

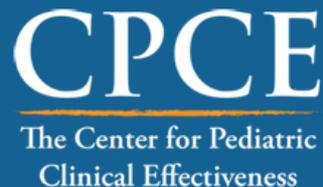


OUTPATIENT ANTIMICROBIAL STEWARDSHIP

Jeffrey S Gerber, MD, PhD

Children's Hospital of Philadelphia

University of Pennsylvania School of Medicine



DISCLOSURE STATEMENT

I have no conflicts of interest to report



LEARNING OBJECTIVES



- Explain the need for outpatient antimicrobial stewardship
- Describe outpatient antimicrobial stewardship interventions that have been effective
- Propose what is needed to further improve outpatient antibiotic prescribing





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. Schrag¹

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

- IMS Health Xponent database
- **262.5 million** antibiotic prescriptions dispensed in 2011
- 842 prescriptions per 1000 persons

Table 2. Antibiotic Courses Prescribed and Prescriptions Per Provider in 2011, by Provider Specialty

Provider Specialty	Prescriptions, No. in Millions (%)	Providers, No.	Prescriptions per Provider, Rate
All Providers	262.5	911 814	289
Persons <20 y	73.8 (29)
Persons ≥20 y	182.8 (71)
Family practice	64.1 (24)	96 073	667
Persons <20 y	12.9 (21)
Persons ≥20 y	49.7 (79)
Dermatology	8.2 (3)	11 329	724
Pediatrics	32.4 (12)	54 228	598
Otolaryngology	4.1 (2)	9536	430
Emergency medicine	13.8 (5)	32 346	427
Internal medicine/ pediatrics	1.4 (1)	3329	421
Internal medicine	32.1 (12)	83 841	383
Physician assistants	17.5 (7)	63 467	276
Infectious diseases	1.3 (1)	6166	211
Dentistry	25.6 (10)	122 706	208
Obstetrics/ gynecology	6.7 (3)	37 590	178
Nurse practitioners	19.5 (7)	109 741	178
Surgery (general)	6.9 (3)	69 536	99
Pediatric subspecialty	0.8 (<1)	8273	97
Medical subspecialty	6.9 (3)	74 424	93
Other	8.2 (3)	113 783	72
Urology	6.0 (2)	10 131	59



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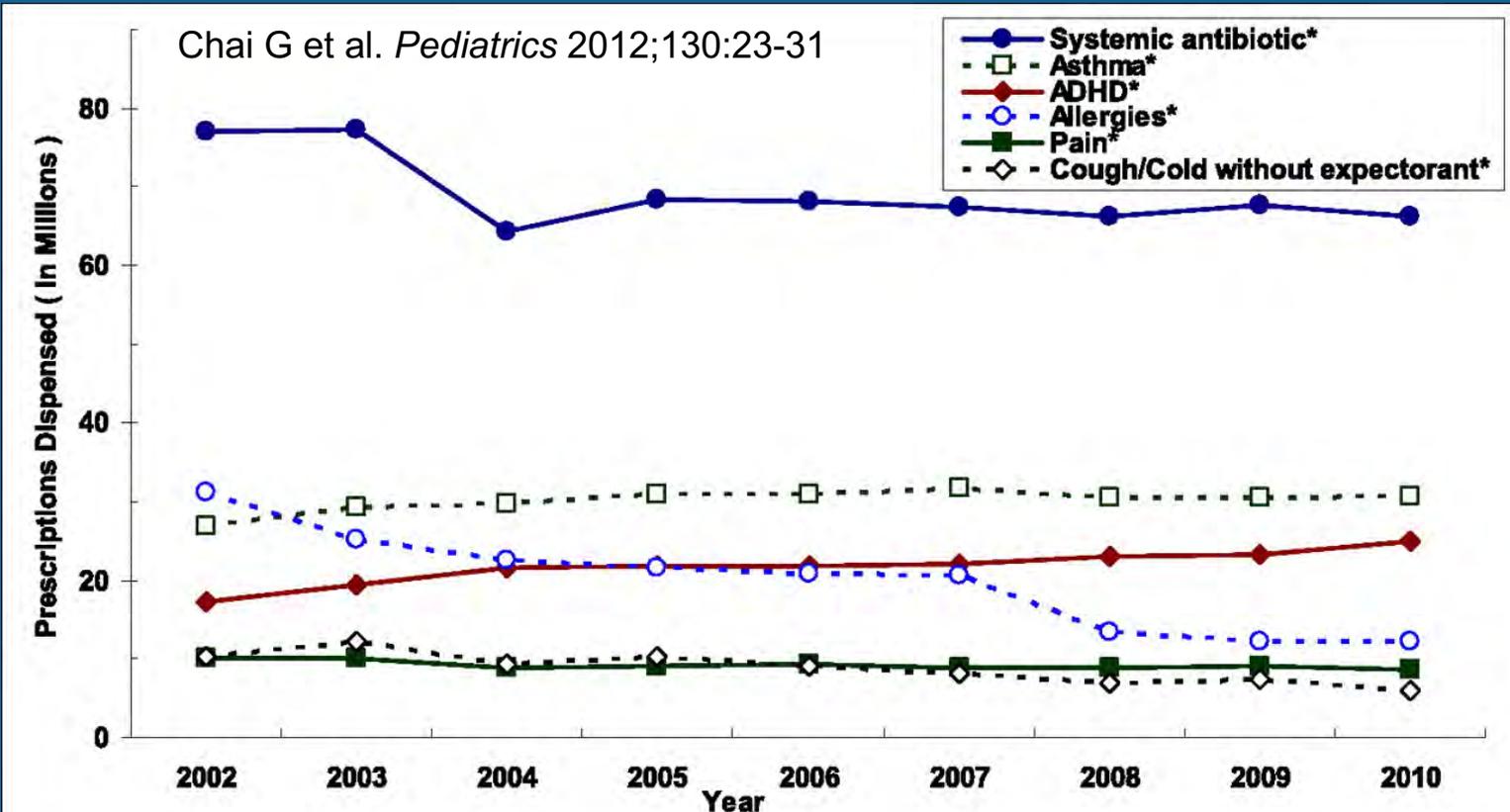


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ANTIBIOTIC USE: OUTPATIENT CHILDREN



