

OUTPATIENT ANTIMICROBIAL STEWARDSHIP: INTERVENTIONS THAT WORK

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LEARNING OBJECTIVES

- Justify the rationale for outpatient antimicrobial stewardship
- Appraise the effectiveness of outpatient antimicrobial stewardship interventions
- Recognize some novel stewardship strategies

WHY OUTPATIENT STEWARDSHIP?

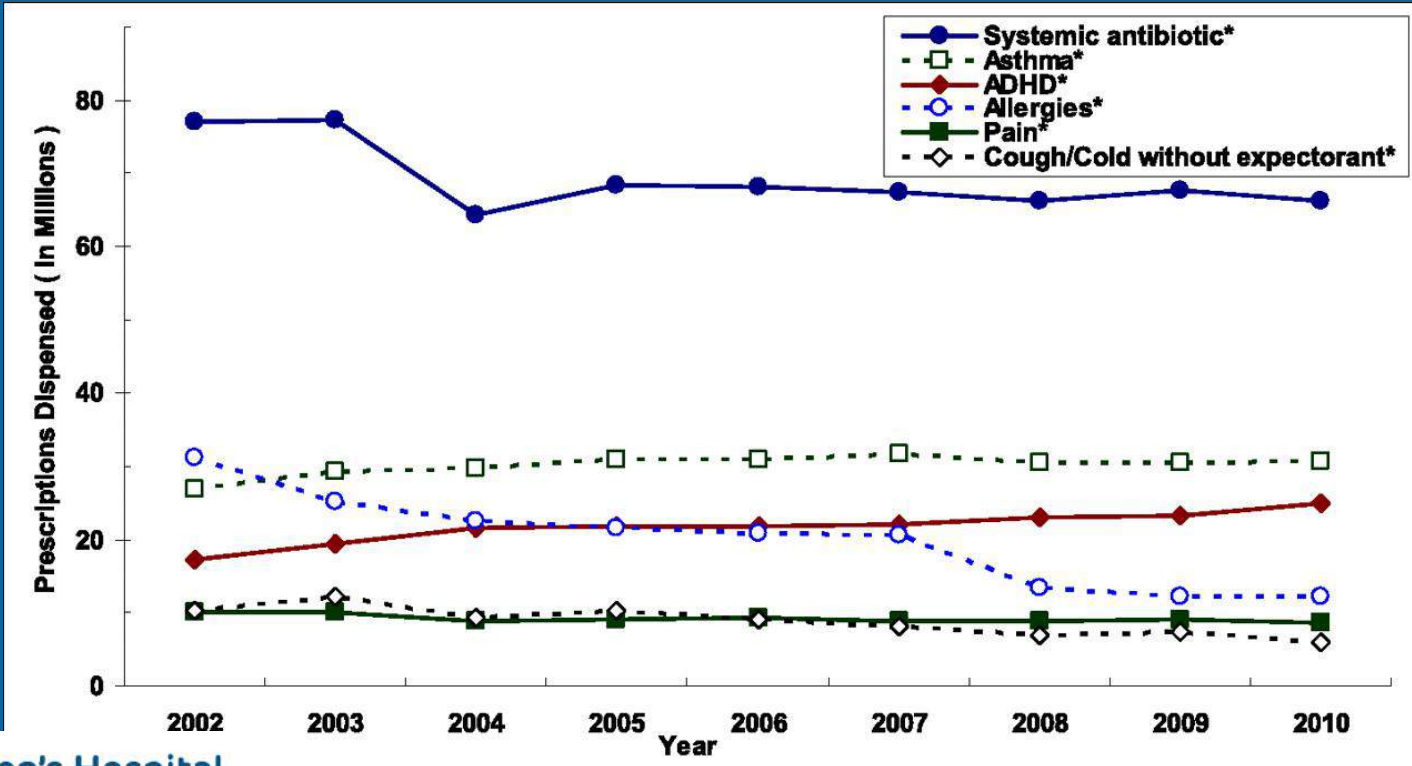


“...because that’s where the money is.”

- Willie Sutton, criminal (1901-1980)

>90% of antibiotic exposure in outpatients

ANTIBIOTIC USE: OUTPATIENT CHILDREN



OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

	US	
All	833	

OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

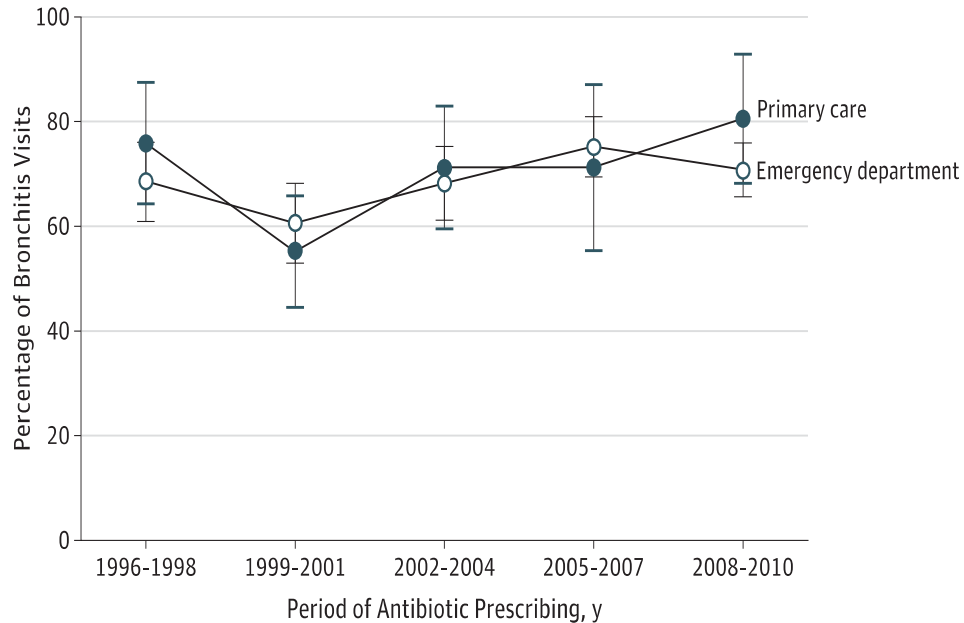
	US	Sweden
All	833	388
0-2	1,365	462
3-9	1,021	414

OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

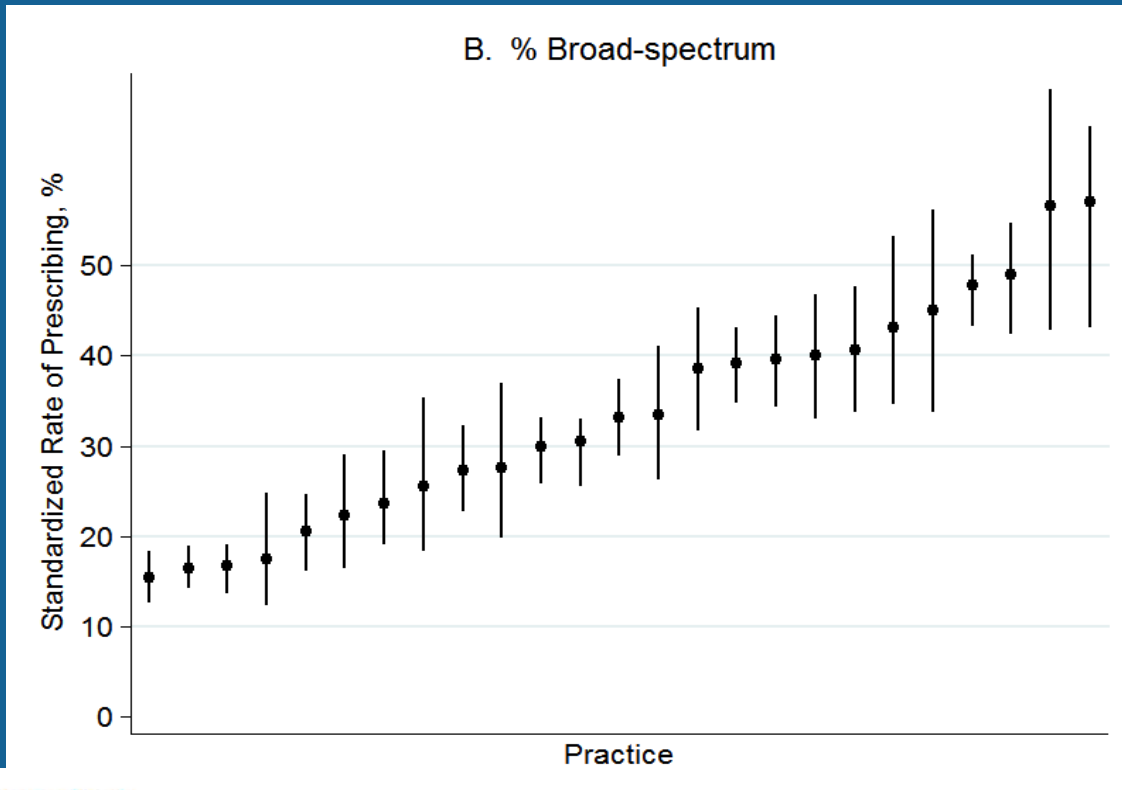
	US	Sweden
All	833	388
quinolones	105	25
macrolides	185	12
cephalosporins	117	12

Antibiotic Prescribing for Adults With Acute Bronchitis in the United States, 1996-2010

Figure. Antibiotic Prescribing for Acute Bronchitis in the United States by Site of Care, 1996-2010



OFF-GUIDELINE ANTIBIOTIC PRESCRIBING



BUT, THERE ARE DOWNSIDES...

- use drives resistance

NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least  **2,049,442** illnesses,
 **23,000** deaths

**bacteria and fungus included in this report*



Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least  **250,000** illnesses,
 **14,000** deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.



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

INDIVIDUAL HARM

- 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 ARTI

A detailed microscopic image showing a dense population of various bacteria. The bacteria are primarily rod-shaped and come in several colors: teal, purple, and red. Some are arranged in long, parallel chains, while others are more isolated. The background is dark, making the colorful bacteria stand out. A white L-shaped graphic element is positioned in the top-left corner, framing the main title.

Your body is mostly microbes

- **10 x** more cells
- **100 x** more genes
- **1000** different species

The Human Microbiome and the Future Practice of Medicine

- benefits derived from microbiota may have profound consequences for health
 - food digestion and nutrition
 - regulation of metabolism
 - processing and detoxification of environmental chemicals
 - development and regulation of the immune system
 - prevention of invasion and growth of pathogens

INCREDIBLY BASIC PRIMER ON THE MICROBIOME

- Its pretty complicated, but ...

- **DIVERSITY IS GOOD.**

- (for the real scoop, visit tutorial by Dan Knights)

