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Beyond the Tip of the Iceberg: Extending Pediatric Antimicrobial Stewardship to Ambulatory Settings

UW TASP Regional Meeting
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Disclosure

I have no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.

Objectives

1. Describe importance of antimicrobial stewardship for children in ambulatory settings
2. Review antibiotic prescribing practices in ambulatory settings
3. Describe effective outpatient stewardship interventions
4. Identify future directions for outpatient stewardship

Pediatric Antibiotic Prescribing

Inpatient: ~3.5 million prescriptions/year[1]
-$3.6 billion/year[2] (all ages)

Ambulatory: ~75 million prescriptions/year[3]
-$6.5 billion/year[2]

Inpatient antibiotic stewardship addresses just ~5% of pediatric antibiotic prescribing

(1- Witt, 2012; 2- Suda 2012; 3- Hicks, *CID* 2015)

Risks associated with antibiotic use

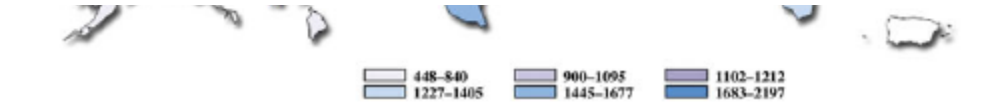
- Resistance in for outpatient conditions increasing
- Increased risk of IBD[1] and JIA[2]
- ED visits for adverse drug events[3]
  - 0-5 y/o: 56% of ED visits for ADE

1 – Kronman, *Pediatrics* 2012; 2 – Horton, *Pediatrics* 2015; 3 – Shehab, *JAMA* 2016

How big is the pediatric outpatient problem?

- Used IMS Health Xponent database
- Estimated 262.5 million overall prescriptions, with ~75 million (~30%) to children

Characteristic	Prescriptions, No. in Millions (%)[a]	Prescriptions per 1000 Persons, Rate
Age group, y		
0–2	15.4 (21)	1287
3–9	29.1 (40)	1018
10–19	29.3 (40)	691
Antibiotic agent (top 5)		
Amoxicillin	24.9	300
Azithromycin	15.2	183
Amoxicillin-clavulanate	7.2	87
Cefdinir	6.1	74
Cephalexin	4.6	56



(Hicks, *CID* 2015; Fleming-Dutra 2016)

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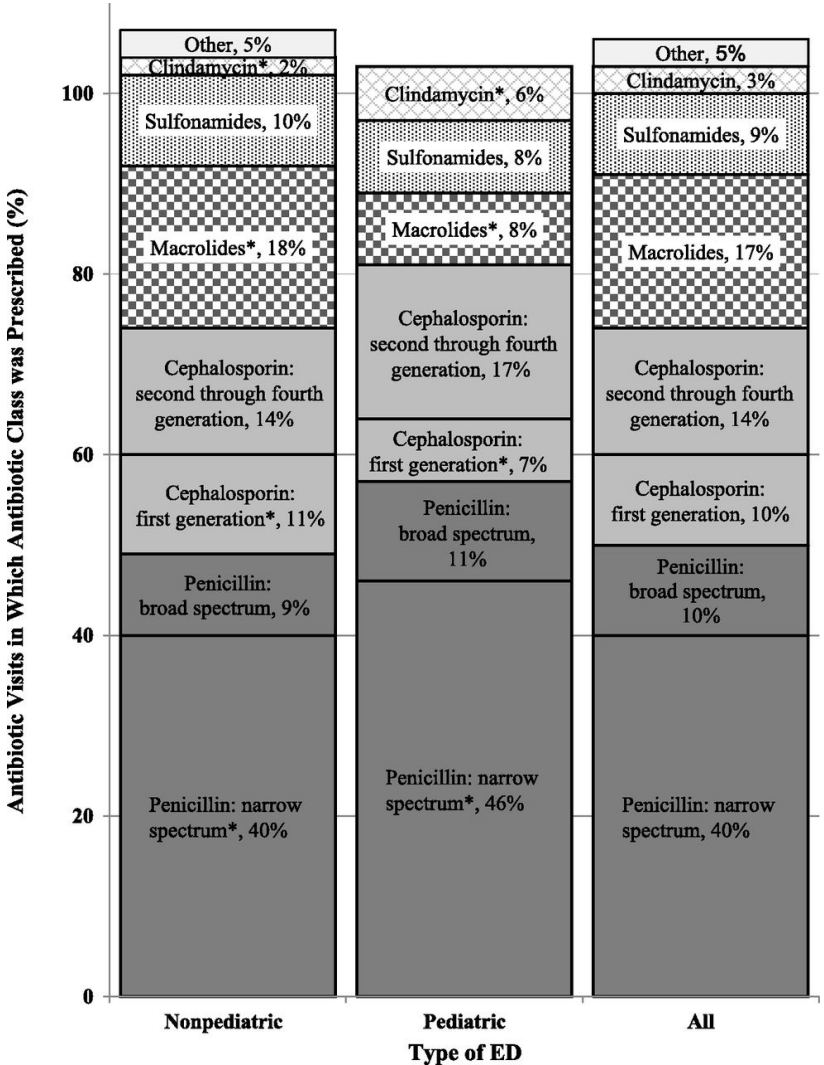
Prescribing in Emergency Departments

- 29 million annual visits by children to EDs nationwide
  - 25m to General ED's; 4m to Pediatric EDs (>75% peds)
- 23% of all visits prescribed an antibiotic (~7m/year)
  - 25% at General EDs; 22% at Pediatric EDs (P<0.01)
- 60% of antibiotics prescribed for respiratory illnesses

Poole, *Pediatrics* 2019


Antibiotic Visits in Which Antibiotic Class was Prescribed (%)
0
20
40
60
80
100
Other, 5%
Clindamycin*, 2%
Sulfonamides, 10%
Macrolides*, 18%
Cephalosporin: second through fourth generation, 14%
Cephalosporin: first generation*, 11%
Penicillin: broad spectrum, 9%
Penicillin: narrow spectrum*, 40%
Clindamycin*, 6%
Sulfonamides, 8%
Macrolides*, 8%
Cephalosporin: second through fourth generation, 17%
Cephalosporin: first generation*, 7%
Penicillin: broad spectrum, 11%
Penicillin: narrow spectrum*, 46%
Other, 5%
Clindamycin, 3%
Sulfonamides, 9%
Macrolides, 17%
Cephalosporin: second through fourth generation, 14%
Cephalosporin: first generation, 10%
Penicillin: broad spectrum, 10%
Penicillin: narrow spectrum, 40%
Nonpediatric
Pediatric
All
Type of ED

Indication for Antibiotic by selected visit characteristics

Percent visits in which the diagnosis was made of all visits for children			
Antibiotics	**General**	**Pediatric**	**Chi²**
Almost Always indicated	10%	11%	0.28
Sometimes Indicated	23%	24%	
Generally Not Indicated	67%	65%	

Factors associated with Guideline Concordant Antibiotic Use			
Characteristic		Pediatric ED visits a/w GCAU (% antibiotic visits)	AOR (CI)
US Census Region	Northeast	86%	1.00
	Midwest	78%	0.51 (0.34-0.77)
	South	76%	0.46 (0.32-0.67)
	West	77%	0.55 (0.35-0.87)
Region	Urban	71%	1.00
	Rural	79%	1.26 (0.99-1.60)
Type of ED	General	77%	1.00
	Pediatric	87%	2.01 (1.38-2.92)
NP/PA at visit?	No	78%	1.00
	Yes	79%	1.08 (0.84-1.39)
Diagnosis	Suppurative OM	81%	1.00
	Sinusitis	70%	0.51 (0.32-0.82)
	Pharyngitis	74%	0.72 (0.53-0.96)

Pediatric outpatient prescribing

- ED prescribing similar to outpatient clinic prescribing
- Outpatient antibiotics prescribed during ~50 million pediatric visits annually
  - Half of this is broad-spectrum

TABLE 1 Antibiotic-Prescribing Patterns Across Diagnostic Conditions

Condition	Across-Condition Contribution to Antibiotic Prescribing, %
Respiratory	72.3
ARTIs for which antibiotics are indicated	48.9
ARTIs for which antibiotics are not indicated	13.1
Other respiratory conditions for which antibiotics are not definitely indicated	10.3
Other	27.7
Skin/cutaneous/mucosal	11.9
Urinary tract infections[a]	2.0
Gastrointestinal infections	0.3
Miscellaneous infections	1.9
Other	11.6
Total	100[a]

