OUTPATIENT ANTIMICROBIAL STEWARDSHIP: **INTERVENTIONS THAT WORK**

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LEARNING OBJECTIVES

- recognize the need for outpatient antimicrobial stewardship
- understand examples of outpatient antimicrobial stewardship interventions
- recognize some novel stewardship strategies

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PRESENTATION OUTLINE

- explain the need for outpatient antimicrobial stewardship
- describe a relevant stewardship CE study generating targets for improvement
- describe an outpatient antimicrobial stewardship intervention focused on this target
- 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

US Outpatient Antibiotic Prescribing Variation According to Geography, Patient Population, and Provider Specialty in 2011

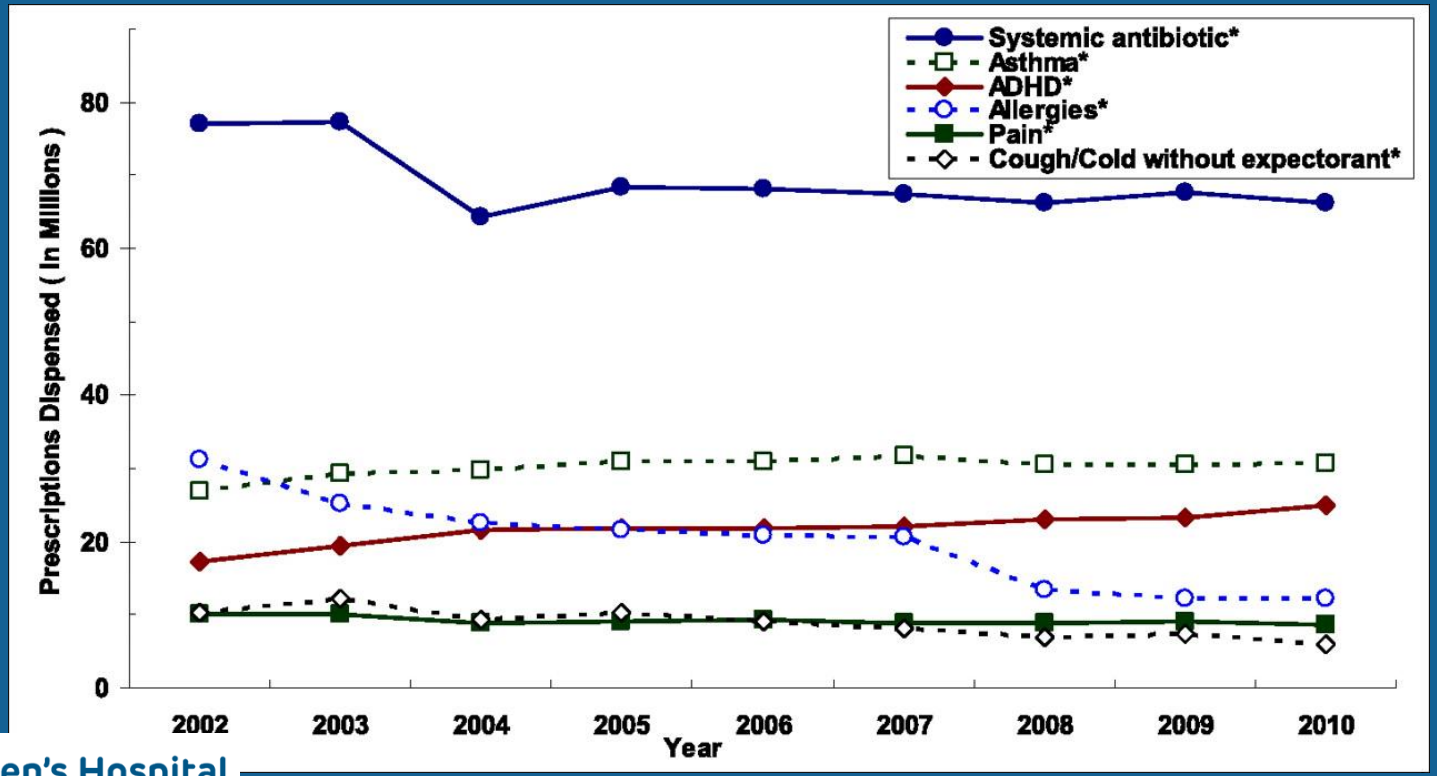
Lauri A. Hicks,[1] Monina G. Bartoces,[1] Rebecca M. Roberts,[1] Katie J. Suda,[2] Robert J. Hunkler,[3] Thomas H. Taylor Jr,[1] and Stephanie J. Schrag[1]

[1]Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Department of Veterans Affairs, University of Illinois at Chicago; and [3]IMS Health, Plymouth Meeting, Pennsylvania

- IMS Health Xponent database
- 262.5 million antibiotic prescriptions dispensed in 2011
- 842 prescriptions per 1000 persons
- 29% for kids

Clinical Infectious Diseases 2015;60(9):1308–16

ANTIBIOTIC USE: OUTPATIENT CHILDREN



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

OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

	US	
All	833	

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Ternhag A. NEJM 2013;369:1175-1176.
Hicks LA et al. NEJM 2010;368:1461-2

OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

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

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Ternhag A. NEJM 2013;369:1175-1176.
Hicks LA et al. NEJM 2010;368:1461-2

OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

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

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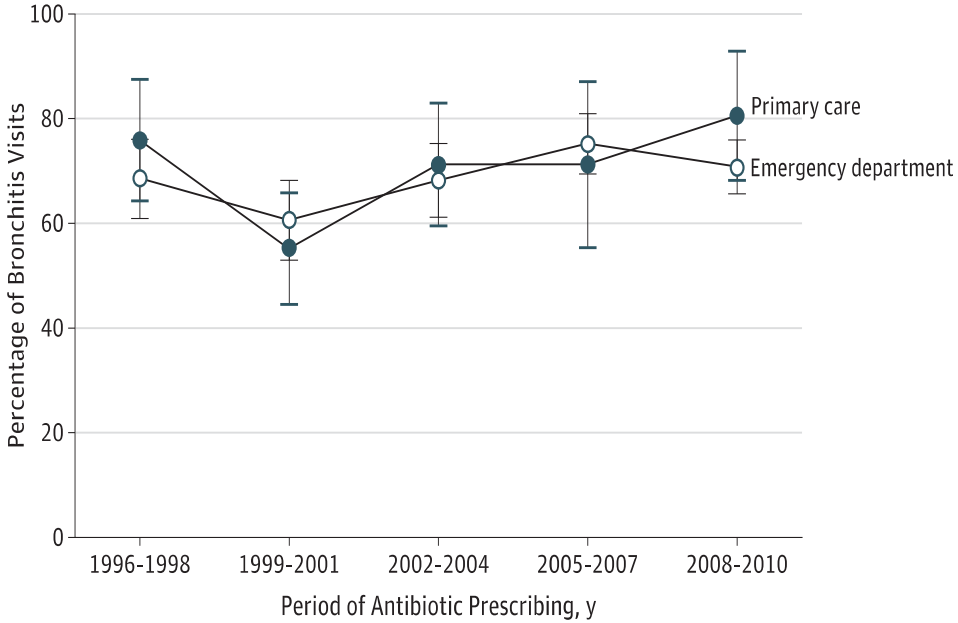
Ternhag A. NEJM 2013;369:1175-1176.
Hicks LA et al. NEJM 2010;368:1461-2

RESEARCH LETTER

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



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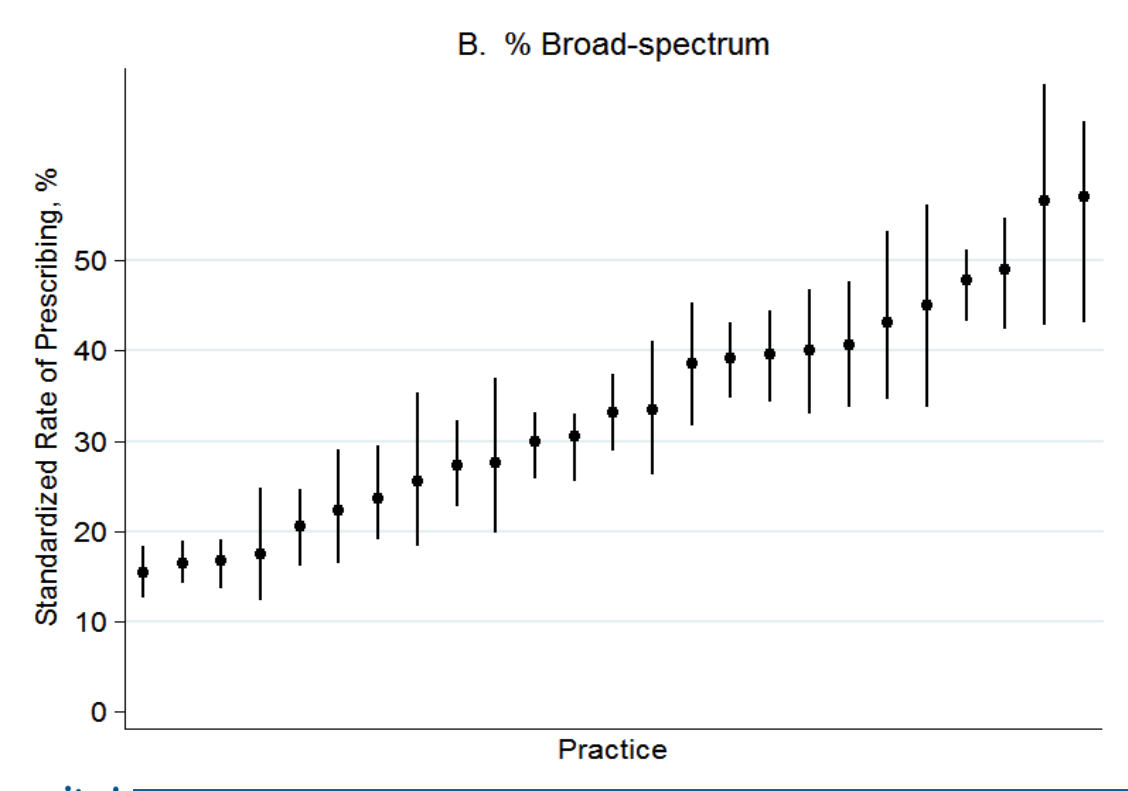
Barnett and Linder. *JAMA*. 2014;311(19):2020-2022

OFF-GUIDELINE ANTIBIOTIC PRESCRIBING



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Gerber et al., *JPIDS*, 2014

BUT ANTIBIOTICS ARE WONDERFUL…

"I am a fan of antibiotics just because of the fact that it does heal them pretty quickly." [H]

"I think [antibiotics] are wonderful. They clear up everything quickly. As long as you take them how the doctor prescribes, the infection is gone." [K]

"All I can say is, antibiotics work. That is the only thing I can say. When we use it right it works. It helps them get better quickly." [SP]