- <https://www.youtube.com/playlist?list=PLOPiWVjg6aTzsA53N19YqJQeZpSCH9QPc>

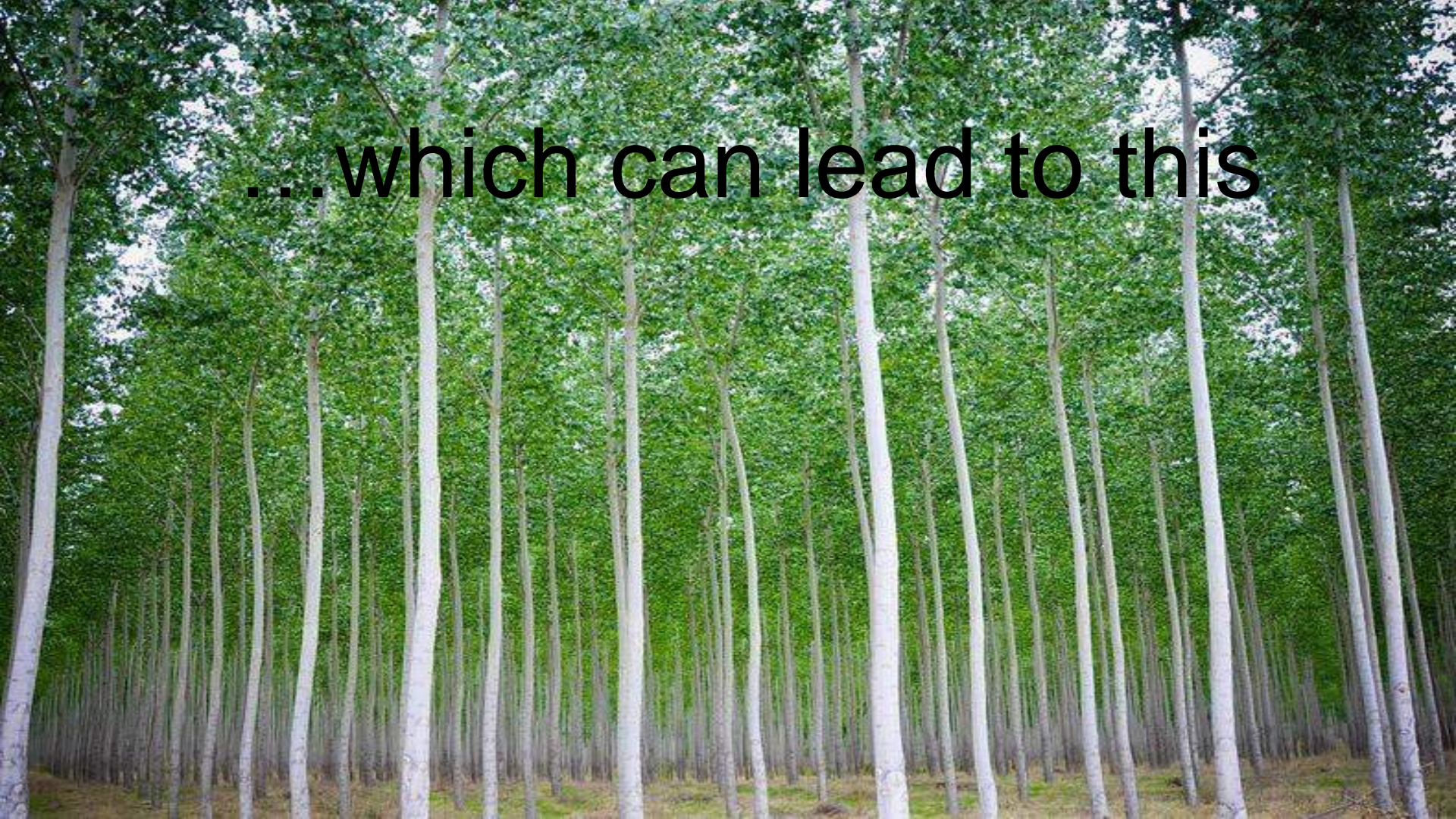
A lush, dense tropical jungle scene. Sunlight filters through the thick canopy of various green plants, including palm trees and broad-leafed species. The ground is covered in a dense layer of undergrowth. The overall atmosphere is vibrant and natural.

This is your gut.

This is your gut on drugs.



...which can lead to this





BROAD-SPECTRUM ANTIBIOTICS

CEARI

COMPARATIVE EFFECTIVENESS OF ANTIBIOTICS FOR RESPIRATORY INFECTIONS

Family Advisory Council

- Kathryn Conaboy, Darlene Barkman

Primary Care Pediatrics

- Lou Bell, Alex Fiks, Mort Wasserman

Infectious Diseases Epidemiology

- Rachael Ross, Julie Szymczak, Theo Zaoutis, Folasade Odeniyi

Biostatistics

- Russell Localio, Matt Bryan

Funding: PCORI contract no. CE-1304-7279

WHY COMPARE BROAD VS. NARROW?

Conflicting guidelines

- AOM
 - AAP recommends amoxicillin; RCTs used amoxicillin-clavulanate for AOM
- Sinusitis:
 - AAP recommends amoxicillin; IDSA recommends amoxicillin-clavulanate
- GAS pharyngitis:
 - cephalosporins?

Pneumococcal vaccination?

(50% of antibiotic use for children is broad-spectrum)

METHODS

- prospective cohort study (2015 – 2016)
- 31 pediatric primary care practices
- 6m-12y Dx with ARTI and Rx oral antibiotic
- excluded multiple ARTIs, another bacterial infection, antibiotics within past 30 days



DATA COLLECTION

- parents/guardians contacted by phone 5 days after diagnosis to confirm eligibility and initiation of antibiotic
- 2 structured telephone interviews completed 5 and 14 days after diagnosis

EXPOSURES

- exposed = narrow-spectrum antibiotics
 - penicillin, amoxicillin
- unexposed = broad-spectrum antibiotics
 - amoxicillin-clavulanate
 - cephalosporins
 - macrolides

OUTCOMES



- qualitative interviews with 109 parents and 24 children from 4 practices presenting for care with ARTI symptoms
- identified **missed school and work, child suffering, child sleep quality, side effects, and speed of symptom resolution** as important outcomes

RESULTS

- Clinical and patient-centered outcomes similar
- More side effects with broad-spectrum antibiotics

JAMA December 19, 2017 Volume 318, Number 23

CONCLUSIONS

- according to patient-centered outcomes generated in partnership with patients and their caregivers, **broad-spectrum agents offered no benefit** over narrow-spectrum agents for the treatment ARTIs
- **broad-spectrum agents were associated with more adverse drug effects**
- these data confirm and extend recommendations to use narrow-spectrum antibiotics for most children, a choice that will maximize patient outcomes while reducing unnecessary antimicrobial resistance pressure, adverse drug effects, and healthcare costs