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Family medicine clinics

Family medicine clinicians:

- Care for 1 in 3 US children, higher in rural regions[1,2]
- Prescribe 13 million courses of antibiotics to children each year[3]

1- Phillips, *Pediatrics* 2006
2- Makaroff, *Ann Fam Med* 2014
3- Hicks, *CID* 2011

WWAMI region Practice and Research Network (WPRN)

- 20 clinics across WWAMI region

Characteristic		Patient Visits, N	Visits Prescribed an Antibiotic, N	Broad Spectrum Antibiotics, N (% of abx)	Antibiotics Rx "Not Indicated" N (% of abx)
	Total	97,228	10,922 (11)	5821 (53)	4,250 (40)

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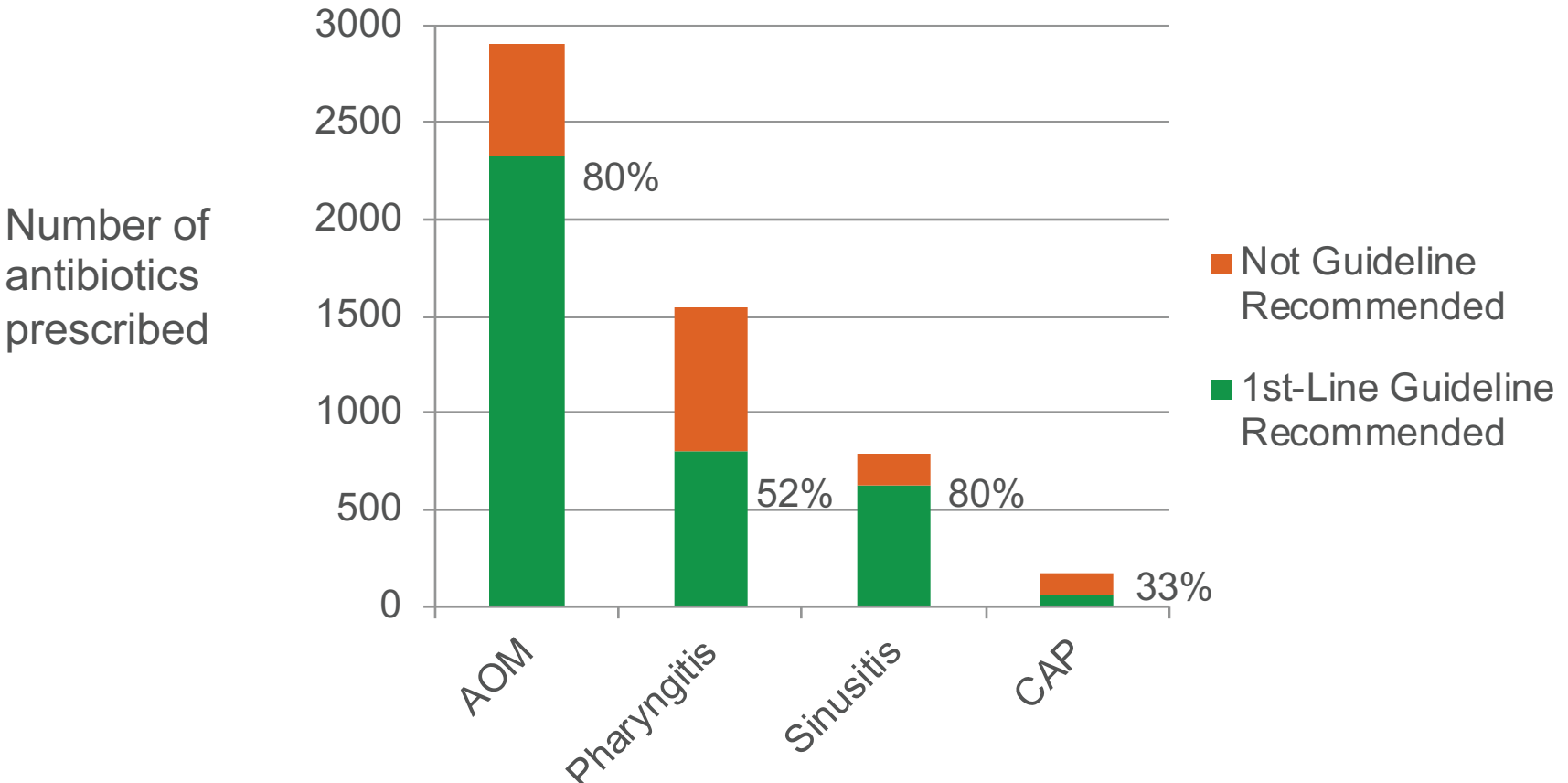
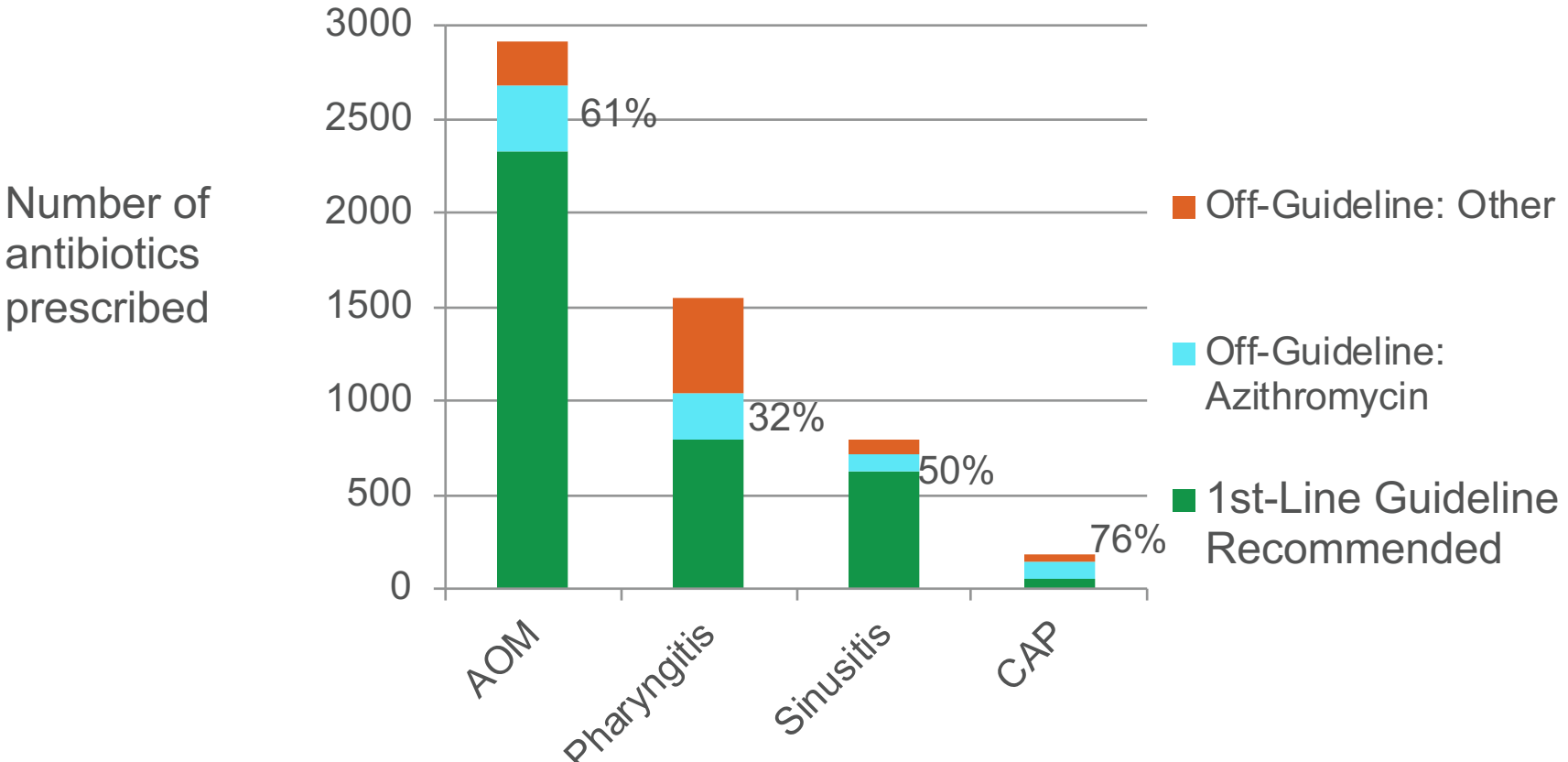
First-line guideline recommended antibiotics