BUT, THERE ARE DOWNSIDES…

- use drives resistance
- bacteria have shown the ability to become resistant to every antibiotic that has been developed

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

CS239559

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

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


1
Your body is mostly microbes
• 10 x more cells
• 100 x more genes
• 1000 different species
http://www.knightslab.org

VIEWPOINT

SCIENTIFIC DISCOVERY AND THE FUTURE OF MEDICINE

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

JAMA September 15, 2015 Volume 314, Number 11

INCREDIBLY BASIC PRIMER ON THE MICROBIOME

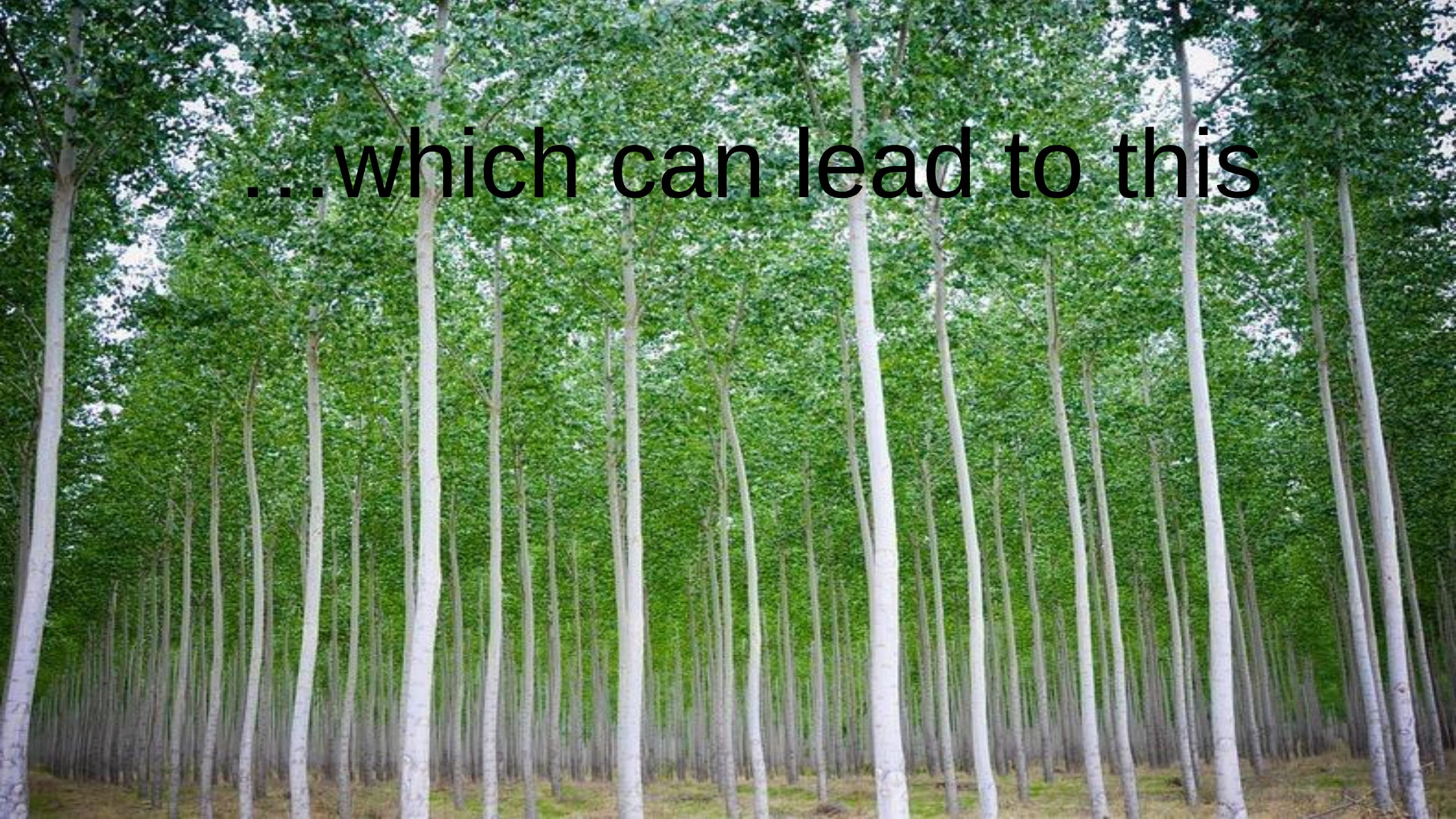
- Its pretty complicated, but …
- DIVERSITY IS GOOD.