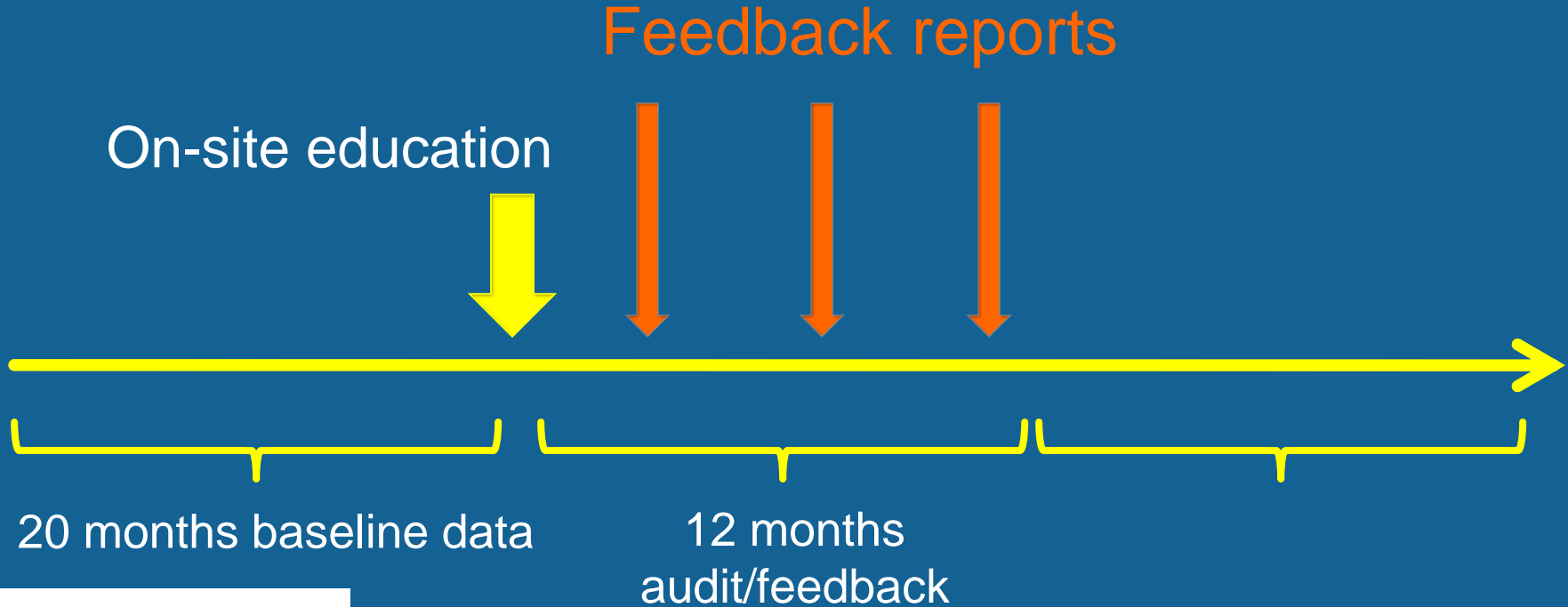
HOW DO WE IMPLEMENT THIS?

Effect of an Outpatient Antimicrobial Stewardship Intervention on Broad-Spectrum Antibiotic Prescribing by Primary Care Pediatricians

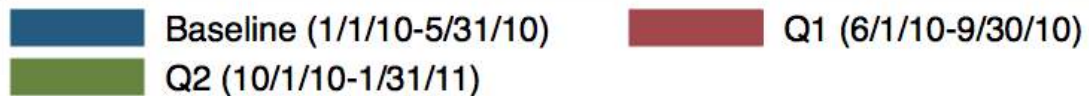
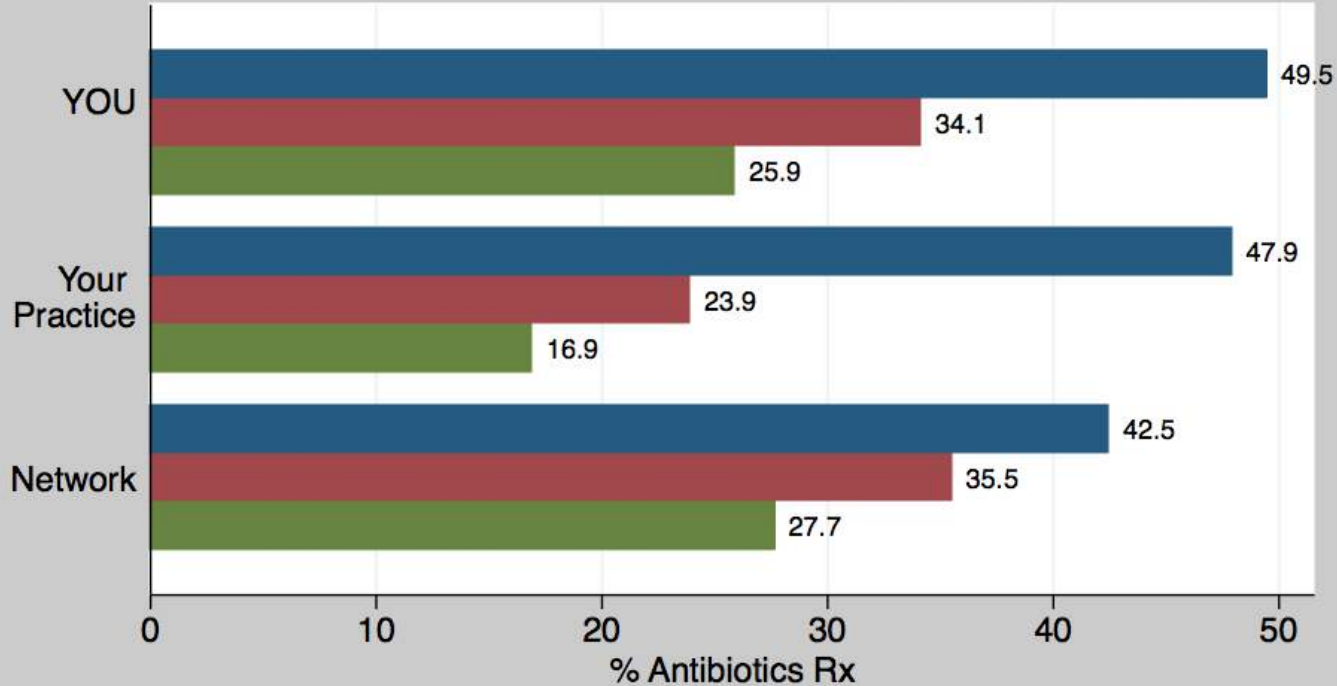
A Randomized Trial

