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Antimicrobial Stewardship: Pediatric Applications

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Agenda

- The case for Antimicrobial Stewardship
- The CHOP ASP
- Examples of Stewardship
  - Surgery
  - Primary care

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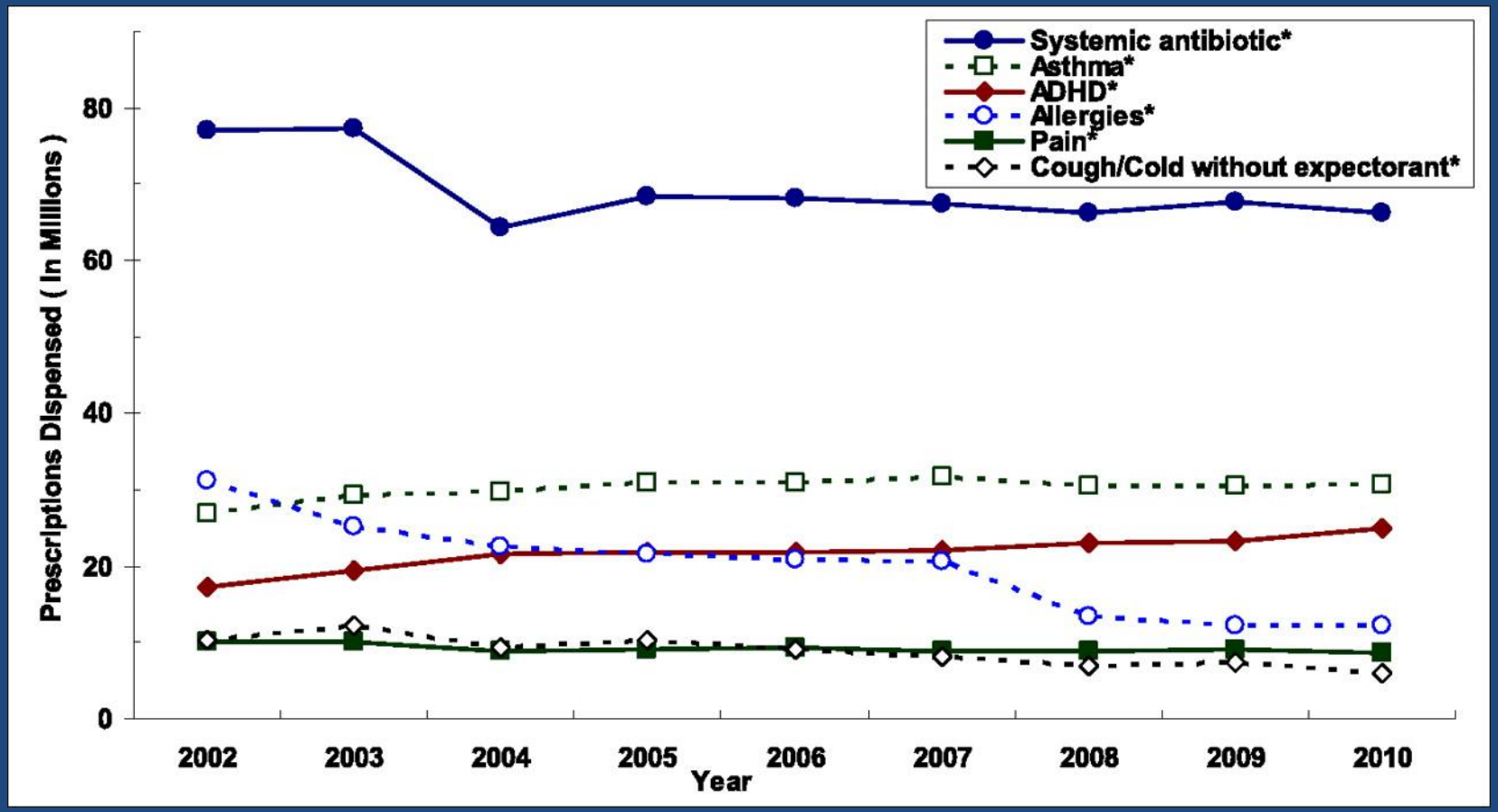
Antibiotic Use: Outpatient Children



Chai G et al. *Pediatrics* 2012;130:23-31

Antibiotic Use: Outpatient Children

Antibiotic Prescription Rates for Acute Respiratory Tract Infections in US Ambulatory Settings

Carlos G. Grijalva, MD, MPH
J. Pekka Nuorti, MD, DSc
Marie R. Griffin, MD, MPH

Context During the 1990s, antibiotic prescriptions for acute respiratory tract infection (ARTI) decreased in the United States. The sustainability of those changes is unknown.

Objective To assess trends in antibiotic prescriptions for ARTI.

Design, Setting, and Participants The National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey data (1995-2006) were used t
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JAMA.

INFECTIONS CAUSED BY ANTIBIOTIC-resistant microorganisms are associated with increased morbidity, mortality, and substantial economic burden.[1] Antibiotic use creates selective pressure for the emergence of antibiotic-resistant bacteria.[2-4] During the past decade, a variety of US initiatives have promoted the judicious use of antibiotics,[5,6] particularly for acute respiratory tract infection (ARTI), which is a common cause of health care encounters and antibiotic prescriptions, especially in young children. In the late 1990s, antibiotic prescription rates in both children and adults decreased,[7-10] but these decreases were initially accompanied by increased prescription of broad-spectrum antibiotics.[9-11]

Interventions not directly targeting antibacterial use may also have reduced antibiotic prescriptions and limited the spread of antibiotic resistance. For example, routine US infant immunization with a 7-valent pneumococcal conjugate vaccine (PCV-7) resulted in decreases in rates of inva-

Antibiotic Prescribing in Ambulatory Pediatrics in the United States

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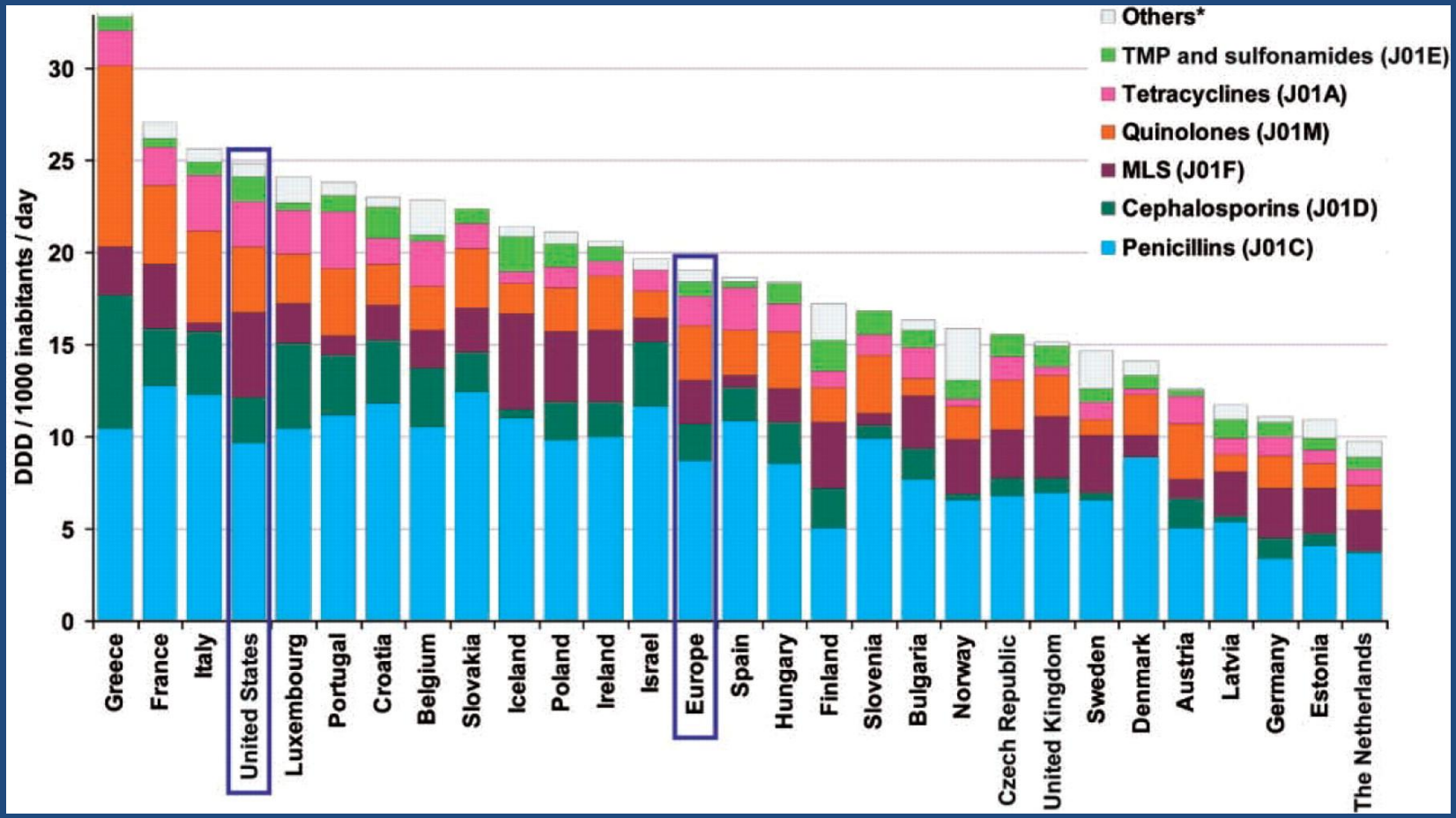
KEY WORDS
antibacterial agents, respiratory tract infections, pediatrics, physician's practice patterns, inappropriate prescribing

WHAT'S KNOWN ON THIS SUBJECT: Results of previous studies have indicated that most antibiotic prescriptions for children are for respiratory conditions, and many of them are inappropriate. Although antibiotic prescribing is declining overall, broad-spectrum antibiotic prescribing for respiratory conditions is increasing. Unnecessary antibiotic prescribing promotes resistance and adverse events.

WHAT THIS STUDY ADDS: Respiratory conditions account for >70% of antibiotic prescriptions in ambulatory pediatrics. Broad-spectrum antibiotics, especially macrolides, represent 50% of pediatric antibiotic use. Broad-spectrum antibiotics are frequently prescribed unnecessarily for conditions for which antibiotics are unlikely to provide benefit.

Outpatient Antibiotic Use: US and Europe, 2004



Goossens H et al. *Clin Infect Dis*. 2007;44:1091-1095

Outpatient Antibiotic Dispensing: US, 2010

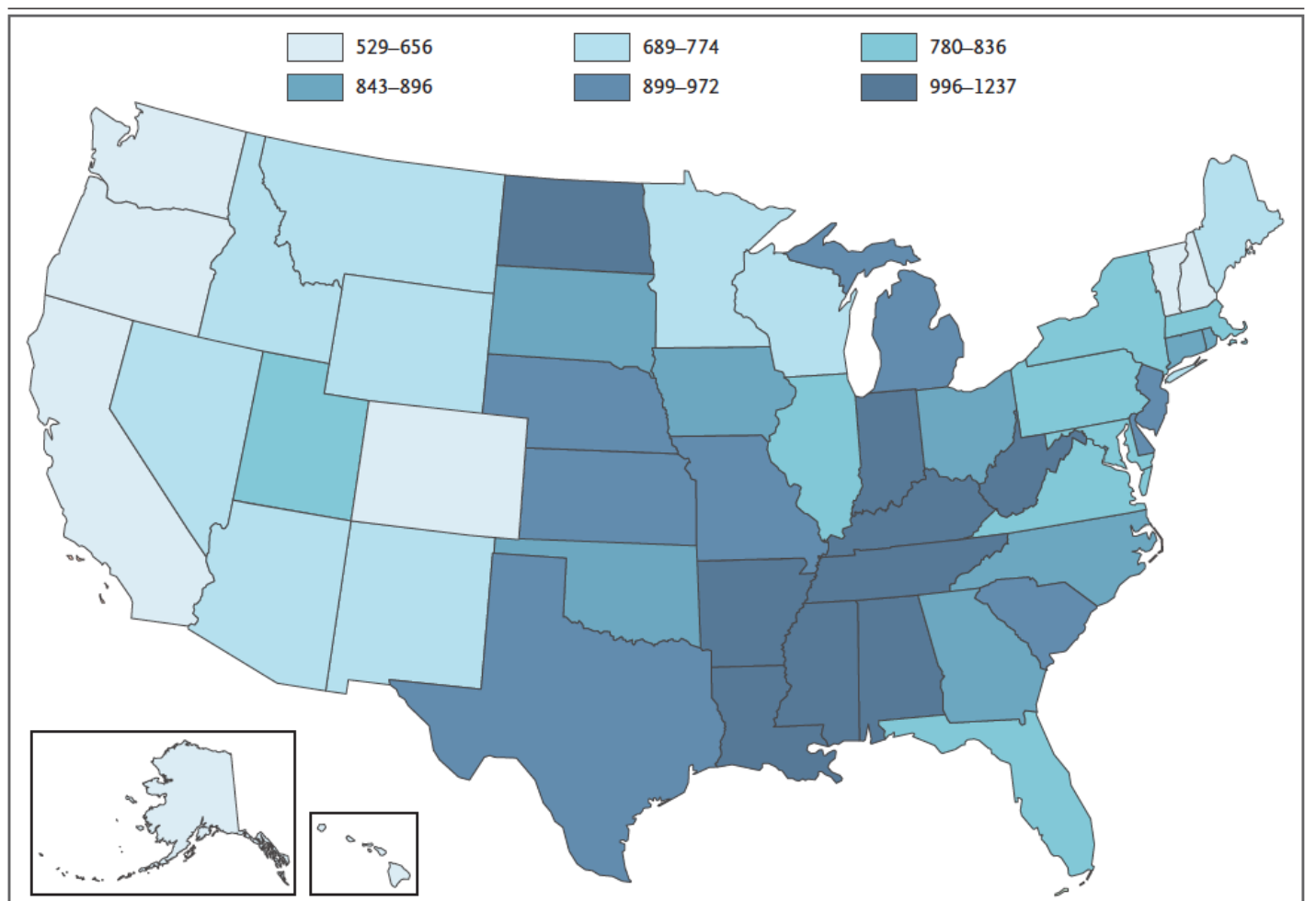


Figure 1. Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010.

Hicks L et. Al. NEJM April 11, 2013

So What?

- We use a LOT of antibiotics
- We use them variably

- But … so what?

ANTIBIOTIC RESISTANCE THREATS
in the United States, 2013

U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

Impact of Antibiotic Resistance

Each Year in the US:

- > 2 million serious infections with antibiotic-resistant bacteria
- > 23,000 die as a direct result of antibiotic-resistant infections
- 250,000 hospitalizations for *C. difficile* infections; >14,000 deaths
- $20 billion direct healthcare costs (2008)
- Many of these infections could have been prevented

Core Actions to Combat Resistance

- preventing infections and preventing the spread of resistance
- tracking resistant bacteria
- improving the use of today's antibiotics
- promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria

Bacteria will inevitably find ways of resisting the antibiotics we develop, which is why aggressive action is needed to keep new resistance from developing and prevent the resistance that already exists from spreading

Antibiotic use is the most important factor leading to antibiotic resistance

Resistance Aside

- 5%–25% diarrhea
- 1 in 1000 visit emergency department for adverse effect of antibiotic
  - comparable to insulin, warfarin, and digoxin
- 1 in 4000 chance that an antibiotic will prevent serious complication from URI

Shehab N. **CID 2008:47**; Linder JA. **CID 2008:47**

COMMENT

HOMININS Did modern humans replace Neanderthals or co-exist with them? **p.395**

HISTORY Sigmund Freud and William Halstead on cocaine **p.397**

BIODIVERSITY DNA bank needed to conserve all species, not just plants **p.399**

OBITUARY Jonathan Widom, genomic map-maker, remembered **p.400**

P. DUREUIL PHOTOALTO/ALAMY

Dosed up: could excessive prescription of antibiotics be hampering children's ability to fight disease?

Stop the killing of beneficial bacteria

Concerns about antibiotics focus on bacterial resistance — but permanent changes to our protective flora could have more serious consequences, says **Martin Blaser**.

The average child in the United States and other developed countries has received 10–20 courses of antibiotics by the time he or she is 18 years old[1]. In many respects, this is a life-saving development. The average US citizen born in 1940 was expected to live to the age of 63; a baby born today should reach 78, in part because of antibiotics. But the assumption that antibiotics are generally safe has fostered overuse and led to an increase in bacterial resistance to treatments.

Other, equally serious, long-term consequences of our love of antibiotics have received far less attention. Antibiotics kill the bacteria we do want, as well as those we don't. Early evidence from my lab and others hints that, sometimes, our friendly flora never fully recover. These long-term changes to the beneficial bacteria within people's bodies may even increase our susceptibility to infections and disease. Overuse of antibiotics could be fuelling the dramatic increase in conditions such as obesity, type 1 diabetes, inflammatory bowel disease, allergies and asthma, which have more than doubled in many populations (see graph).