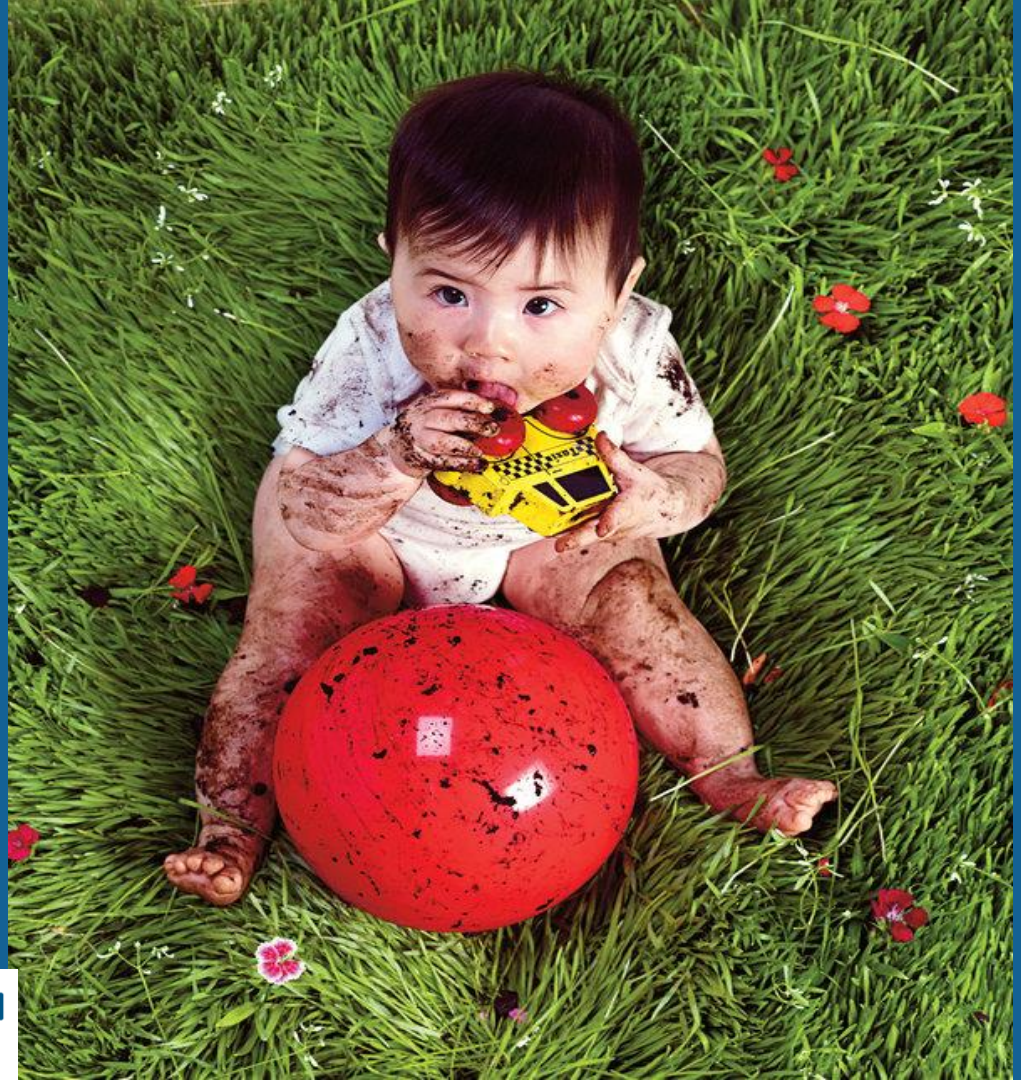
- (for the real scoop, visit tutorial by Dan Knights)
  - https://www.youtube.com/playlist?list=PLOPiWVjg6aTzsA53N19YqJQeZpSCH9QPc

http://www.knightslab.org


This is your gut.


This is your gut on drugs.


…which can lead to this



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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

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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 prescribed oral antibiotic
- excluded multiple ARTIs, another bacterial infection, antibiotics within past 30 days

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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

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Table 4. Patient-Centered Outcomes in the Prospective Cohort

Outcome	No./Total (%)[a]		Stratified Analysis[b]		Full Matched Analysis[c]	
	Broad-Spectrum Antibiotics	Narrow-Spectrum Antibiotics	Risk Difference (95% CI), %[d]	*P* Value	Risk Difference (95% CI), %[e]	*P* Value
Missed school or day care	305/702 (43.4)	503/1199 (42.0)	2.5 (−3.9 to 9.0)	.45	2.4 (−3.1 to 7.9)	.39
Required additional childcare	220/701 (31.4)	390/1190 (32.8)	−0.2 (−5.7 to 5.2)	.94	1.5 (−3.9 to 6.8)	.59
Experienced adverse events	258/725 (35.6)	341/1360 (25.1)	11.6 (6.0 to 17.2)	<.001	12.2 (7.3 to 17.2)	<.001
Symptoms present on day 3[f]	267/647 (41.3)	427/1128 (37.9)	2.3 (−4.5 to 9.1)	.50	4.9 (−0.8 to 10.6)	.09
Sleep disturbance	378/860 (44.0)	582/1570 (37.1)	4.6 (−0.5 to 9.6)	.08	4.6 (−0.3 to 9.6)	.07
Pediatric Quality of Life Inventory score[g]	(n = 860) 90.2 (10.5)[h]	(n = 1570) 91.5 (9.4)[h]	−1.6 (−2.8 to −0.5)[i]	.006	−1.4 (−2.4 to −0.4)[j]	.008

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LIMITATIONS

- relied on clinician diagnosis; many were likely viral
- 30% enrollment rate
- PedsQL™ might not be sensitive enough to detect minor differences in symptoms
- unobserved confounding?
- generalizability

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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

