Antibiotic Stewardship:
Peeling Back the Layers

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Disclosures

- The content of this presentation does not relate to any product of a commercial interest.

- No relevant financial relationships to disclose.

Learning Outcomes

- Appreciate the impact of drug-resistant organisms on the community and on his or her own health care.
- Understand the primary goals of practicing antimicrobial stewardship and what types of activities qualify as antimicrobial stewardship.
- Identify certain activities that he/she can perform at his/her practice setting that would contribute to the goals of antimicrobial stewardship

WHY STEWARDSHIP

Why Stewardship

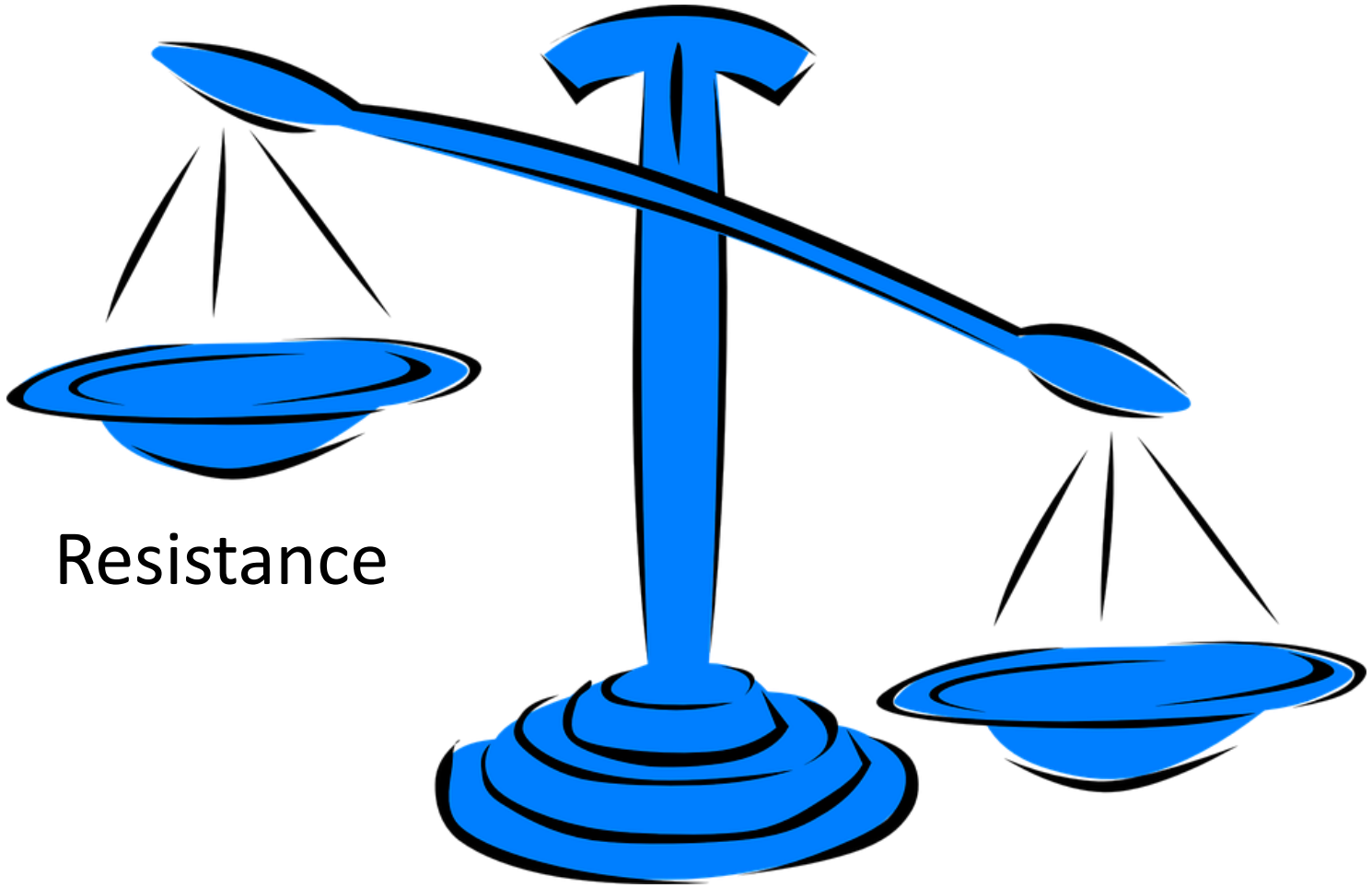
- Death tolls
  - At least 2 million people infected with antibiotic resistant bacteria
  - At least 23,000 deaths resulting from drug-resistant bacteria

- Financial burden on society
  - Compared to drug-susceptible infection episodes, drug-resistant infection episodes have higher costs ($6,000-$30,000 per episode)

- Ability to respond to resistance and increasing mortality

1. Centers for Disease Control and Prevention. Antibiotic / Antimicrobial Resistance. Available at: https://www.cdc.gov/drugresistance/about.html. Accessed November 6, 2018.
2. Maragakis LL et al. *Expert Rev Anti Infect Ther* 2008;6:751-63.

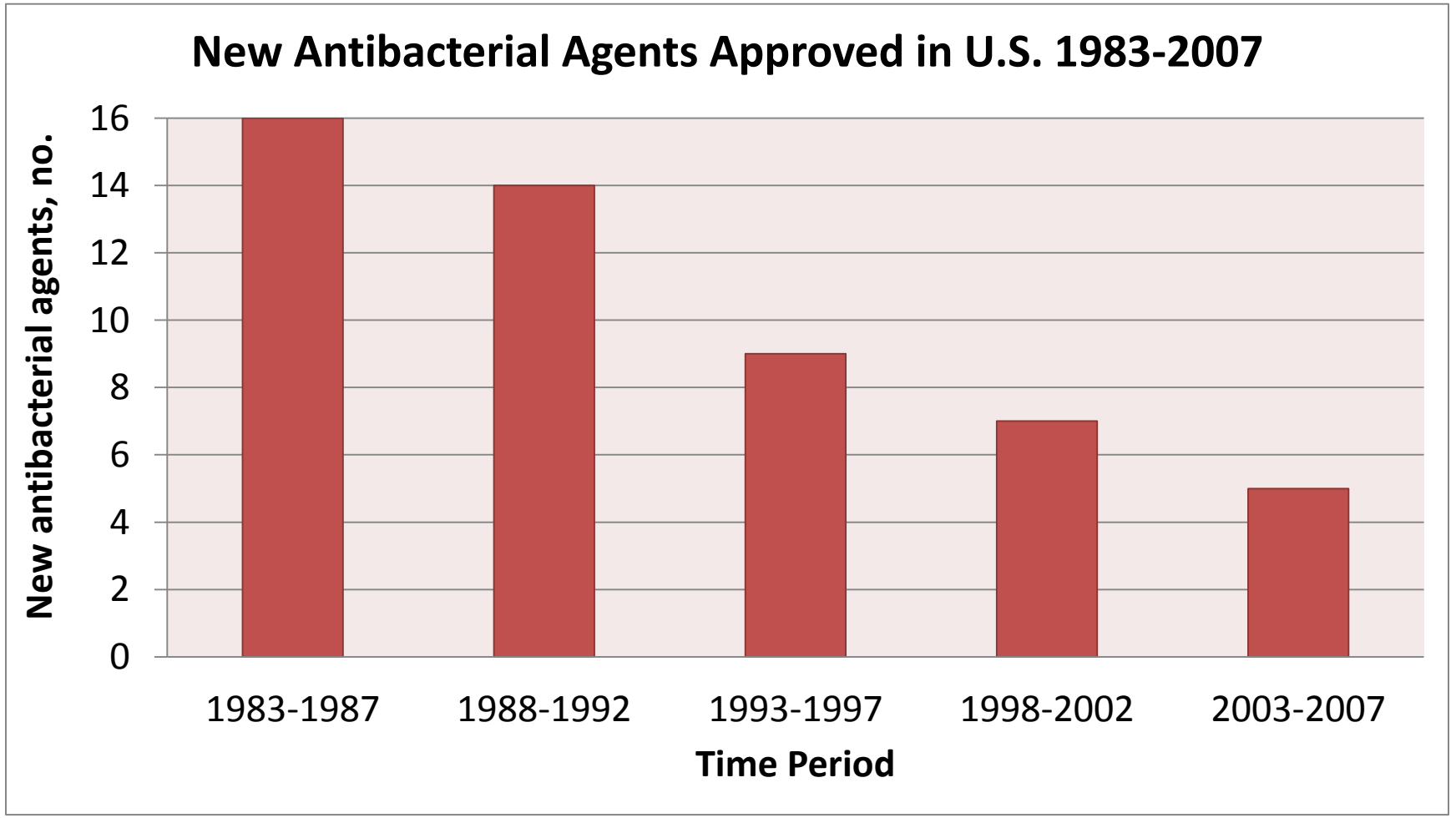
Balancing Act of Antimicrobial Stewardship



Resistance

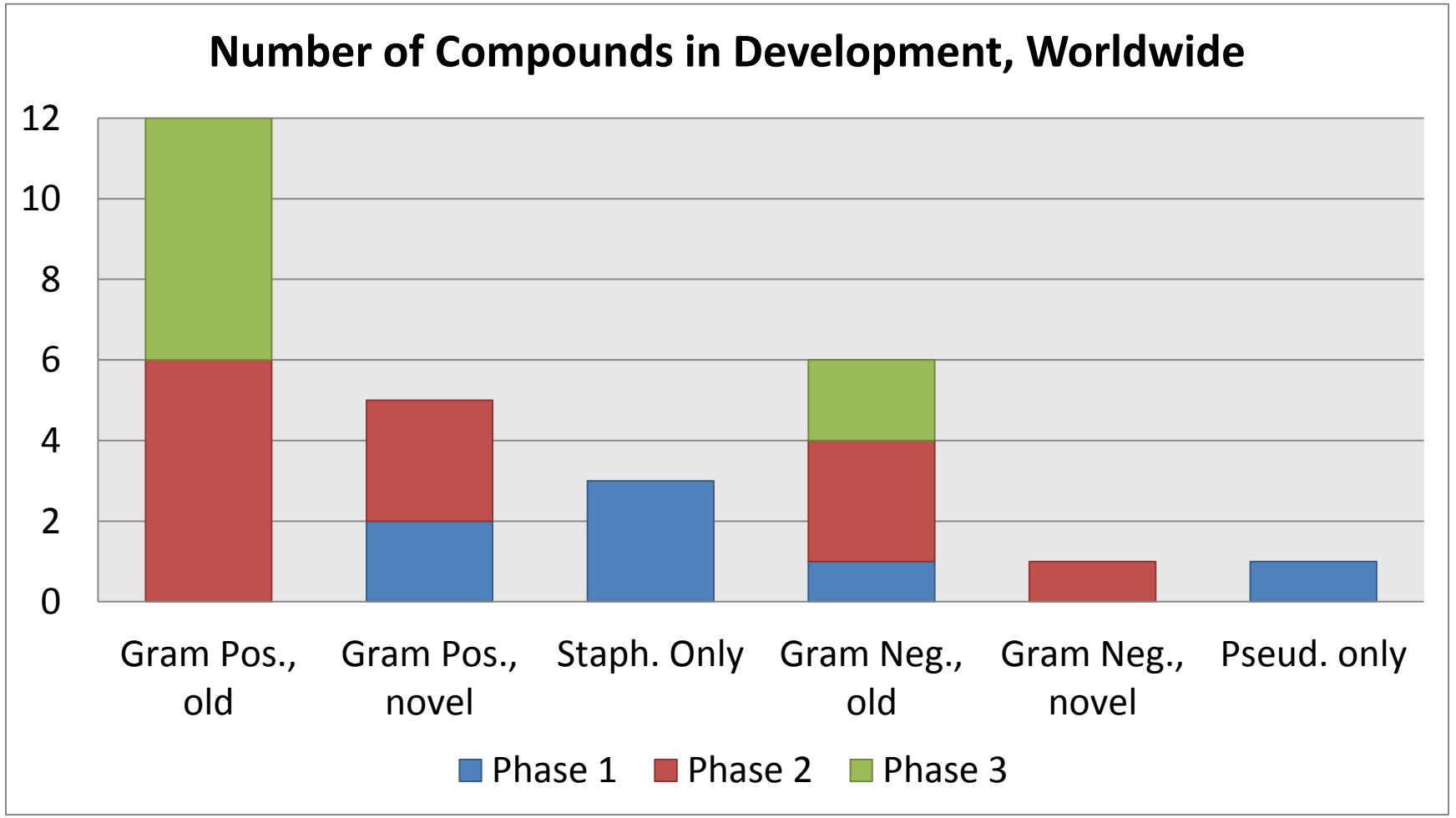
Available Antimicrobial Agents

“Post-Antibiotic Era”



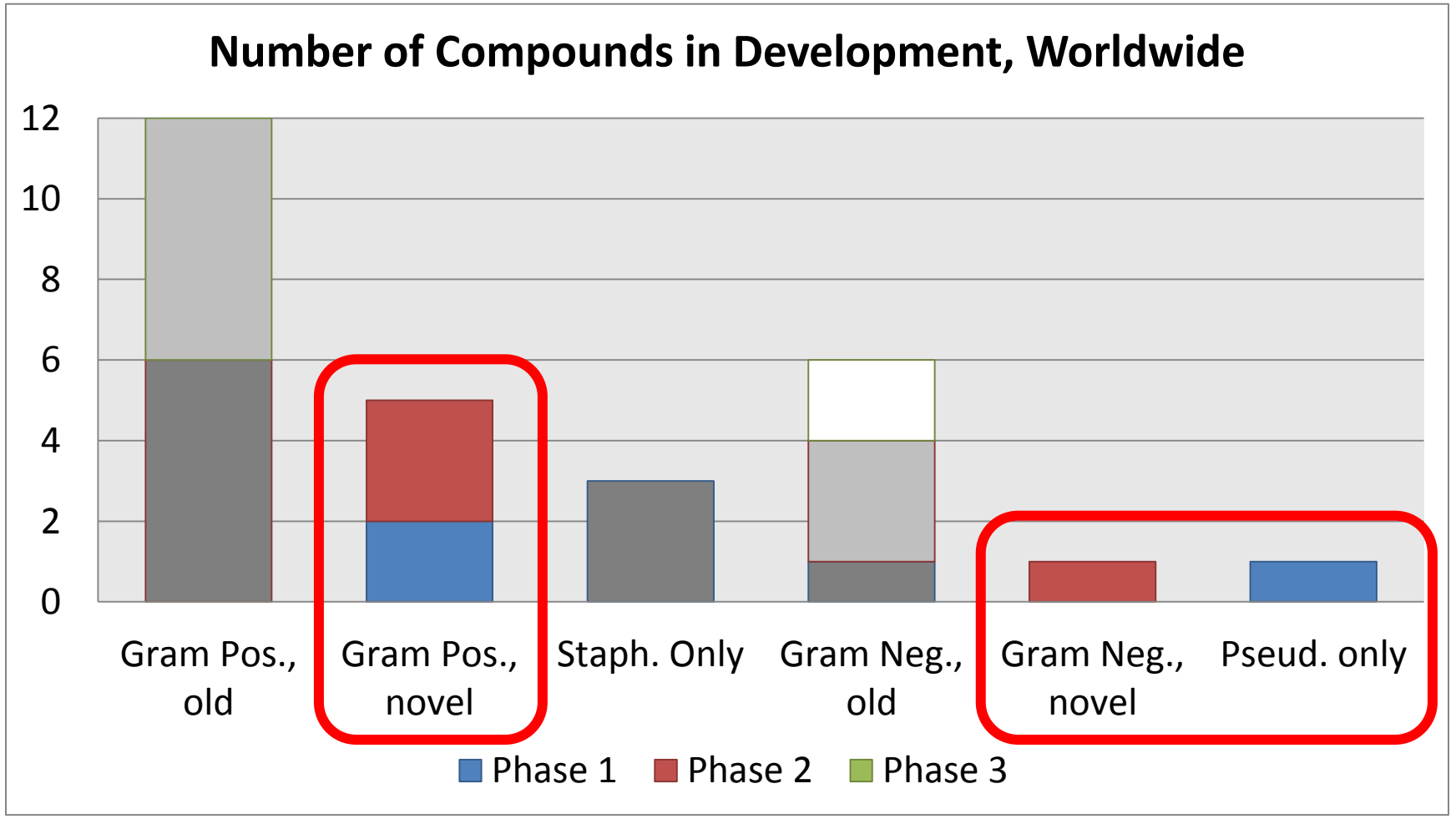
Adapted from: Boucher HW et al. *Clin Infect Dis*. 2009; 48:1-12.

Antimicrobial Pipeline



Adapted from: Theuretzbacher U. *Int J Antimicrob Agents*. 2012; 39:295-9.

Dry Pipeline – Lack of Novelty



Adapted from: Theuretzbacher U. *Int J Antimicrob Agents*. 2012; 39:295-9.

Antibacterials: Low Return on Investment

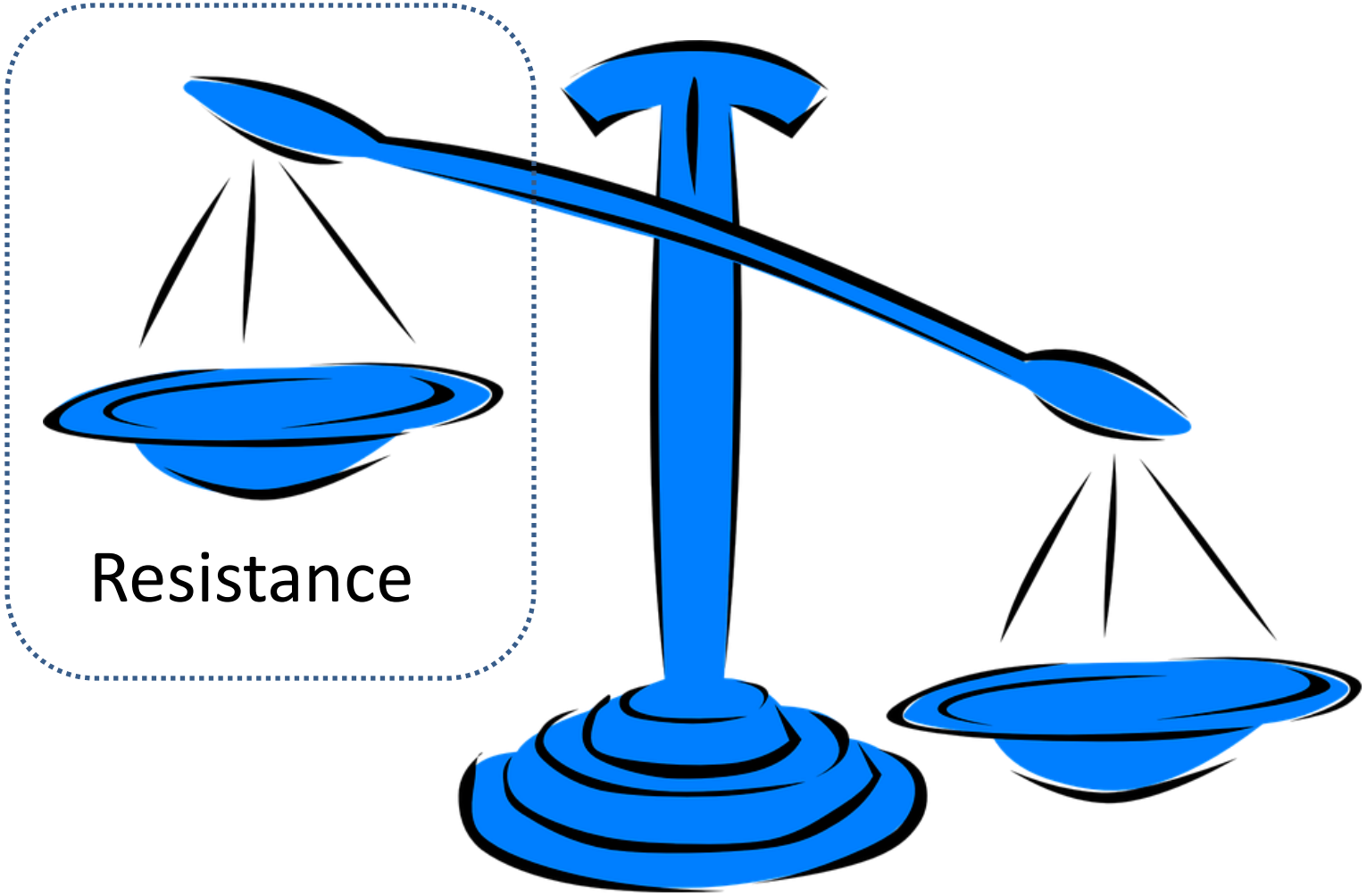
Agent	Average Cost
Harvoni®	
50% of market	$165 billion
Triumeq®	
50% of market	$14.8 billion / year
Entresto® (sacubitril/valsartan)	
50% of market	$13 billion / year
25% of market	$6.5 billion / year