We urgently need to investigate this possibility. And, even before we understand the full scope, there is action we should take. ▶

Antibiotics and Obesity

- Mice fed sub-therapeutic doses of antibiotics exhibited:
  - taxonomic changes of microbiome
  - changes in copies of key genes involved in metabolism of carbohydrates to short-chain fatty acids
  - alterations in hepatic metabolism of lipids and cholesterol
  - increased adiposity

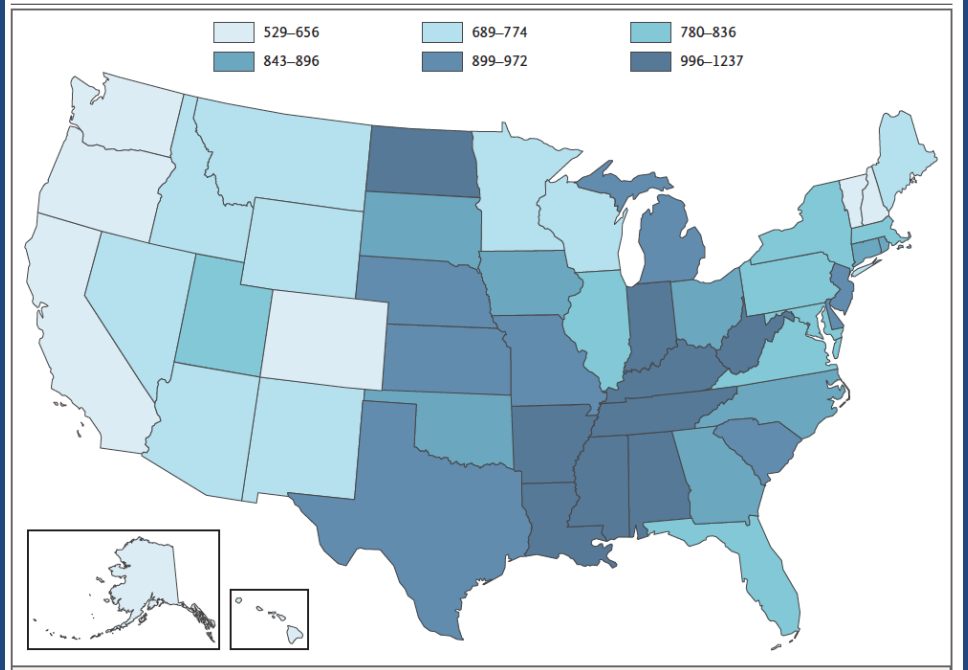
Cho I et al. Nature 2012

Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Vanessa K. Ridaura, Jeremiah J. Faith, Federico E. Rey, Jiye Cheng, Alexis E. Duncan, Andrew L. Kau, Nicholas W. Griffin, Vincent Lombard, Bernard Henrissat, James R. Bain, Michael J. Muehlbauer, Olga Ilkayeva, Clay F. Semenkovich, Katsuhiko Funai, David K. Hayashi, Barbara J. Lyle, Margaret C. Martini, Luke K. Ursell, Jose C. Clemente, William Van Treuren, William A. Walters, Rob Knight, Christopher B. Newgard, Andrew C. Heath, Jeffrey I. Gordon*

The role of specific gut microbes in shaping body composition remains unclear. We transplanted fecal microbiota from adult female twin pairs discordant for obesity into germ-free mice fed low-fat mouse chow, as well as diets representing different levels of saturated fat and fruit and vegetable consumption typical of the U.S. diet. Increased total body and fat mass, as well as obesity-associated metabolic phenotypes, were transmissible with uncultured fecal communities and with their corresponding fecal bacterial culture collections. Cohousing mice harboring an obese twin's microbiota (Ob) with mice containing the lean co-twin's microbiota (Ln) prevented the development of increased body mass and obesity-associated metabolic phenotypes in Ob cage mates. Rescue correlated with invasion of specific members of Bacteroidetes from the Ln microbiota into Ob microbiota and was diet-dependent. These findings reveal transmissible, rapid, and modifiable effects of diet-by-microbiota interactions.

SCIENCE VOL 341 6 SEPTEMBER 2013



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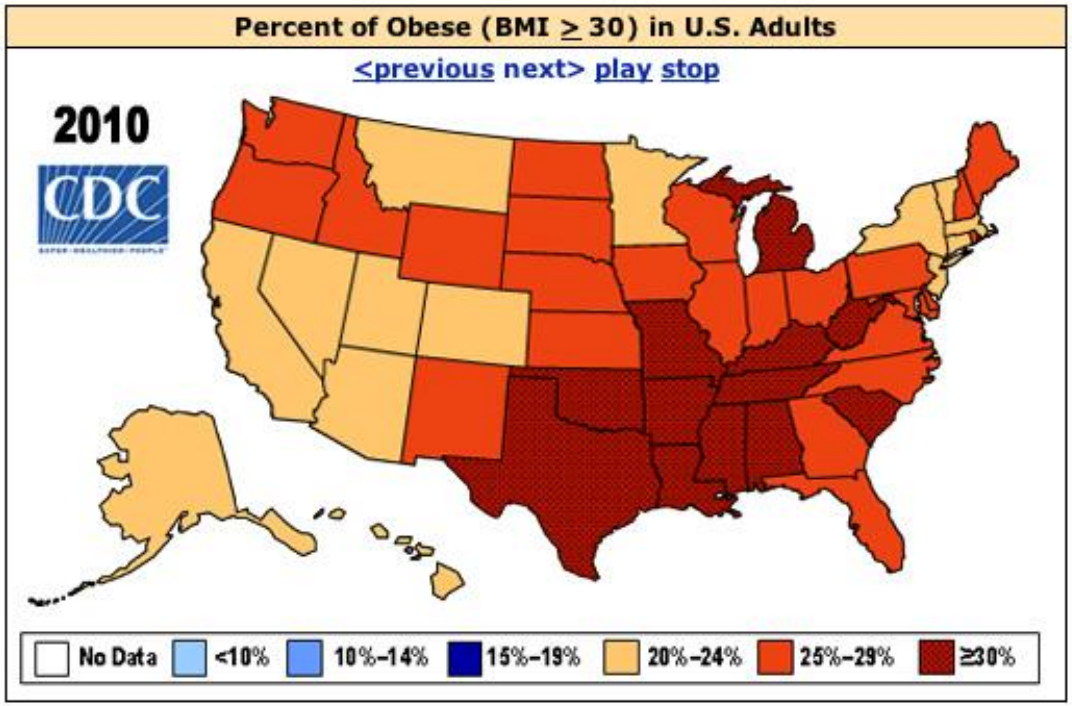
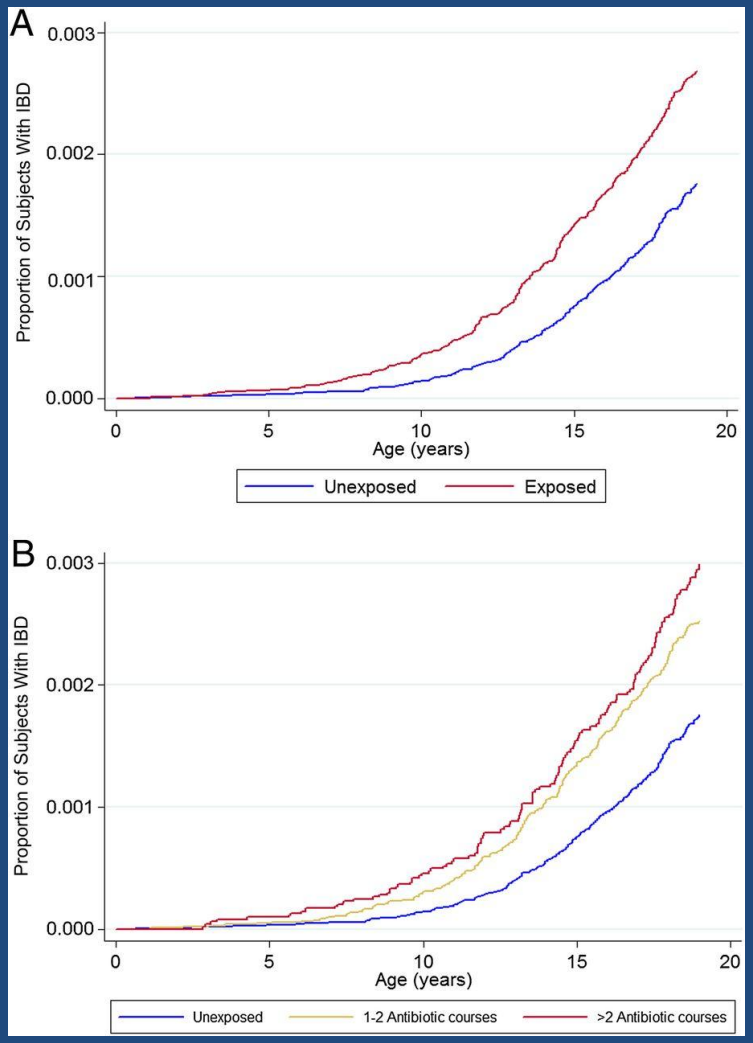


Antibiotics and IBD



Proportion of subjects developing IBD according to age and anti-anaerobic antibiotic exposure status

Kronman MP et al. Pediatrics 2012;130

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2013 VOL. 368 NO. 5

Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

CONCLUSIONS

The infusion of donor feces was significantly more effective for the treatment of recurrent *C. difficile* infection than the use of vancomycin. (Funded by the Netherlands Organization for Health Research and Development and the Netherlands Organization for Scientific Research; Netherlands Trial Register number, NTR1177.)

Summary: Background

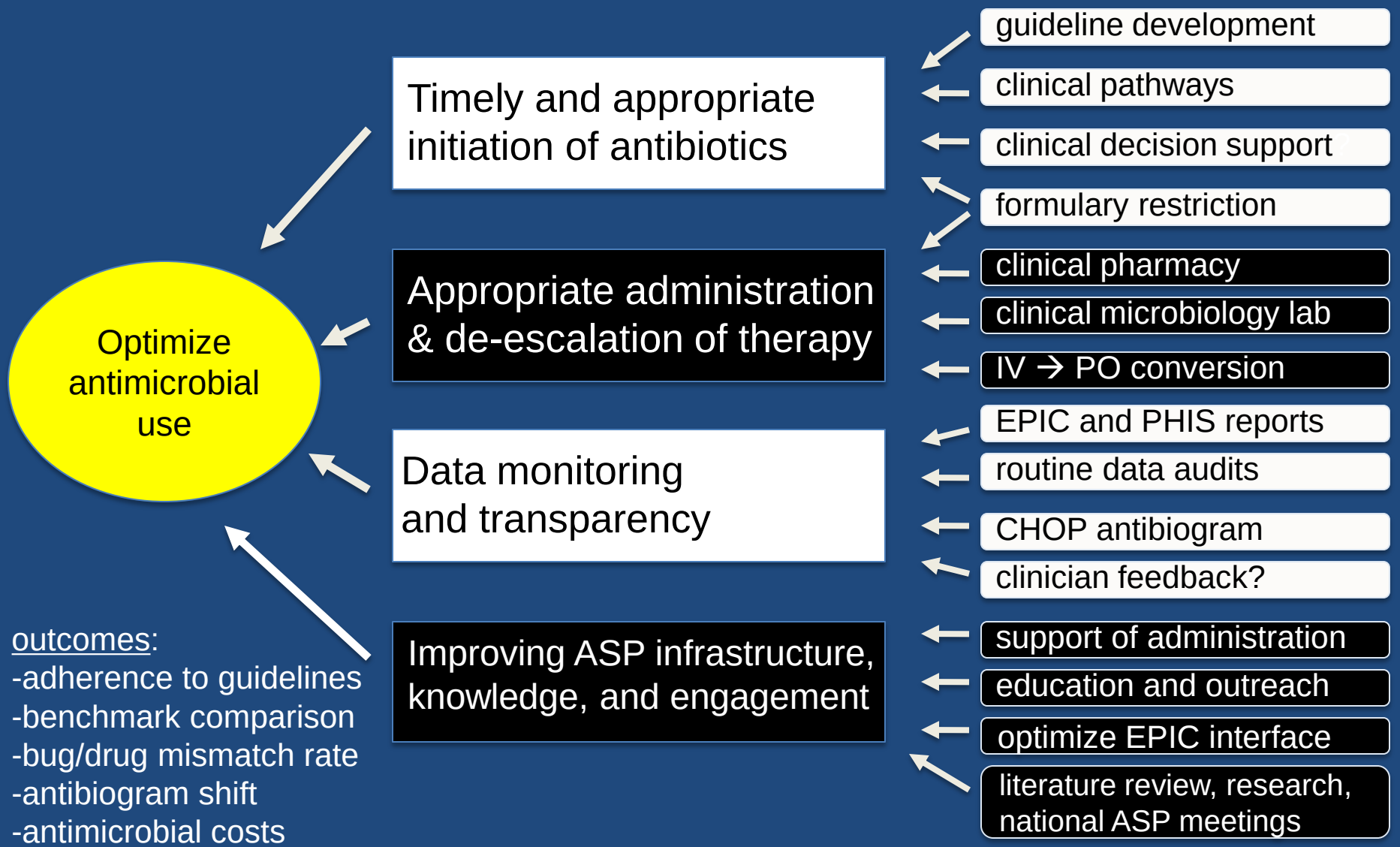
- Antibiotic use is both frequent and variable
- There is a downside to antibiotic use
  - antibiotic resistance
  - patient-specific adverse drug effects
  - disruption of “healthy” flora

Agenda

- The case for Antimicrobial Stewardship
- The CHOP ASP
- Examples of Stewardship

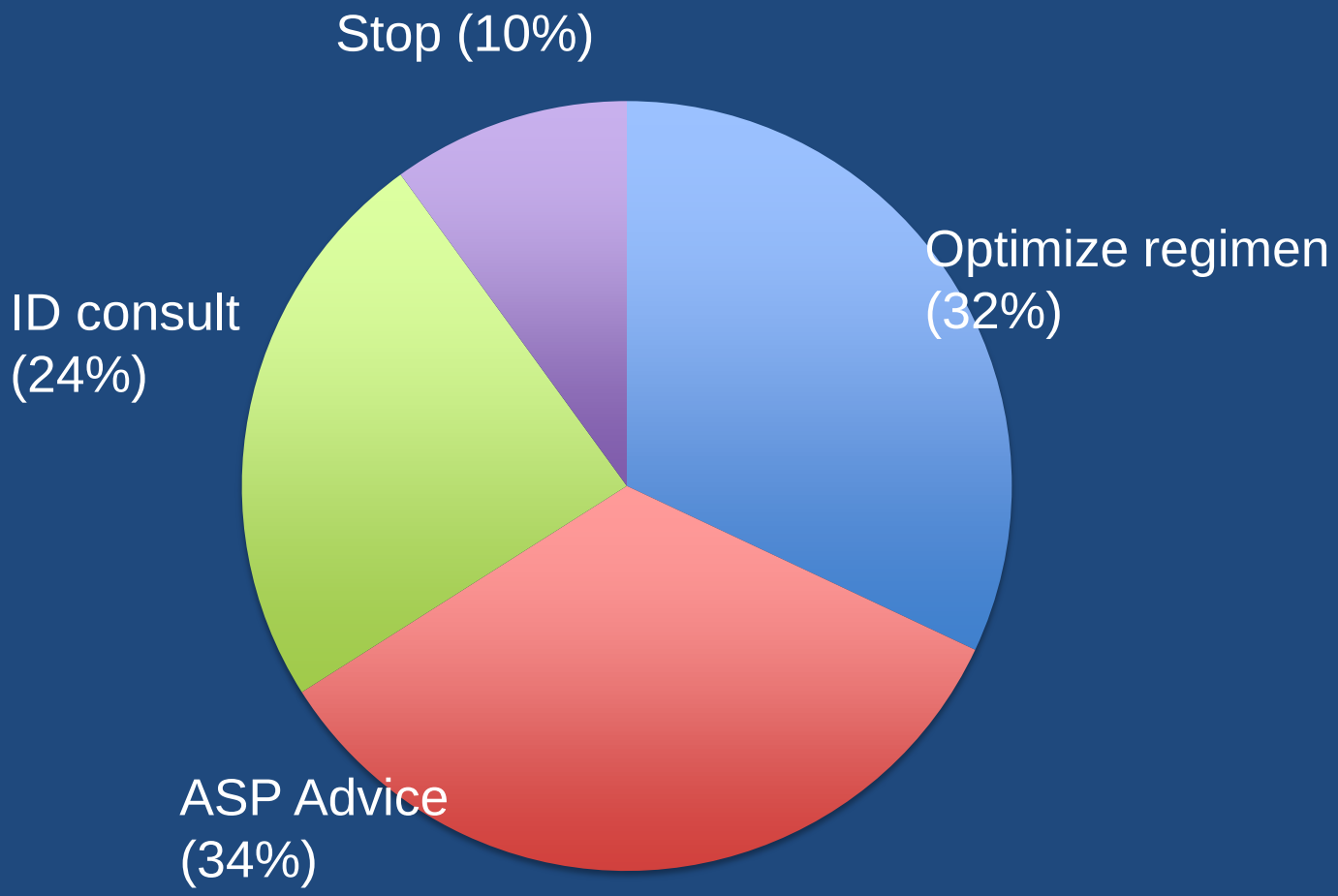

HAI, Influenza clinical resource
Infection Prevention & Control
ASP-EPIC Workflow Pathways, Safety-Net
Office of Patient Safety & Quality
Pandemic Influenza Clinical resource
Emergency Preparedness
clinical guidelines; content experts/support
Division of Infectious Diseases
CHOP ASP
ASP support/consultation education, ASP-Epic workflow
Residents, Fellows, & Nursing
antibiotic DUE, formulary, clinical resource, assist in drug shortages
Department of Pharmacy Services
Division-specific pathways and guidelines; Operating Plan Initiatives (HAI)
Divisions & Departments & Hospital
Microbiology & Virology
antibiogram, clinical resource antimicrobials, & antivirals
Vascular Access Service
clinical resource, lock therapy, damaged CVC CLABSI

