Outpatient Antimicrobial Stewardship

Friday, March 31, 2023

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Monroe Carell Jr.
Children's Hospital
at Vanderbilt

Disclosures

- Research grant from Pfizer (rural antimicrobial tele-stewardship)
- Consultant for Optum (surveillance for biologic products)

Objectives

1. Discuss the rising prevalence of antibiotic-resistant pathogens and increasing awareness of antibiotic-associated adverse events

2. Describe the factors that drive inappropriate antibiotic use in the outpatient setting

3. List strategies for optimizing antibiotic use in the outpatient setting

Outline

1. **Why should we care?**
   - Discuss the rising prevalence of antibiotic-resistant pathogens and increasing awareness of antibiotic-associated adverse events

2. **What's causing the problem?**
   - Describe the factors that drive inappropriate antibiotic use in the outpatient setting

3. **What can we do about it?**
   - List strategies for optimizing antibiotic use in the outpatient setting

Why Should We Care?

Discuss the rising prevalence of antibiotic-resistant pathogens and increasing awareness of antibiotic-associated adverse events

Case

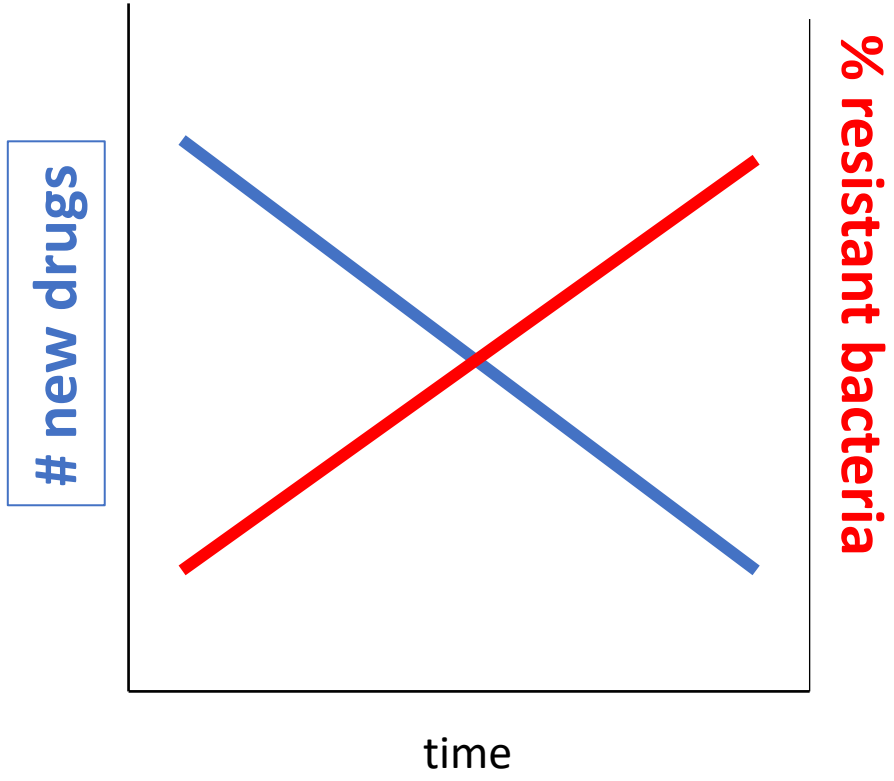
- Previously healthy, 22-month-old female presents to clinic with 5 days of yellow discharge from a nasal dermoid cyst. Low-grade fever, but otherwise well-appearing.

- Wound culture + for *E. coli*

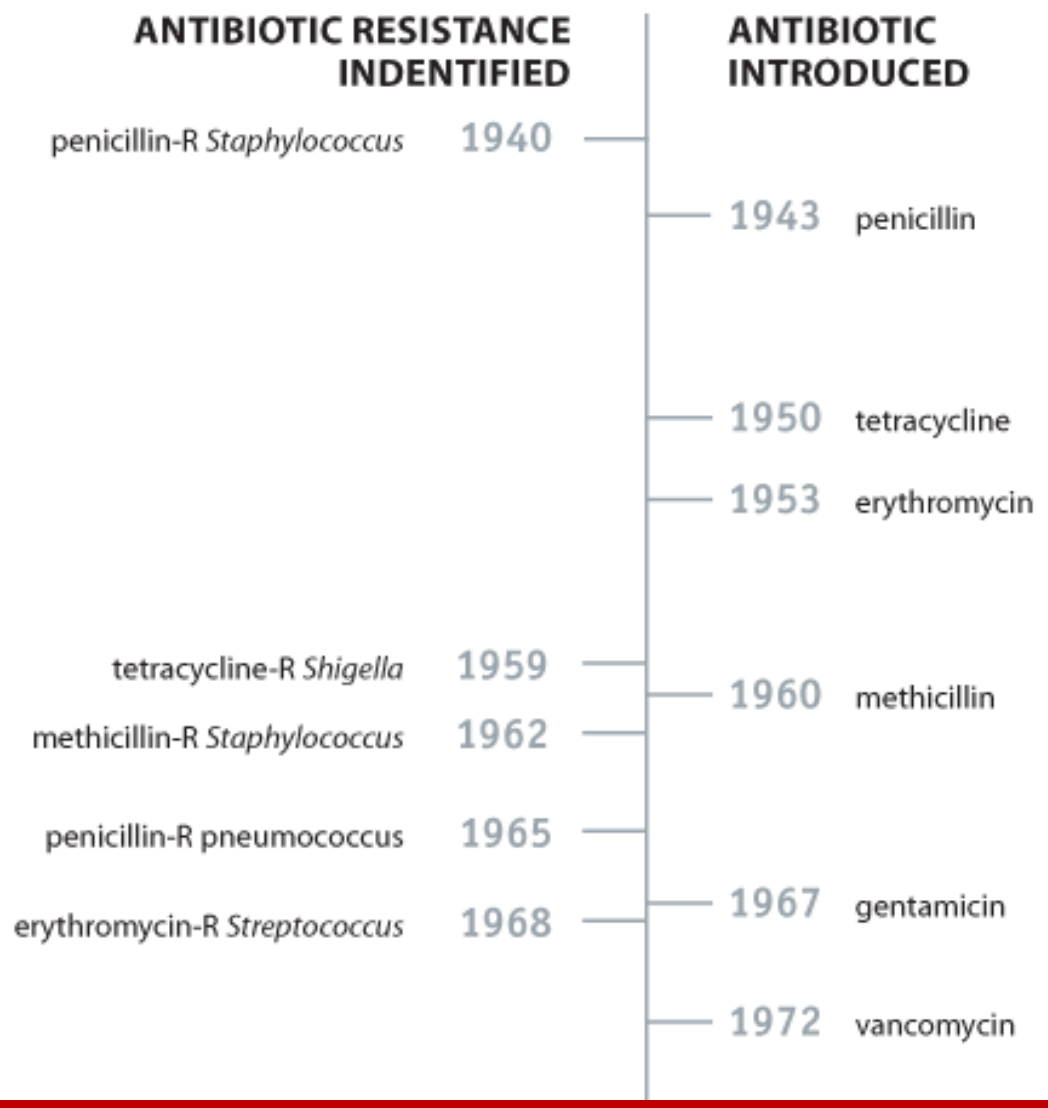
- What antibiotic do you start?

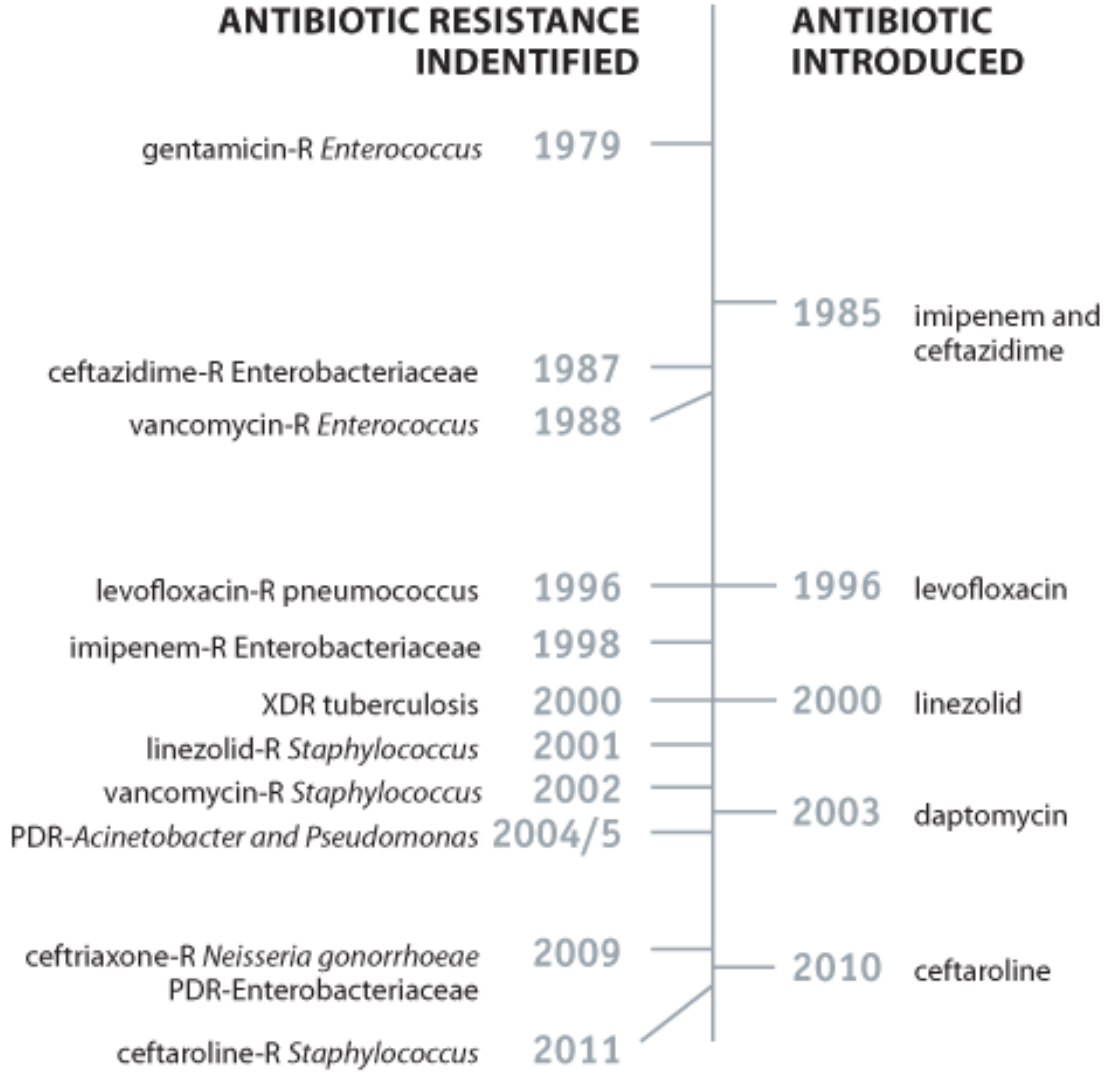
	Escherichia coli MIC	
Amikacin	<=8	Susceptible
Amoxicillin/Clavulanate	8/4	Resistant
Ampicillin	>16	Resistant
Aztreonam	16	Resistant
Cefazolin	>16	Resistant
Cefepime	8	Resistant
Ceftriaxone	>32	Resistant
Ciprofloxacin	>2	Resistant
Gentamicin	<=2	Susceptible
Levofloxacin	>4	Resistant
Piperacillin/Tazobactam	4/4	Susceptible
Tetracycline	>8	Resistant
Tobramycin	<=2	Susceptible
Trimethoprim/Sulfa	>2/38	Resistant

The Problem



The Problem


ANTIBIOTIC RESISTANCE INDENTIFIED
ANTIBIOTIC INTRODUCED
penicillin-R *Staphylococcus* 1940
1943 penicillin
1950 tetracycline
1953 erythromycin
tetracycline-R *Shigella* 1959
1960 methicillin
methicillin-R *Staphylococcus* 1962
penicillin-R pneumococcus 1965
erythromycin-R *Streptococcus* 1968
1967 gentamicin
1972 vancomycin