Agent	Average Cost
Daptomycin	
$1,000 for 14d Assume 50% treat	$1 billion / year

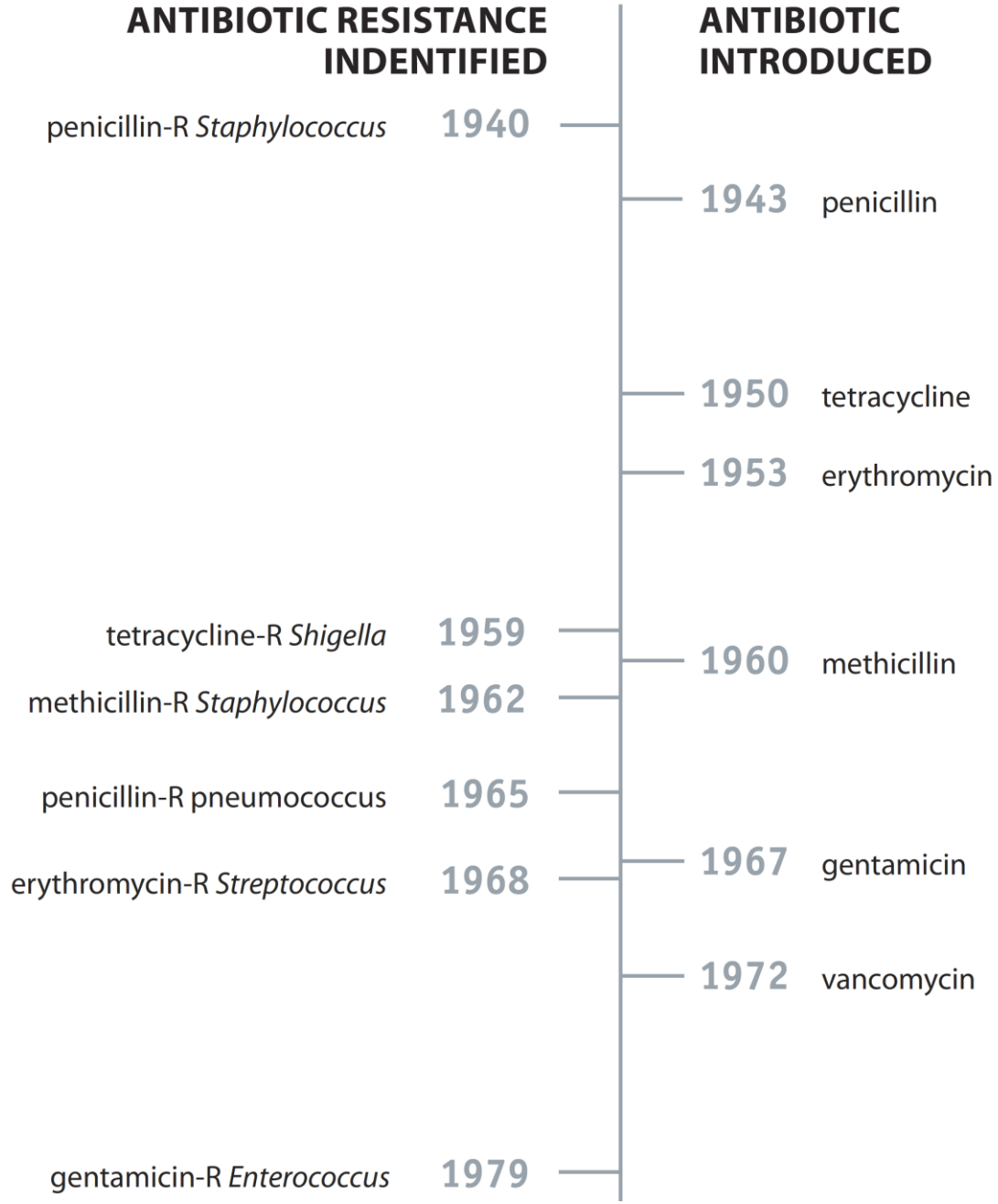
1. Number of affected individuals X Duration requiring medication therapy

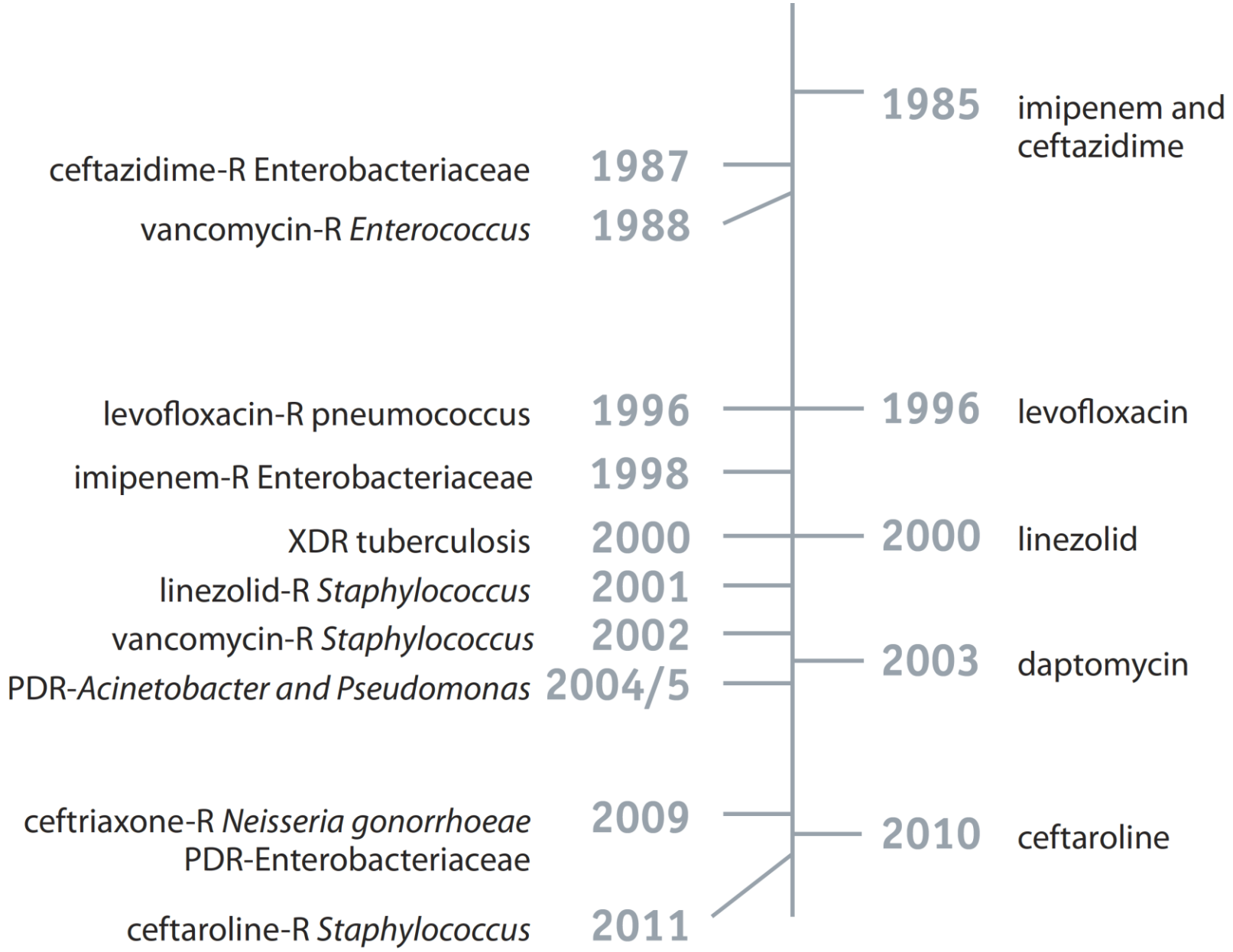
2. Rarity of disease

Are We Winning the Battle Against Resistance?



- Antibiotic resistance observations by epidemiologists in late 1980s to early 1990s
- Resistance non-existent until that time period?
- *Staphylococcus* resistance observed by Alexander Fleming upon discovery of penicillin in 1930-40s


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
1967 gentamicin
erythromycin-R Streptococcus 1968
1972 vancomycin
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
PDR-Acinetobacter and Pseudomonas
2004/5
2003
daptomycin
ceftriaxone-R Neisseria gonorrhoeae
PDR-Enterobacteriaceae
2009
2010
ceftaroline
ceftaroline-R Staphylococcus
2011

CDC Urgent Threats	CDC Serious Threats	CDC Concerning Threats
Clostridioides difficile	MDR *Acinetobacter*	Vancomycin-resistant *Staphylococcus aureus* (VISA)
Carbapenem-resistant Enterobacteriaceae (CRE)	Drug-resistant *Campylobacter*	Erythromycin-resistant Group A *Streptococcus*
Drug-resistant *Neisseria gonorrhoeae*	Fluconazole-resistant *Candida*	Clindamycin-resistant Group B *Streptococcus*
	Extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae	
	Vancomycin-resistant *Enterococcus* (VRE)	
	MDR *Pseudomonas aeruginosa*	
	Drug-resistant non-typhoidal *Salmonella*	
	Methicillin-resistant *Staphylococcus aureus* (MRSA)	
	Drug-resistant *Streptococcus pneumoniae*	
	Drug-resistant Tuberculosis	

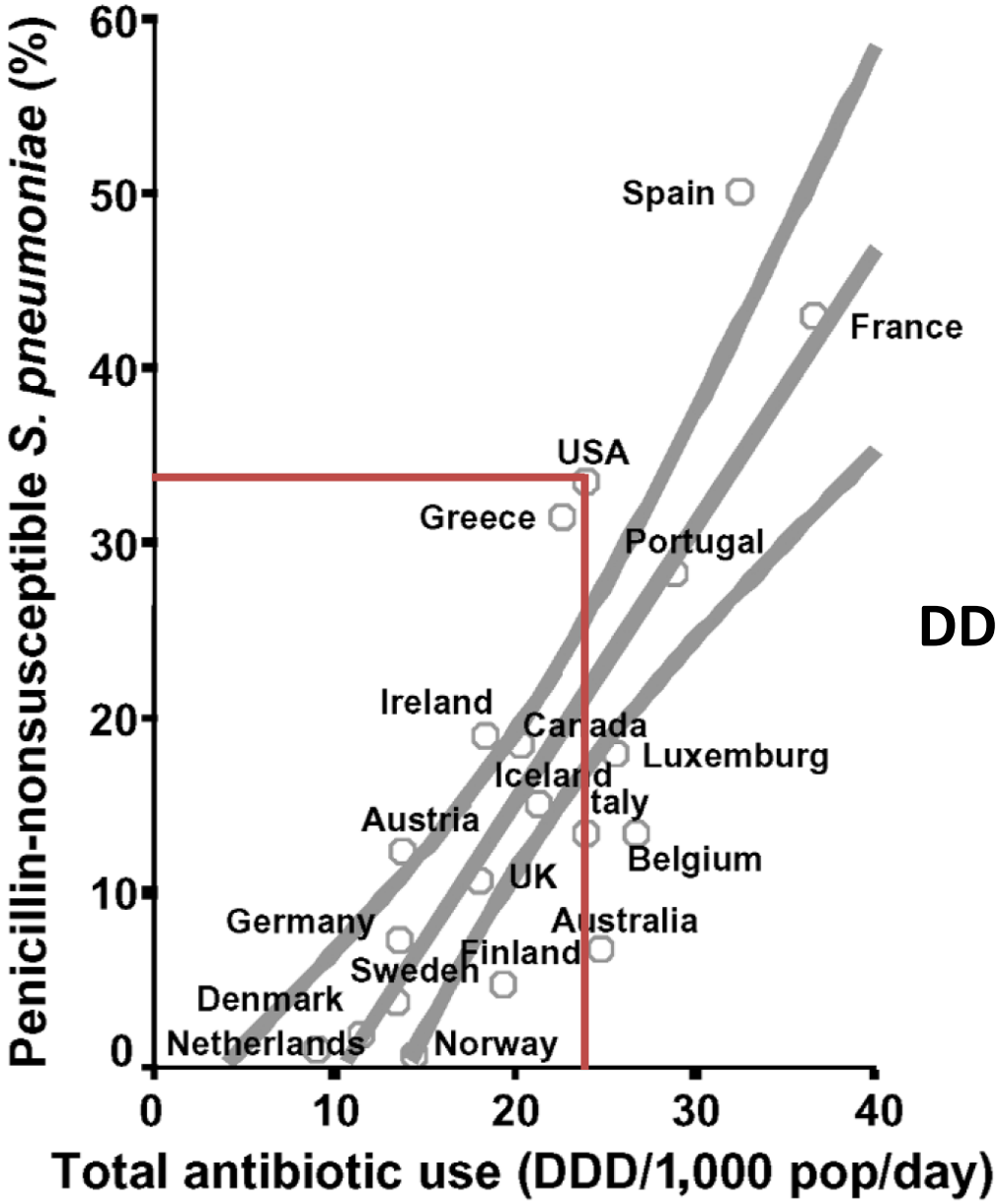
MDR : Multi-drug resistant

Available at: https://www.cdc.gov/drugresistance/biggest_threats.html.
Accessed October 28, 2018

Biggest Threats in Antimicrobial Resistance

Threat	Infections	Deaths
C.difficile	**500,000**	**15,000**
CRE	9,000	600
Drug-resistant *Neisseria gonorrhoeae*	**246,000**	
MDR *Acinetobacter*	7,300	500
Drug-resistant *Campylobacter*	310,000	
Fluconazole-resistant *Candida*	3,400	220
ESBL Enterobacteriaceae	**26,000**	**1,700**
VRE	**20,000**	**1,300**
MDR *Pseudomonas aeruginosa*	6,700	440
MRSA	**80,461**	**11,285**
Drug-resistant *S.pneumoniae*	**1.2 million**	**7,000**

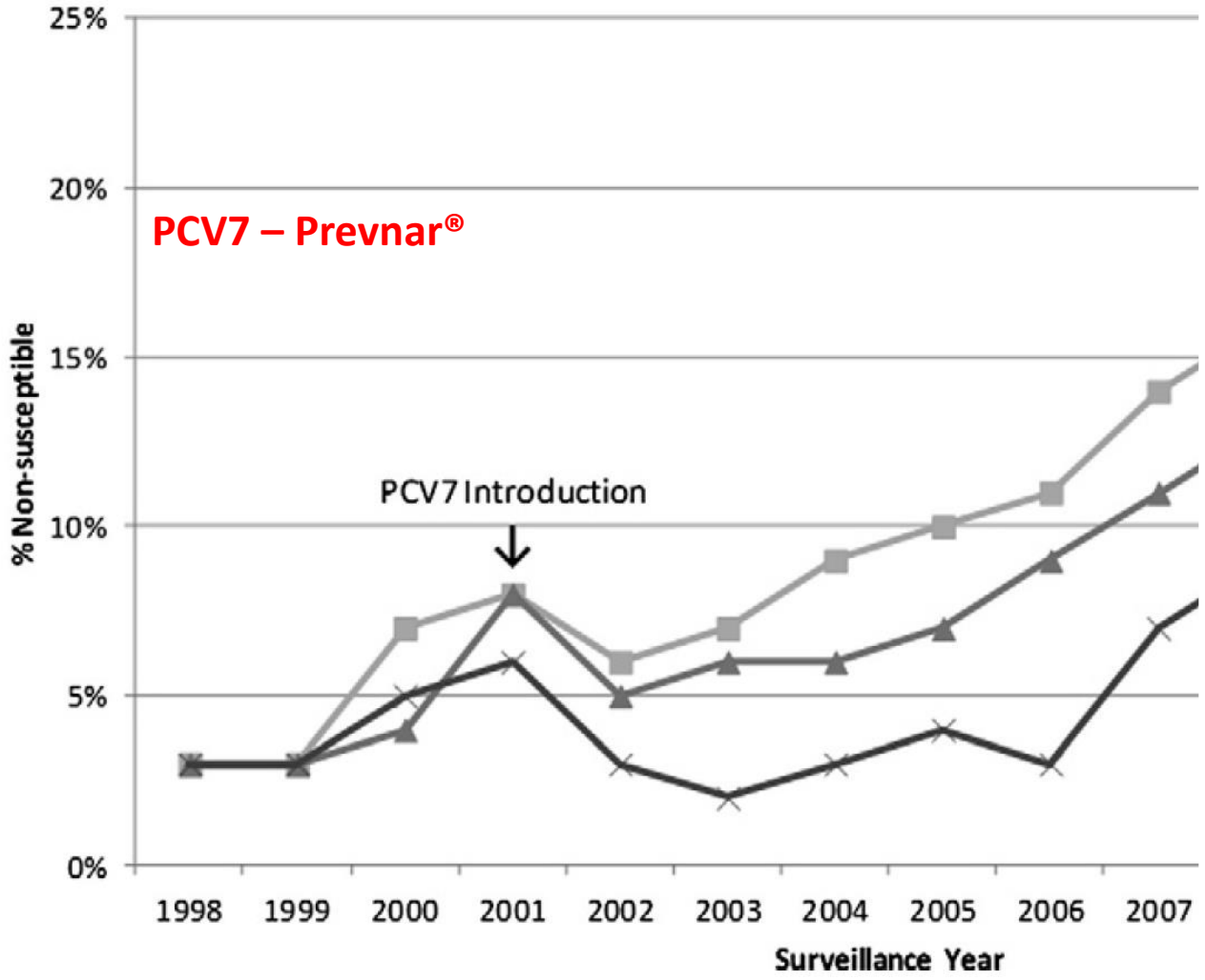
Available at: https://www.cdc.gov/drugresistance/biggest_threats.html.
Accessed October 28, 2018



DDD : defined daily dose

Adapted from: Albrich WC et al. *Emerg Infect Dis* 2004;10:514-7.

Resistance Correlative to Antibiotic Consumption



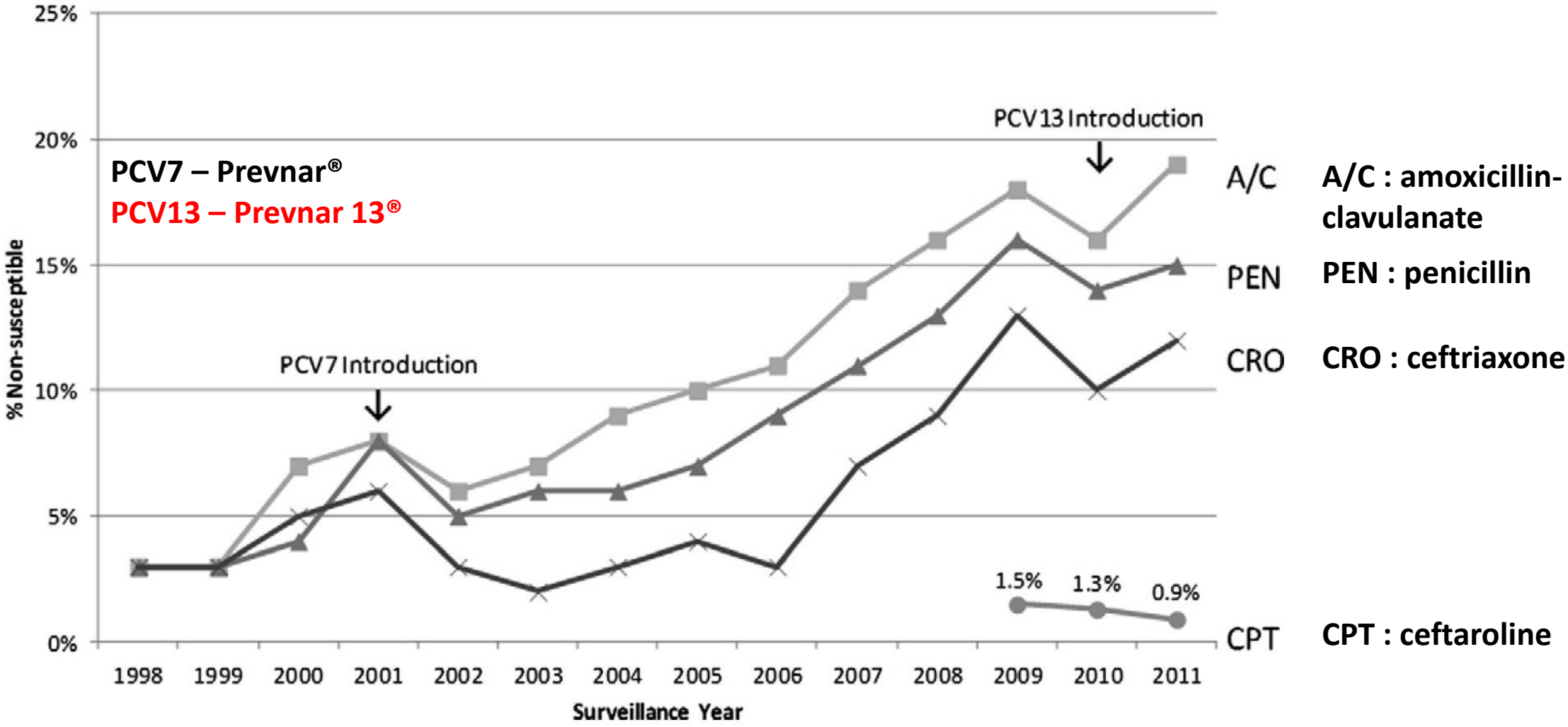
A/C : amoxicillin-clavulanate

PEN : penicillin

CRO : ceftriaxone

Adapted from: Jones RN et al. *Diagn Microbiol Infect Dis* 2013;75:107-9.

Resistance Correlative to Antibiotic Consumption



Adapted from: Jones RN et al. *Diagn Microbiol Infect Dis* 2013;75:107-9.

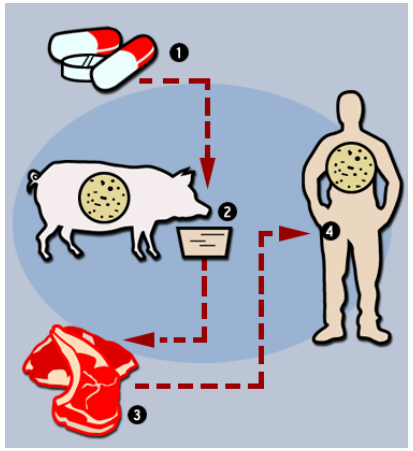
ANTIBIOTIC STEWARDSHIP

Multi-faceted, multi-disciplinary approach to making life miserable for bacteria…

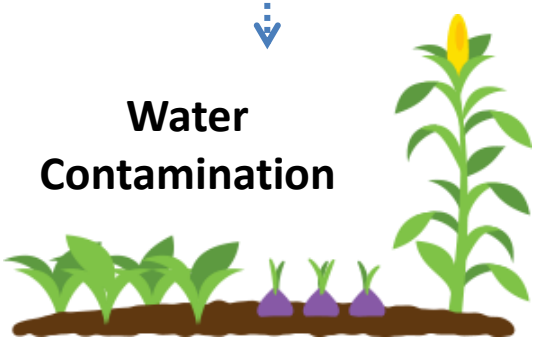
10,000-foot View of Stewardship

ZONE 1

Antibiotic Overutilization in **Livestock and Farming**



Water Contamination



ZONE 2

Outpatient/Ambulatory Settings

- Primary care
- Urgent care
- Emergency department

ZONE 3

Acute Care Settings

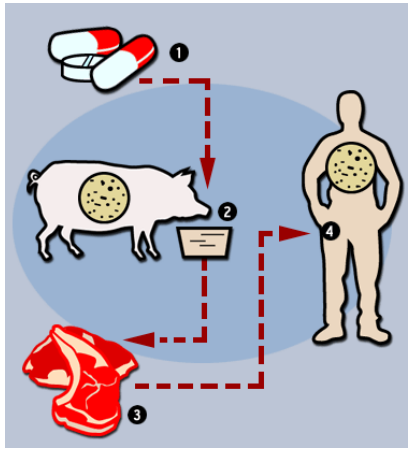
- Hospital

Rehabilitation Facilities

Long-term Care Facilities

ZONE 1

Antibiotic Overutilization in **Livestock and Farming**



- Approximately 70% of medically important antibiotics sold in U.S. used in livestock and agriculture.
  - Disease treatment
  - Disease prevention
  - Growth promotion/feed efficiency
- Estimated global consumption in 2013: 131,109 tons

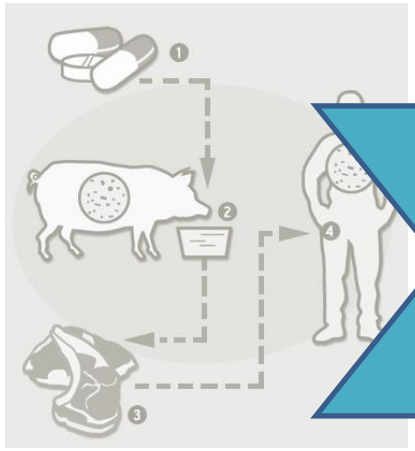
1. U.S. Food and Drug Administration, Center for Veterinary Medicine, 2016 *Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals.* Available at: https://www.fda.gov/downloads/forindustry/userfees/animaldruguserfeeactadufa/ucm588085.pdf. Accessed October 30, 2018.
2. Van Boeckel TP et al. *Science* 2017;357;1350-1352.