- cluster-RCT of 18 practices, 170 clinicians
- common EHR
- focused on **antibiotic choice** for encounters for bacterial infections with established guidelines
 - streptococcal pharyngitis
 - acute sinusitis
 - pneumonia

INTERVENTION: TIMELINE

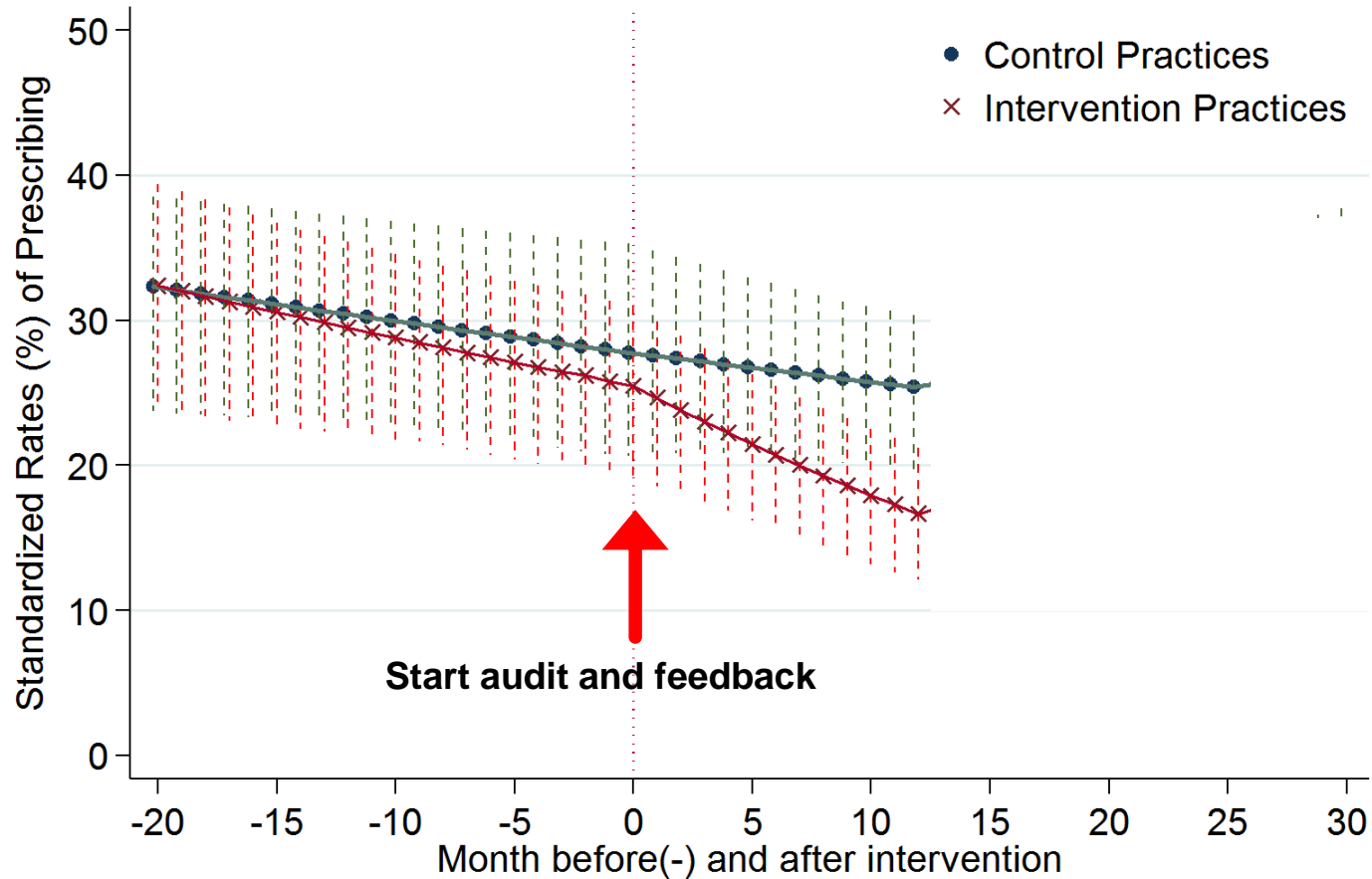


Broad Spectrum Antibiotics for Acute Sinusitis (amoxicillin-clavulanate, 2nd/3rd cephalosporins, or azithromycin)