CHOP ASP: Driver Diagram



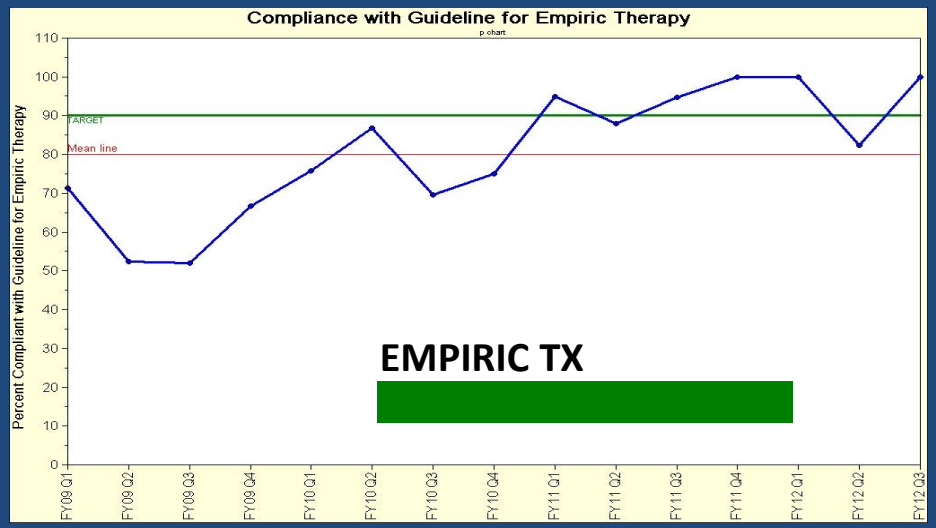
CHOP ASP: 2012

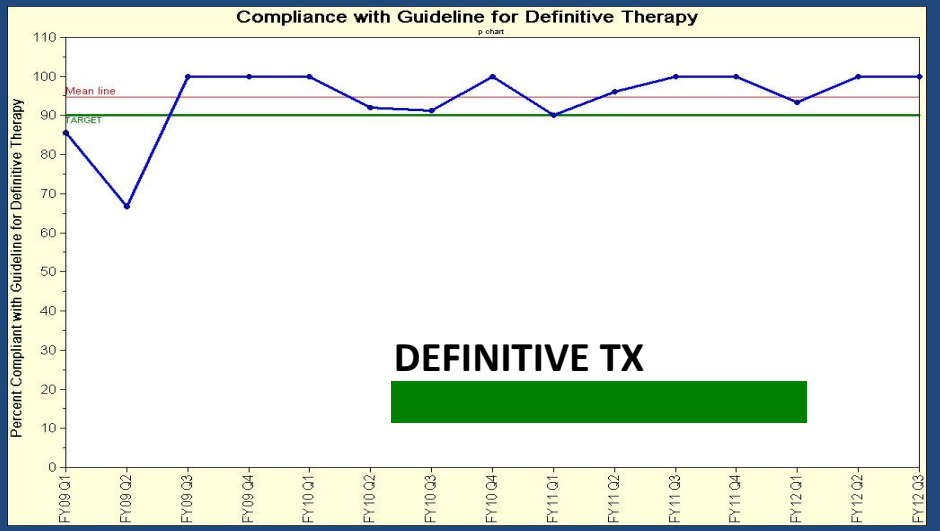
- 1.5 months
- **55% received intervention:**