ANTIBIOTIC RESISTANCE INDENTIFIED
ANTIBIOTIC INTRODUCED
gentamicin-R *Enterococcus* 1979
1985 imipenem and ceftazidime
ceftazidime-R Enterobacteriaceae 1987
vancomycin-R *Enterococcus* 1988
levofloxacin-R pneumococcus 1996
1996 levofloxacin
imipenem-R Enterobacteriaceae 1998
XDR tuberculosis 2000
2000 linezolid
linezolid-R *Staphylococcus* 2001
vancomycin-R *Staphylococcus* 2002
2003 daptomycin
PDR-*Acinetobacter and Pseudomonas* 2004/5
ceftriaxone-R *Neisseria gonorrhoeae* 2009
PDR-Enterobacteriaceae
2010 ceftaroline
ceftaroline-R *Staphylococcus* 2011

CDC Antibiotic Resistance Threats Report, 2019

- Carbapenem-resistant Enterobacteriaceae (CRE)
- *Candida auris*
- *C. difficile*
- *Neisseria gonorrhea*
- *Acinetobacter*
- *Campylobacter*
- ESBL-producing Enterobacteriales
- Erythromycin-resistant GAS
- *Pseudomonas*
- *Salmonella* (typhi and non-typhi)
- *Shigella*
- *Candida*
- Tuberculosis
- VRE
- MRSA
- *S. pneumoniae*
- Clindamycin-resistant GBS

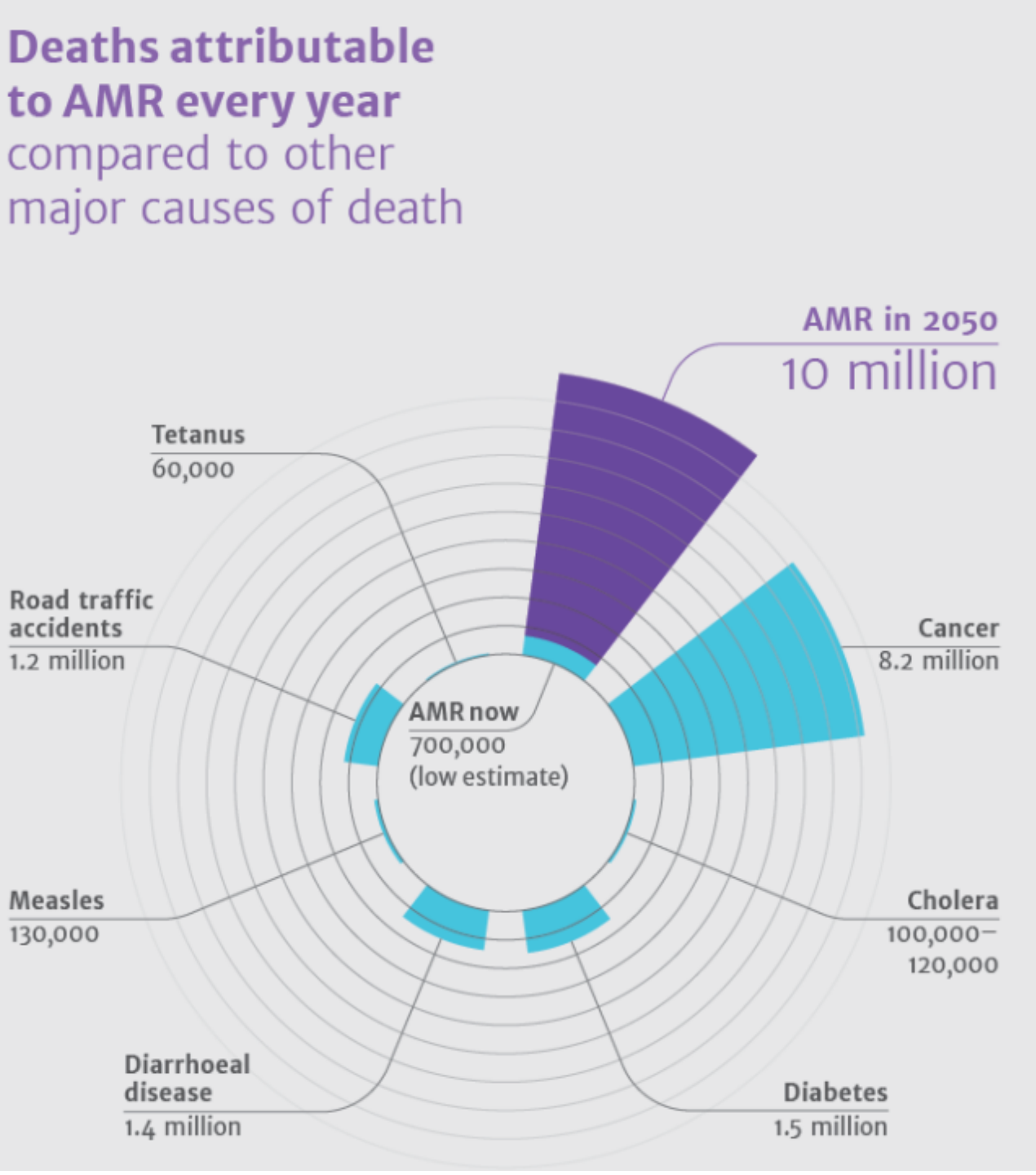
CDC, Antibiotic Resistance Threats in the US, 2019

Pre-antibiotic era?

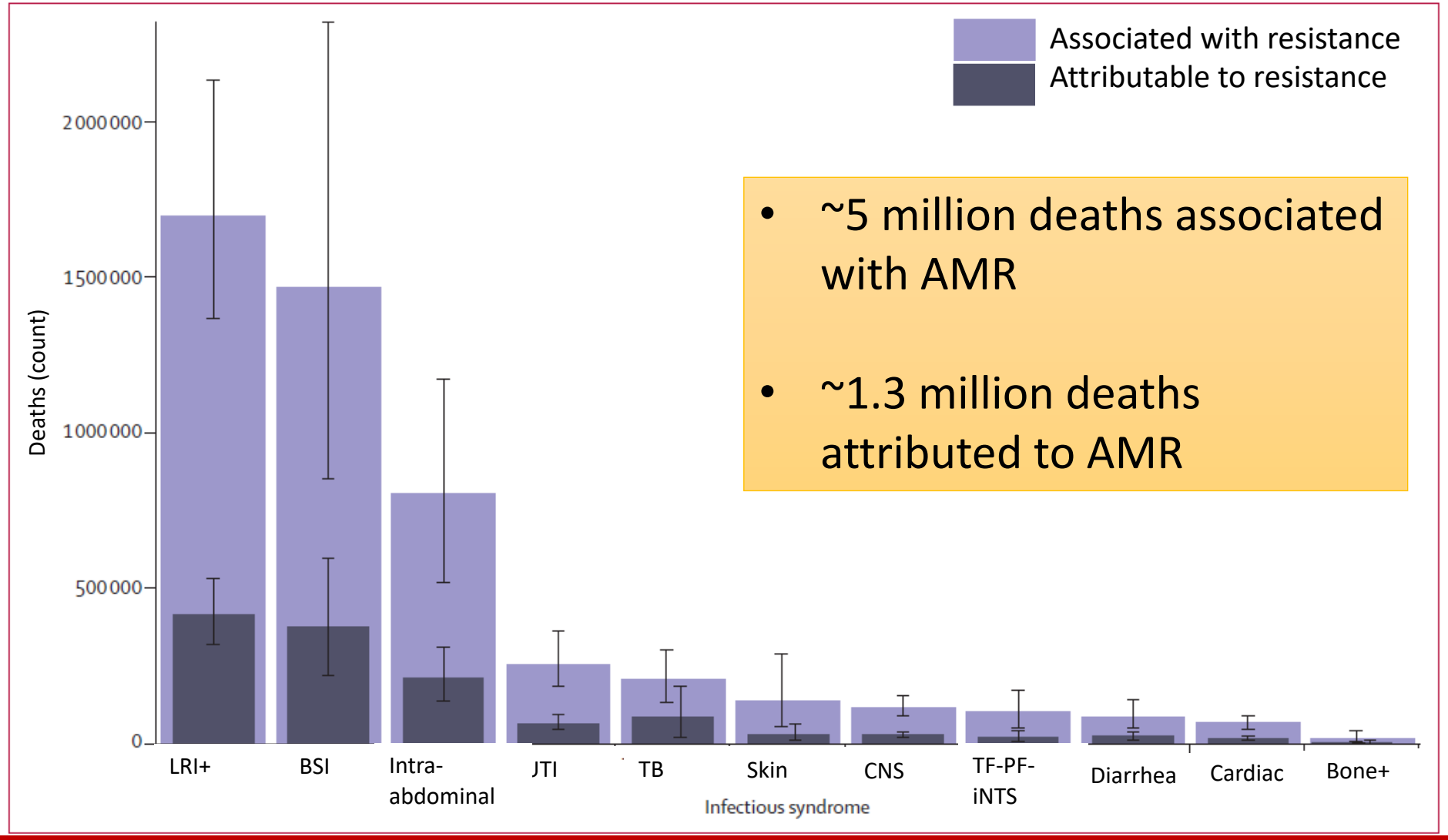
Antimicrobial resistant infections

- High morbidity/mortality
- Sicken 3 million people/yr in US
- $20-35 billion/yr in US
- >8 million add'l hospital days/yr
- 10 million deaths/year by 2050

CDC, Antibiotic Resistance Threats in the US, 2019
Review on Antimicrobial Resistance, chaired by Jim O'Neill, 2014



Global deaths from antimicrobial-resistant bacteria, 2019



- ~5 million deaths associated with AMR
- ~1.3 million deaths attributed to AMR

Lancet, 2022

Alexander Fleming

Antimicrobial misuse

"…the ignorant man may easily underdose himself and by exposing microbes to non-lethal quantities of the drug make them resistant." (1945)

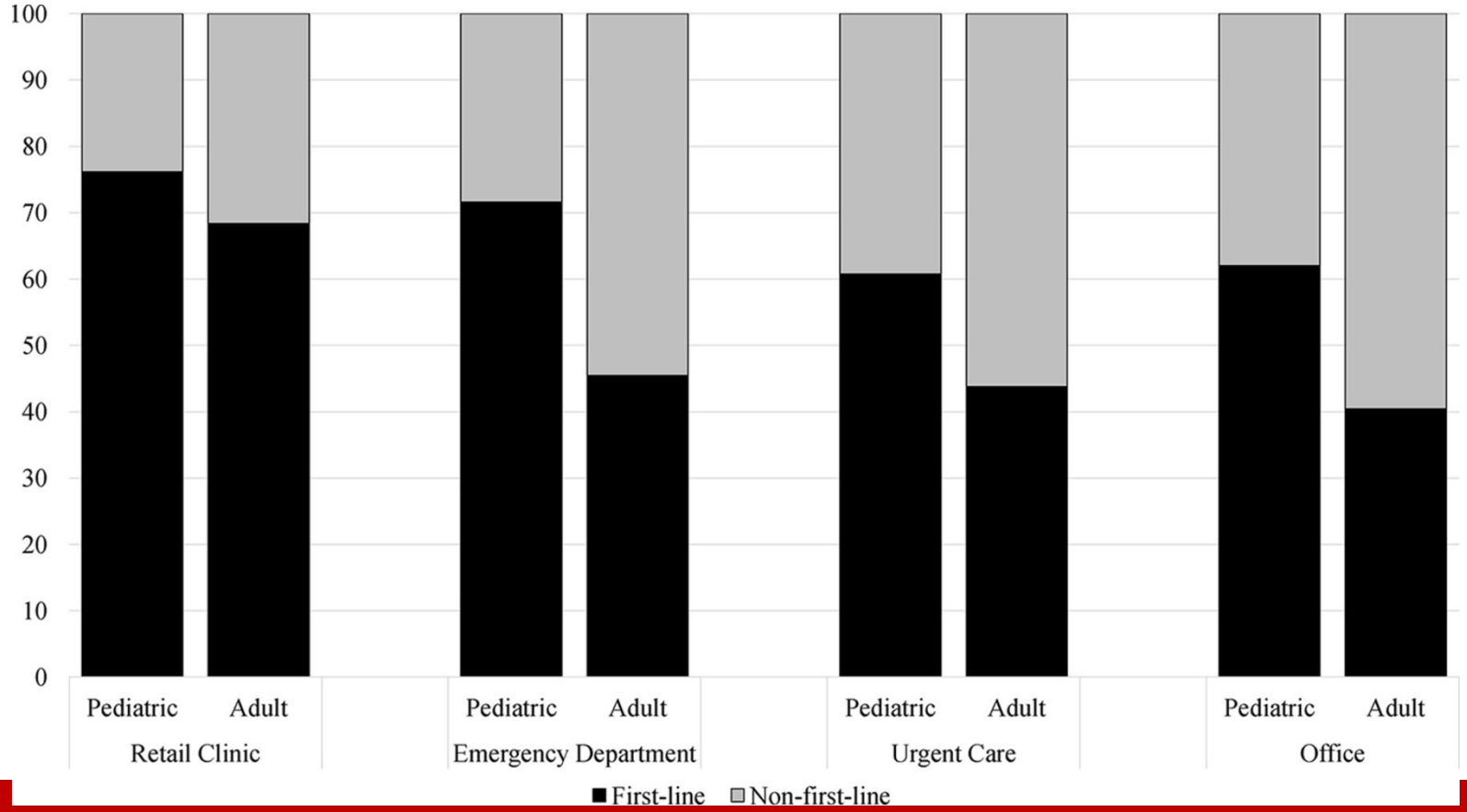
Antibiotic Use in the Outpatient Setting

- The majority (>60%) of antibiotic expenditures are associated with the outpatient setting.[1]
- An estimated 80-90% of the volume of human antibiotic use occurs in the outpatient setting.[2,3]
- 20% of pediatric outpatient visits per year result in an antibiotic prescription.[4]
- 28% of outpatient antibiotic prescriptions are unnecessary.[5]
  - 19% in children

1. Suda et al, *J Antimicrob Chemother*, 2013.
2. Public Health England, 2014.
3. Public Health Agency of Sweden, 2015.
4. Hersh AL et al, *Pediatrics*, 2011.
5. Hersh AL et al, *CID*, 2021.