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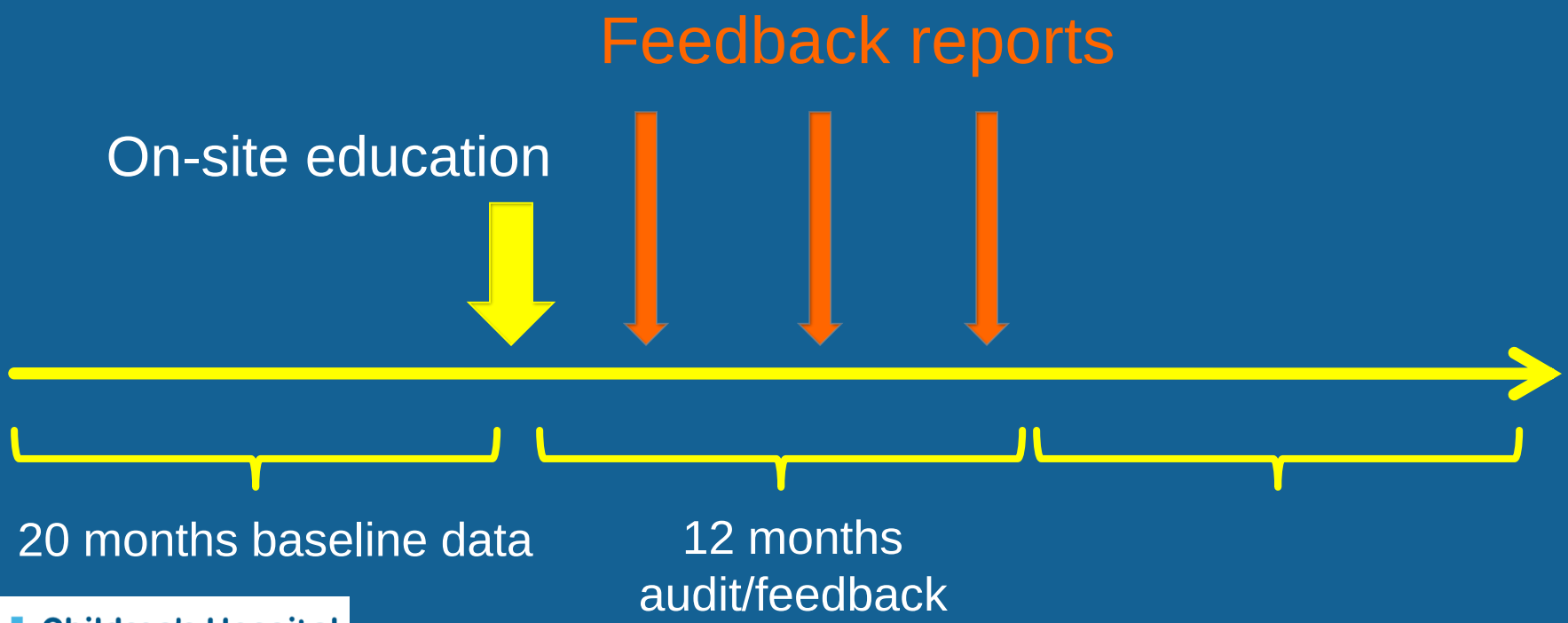
Gerber et al. *JAMA*.2013;309(22):2345

INTERVENTION: TIMELINE



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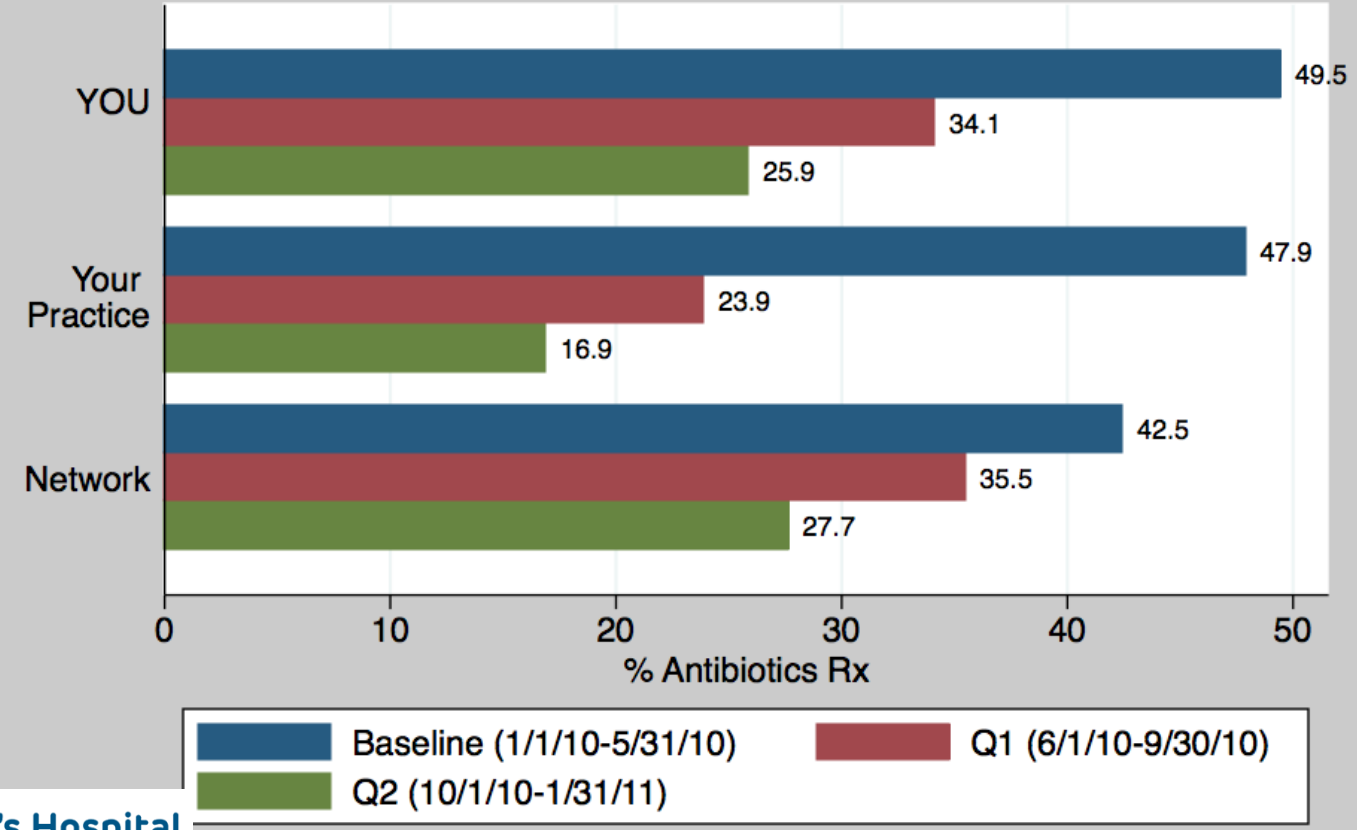
Broad Spectrum Antibiotics for Acute Sinusitis