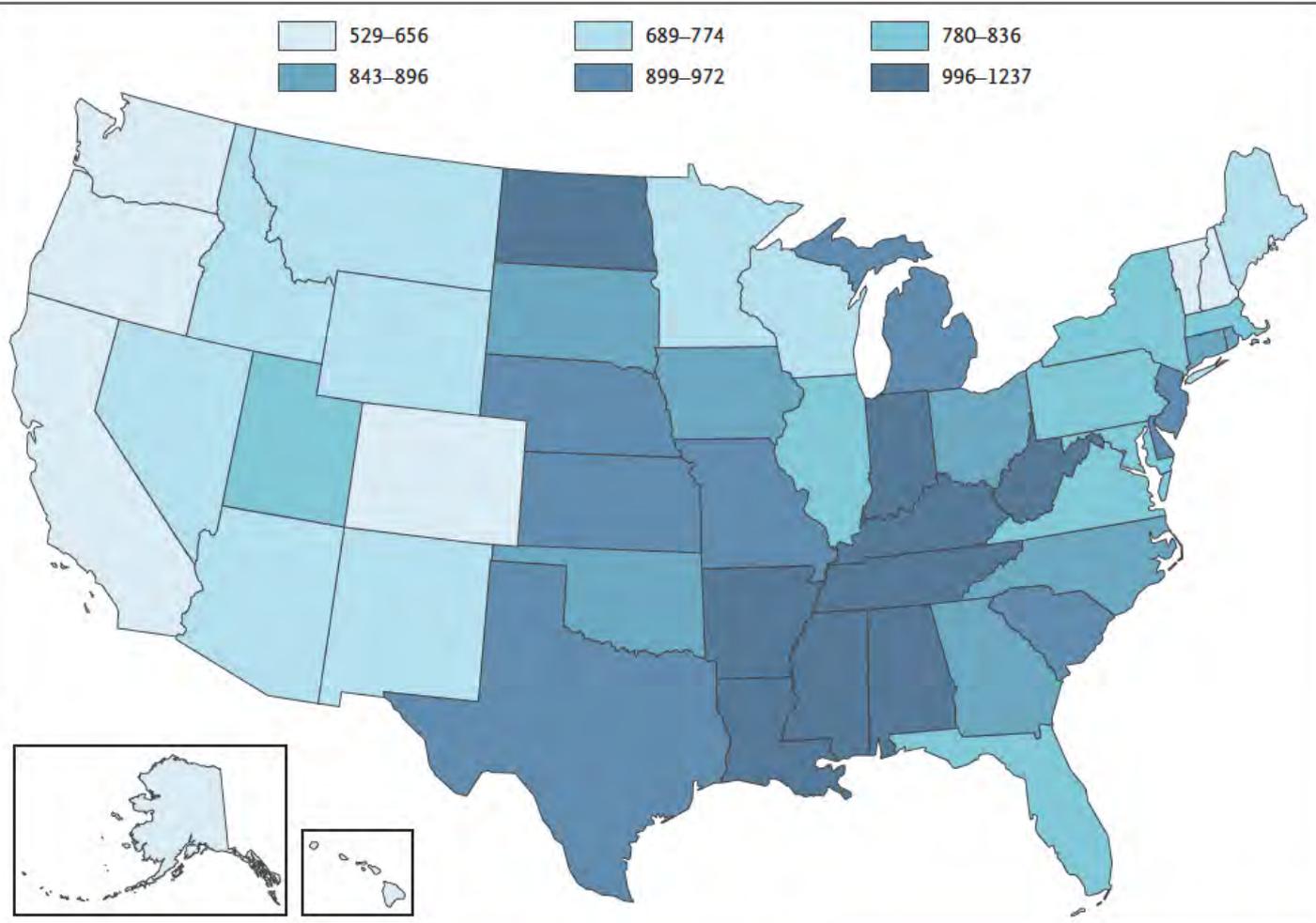


Figure 1. Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010. Hicks L et. Al. *NEJM* April 11, 2013

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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OUTPATIENT ANTIBIOTIC PRESCRIBING (Rx/1000)

Age	US	Sweden
0-2	1,365	462
3-9	1,021	414
10-19	677	252
20-39	669	296
40-64	797	339
>65	1020	556

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

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

Association Between Outpatient Antibiotic Prescribing Practices and Community-Associated *Clostridium difficile* Infection

Raymund Dantes,¹ Yi Mu,¹ Lauri A. Hicks,¹ Jessica Cohen,^{1,2} Wendy Bamberg,³ Zintars G. Beldavs,⁴ Ghinwa Dumyati,⁵ Monica M. Farley,^{6,7} Stacy Holzbauer,⁸ James Meek,⁹ Erin Phipps,¹⁰ Lucy Wilson,^{11,12} Lisa G. Winston,^{13,14} L. Clifford McDonald,¹ and Fernanda C. Lessa¹

- 32% of CDI are community-associated
- reducing antibiotic prescribing rates by 10% among persons ≥ 20 years old was associated with a 17% decrease in CDI
- reductions in prescribing penicillins and amoxicillin/clavulanate were associated with the greatest decreases in CA-CDI rates

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 ARTI





ANTIBIOTIC USE FOR ARTIs

- 21% of all ambulatory visits for children receive an antibiotic RX
- **72% for ARTI**



IS THERE ROOM FOR IMPROVEMENT?

although prescribing rate for ARTIs has declined significantly, this has been modest, and ...

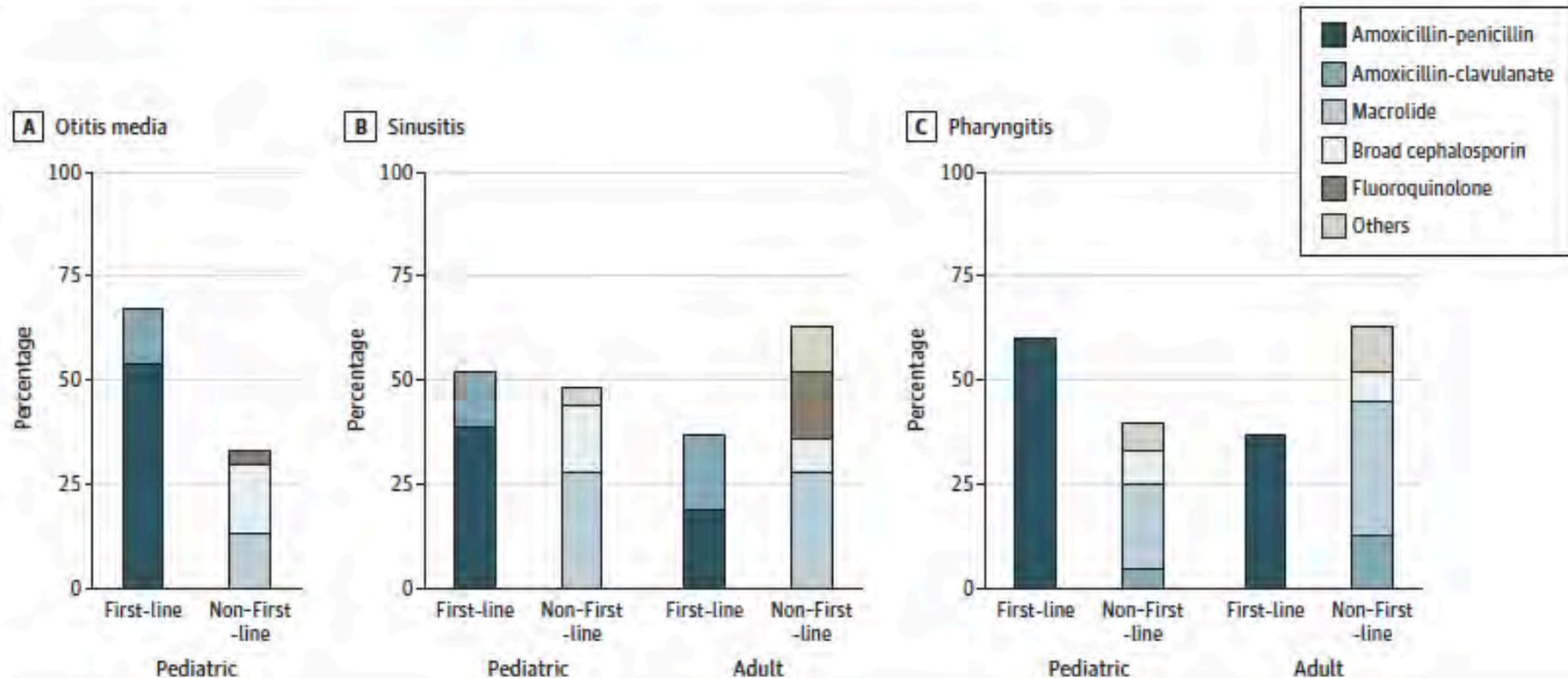
- antibiotic use for ARTIs remains common
- most are caused by viruses
- use of broader-spectrum antibiotics for ARTI has increased
- the most commonly prescribed individual antibiotic agent was **azithromycin**