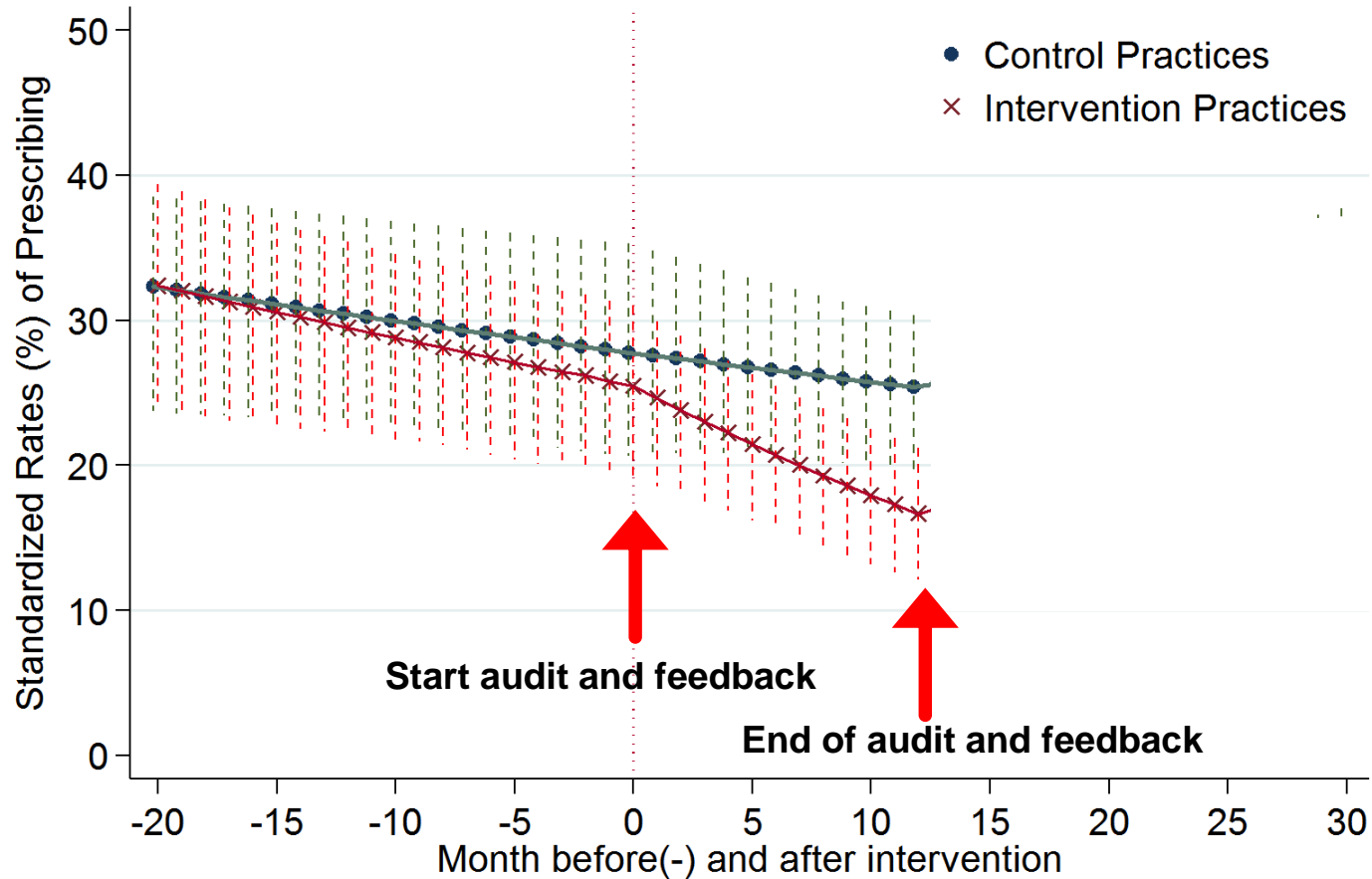
Broad spectrum antibiotics use for acute visits

Rate (95% CI) of prescribing before, during, and after intervention



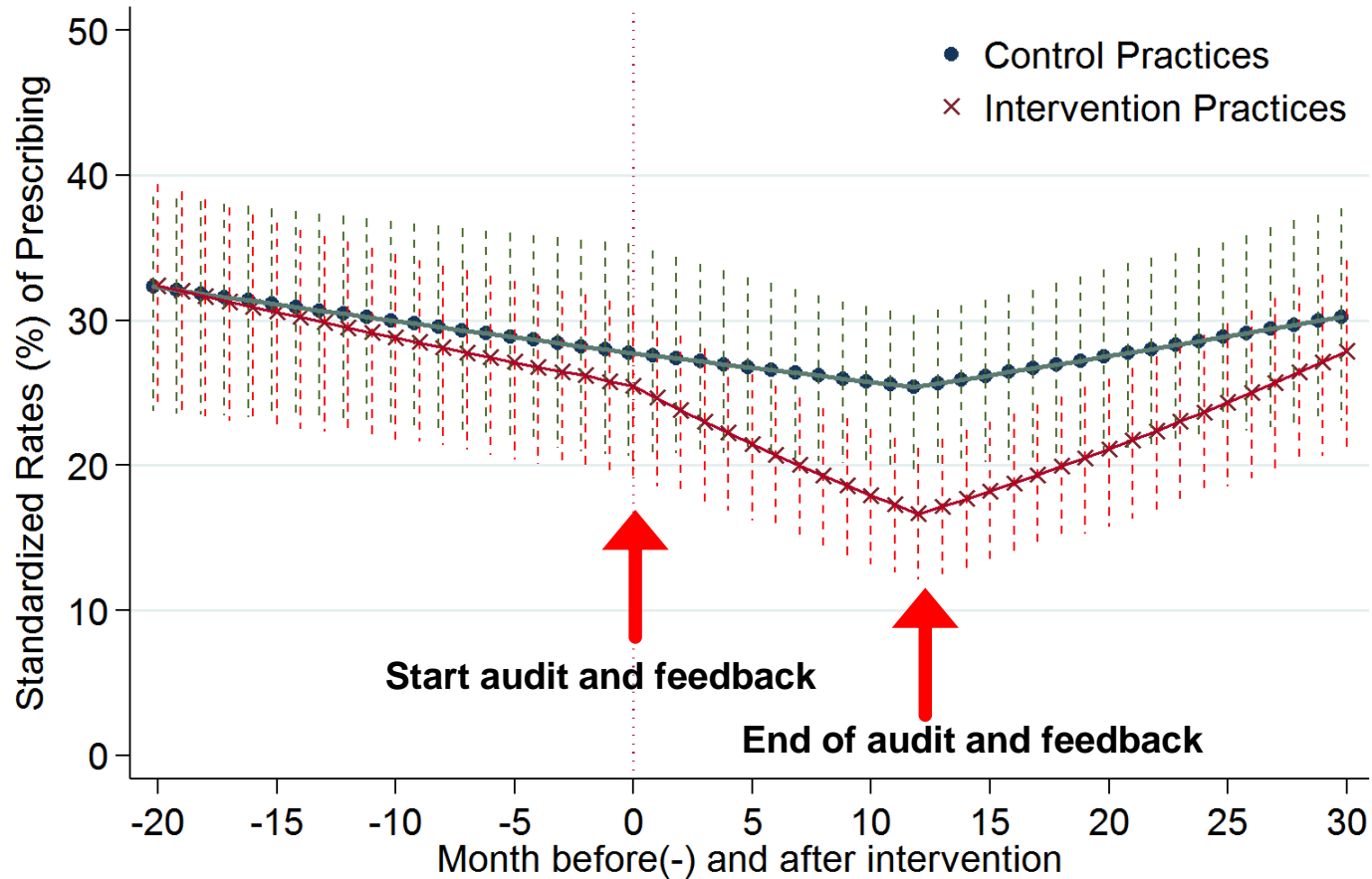
Broad spectrum antibiotics use for acute visits

Rate (95% CI) of prescribing before, during, and after intervention



Broad spectrum antibiotics use for acute visits

Rate (95% CI) of prescribing before, during, and after intervention



QUALITATIVE ANALYSES

- most **did not believe** that their prescribing behavior **contributed** to antibiotic overuse
- reported frequently **confronting parental pressure**
- sometimes acquiescing to avoid losing patients to other practices that would “give them what they want”

“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.”