Outpatient Antibiotic Appropriateness

First-line prescribing



- 2014 IBM MarketScan commercial database
- Overall, 50% of visits for pharyngitis, sinusitis and acute otitis media received first-line therapy

Palms DL et al. *Antimicrob Agents Chemother*, 2019

Antimicrobial use: U.S. ambulatory visits

30% of outpatient oral antibiotic prescriptions for adults and children in the US are inappropriate

Pharyngitis in children
30% caused by bacteria
60% receive antibiotics

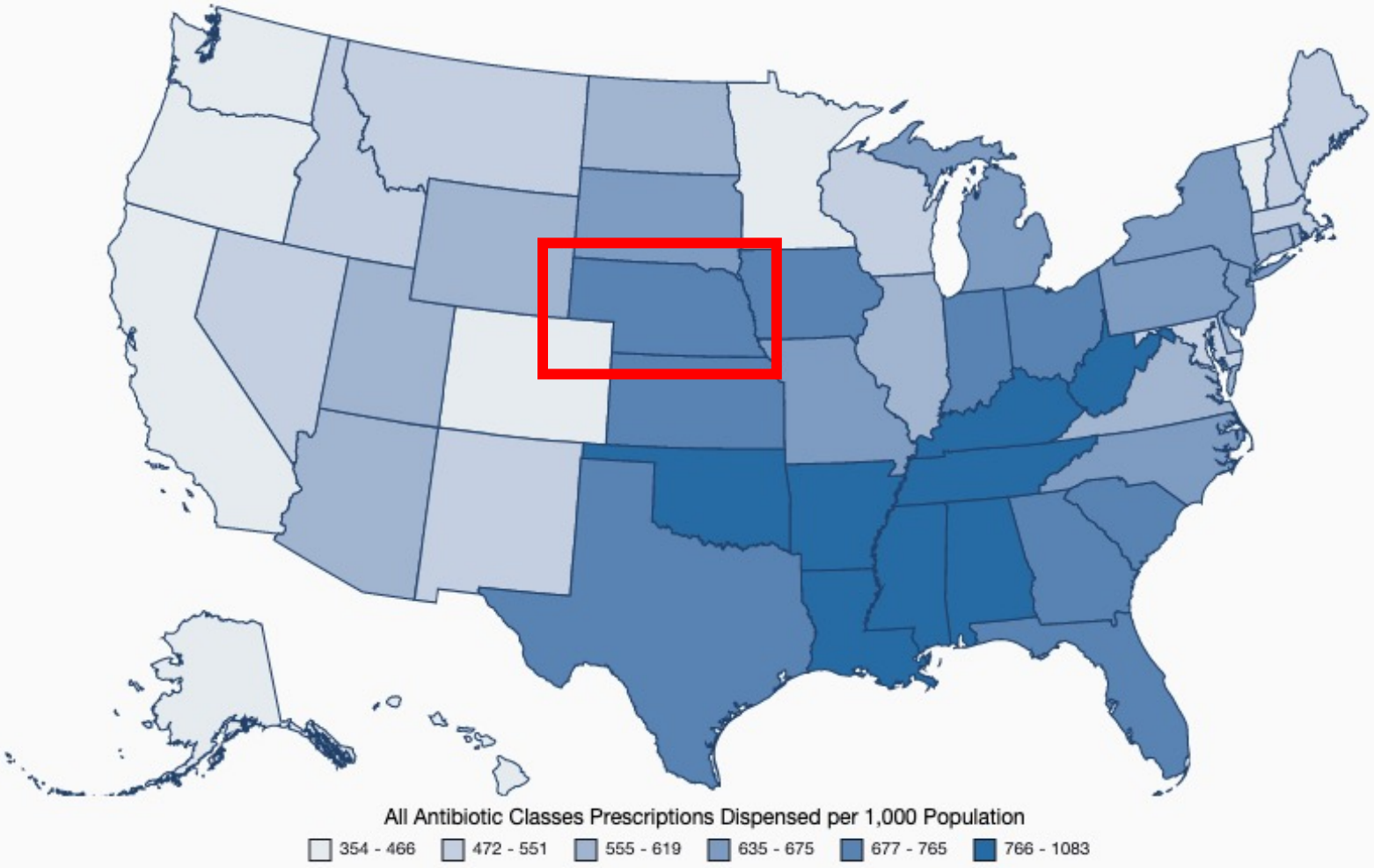
Fleming Dutra, JAMA, 2016, 315: 1864
Dooling et.al., JAMA Pediatrics 2014, 168: 1073

Antibiotic use in the U.S. 2021

Nebraska rate:
760 per 1000 population

National rate:
636 per 1000 population

Community Antibiotic Prescriptions per 1,000 Population by State - 2021



Centers for Disease Control

Antibiotics Cause Collateral Damage

Abx-Associated Toxicities

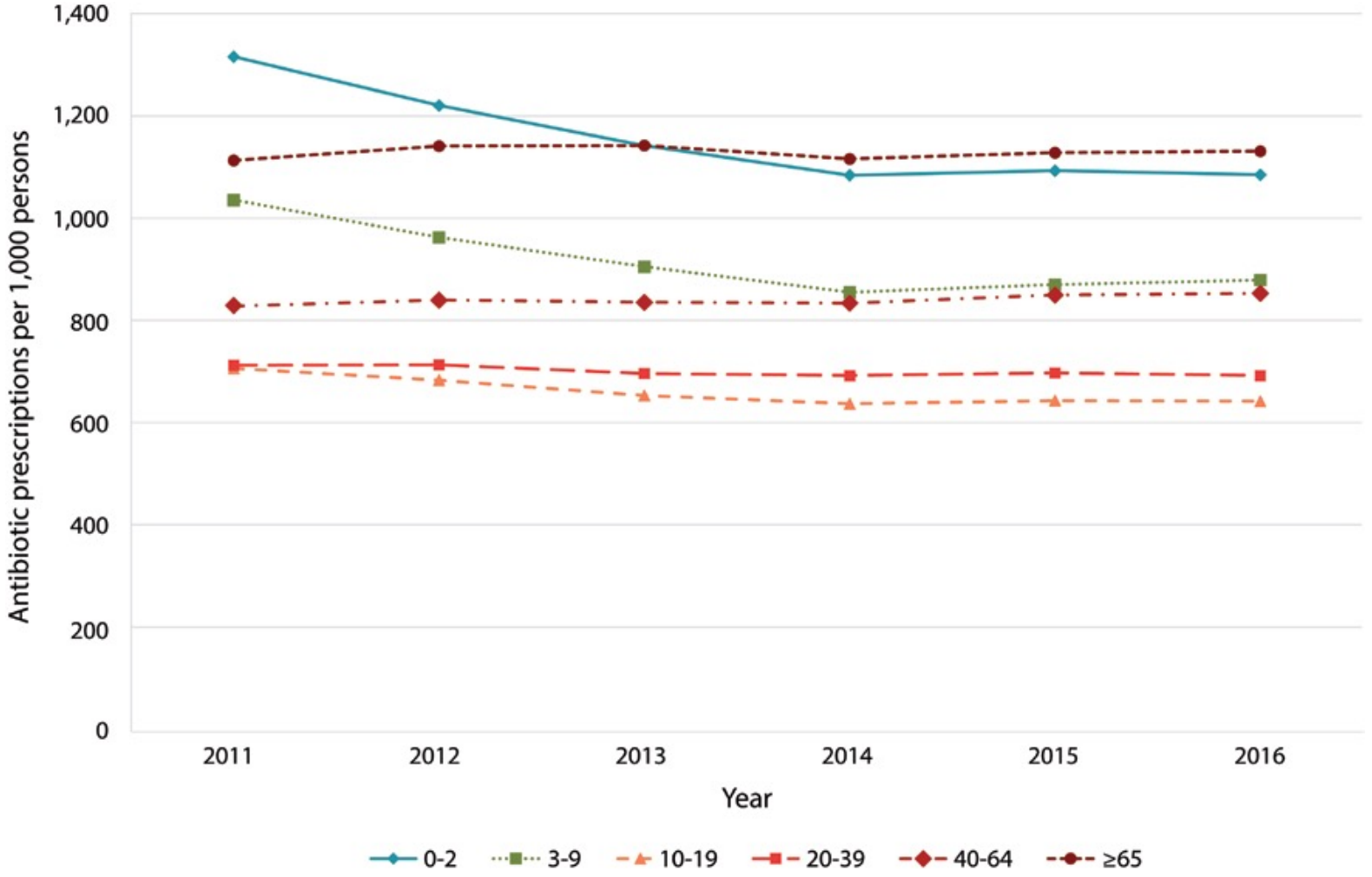
Increased Healthcare Costs

C. difficile Epidemic

Drug Resistance

Microbiome Alterations

Trends in Antibiotic Prescribing, 2011-2016



King, *Clin Inf Dis*, 2020

World Health Organization (WHO)

- **Global Action Plan on Antimicrobial Resistance** (2015)
    1. Improve awareness and understanding of antimicrobial resistance
    2. Strengthen knowledge through surveillance and research
    3. Reduce the incidence of infection
    4. Optimize the use of antimicrobial agents
    5. Ensure sustainable investment in countering antimicrobial resistance
    - Provides a framework for developing national action plans

World Health Organization

AWaRe

HANDLE ANTIMICROBIALS WITH CARE

Antibiotics
Antivirals
Antifungals
Antiparasitics

- **AWaRe** (2018)
    - Antibiotic groupings: Access, Watch, Reserve
    - Goal: By 2023, 60% of all antibiotics consumed must come from Access

- **World Antibiotic Awareness Week** (Nov 18-24)

https://www.emro.who.int/health-topics/drug-resistance/global-action-plan.html

American Rescue Plan

- Sept 2021, Biden/Harris Administration working through CDC
- $2.1 billion for infection prevention and antibiotic stewardship
  - $120 million supplemental funding to state and local jurisdictions
  - Expand access to antibiotic stewardship expertise and support antibiotic stewardship interventions in all healthcare settings

The National Action Plan for Combating Antibiotic-Resistant Bacteria

- First published in 2015, updated in 2020
- 5 goals
  1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections
  2. Strengthen national One-Health surveillance efforts to combat resistance
  3. Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria
  4. Accelerate basic and applied research and development for new antibiotics, other therapeutics and vaccines
  5. Improve international collaboration and capacities for antibiotic resistance, prevention, surveillance, control and antibiotic research and development

Centers for Disease Control and Prevention (CDC)

- Core elements for inpatient and outpatient antibiotic stewardship
- U.S. Antibiotic Awareness Week (Nov 18– 24)
- Annual reports of national prescribing trends