Grijalva *JAMA* 2009;302(7):758-766

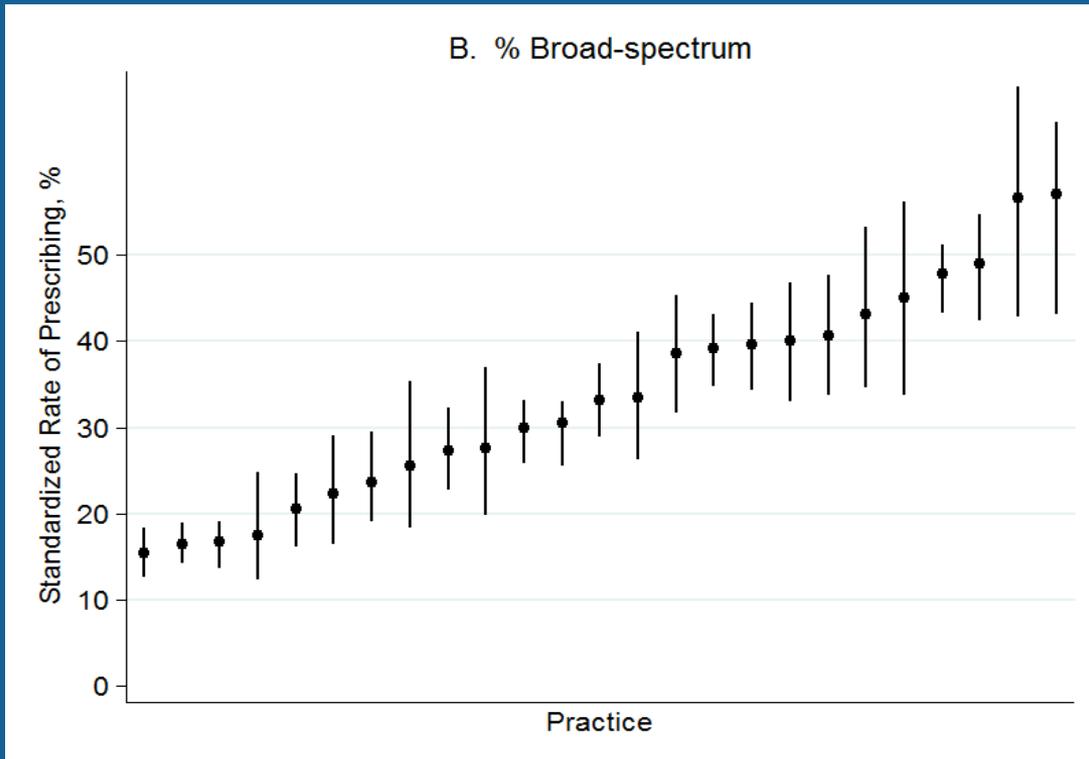
Hersh *Pediatrics* 2011;128;1053

Hicks LA et al. *NEJM* 2010;368:1461-2

Figure. Percentage of Visits in Which Antibiotics Were Prescribed That Are First-line and Non-First-line for Otitis Media, 2010-2011



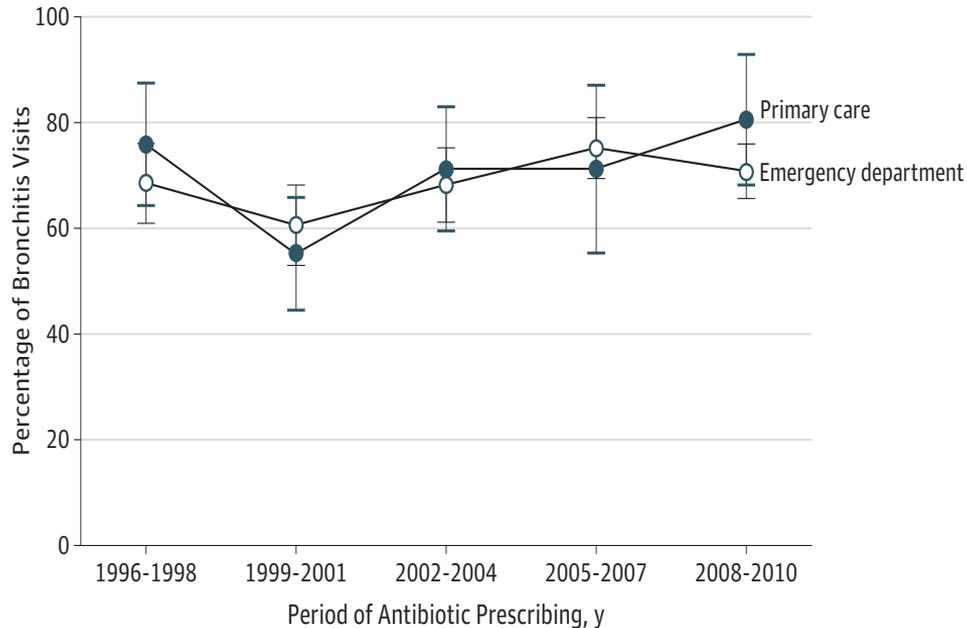
OFF-GUIDELINE ANTIBIOTIC PRESCRIBING



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

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



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

HOW CAN WE DO THIS?

