North Carolina SPICE
Statewide Program for Infection Control & Epidemiology

Five Common Missed Opportunities for Antibiotic Stewardship

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North Carolina Clinical Antibiotic Stewardship Partners

Conflict of interest Disclosures

- The views and opinions expressed in this presentation are those of the speaker and do not reflect the official policy or position of any agency of the U.S. or NC government or UNC.
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- The speaker has no financial conflicts of interest.

Objectives

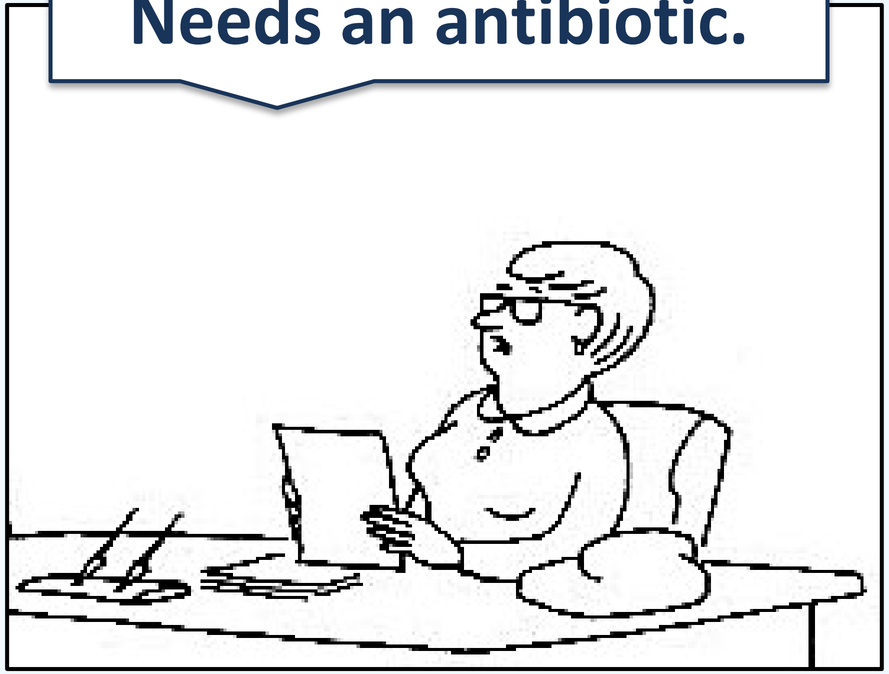
- Identify when and why we should not over-rely on test results.
- Discuss common clinical situations in which clinicians should avoid jumping to diagnostic conclusions.
- Explain how antibiotic stewardship teams can avoid a common missed opportunity.

Missed Opportunity #1:

Putting Too Much Trust in Test Results

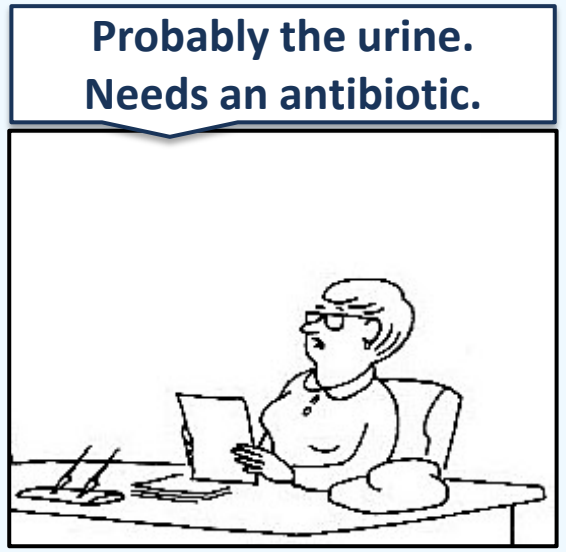
The Myth of “It Must Be the Urine”

Probably the urine. Needs an antibiotic.



What's Behind the Myth of "It Must Be the Urine"

- Ordering a urinalysis and/or culture whenever any adverse event happens to an older person
- Thinking white blood cells and/or bacteria in the urine mean infection
- Thinking a positive culture means "UTI" and the need for antibiotics



Case 1: Positive Urine in the Emergency Department

- 84 y/o woman with moderate dementia. Assisted living resident for 9 months. Requires assistance with bathing, dressing and toileting.
- Fell while walking to breakfast this morning. Per protocol, the facility called EMS, who found her confused and took her to the ED.
- T 98.4 HR 88 BP 114/76. Assessment showed confusion but no significant injury.
- Urinalysis positive for leukocyte esterase and nitrites.
- She is returned to the assisted living community with a 10-day course of ciprofloxacin.
- Does this ever happen in your experience? What do you do?

Urinalysis is Useless in Diagnosing UTI

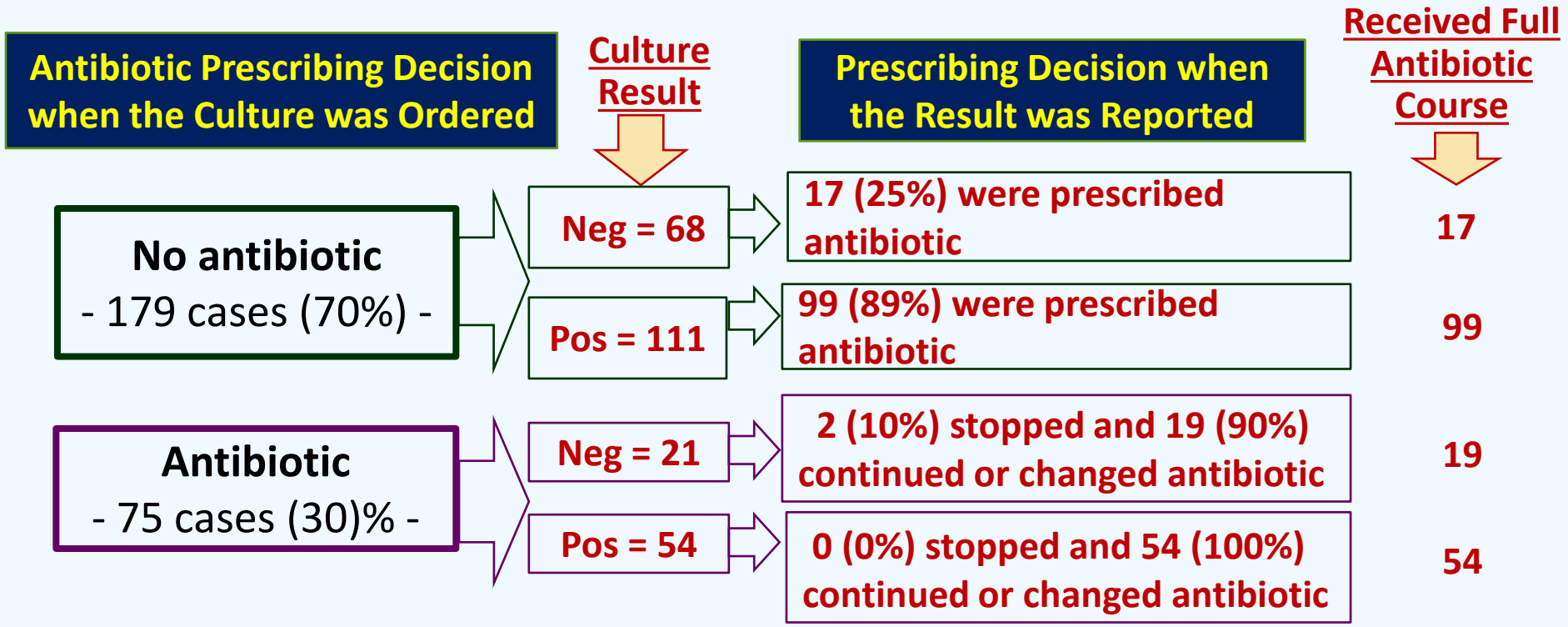
- Recent study of 3,392 adult patients (mean age 67, 60% female) from 5 hospitals who had a urinalysis in the ED or on admission and a culture.
- Diagnostic criteria for infection: + culture (>100,000 colonies) + either urinary symptoms (e.g. dysuria) or two systemic signs (e.g. fever) without other cause

Parameter	Pos Predict Value	Neg Predict Value
Leukocyte Esterase ≥ Trace LE	.33	.95
Leukocyte Esterase ≥ 1+ LE	.33	.94
WBC ≥ 5/hpf	.32	.95
WBC ≥ 10/hpf	.35	.92
WBC ≥ 20/hpf	.37	.89
Nitrite Positive	.43	.86
Bacterial count 5-50/hpf	.20	.77
Bacterial count > 50/hpf	.41	.90

Advani SD, et al. Performance of Urinalysis Parameters in Predicting Urinary Tract Infection. Clin Infect Dis. 2024 Apr 26:ciae230.