Others

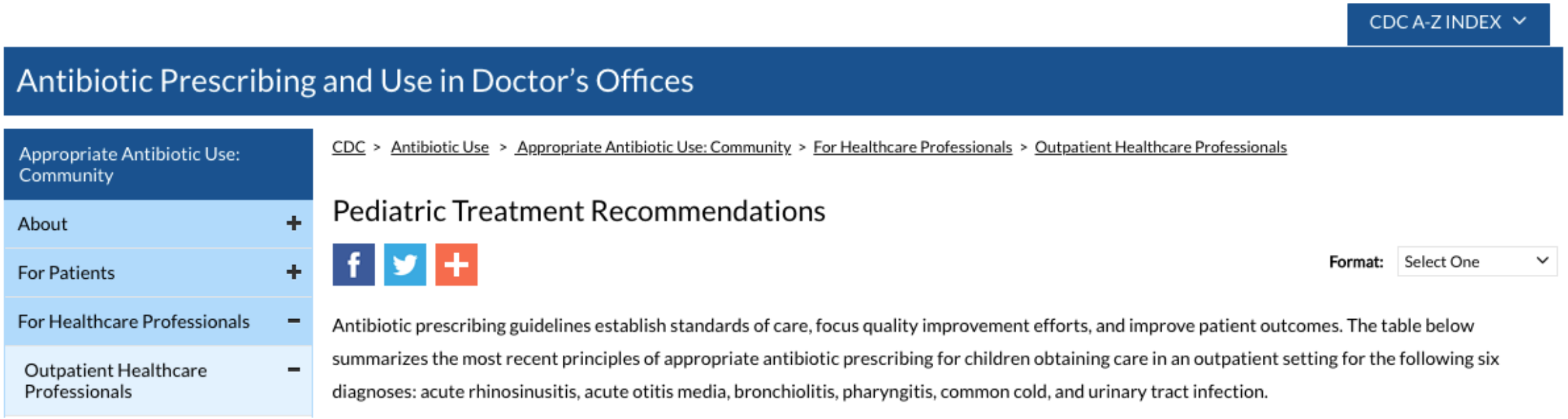
- The Joint Commission
  - Inpatient and outpatient standards
- The Leapfrog Group
  - Scores hospitals on their commitment to stewardship
- Infectious Diseases Society of America (IDSA)
  - 10 x ‘20 Initiative (Surpassed! 14 new anti-infectives)
- Federal Legislation
  - PASTEUR Act (Pioneering Antimicrobial Subscriptions to End Upsurging Resistance)

What's Causing the Problem?

Describe the factors that drive inappropriate antibiotic use in the outpatient setting

Lack of Awareness of Treatment Guidelines

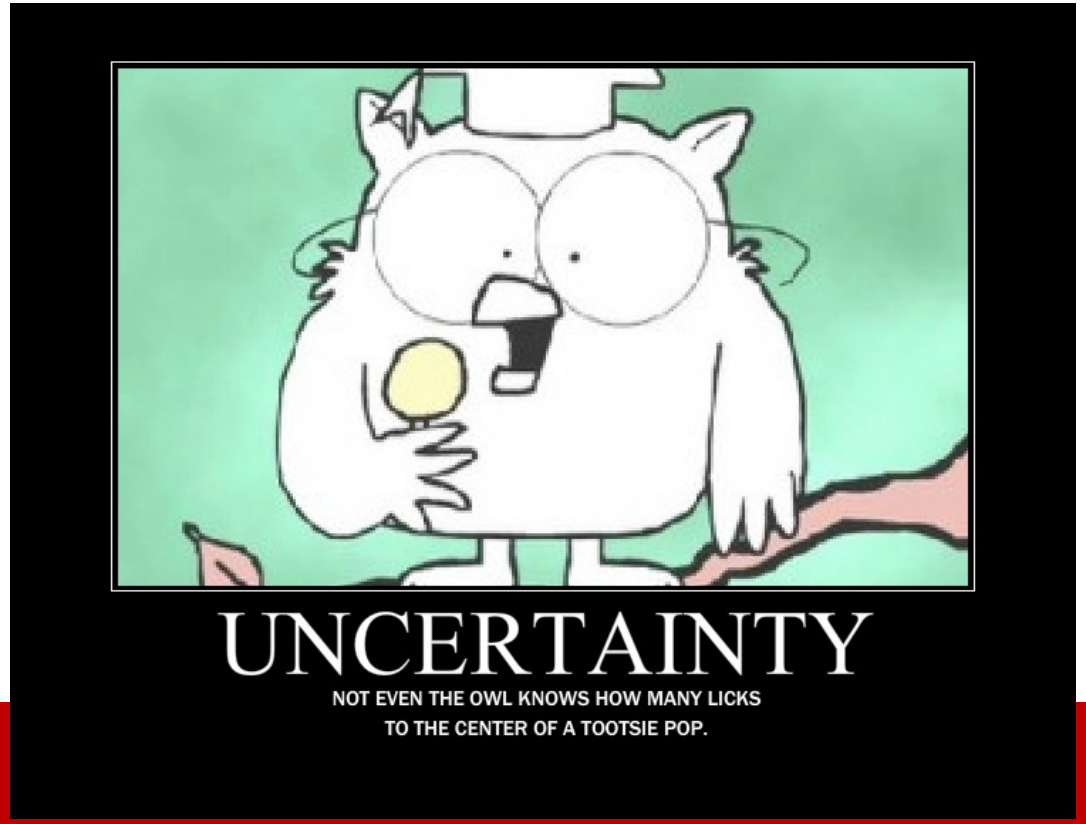
- Too many recommendations
- Difficult to keep up with new recommendations



https://www.cdc.gov/antibiotic-use/community/for-hcp/outpatient-hcp/pediatric-treatment-rec.html

Diagnostic Uncertainty / Fear of Complications

- Sometimes it feels safer to prescribe antibiotics
- Must weigh risks and benefits



http://www.financialtipoftheday.com/financial-tip-of-the-day/the-uncertainty-of-saving-for-retirement-and-your-childs-education

Journal of the Pediatric Infectious Diseases Society

ORIGINAL ARTICLE

US Emergency Department Visits for Adverse Drug Events From Antibiotics in Children, 2011–2015

Maribeth C. Lovegrove, Andrew I. Geller, Katherine E. Fleming-Dutra, Nadine Shehab, Mathew R. P. Sapiano, and Daniel S. Budnitz

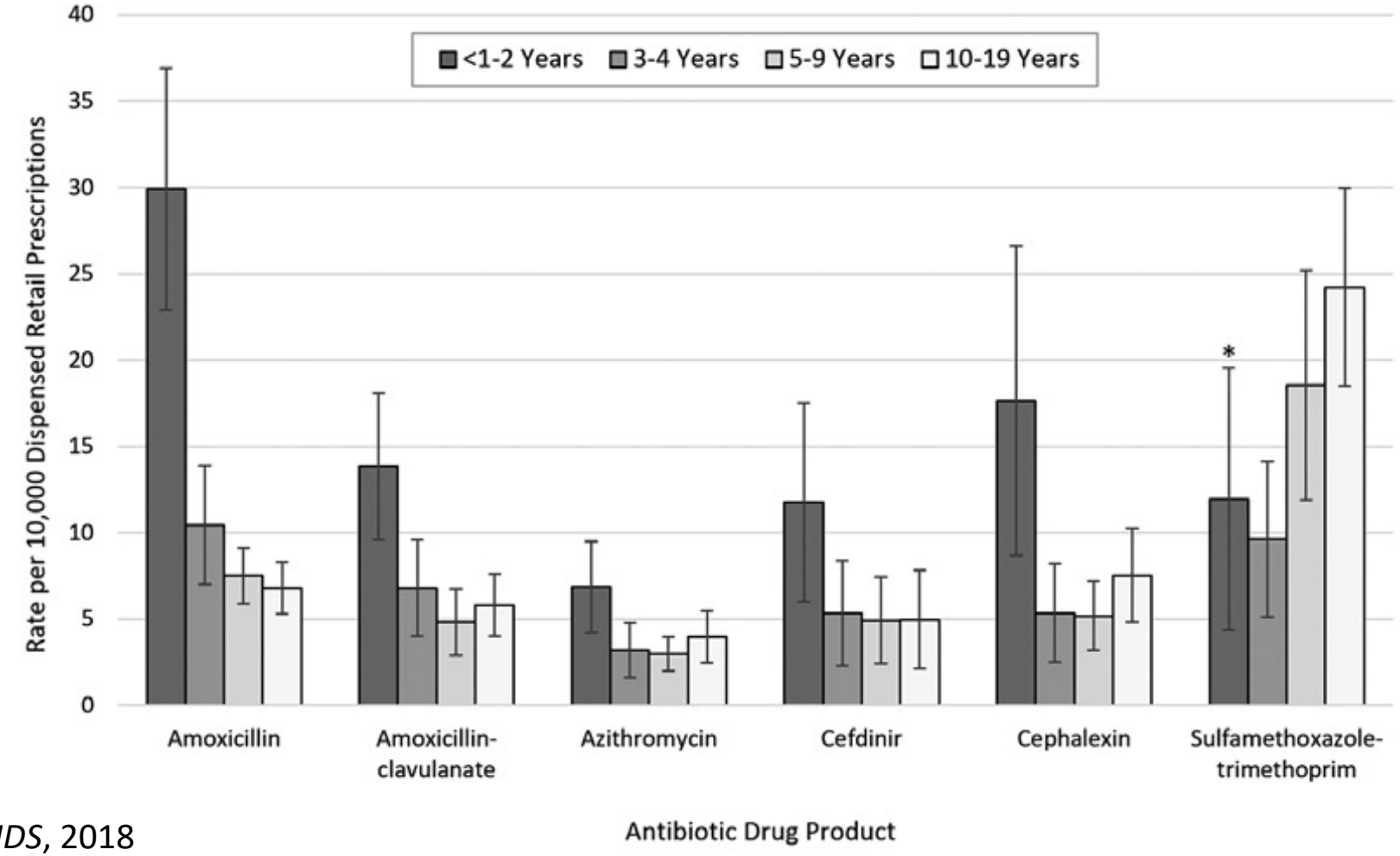
Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

- National estimates of ED visits for antibiotic adverse drug events (ADEs) were based on data from CDC, US Consumer Product Safety Commission and the US FDA

- Est. 69,464 ED visits annually in the U.S. for pediatric antibiotic ADEs

Lovegrove, *JPIDS*, 2018

Rates of Pediatric ED Visits for ADEs



Lovegrove, *JPIDS*, 2018

Patient Pressure and Satisfaction

Effects of Knowledge, Attitudes, and Practices of Primary Care Providers on Antibiotic Selection, United States
***Emerg. Infect. Dis.*, 2014**

Guillermo V. Sanchez, Rebecca M. Roberts, Alison P. Albert, Darcia D. Johnson, and Lauri A. Hicks

- In-depth interviews with 36 PCPs in the U.S.

Patient Pressure and Satisfaction

- "*We as doctors are business people. We're no different than running a shoe store. If somebody comes in and wants black shoes, you don't sell them white shoes. And if you do, they get upset. You can convince a patient, look if I were you I wouldn't take this antibiotic… but patients in general don't understand that concept of not taking it if you don't need it… [and] if you don't give it to them, they don't come back to you.*"

Others

Habit

Workload

Time Constraints

Decision Fatigue

Unnecessary Testing

- Nationally, antibiotics are prescribed during 60% of pediatric visits for pharyngitis, but the expected prevalence of GAS pharyngitis is 30%.

- Guidelines recommend testing only for patients
  - Age > 2 years
  - WITHOUT evidence of viral URI (congestion, cough, etc) and
  - WITH physical exam signs consistent with Strep pharyngitis (exudate, tender cervical nodes, palatal petechiae)

What Can We Do About It?

List strategies for optimizing antibiotic use in the outpatient setting

Antimicrobial Stewardship Programs (ASPs)

- Definition:
  - The optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance

Patient safety &
delivering high quality healthcare!