(amoxicillin-clavulanate, 2nd/3rd cephalosporins, or azithromycin)



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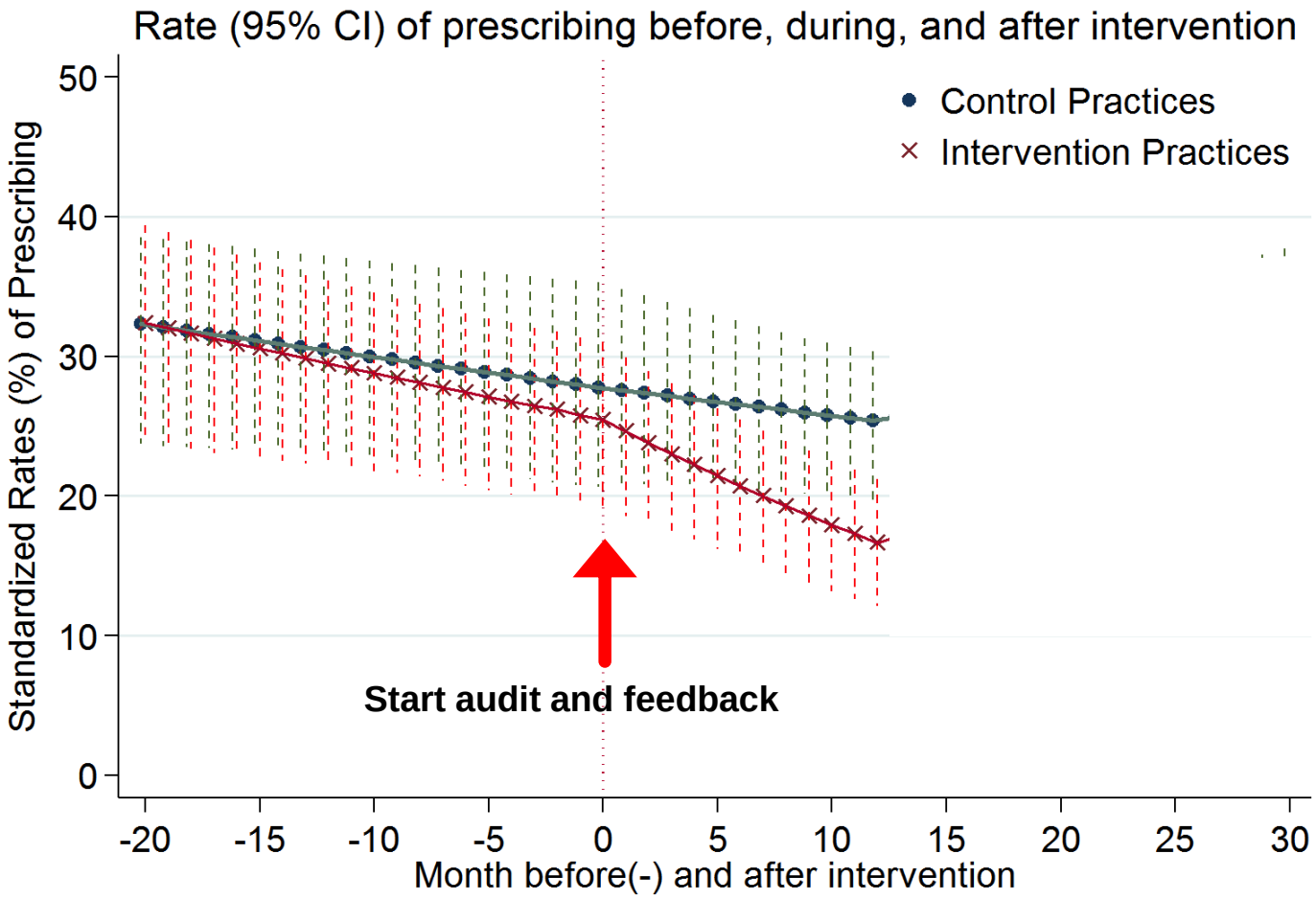
Broad spectrum antibiotics use for acute visits