Ordering a Urine Culture: A "Gateway" to Overprescribing

- results of 254 randomly sampled cultures from 31 nursing homes -



Bottom Line: 189 (74%) received a course of antibiotics, although 86% had a temperature less than 99ºF, 74% lacked documentation of any urinary tract-specific signs or symptoms, and only 18% met the modified McGeer criteria for urinary tract infection.

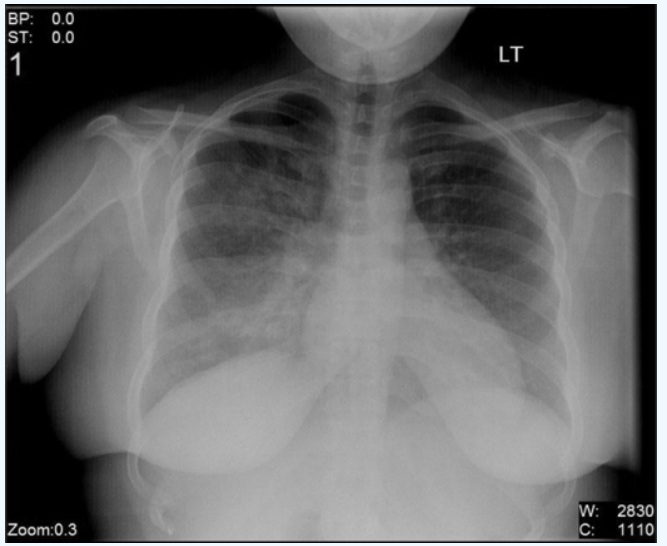
Case Discussion

- Belief that a positive urinalysis or urine culture needs antibiotics is the #1 opportunity for antibiotic stewardship in older persons.
- Addressing this issue must be done both on a policy level and on a case-by-case basis
- Examples of policy level interventions that work:
  - ✓ "Time out" 2-3 days after initiating antibiotic
  - ✓ Protocol for when to (and when not to) order urine testing
  - ✓ Protocol for comprehensive evaluation and management of status changes
- Examples of individual (case-by-case) level interventions that work:
  - ✓ Educational materials about bladder physiology in older women
  - ✓ One-on-one discussion of issues and options
  - ✓ Focusing on providers who are outliers from standard practice

Case 2: Portable X-Ray Report

- You are on call at night for a nursing home
- The nurse on duty phones to read you the report of a portable chest x-ray that was done that afternoon and just came back now
- It reads: “Patchy area in left lower lobe. Underlying atelectasis or pneumonia cannot be excluded.”
- Is this an indication to start antibiotics?

Mobile Chest-X-Rays Often Aren't Very Good



- Inability of frail older persons to maintain a stationary, upright sitting position
- Relatively poor image quality
- A lack of availability of previous films for comparison

- Radiologists disagree frequently on
  - If infiltrate present (K = 0.54)
  - If pleural effusion (K = 0.8),
  - If hilar lymphadenopathy (K = 0.54)
  - if mediastinal lymphadenopathy (K =0.49)

Loeb MB, et al. JAMDA 2006; 7: 2006, 7:416–419. Drinka PJ, et al. J AMDA 2006:7:467-469

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Radiologists Have Many Ways to Say “I’m Not Sure”

Atelectasis without pneumonia	**Identifies atelectasis without mention of possibility of pneumonia:** terms included linear opacities, streaky opacities, right lower lobe atelectasis, atelectasis at lung bases, possible atelectasis, likely atelectasis	Low Likelihood of Pneumonia
Cannot exclude pneumonia	**Pneumonia is not likely but cannot be excluded:** terms included pneumonia could be missed, pneumonia not excludable, pneumonia would be considered, may reflect pneumonia, suggesting pneumonia, infiltrate may not be seen, possible infiltrate	Intermediate Likelihood of Pneumonia
Atelectasis or pneumonia	**Reports both pneumonia/infiltrate and atelectasis as possibilities:** terms included patchy atelectasis or pneumonitis, patchy atelectasis or interstitial pneumonitis, may reflect atelectasis or pneumonia, pneumonia vs. atelectasis, infiltrate vs. atelectasis, consistent with atelectasis or developing acute infiltrate, underlying atelectasis or infiltrate cannot be excluded, right lower lobe atelectasis or infiltrate	Intermediate Likelihood of Pneumonia
Infiltrate without pneumonia	**Infiltrate is identified without use of the word pneumonia:** terms included possible infiltrate suggested, right lower lung infiltrate, right base infiltrate, minimal infiltrate persists, infiltrate and linear atelectasis in both, bilateral lower lobe infiltrates with linear atelectasis	Intermediate Likelihood of Pneumonia

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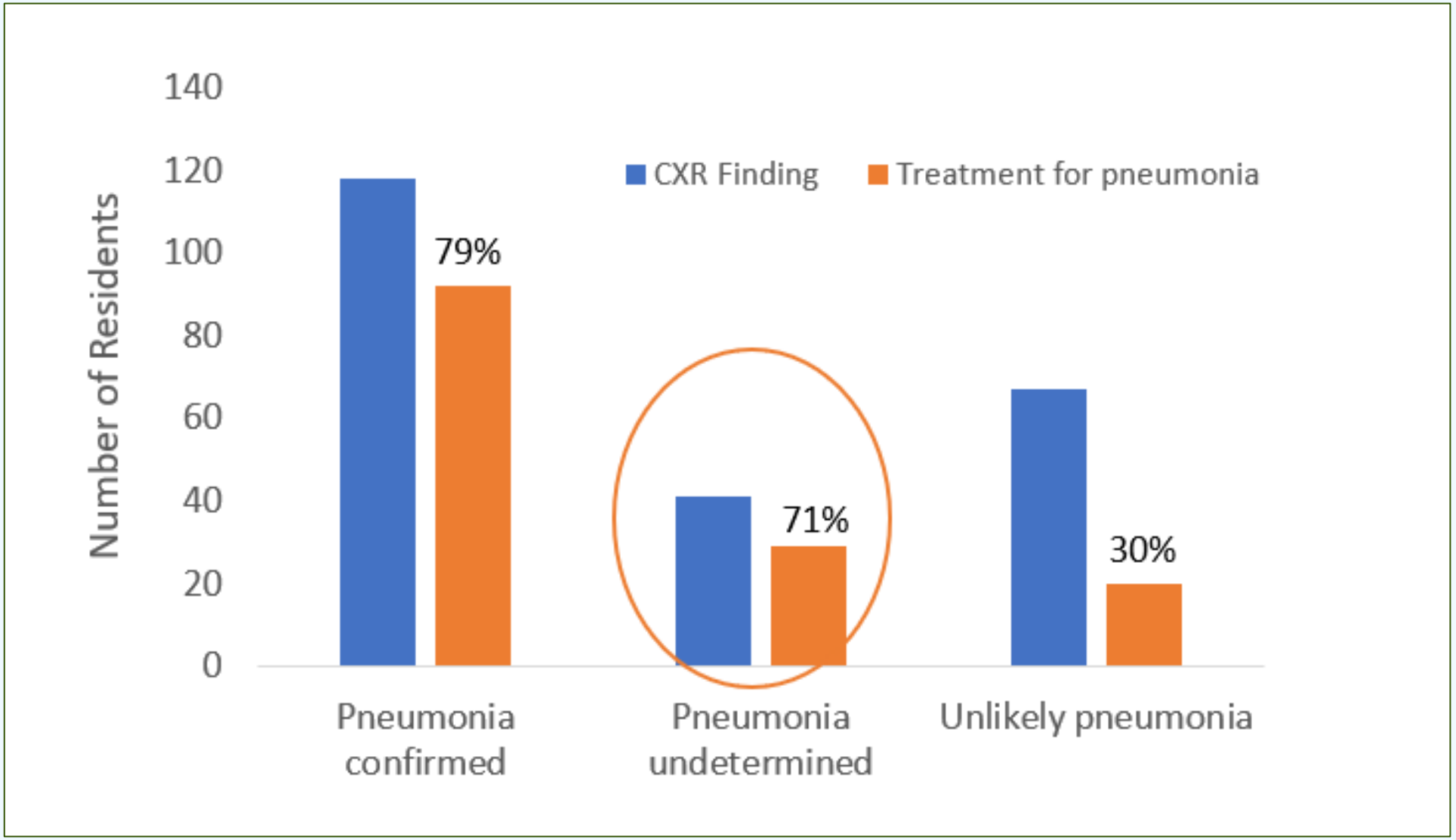
Unfortunately, Doctors Prescribe When Radiologists Equivocate