ZONE 1

ZONE 2

ZONE 3

Antibiotic Overutilization in **Livestock and Farming**



Increasing resistance profile

Outpatient/Ambulatory Settings

- Primary care
- Urgent care
- Emergency department

Acute Care Settings

- Hospital

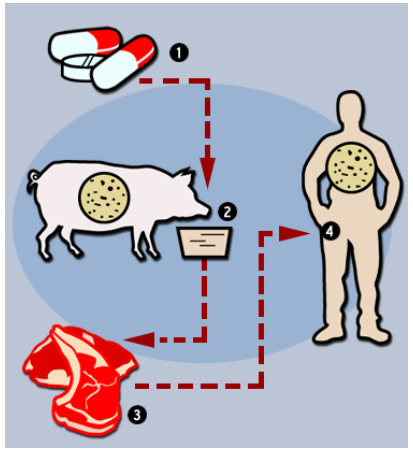
Rehabilitation Facilities

Water Contamination

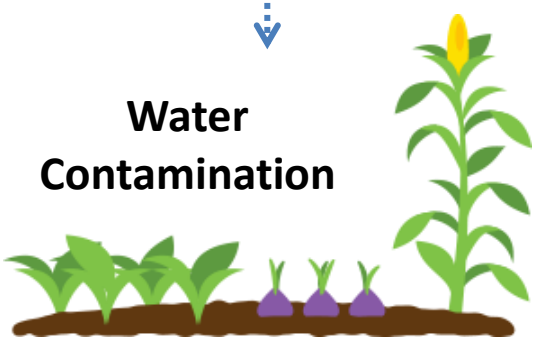
Long-term Care Facilities

ZONE 1

Antibiotic Overutilization in **Livestock and Farming**



Water Contamination



ZONE 2

Outpatient/Ambulatory Settings

- Primary care
- Urgent care
- Emergency department

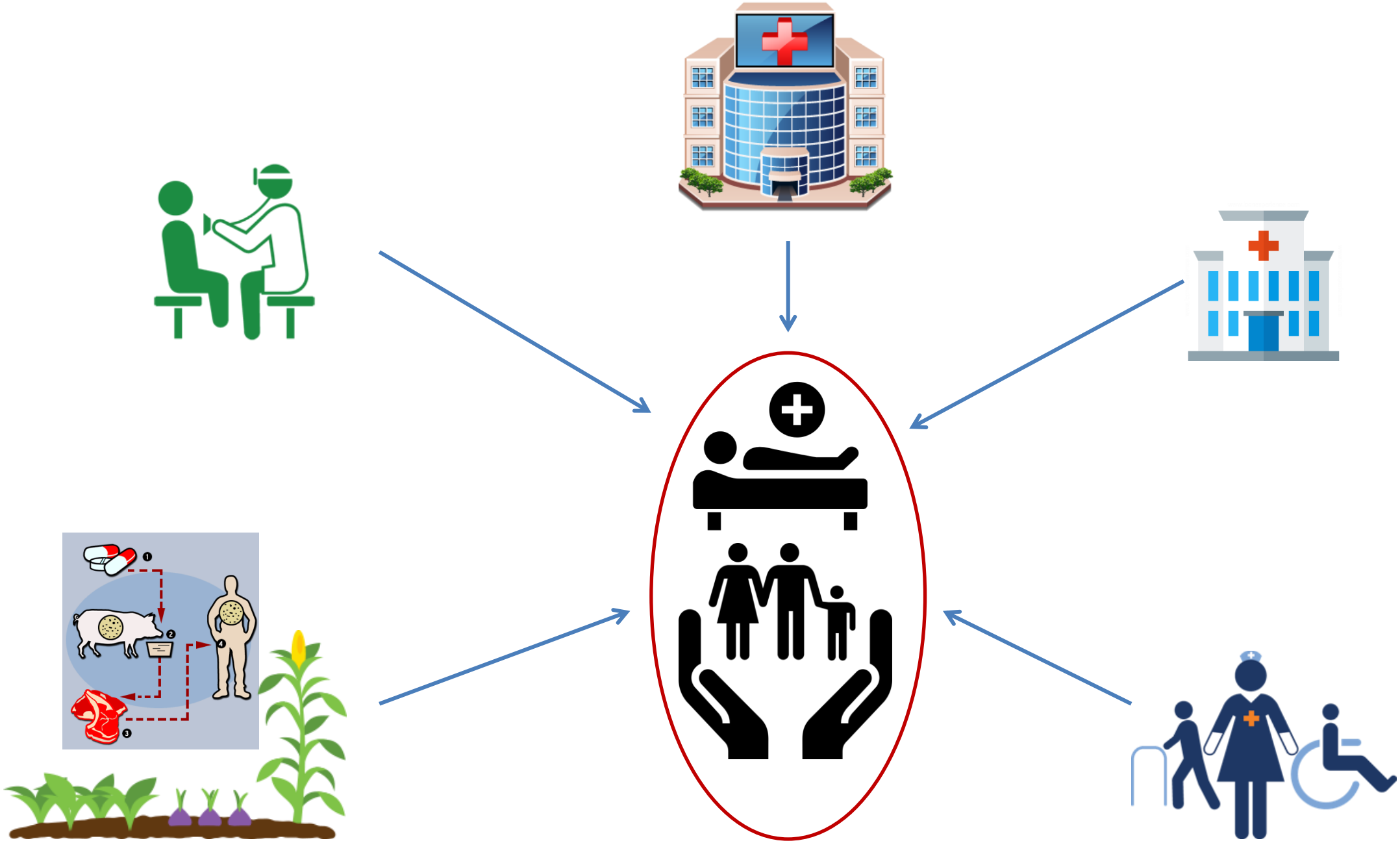
ZONE 3

Acute Care Settings

- Hospital

Rehabilitation Facilities

Long-term Care Facilities

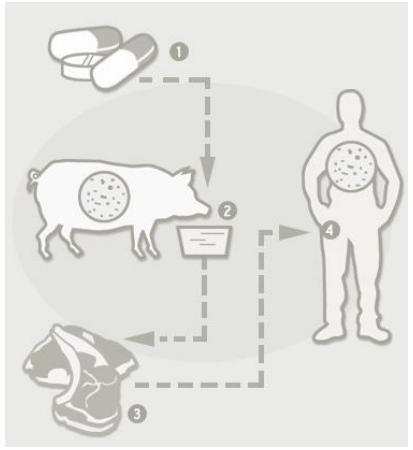


ZONE 1

ZONE 2

ZONE 3

Antibiotic Overutilization
in **Livestock and Farming**



INPATIENT EXAMPLE OF RESISTANCE

Outpatient/Ambulatory Settings
- Primary care
- Urgent care
- Emergency department

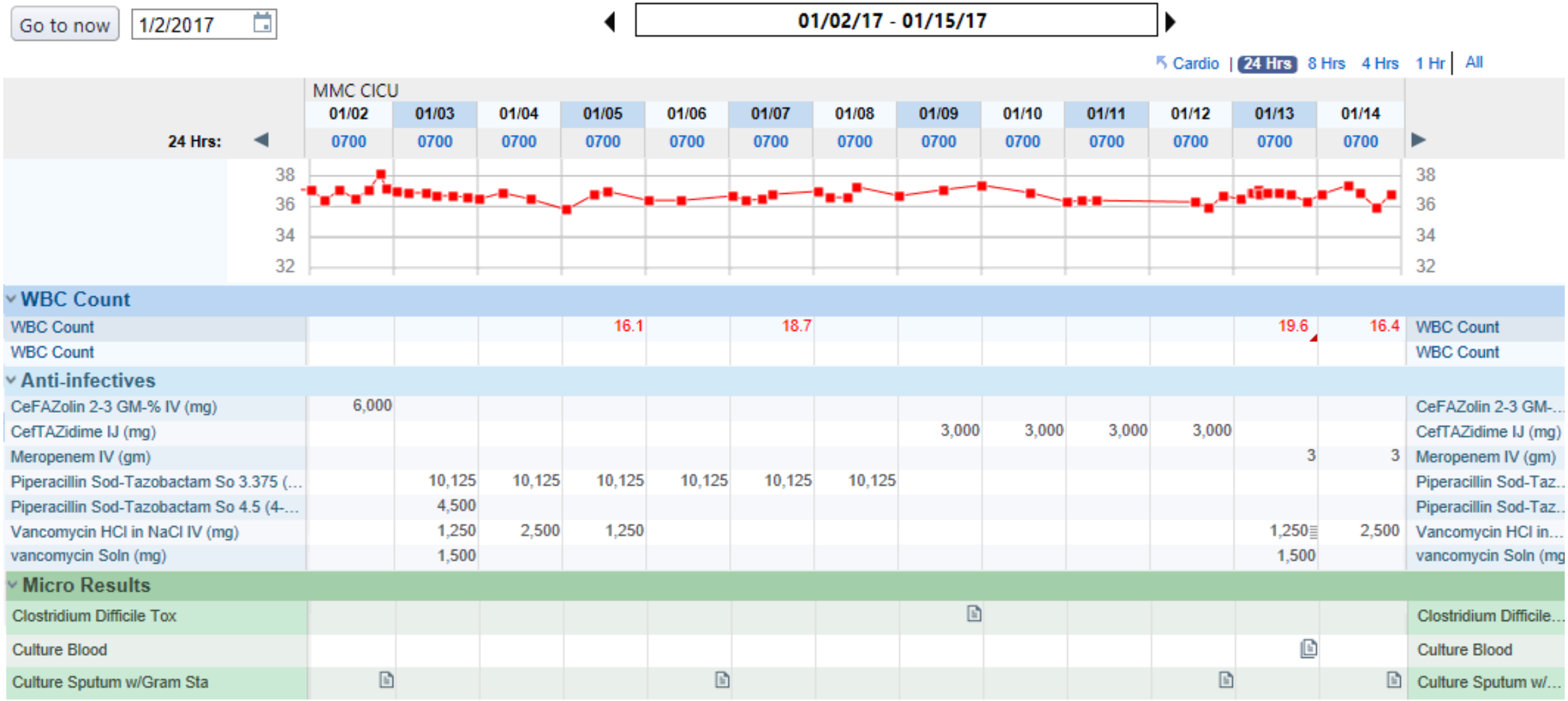
Acute Care Settings
- Hospital

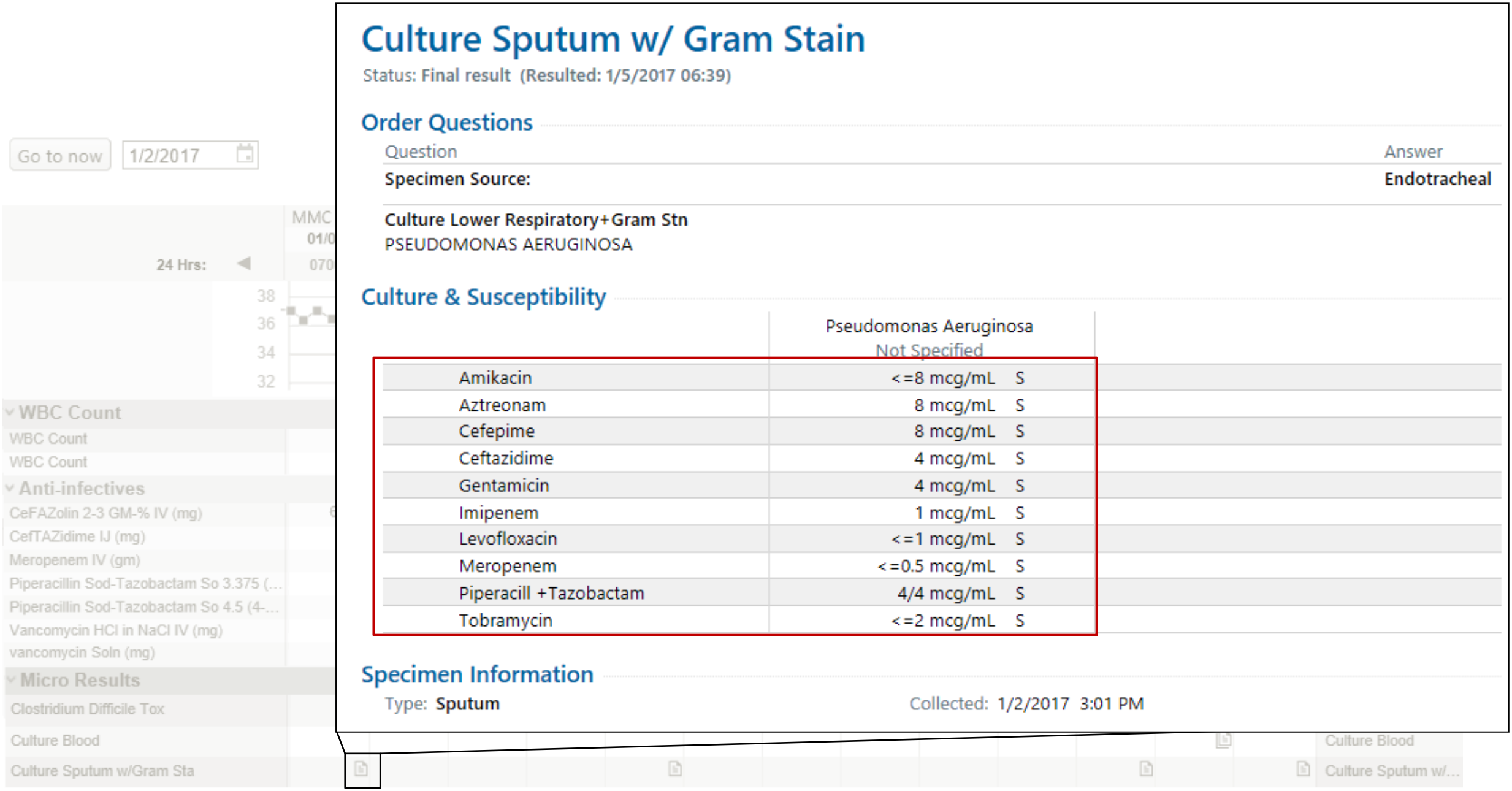
Rehabilitation Facilities

Water Contamination

Long-term Care Facilities

Challenges in Hospital Pathogens





Culture Sputum w/ Gram Stain

Status: **Final result** (Resulted: 1/5/2017 06:39)

Order Questions

Question	Answer
Specimen Source:	**Endotracheal**

Culture Lower Respiratory+Gram Stn
PSEUDOMONAS AERUGINOSA

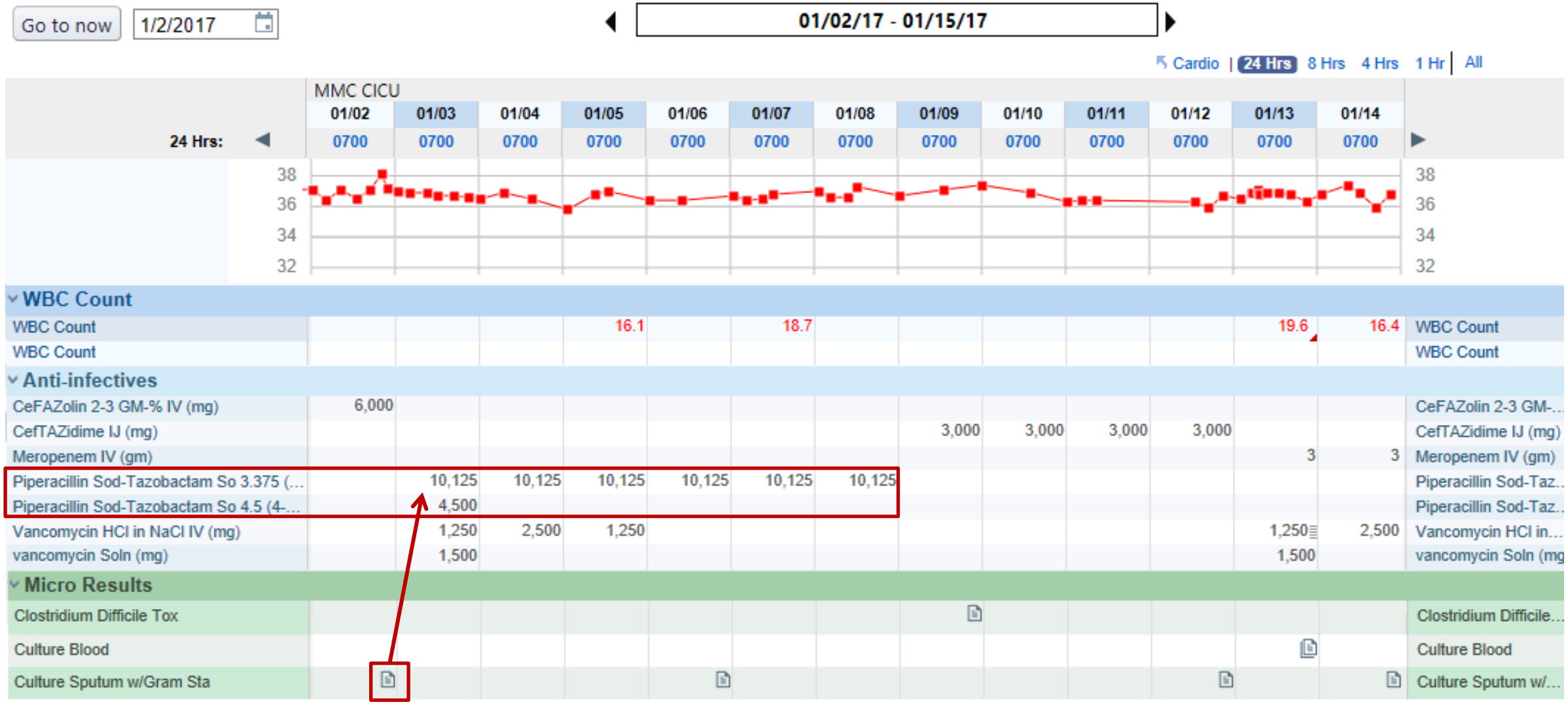
Culture & Susceptibility

	Pseudomonas Aeruginosa Not Specified	
Amikacin	<=8 mcg/mL	S
Aztreonam	8 mcg/mL	S
Cefepime	8 mcg/mL	S
Ceftazidime	4 mcg/mL	S
Gentamicin	4 mcg/mL	S
Imipenem	1 mcg/mL	S
Levofloxacin	<=1 mcg/mL	S
Meropenem	<=0.5 mcg/mL	S
Piperacill +Tazobactam	4/4 mcg/mL	S
Tobramycin	<=2 mcg/mL	S