WHAT DO PARENTS THINK?

- interviewed >100 parents of kids presenting with ARTIs from waiting rooms
- parents **did not plan to demand an antibiotic** for their child
 - **deferred to medical expertise** about the need for antibiotic therapy
 - parents are aware of the downsides of antibiotics and may be willing to partner to improve appropriate use

NON-CLINICAL DRIVERS OF ANTIBIOTIC PRESCRIBING?

- perceived parental pressure
- presence of trainees
- time of day
- patient race
- practice location

Roumie CL et al., *Am J Med.* 2005;118(6):614-648

Linder, *JAMA Internal Medicine* 2014;174(12)

Gerber et al., *Pediatrics* 2013;131:677–684

Handy LK, *Pediatrics* 2017

Nudging Guideline-Concordant Antibiotic Prescribing A Randomized Clinical Trial

Daniella Meeker, PhD; Tara K. Knight, PhD; Mark W. Friedberg, MD, MPP; Jeffrey A. Linder, MD, MPH;
Noah J. Goldstein, PhD; Craig R. Fox, PhD; Alan Rothfeld, MD; Guillermo Diaz, MD; Jason N. Doctor, PhD

- intervention that takes advantage of clinicians' desire to be consistent with their public commitments
- simple, **low-cost behavioral “nudge” in form of a public commitment device**: a poster-sized letter signed by clinicians and posted in their examination rooms indicating their commitment to reducing inappropriate antibiotic use for ARTIs

Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices A Randomized Clinical Trial

Daniella Meeker, PhD; Jeffrey A. Linder, MD, MPH; Craig R. Fox, PhD; Mark W. Friedberg, MD, MPP;
Stephen D. Persell, MD, MPH; Noah J. Goldstein, PhD; Tara K. Knight, PhD; Joel W. Hay, PhD; Jason N. Doctor, PhD

Suggested alternatives

- “antibiotics are generally not indicated for this”

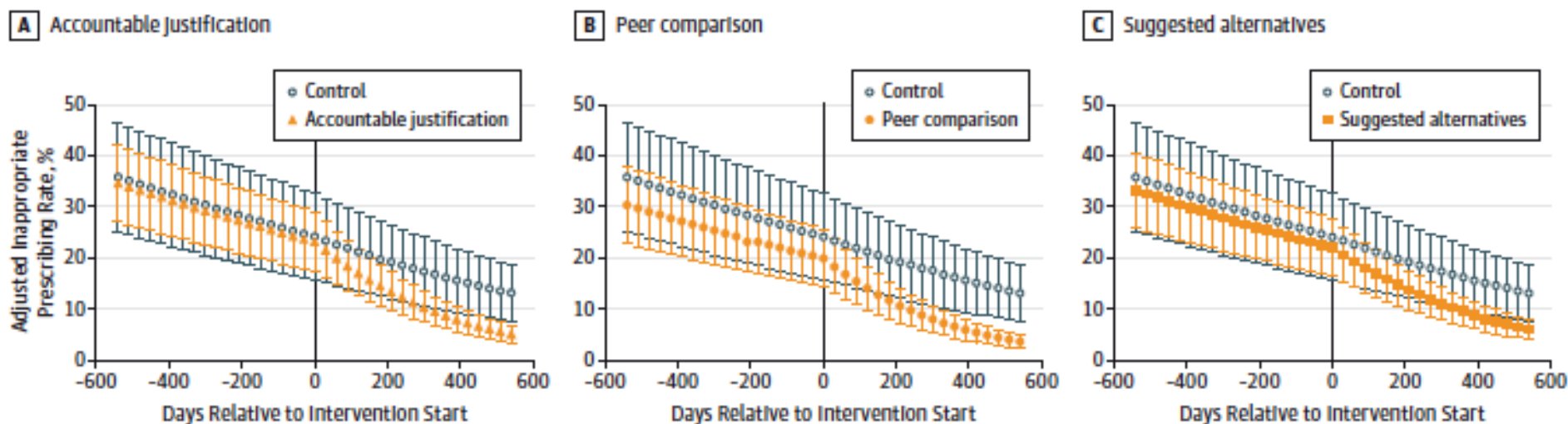
Accountable justification

- free text, or “no justification given”

