ANTIMICROBIAL STEWARDSHIP
FOR AMBULATORY CARE SETTINGS

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DISCLOSURE STATEMENT

I have no conflicts of interest to report

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

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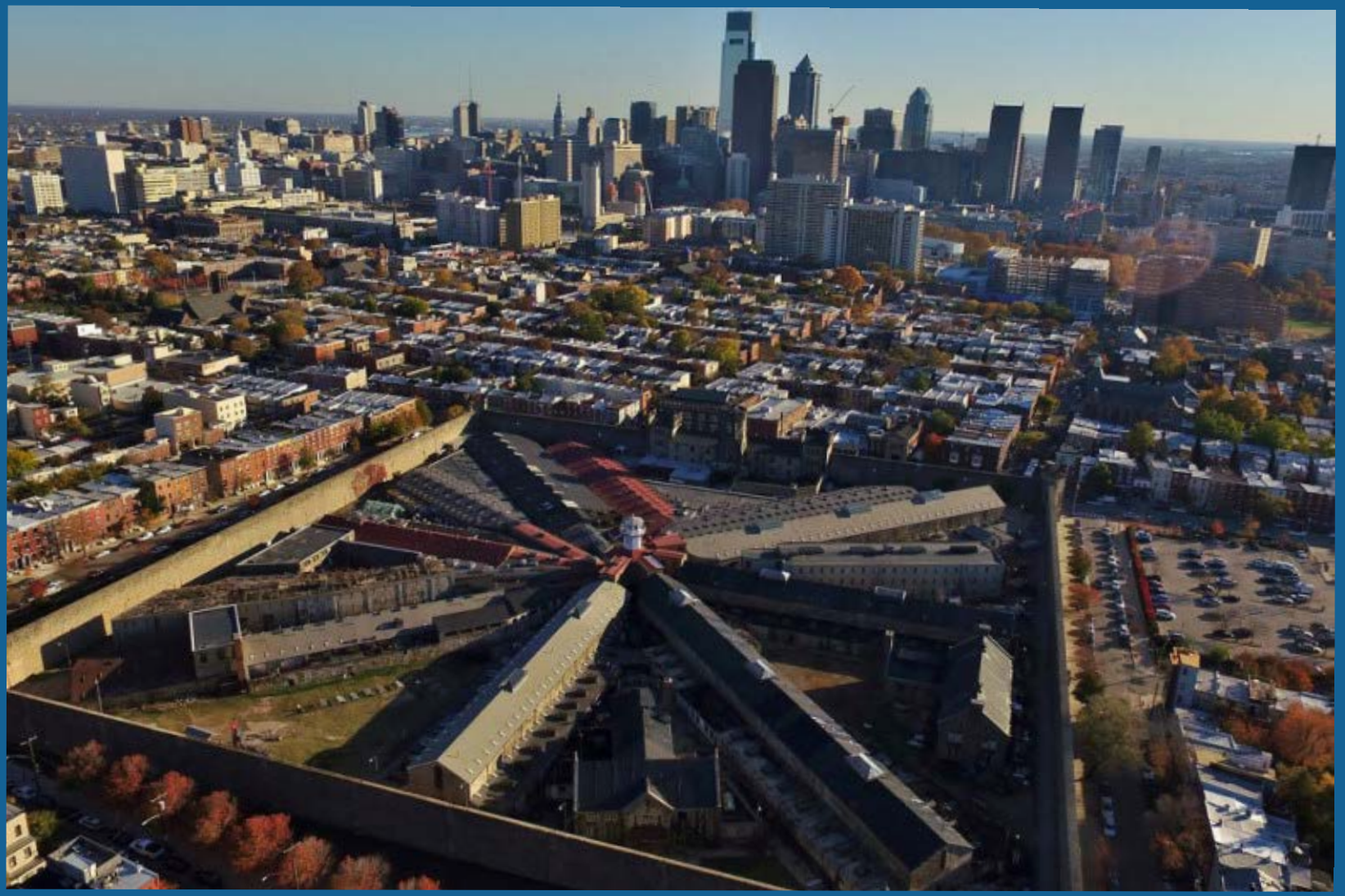


WHY OUTPATIENT STEWARDSHIP?