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
HOSPITAL 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. Hooton¹²

- 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

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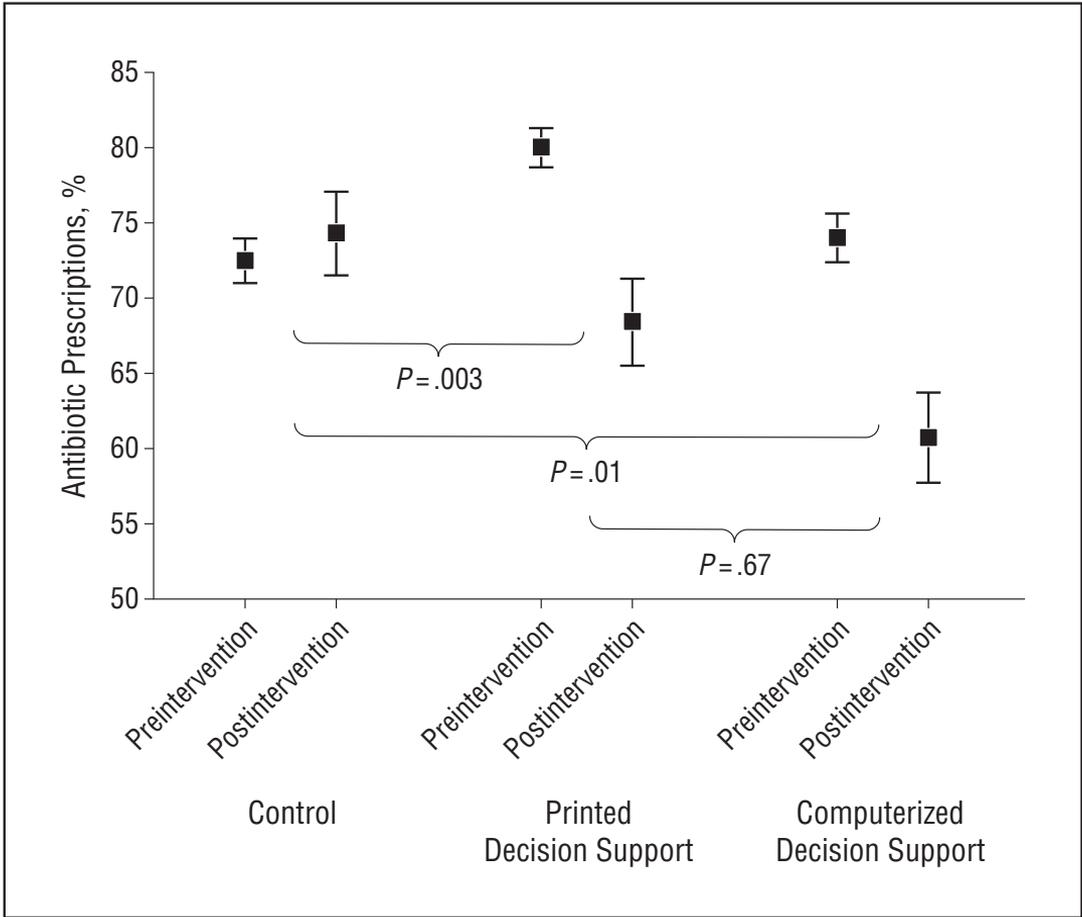
WHAT HAS BEEN DONE?

CLINICAL DECISION SUPPORT

A Cluster Randomized Trial of Decision Support Strategies for Reducing Antibiotic Use in Acute Bronchitis

Ralph Gonzales, MD, MSPH; Tammy Anderer, PhD, CRNP; Charles E. McCulloch, PhD;
Judith H. Maselli, MSPH; Frederick J. Bloom Jr, MD; Thomas R. Graf, MD; Melissa Stahl, MPH;
Michelle Yefko; Julie Molecavage; Joshua P. Metlay, MD, PhD

- **3-arm cluster RCT:** 33 primary care practices within integrated health care system
- **11 sites:** print-based decision support
- **11 sites:** computer-assisted (EHR) decision support
- both intervention sites also received clinician and patient education
- **11 control sites**



EDUCATION OF CLINICIANS AND PATIENTS

Impact of a 16-Community Trial to Promote Judicious Antibiotic Use in Massachusetts

Jonathan A. Finkelstein, MD, MPH^{a,b}, Susan S. Huang, MD, MPH^{a,c}, Ken Kleinman, ScD^a, Sheryl L. Rifas-Shiman, MPH^a, Christopher J. Stille, MD, MPH^d, James Daniel, MPH^e, Nancy Schiff, MPH^f, Ron Steingard, MD^g, Stephen B. Soumerai, ScD^a, Dennis Ross-Degnan, ScD^a, Donald Goldmann, MD^h, Richard Platt, MD^a

- cluster RCT in 16 MA communities (1998 to 2003)
- **clinician** guideline dissemination, small-group education, frequent updates and educational materials, and prescribing feedback
- **parents** received educational materials by mail and in primary care practices, pharmacies, and child care settings
- using health-plan data, measured changes in antibiotics dispensed among children aged 3 to \leq72 months

TABLE 2 Impact of Community-Level Intervention According to Age Group and Insurance Type

Parameter	Control		Intervention		Intervention Impact ^c	P
	Unadjusted Rate, Baseline Year 1 ^a	Adjusted % Change ^b	Unadjusted Rate, Baseline Year 1 ^a	Adjusted % Change ^b		
Overall						
3 to <24 mo	2.8	-20.7	2.9	-21.2	-0.5	.69
24 to <48 mo	1.7	-10.3	1.7	-14.5	-4.2	<.01
48 to <72 mo	1.4	-2.5	1.4	-9.3	-6.7	<.0001