Peer comparison

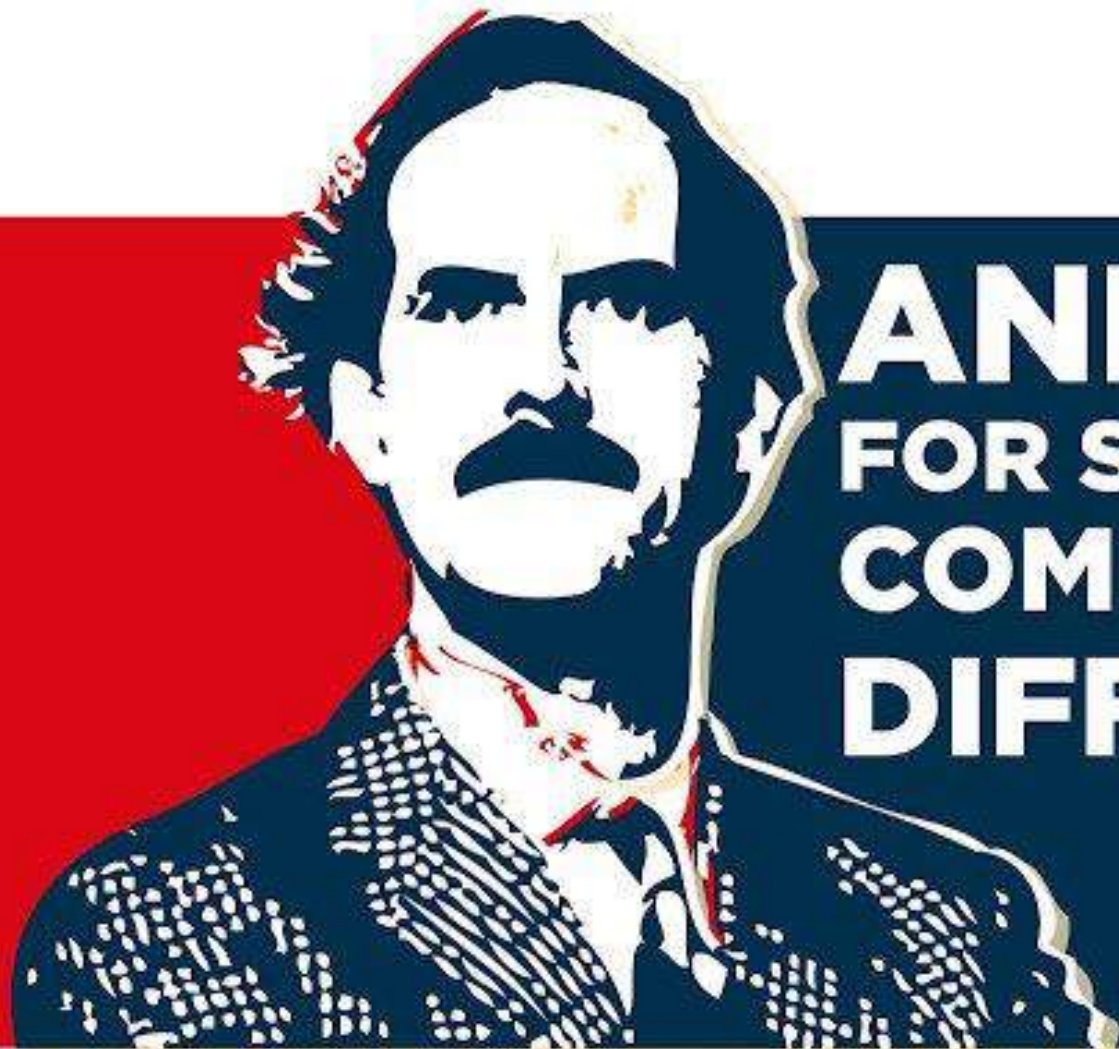
- top decile “top performer” or “not top performer”

Figure 2. Adjusted Rates of Antibiotic Prescribing at Primary Care Office Visits for Antibiotic-Inappropriate Acute Respiratory Tract Infections Over Time



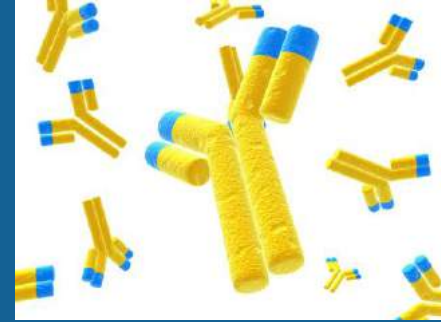
Prescribing rates for each intervention are marginal predictions from hierarchical regression models of intervention effects, adjusted for concurrent exposure to other interventions and clinician and practice random effects. Error bars indicate 95% CIs. Model coefficients are available in eTable 3 in Supplement 2.

Table 2. Unadjusted Visit Counts and Antibiotic Prescribing Rates for Antibiotic-Inappropriate Acute Respiratory Tract Infections During the Baseline and Intervention Periods, by Study Group



**AND NOW
FOR SOMETHING
COMPLETELY
DIFFERENT.**

ANTIBIOTIC ALLERGY



- **Antibiotics** the most common reported cause of medication allergies
- **penicillin** is the most common antimicrobial allergy
 - reported in 5-10% of all patients
- <10% of patients with reported penicillin allergies actually have a positive reaction to penicillin skin testing
- **more than 80% of all adverse drug reactions are non-immunologically mediated**

IMPLICATIONS OF ANTIBIOTIC ALLERGIES

- LOTS of kids get antibiotics, most SHOULD be penicillins
- LOTS of kids are labeled as penicillin allergic (5 million)
- Therefore, LOTS of kids “can’t” get 1st line drugs
- When they need an antibiotic, they might get a drug with:
 - different spectrum
 - more side effects
 - more expensive
 - less familiar to prescriber (dose, interactions)

Allergy Testing in Children With Low-Risk Penicillin Allergy Symptoms

David Vyles, DO,^a Juan Adams, MD,^b Asriani Chiu, MD,^b Pippa Simpson, PhD,^c
Mark Nimmer, BA,^d David C. Brousseau, MD, MS^e

- Parents of kids 4-18 y with Hx of PCN allergy presenting to ED
- 597 kids took Allergy questionnaire
- 50% met low risk criteria
- 100 enrolled and were tested
 - 97 negative skin tests
 - 100 negative oral challenge
 - **100 de-labeled**

DE-LABEL

- By history alone:
 - family history
 - GI symptoms
 - subsequently took drug
- Refer to allergy for skin testing
 - Delayed reaction
 - Hx of anaphylaxis

SUMMARY

- Most kids labeled as allergic aren't truly allergic
- Allergy labels are associated with more adverse events, lower clinical cure rates, and higher cost
- Consider implementing protocols for de-labeling in partnership with allergists and with reassurance and clear communication

SUMMARY

- antibiotic prescribing in the ambulatory setting is common and can be harmful to the patient and society
- audit with feedback can be an effective strategy to improve prescribing
- other socio-behavioral approaches, such as improving communication and holding clinicians accountable can also be effective
- Most kids aren't allergic to penicillins, and use of 2nd line agents might be harmful

THANK YOU

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The Children's Hospital
of Philadelphia®

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School of Medicine
UNIVERSITY of PENNSYLVANIA



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to do everything exactly the same way it's
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