"…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

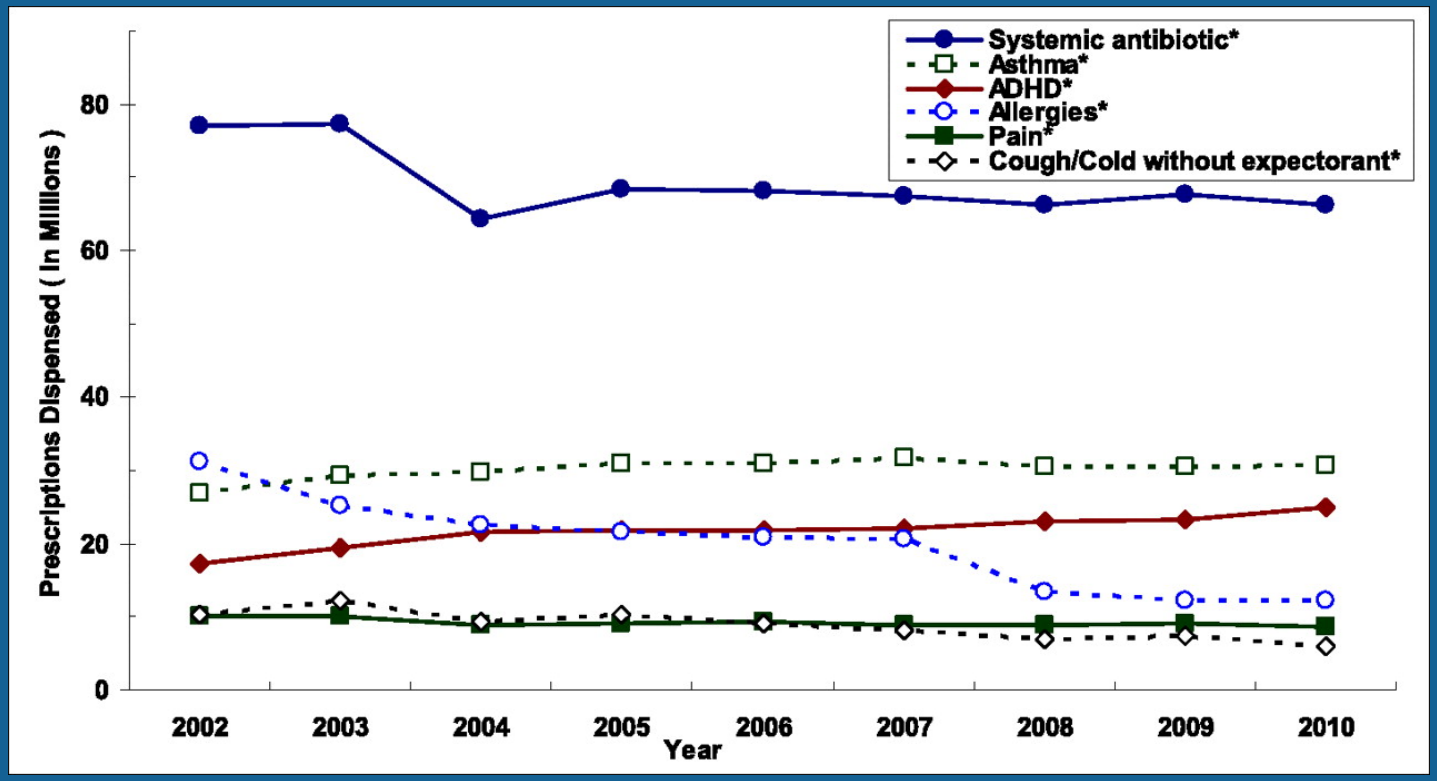
Lauri A. Hicks,[1] Monina G. Bartoces,[1] Rebecca M. Roberts,[1] Katie J. Suda,[2] Robert J. Hunkler,[3] Thomas H. Taylor Jr,[1] and Stephanie J. Schrag[1]

[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	

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

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OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

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

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

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OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

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

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

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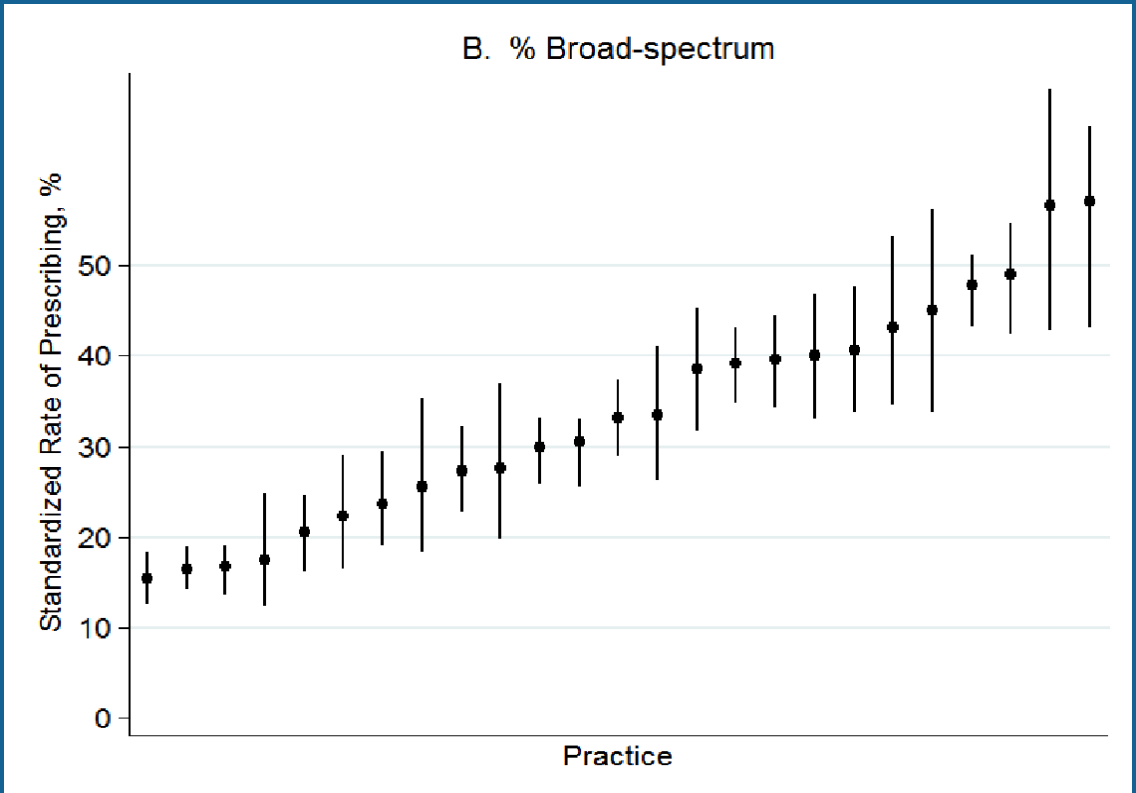
OFF-GUIDELINE ANTIBIOTIC PRESCRIBING