Off-guideline recommended antibiotics



National Strategy for Combating Antibiotic Resistant Bacteria

March 2015: National Action Plan

Goal 1: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

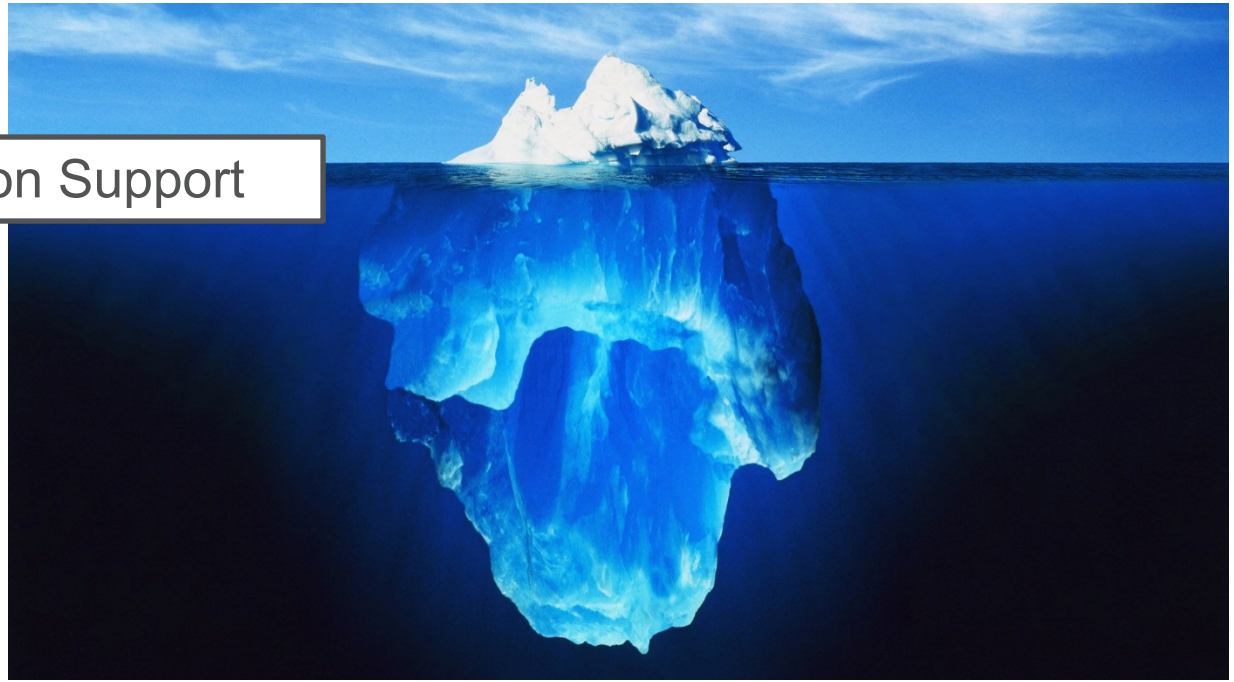
By 2020, significant outcomes of Goal 1 will include:

- Establishment of antibiotic stewardship programs in all acute care hospitals and improved antibiotic stewardship across all healthcare settings.
- Reduction of inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient

OUTPATIENT STEWARDSHIP TOOLS

Stewardship Tools

Decision Support

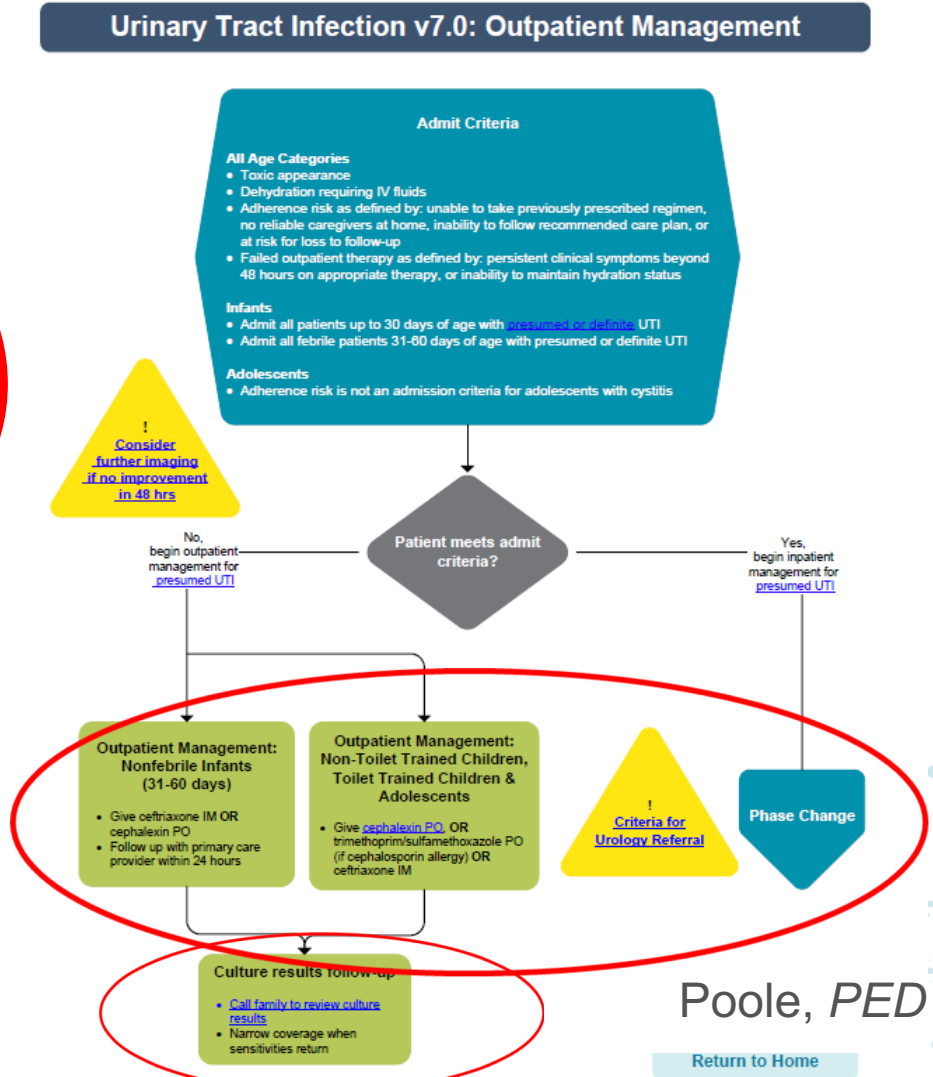


Antibiotic Choice:
Oral Cephalexin

If allergic:
Trimethoprim-sulfamethoxazole

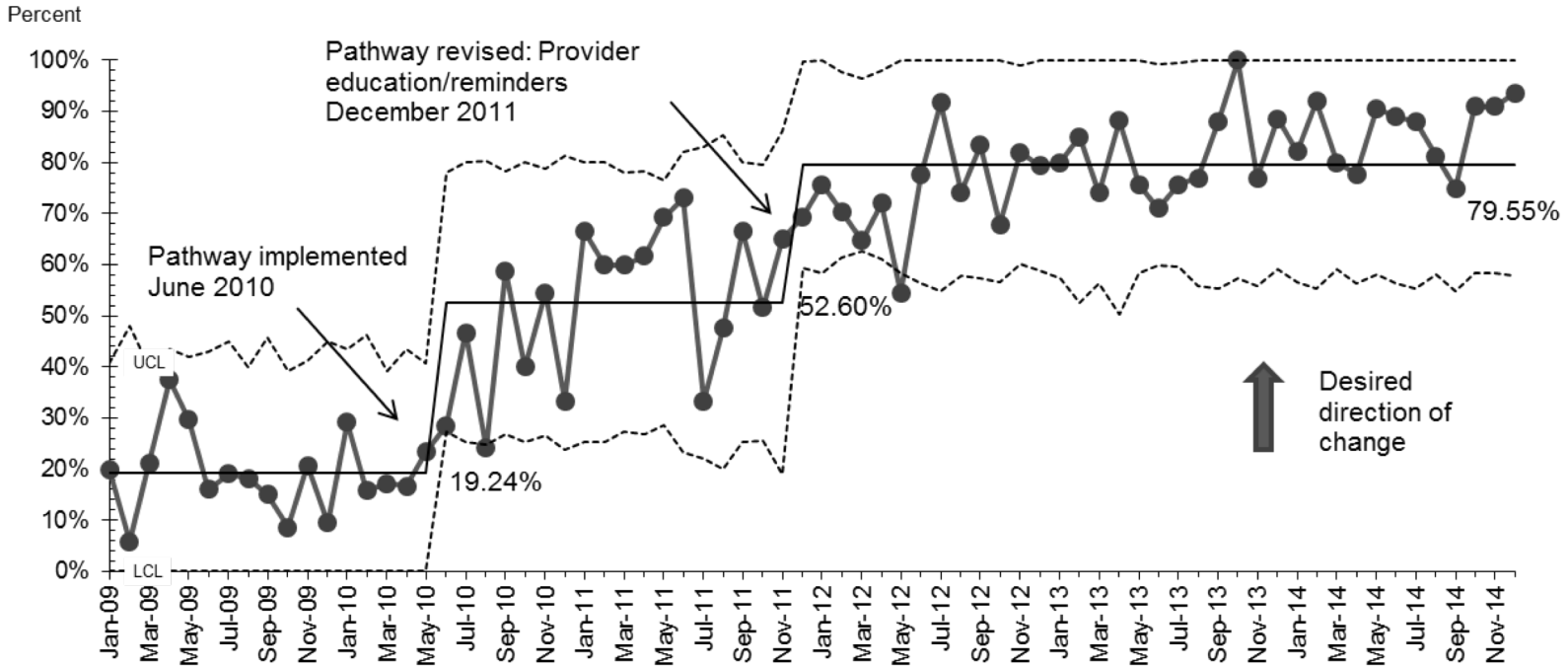
Follow up:
Review results with family

Narrow coverage after sensitivities

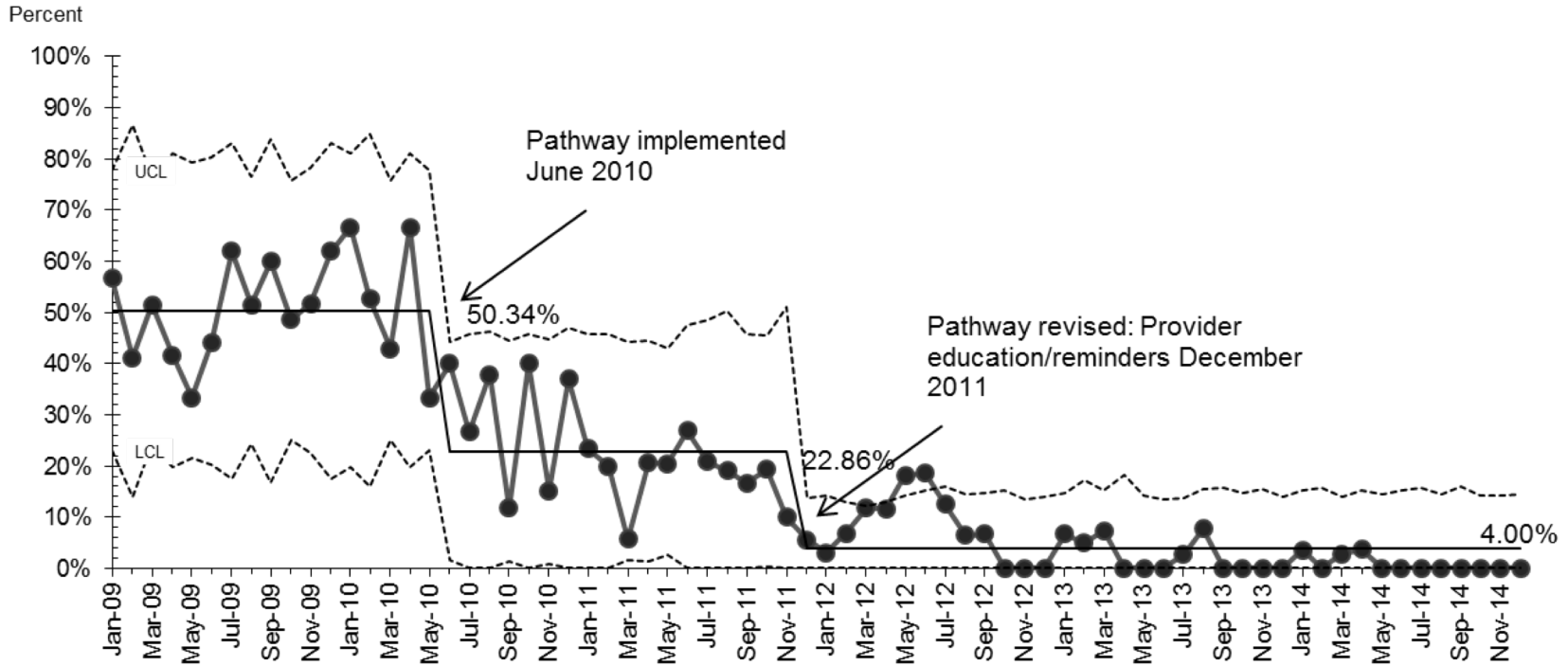


Poole, *PED* 2018

1st-gen cephalosporin use (cephalexin)



3rd-gen cephalosporin use (cefixime)



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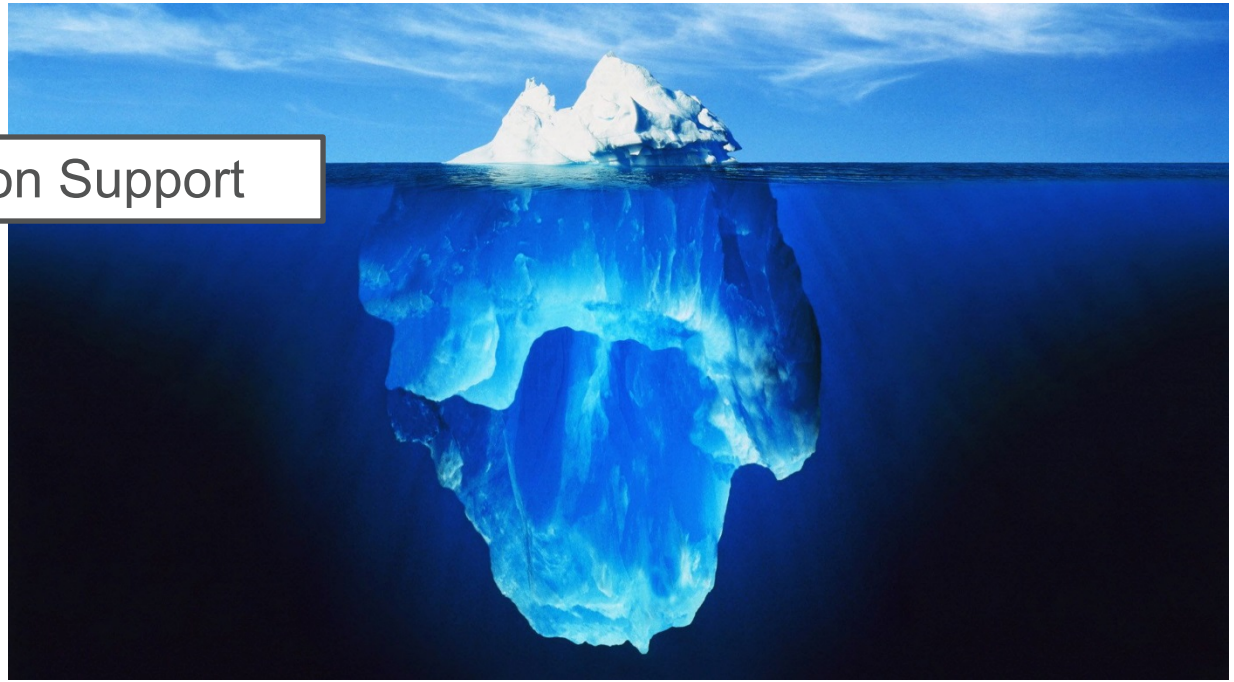
Conclusion