Mc Clester Brown et al. JAMDA 17 (2016) 1164.e1e1164.e5

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Missed Opportunity #2:

Not Using Alternatives to Antibiotics for Older Persons with Recurrent UTIs

Case 3: Is UTI Prophylaxis Working?

- Ms. B is an 82-year-old woman with hemiparesis and moderate dementia. She lives with her daughter and son-in-law.
- She is followed by a urologist, who has her on prophylactic antibiotics for recurrent UTIs
- Despite receiving daily prophylaxis with nitrofurantoin 50 mg HS daily for a year, she's had 3 UTI episodes over the past year
- She visits her urologist for a routine check up

Culture Results from Urologist

1. >100,000 ESCHERICHI COLI
2. >100,000 PROVIDENCIA STUARTII

ANTIBIOTIC SUSCEPTIBILITY TEST RESULTS:

	1. ESCHERICHIA COLI		2. PROVIDENCIA STUARTII		
	SUSC	INTP	SUSC	INTP	
AMPICILLIN	4	S	>=32	R	MCG/ML
CEFAZOLIN	<=4	S	>=64	R	MCG/ML
CIPROFLOXACIN	4	R	>=4	R	MCG/ML
TRIMETH/SULFA	>=320	R	<=20	S	MCG/ML
NITROFURANTOIN	<=16	R	>=256	R	MCG/ML
AMPICILLIN/SUL	<=2	S	>=64	R	MCG/ML

Case Discussion

- The urologist recommends switching prophylactic antibiotics to trimethoprim / sulfamethoxazole
- The daughter asks if there are antibiotic alternatives that would work in this situation
- What's going on?
- What would you recommend?

Basic Hygiene to Reduce UTI Recurrence

- Drink plenty of fluids
- Perineal hygiene i.e., wiping front to back, consider using non-scented wipes
- Vaseline or other barrier cream post-void
- Reduce constipation
- Empty bladder frequently (timed toileting) – some say as much as every 2 hours (consider 2 x a shift)
- No data from trials

https://www.auanet.org/guidelines-and-quality/guidelines/recurrent-uti#x14424
https://www.nottsapc.nhs.uk/media/1815/uti-prophylaxis.pdf
https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Urological-infections-2023.pdf

Topical Estrogens to Prevent Recurrent UTIs in Women

- Recent (2022) review found six studies conducted 1993-2005 with total of 258 patients
- 3 methods studied: cream, ring/pessary, and intravaginal tablet
- All included studies concluded that topical estrogen is effective prophylaxis, with higher efficacy associated with weekly doses of ≥850 µg.

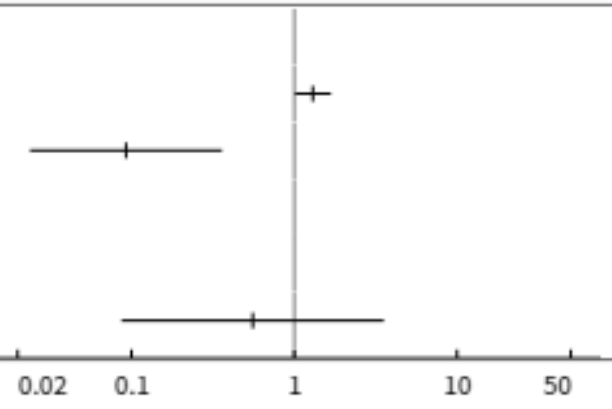
Antoniou & Somani. Eur Urol Focus. 2022 Nov;8(6):1768-1774
Perrotta et al. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD005131

Paltry Amount of Research on Topical Estrogens Identified in Cochrane Review (2008)

- Review contained only two studies comparing oral antibiotics with vaginal estrogens.

Analysis 3.1. Comparison 3 Vaginal oestrogens versus antibiotics, Outcome 1 UTI.

Study or subgroup	Vaginal oestrogens n/N	Antibiotics n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
3.1.1 UTI at end of treatment period				
Raz 2003	58/86	44/85		1.3[1.01,1.68]
Xu 2001	2/27	12/15		0.09[0.02,0.36]
3.1.2 UTI - recurrence 2 months after treatment				
Xu 2001	2/27	2/15		0.56[0.09,3.55]



Perrotta et al. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD005131

Cochrane Review (2023) – Cranberry Products and UTI Rate

Cranberry Juice or Syrup vs Placebo	# Studies	Effect Size [90% CI] <1 favors Cranberry
Women with recurrent UTI	6	0.84 [0.63, 1.10]
Elderly men and women in institutions	1	0.51 [0.21 , 1.22]
Cranberry Tablets or Powder vs Placebo or Control	**# Studies**	**Effect Size [90% CI]**
Women with recurrent UTI	3	0.45 [0.28 , 0.72]
Elderly men and women in institutions	2	1.02 [0.75 , 1.39]
Cranberry Product vs Antibiotics	**# Studies**	**Effect Size [90% CI]**
Women with recurrent UTIs	1	1.02 [0.76, 1.37]
Culture-verified UTI	2	1.03 [0.80, 1.33]
Clinical UTI (symptoms) without culture	2	1.30 [0.79, 2.14]

Methenamine vs Antibiotics in NH Patients (ALTAR Trial)

- 102 with daily antibiotics vs 103 with methenamine Hippurate over 12 months
  - Abx Rx: 0.89 episodes/person/year (95% CI, 0.65-1.12); Methenamine RX: 1.38 episodes/person/year (95% CI, 1.05-1.72)
  - Development of resistance among E Coli: 72% of participants in daily antibiotics group vs 56% in the methenamine arm (p = 0.05)
  - 52% of cultures during “symptomatic UTIs” grew bacteria.
- Editorial: Methenamine was non-inferior in this trial of non-NH women

Saul H, et al. C. Methenamine is as effective as antibiotics at preventing urinary tract infections. BMJ. 2023 Jan 17;380:72.
Harding C, et al. Alternative to prophylactic antibiotics for the treatment of recurrent urinary tract infections in women: multicentre, open label, randomised, non-inferiority trial. BMJ 2022;376:e068229.

Effectiveness of Antibiotic Stewardship in Older Women with Recurrent UTIs

- ImpresU cluster randomized trial in 1,041 frail older adults aged 70 +
- Intervention: Multifaceted antibiotic stewardship program – decision tool for antibiotic use and educational material. Control Group: Usual care.
- Results
  - Abx prescription rate in intervention group: 27 courses/person-year; rate in control group: 58 courses/person-year ($p<0.001$)
  - No difference in incidence of complications, hospital admissions, or mortality
- Take Home: A multifaceted antibiotic stewardship intervention reduced antibiotic prescribing for suspected UTIs in older adults

Hartman E, et al. BMJ. 2023;380:e072319. Published 2023 Feb 23.

Conclusions

- Lots of opinion, modest data
- My opinion:
  - Everyone should employ and foster good perineal hygiene
  - Antibiotic stewardship is best option to reduce “recurrences” because many “UTI’s” are misdiagnosis of asymptomatic bacteriuria
  - Second best option: Topical Estrogens or Methenamine Hippurate

Missed Opportunity #3:

Avoiding a “Test for Cure” when It Isn’t Indicated

Case 4: Re-test after Treatment for *C Difficile*?