Patient/Family Education

- Family focus group; 8 parents
- Ideas on topics for education, best places for and methods of education

Address in non-acute visits ("set expectations")

Community partners / educational seminars / social media pushes

Add guidance on when antibiotics might be appropriate to clinic website

Interested in education on all topics suggested

- Prophylaxis (pros/cons)
- Non-infectious use of abx
- Specific diseases
- Allergies
- Side effects, resistance

BMJ

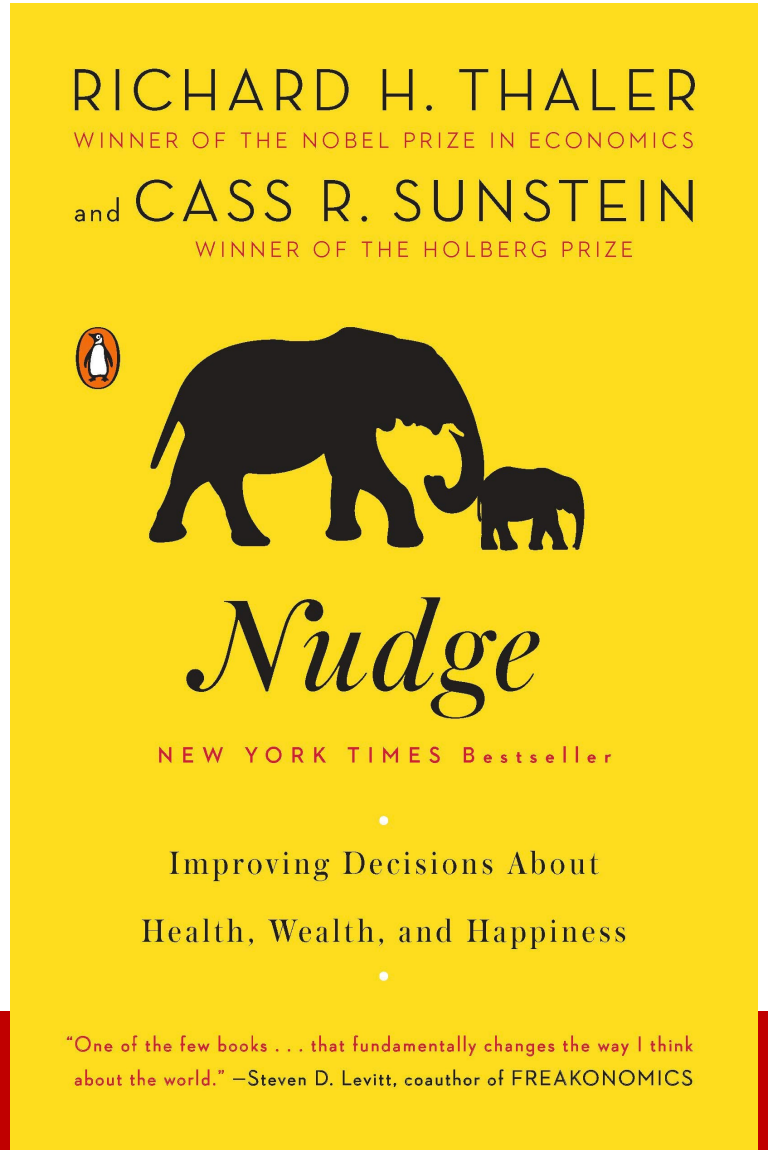
RESEARCH

Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial

Nick A Francis, medical research council health services fellow,[1,2] Christopher C Butler, professor of primary care medicine, head of department of primary care and public health,[1] Kerenza Hood, reader in statistics, director of south east Wales trials unit,[1,2] Sharon Simpson, senior research fellow,[1,2] Fiona Wood, lecturer,[1] Jacqueline Nuttall, senior trial manager[1,2]

- Used interactive pictorial booklet during URI visits with PCPs
- Significantly lowered antibiotic prescribing rates – 19.5% vs 40.8% ($p<0.001$)
- Similar return visit rates and patient satisfaction scores

Behavioral Science in Practice



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

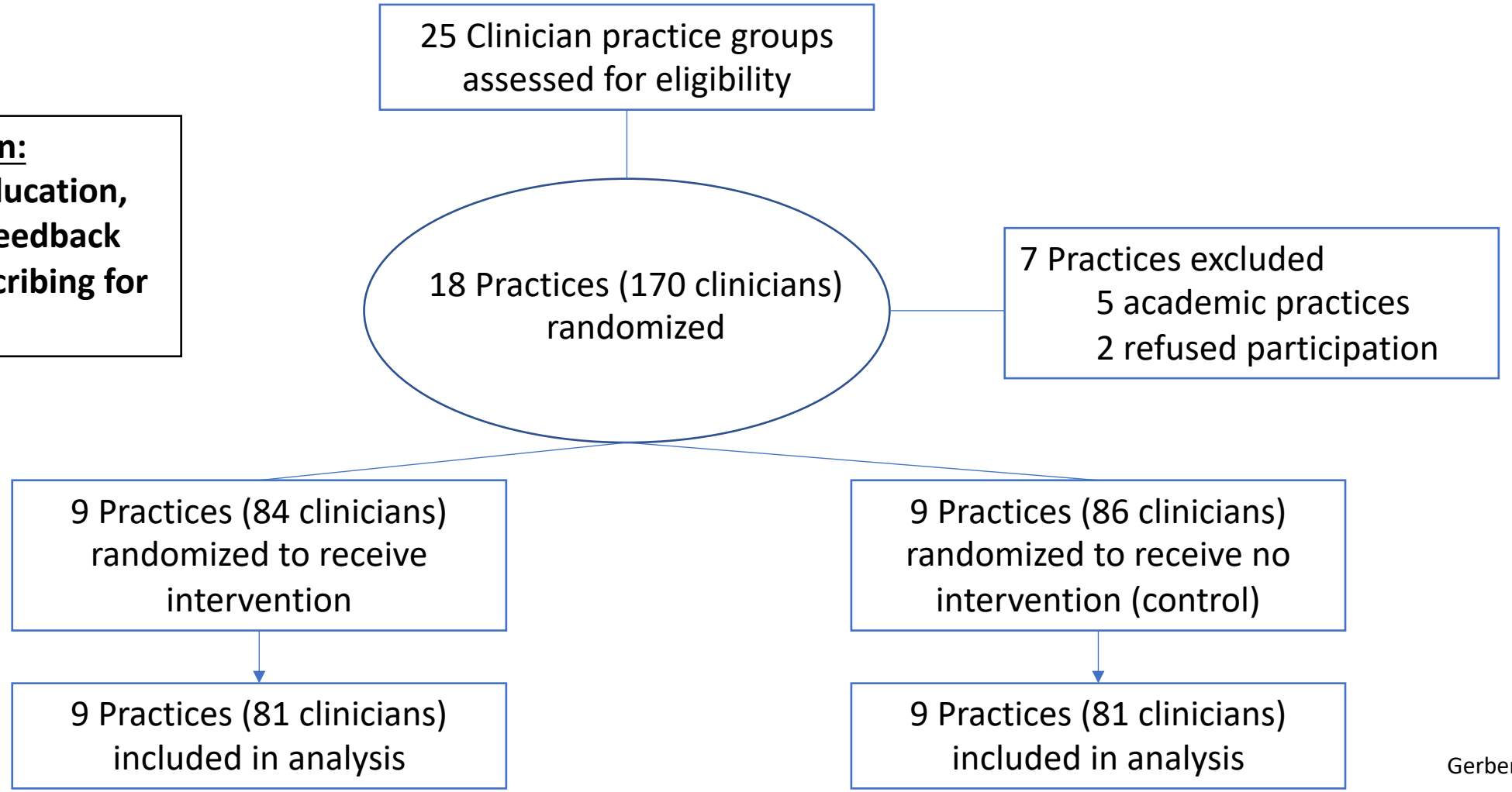
A Randomized Trial

Jeffrey S. Gerber, MD, PhD
Priya A. Prasad, MPH
Alexander G. Fiks, MD, MSCE
A. Russell Localio, PhD
Robert W. Grundmeier, MD
Louis M. Bell, MD
Richard C. Wasserman, MD
Ron Keren, MD, MPH
Theoklis E. Zaoutis, MD, MSCE

JAMA. 2013;309(22):2345-2352

Cluster Randomized Trial

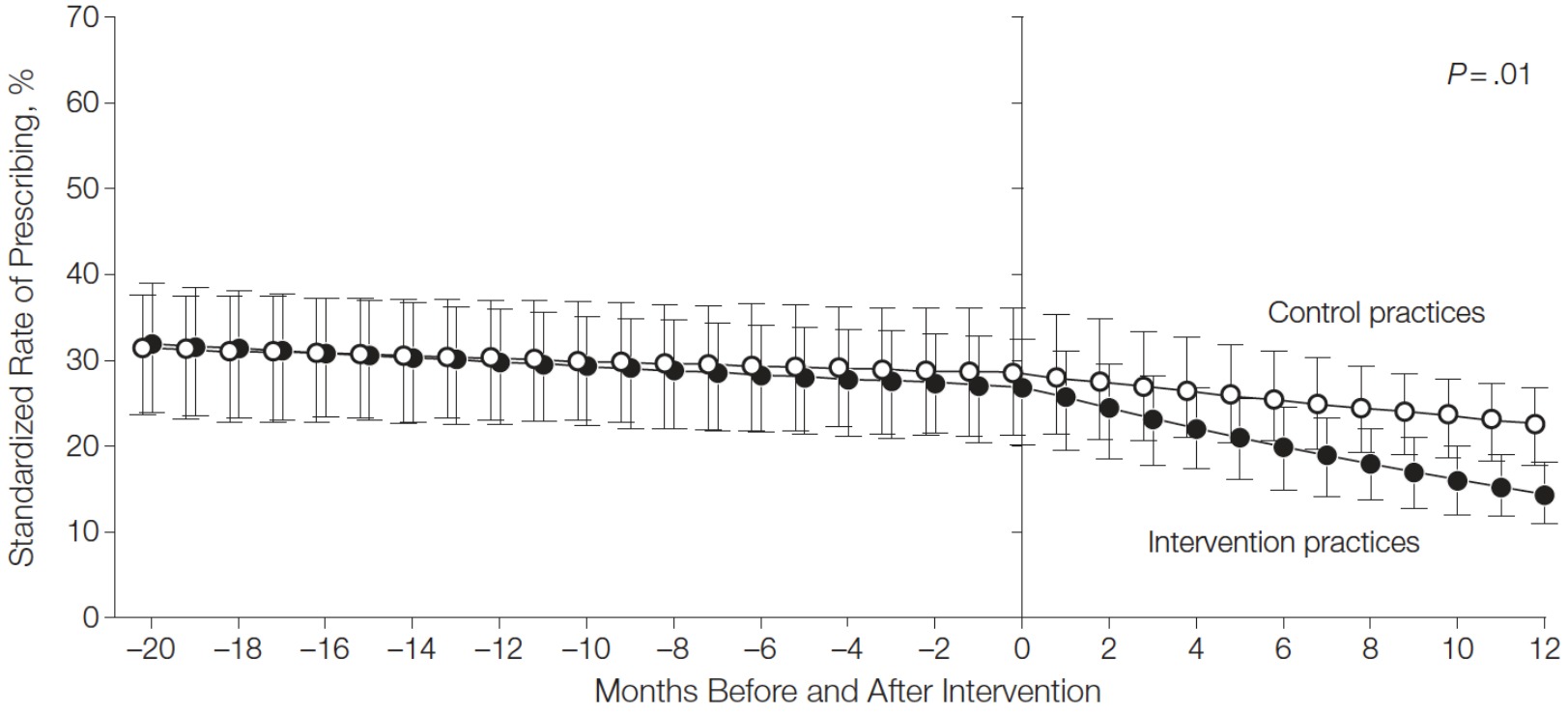
Intervention:
provider education, audit and feedback about prescribing for ARTIs