Implementation of a UTI pathway led to:

- ***Improvement*** in empiric selection of narrow spectrum antimicrobials
- ***No change*** in 72 hour revisits
- ***No change*** in inpatient admissions for UTI

Stewardship Tools

Decision Support



Outpatient stewardship: decision support

- Outpatient adult practices in Denver
- 8 clinical pathways
- Only one integrated into electronic charting
- Improved overall and broad-spectrum antibiotic prescribing

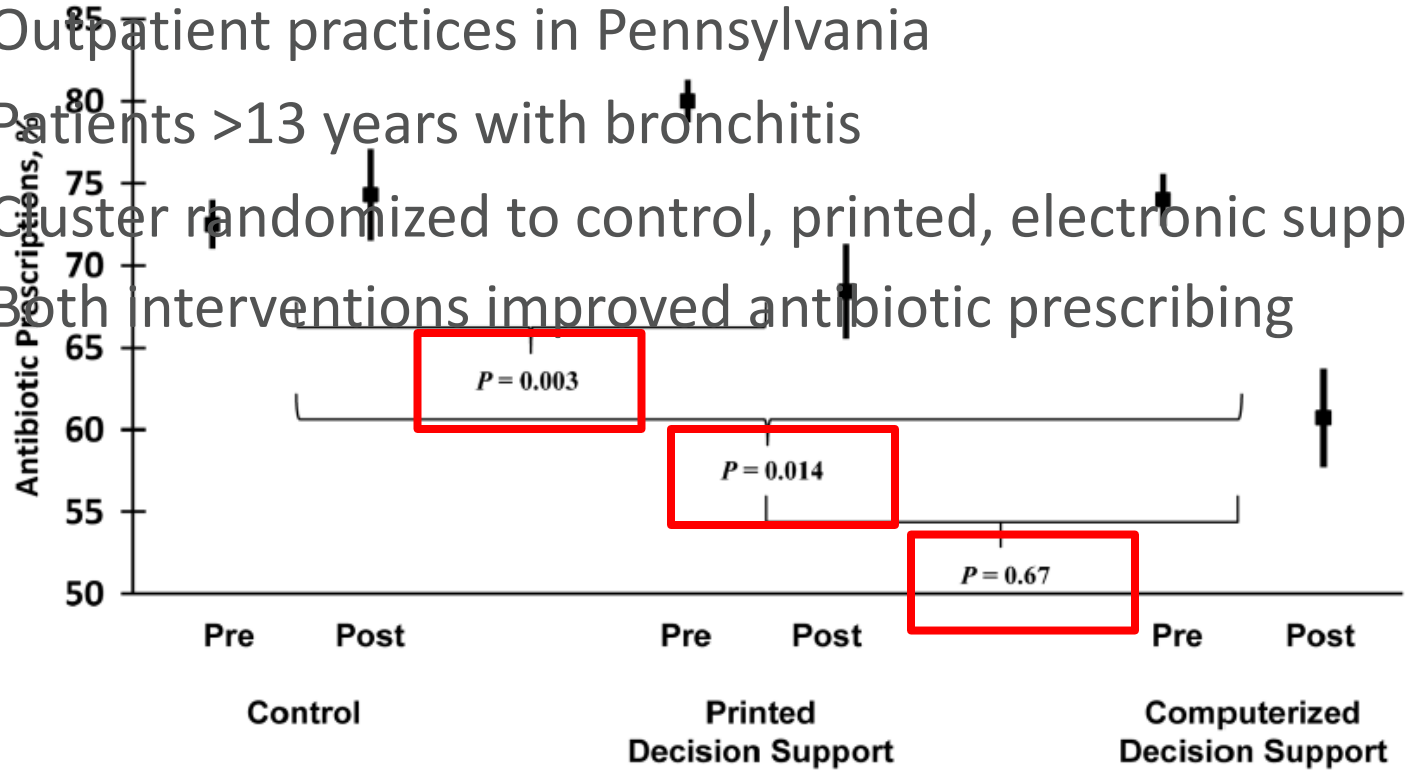
Table 4 Antibiotic Prescriptions for Non-pneumonia Acute Respiratory Infections*

	Study Group			Control Group		
	Baseline Period N = 15,114	Intervention Period N = 7897	P	Baseline Period N = 7650	Intervention Period N = 4052	P
Antibiotic prescribed for acute respiratory infection	6460 (42.7)	2991 (37.9)	<.0001	3045 (39.8)	1569 (38.7)	.25
Upper respiratory infection	1135 (21.6)	468 (15.6)		371 (12.8)	182 (14.2)	
Acute bronchitis	1773 (60.5)	737 (54.9)		625 (57.2)	289 (51.1)	
Pharyngitis	715 (29.9)	426 (31.5)		565 (40.6)	364 (37.3)	
Acute rhinosinusitis	2242 (66.5)	1060 (65.9)		999 (70.2)	524 (65.8)	
Acute otitis media	595 (50.6)	300 (51.2)		485 (57.5)	210 (48.5)	

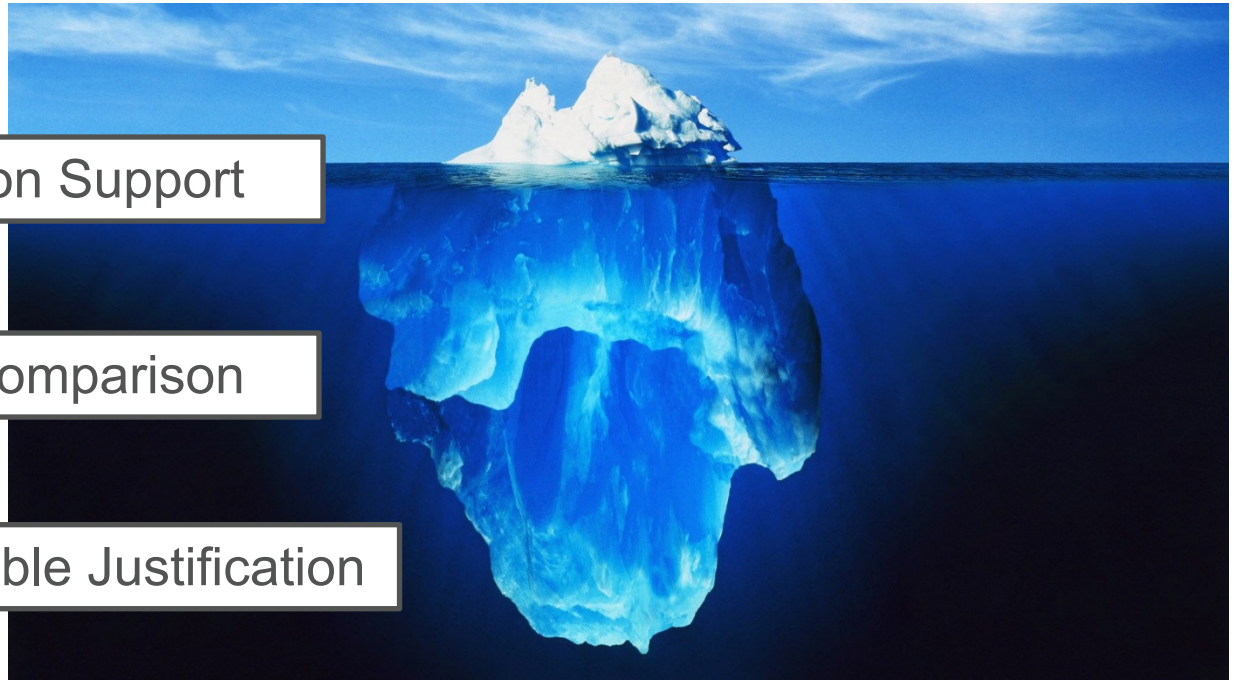
*Denominator for individual conditions is the number of cases of each condition from **Table 3**.