- Mr. JD, a 60 y/o attorney, was hospitalized for community-acquired pneumonia, treated with levofloxacin and discharged
- 7 days later, seen at another hospital because of 4-6 loose stools over prior 24 hours and a low-grade fever
- Stool test positive for *C diff*
- Treated with vancomycin 125 mg PO QID for 10 days
- Treatment is completed
- His wife, who has read recurrence, asks that he be tested to assure that the disease has been eliminated
- What do you advise and why?

C difficile Colonization Is Common in Healthy People

Population type		Range of carriage rates
Healthy neonates and infants		18–90 %
Healthy adults – general population		0–15 %
Elderly in long-term care facilities, chronic care, or nursing homes		0–51 %
Hospital	*Elderly*	0.6–15 %
	Inpatients (not specifically elderly)	4–29 %
	Rehabilitation (spinal)	11–50 %
	HIV	4 %
	Healthcare workers	0–13 %

Furuya-Kanamori L, et al. Asymptomatic Clostridium difficile colonization: epidemiology and clinical implications. BMC Infect Dis. 2015 Nov 14;15:516.

Asymptomatic Carriage of *C difficile* among Inpatients

Table 1
Asymptomatic carriage and CDI on hospital admission versus acquired during hospitalization

Ref. #	2	3	4	5	6	15
Setting	Medical Ward, n (%)	Medical-Surgical Ward, n (%)	3 ICUs/2 Medical-Surgical Wards, n (%)	2 Medical Wards, n (%)	6 Hospitals, n (%)	Medical Wards, n (%)
C difficile positive on admission	29 of 428 (7)	65 of 634 (10)[a]	55 of 496 (11)[b]	37 of 271 (14)	—	16 of 168 (10)[c]
Asymptomatic carriage	17 of 29 (59)	61 of 65 (94)	44 of 55 (80)[d]	19 of 37 (51)[e]	184 of 4143 (4)	16 of 168 (10
CDI	12 of 29 (41)	4 of 65 (6)	11 of 55 (20)	18 of 37 (49)	[f]	Excluded
C difficile acquired during hospital stay	83 of 399 (21)	54 of 569 (10)	34 of 234 (15)[g]	47 of 253 (19)	240 of 3959 (6)	12 of 152 (8)
Asymptomatic carriage	52 of 83 (63)	51 of 54 (94)	25 of 34 (74)	19 of 47 (40)	123 of 240 (51)	8 of 12 (75)
CDI	31 of 83 (37)	3 of 54 (6)	9 of 34 (26)	28 of 47 (60)	117 of 240 (49)	4 of 12 (25)
Persistence of carriage	68 of 83 (82) colonized on discharge[h]	—	44 of 71 (62) colonized on follow-up cultures	—	—	—

Donskey CJ, et al. Colonization versus carriage of Clostridium difficile. Infect Dis Clin North Am. 2015 Mar;29(1):13-28.

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IDSA Recommendations about *C difficile* Testing

- Do not perform repeat testing (within 7 days) during the same episode of diarrhea
- Do not test stool from asymptomatic patients, except for epidemiological research
- Do not submit stool specimens on patients receiving laxatives
- Only submit specimens from patients with unexplained, new onset of ≥ 3 unformed stools in 24 hours
- Bottom line – as with all testing, don't test unless a positive test will lead to a change in management

McDonald LC, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018 Mar 19;66(7):e1-e48.

What to Advise JD and his Wife about Minimizing Recurrences of *C difficile*

- Control modifiable risk factors
  - Minimize antibiotic use
  - Avoid gastric acid suppression (H2 blockers, PPIs)
- Avoid laxatives
- Only re-test if symptomatic and meeting diagnostic criteria

Case 5: Test for Cure after Treatment for UTI?

- Mrs. B is back again
- She did well on cranberry tablets for 4 months and then had an episode of dysuria, low grade fever, and worsened incontinence. She was treated with 3 days of trimethoprim-sulfamethoxazole.
- She returns with her daughter, who says that her urinary symptoms are gone, but that she seems more tired than usual. "Can you please do a repeat culture so we can be sure the infection is gone?" she asks. "My doctor always does that when I have an infection."
- What do you advise and why? And when is "test for cure" appropriate?

Missed Opportunity #4:

Thinking All Red Legs are Infected

Case 6: Walk-In Clinic -- Student Case Presentation

- 66 year old Latino man
- Has red foot
- Ambulatory, complains of discomfort when walking
- Temperature 98.2º F
- Student wants to know which antibiotic to prescribe

Additional History

- Had rash on and off for a year
- Similar, less intense rash on other foot
- Works as a cook in a kitchen
- Wears leather boots
- Feet sweat and/or get wet frequently.

Diagnosis: Contact Dermatitis

Case 7: Nonhealing Wound

- A 62 year old man who injured his left leg at a pool
- Self-treated for several weeks
- MD treated with Bactrim; then (when he failed to respond) a course of Augmentin
- Main symptom is itching
- What's the likely cause?

Diagnosis: Contact Dermatitis

Case 8: Red Leg with Nonhealing Wound

- 70-year-old cruise ship passenger
- Had banged shin getting into a taxi a week beforehand
- Had been treated by another provider with cephalexin, then azithromycin
- Leg swollen and red, with nonhealing wound
- What's going on here?

NERDS and STONEES

NERDS – Signs of Superficial Infection

- ☑ **N**onhealing
- ☑ **E**xudate (increased drainage)
- ☑ **R**ed, friable, bleeding wound bed
- ☑ **D**ebris (yellow film)
- ☐ **S**mell (increased)

STONEES – Signs of Deep Infection

- ☐ **S**ize of wound (increasing)
- ☐ **T**emperature of wound (increased)
- ☐ **O**s (probes to bone)
- ☐ **N**ew breakdown
- ☑ **E**dema/**E**rythema (more than 1 cm)
- ☐ **E**xudate (or profuse drainage)
- ☐ **S**mell (prominent)

Adv Skin Wound Care. 2006 Oct;19(8):447-61

Case Discussion

- Diagnosis: nonhealing, superficially infected wound with dependent edema
- Treatment:
  - Systemic antibiotics discontinued
  - Leg elevated much of time for several days
  - Debridement
  - Topical antibacterials such as xeroform (has bismuth), cadexomer iodine, or silver impregnated products

Case 9: Early Cellulitis or Not? Antibiotics or No?

- 62 year old man
- Largely confined to wheelchair due to obesity, arthritis, and weakness from stroke
- Bumped leg 1 week ago; has self-treated by cleansing and covering with a band-aid
- Not painful
- Nurse wonders if wound needs an antibiotic