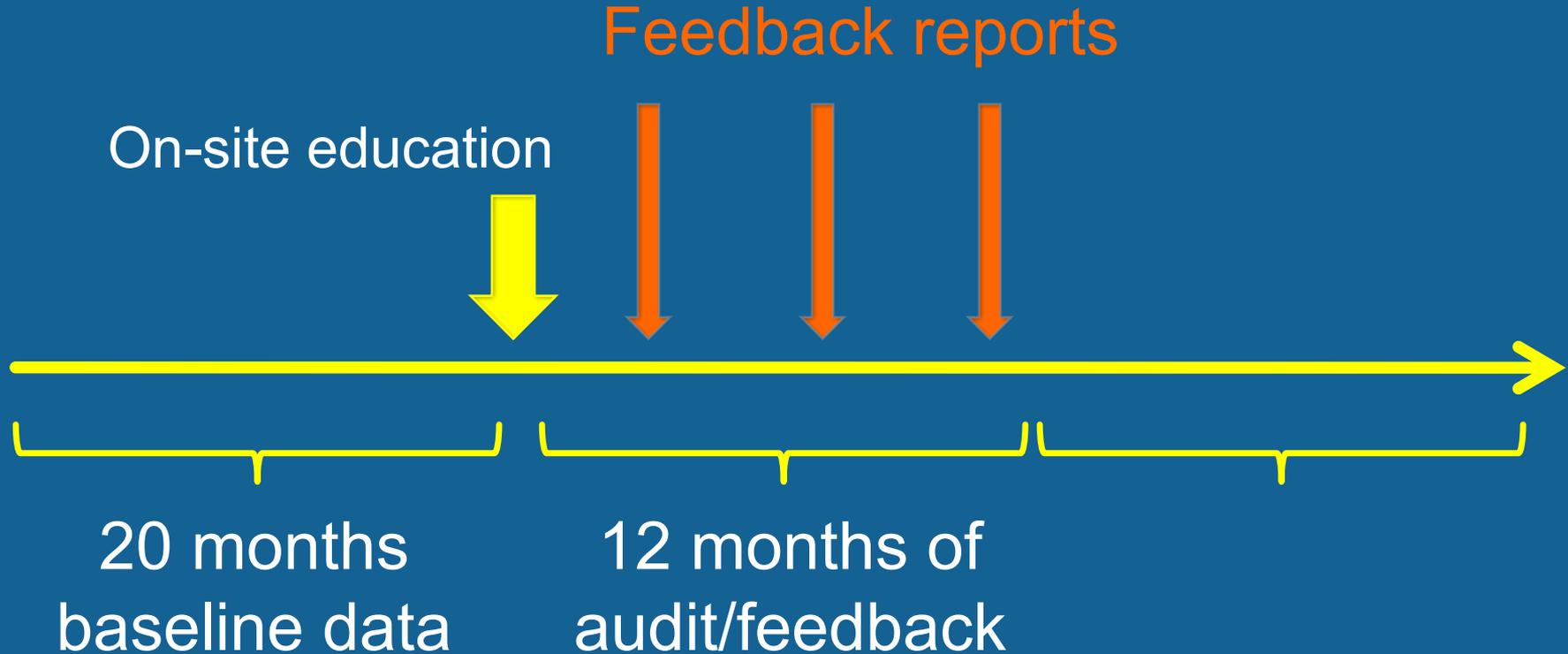
AUDIT AND FEEDBACK

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

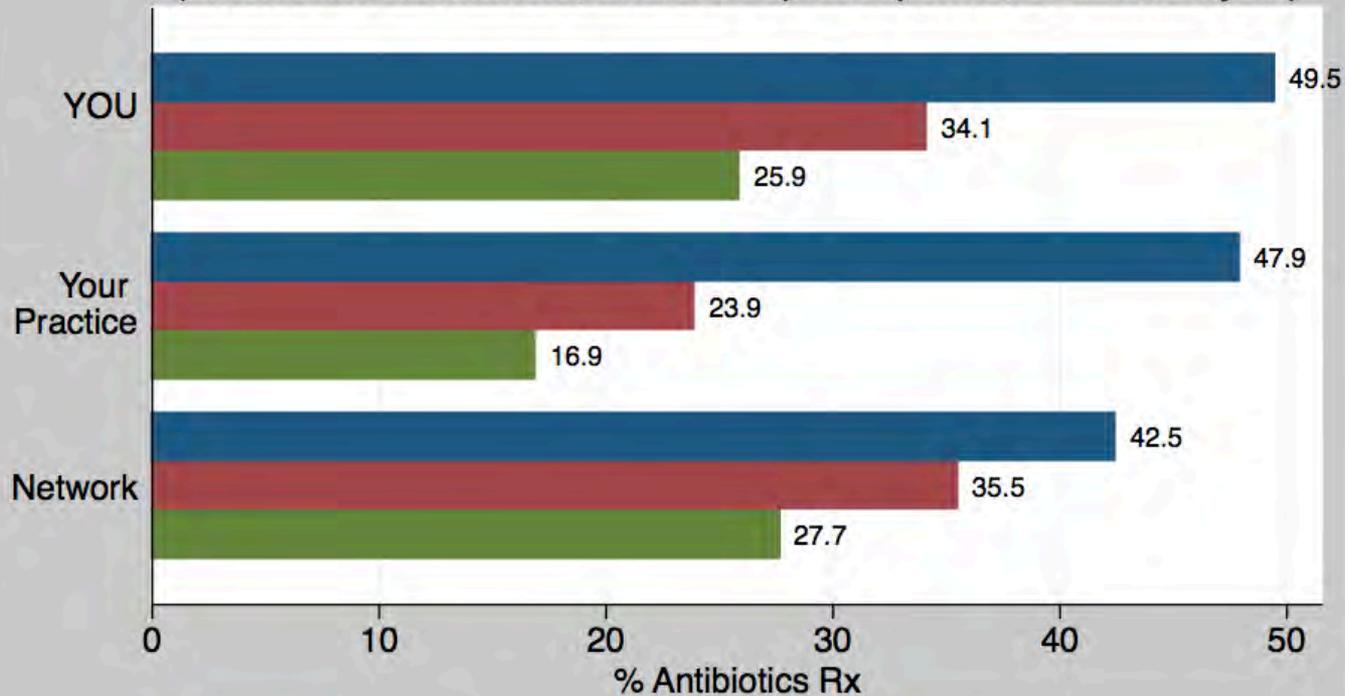
A Randomized Trial

- 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
- (all should get penicillin or amoxicillin)