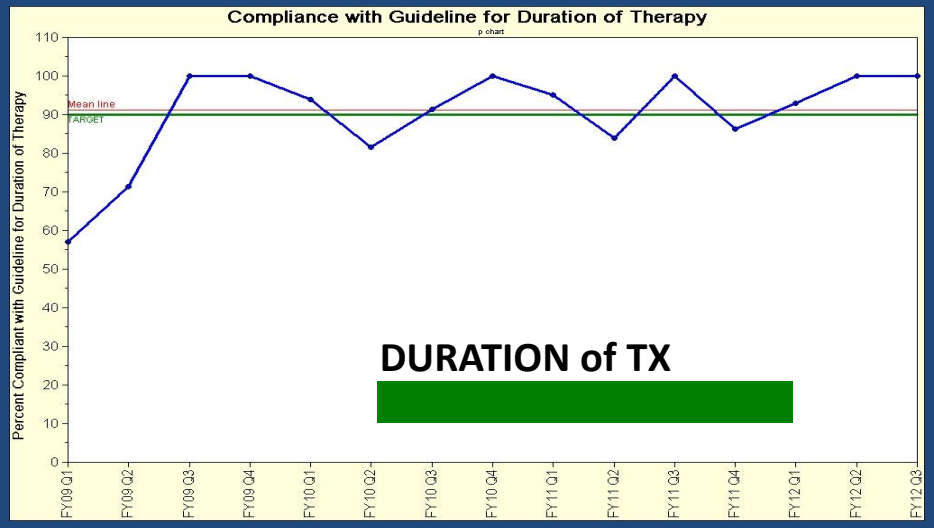


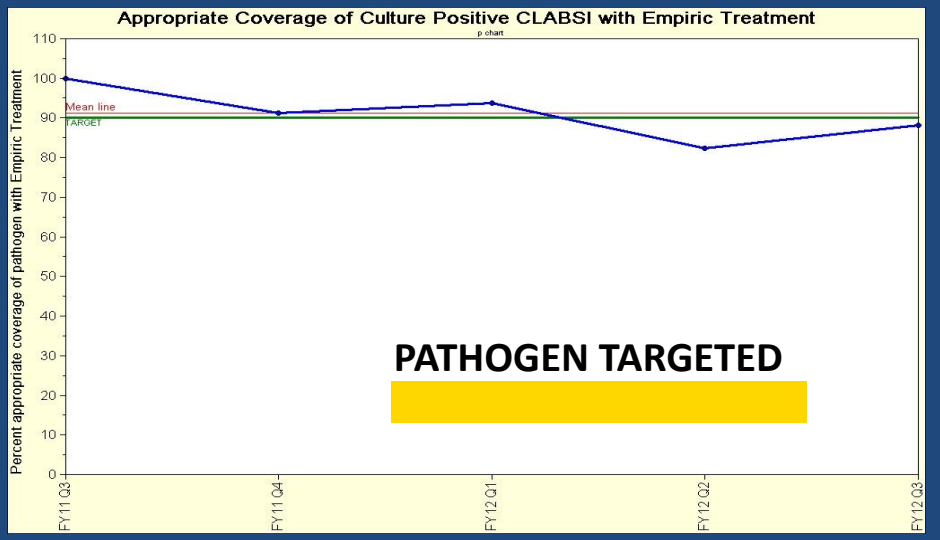
CLABSI: Tx Compliance

= at or above target
= within 15% of Target
= >15% from Target

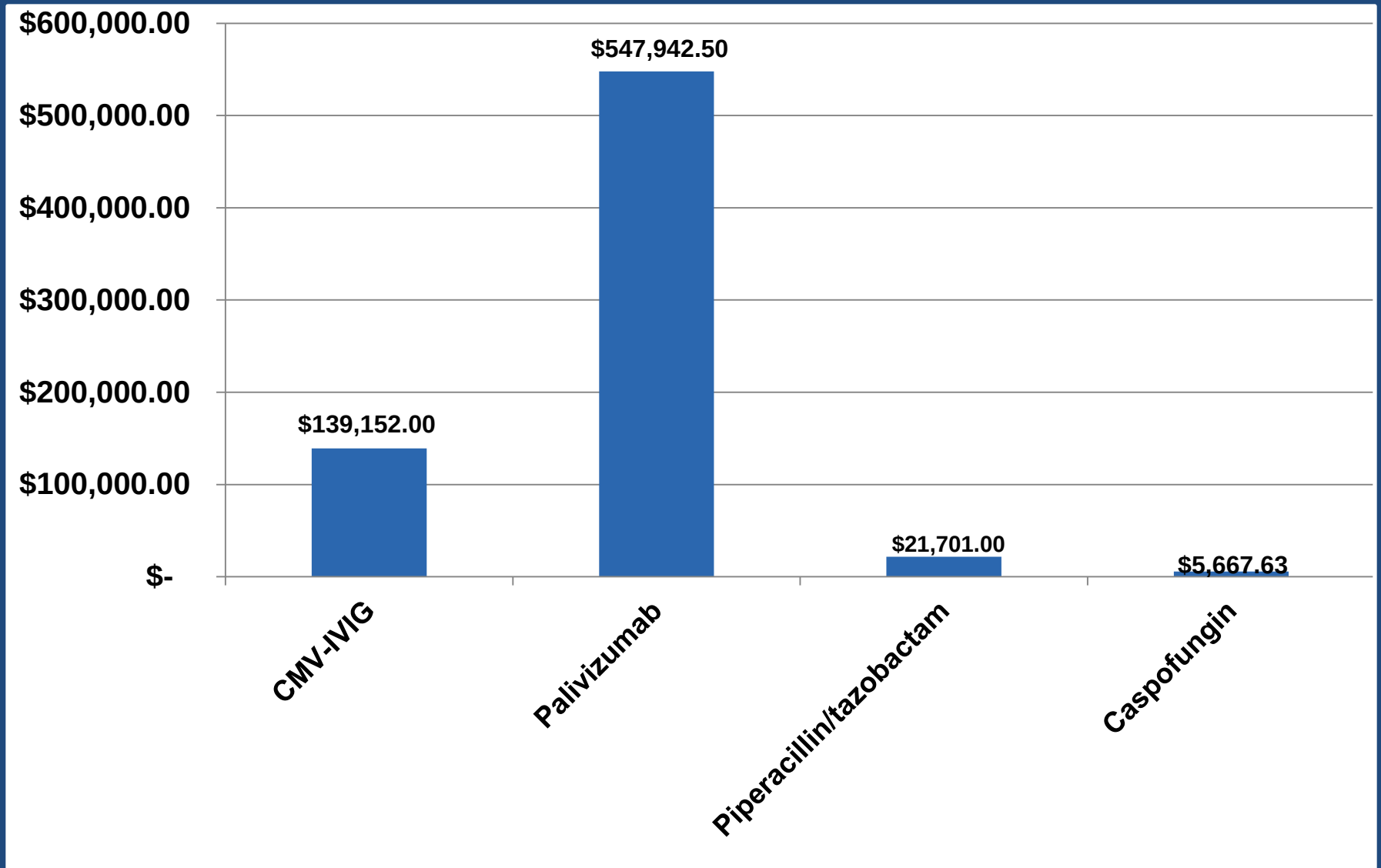






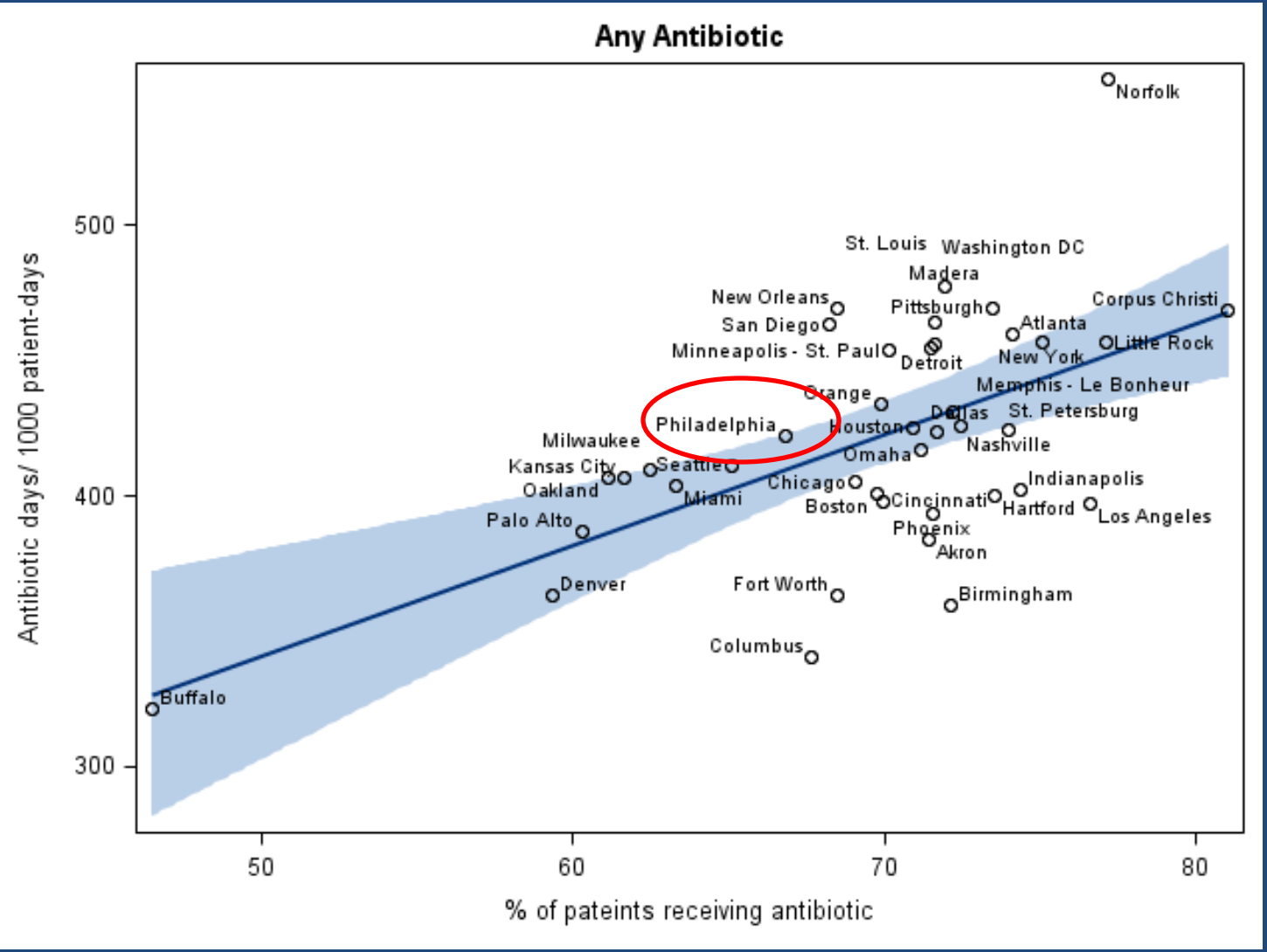


Cost savings: $714,463



Benchmarking

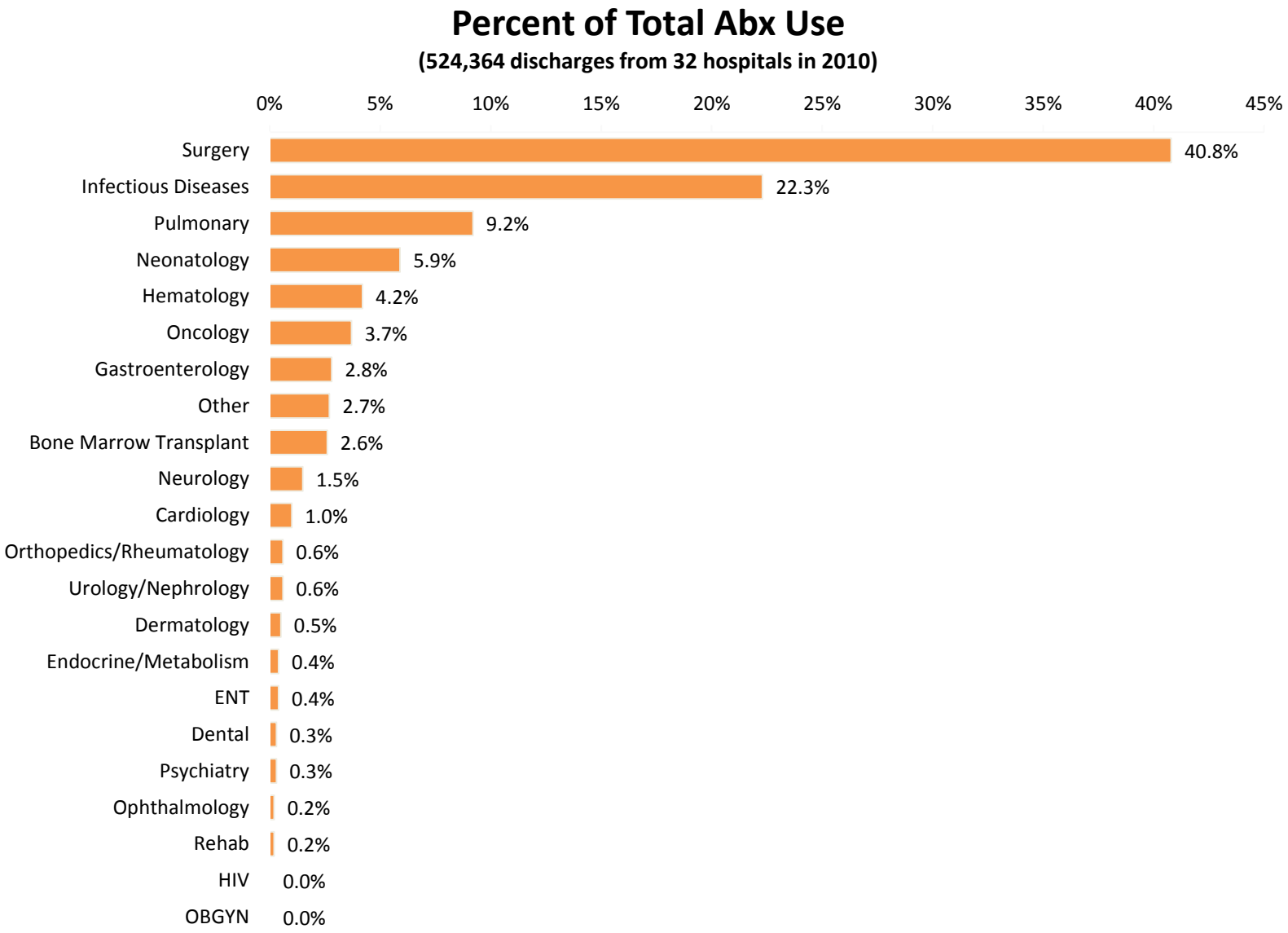
Benchmarking



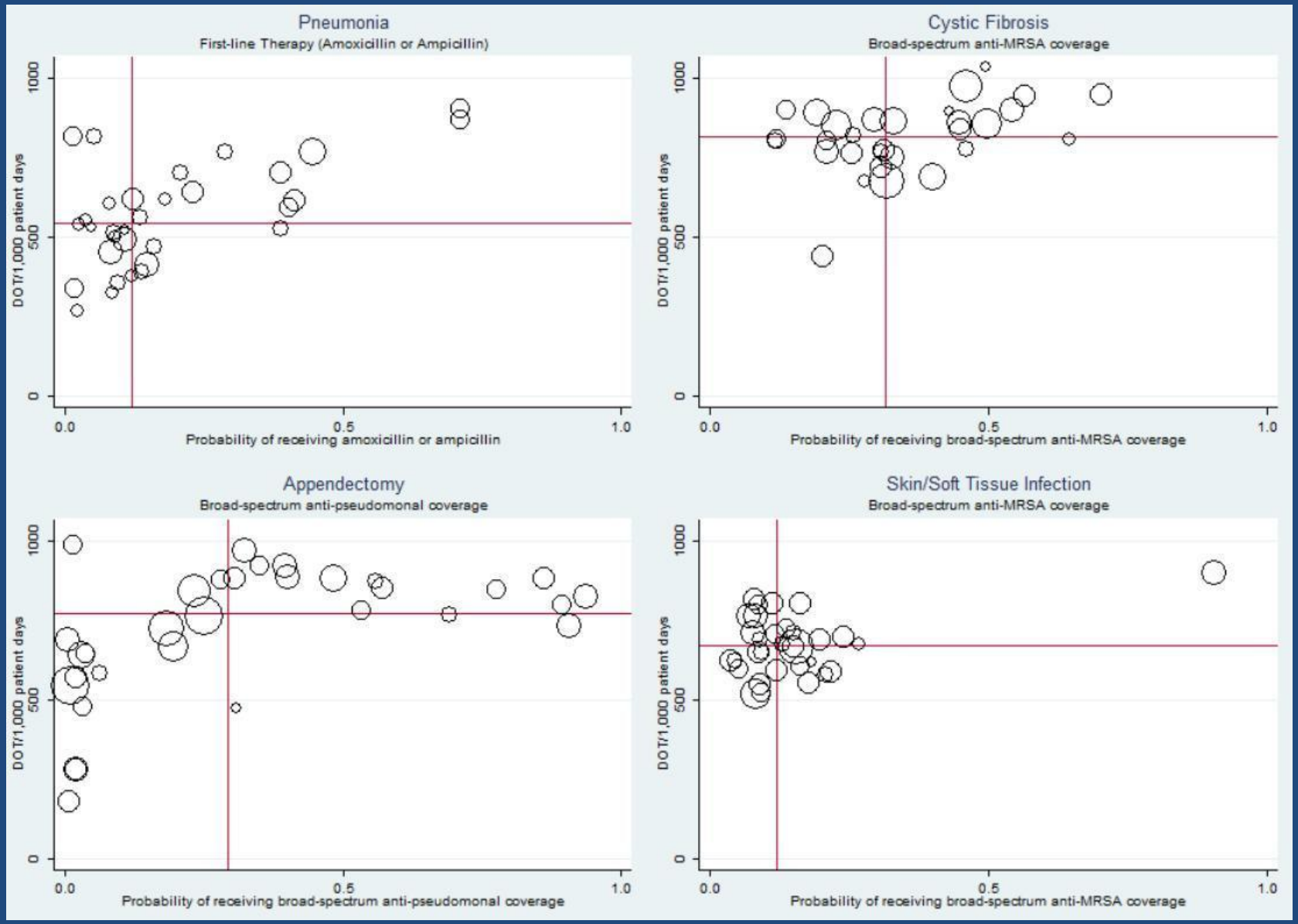
Gerber et al. *Pediatrics* 2010

Where should we focus stewardship efforts?

Antibiotic Use at Children's Hospitals, by Service Line



Variability of Antibiotic Use Across Hospitals, Top Four APR-DRGs

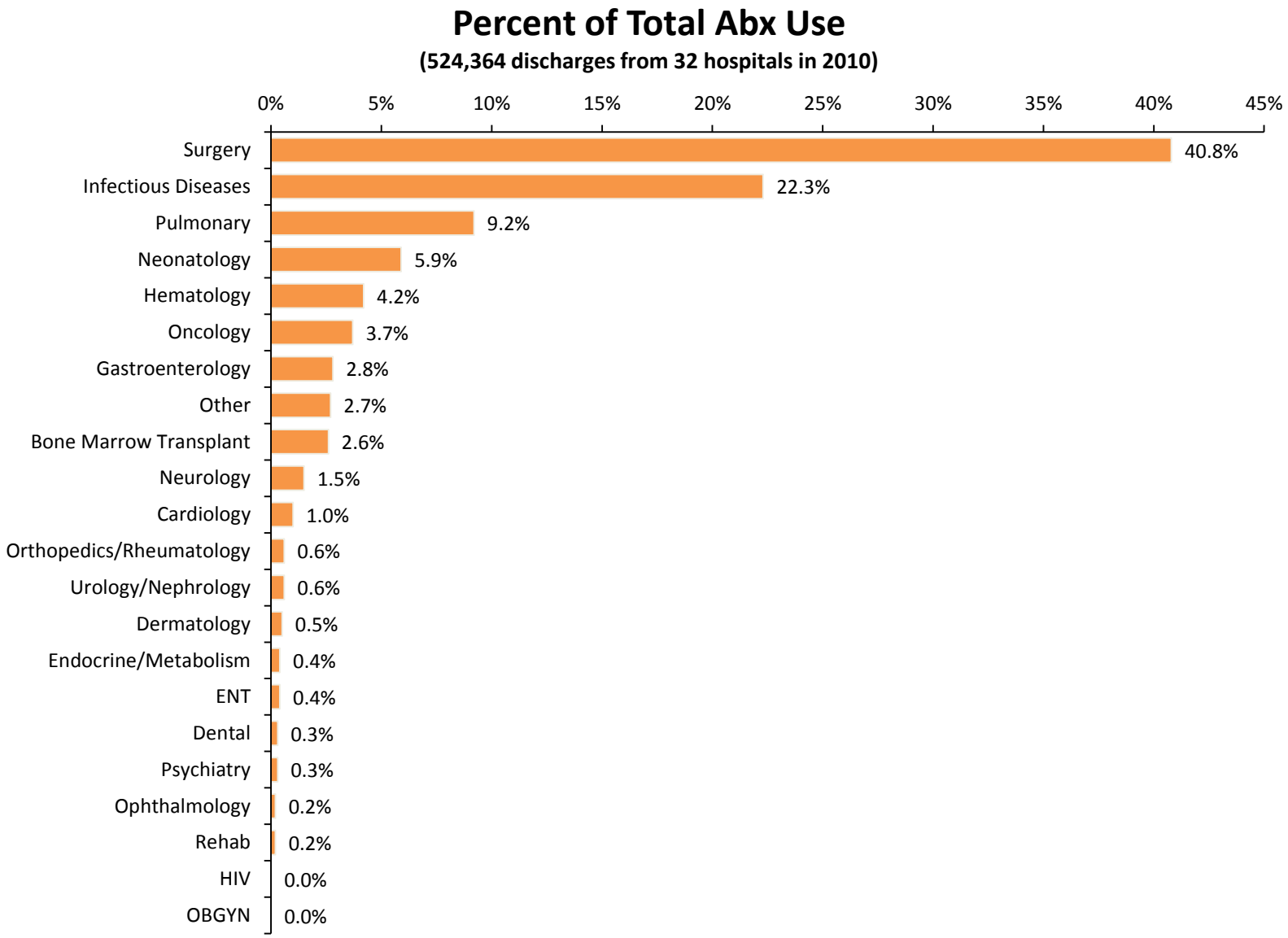


Each circle represents one hospital. Size of circles corresponds to number of discharges with diagnosis receiving antibiotics. Red lines represent median values.
Broad-spectrum anti-MRSA coverage: vancomycin, linezolid, tigecycline, daptomycin
Broad-spectrum anti-pseudomonal coverage: imipenem, meropenem, cefepime, piperacillin, ticarcillin, piperacillin-tazobactam, ticarcillin-clavulanate, ceftazidime

Agenda

- The case for Antimicrobial Stewardship
- The CHOP ASP
- Examples of Stewardship
  - Surgery: prophylaxis and treatment

Antibiotic Use at Children's Hospitals, by Service Line



Surgical Antimicrobial Prophylaxis

- surgical AMP is used to reduce the microbial burden of skin colonization that may contribute to intraoperative contamination = SSI
- **most common Healthcare Associated Infection (HAI)**
- SSIs cause harm, prolong hospitalizations, can cause readmissions, and can increases mortality rate
- **Prophylaxis; not treatment**

When appropriately used, AMP reduces SSI rate by 50-70%

Surgical Wound Classes

I. Clean: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered

II. Clean-Contaminated: Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination

III. Contaminated: Open, fresh, accidental wounds; operations with major breaks in sterile technique or gross spillage from GI tract, and incisions in which acute, nonpurulent inflammation is encountered

IV. Dirty or Infected: Includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera

Antimicrobial Prophylaxis: Timing

Goal is to have peak antibiotic serum/tissue levels at the time of incision.

Therefore, complete antibiotic infusion **0 - 60 minutes prior to incision**

- ✓ Start 0-60 minutes prior to incision for agents with brief infusion times
- ✓ Start 60-120 minutes prior to incision for vancomycin and fluoroquinolones

cal-wound infections in 2847 patients undergoing elective clean or "clean–contaminated" surgical procedures at a large community hospital. The administration of antibiotics 2 to 24 hours before the surgical incision was defined as early; that during the 2 hours before the incision, as preoperative; that during the 3 hours after the incision, as perioperative; and that more than 3 but less than 24 hours after the incision, as postoperative.

Results. Of the 1708 patients who received the prophylactic antibiotics preoperatively, 10 (0.6 percent) subsequently had surgical-wound infections. Of the 282 pa-

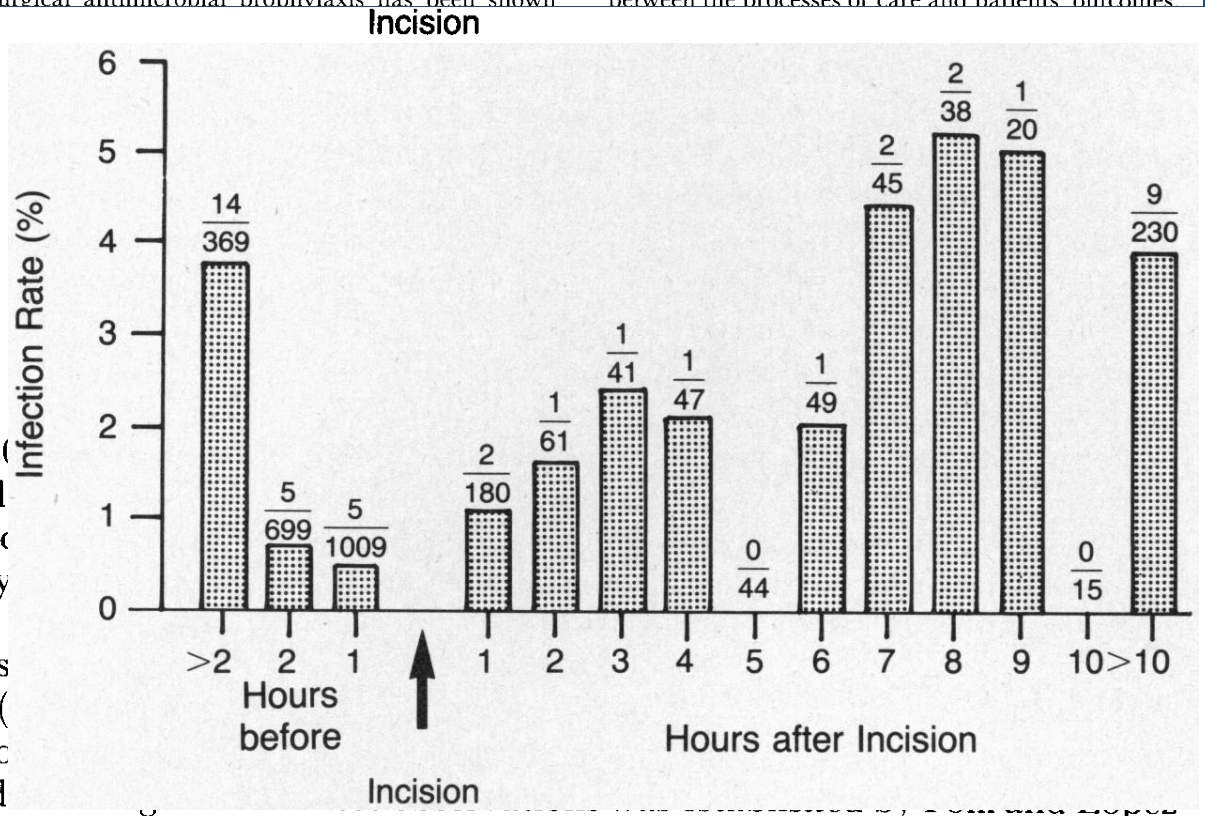
14 (3.8 percent) had wound infections ($P<0.0001$; relative risk, 6.7; 95 percent confidence interval, 2.9 to 14.7). Stepwise logistic-regression analysis confirmed that the administration of antibiotics in the preoperative period was associated with the lowest risk of surgical-wound infection.

Conclusions. In surgical practice there is considerable variation in the timing of the prophylactic administration of antibiotics, and administration in the two hours before surgery reduces the risk of wound infection. (N Engl J Med 1992;326:281-6.)

THE widespread use of antimicrobial agents for prophylaxis has altered surgical practice markedly in the past 20 years and now represents one of the most frequent uses of antibiotics in hospitals, accounting for as many as half of all antibiotics prescribed.[1-5] Surgical antimicrobial prophylaxis has been shown

variations in the timing of prophylaxis affect the occurrence of surgical-wound infections in actual clinical practice.