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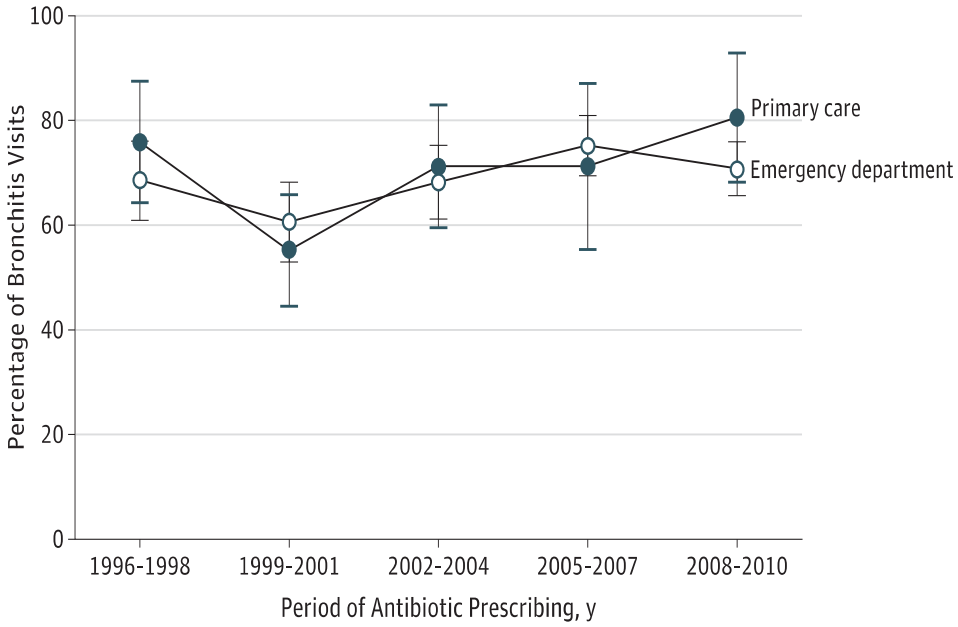
Gerber et al., *JPIDS*, 2014

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



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

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Original Investigation

Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011

Katherine E. Fleming-Dutra, MD; Adam L. Hersh, MD, PhD; Daniel J. Shapiro; Monina Bartoces, PhD; Eva A. Enns, PhD; Thomas M. File Jr, MD; Jonathan A. Finkelstein, MD, MPH; Jeffrey S. Gerber, MD, PhD; David Y. Hyun, MD; Jeffrey A. Linder, MD, MPH; Ruth Lynfield, MD; David J. Margolis, MD, PhD; Larissa S. May, MD, MSPH; Daniel Merenstein, MD; Joshua P. Metlay, MD, PhD; Jason G. Newland, MD, MEd; Jay F. Piccirillo, MD; Rebecca M. Roberts, MS; Guillermo V. Sanchez, MPH, PA-C; Katie J. Suda, PharmD, MS; Ann Thomas, MD, MPH; Teri Moser Woo, PhD; Rachel M. Zetts; Lauri A. Hicks, DO

- diagnosis-specific rates of total and appropriate antibiotic prescribing determined based on national guidelines and regional variation
  - 30% overall reduction suggested
  - 50% for ARTIs

JAMA May 3, 2016 Volume 315, Number 17

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]

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…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

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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