Outpatient stewardship: decision support

- Outpatient practices in Pennsylvania
- Patients >13 years with bronchitis
- Cluster randomized to control, printed, electronic support
- Both interventions improved antibiotic prescribing

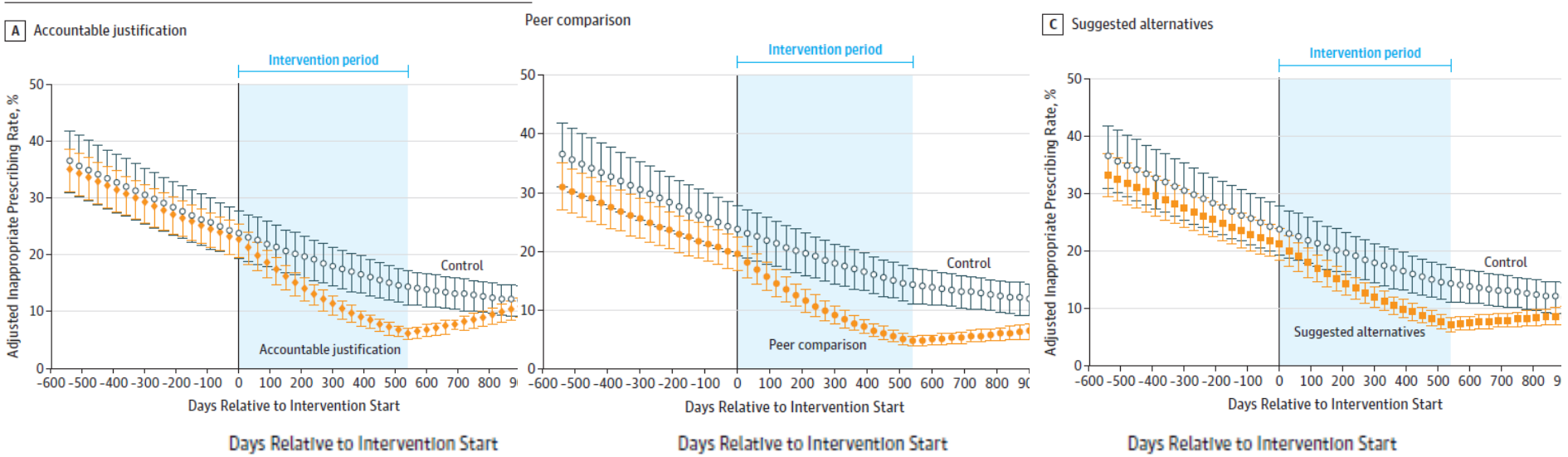


Stewardship Tools

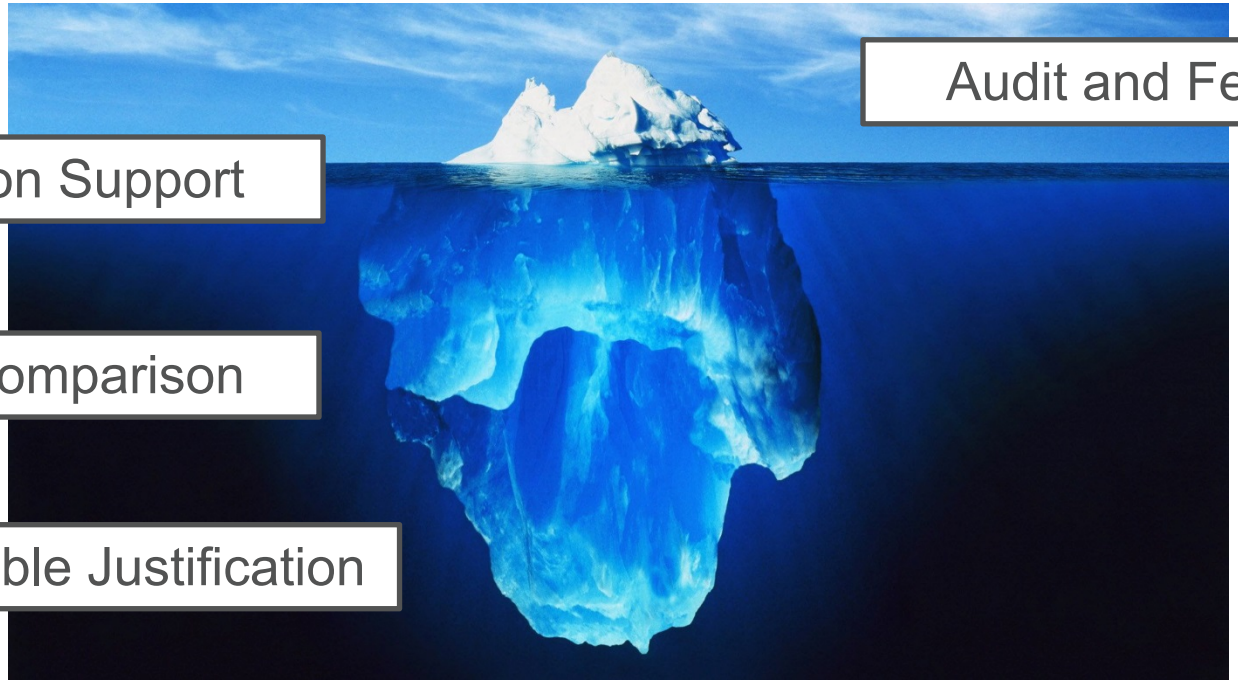


Outpatient stewardship: behavior: RCT

- RCT 47 outpatient adult clinics in LA, Boston



Stewardship Tools



Audit and Feedback

Decision Support

Peer Comparison

Accountable Justification

Outpatient stewardship: audit & feedback

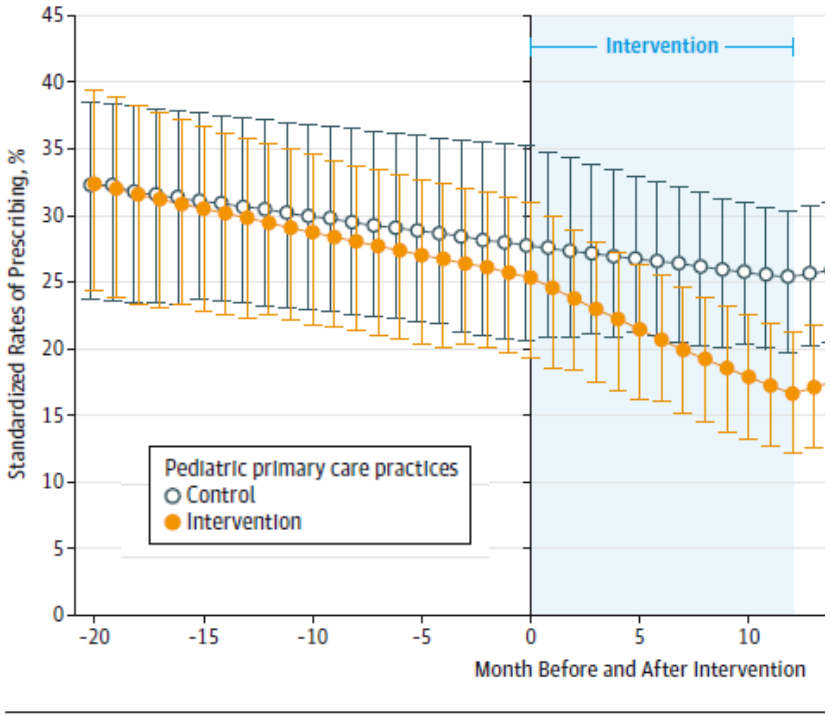
One hour education

Personalized audit and feedback

Really works!