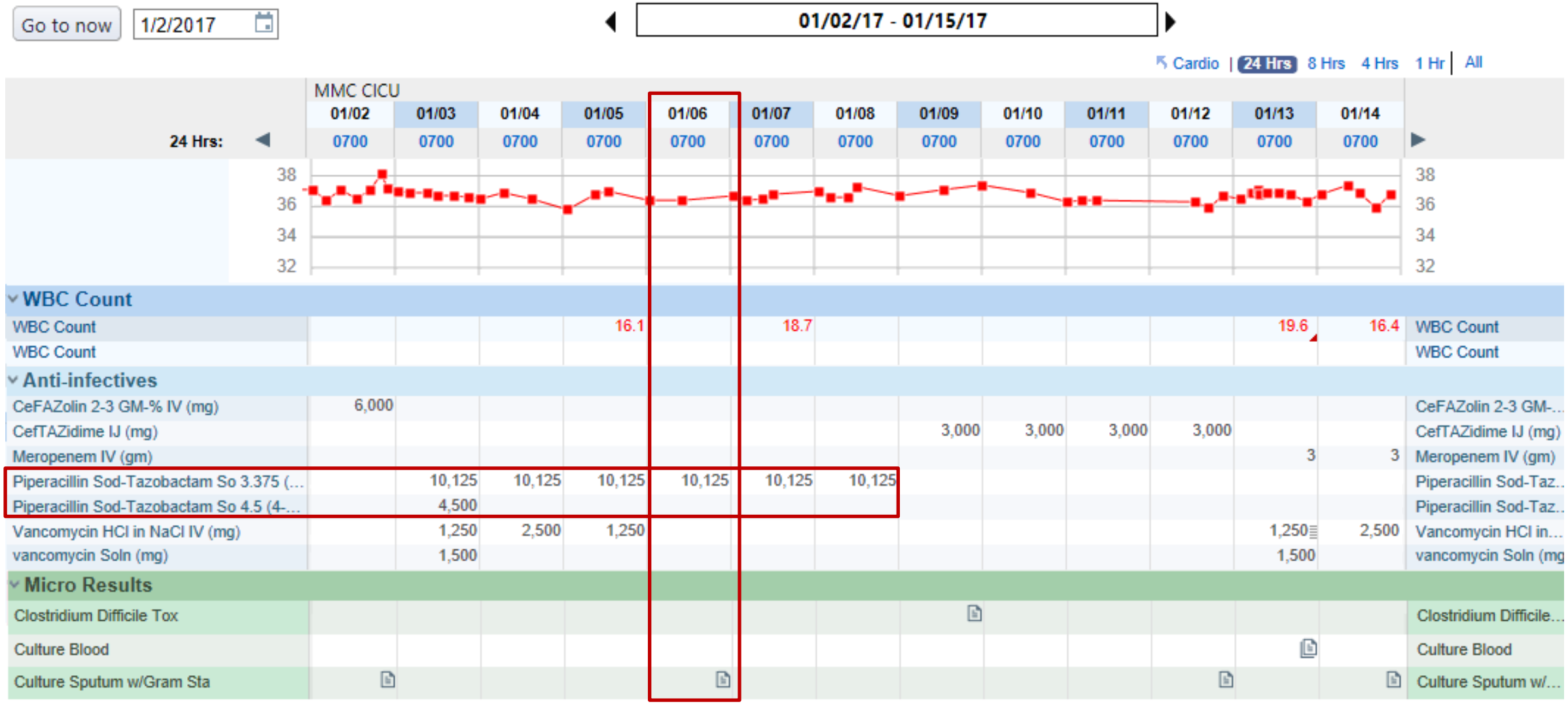
Specimen Information

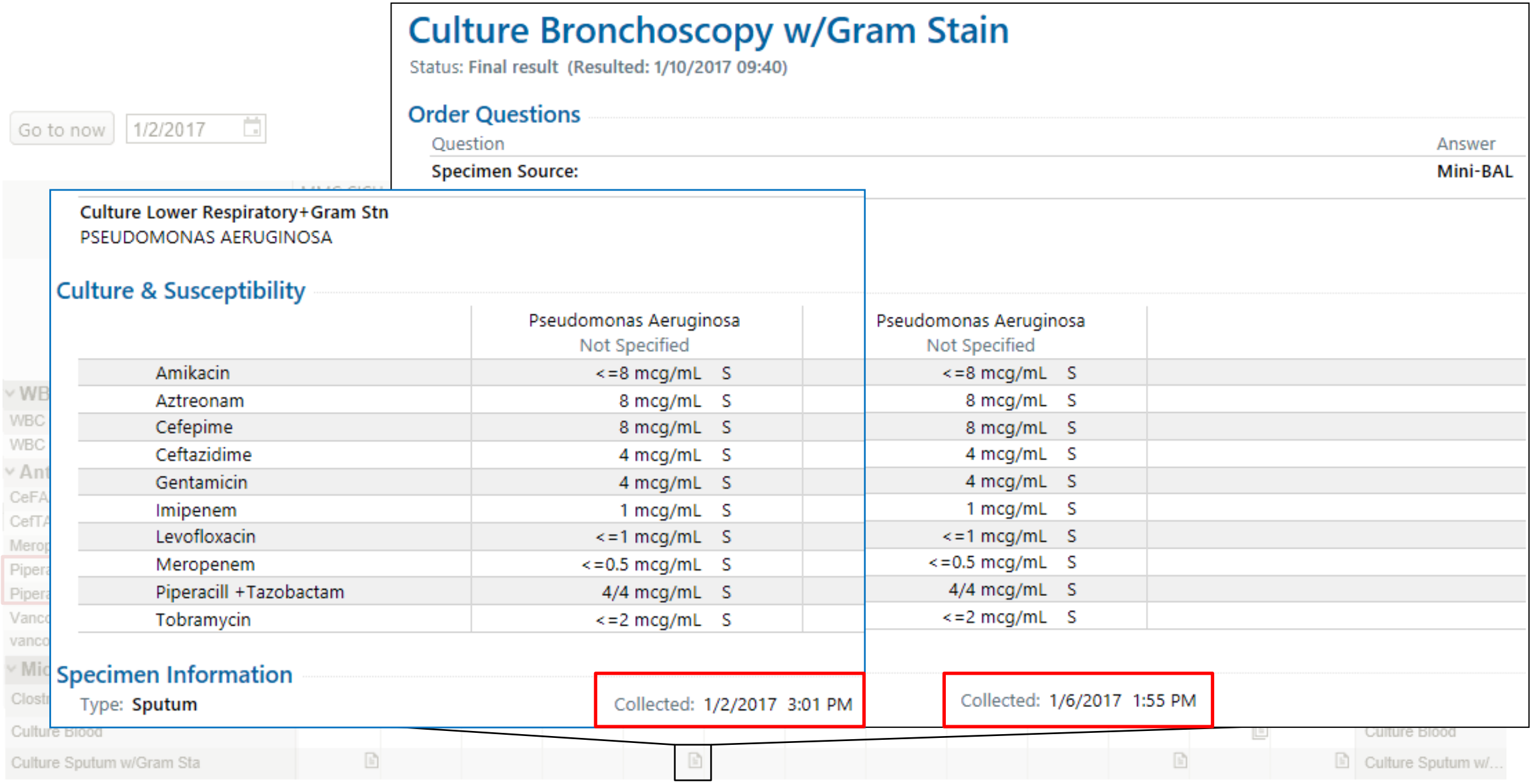
Type: **Sputum** Collected: 1/2/2017 3:01 PM

Initiation of Piperacillin-Tazobactam on 1/3

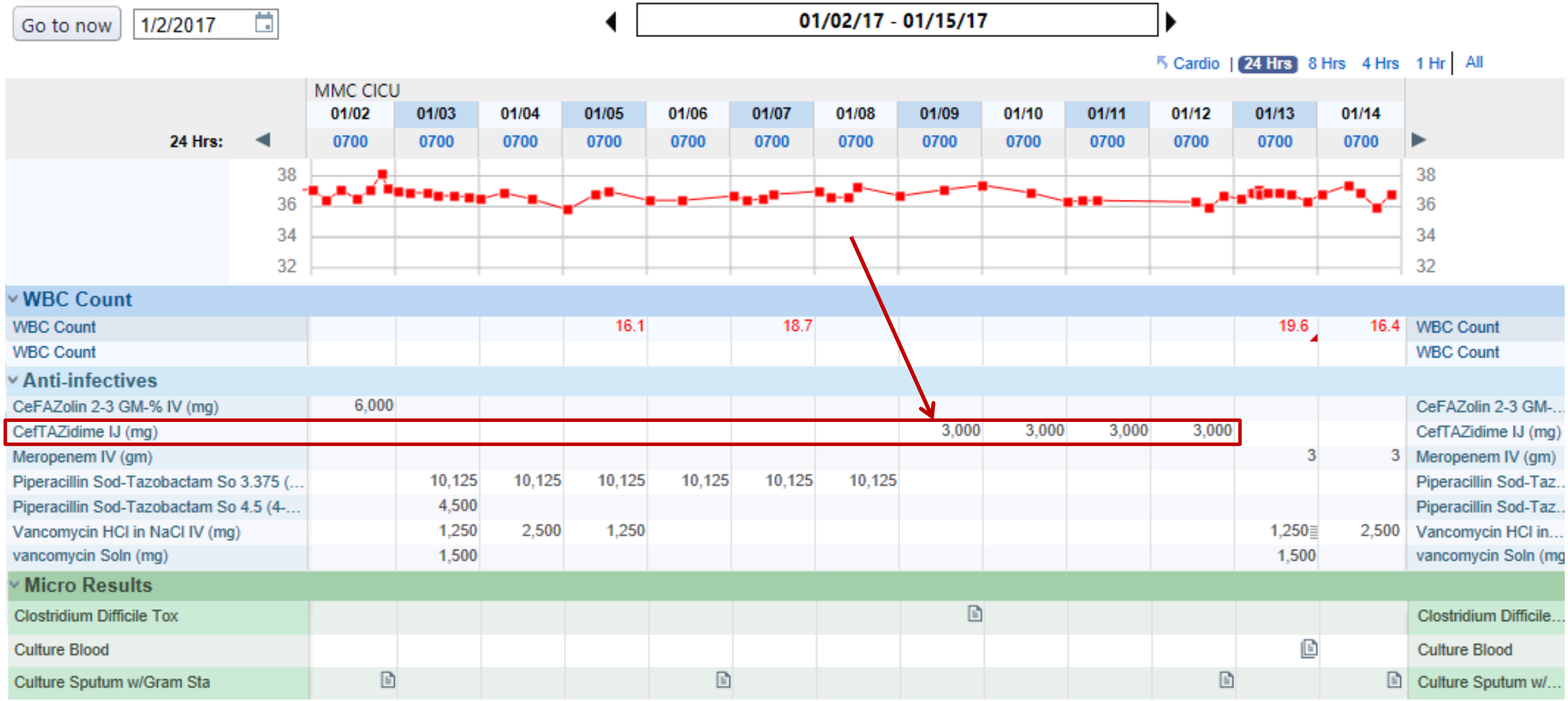


Mini-BAL Culture 1/6

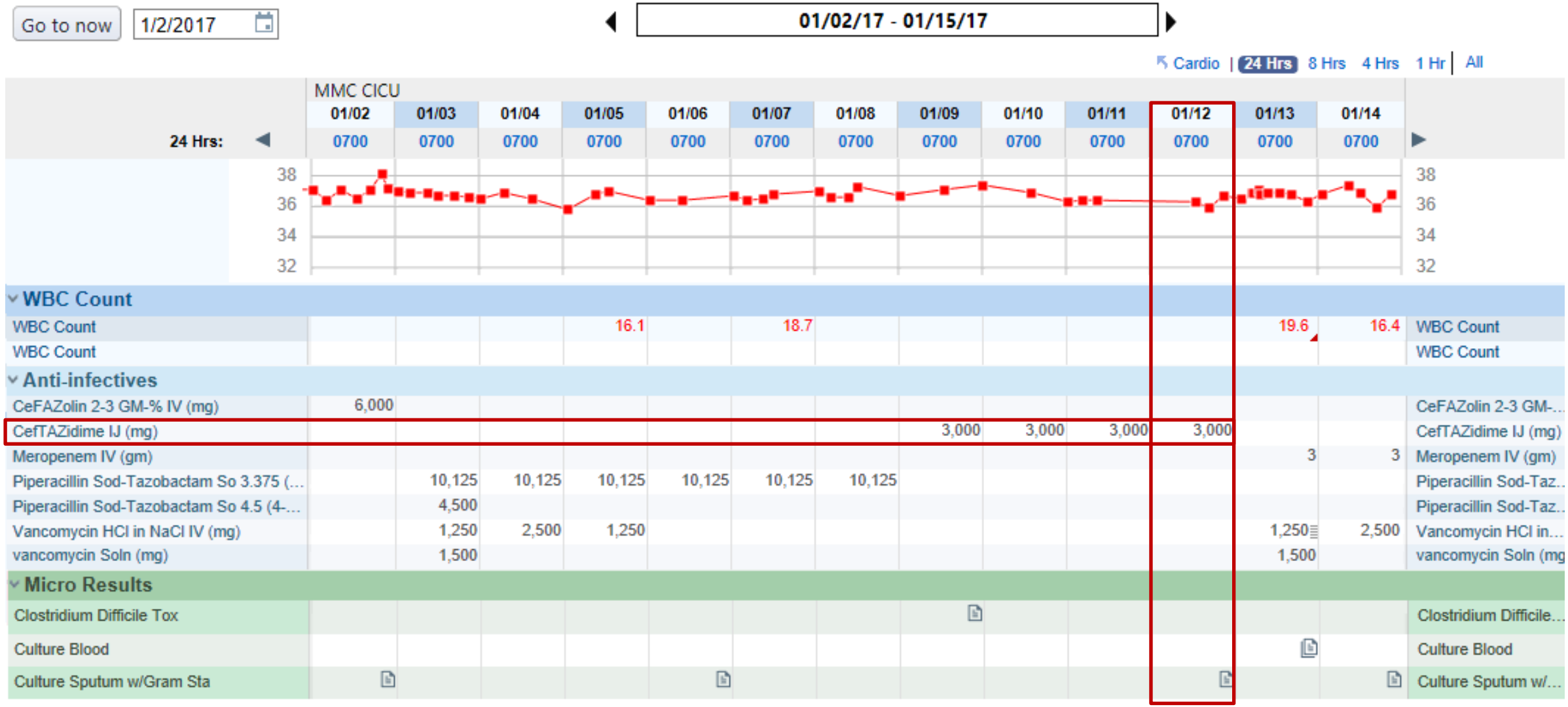



Go to now
1/2/2017
Culture Bronchoscopy w/Gram Stain
Status: Final result (Resulted: 1/10/2017 09:40)
Order Questions
Question
Answer
Specimen Source:
Mini-BAL
Culture Lower Respiratory+Gram Stn
PSEUDOMONAS AERUGINOSA
Culture & Susceptibility
Pseudomonas Aeruginosa
Not Specified
Pseudomonas Aeruginosa
Not Specified
Amikacin <=8 mcg/mL S <=8 mcg/mL S
Aztreonam 8 mcg/mL S 8 mcg/mL S
Cefepime 8 mcg/mL S 8 mcg/mL S
Ceftazidime 4 mcg/mL S 4 mcg/mL S
Gentamicin 4 mcg/mL S 4 mcg/mL S
Imipenem 1 mcg/mL S 1 mcg/mL S
Levofloxacin <=1 mcg/mL S <=1 mcg/mL S
Meropenem <=0.5 mcg/mL S <=0.5 mcg/mL S
Piperacill +Tazobactam 4/4 mcg/mL S 4/4 mcg/mL S
Tobramycin <=2 mcg/mL S <=2 mcg/mL S
Specimen Information
Type: Sputum
Collected: 1/2/2017 3:01 PM
Collected: 1/6/2017 1:55 PM
Culture Sputum w/Gram Sta
Culture Sputum w/...

Therapy Change to Ceftazidime



Induction of Resistance in *P.aeruginosa*



Culture Sputum w/ Gram Stain

Status: Final result (Resulted: 1/16/2017 11:36)

Order Questions

Question

Specimen Source:

Collection Instructions:

Culture Lower Respiratory+Gram Stn

PSEUDOMONAS AERUGINOSA

Culture & Susceptibility

	Pseudomonas Aeruginosa Not Specified	
Amikacin	<=8 mcg/mL	S
Aztreonam	>16 mcg/mL	R
Cefepime	>16 mcg/mL	R
Ceftazidime	>16 mcg/mL	R
Gentamicin	4 mcg/mL	S
Imipenem	2 mcg/mL	S
Levofloxacin	<=1 mcg/mL	S
Meropenem	<=0.5 mcg/mL	S
Piperacill +Tazobactam	>64/4 mcg/mL	R
Tobramycin	<=2 mcg/mL	S

Specimen Information

Type: **Bronchoscopy**

Collected: 1/14/2017 9:30 AM

Culture Sputum w/ Gram Stain

Status: Final result (Resulted: 1/16/2017 11:36)

Order Questions

Question

Specimen Source:

Collection Instructions:

Culture Lower Respiratory+Gram Stn

PSEUDOMONAS AERUGINOSA

Culture & Susceptibility

	Pseudomonas Aeruginosa Not Specified	
Amikacin	<=8 mcg/mL	S
Aztreonam	>16 mcg/mL	R
Cefepime	>16 mcg/mL	R
Ceftazidime	>16 mcg/mL	R
Gentamicin	4 mcg/mL	S
Imipenem	2 mcg/mL	S
Levofloxacin	<=1 mcg/mL	S
Meropenem	<=0.5 mcg/mL	S
Piperacill +Tazobactam	>64/4 mcg/mL	R
Tobramycin	<=2 mcg/mL	S

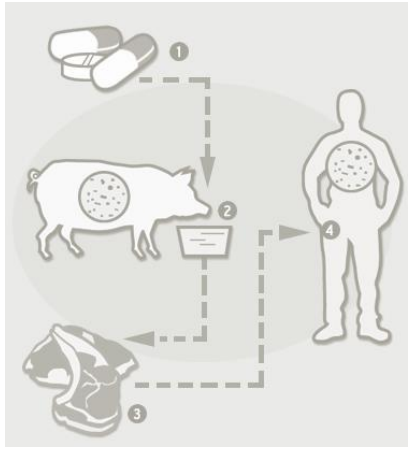
Specimen Information

Type: **Bronchoscopy**

Collected: 1/14/2017 9:30 AM

ZONE 1

Antibiotic Overutilization in **Livestock and Farming**



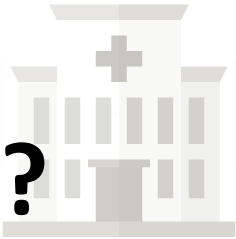
Water Contamination

HOW DID WE GET TO THIS POINT?