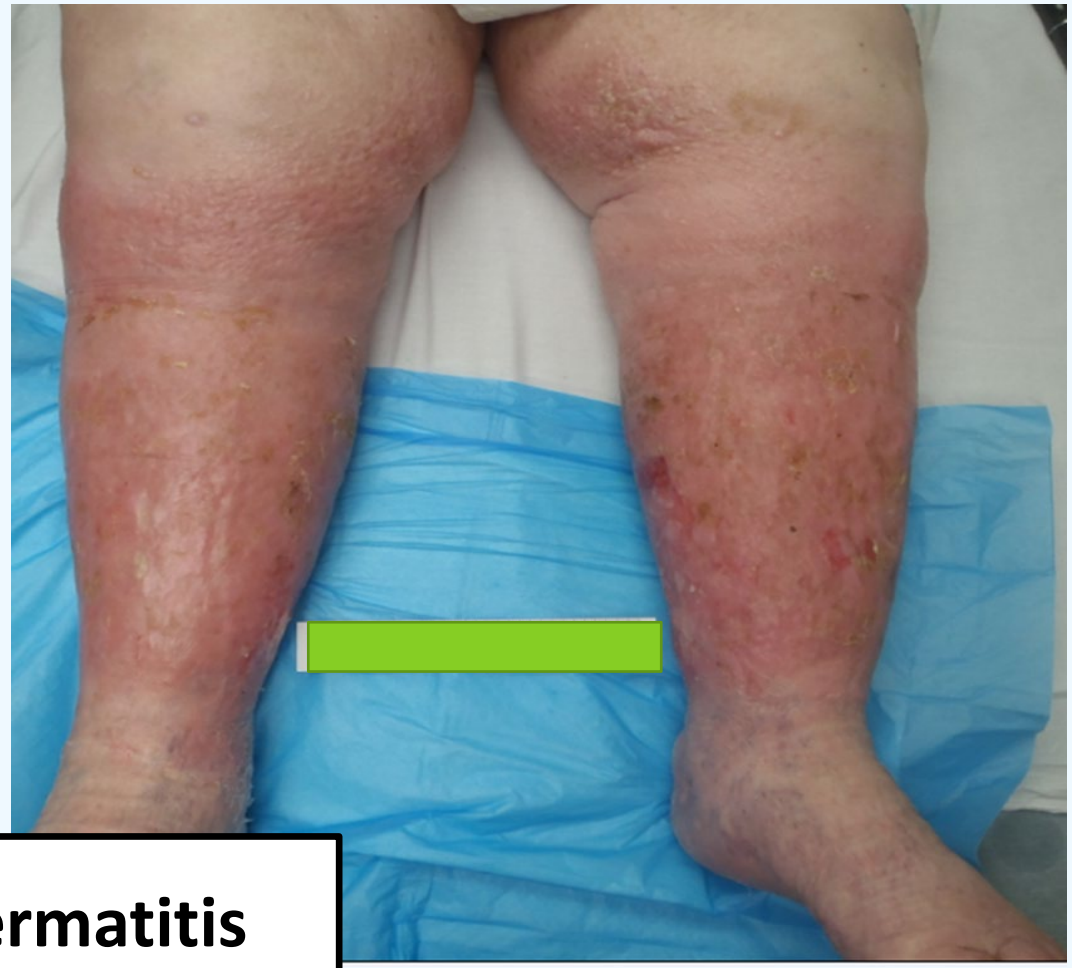
One Week Later

After treatment with elevation, xeroform gauze and Tegaderm

Case 10: Horrible Looking Red Legs After Cross-Country Drive

Appearance after 10-day course of levofloxacin

Case Discussion



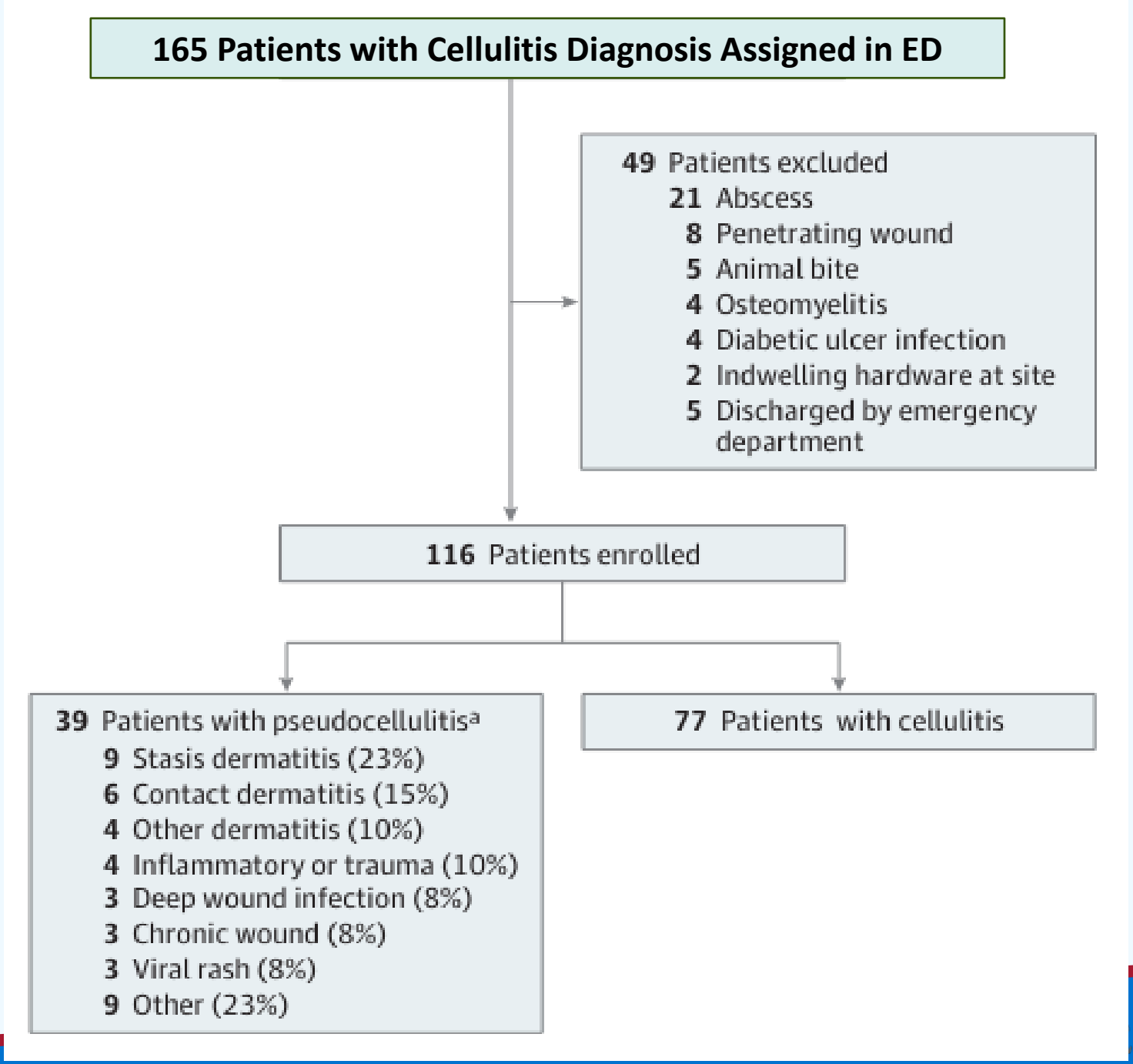
Diagnosis: Stasis Dermatitis

After 1-week course of levofloxacin

After a month of dynamic compression

Outcomes of Early Dermatology Consultation in Inpatients Assigned a Diagnosis of "Cellulitis" by the Emergency Department