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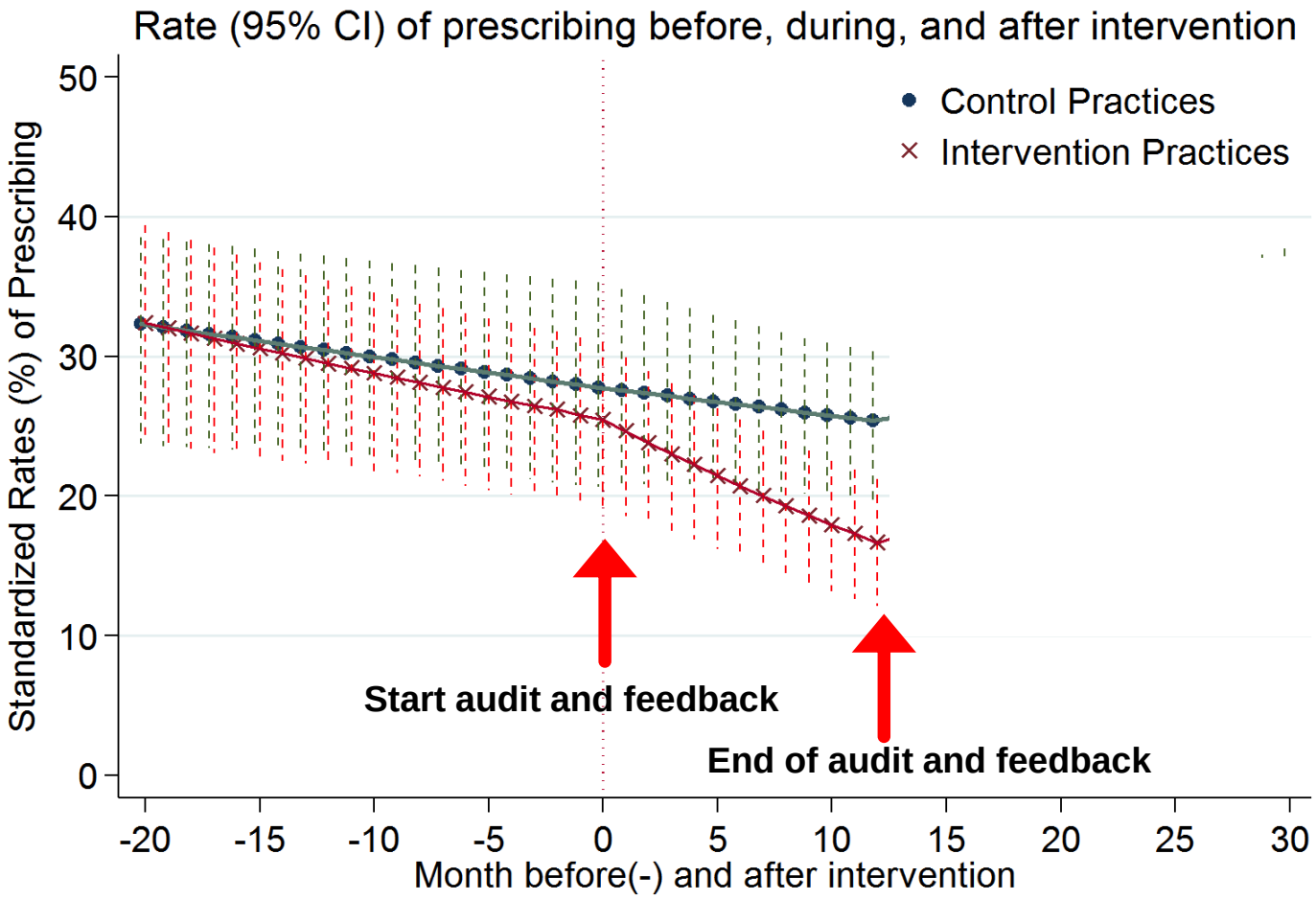

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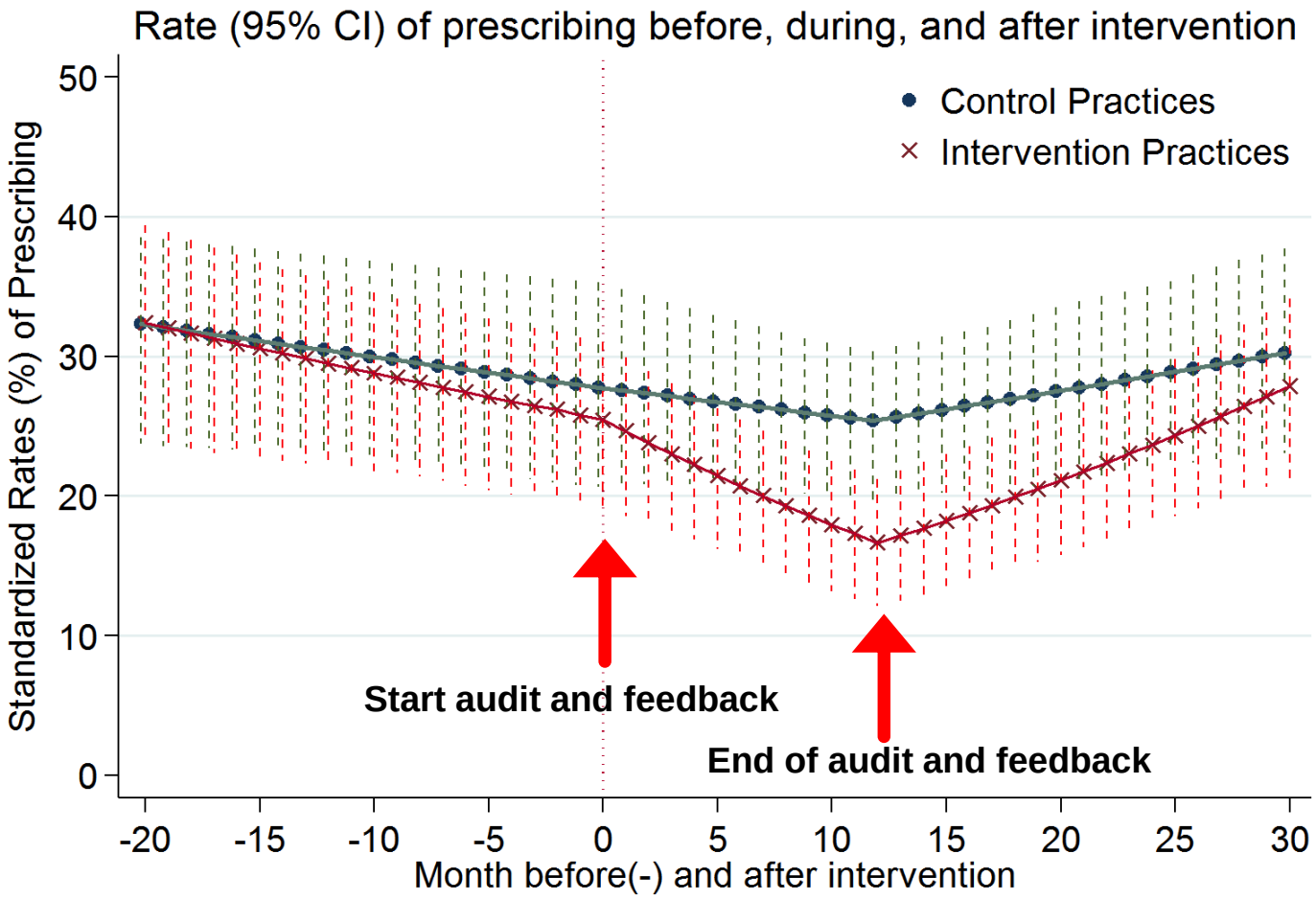