It is increasingly recognized that to assess the quality of care, investigators must examine the linkage between the processes of care and patients' outcomes



71 through 75

he odds ratios

Mayor in a study of perioperative and postoperative administration of cephaloridine in which there was a

Antimicrobial Choice

Staphylococcus aureus is most common cause of SSI

Cefazolin has activity against most strains of *S. aureus*; therefore, Cefazolin is the empiric choice for most procedures

However, Cefazolin may not always be the appropriate choice…

1. procedures involving organs with alternate or additional colonizing bacteria (e.g. GI tract)
2. patients with cephalosporin allergy
3. patients known to be colonized with resistant bacteria

Antimicrobial Selection: **Using CHOP Guidelines**

1) **procedures involving organs with alternate or additional colonizing bacteria**

Antibiotic Prophylaxis by Surgical Procedure

Table 1

Surgery	Antibiotic	Alternative for Penicillin and/or Cephalosporin allergy	MRSA History of colonization or infection
Cardiothoracic			
General	cefazolin	clindamycin	vancomycin[1] + cefazolin
High-risk implants (pacemaker, ICD, L-VAD)	vancomycin + cefazolin	vancomycin + gentamicin	vancomycin[1]+ cefazolin
Lung transplant	targeted therapy[2]	targeted therapy[2]	vancomycin[1]+ targeted therapy[2]
Gastrointestinal			
Appendectomy[3]	ceftriaxone + metronidazole	ciprofloxacin + metronidazole	vancomycin[1] + ceftriaxone + metronidazole
Esophageal, gastroduodenal, jejunal	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Colorectal[3]	ceftriaxone and metronidazole	ciprofloxacin + metronidazole	vancomycin[1]+ ceftriaxone + metronidazole
Liver transplant	piperacillin/tazobactam	ciprofloxacin + metronidazole	vancomycin[1] + piperacillin/tazobactam
NEC	piperacillin/tazobactam	none	vancomycin[1] + piperacillin/tazobactam
Biliary tract			
Open and laparoscopic procedures	cefazolin	clindamycin + gentamicin	vancomycin[1]+ cefazolin
Head and Neck			
Clean	none	none	none
With implant	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Clean-contaminated	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Obstetric or Gynecologic			
Cesarean section	cefazolin or cefoxitin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Orthopedic			
General	cefazolin	clindamycin	vancomycin[1]+ cefazolin
High-risk implants (spinal rods, VEPTR)	vancomycin + cefazolin (+/- gentamicin) [4]	vancomycin + gentamicin	Vancomycin[1]+ cefazolin (+/- gentamicin) [4]
Neurosurgery			
	cefazolin	vancomycin	vancomycin[1] + cefazolin
Urologic			
General	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Cystourethroscopy	targeted therapy[5]	targeted therapy[5]	vancomycin[1] + targeted therapy[5]

Antimicrobial Selection: **Using CHOP Guidelines**

1) procedures involving organs with alternate or additional colonizing bacteria

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Antimicrobial Selection: **Using CHOP Guidelines**

1) procedures involving organs with alternate or additional colonizing bacteria
2) patients with cephalosporin allergy
3) colonization with resistant bacteria
   - ✧ **specific procedures**
   - ✧ MRSA colonization

Antibiotic Prophylaxis by Surgical Procedure
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Gastrointestinal			
Appendectomy[3]	ceftriaxone + metronidazole	ciprofloxacin + metronidazole	vancomycin[1] + ceftriaxone + metronidazole
Esophageal, gastroduodenal, jejunal	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Colorectal[3]	ceftriaxone and metronidazole	ciprofloxacin + metronidazole	vancomycin[1]+ ceftriaxone + metronidazole
Liver transplant	piperacillin/tazobactam	ciprofloxacin + metronidazole	vancomycin[1] + piperacillin/tazobactam
NEC	piperacillin/tazobactam	none	vancomycin[1] + piperacillin/tazobactam
Biliary tract			
Open and laparoscopic procedures	cefazolin	clindamycin + gentamicin	vancomycin[1]+ cefazolin
Head and Neck			
Clean	none	none	none
With implant	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Clean-contaminated	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Obstetric or Gynecologic			
Cesarean section	cefazolin or cefoxitin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Orthopedic			
General	cefazolin	clindamycin	vancomycin[1]+ cefazolin
High-risk implants (spinal rods, VEPTR)	vancomycin + cefazolin (+/- gentamicin)[4]	vancomycin + gentamicin	Vancomycin[1]+ cefazolin (+/- gentamicin)[4]
Neurosurgery			
	cefazolin	vancomycin	vancomycin[1] + cefazolin
Urologic			
General	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Cystourethroscopy	targeted therapy[5]	targeted therapy[5]	vancomycin[1] + targeted therapy[5]

Antimicrobial Selection: **Using CHOP Guidelines**

1) procedures involving organs with alternate or additional colonizing bacteria
2) patients with cephalosporin allergy
3) colonization with resistant bacteria
   - ✧specific procedures
   - ✧**MRSA colonization**

Antibiotic Prophylaxis by Surgical Procedure
Table 1

Surgery	Antibiotic	Alternative for Penicillin and/or Cephalosporin allergy	MRSA History of colonization or infection
Cardiothoracic			
General	cefazolin	clindamycin	vancomycin[1] + cefazolin
High-risk implants (pacemaker, ICD, L-VAD)	vancomycin + cefazolin	vancomycin + gentamicin	vancomycin[1]+ cefazolin
Lung transplant	targeted therapy[2]	targeted therapy[2]	vancomycin[1]+ targeted therapy[2]
Gastrointestinal			
Appendectomy[3]	ceftriaxone + metronidazole	ciprofloxacin + metronidazole	vancomycin[1] + ceftriaxone + metronidazole
Esophageal, gastroduodenal, jejunal	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Colorectal[3]	ceftriaxone and metronidazole	ciprofloxacin + metronidazole	vancomycin[1]+ ceftriaxone + metronidazole
Liver transplant	piperacillin/tazobactam	ciprofloxacin + metronidazole	vancomycin[1] + piperacillin/tazobactam
NEC	piperacillin/tazobactam	none	vancomycin[1] + piperacillin/tazobactam
Biliary tract			
Open and laparoscopic procedures	cefazolin	clindamycin + gentamicin	vancomycin[1]+ cefazolin
Head and Neck			
Clean	none	none	none
With implant	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Clean-contaminated	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Obstetric or Gynecologic			
Cesarean section	cefazolin or cefoxitin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Orthopedic			
General	cefazolin	clindamycin	vancomycin[1]+ cefazolin
High-risk implants (spinal rods, VEPTR)	vancomycin + cefazolin (+/- gentamicin) [4]	vancomycin + gentamicin	Vancomycin[1]+ cefazolin (+/- gentamicin) [4]
Neurosurgery			
	cefazolin	vancomycin	vancomycin[1] + cefazolin
Urologic			
General	cefazolin	clindamycin + gentamicin	vancomycin[1] + cefazolin
Cystourethroscopy	targeted therapy[5]	targeted therapy[5]	vancomycin[1] + targeted therapy[5]

ASHP REPORT

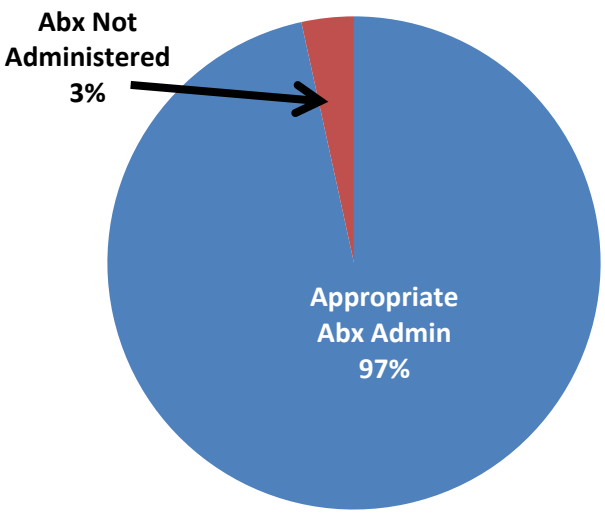
Clinical practice guidelines for antimicrobial prophylaxis in surgery

DALE W. BRATZLER, E. PATCHEN DELLINGER, KEITH M. OLSEN, TRISH M. PERL, PAUL G. AUWAERTER, MAUREEN K. BOLON, DOUGLAS N. FISH, LENA M. NAPOLITANO, ROBERT G. SAWYER, DOUGLAS SLAIN, JAMES P. STEINBERG, AND ROBERT A. WEINSTEIN

Am J Health-Syst Pharm. 2013; 70:195-283

How do we do at CHOP?

Orhtopedic Surgery
n=175 for antibiotics



Cardiac Surgery
n = 48 for antibiotic

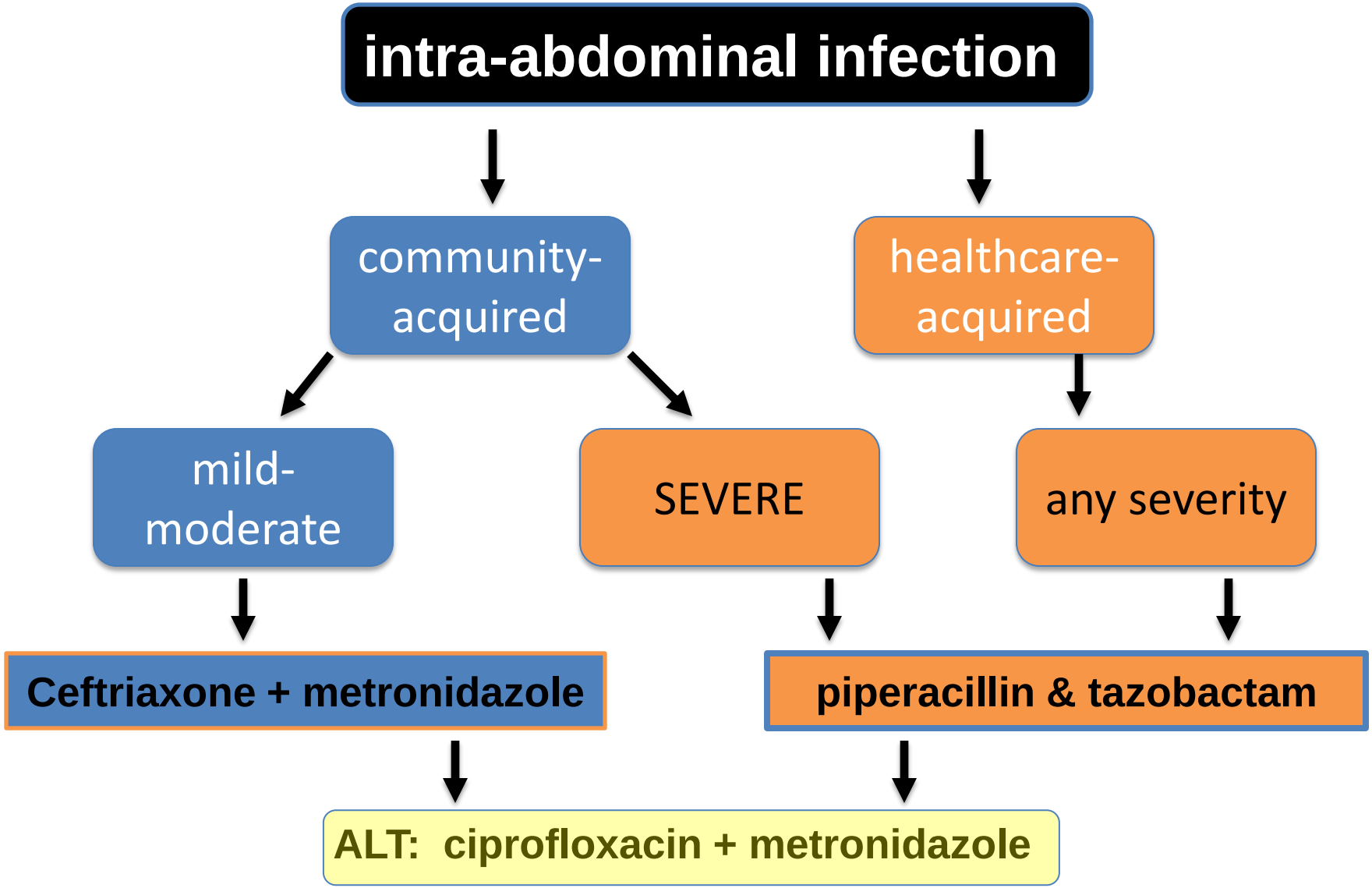
Intra-abdominal Infections

Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America

Joseph S. Solomkin,[1] John E. Mazuski,[2] John S. Bradley,[3] Keith A. Rodvold,[7,8] Ellie J. C. Goldstein,[5] Ellen J. Baron,[6] Patrick J. O'Neill,[9] Anthony W. Chow,[16] E. Patchen Dellinger,[10] Soumitra R. Eachempati,[11] Sherwood Gorbach,[12] Mary Hilfiker,[4] Addison K. May,[13] Avery B. Nathens,[17] Robert G. Sawyer,[14] and John G. Bartlett[15]

Clinical Infectious Diseases 2010; 50:133–64

Intra-abdominal Infections



Intra-abdominal Infections: duration

- antimicrobial tx of established infection should be **limited to 4–7 days**, unless difficult to achieve adequate source control

Intra-abdominal Infections: prophylaxis

- acute appendicitis without evidence of perforation, abscess, or local peritonitis requires only prophylactic administration of narrow spectrum regimens; **treatment should be discontinued within 24h**

Agenda

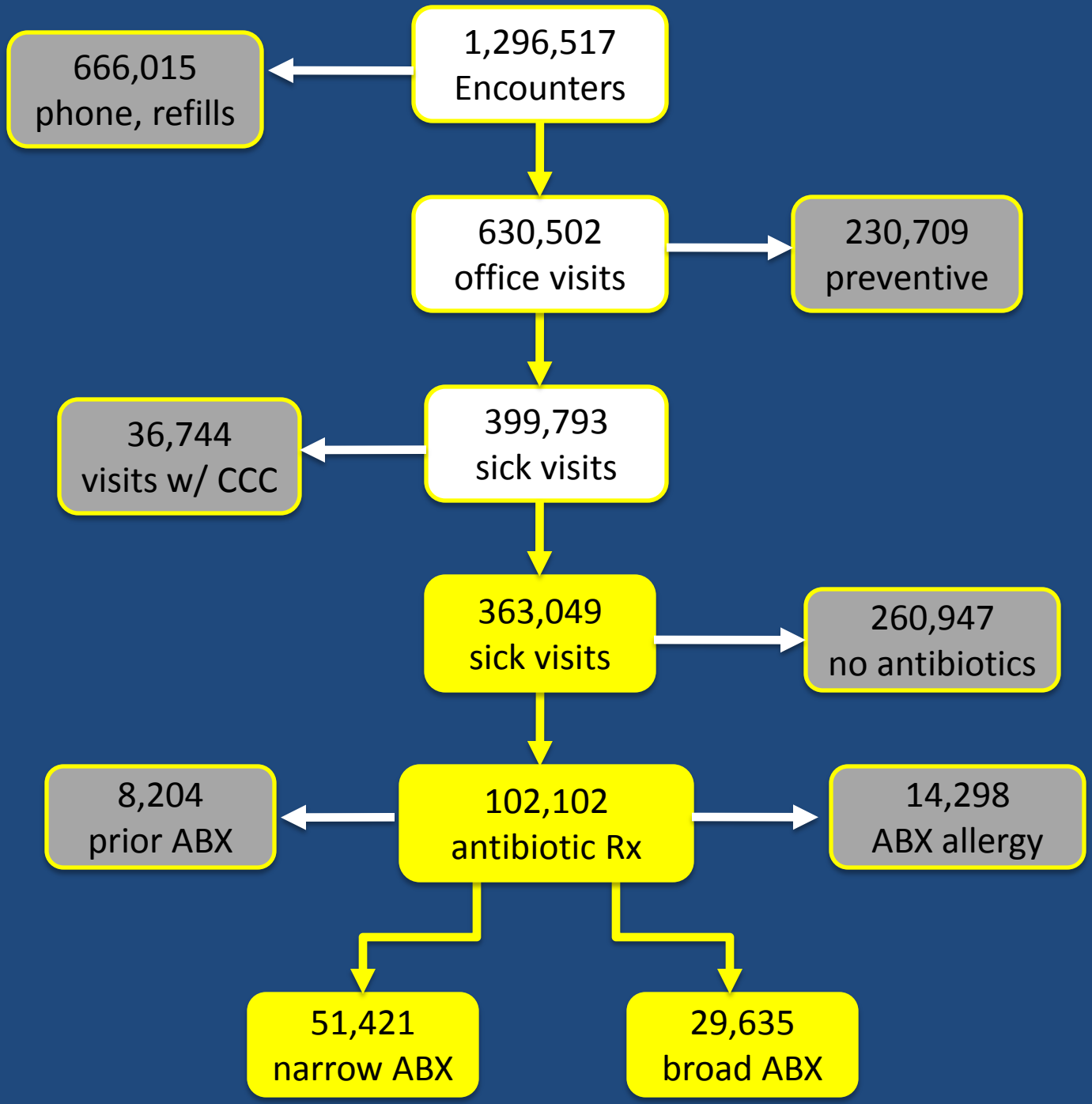
- The case for Antimicrobial Stewardship
- The CHOP ASP
- Examples of Stewardship
  - Surgery
  - Primary care