Outpatient/Ambulatory Settings

- Primary care
- Urgent care
- Emergency department

ZONE 3



Rehabilitation Facilities

Acute Care Settings

- Hospital

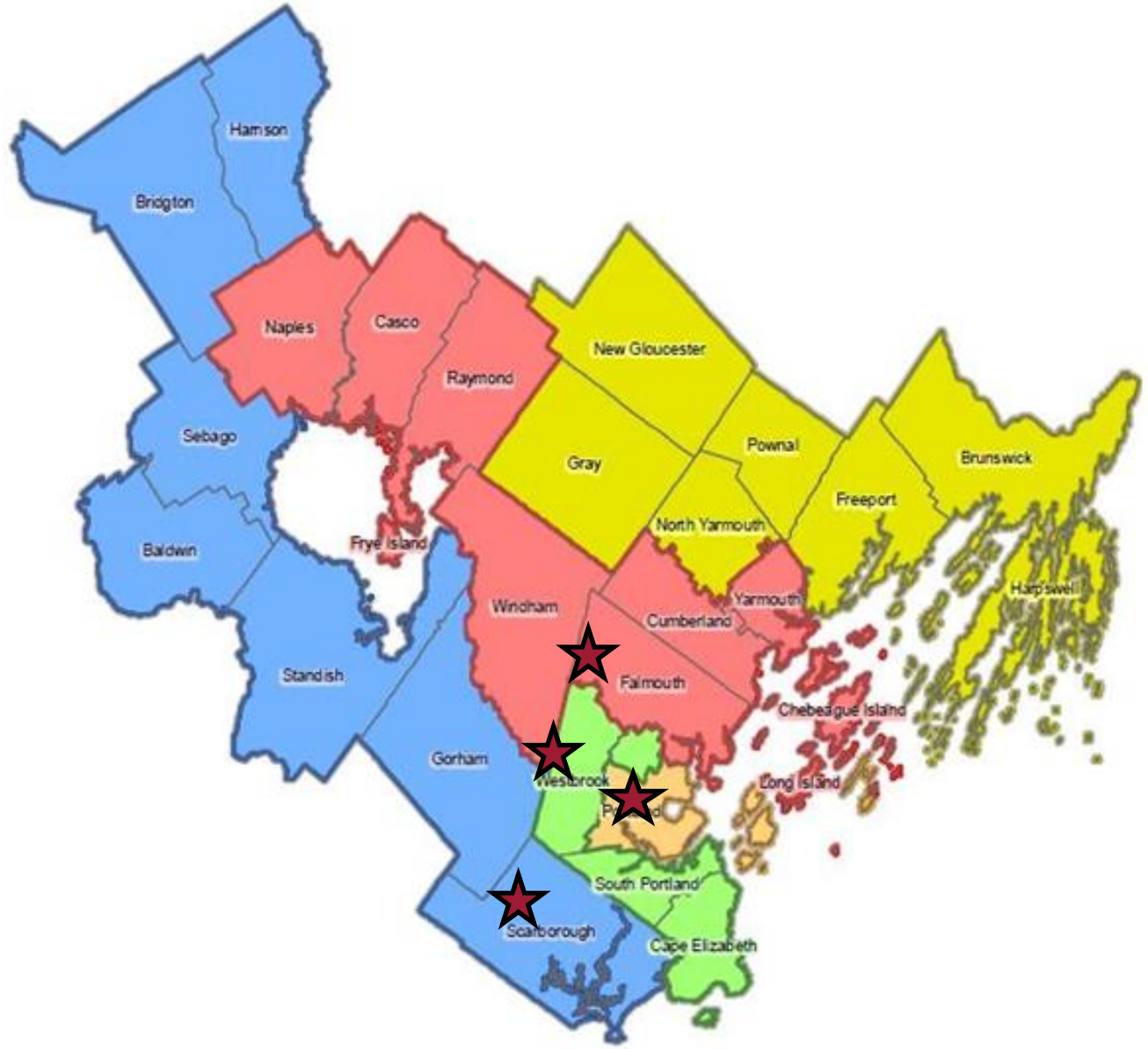
Long-term Care Facilities

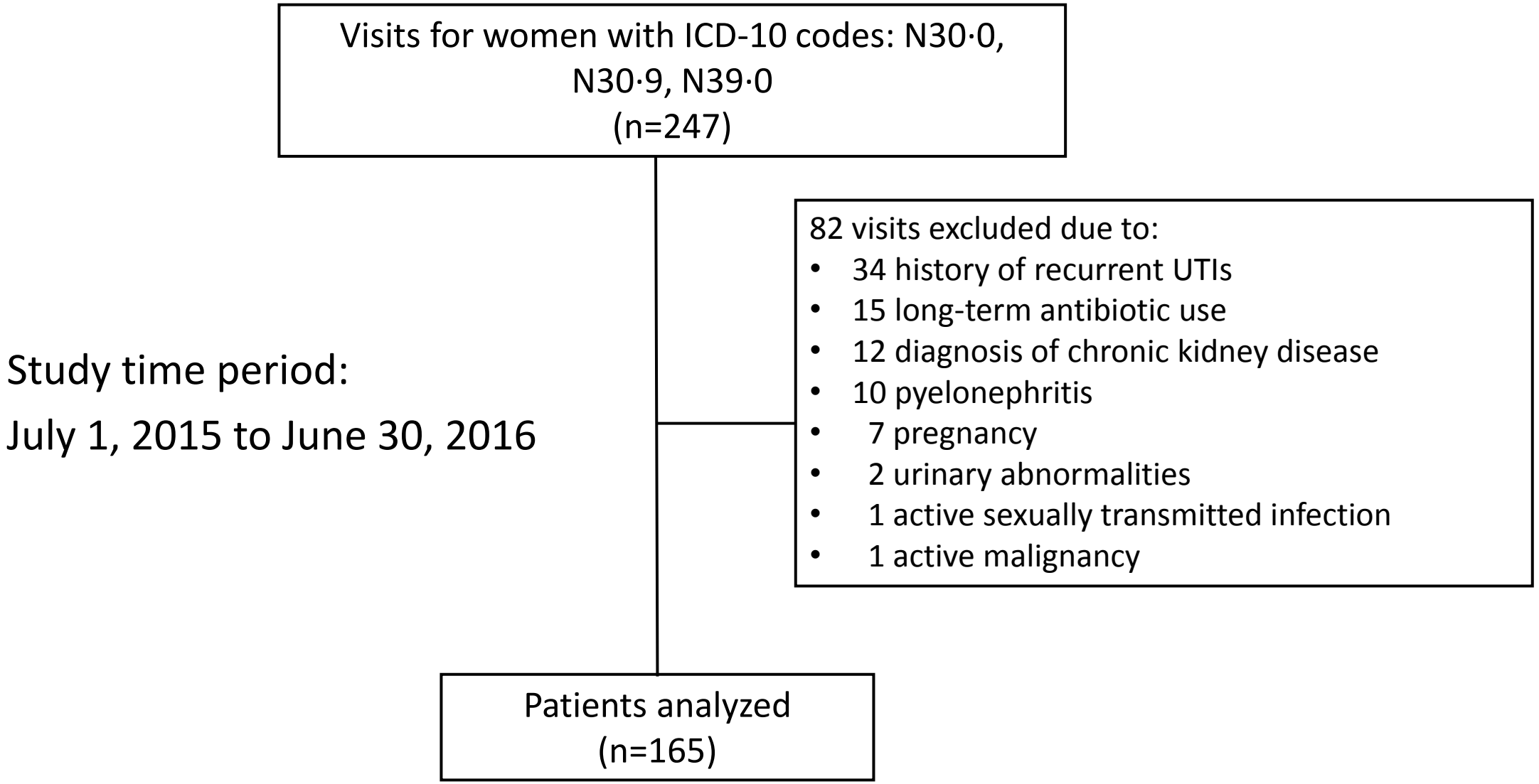
OUTPATIENT PRESCRIBING FOR UNCOMPLICATED CYSTITIS IN WOMEN

Retrospective assessment of 4 family medicine clinics

Study Setting

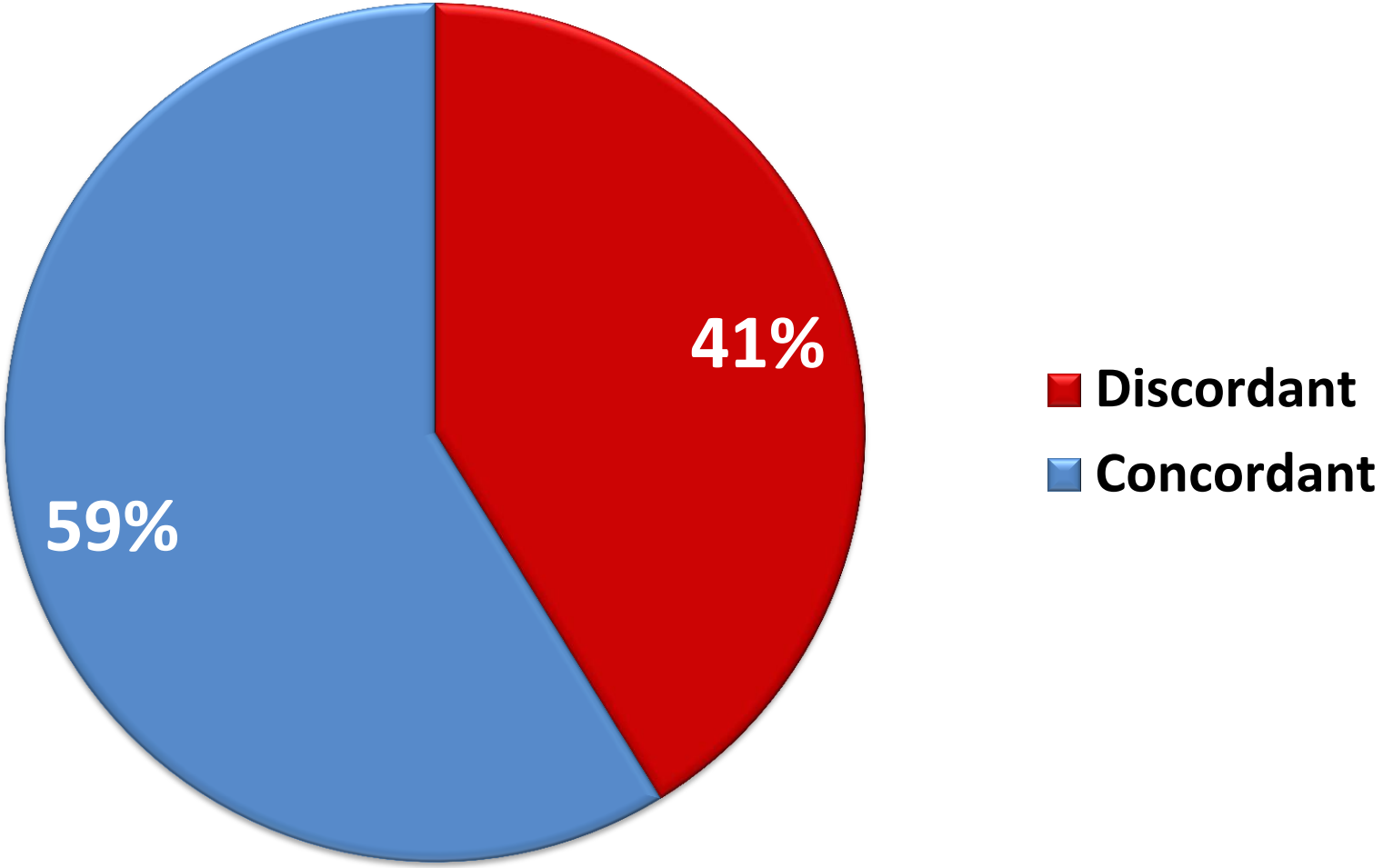
- Four family medicine clinics
- Across all primary care clinics
  - Staffed by 90 physicians, 100 residents, and 23 advanced practice providers
  - Perform >170,000 patient exams per year





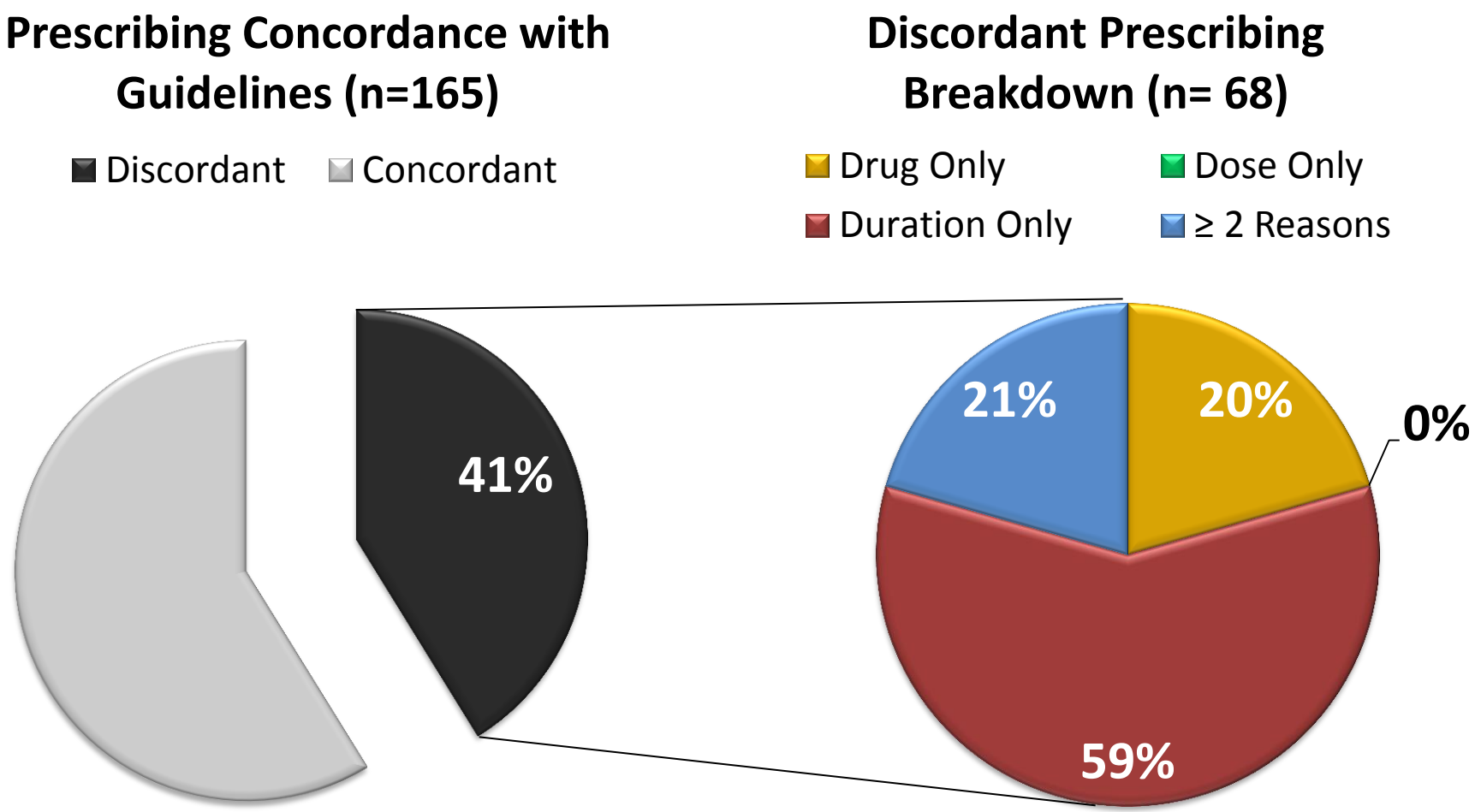
Data from internal analysis. Publication in process.

Prescribing Concordance to Guidelines



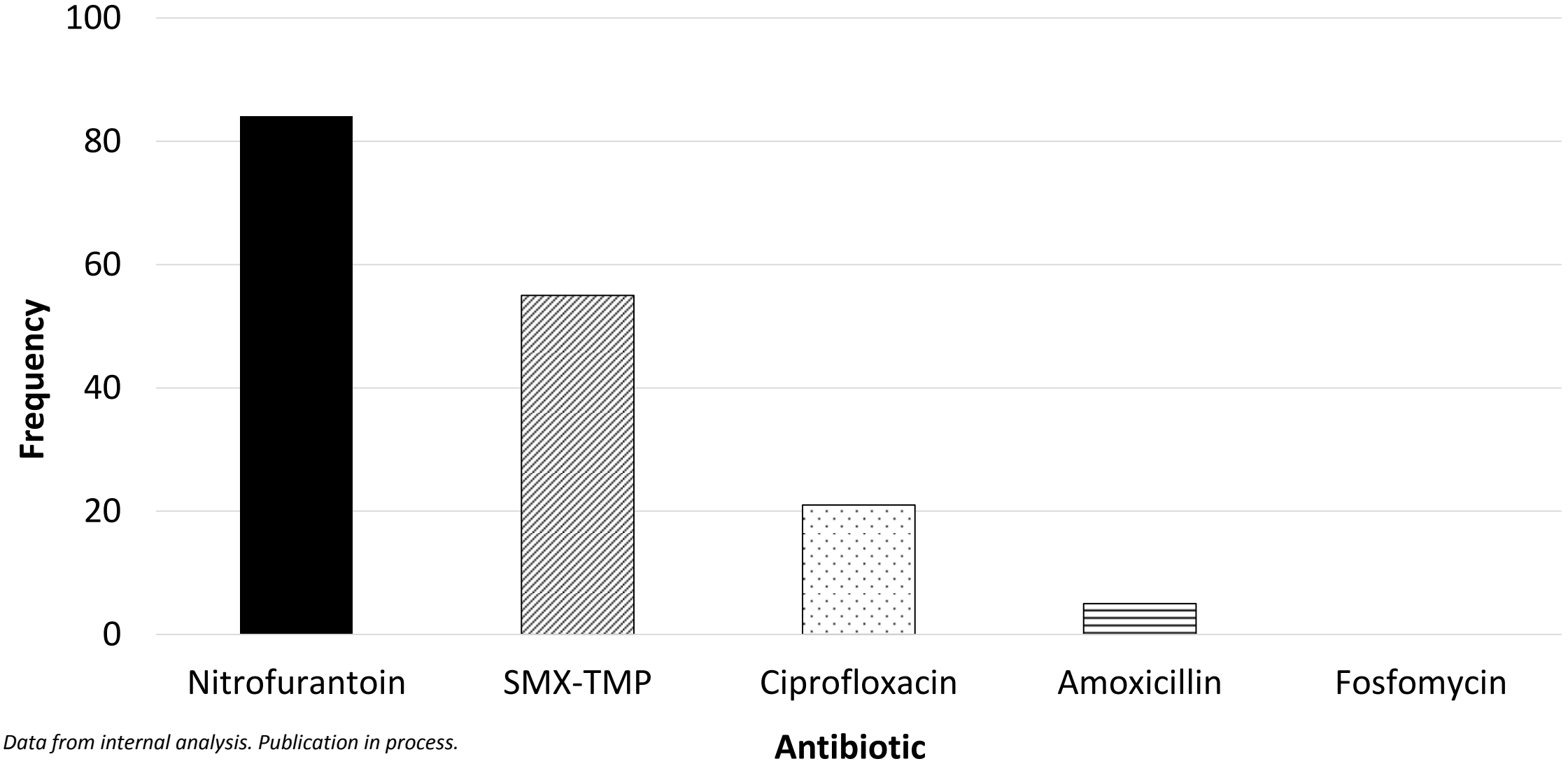
Data from internal analysis. Publication in process.

Dig A Little Deeper



Data from internal analysis. Publication in process.

Distribution of Prescribed Antibiotics



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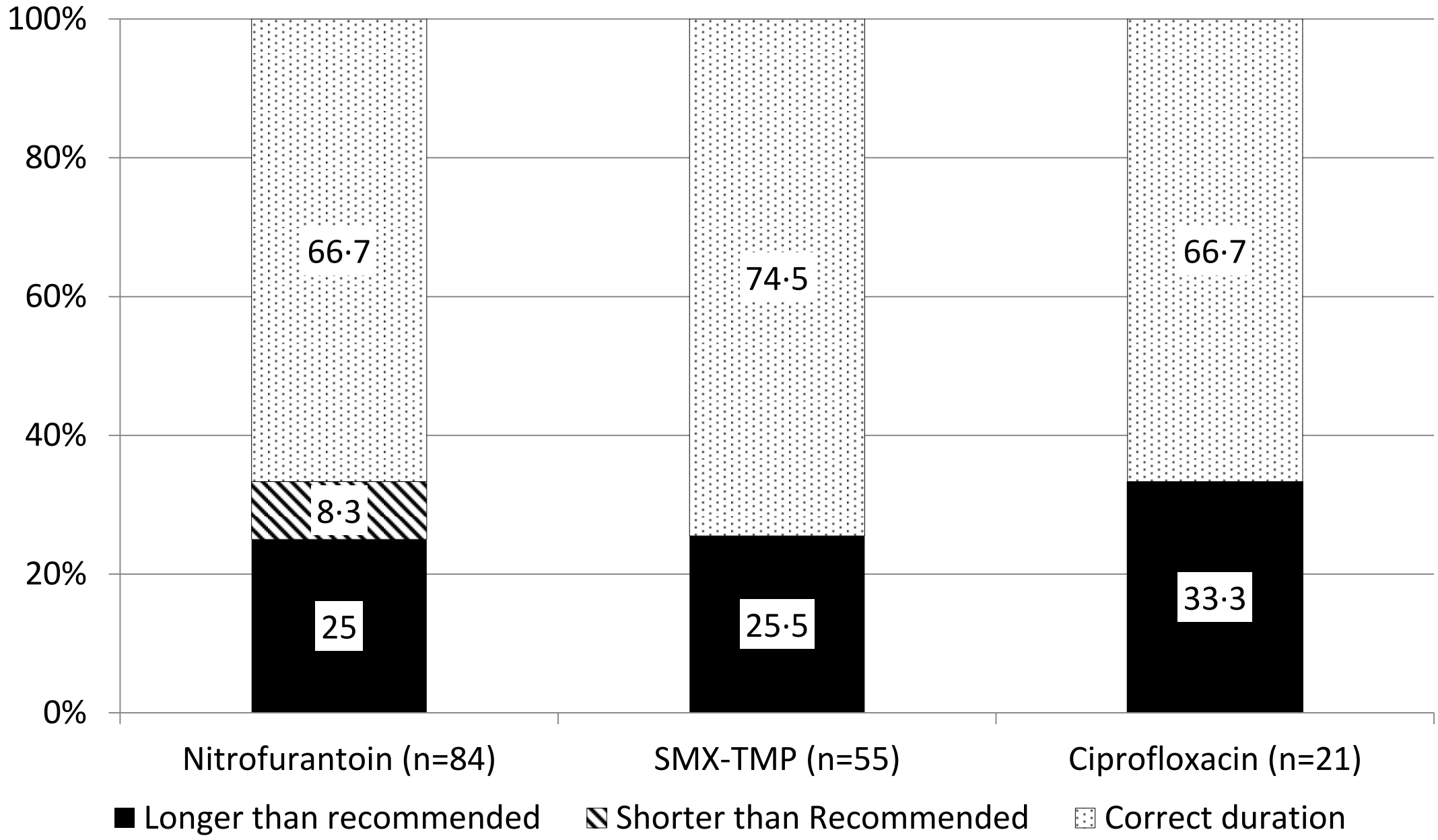
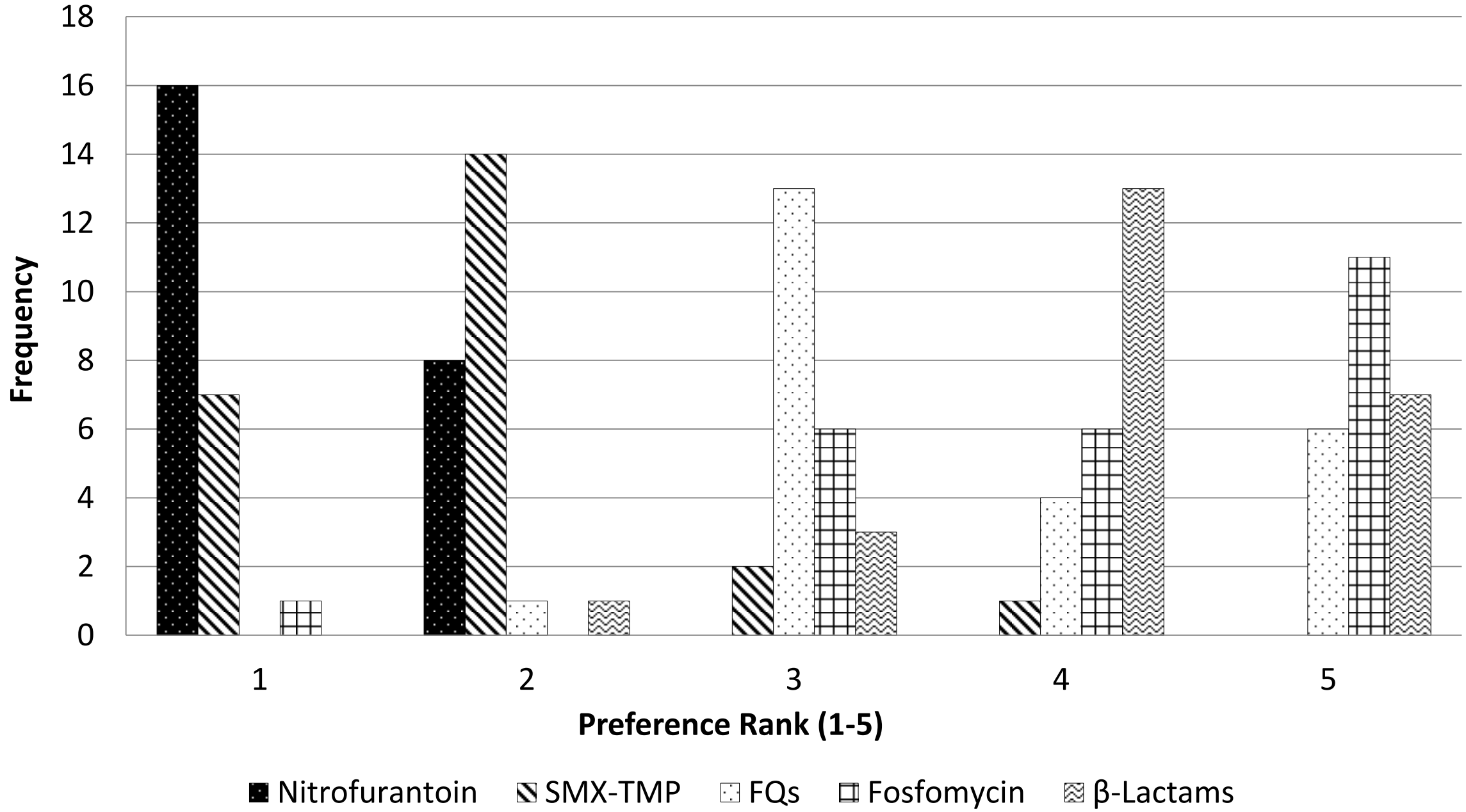


Data from internal analysis. Publication in process.

Questions	Answer Choices
1. Please select your title	• Attending physician • Medical resident (specify year in training) • Physician's assistant • Nurse practitioner
2. How long have you been a practicing clinician?	Specify years in practice (free text response)
3. Rank the following antibiotics 1 through 5 according to preference and select reason(s) for selection #1 and #5: • β-lactams (i.e. amoxicillin-clavulanate, cephalexin) • Fluoroquinolones (i.e. ciprofloxacin, levofloxacin) • Fosfomycin trometamol • Nitrofurantoin • Sulfamethoxazole-trimethoprim	1 = most preferred 5 = least preferred Reasons that may be selected: • Efficacy • Side effect profile • Ease of dosing (i.e. frequency, pill burden) • Cost
5. For selections ranked #1 and #2, please provide duration of therapy you would prescribe	Specify number of days (free text response)
6. Do you use any resources to aid you in providing treatment to patients with acute uncomplicated cystitis?	Select all that may apply: • I do not utilize any resources • Institution-specific order set • Drug information resources • MMC AgileMD App (Infectious Diseases) • Johns Hopkins Antibiotic Guide

Data from internal analysis. Publication in process.



Data from internal analysis. Publication in process.

RESULTS OF SURVEY DISTRIBUTED

- Twenty-four out of 37 distributed surveys responded (65% response rate)
- Using first preferred agent selected as criteria for “Appropriate Drug”, all 24 respondents chose a guideline-recommended agent
- Based on agent selected, only 75% of respondents paired the agent with the correct duration
- Six out of 24 respondents correctly identified fluoroquinolones as last line therapy

Data from internal analysis. Publication in process.

FQs for UTIs: Tip of the Iceberg?