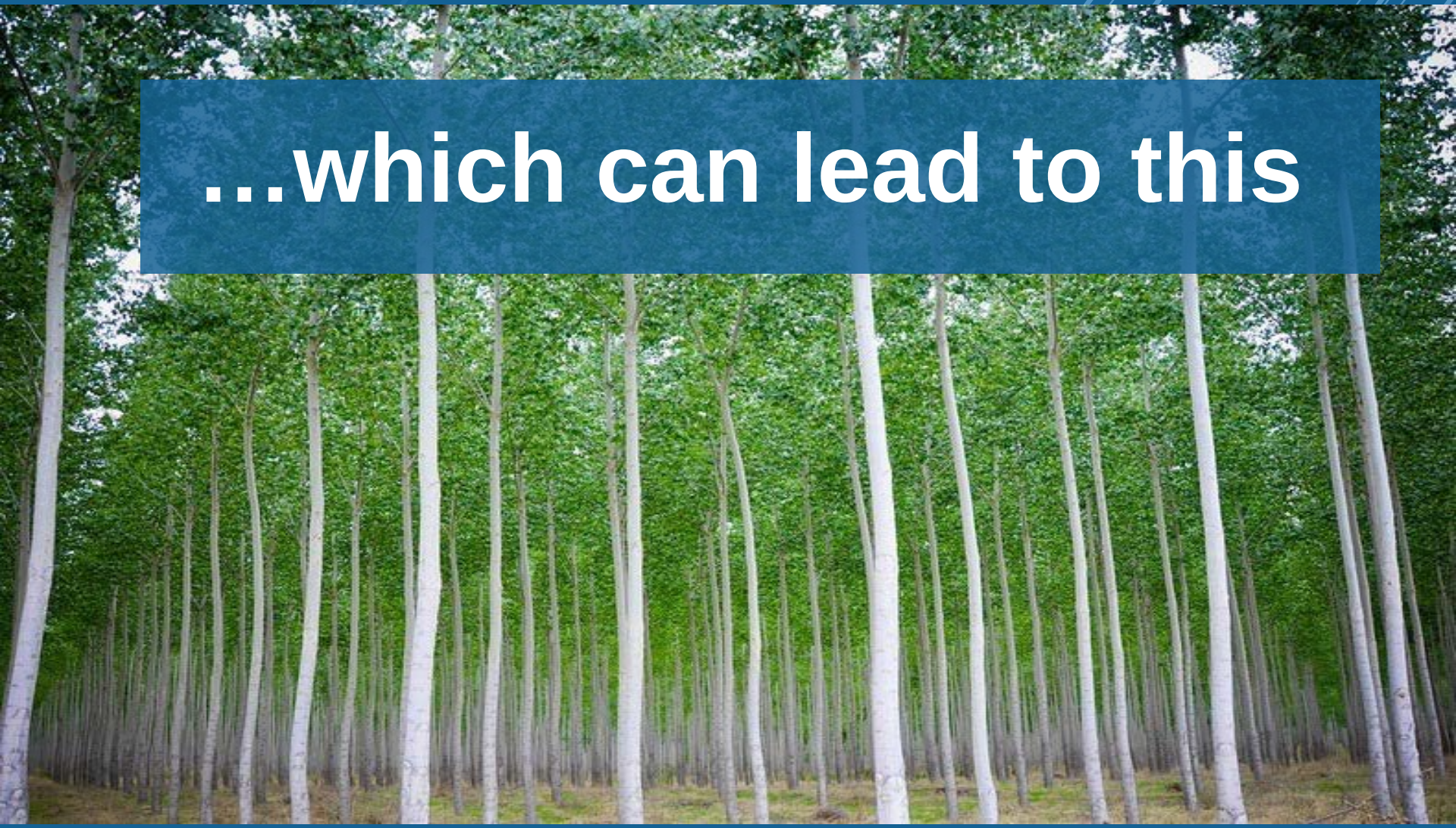
INCREDIBLY BASIC PRIMER ON THE MICROBIOME

- 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

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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)

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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

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EXPOSURES

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

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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

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HOW DO WE IMPLEMENT THIS?

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FIGHTING BACK AGAINST ANTIBIOTIC RESISTANCE

Four Core Actions to Prevent Antibiotic Resistance

1 PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE

Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4 DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS

Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

ANTIBIOTIC STEWARDSHIP

IN YOUR FACILITY WILL

DECREASE

- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE

- GOOD PATIENT OUTCOMES

PROMOTE ANTIBIOTIC BEST PRACTICES— A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN "ANTIBIOTIC TIMEOUT" REASSESSING ANTIBIOTICS AFTER 48–72 HOURS

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A "WIN-WIN" FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM **SAVED A TOTAL OF $17 MILLION** OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS **IMPROVE PATIENT CARE AND SHORTEN HOSPTIAL STAYS,** THUS **BENEFITING PATIENTS AS WELL AS HOSPITALS**

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]

- ASPs recommended for hospitals
- most antibiotic use occurs in the outpatient setting
- is outpatient “stewardship” achievable?

ANTIMICROBIAL STEWARDSHIP

- Core Strategies
  - prior authorization
  - prospective audit & feedback
  - formulary restriction
- Supplemental Strategies
  - education
  - clinical guidelines
  - IV to PO conversion
  - dose optimization

ANTIMICROBIAL STEWARDSHIP

- Core Strategies
  - prior authorization
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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