….if continued

Figure. Standardized Rates of Broad-Spectrum Antibiotic Prescribing Before, During, and After Audit and Feedback



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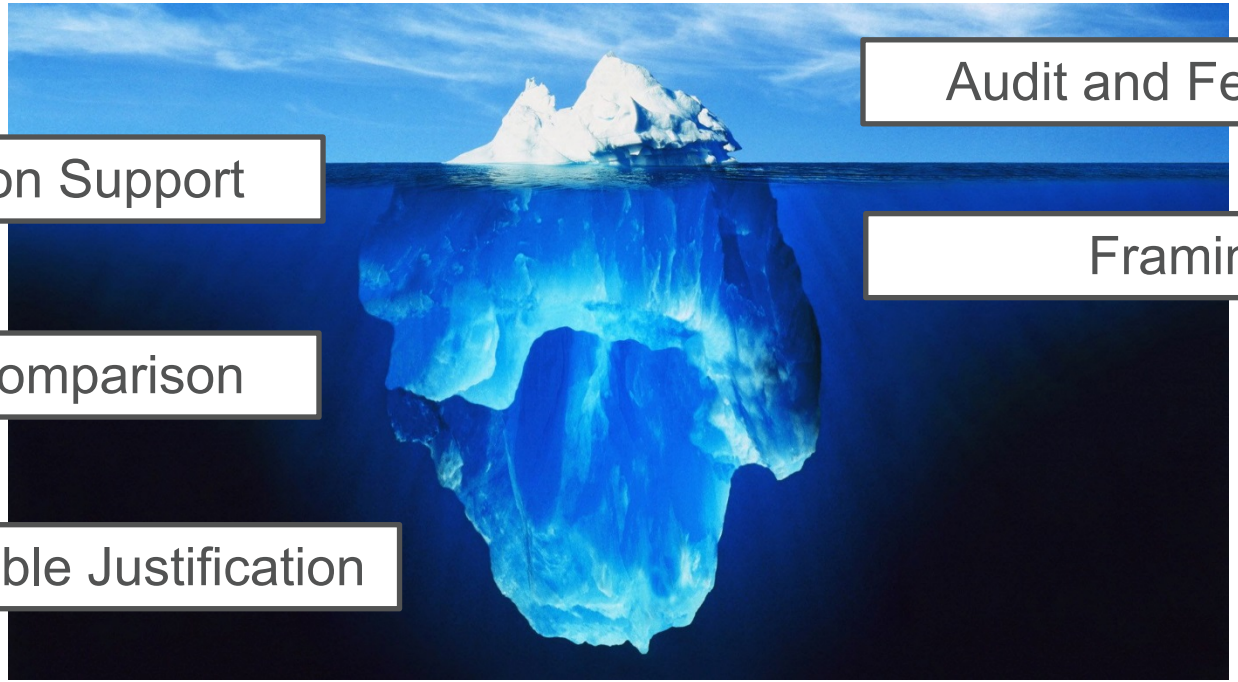
…and it might be an uphill battle

Semi-structured interviews with 24 trial participant pediatricians to evaluate response to the intervention

- Ignored (~30%) or distrusted (~50%) audit reports
- Gamed the system
- Constrained by guidelines
- Parental pressure for antibiotics (>90%)

Szymczak, ** 2016

Stewardship Tools



Audit and Feedback

Framing

Decision Support

Peer Comparison

Accountable Justification

Framing for antibiotics

- Clinicians more likely to prescribe inappropriately if they perceive a parent desires antibiotics
- Negative recommendations
- Positive recommendations

(7) 38-34-05

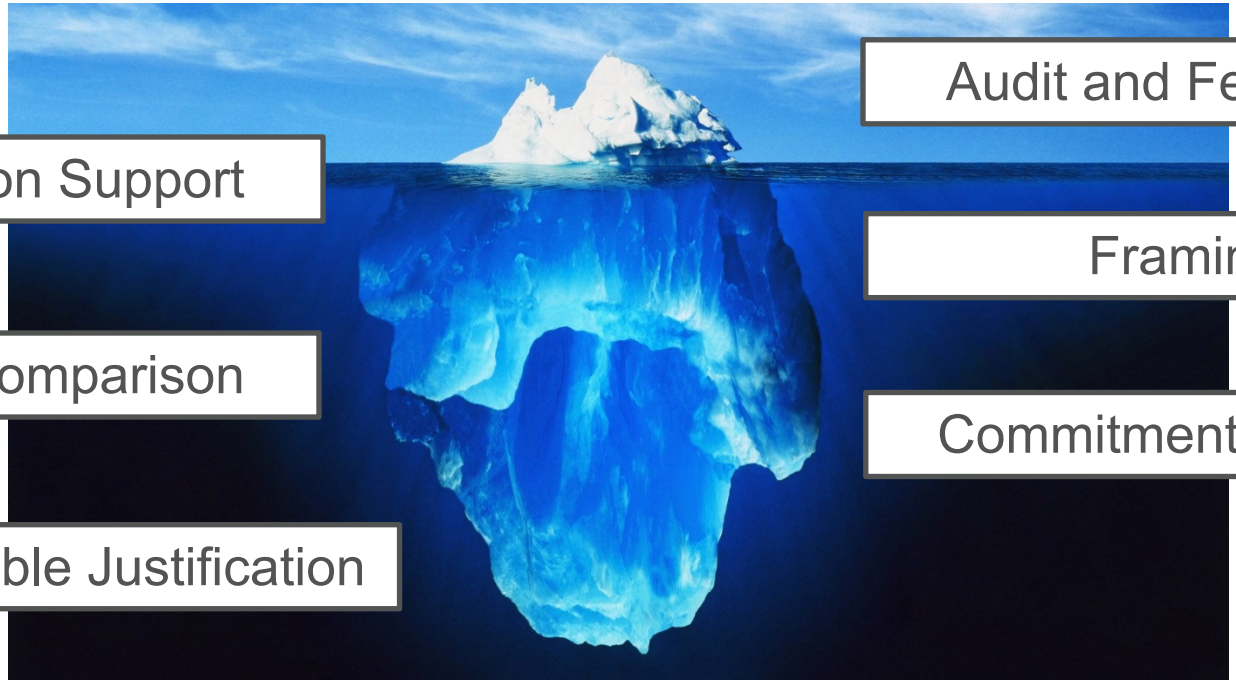
1	DOC:	I think we're in good shape here_
2		I don't think he needs
3		antibiotics, cause (0.5)
4		it wouldn't work.
15	MOM:	[Mm hm,
16	DOC: ->	=so .hh treatment will be:
17		you know medicine-
18		that're gonna make her
19		comfortable and treat her
20		symptoms. so .hh you c'd
21		get her medicine that's
22		gonna make her nose less
23		stuffy an' °make it° less
24		runny, an' uh medicine
25		for thuh cou:gh?,
26	DOC:	.hh An:d=uh you know
27		something for thuh fever
28		like (you've)/(we've) been
29		doing,

Framing for antibiotics

- Study
  - 1,200 children with 800 ARTI seen by 60 pediatricians
  - Antibiotics only given to 5%

Predictor Variable	Adjusted Risk Ratio[a]	95% CI	*P* Value
Communication practices			
Only positive treatment recommendations provided[b]	0.48	0.24-0.95	.04
Only negative treatment recommendations provided[b]	0.18	.02-1.43	.11
Both positive and negative treatment recommendations provided provided[b]	0.15	0.06-0.40	<.001
Contingency plan provided	1.66	0.65-4.23	.29

Stewardship Tools



Audit and Feedback

Decision Support

Framing

Peer Comparison

Commitment Posters

Accountable Justification

Outpatient stewardship: posters

- RCT 5 outpatient adult clinics in LA
- Signed commitment letter with photo in exam rooms
- One year observation period total, with interve
weeks at height of cold and 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.