Study Setting: CHOP Care Network

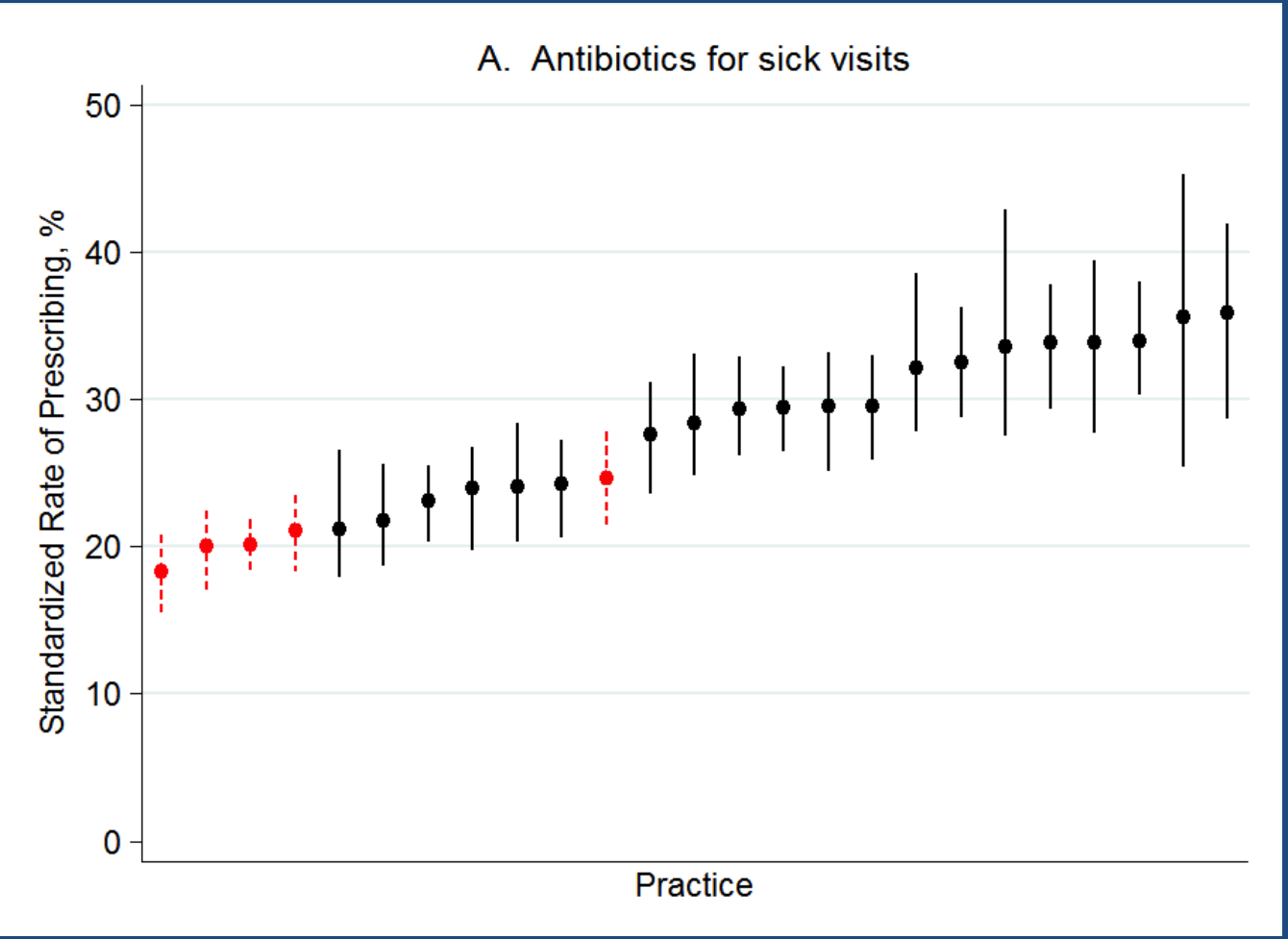
- 5 urban, academic
- 24 "private" practices
  - urban, suburban, rural
  - >200 clinicians
  - >200,000 patients
- common EHR

Case Definitions

- ICD9 codes for common infections
  - AOM, sinusitis, strep throat, pneumonia
  - (+/- GAS testing, antibiotic use)
- Excluding:
  - concurrent bacterial infection
    - AOM, SSTI, UTI, lyme, acne, chronic sinusitis, mycoplasma, scarlet fever, animal bite, proph, oral infections, pertussis, STD, bone/joint
  - complex chronic conditions (Feudtner, *Pediatrics* 2000)
  - antibiotic allergy
  - visit within prior 3 months with antibiotic


1,296,517
Encounters
666,015
phone, refills
630,502
office visits
230,709
preventive
399,793
sick visits
36,744
visits w/ CCC
363,049
sick visits
260,947
no antibiotics
102,102
antibiotic Rx
8,204
prior ABX
14,298
ABX allergy
51,421
narrow ABX
29,635
broad ABX

Antibiotic Prescribing for Sick Visits



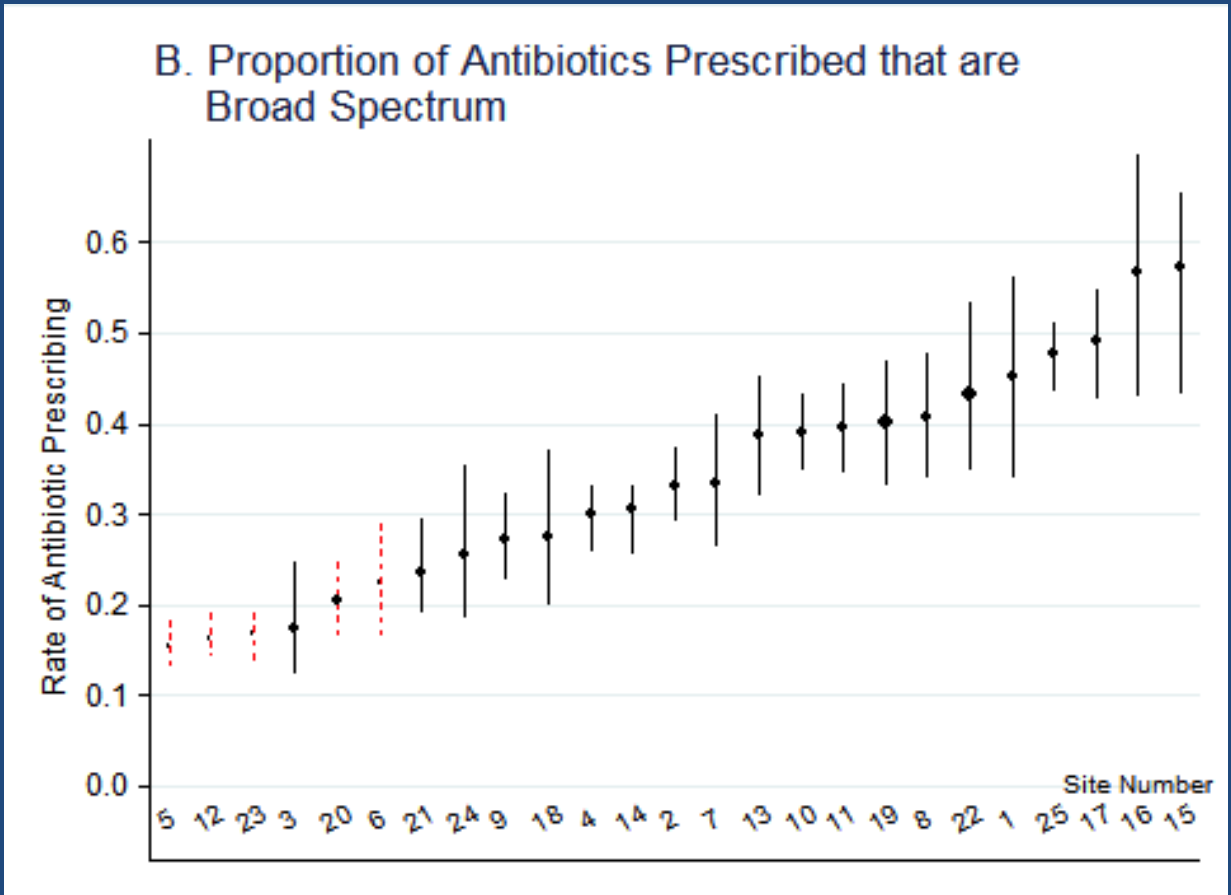
Excluding: preventive visits, CCC
Standardized by: age, sex, race, Medicaid

Broad-Spectrum Antibiotics

- amoxicillin-clavulanate
- cephalosporins
- azithromycin*

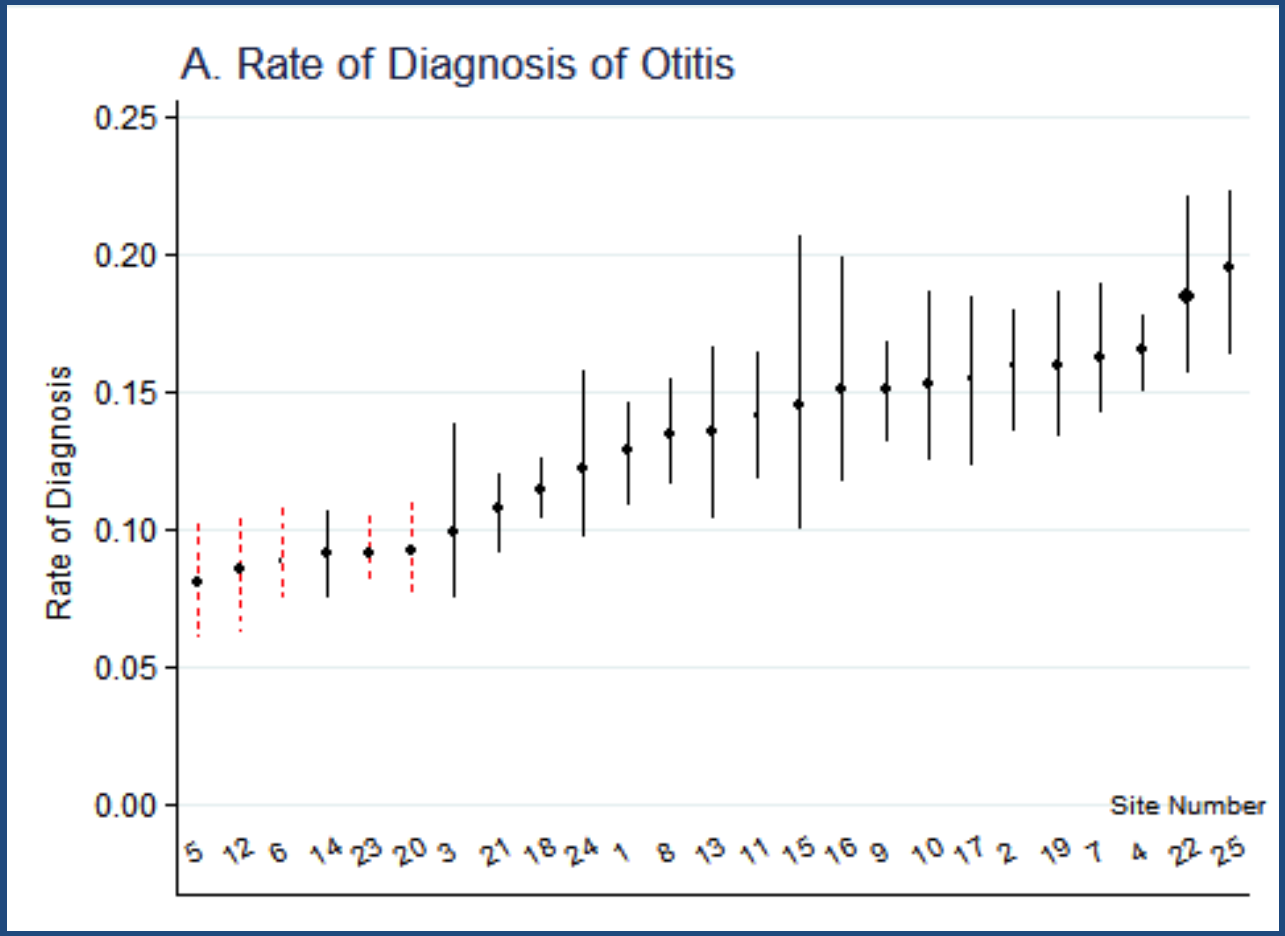
*not considered broad-spectrum therapy for pneumonia

Broad Antibiotic Prescribing



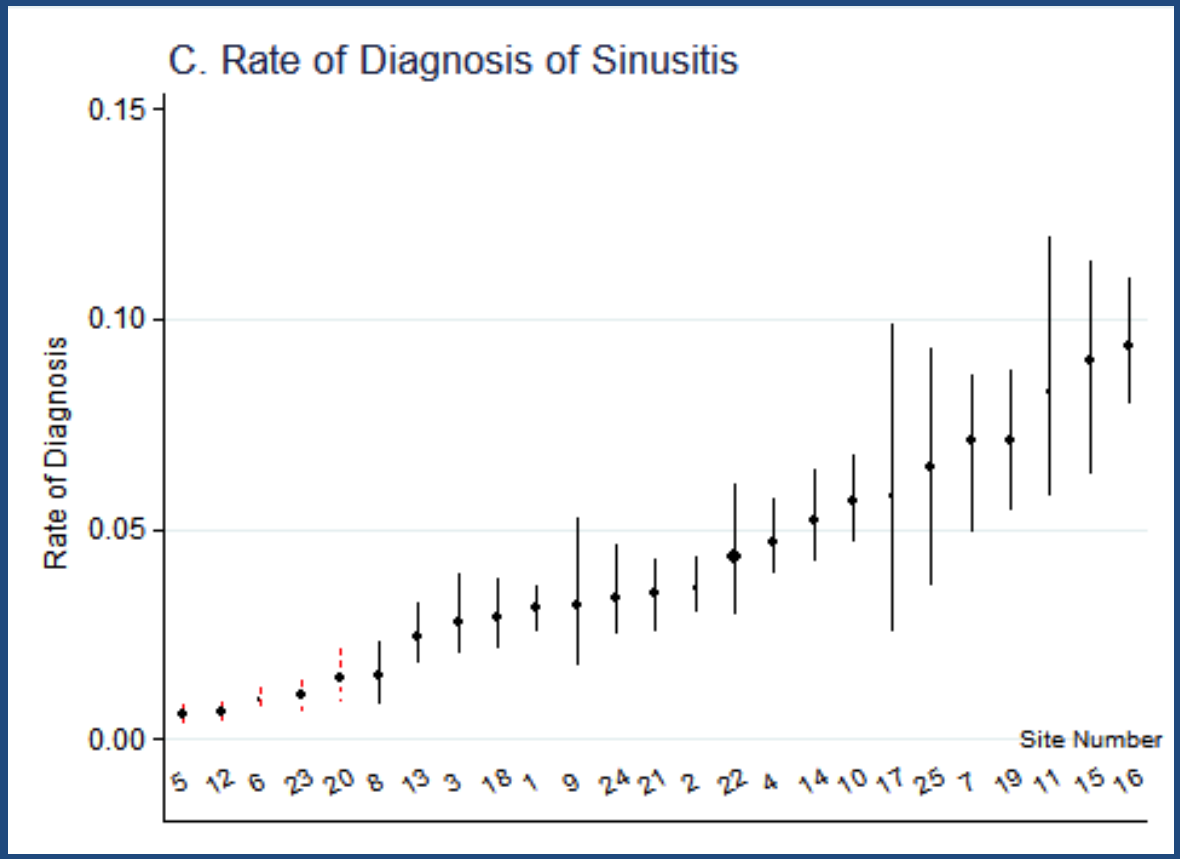
Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics
Standardized by: age, sex, race, Medicaid

Diagnosis rate of AOM



Excluding: preventive visits, CCC, prior antibiotics
Standardized by: age, sex, race, Medicaid

Diagnosis Rate of Sinusitis



Excluding: preventive visits, CCC, prior antibiotics
Standardized by: age, sex, race, Medicaid

Summary of Across-Practice Analyses

- antibiotic prescribing at sick visits varies significantly across practice sites
- broad-spectrum antibiotic prescribing at sick visits varies significantly across practice sites
- the rate of diagnosis of ARTIs varies significantly across practice sites
- adherence to prescribing guidelines for AOM, sinusitis, GAS pharyngitis, and pneumonia varies significantly across practice sites

Antimicrobial Stewardship

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

- Antimicrobial Stewardship Programs recommended for hospitals
- most antibiotic use (and misuse) occurs in the outpatient setting
- is outpatient “stewardship” achievable?