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

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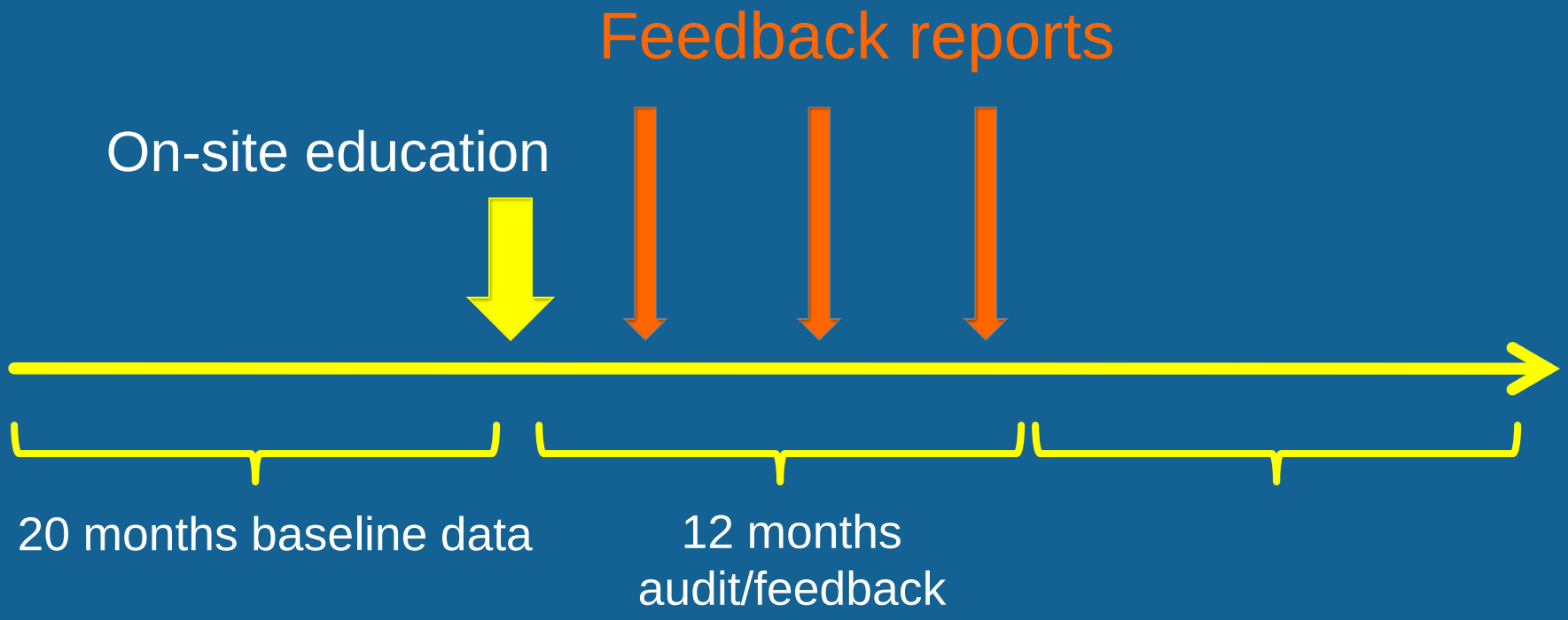
INTERVENTION: TIMELINE



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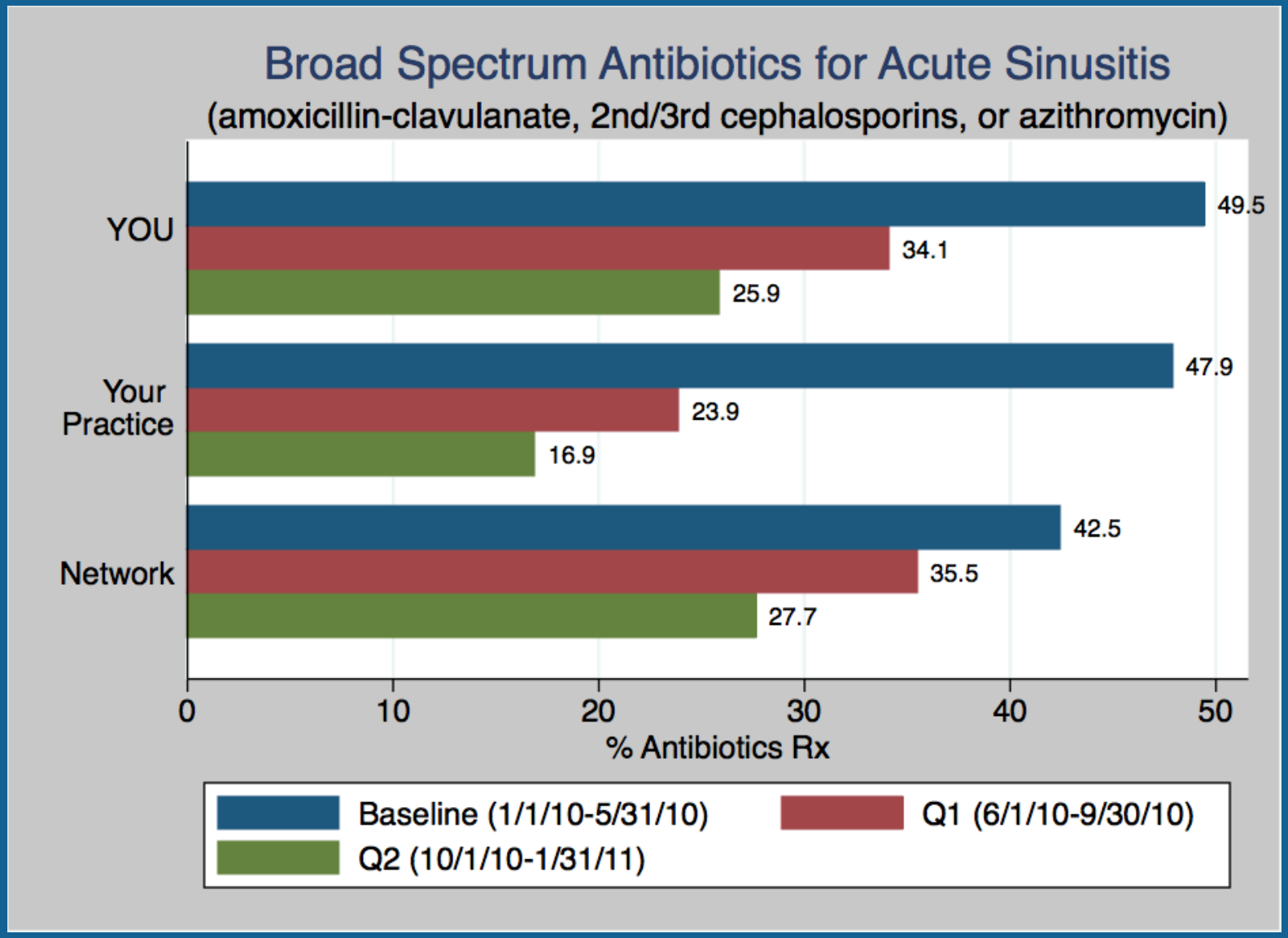