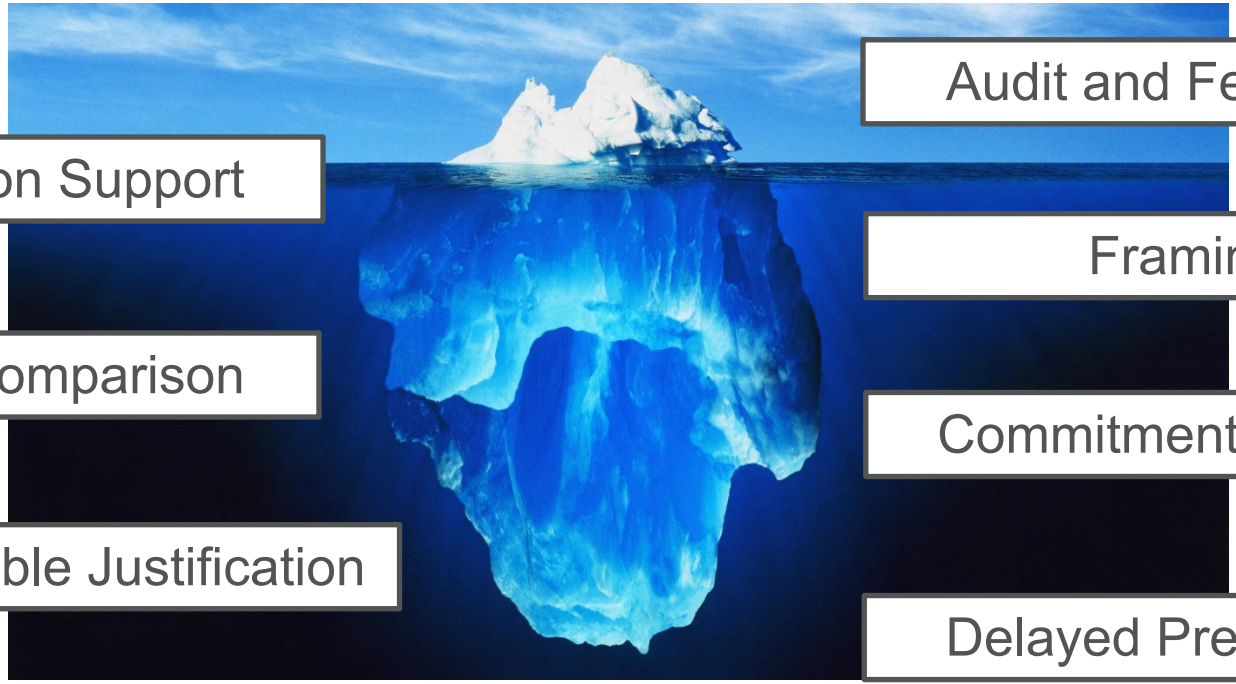
Your health is very important to us. As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do m

Table 4. Chang

Characteristic		ment
Inappropriate		1.9)
Absolute perce measurement		
Difference in c and control (9		

volving more intensive and costlier designs.[40] 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.[12]

Stewardship Tools



Audit and Feedback

Decision Support

Framing

Peer Comparison

Commitment Posters

Accountable Justification

Delayed Prescribing

Outpatient stewardship: delayed prescribing

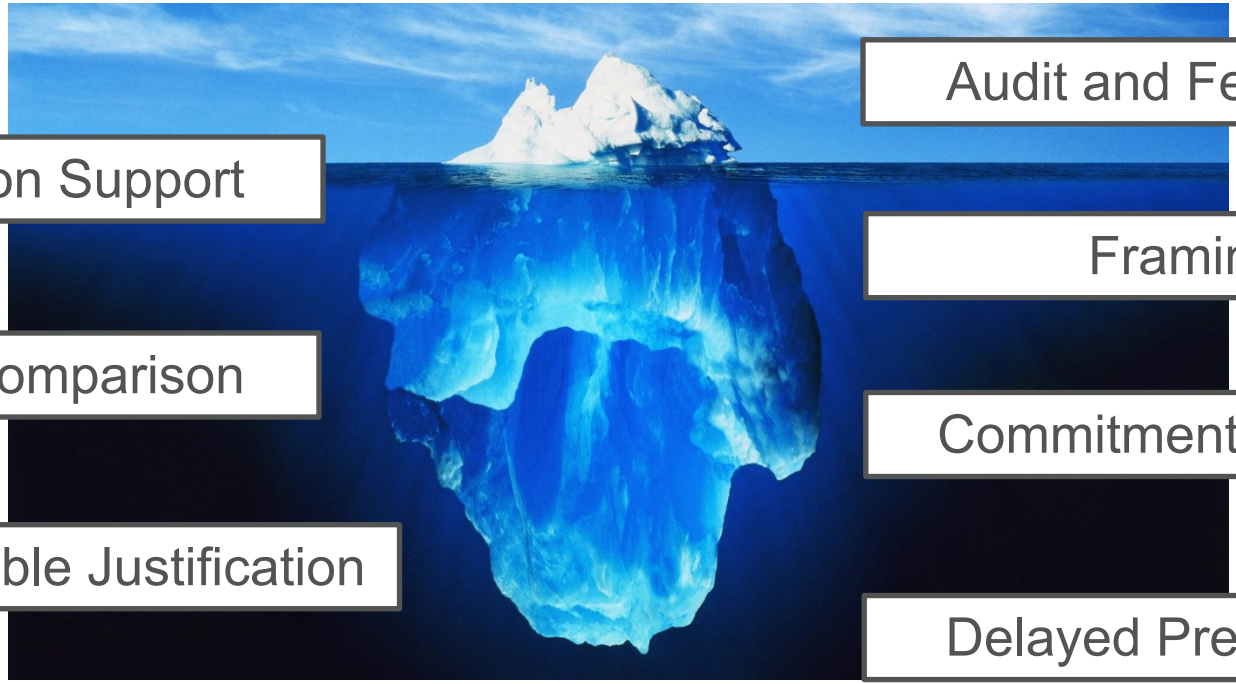
- Patients 2-12 years with AOM seen in an ED
- Randomized to observation (OT) or observation and antibiotic prescription (OT+P)
- Asked not to use antibiotics or visit another MD for 3 days
- All were given education and symptomatic care

TABLE 2 Patient Outcomes by Group

Characteristic Group	OT, *n* (%)[a]	OT+P, *n* (%)[a]	*P*
Used antibiotics or saw another physician within 3 d of PED visit	13 (13)	40 (38)	<.01
Ever used antibiotics between PED visit and follow-up call	19 (19)	49 (46)	<.01
Days of otalgia after PED visit			.29
0	31 (532)	41 (39)	
1	18 (18)	20 (19)	
2	20 (20)	18 (17)	
3	18 (18)	13 (12)	
>4	11 (11)	13 (12)	
Days of fever after PED visit			.03
0	69 (70)	60 (57)	
1	9 (9)	10 (10)	
2	12 (12)	17 (16)	
3	6 (6)	9 (9)	
>4	2 (2)	9 (9)	
Used medications after PED visit for pain or fever	94 (94)	95 (90)	.26

[a] Denominators differ slightly because of missing data.

Stewardship Tools



Audit and Feedback

Decision Support

Framing

Peer Comparison

Commitment Posters

Accountable Justification

Delayed Prescribing

Stewardship Tools

- CDC Core Elements of Outpatient Stewardship
- SHEA Mitigate Antimicrobial Stewardship Toolkit
- WA State Department of Health
- TASP!

THANK YOU!!

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ANTIBIOGRAM
2017
NUMBERS ARE PERCENT SUSCEPTIBLE

GRAM NEGATIVE ORGANISMS (Some antimicrobial agents known to lack clinical efficacy are not included)	Number tested (U = Urine)	Amikacin	Ampicillin	Amp-Sulbactam	Augmentin	Aztreonam	Cefazolin (Ur | non Ur)	Cefepime	Ceftazidime	Ceftriaxone	Cefuroxime (Parenteral | Oral)	Ciprofloxacin	Gentamicin	Imipenem	Meropenem	Minocycline	Nitrofurantoin U	Piperacillin-Tazo	Tobramycin	Trim-Sulfa
Acinetobacter species	43	93		95				88	88			80	92		97			67	90	80
Enterobacter cloacae[β]	83(U47)		0		0		0	97	71	69		93	96		96		53	71		84
Escherichia coli	940(U872)		51		79		92 |60	97	95	94	90 |32	88	93		99.9		99	96		68
Haemophilus influenzae	25		69		100						100	100								81
Klebsiella oxytoca	39(U31)		0		88		87 |33	100	100	95	90 |53	90	95		100		90	85		77
Klebsiella pneumoniae	111(U79)		1		83		91 |65	96	94	94	86 |41	85	95		98		52	87		76
Proteus mirabilis	68(U60)		74		88		97 |22	99	99	99	99 |88	94	91		100		0	100		79
Salmonella species	27		78						89	89		45								96
Serratia marcescens[β]	30(U15)		0		0		0	100				97	97		97		0	90		97
Pseudomonas aeruginosa-nonCF	221(U62)	89				65		93	90			90	83		90			90	95	3
Pseudomonas aeruginosa-CF	[α]414	38				74		51	81			81		75	81			86	62	51
Stenotrophomonas maltophilia	60(CF50)											44				100				[γ]93