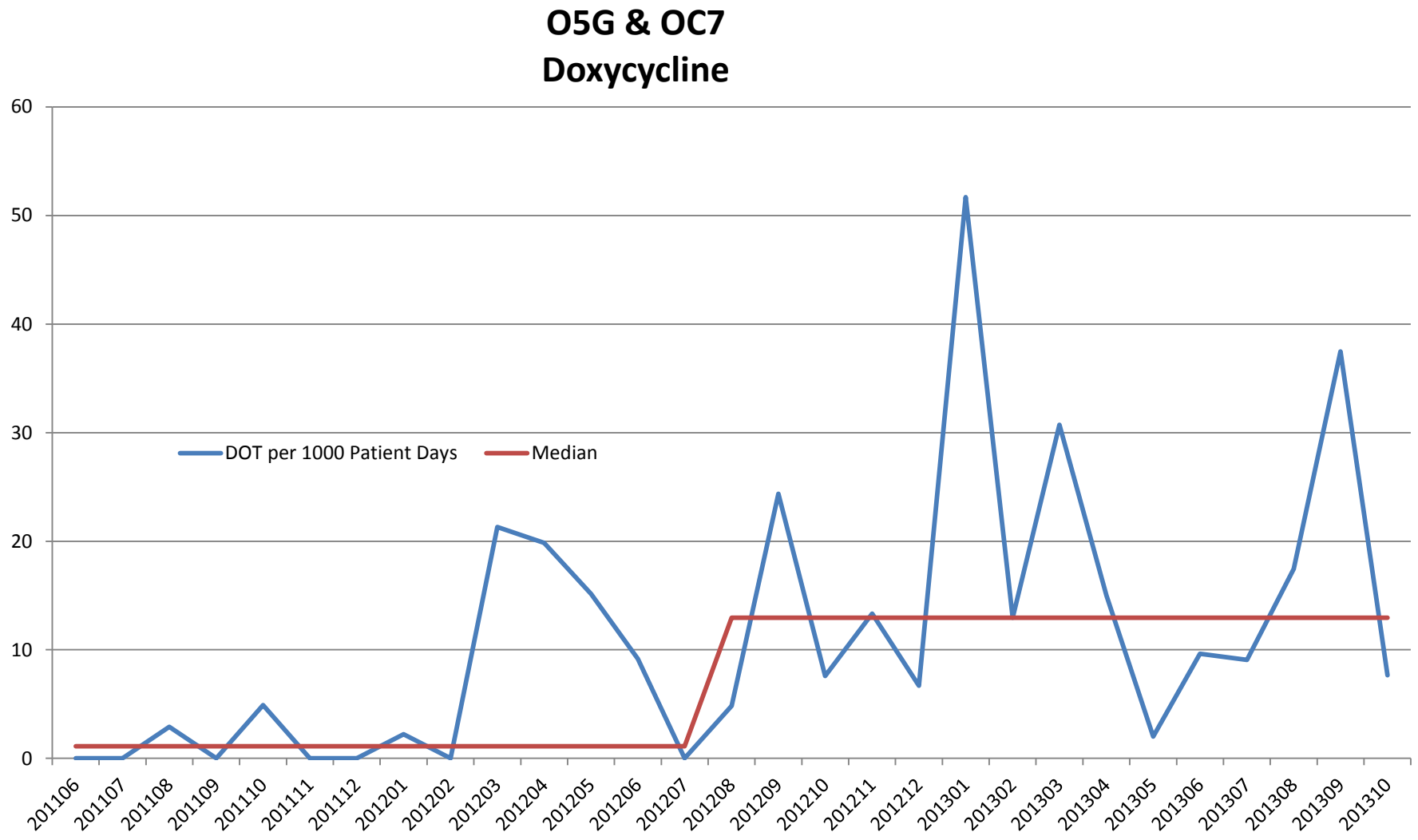