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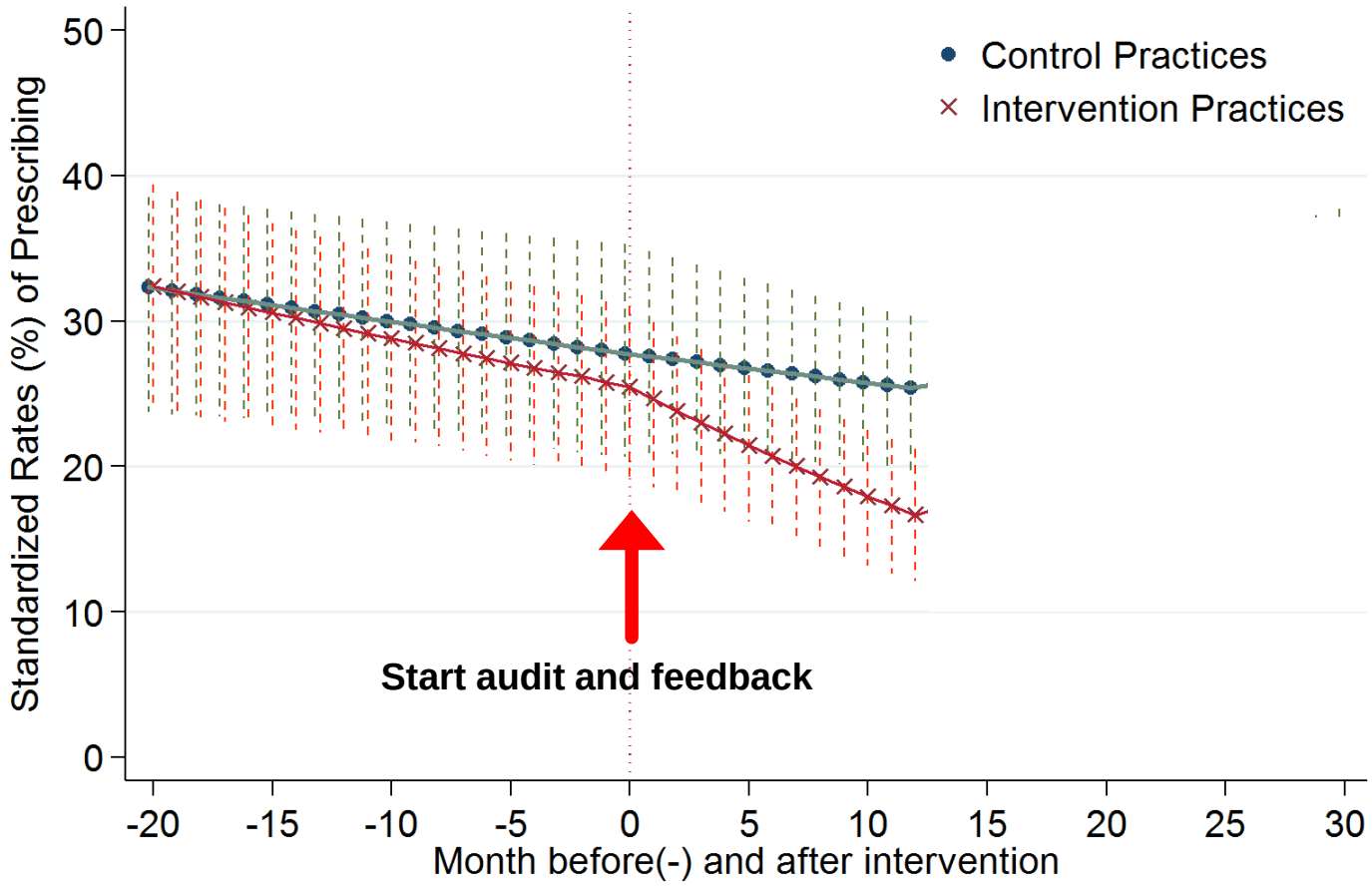