JAMA.2013;309(22):2345

WHAT DO CLINICIANS THINK?

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”

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Szymczak, *ICHE*, 2014, vol. 35, no. s3

“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.”

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Szymczak, *ICHE*, 2014, vol. 35, no. s3

CLINICIAN PERCEPTIONS

- interviewed 10 physicians, 306 parents
- physician perception of parental expectations for antimicrobials was the only predictor of prescribing antimicrobials for viral infections
  - when they thought parents wanted antimicrobial:
    - 62% vs. 7% prescribed antibiotic

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Mangione-Smith et al. *Pediatrics* 1999;103(4)

WHAT DO PARENTS THINK?

WHAT DO PARENTS WANT?

- direct parental request for antibiotics in 1% of cases
- parental expectations for antibiotics were not associated with physician-perceived expectations
- parents who expected antibiotics but did not receive them were more satisfied if the physician provided a contingency plan
- failure to meet parental expectations regarding communication events during the visit was the only significant predictor of parental satisfaction (NOT failure to provide expected antimicrobials)

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Mangione-Smith et al. *Arch Pediatr Adolesc Med* 2001;155:800-806

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

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Szymczak, ID Week, San Diego, 2015

COMMUNICATION

- parent and clinician surveys after 1,285 pediatric ARTI visits to 28 pediatric providers from 10 Seattle practices

- positive treatment recommendations (suggesting actions to reduce child's symptoms) were associated with decreased risk of antibiotic prescribing

Mangione-Smith et al. *Ann Fam Med* 2015;13:221-227

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

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Original Investigation

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

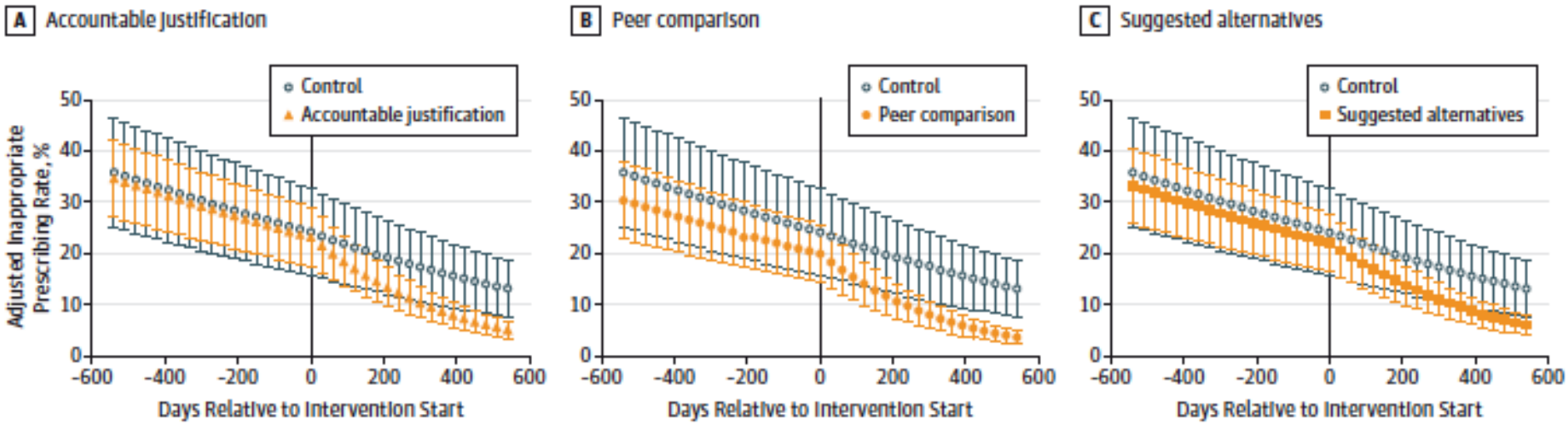
- free text, or "no justification given"

Peer comparison

- top decile "top performer" or "not top performer"

JAMA February 9, 2016 Volume 315, Number 6

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

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
- more to come…

THANK YOU

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