INTERVENTION: TIMELINE



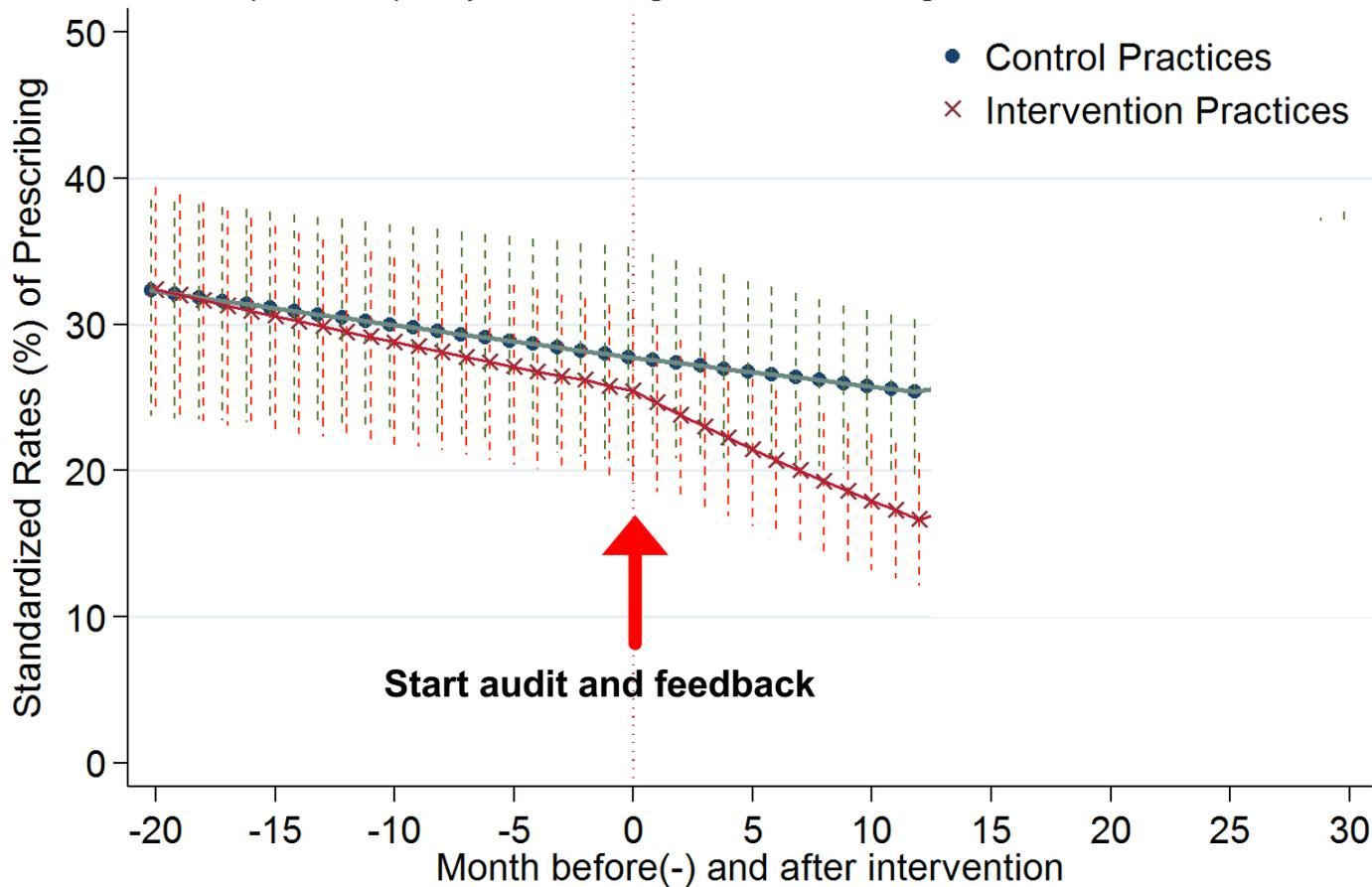
Broad Spectrum Antibiotics for Acute Sinusitis (amoxicillin-clavulanate, 2nd/3rd cephalosporins, or azithromycin)



■ Baseline (1/1/10-5/31/10) ■ Q1 (6/1/10-9/30/10)
■ Q2 (10/1/10-1/31/11)

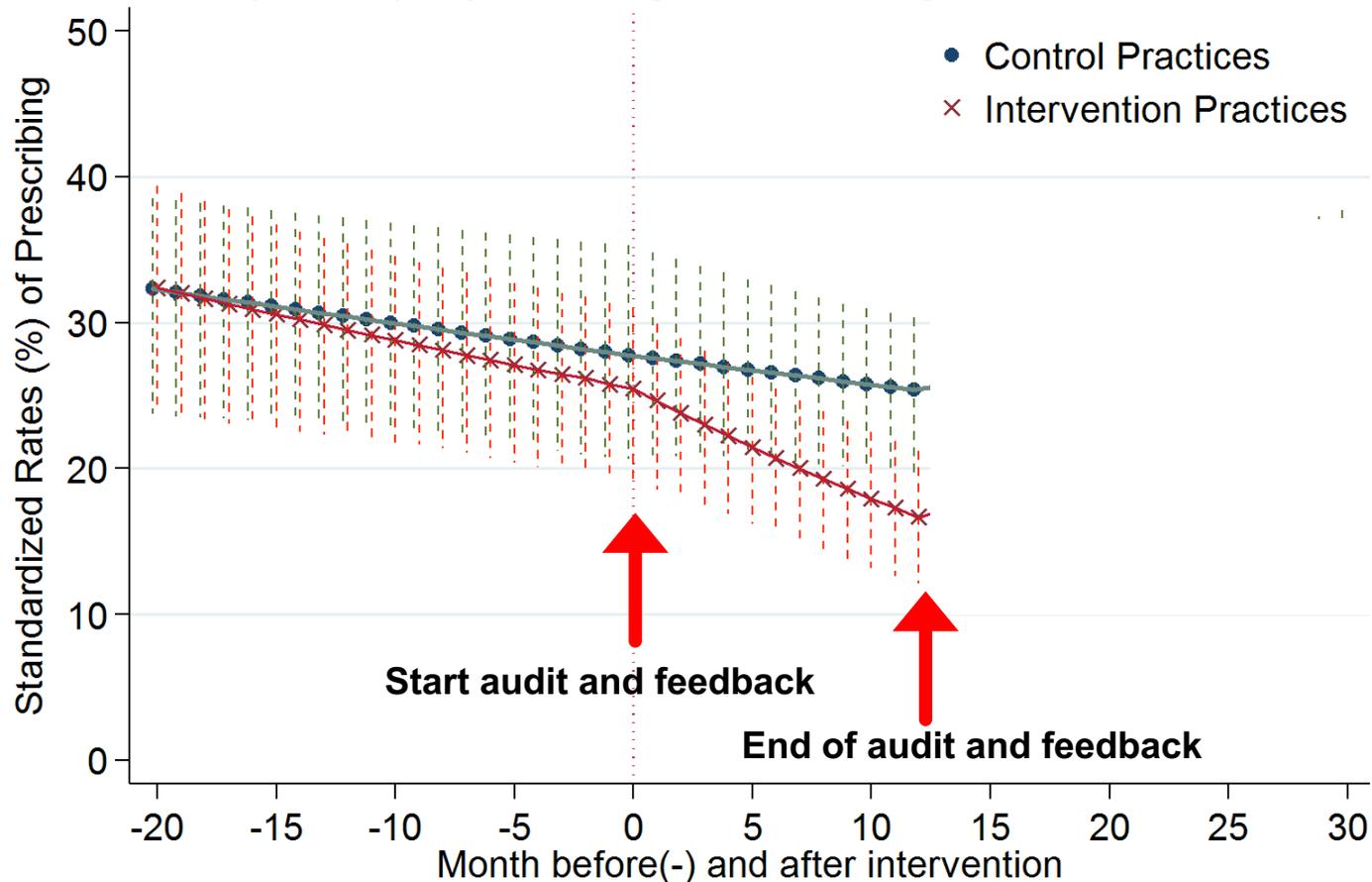
Broad spectrum antibiotics use for acute visits