- Drug use evaluation to compare two time periods (pre- vs. post- FDA drug label change in May 2016)
- Cohort included individuals age 18-65

Diagnoses reviewed:

- Acute sinusitis
- Acute exacerbation of chronic bronchitis
- Acute uncomplicated cystitis

Uncomplicated UTI	2016	2017
n	10,900	14,110
Rx with FQ	1209 (11%)	1348 (9.5%)
Overlapping antibiotic	151 (12%)	145 (11%)

COPD w/ acute exacerbation	2016	2017
n	5,210	6,876
Rx with FQ	308 (6%)	357 (5%)
Overlapping antibiotic	62 (20%)	50 (14%)

Acute sinusitis	2016	2017
n	7,697	9,166
Rx with FQ	452 (6%)	428 (5%)
Overlapping antibiotic	135 (30%)	95 (22%)

Data used with permission from single insurer.

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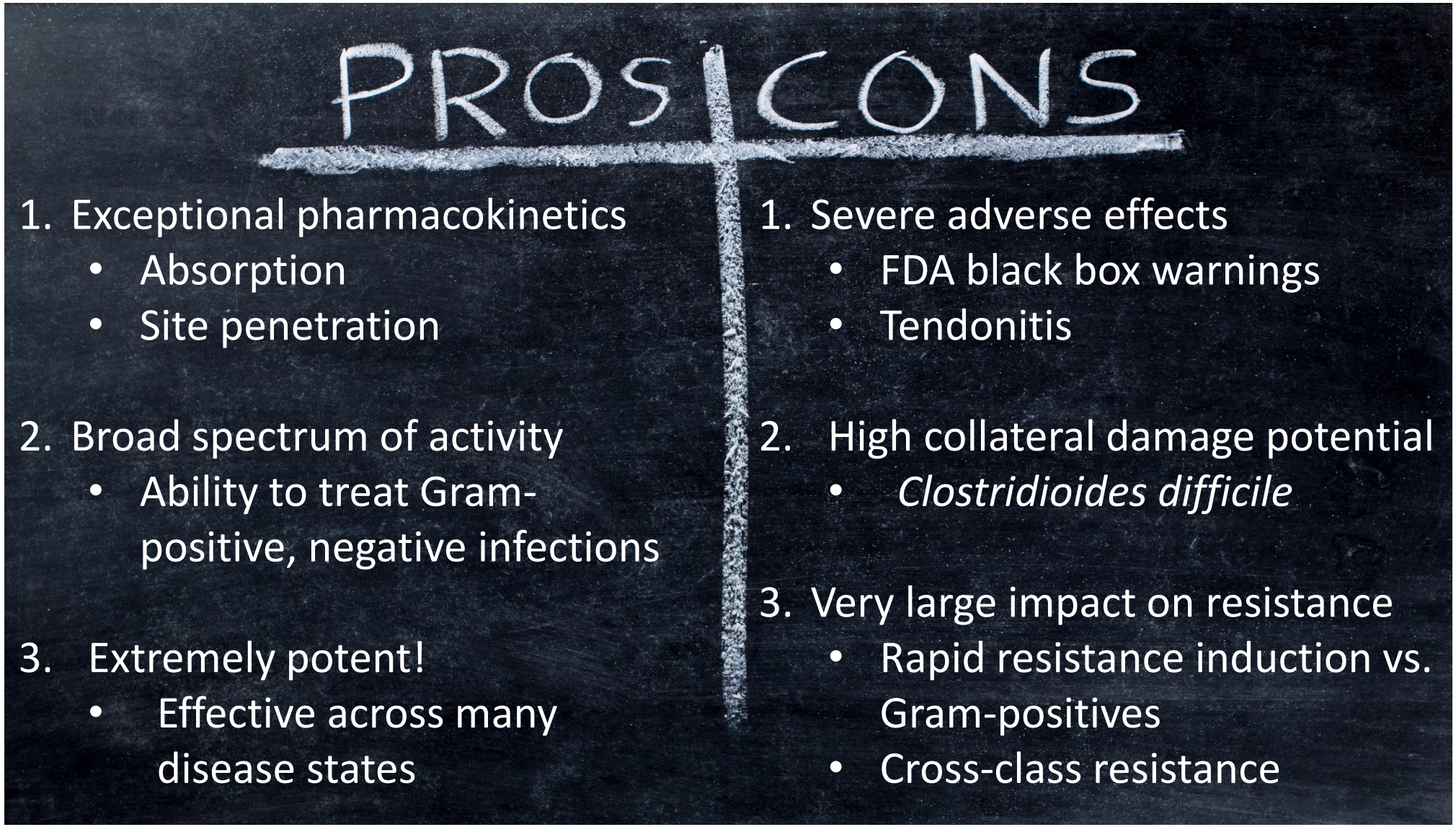
With Great Power Comes Great Responsibility..



ANTIBIOTICS IN DENTISTRY

Provider Prescribing Distribution, 2011

Provider Specialty	Prescriptions, No. in Millions (%)	Providers, No.	Prescriptions per Provider, Rate
All Providers	262.5	911,814	289
Family Practice	64.1 (24)	96,073	667
Dermatology	8.2 (3)	11,329	724
Pediatrics	32.4 (12)	54,228	598
Otolaryngology	4.1 (2)	9,536	430
Emergency medicine	13.8 (5)	32,346	427
Internal medicine/pediatrics	1.4 (1)	3,329	421
Internal medicine	32.1 (12)	83,841	383
Infectious diseases	1.3 (1)	6,166	211
Dentistry	25.6 (10)	122,706	208
Obstetrics/gynecology	6.7 (3)	37,590	178
Surgery (general)	6.9 (3)	69,536	99

Hicks LA et al. *Clin Infect Dis* 2015;60:1308-16.

General Practitioner Prescribing

Provider Specialty	Prescriptions, No. in Millions (%)	Providers, No.	Prescriptions per Provider, Rate
All Providers	262.5	911,814	289
Family Practice	64.1 (24)	96,073	667
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Fourth Highest Antibiotic Prescribing

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Significant Antibiotic Footprint

- Dentists prescribed 24.5 million courses of outpatient antibiotics in 2013
- 77.5 prescriptions per 1,000 people

Characteristic	Prescriptions, No. in Millions (%)[a]	Prescriptions per 1000 Persons, Rate
Overall		
Antibiotic category		
Penicillins	60.3 (23)	193
Macrolides	59.1 (23)	190
Cephalosporins	35.6 (14)	114
Quinolones	27.6 (11)	89
β-lactams, increased activity	21.6 (8)	69
Tetracyclines	21.1 (8)	68
Trimethoprim-sulfamethoxazole	20.3 (8)	65
Urinary anti-infectives	8.5 (3)	27
Lincosamides	7.8 (3)	25
Other	0.5 (0.2)	2
Total	262.5	842

1. Roberts RM et al. *J Am Dent Assoc* 2017; 148:172-178.
2. Hicks LA et al. *Clin Infect Dis* 2015; 60:1308-16.

Cost-effectiveness of antibiotic prophylaxis for dental patients with prosthetic joints

Comparisons of antibiotic regimens for patients with total hip arthroplasty

Daniel D. Skaar, DDS, MS, MBA;
Taehwan Park, PhD; Marc F. Swiontkowski, MD;
Karen M. Kuntz, ScD

ABSTRACT

Background. Clinician uncertainty concerning the need for antibiotic prophylaxis to prevent prosthetic joint

Skaar DD et al. *J Am Dent Assoc* 2015;146:830-9.

Cost-effectiveness of antibiotic prophylaxis prosthetic j

Comparisons of with total hip a

Daniel D. Skaar, DDS, MS, MBA;
Taehwan Park, PhD; Marc F. Sw
Karen M. Kuntz, ScD

Conclusions. The results of Markov decision modeling indicated that a no-antibiotic prophylaxis strategy was cost-effective for dental patients who had undergone THA. These results support the findings of case-control studies and the conclusions of an American Dental Association Council on Scientific Affairs report that questioned general recommendations for antibiotic prophylaxis before dental procedures.

Practical Implications. The results of cost-effectiveness decision modeling support the contention that routine antibiotic prophylaxis for dental patients with total joint arthroplasty should be reconsidered.

Skaar DD et al. *J Am Dent Assoc* 2015;146:830-9.

PERSPECTIVE

Myths of Dental-Induced Prosthetic Joint Infections

Michael J. Wahl, D.D.S. *Medical Center of Delaware, Wilmington, Delaware*

The overwhelming majority of orthopedists and dentists surveyed recommend antibiotic prophylaxis for dental procedures to prevent late prosthetic joint infection. It is time to stop this practice, which is not based on scientific evidence but rather on "myths" of prosthetic joint infections after dental procedures. The first myth is that there are close similarities between late prosthetic valve endocarditis and late prosthetic joint infection. The second myth is that dental treatment is the probable cause of a large percentage of prosthetic joint infections. The third myth is that results of animal experiments have shown that transient bacteremia due to dental procedures can cause prosthetic joint infections in humans. The fourth myth is that the benefits of antibiotic prophylaxis for patients with prosthetic joints outweigh the risks and costs. The fifth and final myth is that clinicians should recommend antibiotic prophylaxis before dental treatment for patients with prosthetic joints to protect themselves legally.

Wahl MJ. *Clin Infect Dis* 1995;20:1420-1425.

Debunking the Myths of Antibiotics in Dentistry

1. Close similarities between late prosthetic valve endocarditis and late prosthetic joint infection

2. Dental treatment is probable cause of large percentage of prosthetic joint infections

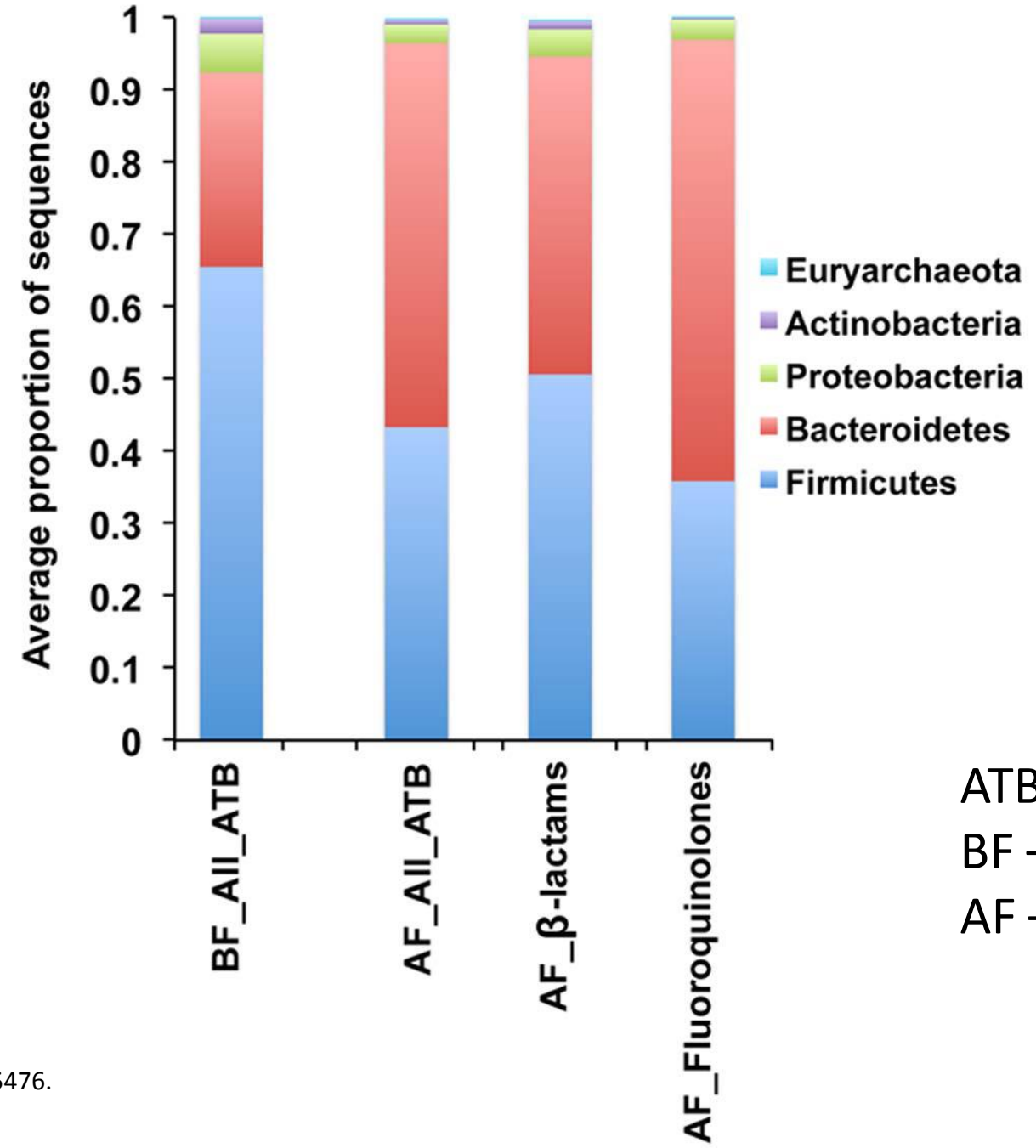
3. Animal experiments show transient bacteremia due to dental procedures can cause prosthetic joint infections in humans

4. Benefits of antimicrobial prophylaxis for patients with prosthetic joints outweigh the risks and costs

Wahl MJ. *Clin Infect Dis* 1995;20:1420-1425.


FACTS
MYTHS

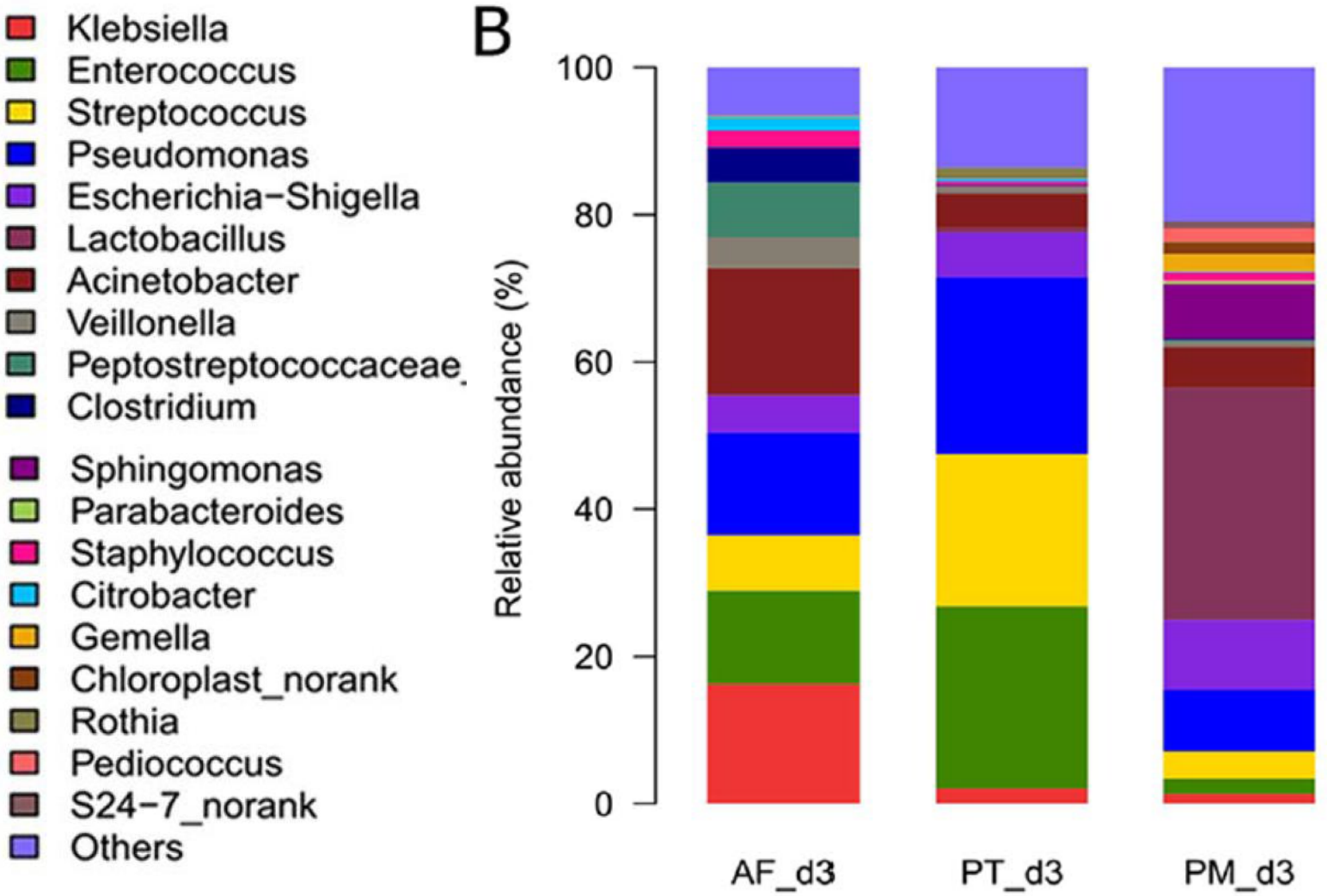
NORMAL FLORA DISTURBANCE SECONDARY TO ANTIBIOTICS



ATB – antibiotics
BF – before treatment
AF – after treatment

Panda S et al. *PLoS One* 2014;9:e95476.

Effect of 1-week Empirical Antibiotic Therapy in Preterm Infant Microbiota



AF – antibiotic free
PT – piperacillin/tazobactam
PM – penicillin/moxalactam

Zhu D et al. *Sci Rep* 2017;7:8025.

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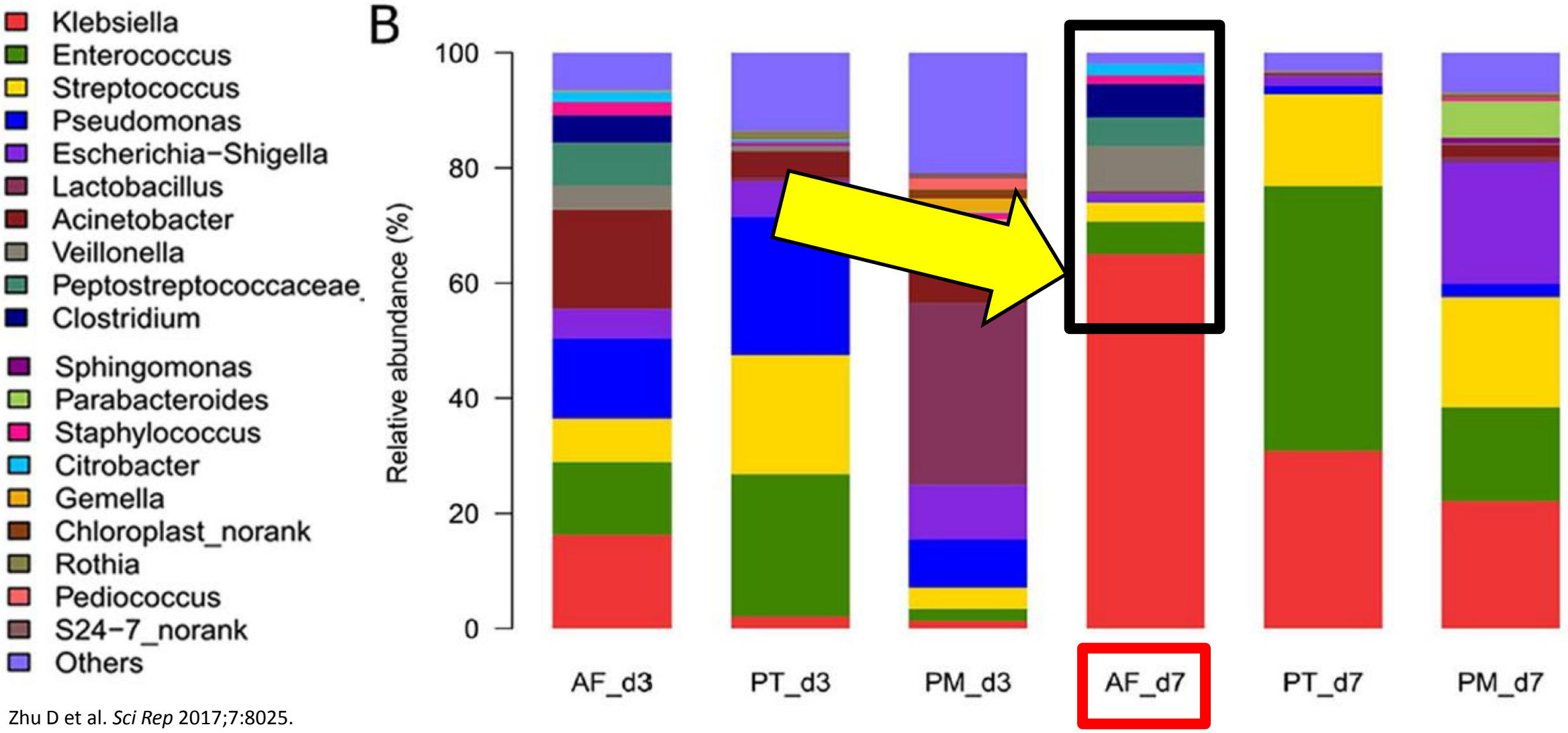