Specific Aim

- To determine the impact of an outpatient antimicrobial stewardship bundle within a pediatric primary care network on antibiotic prescribing for common ARTI:

1. Antibiotic prescribing for viral infections

1. Broad-spectrum antibiotic prescribing for conditions for which narrow-spectrum antibiotics are indicated

Antimicrobial Stewardship

- Core strategies
  - Prior authorization
  - Prospective audit & feedback
  - Formulary restriction
- Supplemental Strategies
  - Education
  - Clinical guidelines
  - IV to PO conversion
  - Dose optimization
  - Antimicrobial order forms

Antimicrobial Stewardship

- Core strategies
  - Prior authorization
  - **Prospective audit & feedback**
  - Formulary restriction
- Supplemental Strategies
  - **Education**
  - **Clinical guidelines**
  - IV to PO conversion
  - Dose optimization
  - Antimicrobial order forms

Study Design

- cluster-randomized controlled trial
- bundled intervention vs. no intervention
- unit of observation will be the practitioner but randomized at practice level
  - natural distribution of physicians
  - avoids intra-practice contamination

Intervention

1. guideline development
2. education
3. audit and feedback

Hypotheses

1. clinicians have incomplete knowledge of the data regarding the effectiveness of antibiotics for ARTIs
   - GAS and broad spectrum antibiotics
   - antibiotic activity against pneumococcus
   - prevention of bacterial superinfection
   - role of *moraxella* and *Hflu* in disease

2. clinicians might be influenced by presentation of their prescribing habits relative to peer benchmarking data

Study Setting: CHOP Care Network

- 5 urban, academic
- 24 non-academic practices
- common EHR

Outcomes

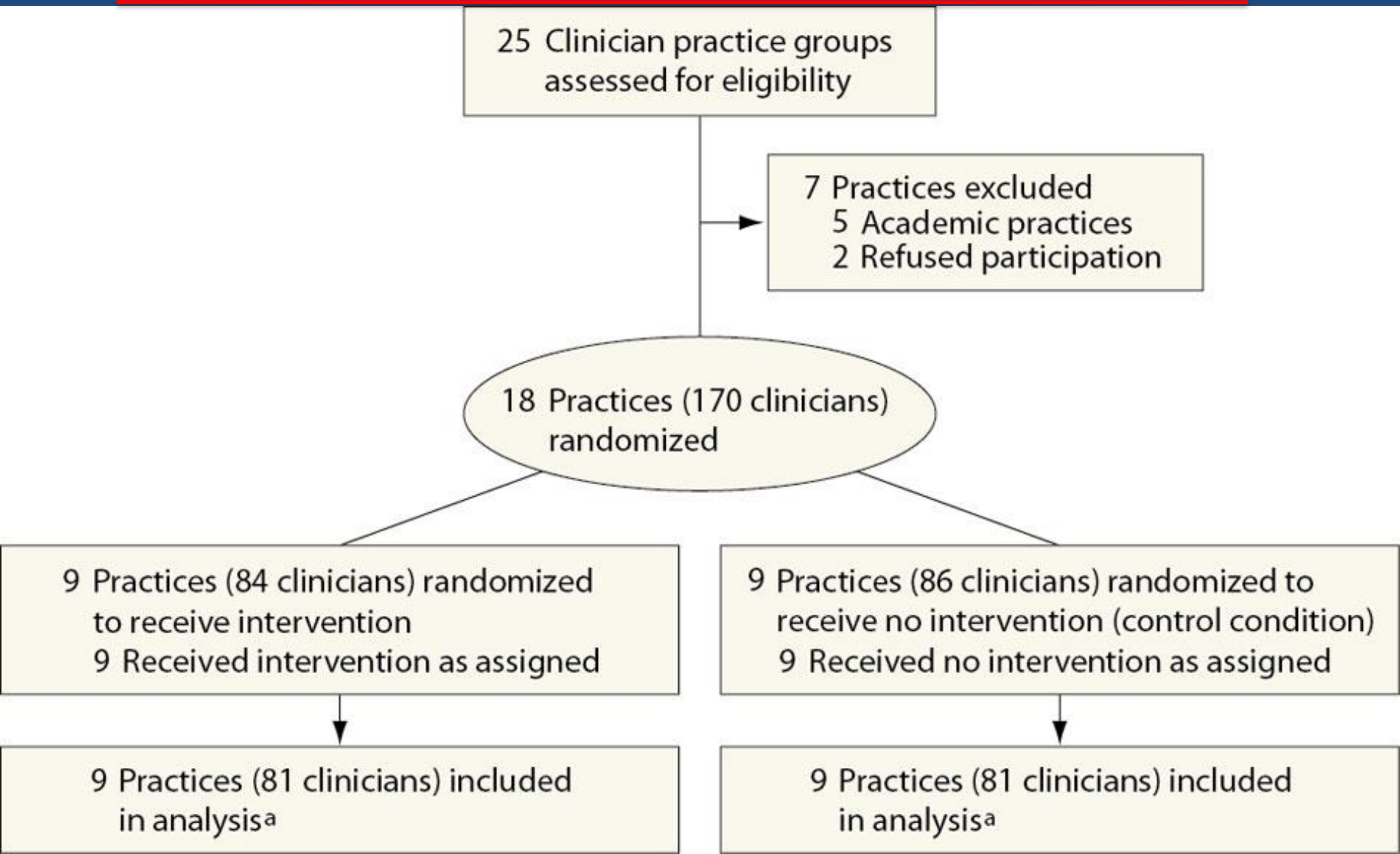
VIRAL
common cold
URI
acute bronchitis
tonsillitis
pharyngitis (non-strep)

no antibiotics

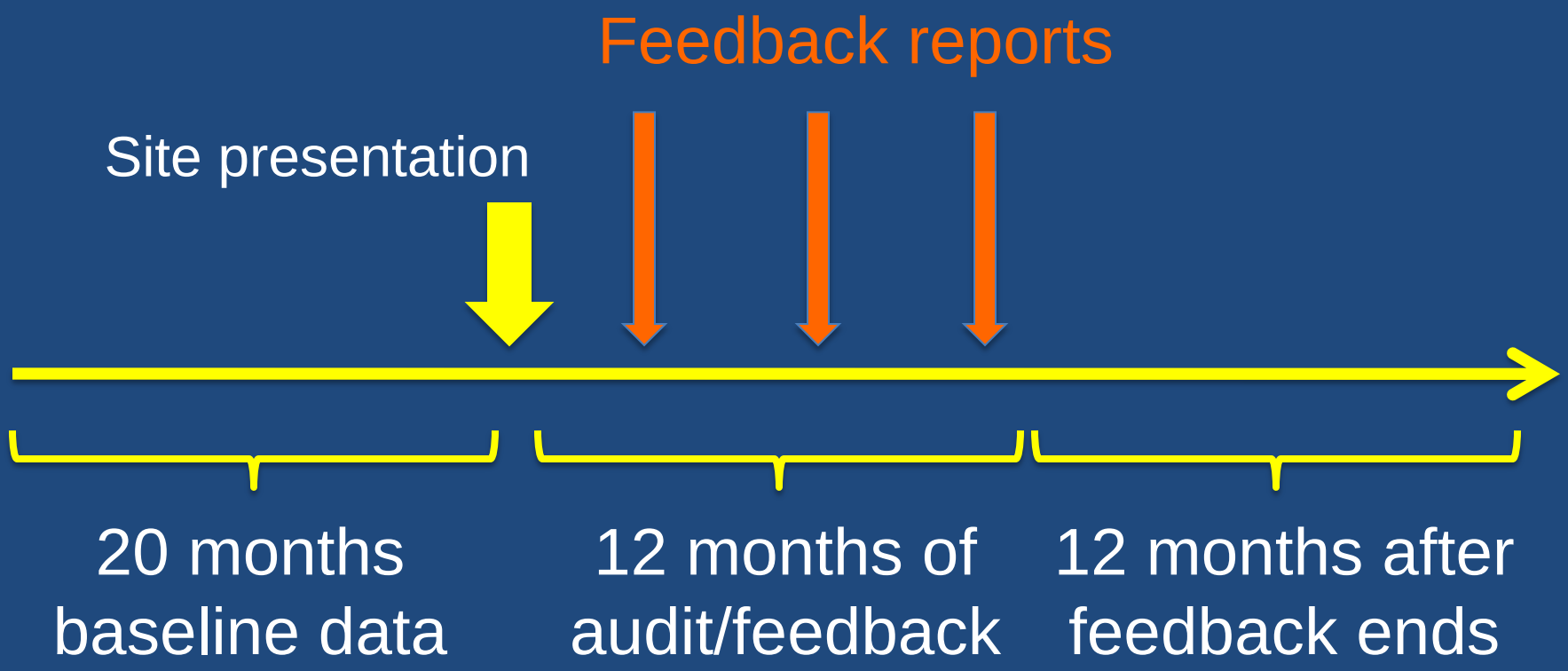
BACTERIAL
acute sinusitis
Strep pharyngitis
pneumonia

penicillin/amoxicillin

Randomization

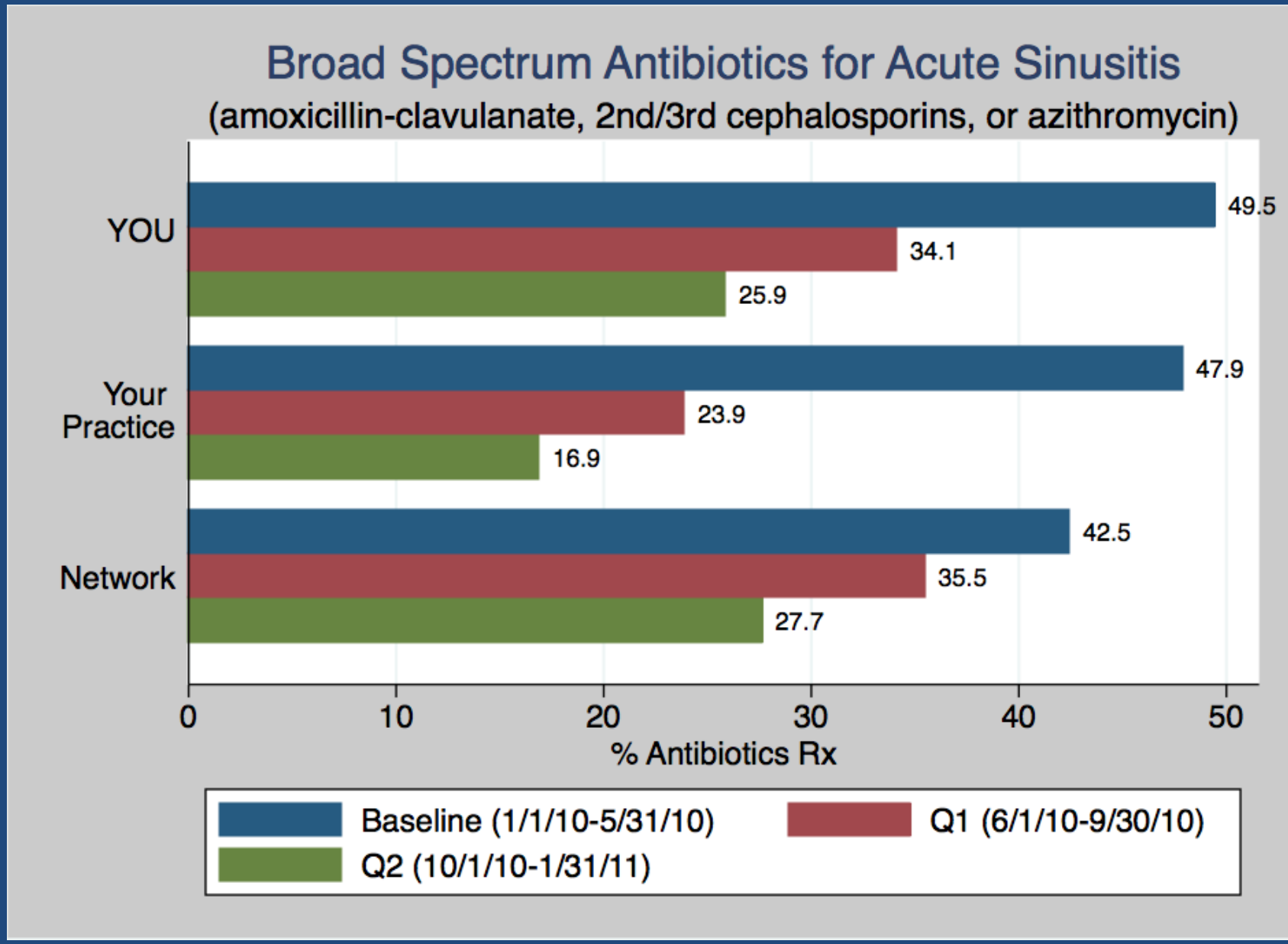


Intervention: Timeline

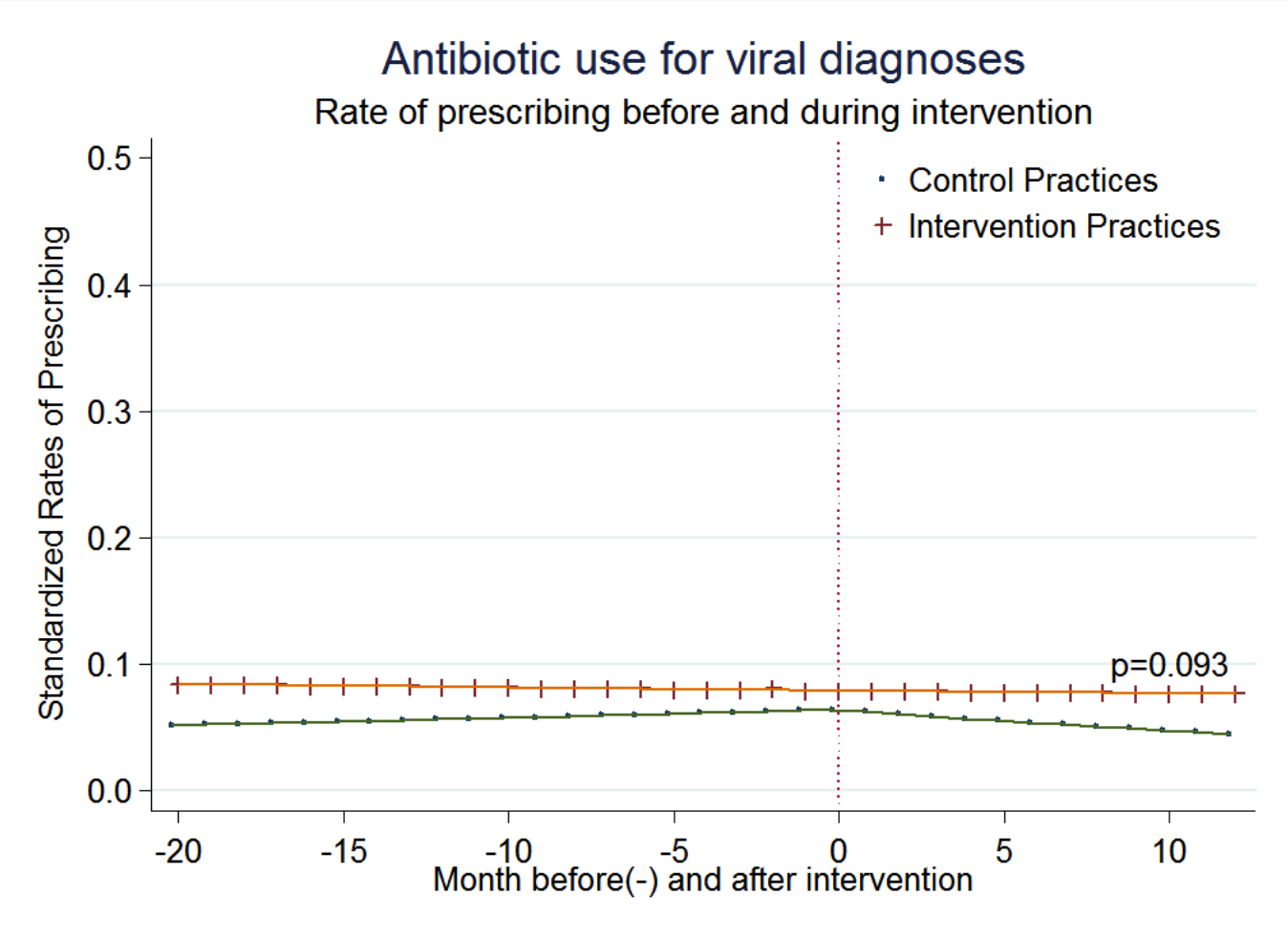


Over 32 month study period (so far):

- 185,212 patients
- 1,435,605 encounters


Broad Spectrum Antibiotics for Acute Sinusitis
(amoxicillin-clavulanate, 2nd/3rd cephalosporins, or azithromycin)
YOU
Your Practice
Network
49.5
34.1
25.9
47.9
23.9
16.9
42.5
35.5
27.7
0
10
20
30
40
50
% Antibiotics Rx
Baseline (1/1/10-5/31/10)
Q1 (6/1/10-9/30/10)
Q2 (10/1/10-1/31/11)