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



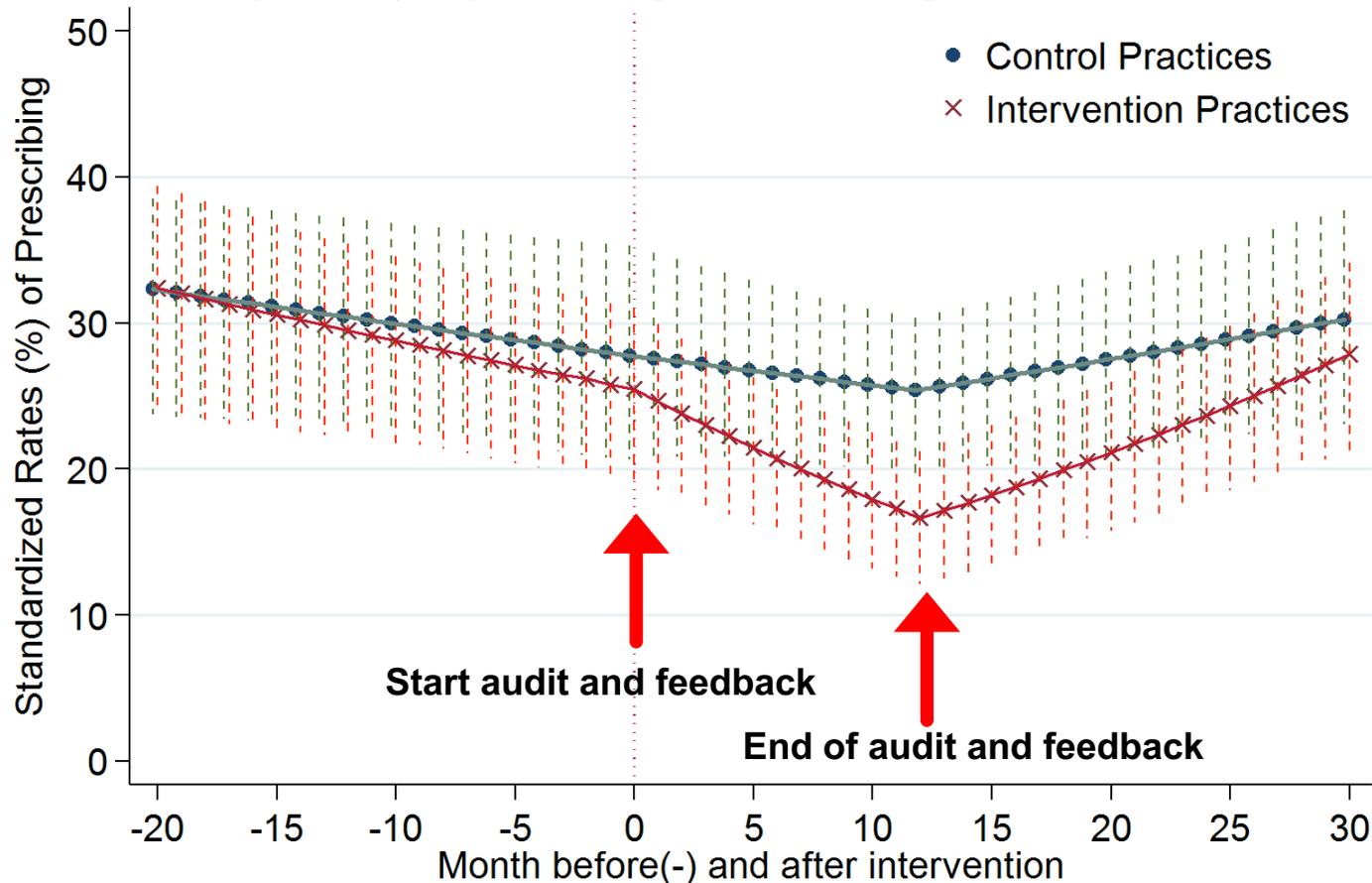
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Broad spectrum antibiotics use for acute visits

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



WHAT DO CLINICIANS THINK?



Julia Szymczak, PhD

QUALITATIVE ANALYSES

- most **did not believe** that their prescribing behavior **contributed** to antibiotic overuse
- reported frequently **confronting parental pressure**, sometimes acquiescing to:
 - appear competent
 - 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.”

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

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)

PARENT PERCEPTIONS

- survey of 1500 Massachusetts parents in 2013
 - high level of trust in physicians
- 5 focus groups (31 parents) – knowledge/attitudes surrounding antibiotic use in 2011:
 - concerned about antibiotic resistance
 - expressed desire to use antibiotics only when necessary
 - it appears that parents have become more informed and sophisticated regarding appropriate uses of antibiotics

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, contrary to what pediatricians report
 - parents are aware of the downsides of antibiotics and may be willing to partner to improve appropriate use

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

Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial

Paul Little, Beth Stuart, Nick Francis, Elaine Douglas, Sarah Tonkin-Crine, Sibyl Anthierens, Jochen W L Cals, Hasse Melbye, Miriam Santer, Michael Moore, Samuel Coenen, Chris Butler, Kerenza Hood, Mark Kelly, Maciek Godycki-Cwirko, Artur Mierzecki, Antoni Torres, Carl Llor, Melanie Davies, Mark Mullee, Gilly O'Reilly, Alike van der Velden, Adam W A Geraghty, Herman Goossens, Theo Verheij, Lucy Yardley, on behalf of the GRACE consortium

- 246 practices, 4264 patients, 6 European countries
- training in enhanced communication skills:
 - gathering information on patient concerns/expectations
 - exchange of information on symptoms, natural disease course
 - Tx; agreement of a management plan
- **communication training led to a >30% reduction in antibiotic prescribing for ARTI**

NON-CLINICAL DRIVERS OF ANTIBIOTIC PRESCRIBING?