Gerber et al, JAMA 2013

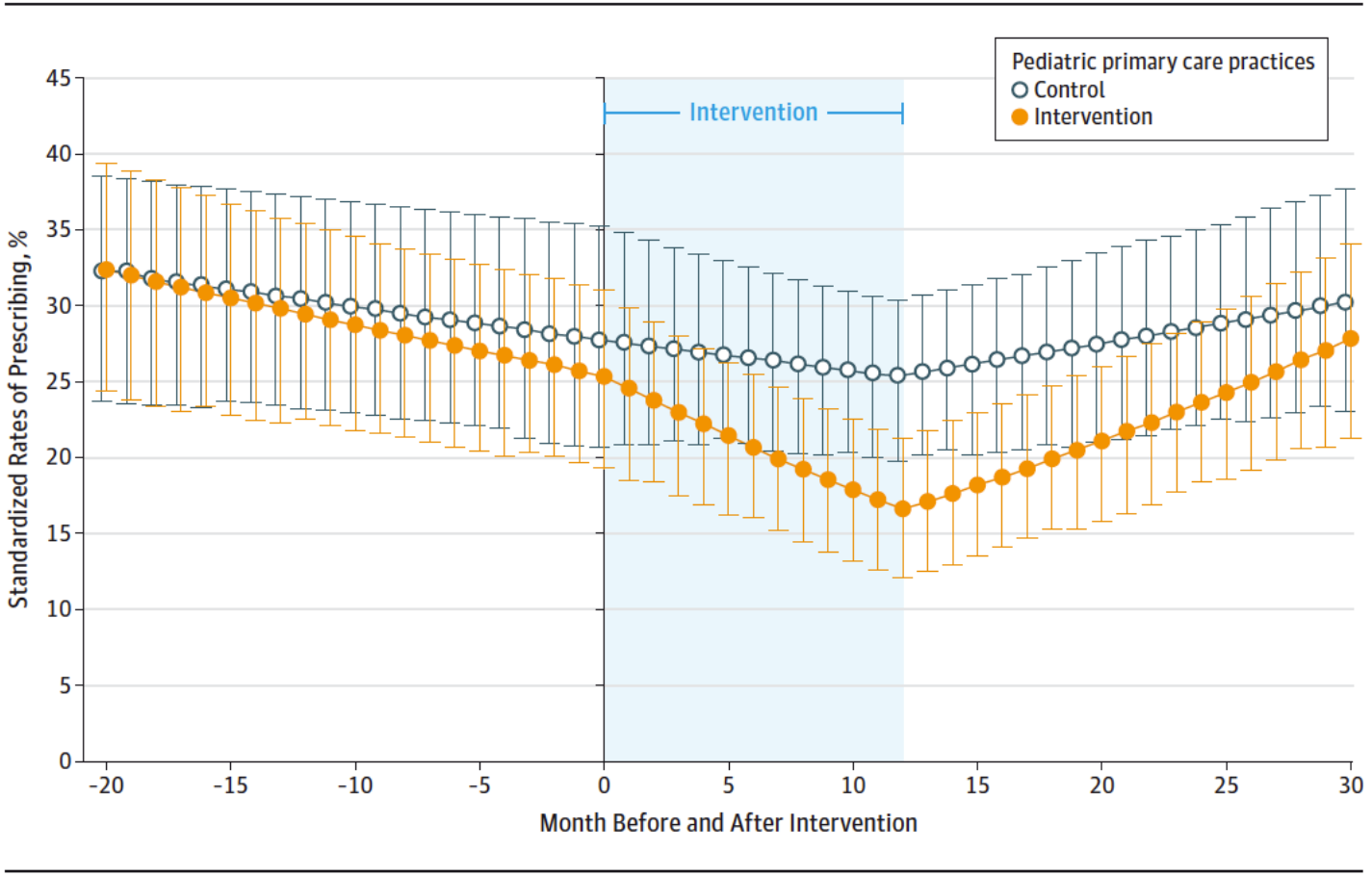
Cluster Randomized Trial: Intervention Practices Had Significantly Less Off-Guideline Prescribing for ARTIs

Figure 2. Standardized Rates of Broad-Spectrum Antibiotic Prescribing at Acute Care Office Visits Over Time



Gerber et al, JAMA 2013

However… the Effect Was Not Long-Lasting



Gerber et al, JAMA 2014

Study Conclusions

- Outpatient antimicrobial stewardship (provider education and audit and feedback) is feasible.
- Continued feedback to clinicians is required to sustain improvements in antimicrobial prescribing.

- ***Expand antimicrobial stewardship programs to outpatient settings***

Gerber et al, JAMA 2014

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

JAMA. 2016;315(6):562-570. doi:10.1001/jama.2016.0275

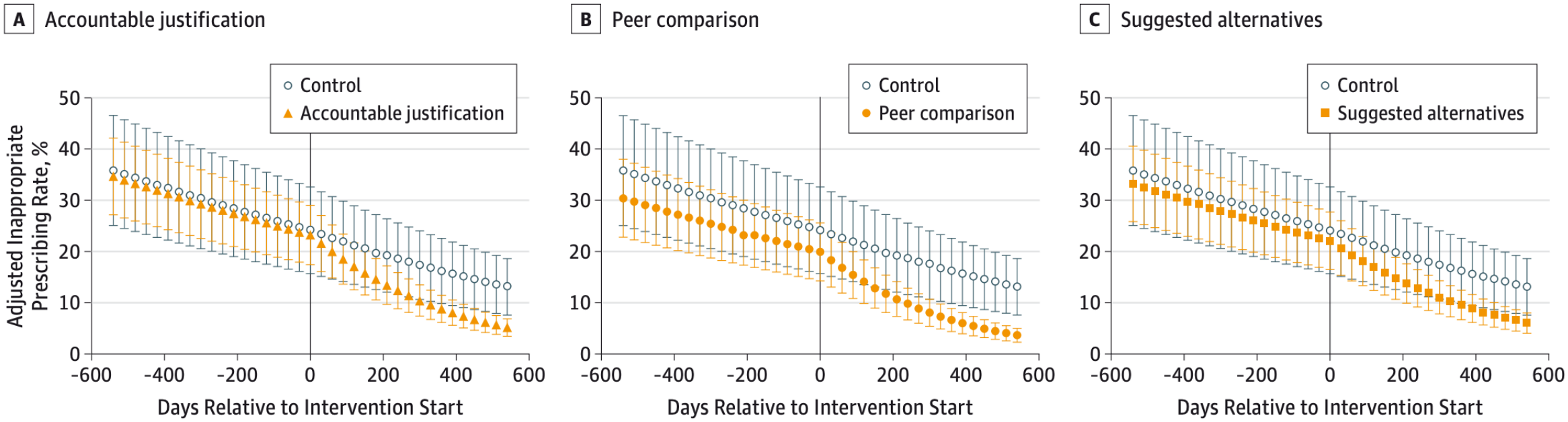
Cluster Randomized Trial

- 47 Primary Care Practices in Boston and LA, 2011-2012
- Randomized to control vs. 1 or more interventions:
  - Non-antibiotic alternatives in order sets
  - Accountable justification for prescribing
  - Peer comparison

Meeker et al, JAMA 2016

Accountable Justification and Peer Comparison Reduced Antibiotic Prescribing for ARTI

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



Meeker et al, JAMA 2016

Study Conclusions

- Simple, inexpensive tactics grounded in human behavior can reduce inappropriate antibiotic prescribing in the outpatient setting

- ***"Nudge" prescribers to do the right thing***

Meeker et al, JAMA 2016

Original Investigation

March 2014

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 Rothfield, MD; Guillermo Diaz, MD; Jason N. Doctor, PhD

JAMA Intern Med. 2014;174(3):425-431. doi:10.1001/jamainternmed.2013.14191

Public Commitments

- Randomized Clinical Trial, 5 outpatient adult clinics in LA
- Signed commitment letter with photo in exam rooms
- One year observation period total intervention in 12 weeks at height of influenza season

When you have a cough, sore throat or other illness, your doctor will help you select the best possible treatments. If an antibiotic would do more harm than good, your doctor will explain this to you, and may offer other treatments that are better for you.

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.

Meeker, *JAMA Int Med* 2014

Public Commitments

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]			

"When extrapolated to the entire United States, the posted-commitment-letter intervention could eliminate 2.6 million unnecessary antibiotic prescriptions and save $70.4 million annually on drug costs alone."

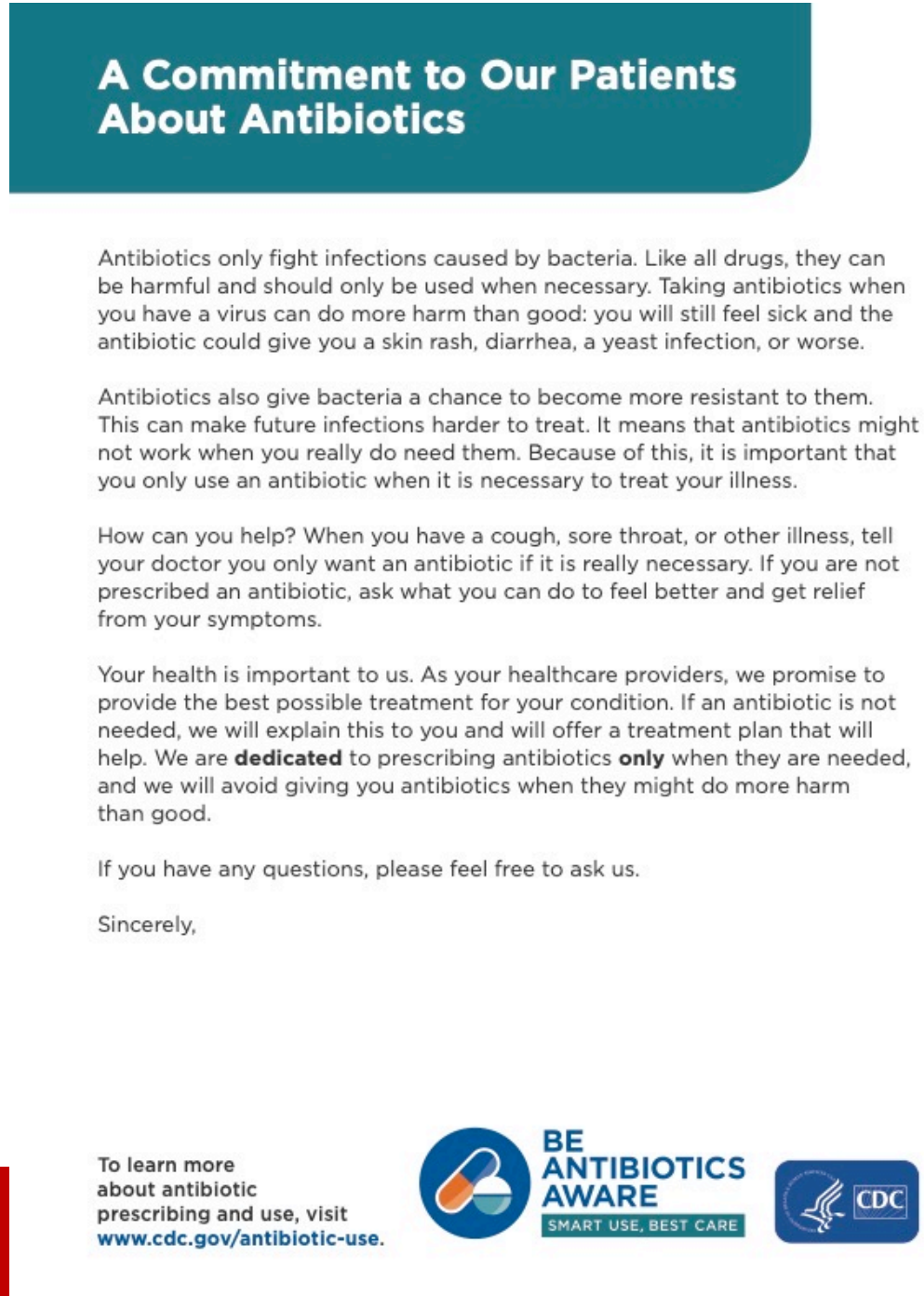
Meeker, *JAMA Int Med* 2014

CDC Resources

https://www.cdc.gov/antibiotic-use/community/materials-references/print-materials/hcp/index.html

Also on the website:

- Fact sheets and posters
- Return to day care letter
- Prescription pads
  - Delayed prescribing
  - Symptom relief for viral illness
  - Instructions on taking antibiotics correctly
  - Watchful waiting



A Commitment to Our Patients About Antibiotics

Antibiotics only fight infections caused by bacteria. Like all drugs, they can be harmful and should only be used when necessary. Taking antibiotics when you have a virus can do more harm than good: you will still feel sick and the antibiotic could give you a skin rash, diarrhea, a yeast infection, or worse.

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

How can you help? When you have a cough, sore throat, or other illness, tell your doctor you only want an antibiotic if it is really necessary. If you are not prescribed an antibiotic, ask what you can do to feel better and get relief from your symptoms.

Your health is important to us. As your healthcare providers, we promise to provide the best possible treatment for your condition. If an antibiotic is not needed, we will explain this to you and will offer a treatment plan that will help. We are **dedicated** to prescribing antibiotics **only** when they are needed, and we will avoid giving you antibiotics when they might do more harm than good.

If you have any questions, please feel free to ask us.

Sincerely,

To learn more about antibiotic prescribing and use, visit www.cdc.gov/antibiotic-use.