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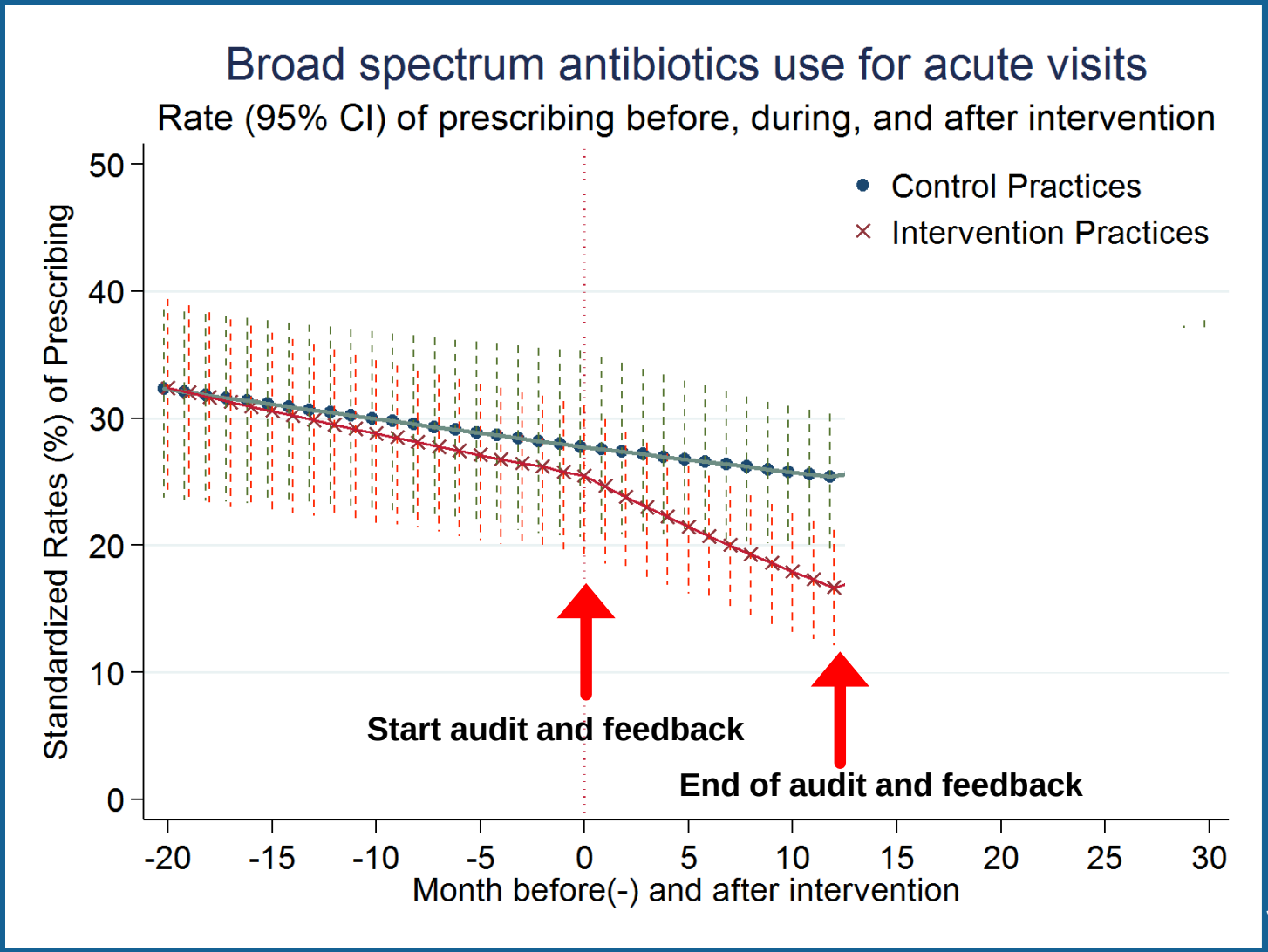
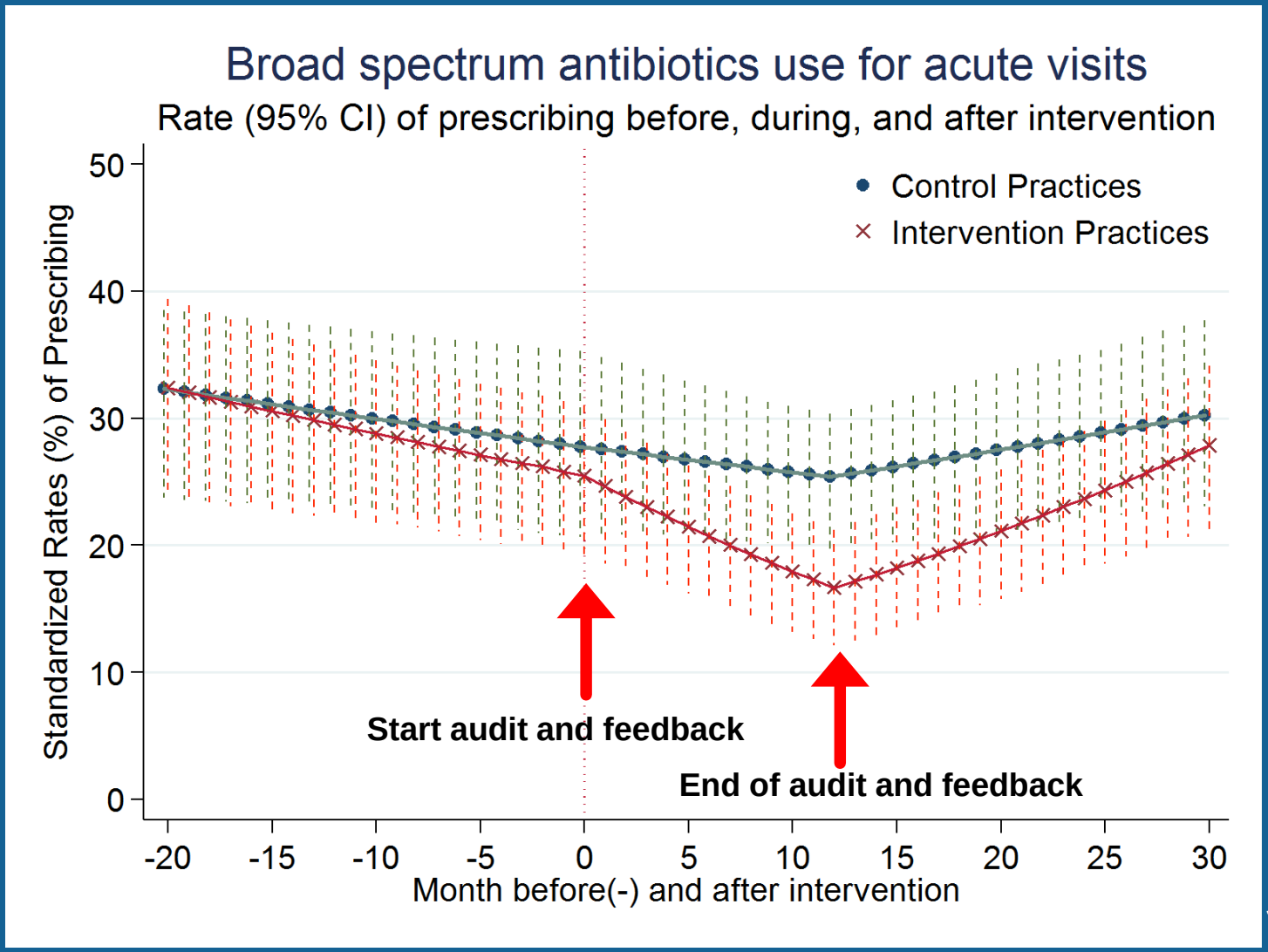