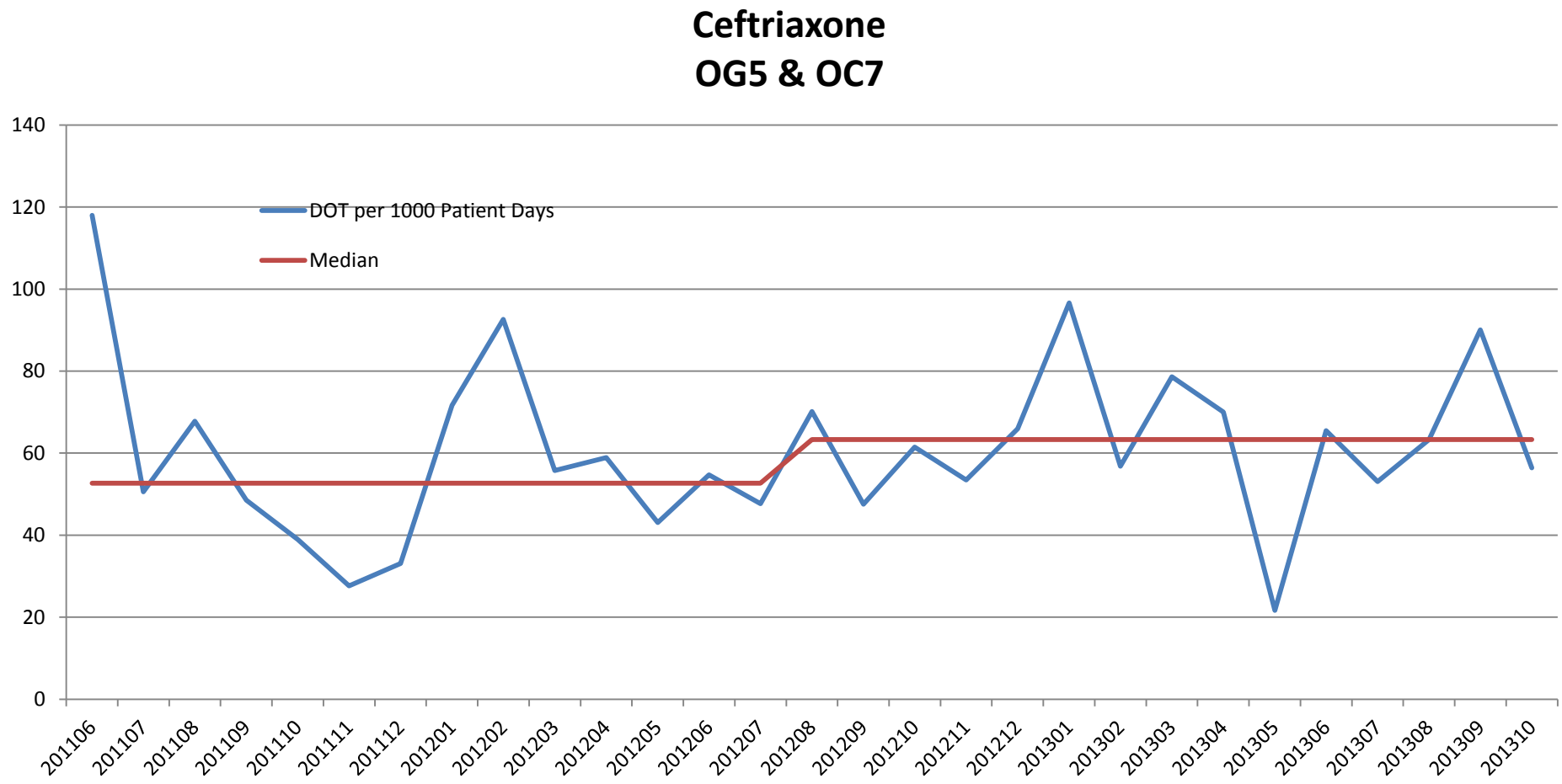
LH ASP: CAP Experience