BE ANTIBIOTICS AWARE
SMART USE, BEST CARE

CDC

Effective Communication

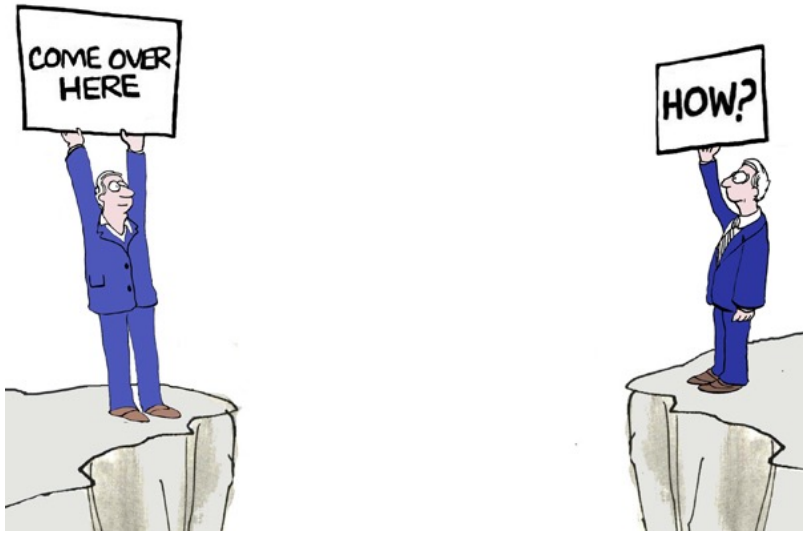
Dialogue Around Respiratory Illness Treatment: Optimizing Communication with Parents

Jeffrey D. Robinson, PhD
John Heritage, PhD
Rita Mangione-Smith, MD, MPH

https://www.uwimtr.org/dart/

Effective Communication

- Four easy steps
    1. Review your physical exam findings
    2. Give a clear diagnosis
    3. Use positive treatment recommendations
    4. Provide a contingency plan



http://www.teamworkandleadership.com/2014/10/3-funny-communication-videos-share-at-your-next-staff-meeting.html

Effective Communication

- Explain why antibiotics are not needed
  1. Review your physical exam findings
  2. Deliver a clear diagnosis

https://www.healthline.com/health/getting-physical-examination

Fleming-Dutra, Amer Fam Phys (2016) 94(3):200, Mangione-Smith, Ann Fam Med (2015) 13(3)

Effective Communication

- Negative, then positive treatment recommendations
- “On the one hand…” “On the other hand….”
- Lowest association with unwarranted prescribing and strongest association with satisfaction with quality of care

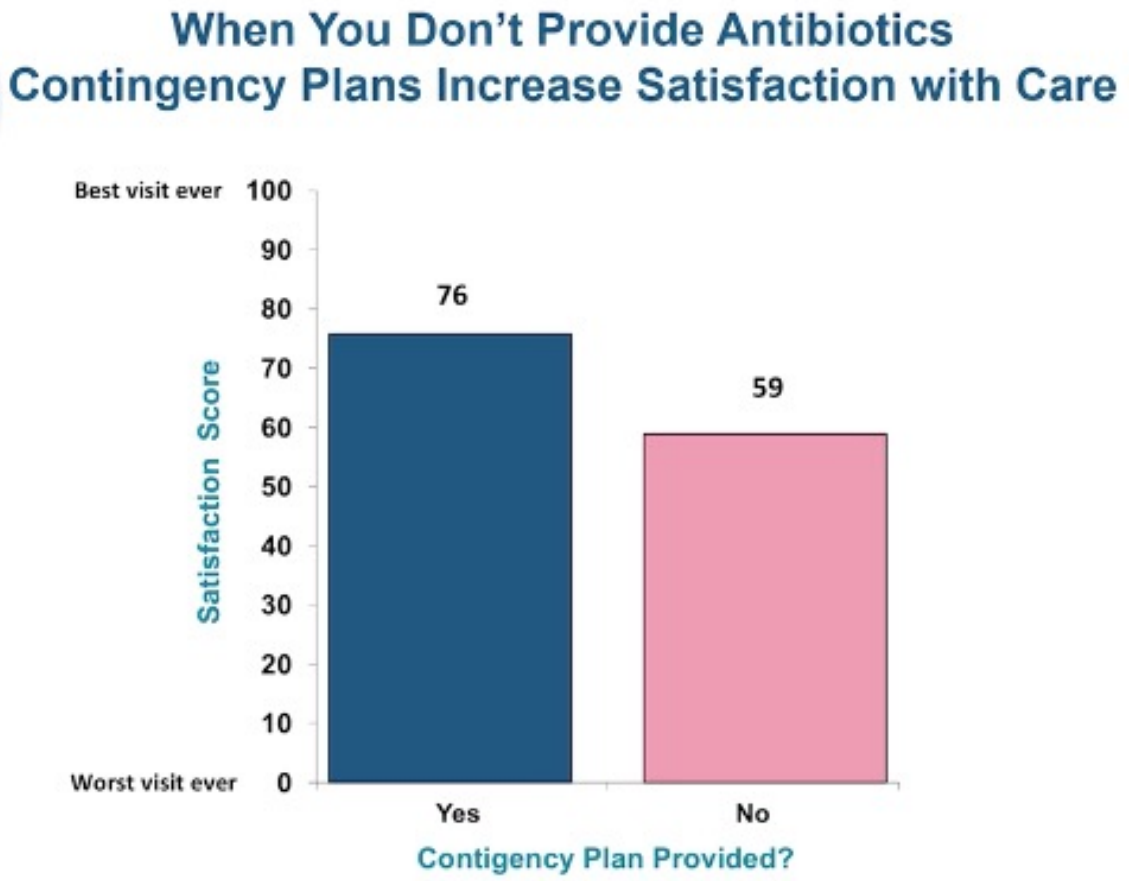
"The good news is we were able to re-attach your severed hand."

CartoonStock.com

Fleming-Dutra, Amer Fam Phys (2016) 94(3):200, Mangione-Smith, Ann Fam Med (2015) 13(3)

Effective Communication

- Contingency plan
  - Delayed antibiotic prescriptions



Fleming-Dutra, Amer Fam Phys (2016) 94(3):200, Mangione-Smith, Ann Fam Med (2015) 13(3)

Reducing Antibiotic Prescribing in Primary Care for Respiratory Illness

PEDIATRICS Volume 146
(3) September 2020

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Jeffrey D. Robinson, PhD,[d] John Heritage, PhD,[e] James Stout, MD,[a] Dennis Burges, BA,[a] Benjamin Hedrick, BA,[a]
Louise Warren, MPH,[a] Madeleine Shalowitz, MD, MBA,[f] Laura P. Shone, DrPH, MSW,[g] Jennifer Steffes, MSW,[g]
Margaret Wright, PhD,[g] Alexander G. Fiks, MD, MSCE,[c,g] Rita Mangione-Smith, MD, MPH[h]

- Stepped-wedge clinical trial, Nov 2015 – June 2018
- 19 pediatric practices, 57 clinicians
- Intervention: 3 program modules; 11 months
  - Online tutorials and webinars on evidence-based strategies and antibiotic prescribing
  - Booster video vignettes
  - Individualized antibiotic prescribing feedback reports

Effective Communication

- 72,723 acute respiratory tract illness (ARTI) visits by 29,762 patients
  - 41 clinicians (72%) engaged actively with the intervention

Rate Ratios of Antibiotic Prescribing During All ITT Analysis Visits for ARTI Overall and by Condition

Condition	Module 1	Module 2	Module 3	Postintervention
ARTI overall	0.96	0.84	0.89	0.93
Viral ARTI	0.63	0.65	0.64	0.6
All pharyngitis	1.06	0.9	0.85	0.96
AOM*	1.01	0.69	0.96	0.93
Strep pharyngitis*	0.71	0.61	0.46	0.66
Sinusitis*	0.75	0.51	0.66	0.59

Kronman et al, *Pediatrics* 2020

* measured second-line prescribing
ARTI = acute respiratory tract infection; AOM = acute otitis media

Study Conclusions

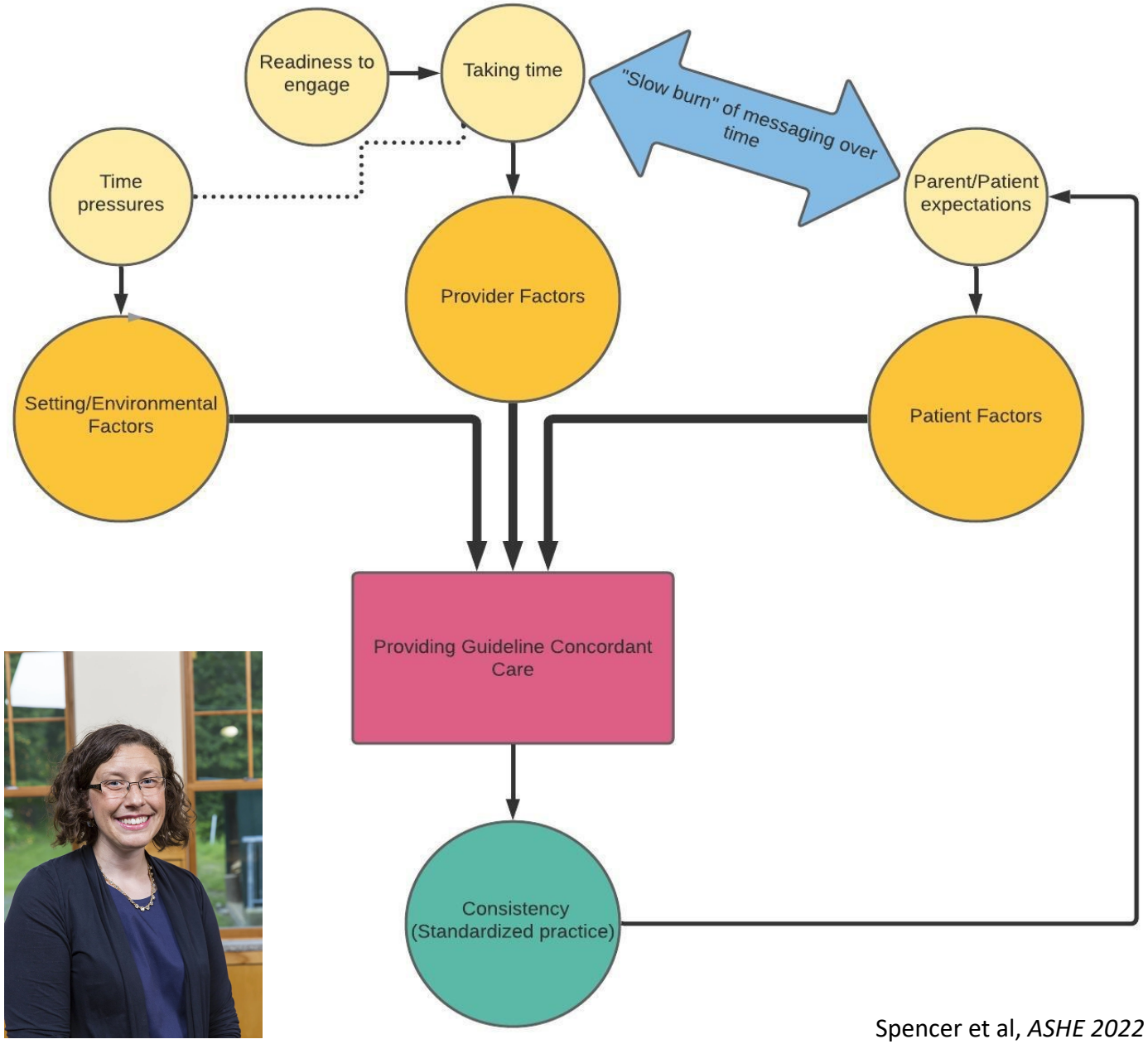
- Decrease in overall antibiotic prescribing during pediatric ARTI visits using the DART QI program
- Reduction in antibiotic prescribing was sustained in the post-intervention period

Kronman et al, *Pediatrics* 2020

Data - Provider Interviews: Drivers of antibiotic prescribing in ambulatory settings

- 38 providers interviewed
  - Primary care, urgent care, retail settings
  - 22 (58%) advanced practice providers
  - In-person or telephone (thanks, COVID)