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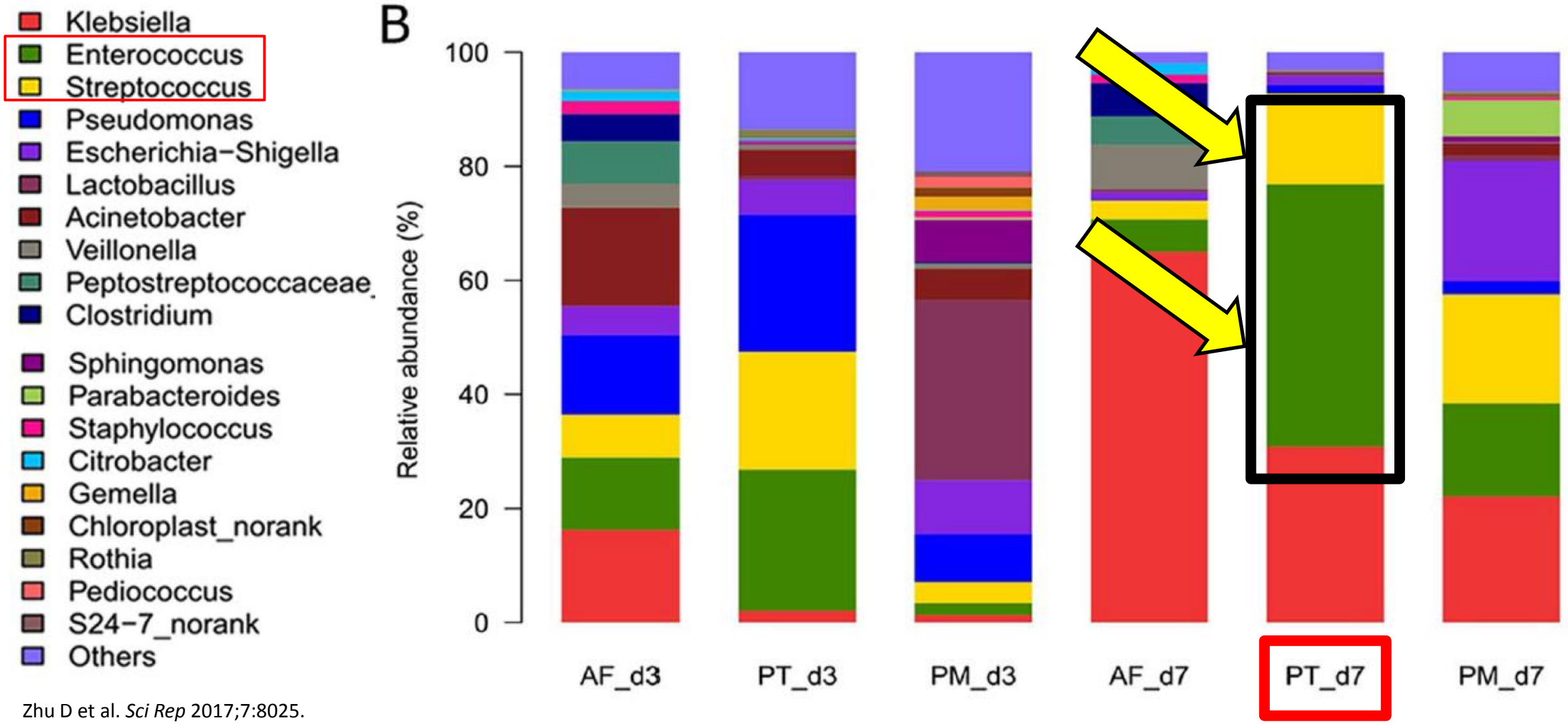

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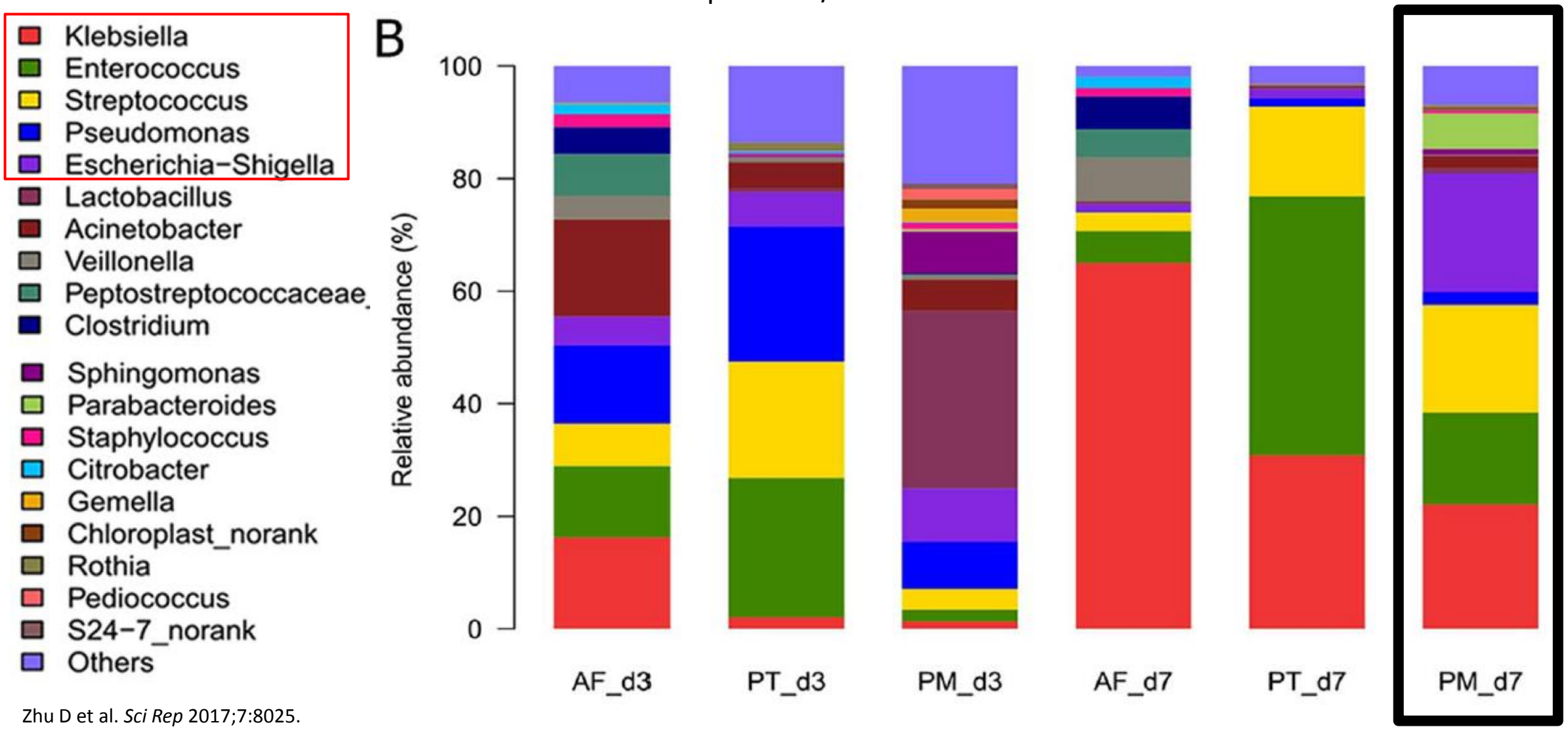
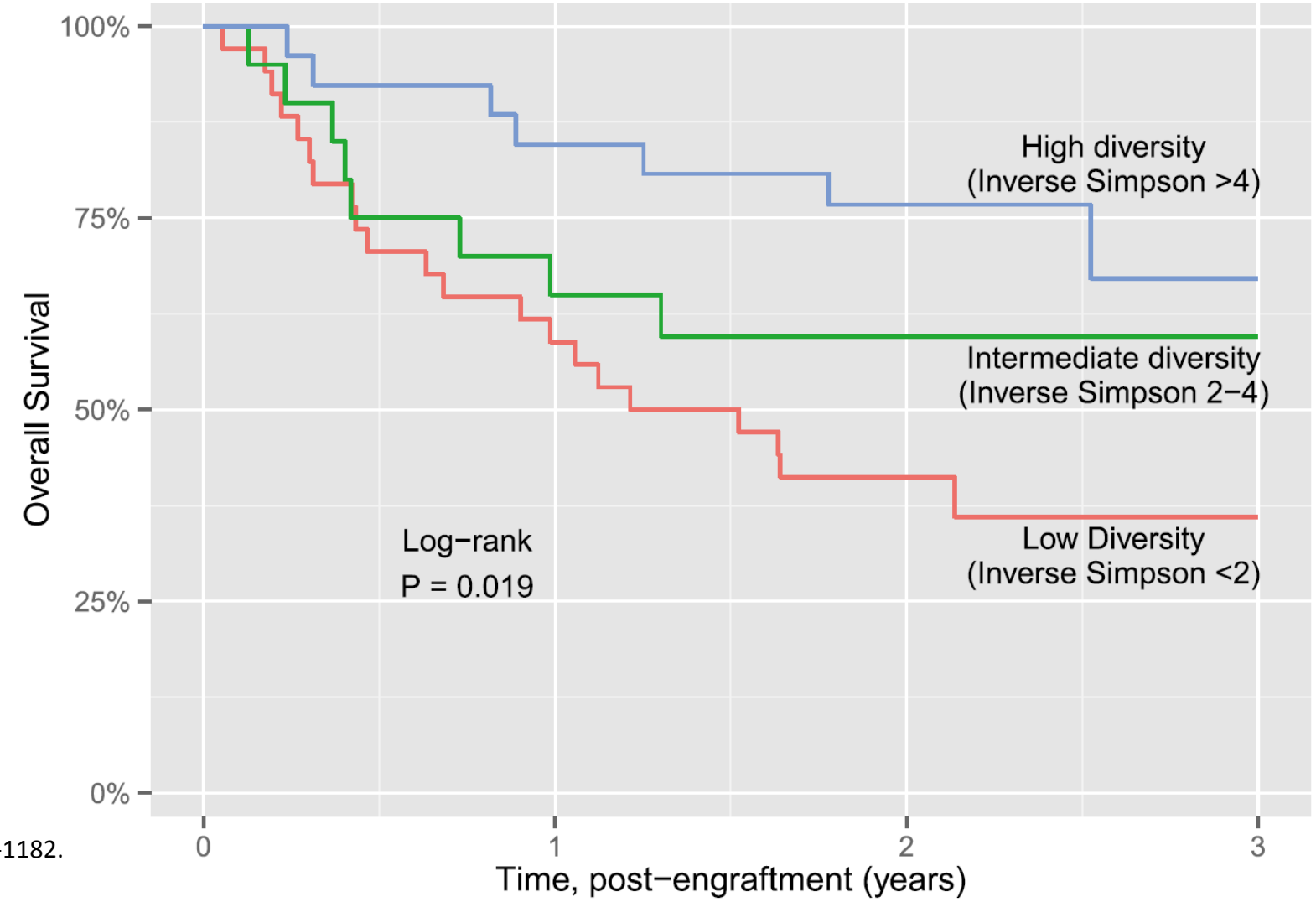


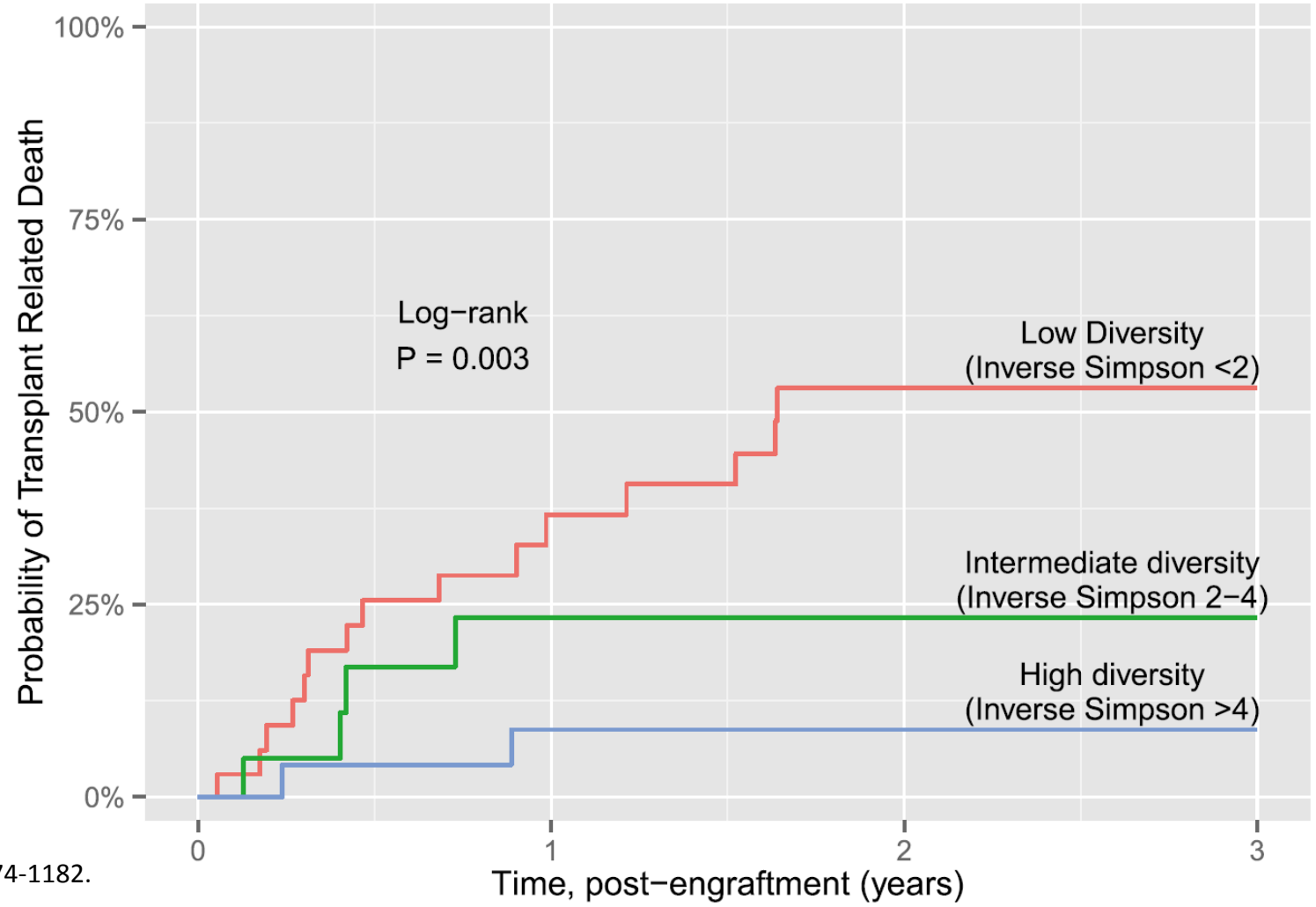
Zhu D et al. *Sci Rep* 2017;7:8025.

Impact of Diversity in Stem-Cell Transplant Recipients



Taur Y et al. *Blood* 2014;24:1174-1182.

Less Diverse? More Complications?



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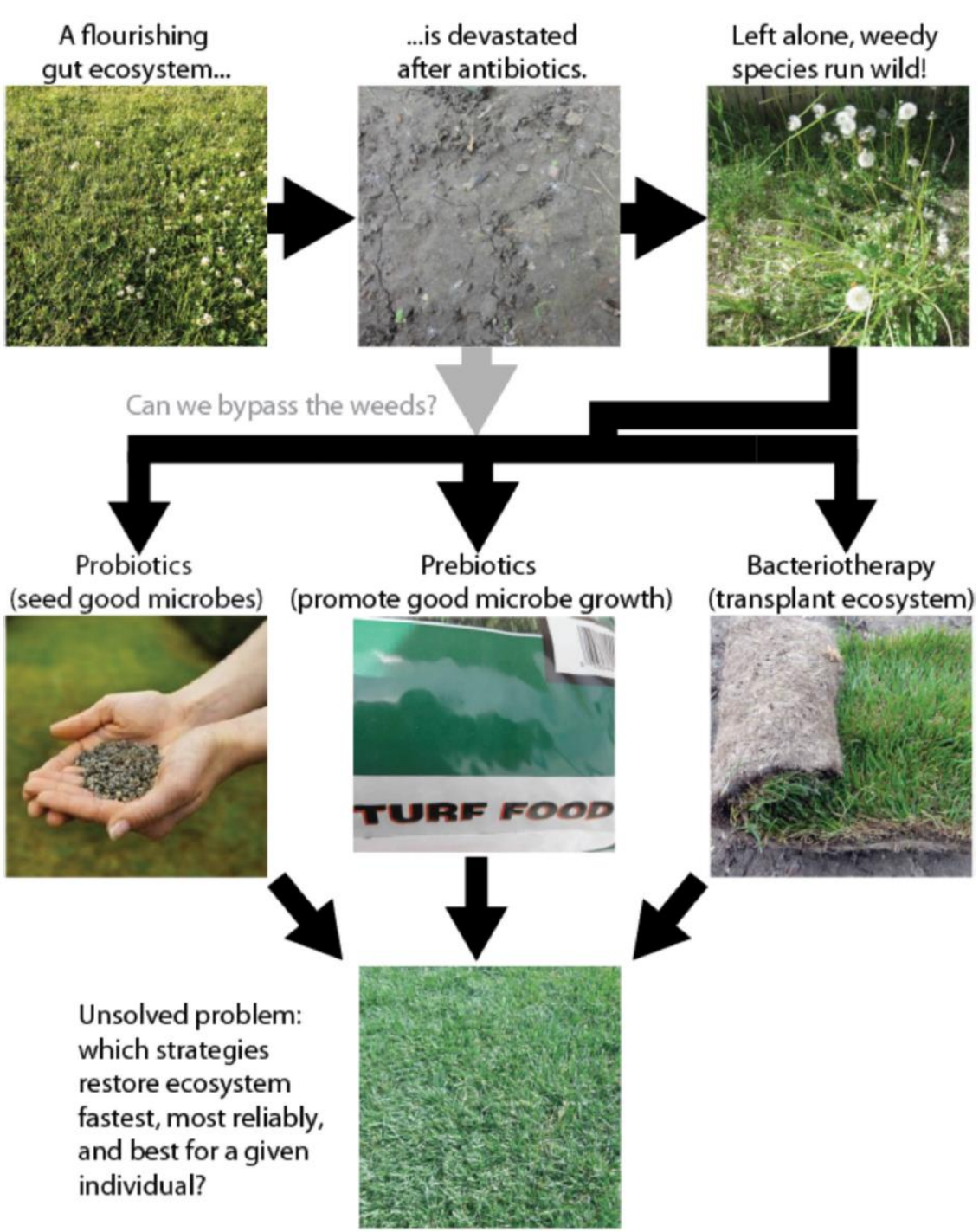
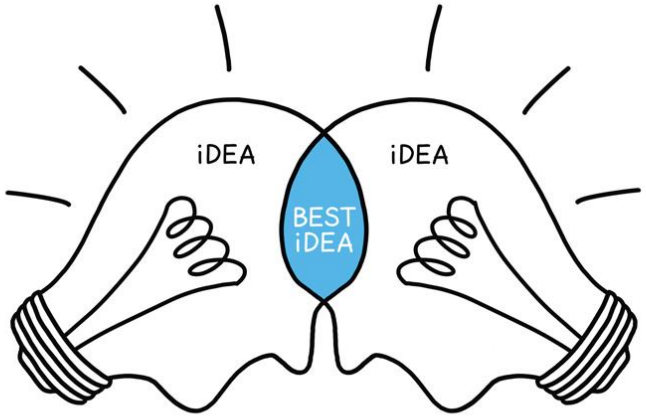


Lozupone CA et al. *Nature* 2012;489:220-230.

IMPLEMENTING STEWARDSHIP INTO YOUR PRACTICE

Step 1: Identify the “Low Hanging Fruit”

- Determine the needs and goals within your practice or practice site
- Variable from site-to-site
  - Regional challenges
  - Institutional considerations
  - Patient demographics



- Multi-disciplinary approach leads to high level involvement
- “What makes sense for me and/or my site?”

Step 2: Perform Assessment of Current Practice

- Is it worth time/effort to tackle an area of stewardship that is already performing at a high level?
- Baseline assessment allows for measured or calculated expectations post-intervention implementation
- Data collection & analysis can be daunting!
  - Work as a team
  - Consult experts

Step 3: Formulate Intervention

- A well thought out approach leads to:
  - Successful adoption by individuals involved
  - Sustained “response”
- Multi-disciplinary
  - Include key stakeholders with “skin in the game”
  - Discussion of varying viewpoints
  - Physician/provider champion

Step 4: Implementation

- Understand metrics to review post-implementation
  - How would you define a successful implementation?
  - Are expectations realistic?
- Promote the "**WHY**"
  - Present data to front-line staff
  - Financials are great for C-suite, bedside clinicians want to see patient impact!
- Change mentality from "have to do it" to "want to do it"

Common low hanging fruit stewardship initiative..

IV TO PO

Table 1. Low-Hanging Fruit Antimicrobial Stewardship Initiatives

ASP Activity	Reference	Setting	Description of ASP Intervention	Cost Savings/Avoidance
Intravenous-to-oral conversion	Davis et al 2005 [10]	Detroit Receiving Hospital and University Health Center	Prospective pharmacy intervention involving sequential intravenous/oral therapy for patients with pneumonia	Drug acquisition cost savings of $110/patient
	Kuti et al 2002 [11]	Hartford Hospital	A pharmacist-managed proactive program that used predetermined clinical criteria for converting levofloxacin therapy from intravenous to oral	Length of stay and costs were significantly less for the intravenous-to-oral converted patients (6 vs 9.5 d [$P = .031$]) and ($13 931 vs $17 198)
	Paladino et al 1991 [12]	Millard Fillmore Suburban Hospital	After conventional intravenous antibiotics were administered for 3 days, patients were randomly assigned to either continue intravenous antibiotics or switch to oral ciprofloxacin	Ciprofloxacin was associated with an average cost savings of $293 per patient
	Hendrickson and North 1995 [13]	Denver Veterans Affairs Medical Center	Patients converted from intravenous ceftriaxone to oral cefpodoxime	A drug cost savings of $46.05 per patient; patients receiving step-down therapy averaged 1 less day of hospitalization
	Lau et al 2011 [18]	Johns Hopkins Hospital	Evaluated budget impact of voriconazole, pantoprazole, chorothiazide, levetiracetam in patients eligible for oral medication	Potential annual cost reduction of $1 166 759.70
	Jones et al 2012 [19]	VA hospitals throughout United States	Evaluated budget impact of fluoroquinolones in patients eligible for oral medication	Estimated cost savings over 4 years in the range of $4 million
	2010	The Ohio State University Wexner Medical Center	ASP targeted linezolid, moxifloxacin, and fluconazole	Annualized cost avoidance savings for these 3 antimicrobials were $242 713

Goff DA et al. *Clin Infect Dis* 2012;55:587-92.