LH ASP: CAP Experience



LH ASP: CAP Experience



Lesson 3:
Duration: Use Evidence not “experience”

How to Figure Out the Length of an Antibiotic

Paul E. Sax, MD

Editor-in-Chief
NEJM JOURNAL WATCH HIV/AIDS
CLINICAL CARE

- Choose a multiple of 5 (fingers of the hand) or 7 (days of the week).
- Is it an outpatient problem that is relatively mild? If so, choose something less than 10 days. After application of our multiples rule, this should be 5 or 7 days.
- Is it really mild, so much so that antibiotics probably aren't needed at all but clinician or patient are insistent? Break the 5/7 rule and go with 3 days. Ditto uncomplicated cystitis in young women.

How to Figure Out the Length of an Antibiotic

- Is it a serious problem that occurs in the hospital or could end up leading to hospitalization? With the exception of community-acquired pneumonia (5 or 7 days), 10 days is the minimum.
- Patient not doing better at the end of some course of therapy? Extend treatment, again using a multiple of 5 or 7 days.
- Does the infection involve a bone or a heart valve? Four weeks (28 days) at least, often 6 weeks (42 days). Note that 5 weeks (35 days) is not an option — here the 5's and 7's cancel each other out, and chaos ensues.
- The following lengths of therapy are inherently weird, and should generally be avoided: 2, 4, 6, 8, 9, 11, 12, 13 days.

Evidence-based Durations

- CAP: <7 days (usually 5)
- VAP: 8 days
- Cellulitis: 7 days
- UTI: 3 days
- UTI in men: <7days
- Pyelonephritis: 7 days
- Even with bacteremia? 7 days

Evidence-based Durations

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Institute for Safe Medication Practices Canada

A Key Partner in the Canadian Medication Incident Reporting and Prevention System (CMIRPS)

Evidence-Based Summaries for Short-Course Antimicrobial Therapy

- Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD)
- Community-Acquired Pneumonia
- Surgical Prophylaxis
- Uncomplicated Urinary Tract Infection
- Ventilator-Associated Pneumonia

Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection— 7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials

Noa Eliakim-Raz[1,2]*, Dafna Yahav[2,3], Mical Paul[2,3] and Leonard Leibovici[1,2]

Study or subgroup	Short Events	Short Total	Long Events	Long Total	Weight	RR M-H, Random, 95% CI
Peterson 2008	23	265	31	241	38.9%	0.67 [0.41–1.12]
Sandberg 2012	2	73	3	83	10.3%	0.76 [0.13–4.41]
Talan 2000	4	113	19	111	21.5%	0.21 [0.07–0.59]
de Gier 1995	7	18	5	16	24.5%	1.24 [0.49–3.15]
Klausner 2007	1	80	1	76	4.8%	0.95 [0.06–14.92]
Total (95% CI)		549		527	100.0%	0.63 [0.33–1.18]
Total events	37		59			

Heterogeneity: $\tau^2 = 0.20$; $\chi^2 = 6.83$, df = 4 ($P = 0.15$); $I^2 = 41\%$

Test for overall effect: $Z = 1.45$ ($P = 0.15$)

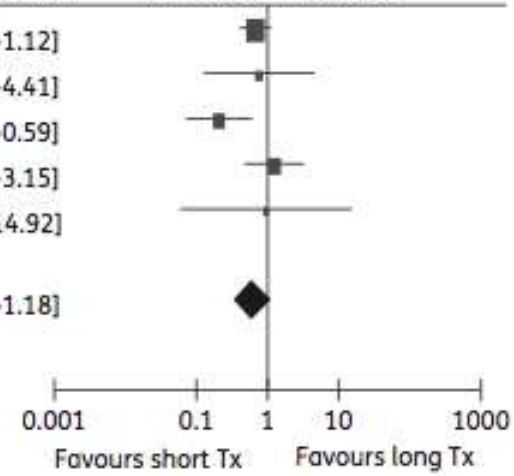

Figure 2. Clinical failure at EOT in patients treated for pyelonephritis, comparing short versus long treatment. EOT was defined as a lack of resolution of fever or signs and symptoms of UTI, or antibiotic modification at the end of the long-treatment arm. Clinical failure was significantly lower in the short-treatment arm. Studies are identified by the name of the first author and year of publication. FE meta-analysis was used for estimation of combined RR (95% CI). The diamond indicates the overall summary estimate for the analysis. Tx, treatment; M-H, Mantel-Haenszel.

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LESS IS MORE

Urinary Tract Infection in Male Veterans

Treatment Patterns and Outcomes

Dimitri M. Drekonja, MD, MS; Thomas S. Rector, PhD; Andrea Cutting, MA; James R. Johnson, MD

Conclusion: Longer-duration treatment (>7 days) for male UTI in the outpatient setting was associated with no reduction in early or late recurrence.