at Brigham and Women's Hospital, Boston

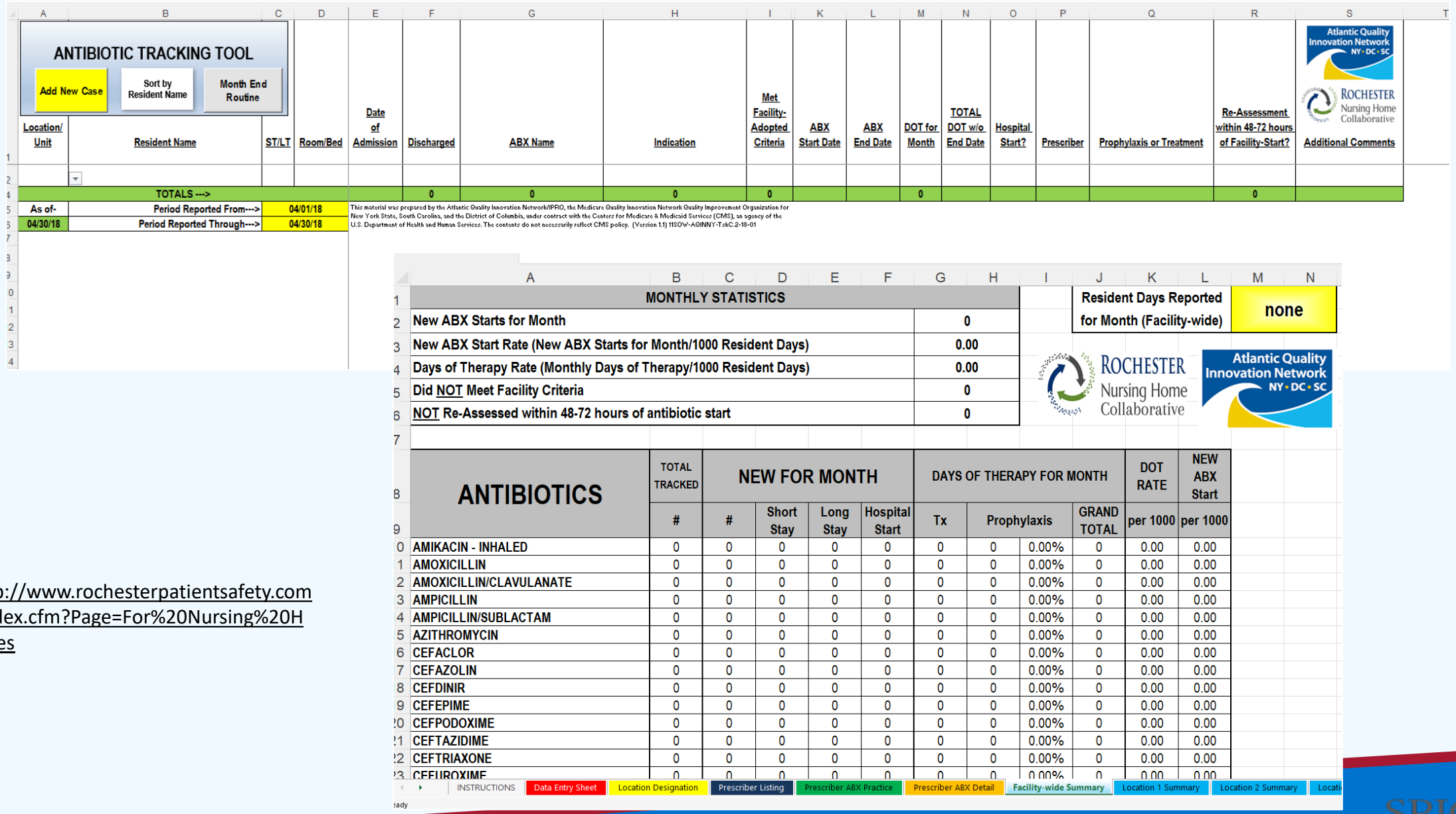


JAMA Dermatol. 2018 May 1;154(5):537-543

Missed Opportunity #5:

Not Using Data to Motivate Change

Top Responsibility of Infection Preventionist / Antibiotic Steward



ANTIBIOTIC TRACKING TOOL

Add New Case | Sort by Resident Name | Month End Routine

Location/ Unit	Resident Name	ST/LT	Room/Bed	Date of Admission	Discharged	ABX Name	Indication	Met Facility-Adopted Criteria	ABX Start Date	ABX End Date	DOT for Month	TOTAL DOT w/o End Date	Hospital Start?	Prescriber	Prophylaxis or Treatment	Re-Assessment within 48-72 hours of Facility-Start?	Additional Comments
TOTALS --->					0	0	0	0			0					0	

As of-	Period Reported From--->	04/01/18
04/30/18	Period Reported Through--->	04/30/18

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MONTHLY STATISTICS	
New ABX Starts for Month	0
New ABX Start Rate (New ABX Starts for Month/1000 Resident Days)	0.00
Days of Therapy Rate (Monthly Days of Therapy/1000 Resident Days)	0.00
Did NOT Meet Facility Criteria	0
NOT Re-Assessed within 48-72 hours of antibiotic start	0

Resident Days Reported for Month (Facility-wide)	none

ANTIBIOTICS	TOTAL TRACKED	NEW FOR MONTH				DAYS OF THERAPY FOR MONTH				DOT RATE	NEW ABX Start
	#	#	Short Stay	Long Stay	Hospital Start	Tx	Prophylaxis		GRAND TOTAL	per 1000	per 1000
AMIKACIN - INHALED	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
AMOXICILLIN	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
AMOXICILLIN/CLAVULANATE	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
AMPICILLIN	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
AMPICILLIN/SUBLACTAM	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
AZITHROMYCIN	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFACLOR	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFAZOLIN	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFDINIR	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFEPIME	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFPODOXIME	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFTAZIDIME	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFTRIAXONE	0	0	0	0	0	0	0	0.00%	0	0.00	0.00
CEFUROXIME	0	0	0	0	0	0	0	0.00%	0	0.00	0.00

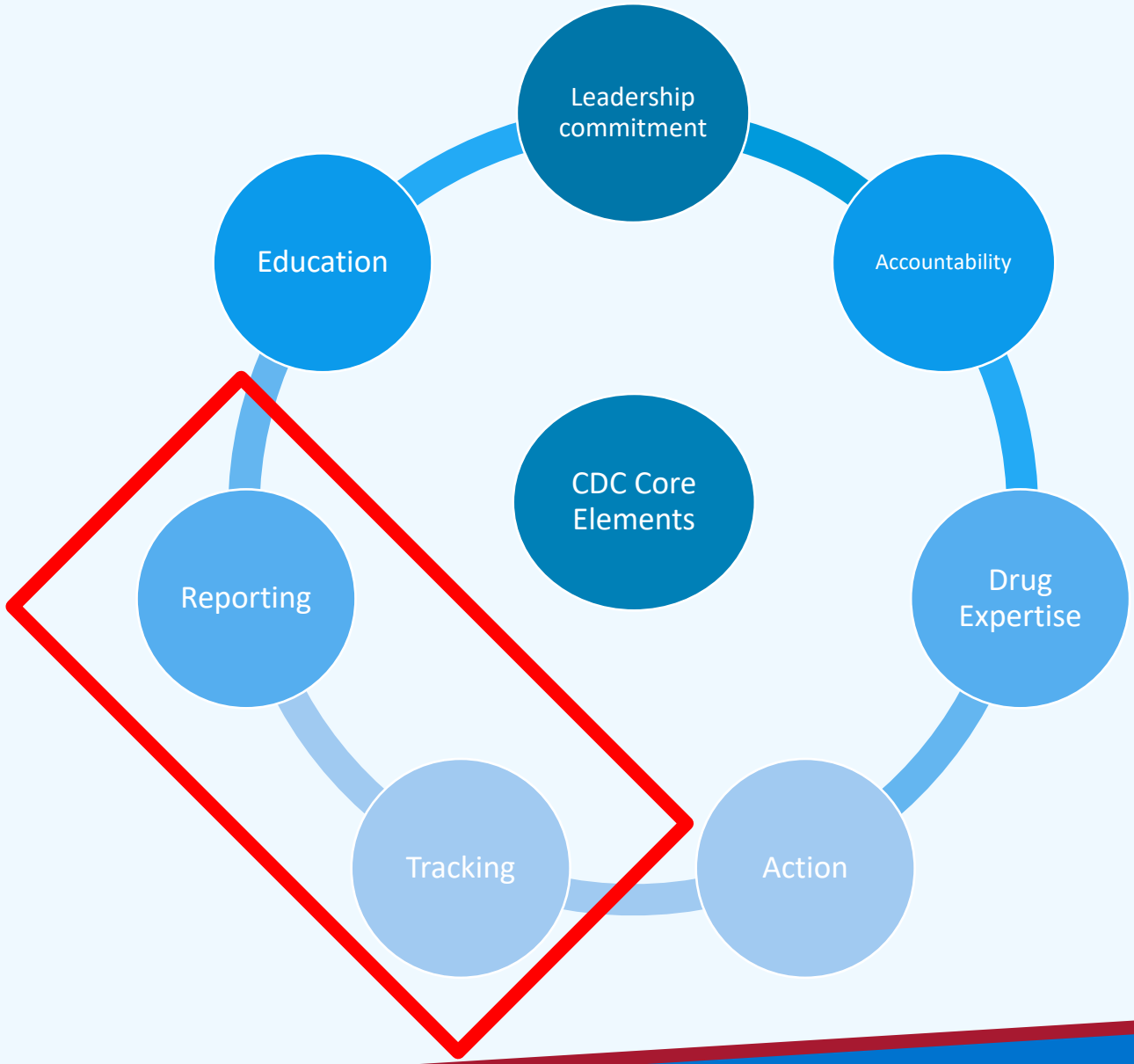
INSTRUCTIONS | Data Entry Sheet | Location Designation | Prescriber Listing | Prescriber ABX Practice | Prescriber ABX Detail | Facility-wide Summary | Location 1 Summary | Location 2 Summary