JAMA.2013;309(22):2345



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”

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

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“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.”

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

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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

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

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WHAT DO PARENTS THINK?

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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)

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

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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

Szymczak, ID Week, San Diego, 2015

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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

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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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NOVEL SOCIO-BEHAVIORAL STRATEGIES

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

Antibiotics, like penicillin, fight infections due to bacteria … but these medicines can cause side effects like skin rashes, diarrhea, or yeast infections. If your symptoms are from a virus and not from bacteria, you won't get better with an antibiotic, and you could still get these bad side effects.

Your health is very important to us. As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do more harm than good.

Table 4. Changes in Adjusted Rates[a] of Inappropriate Antibiotic Prescribing for ARIs

Characteristic	Poster Condition		Control Condition	
	Baseline	Final Measurement	Baseline	Final Measurement
Inappropriate prescribing rate, % (95% CI)	43.5 (38.5 to 49.0)	33.7 (25.1 to 43.1)	42.8 (38.1 to 48.1)	52.7 (44.2 to 61.9)
Absolute percentage change, baseline to final measurement (95% CI)	−9.8 (0.0 to −19.3)		9.9 (0.0 to 20.2)	
Difference in differences between poster condition and control (95% CI)	−19.7 (−5.8 to −33.04)[b]			

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

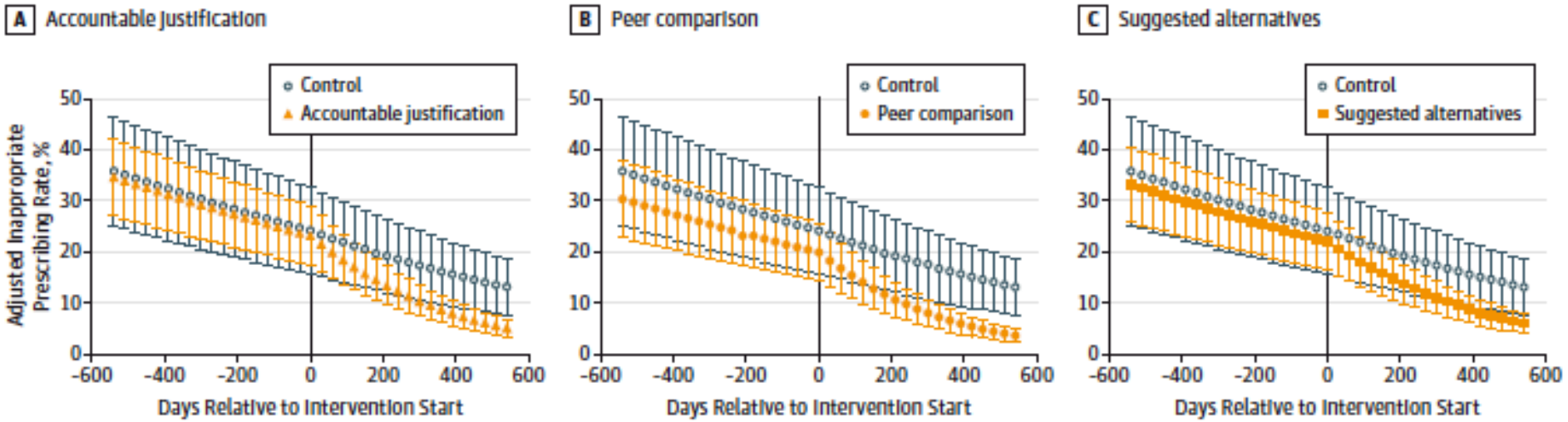
- free text, or "no justification given"

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
- Broad-spectrum antibiotics are probably not better than narrow-spectrum agents, and cause more harm
- 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

THANK YOU

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