Diagram of relationship between major categories and select themes



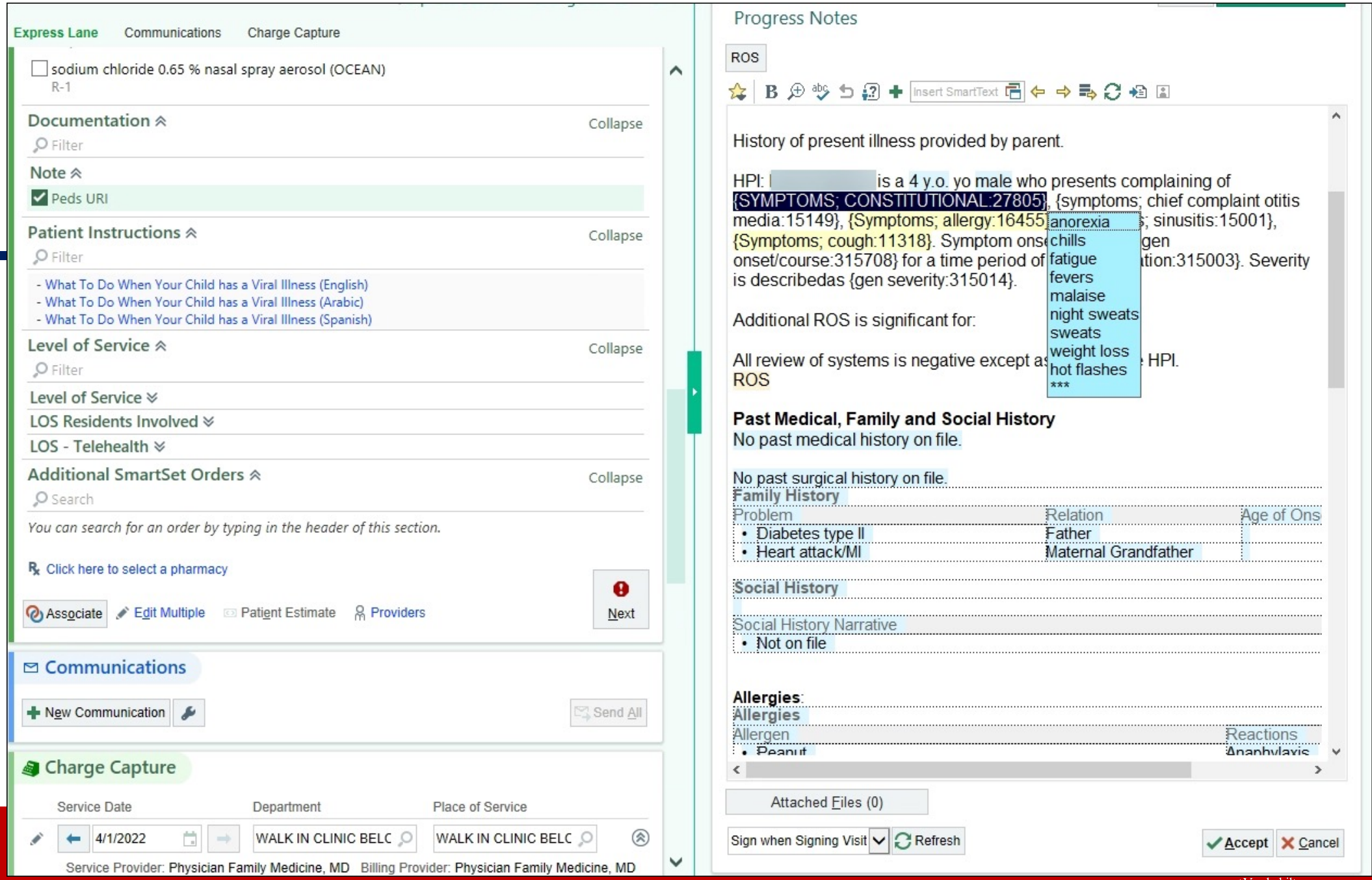
Spencer et al, *ASHE 2022*

Clinical Pathway Guidelines

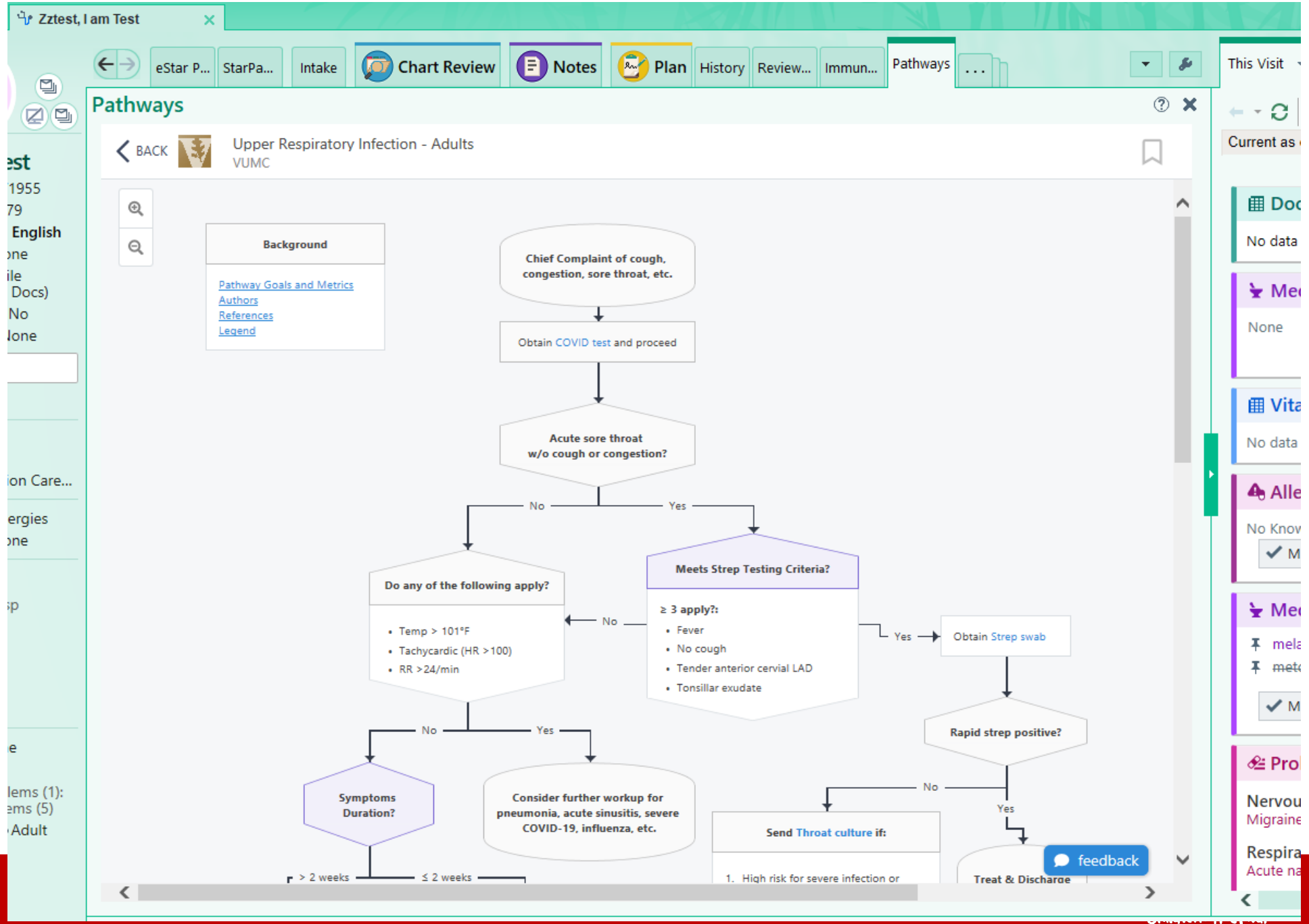
- Wanted by outpatient providers! (Qualitative interview study)
  - ”Blame” not prescribing antibiotics on someone else
- Potential targets:

Rx variability	High-volume diagnoses	Guideline discordance	Diagnostic stewardship
Urinary tract infection Skin/soft tissue infection	Pharyngitis Acute otitis media Viral URI	Sinusitis Pneumonia Strep pharyngitis	Strep pharyngitis Urinary tract infection Viral URI

EHR Decision Support - eStar Express Lane

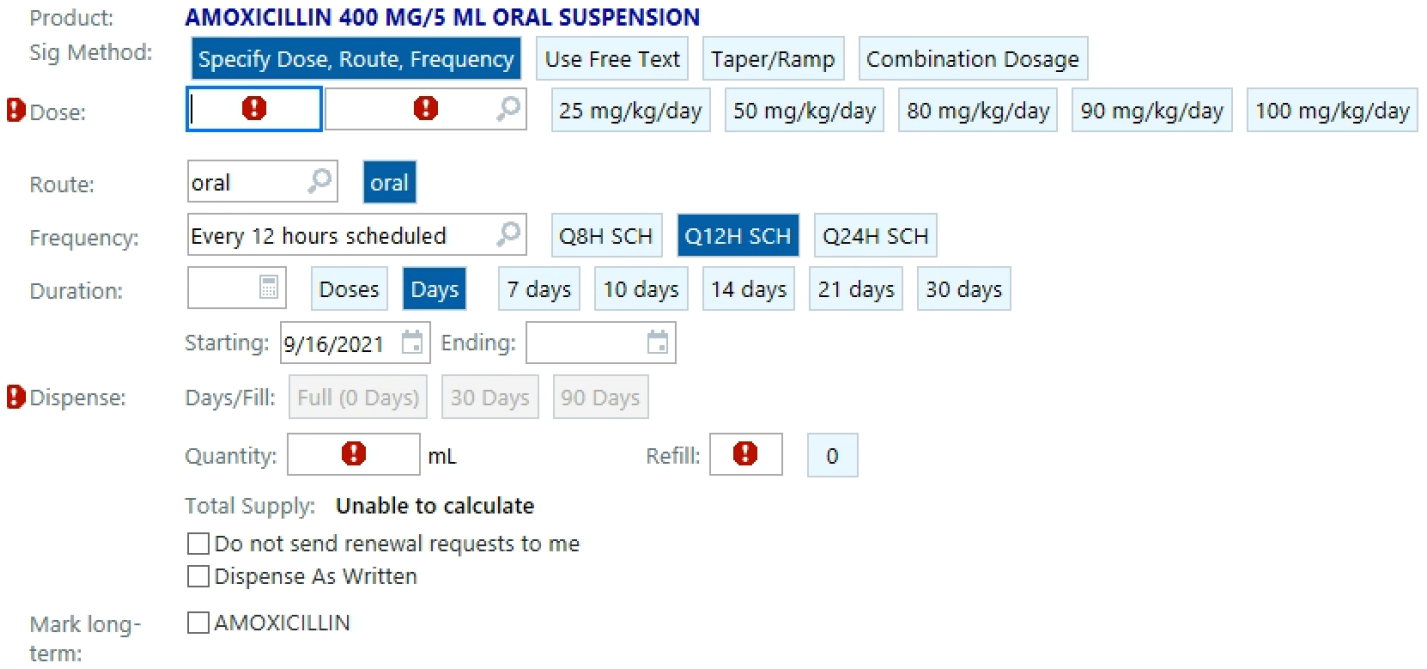


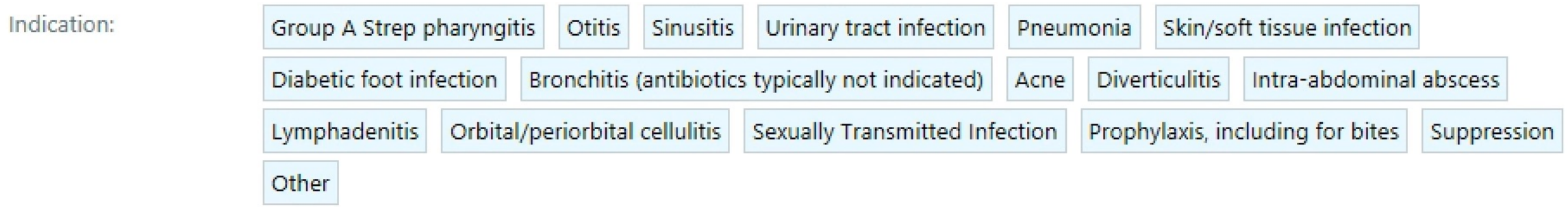
EHR Decision Support - AgileMD



EHR – Antibiotic Indications

- Accountable justification
- Accurate feedback
- Gentle reminder not to prescribe antibiotics for bronchitis





Take Home Points

- The rate of antibiotic resistance is rising faster than the rate of development of new, effective antibiotics.
- The majority of antibiotic use occurs in the outpatient setting.
- Many of the drivers of inappropriate antibiotic use in the outpatient setting can be overcome.
- There are evidence-based methods for reducing inappropriate antibiotic use that can easily be integrated into daily practice.

Thank you!

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