http://www.rochesterpatientsafety.com/index.cfm?Page=For%20Nursing%20Homes

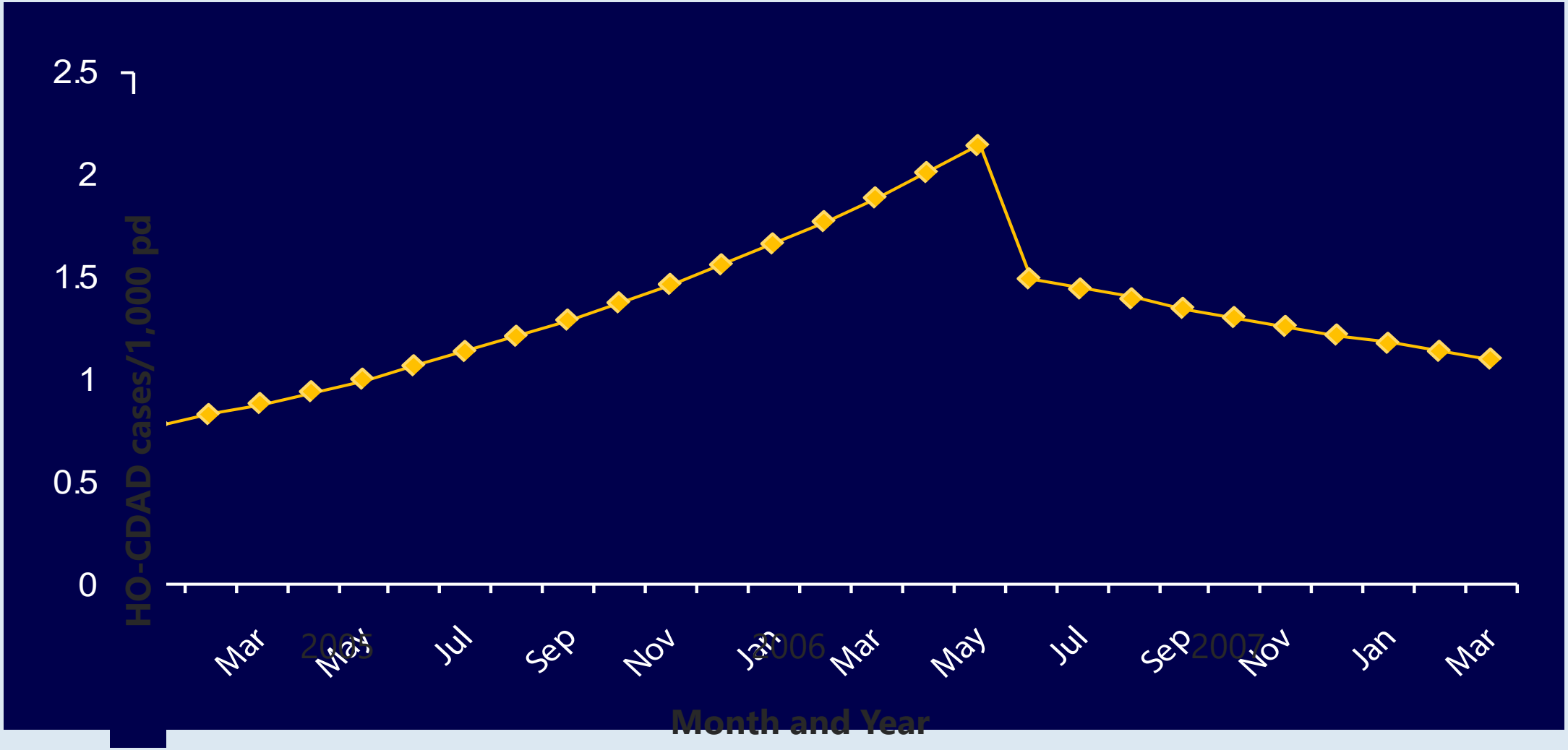
Typical Measures to Record and Report

- Antibiotic use measures:
  - Infection diagnosis / category; antibiotic name; dose and duration; and provider
  - NHSN (National Healthcare Safety Network) reporting
  - Comparing results with benchmarks for antibiotic use: type, starts, days of therapy (DOT).
  - Adherence to surveillance criteria for suspected UTIs, pneumonia, skin/soft tissue infections (McGeer criteria)
- Antibiotic outcome measures:
  - Rates of *c. difficile*, MRSA, CRE, and other MDROs (multi-drug resistant organisms)

How Can Antibiotic Stewards Best Use Their Data?



Impact of Fluoroquinolone Restriction on Rates of *C. difficile* Infection in a Community Hospital



Infect Control Hosp Epidemiol. 2009 Mar;30(3):264-72.