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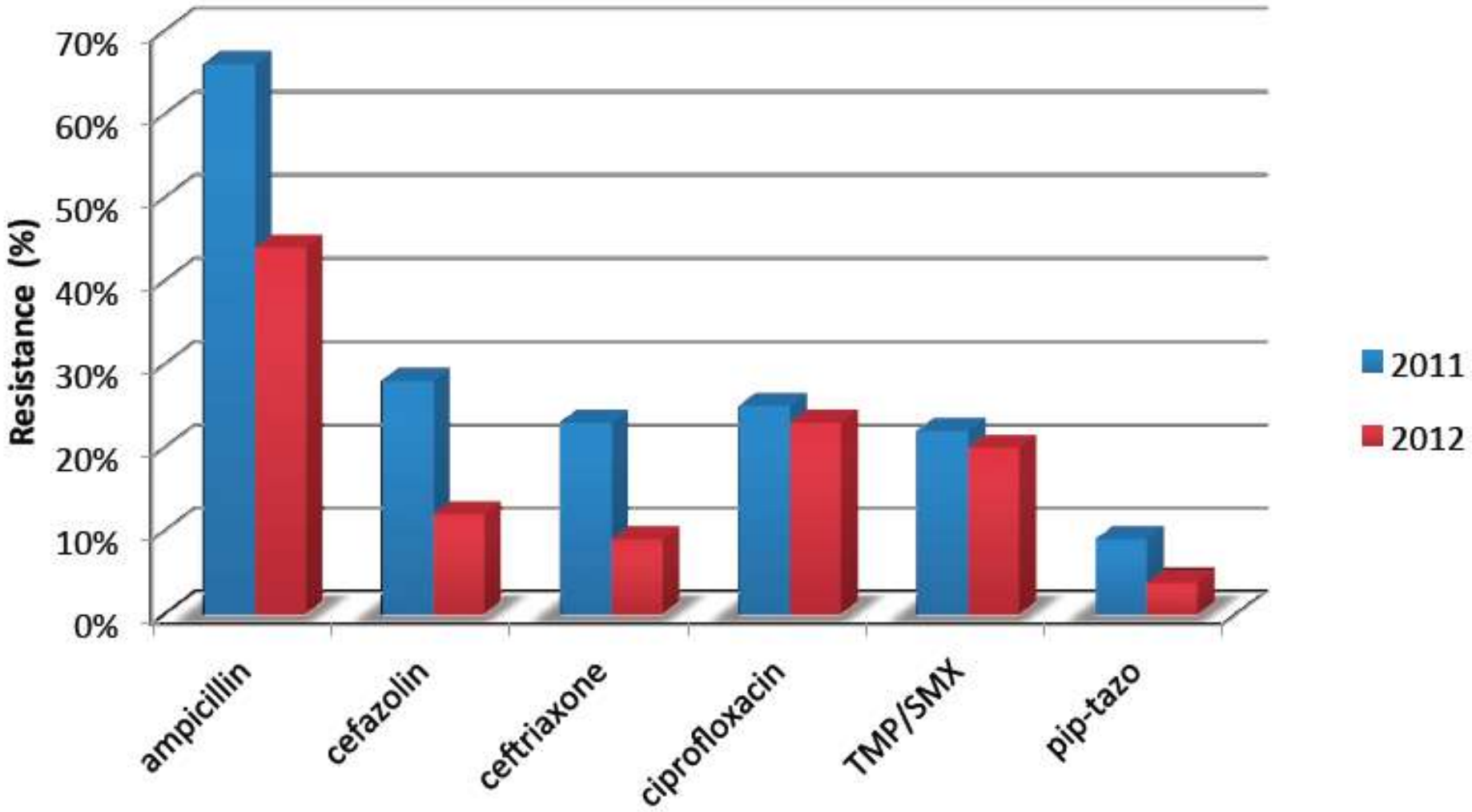
doi:10.1001/2013.jamainternmed.829

Future Directions

- Target antibiotic use in the community
  - EDs; WICs; PCP office
- Target antibiotic use in LTCFs
- Beyond antibiotics
  - Prudent PPI use etc.

Questions?

E. coli Antibiotic Resistance 2011 to 2012



Pseudomonas Antibiotic Resistance 2011 vs 2012