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

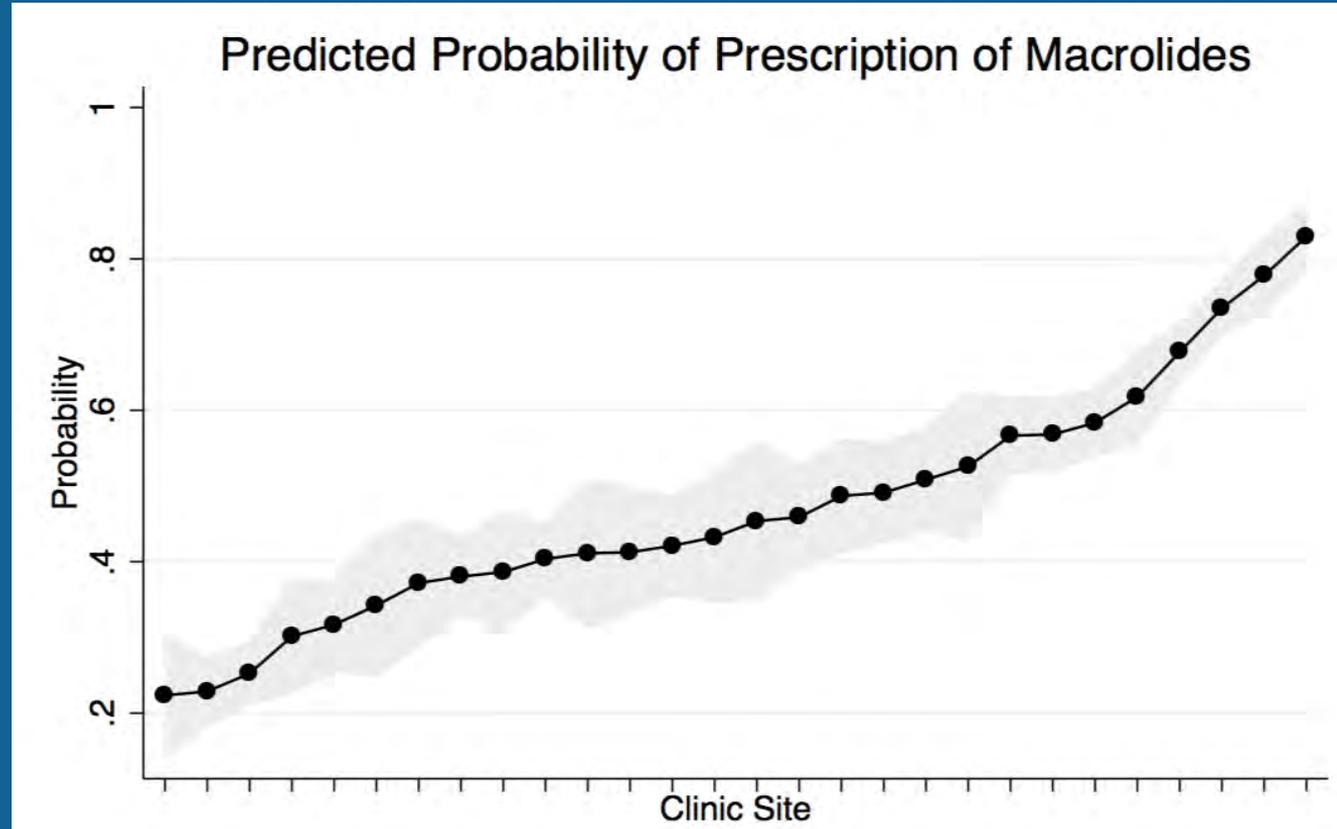
Roumie CL et al., Am J Med. 2005;118(6):614-648

Linder, JAMA Internal Medicine 2014;174(12)

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

Handy LK, ID Week 2015

- 10,414 children Dx with pneumonia
- 30 practices
- 41% amoxicillin
- 43% azithromycin



HUMAN BEHAVIOR AND PRESCRIBING

- behavioral determinants and social norms influence antibiotic prescribing
- therefore, different levers that shape clinician behavior need to be considered at the point of care, where the decision to prescribe is made



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

- QI interventions often neglect psychosocial and professional factors that may affect clinical decisions
- 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.***

*Antibiotics also make bacteria more resistant to them. This can make future infections harder to treat. This means that **antibiotics might not work when you really need them.** Because of this, it is important that you only use an antibiotic when it is necessary ...*

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			

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”

INTERVENTION 3: PEER COMPARISON

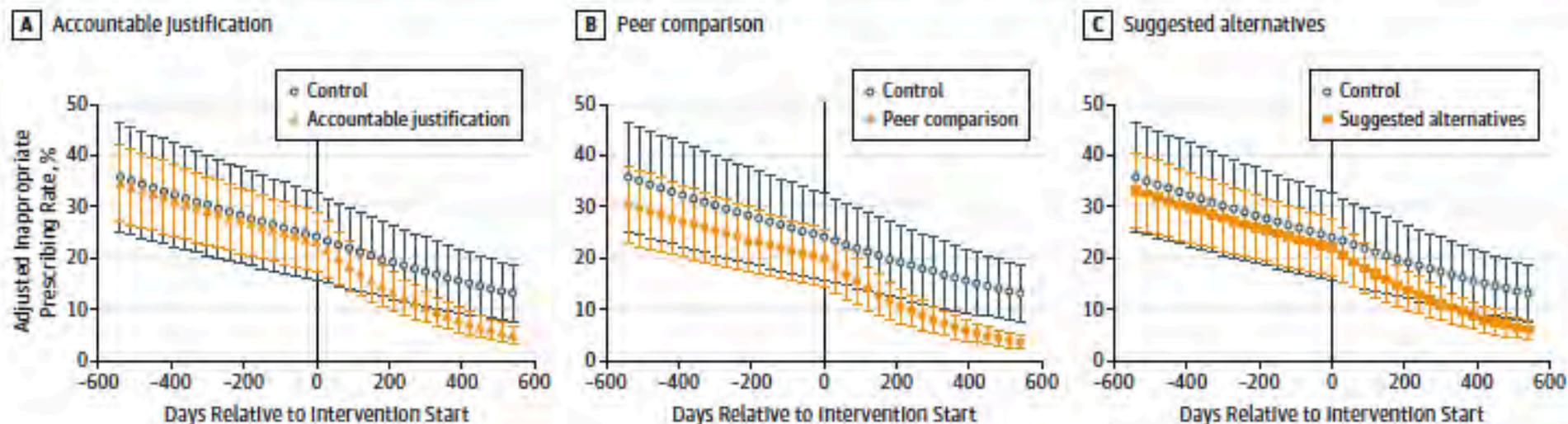
“You are a Top Performer”

You are in the top 10% of clinicians. You wrote 0 prescriptions out of 21 acute respiratory infection cases that did not warrant antibiotics.

“You are not a Top Performer”

Your inappropriate antibiotic prescribing rate is 15%. Top performers' rate is 0%. You wrote 3 prescriptions out of 20 acute respiratory infection cases that did not warrant antibiotics.

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 has only slightly improved in certain areas over time
- many investigators and public health entities have implemented promising strategies to improve use, such as education, audit with feedback, and decision support
- socio-behavioral approaches, such as improving communication and holding clinicians accountable can also be effective

WHAT WE NEED

- Widespread implementation of the approaches we already have
- mechanism for tracking antibiotic use for benchmarking/feedback
 - overall antibiotic use; by condition/setting to identify targets
 - antibiotic choice (FQ, macrolides, 3rd ceph)
- additional targets:
 - duration of Tx (UTI, CAP, AOM)
 - hospital discharge (OPAT, oral)
 - Emergency Department
 - ambulatory surgery

THANK YOU

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Get Smart
About
Antibiotics Week
November 14–20, 2016

**GET
SMART**
Know When Antibiotics Work

www.cdc.gov/getsmart

The image is a promotional graphic for Antibiotics Week. It features a central logo with the text 'GET SMART' in large, bold, blue letters. Below this, the tagline 'Know When Antibiotics Work' is written in a smaller, blue font. To the right of the 'GET SMART' text is a cartoon owl wearing glasses and a white lab coat with a stethoscope, representing a doctor. A yellow speech bubble with a blue outline emanates from the owl, containing the text 'Get Smart About Antibiotics Week November 14–20, 2016'. At the bottom of the graphic, the website address 'www.cdc.gov/getsmart' is displayed in a blue, sans-serif font.