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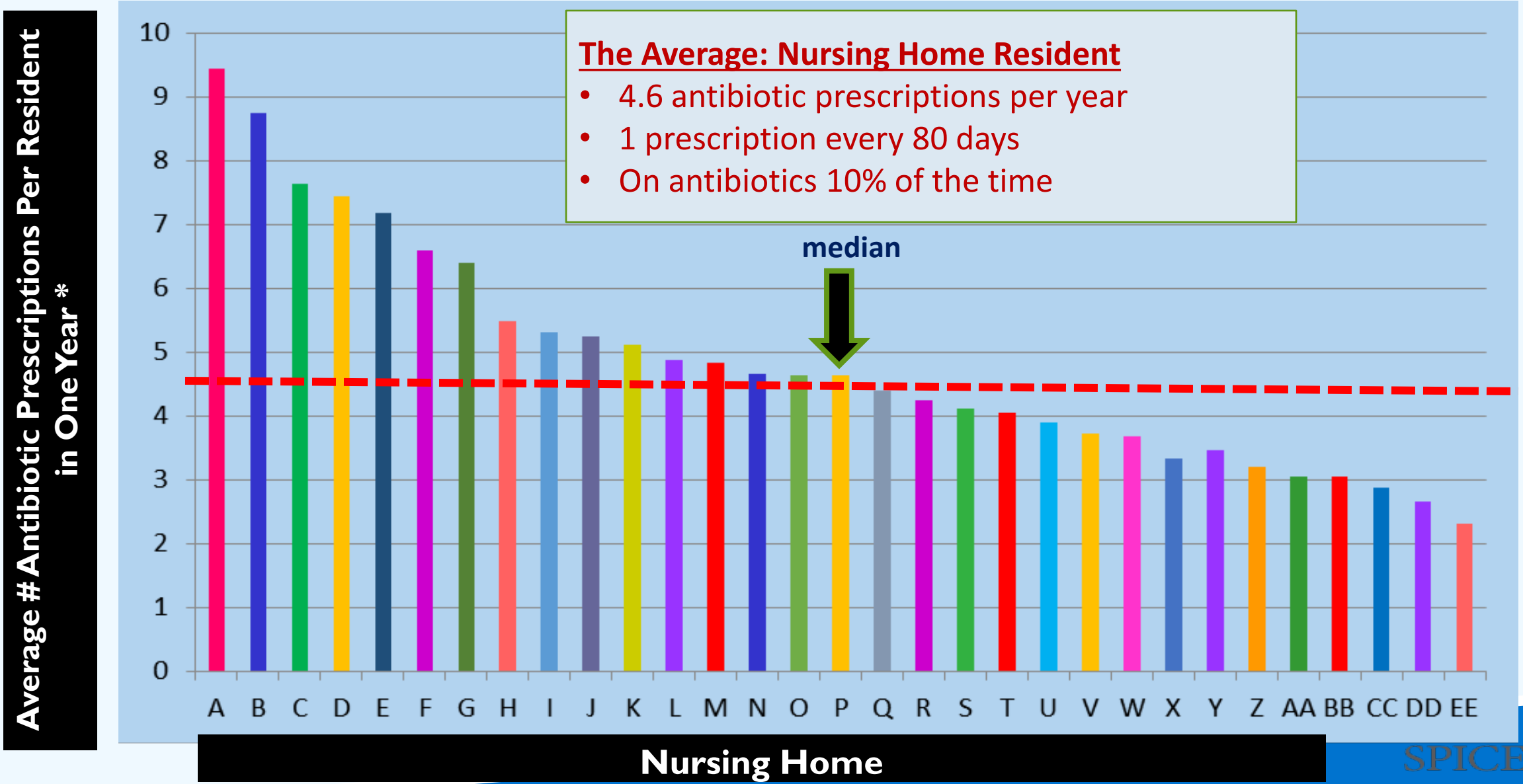
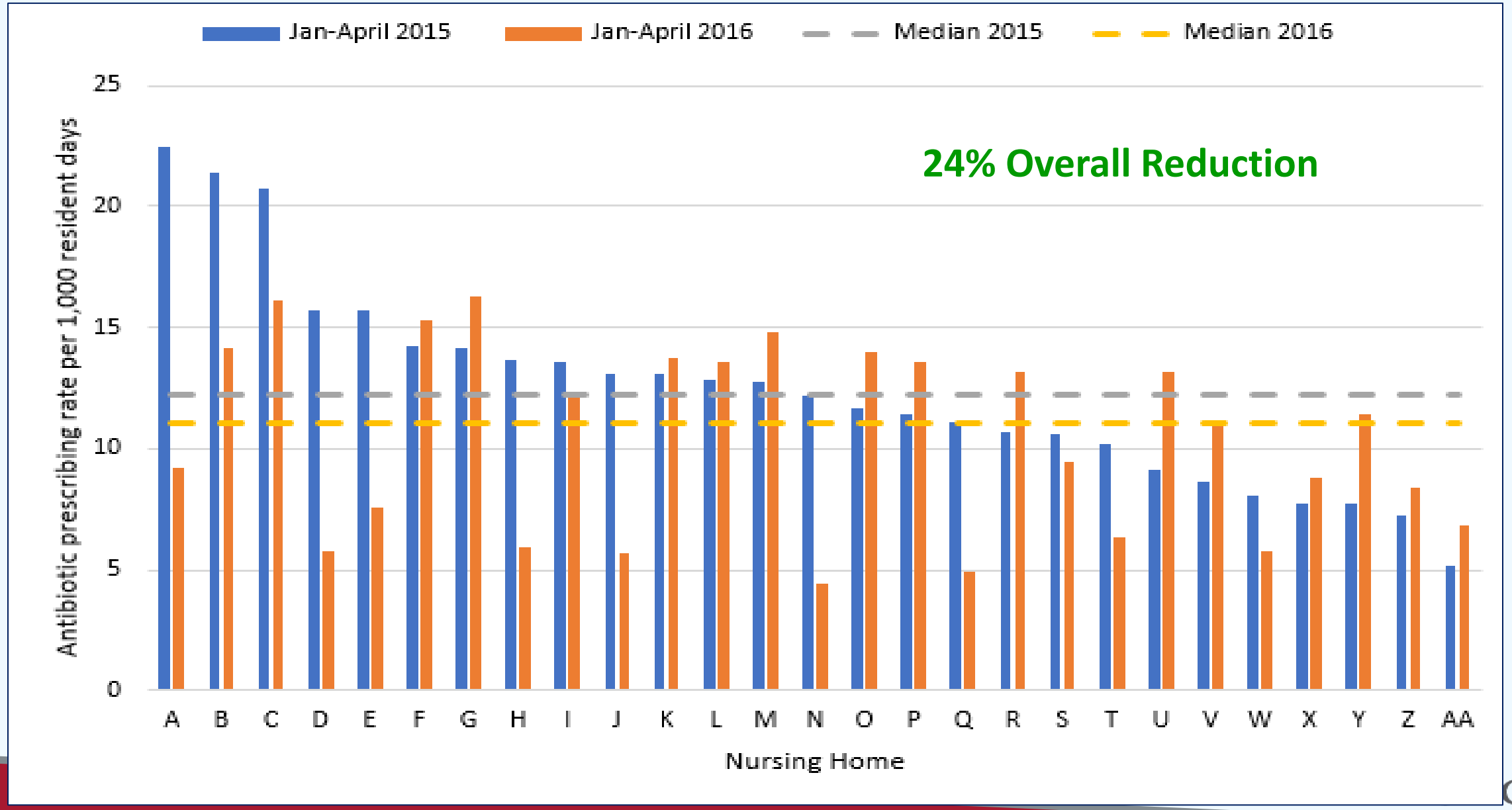
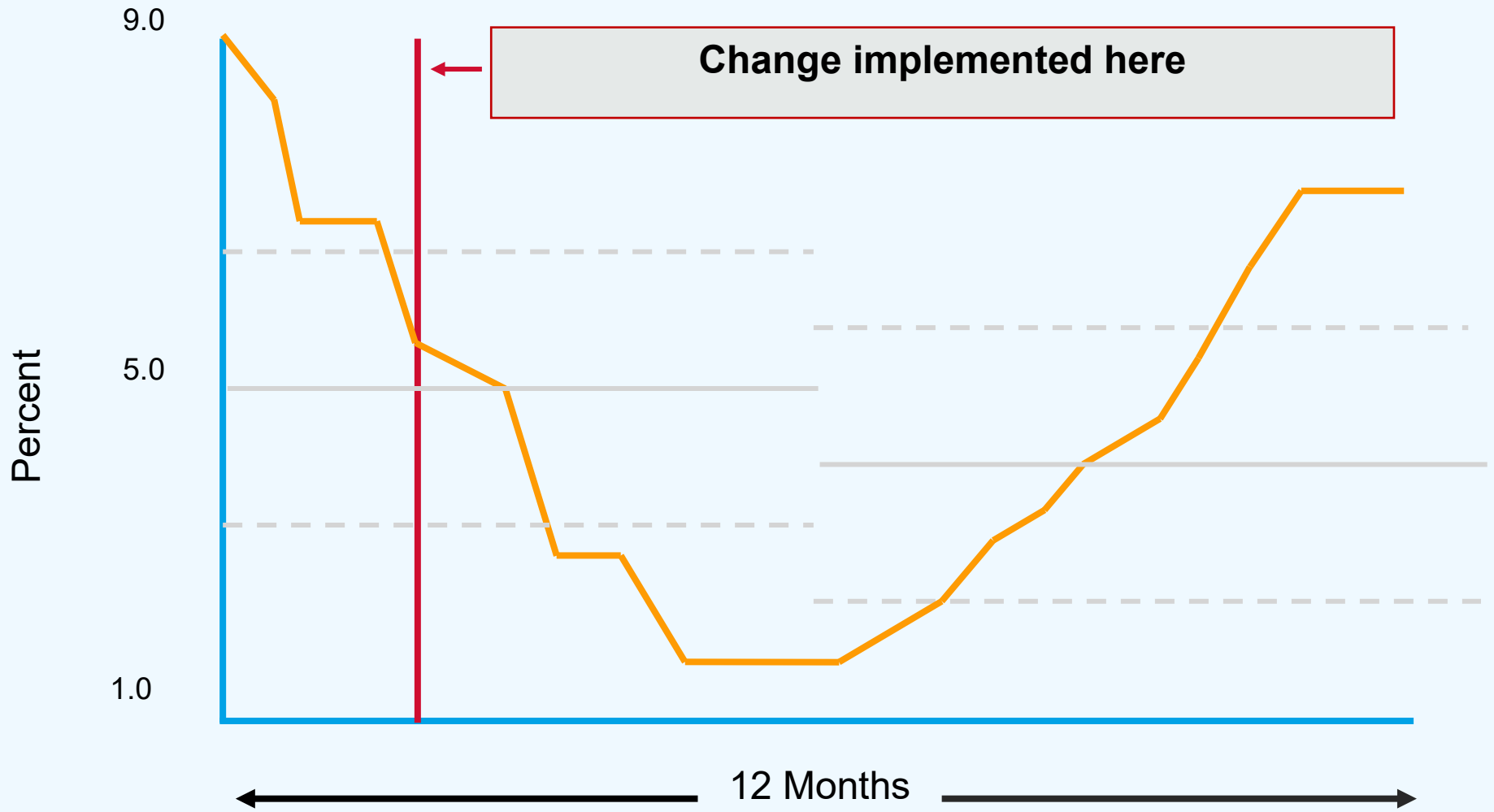
Antibiotic Prescribing Rates across 31 North Carolina Nursing Homes



Prescribing Change During Antibiotic Stewardship Program



An All-Too-Common Curve in Quality Improvement



What Happened? Why?

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To Sum it Up

“In some ways we feel we are as confused as ever, but we believe we are confused on a higher level and about more important things.”

Earl C. Kelley, Professor of Secondary Education, Wayne State University.