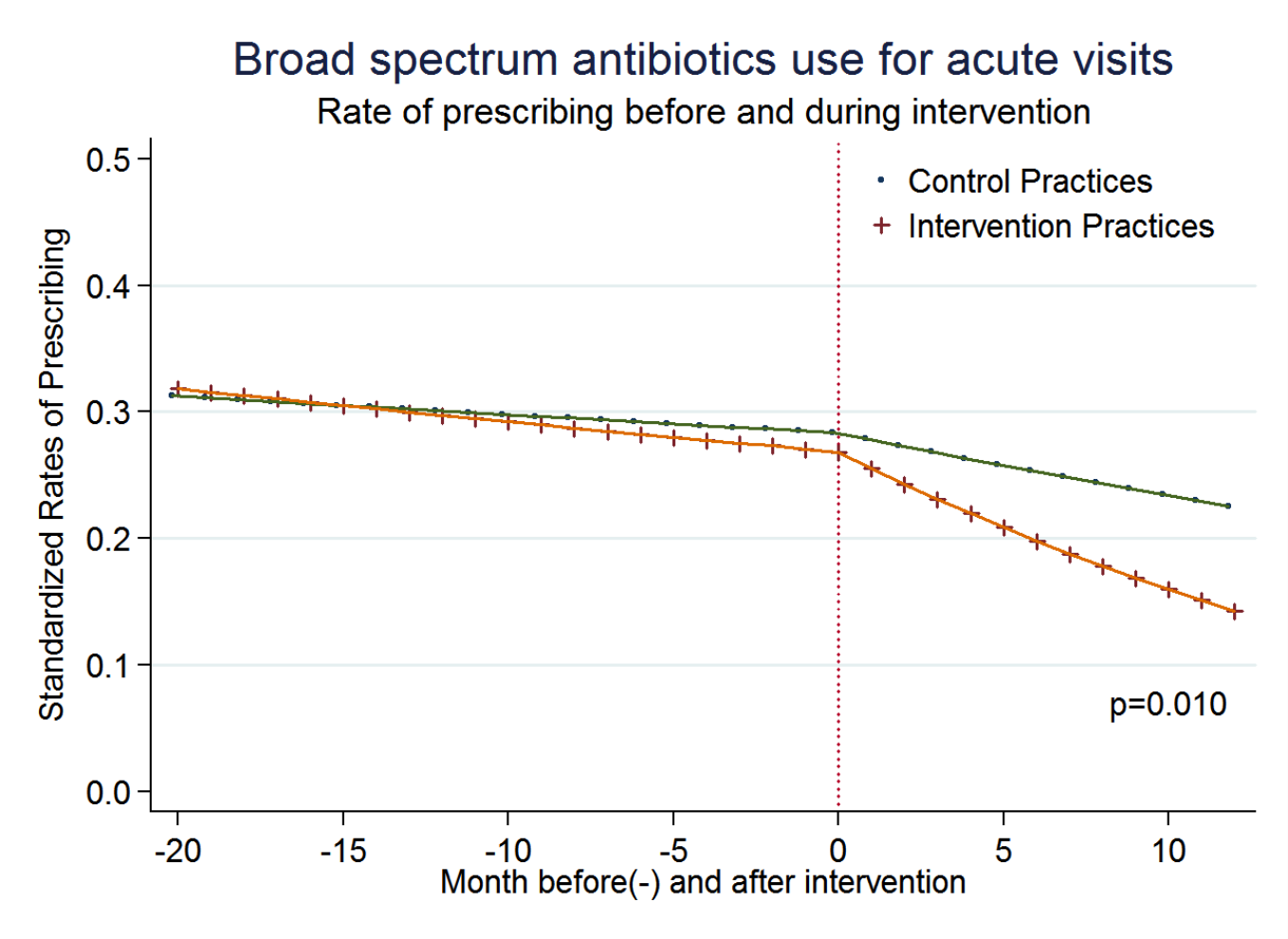
Antibiotics for Viral Infection



Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics

Standardized by: age, sex, race, Medicaid

Broad-Spectrum per Sick Visit

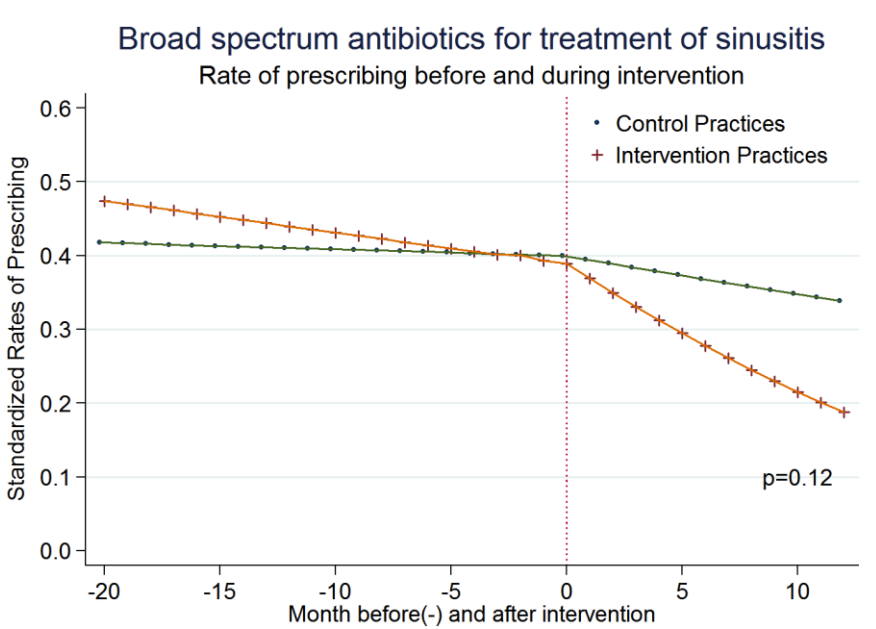


Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics

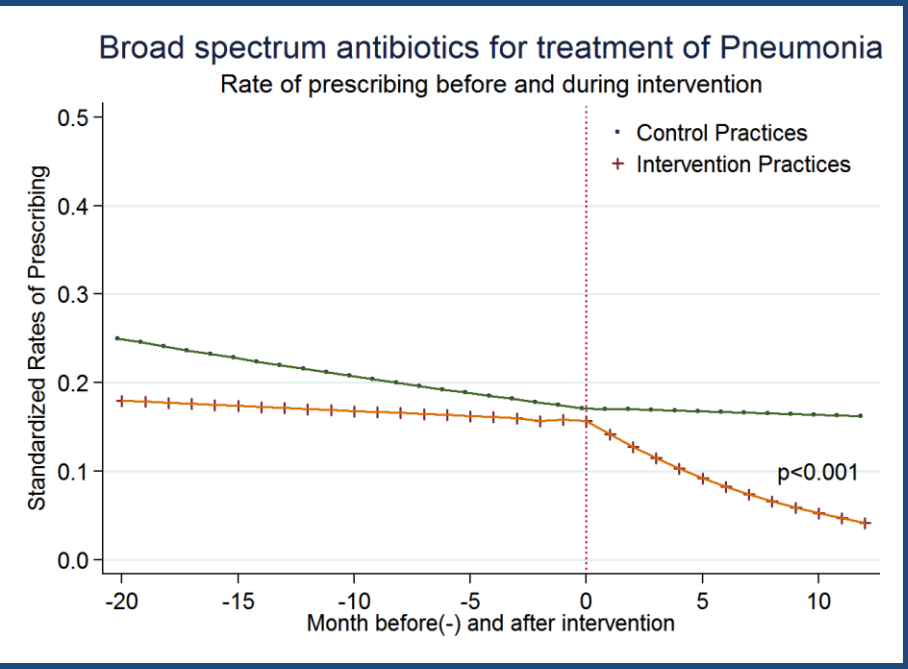
Standardized by: age, sex, race, Medicaid

Broad-Spectrum: by condition

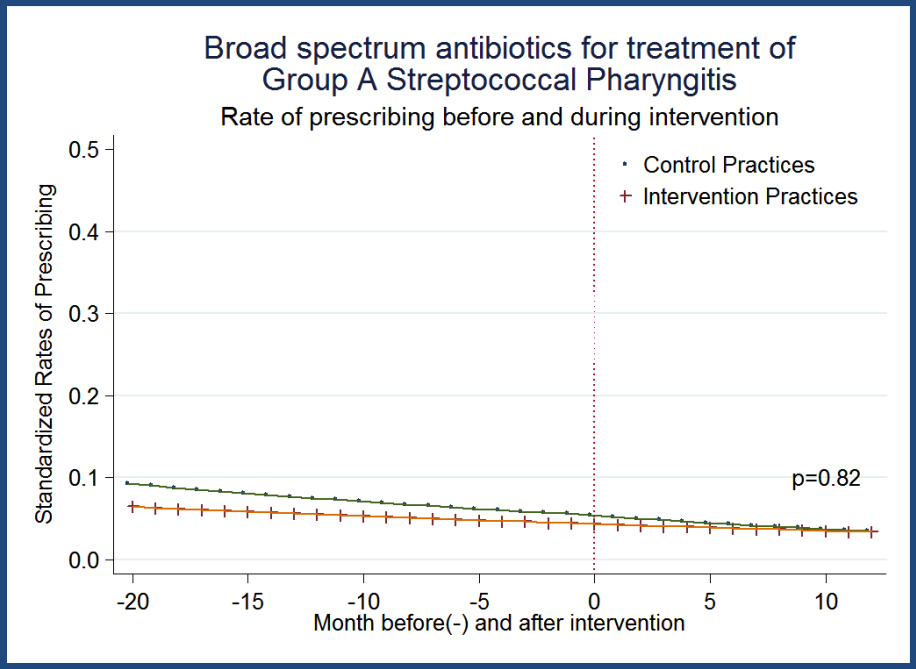
SINUSITIS →



PNEUMONIA



GAS PHARYNGITIS



Summary/Future Directions

- clinician education coupled with audit & feedback significantly improved guideline adherence for the treatment of common ARTI
- this was most pronounced for pneumonia
- need to measure outcomes

Why did it work?
Can we do better?

Qualitative Analyses

- semi-structured interviews of 21 clinicians in the intervention group
- 6/21 ignored or did not remember reports
- 9/15 reported considerable skepticism and distrust of auditing data
- most did not believe that their prescribing behavior contributed to antibiotic overuse

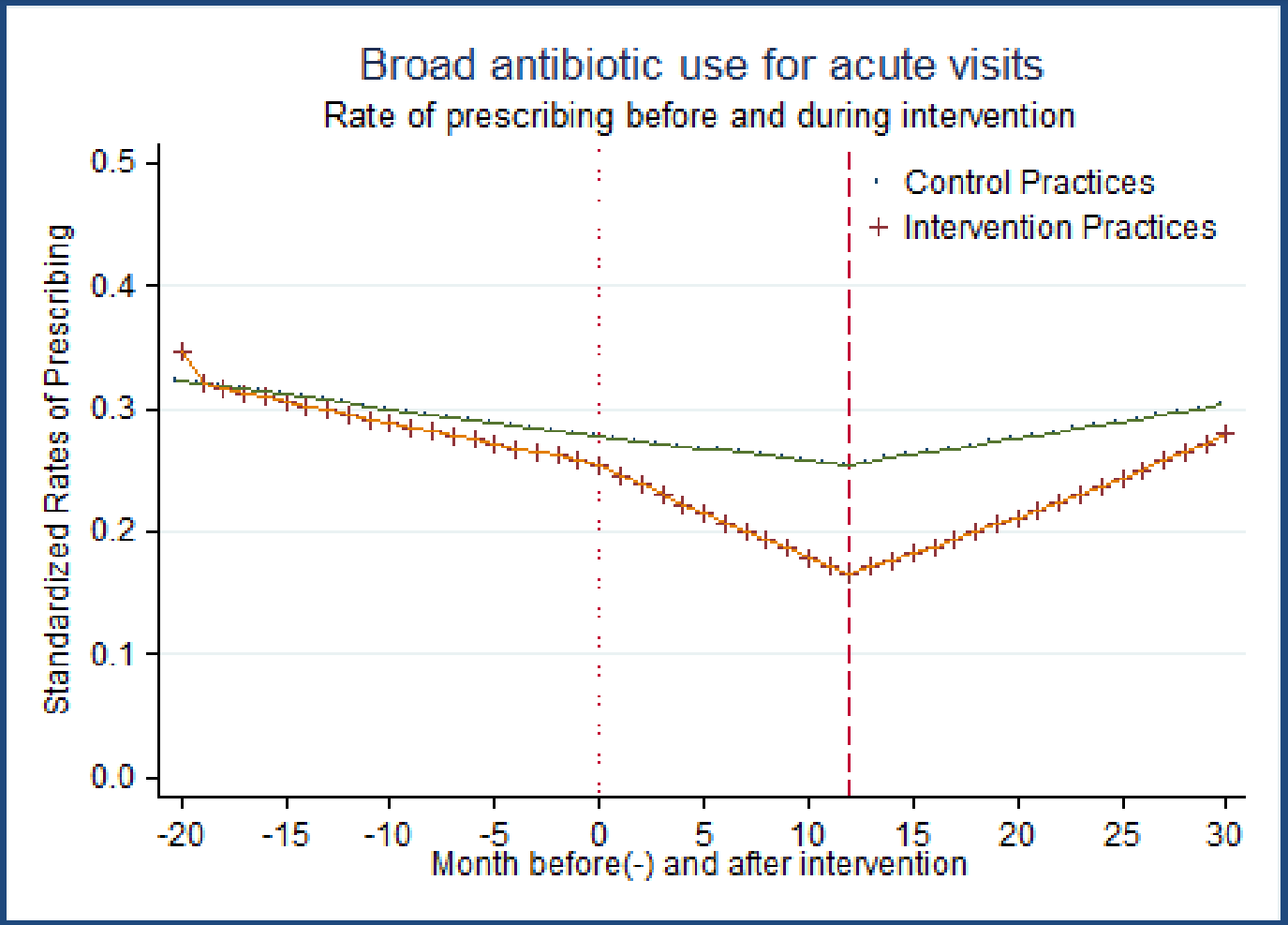
“I did not read my audit reports because honestly, I didn’t really care. To me, it was just another piece of paper. It didn’t impress me at all. They [the study team] gave you a number describing your behavior but they had no deeper understanding of what was really going on.”

Qualitative Analyses

- reported frequently confronting parental pressure, sometimes acquiescing to:
  - appear competent
  - avoid losing patients to other practices that would “give them what they want”
  - provide comfort to anxious parents
  - help with upcoming travel, family celebrations, parent work schedules

“We have lots of parents who come in and they know what they want. They don’t care what we have to say. They want the antibiotic that they want because they know what is wrong with their child.”

Broad-Spectrum Prescribing



Excluding: preventive visits, CCC, antibiotic allergy, prior antibiotics
Standardized by: age, sex, race, Medicaid

Study Team

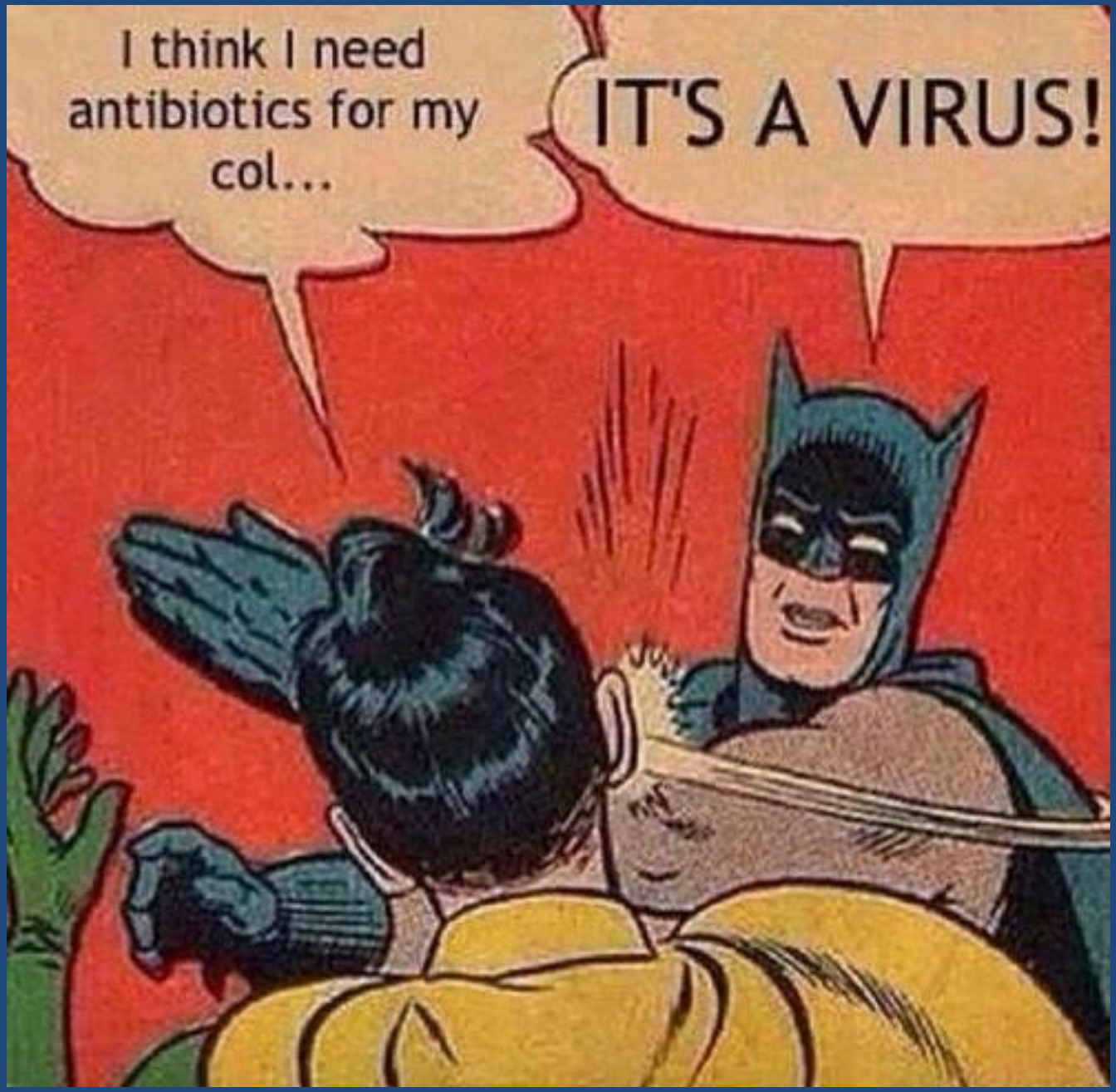
The Children's Hospital of Philadelphia® RESEARCH INSTITUTE

Perelman School of Medicine University of Pennsylvania

CPCE The Center for Pediatric Clinical Effectiveness

- Primary Care Pediatrics
  Bob Grundmeier, Alex Fiks, Mort Wasserman
- General Pediatrics
  Lou Bell, Ron Keren
- Pediatric Infectious Diseases
  Theo Zaoutis, Priya Prasad
- Biostatistics/data management
  Russell Localio, Lihai Song
- PeRC Administrator
  Jim Massey
- Sociology
  Julie Szymczak

*supported by US Agency for Health Care Research and Quality


I think I need antibiotics for my col...
IT'S A VIRUS!