Juice Worth The Squeeze

Setting & Year	Cost Savings/Avoidance
Detroit Receiving Hospital and University Health Center, 2005	Drug acquisition cost savings of **$110/patient**
Hartford Hospital, 2002	Length of stay and costs were significantly less for IV to PO converted (6 vs. 9.5 d, *p* = 0.31) and (**$13,931 vs. $17,198**)
Millard Fillmore Suburban Hospital, 1991	Ciprofloxacin was associated with an average cost savings of **$293 per patient**
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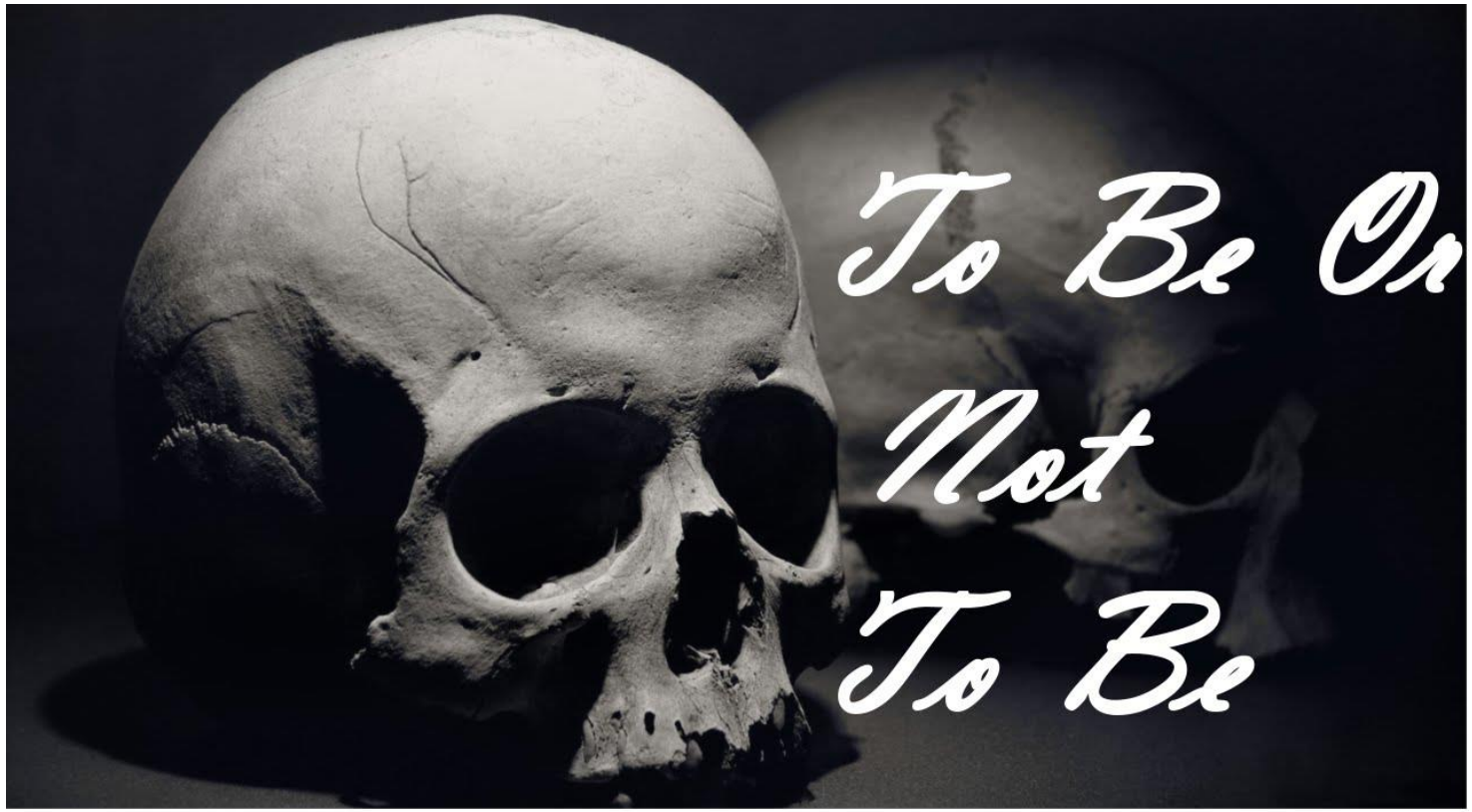
Johns Hopkins Hospital, 2011	Potential annual cost reduction **of $1,166,759.70**
VA hospitals throughout U.S., 2012	Est cost savings **over 4 years of $4 million**
The Ohio State University – Wexner Medical Center, 2010	Annual cost avoidance for 3 antimicrobials (linezolid, moxifloxacin, fluconazole) **$242,713**

Goff DA et al. *Clin Infect Dis* 2012;55:587-92.

RESTRICTIONS



To Restrict, Or No To Restrict?

Formulary restriction	White et al 1997 [22]	Ben Taub General Hospital Houston	Prior ID authorization required for restricted antimicrobials	Total intravenous antimicrobial expenditures decreased by 32% ($863 100)
				Antibiotic cost per patient-day decreased from $18.00 to $12.90
	Po et al 2012 [3]	Banner Estrella Medical Center	Implemented computer physician order entry ASP restrictive template for linezolid	Linezolid use fell from 28 defined daily doses/1000 patient-days to 7 defined daily doses/1000 patient-days over 25 months; cost data not reported
	2010	The Ohio State University Wexner Medical Center	Doripenem added to formulary as a restricted antibiotic, required prior authorization by ASP	Annual antipseudomonal carbapenem cost savings of $61 000

Goff DA et al. *Clin Infect Dis* 2012;55:587-92.

MICRO ROUNDS (IMPACT OF MICROBIOLOGY INVOLVEMENT)

Open Forum Infectious Diseases

BRIEF REPORT

The Role of Antimicrobial Stewardship in the Clinical Microbiology Laboratory: Stepping Up to the Plate

Shawn H. MacVane,[1,2] John M. Hurst,[4] and Lisa L. Steed[3]

[1]Department of Pharmacy Services, [2]Division of Infectious Diseases, College of Medicine; and [3]Department of Pathology and Laboratory Medicine, Medical University of South Carolina; Charleston; [4]Department of Pharmacy, Saint Anthony Hospital, Oklahoma City

Clinical Microbiologist Expertise Crucial

Table 2. Examples of Common ASP Interventions Resulting From Interdisciplinary Microbiology Plate Rounds and Their Potential Clinical Impact

Category	Intervention or Examples	Potential Clinical Impact
Antibiotic allergy	• Identification of penicillin allergic patients prompts earlier *in vitro* susceptibility testing of alternative agents	• Faster *in vitro* susceptibility data • Avoid delay in time to appropriate therapy
Antimicrobial resistance markers	• Methicillin-resistant vs methicillin sensitive *Staphylococcus aureus* (PCR, PBP_{2a}, chromogenic agar) • Vancomycin-resistance in *Enterococcus* spp (PCR) • KPC-producing organisms (in facilities where these are uncommon)	• Shorter time to effective and/or optimal therapy • Cost savings (supplement to anti-MRSA pneumonia therapy duration of treatment limits)
Bug-drug mismatch from emergency department or outpatient clinics	• Alert provider to untreated pathogens (yeast, *S aureus*, GNR) from critical sterile sites (blood, CSF, etc) • Alert provider to discordant result • Suggest alternative agents	• Decrease time to appropriate therapy • Prevent unnecessary hospitalization • Avoid IV/IM administration or PICC insertion (eg, fosfomycin for MDR cystitis)
Clarification of improper specimen/culture ordering	• Endotracheal specimen ordered as a BAL or vice versa • Abdominal abscess ordered as abdominal fluid • CF culture in non-CF patient	• Decrease unnecessary/excessive microbiology workup
Clinical liaison services	• Reporting organism in mixed urine culture of patients with bacteremic urosepsis • Review prior patient history, cultures from OSH	• Established source of bacteremia allows for conversion to oral therapy in some situations • Modification of therapy and/or microbiologic workup based on previous culture and susceptibility results

MacVane SH et al. *Open Forum Infect Dis* 2016:3:ofw201.

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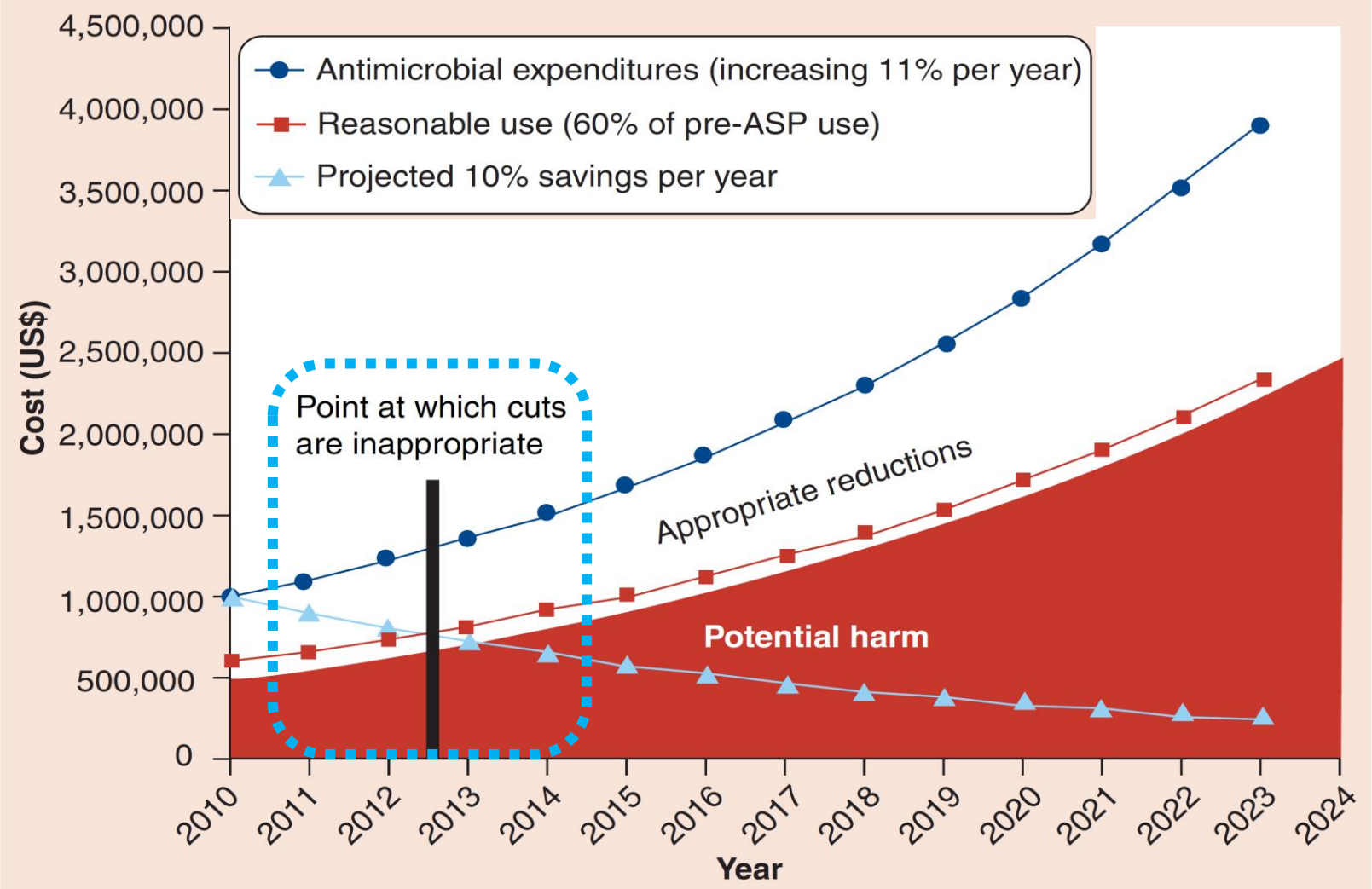
MacVane SH et al. *Open Forum Infect Dis* 2016:3:ofw201.

Better Patient Care!

Infection vs colonization	• Assist with assessment of clinical presentation and clinical correlation for lower respiratory cultures and urine cultures, etc	• Avoid unnecessary antimicrobial utilization • Decrease unnecessary/excessive microbiology workup
MDR organisms	• Earlier *in vitro* susceptibility testing of alternative/salvage antimicrobials (tigecycline, polymyxins) • Earlier involvement of infectious diseases consultant	• Decrease delay in time to approriate therapy • Improve patient outcomes
Mixed cultures	• Predominance vs polymicrobial • Liaison service between provider and microbiologists to determine extent of work up of mixed cultures in a more timely fashion • Requirements for *in vitro* susceptibility testing for all isolates vs selective isolates	• May prevent unnecessary escalation of antibiotic treatment and may decrease time to appropriate therapy • Avoid unnecessary/excessive microbiology workup • Streamlining of antimicrobial regimen for polymicrobial infection
Optimal dose selection	• Actual MIC for a given antimicrobial agent	• Optimize the therapeutic regimen based on pharmacokinetic and pharmacodynamic principles
Rapid diagnostics (PCR, MALDI-TOF)*	• Create clinical pathways to increase utilization of results	• Shorter time to effective and/or optimal therapy • Decrease broad-spectrum antimicrobial utilization
Reporting*	• Avoid inappropriate/suboptimal *in vitro* susceptibility results for site specific cultures (early-generation cephalosporins for inducible AmpC beta-lactamase-producing Gram-negative bacilli in blood cultures)	• Decrease inappropriate prescribing, therapeutic failures, and metastatic infections • Increase appropriate antimicrobial selection

MacVane SH et al. *Open Forum Infect Dis* 2016:3:ofw201.

Striking a Balance



Griffith M et al. *Expert Rev Anti Infect Ther* 2012;10:63-73.

Agricultural, farms, etc.

STEWARDSHIP EFFORTS ASIDE FROM DIRECT PATIENT ANTIBIOTIC INTERVENTIONS

Covering All Bases in Antimicrobial Stewardship

Antibiotic Armamentarium

- Infrastructure to promote drug development
  - Qualified infectious disease product (QIDP)
- Antimicrobial utilization
  - Guideline-based, evidence-based use of antimicrobials
  - Protocols, order-sets
  - ? Restrictions
  - Not limited to acute care settings!
- Policy change advocacy
  - Limit use in agriculture & farming
  - Third-party payers

Combating Resistance

- Responsible antimicrobial utilization
- Optimize infection control practices

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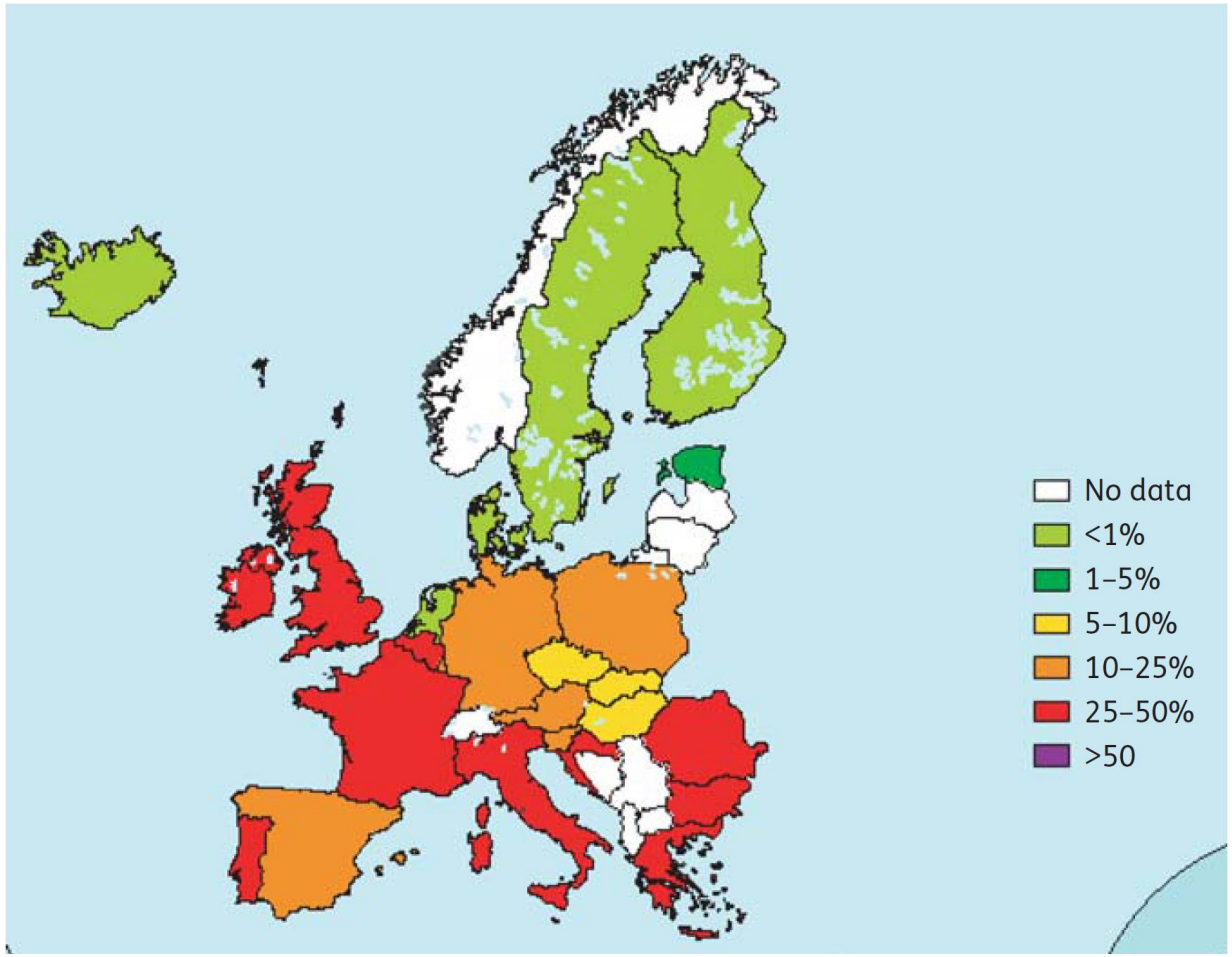
- **Optimize infection control practices**

Proportion of Methicillin-resistance in *S.aureus*



Johnson AP. *J Antimicrob Chemother* 2011;66 Suppl 4: iv43-48.

Covering All Bases in Antimicrobial Stewardship

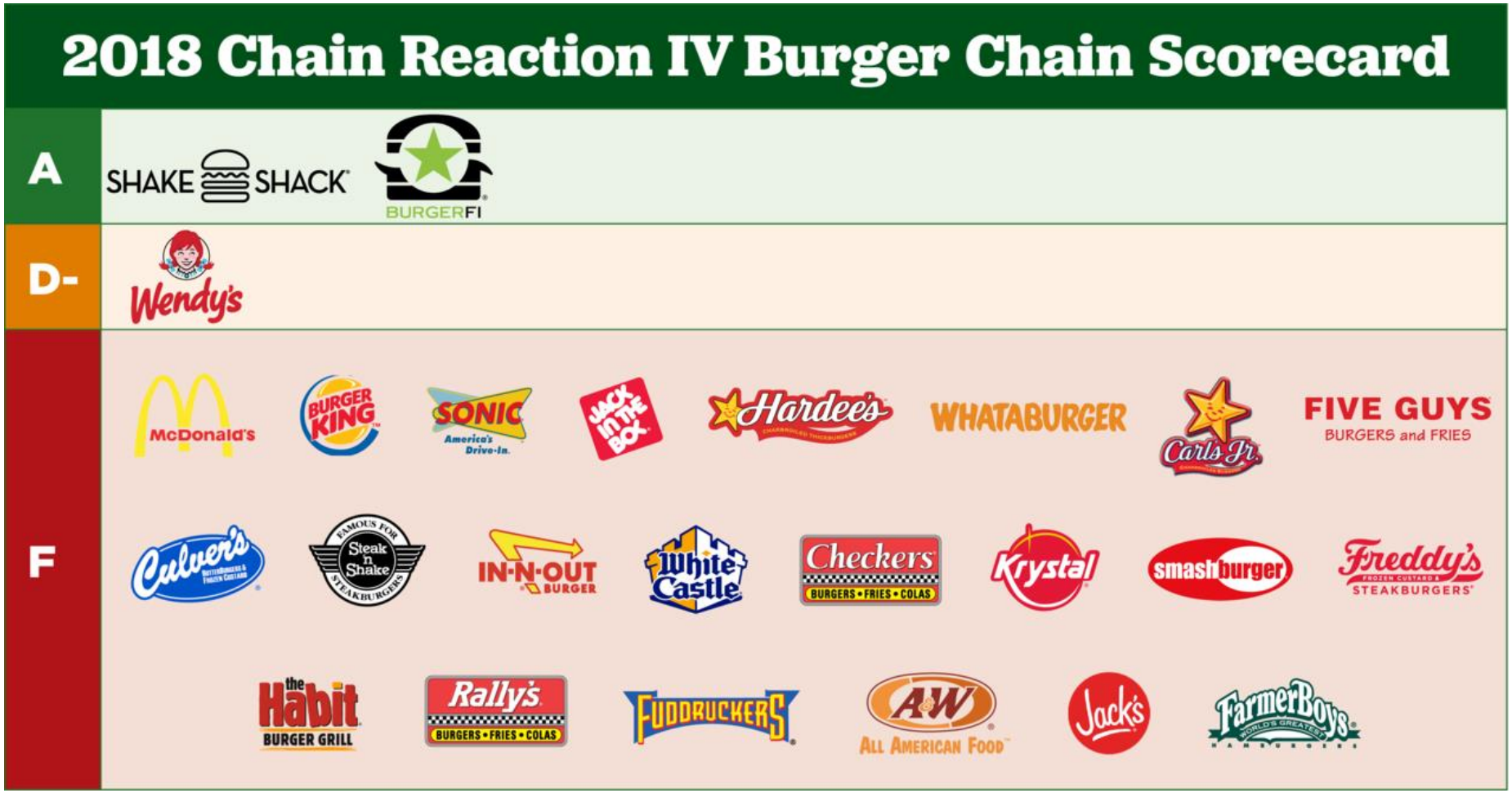
Antibiotic Armamentarium

- Infrastructure to promote drug development
  - Qualified infectious disease product (QIDP)
- Antimicrobial utilization
  - Guideline-based, evidence-based use of antimicrobials
  - Protocols, order-sets
  - ? Restrictions
  - Not limited to acute care settings!
- **Policy change advocacy**
  - **Limit use in agriculture & farming**
  - Third-party payers

Combating Resistance

- Responsible antimicrobial utilization
- Optimize infection control practices

Irresponsible Practices Among Fast Food Chains



Available at: https://www.nrdc.org/sites/default/files/restaurants-antibiotics-use-es-2018.pdf. Accessed October 30, 2018.

Company	Beef Policy	Implementation	Transparency	Total Points	Total Possible Points	%-age Total	Grade*
Shake Shack	40	32	23	95	100	95	A
BurgerFi	40	32	19	91	100	91	A
Wendy's	4.2	4.8	28	37	100	37	D-
McDonald's	0	0	6	6	100	6	F
Sonic America's Drive-In	0	0	6	6	100	6	F
Jack in the Box	0	0	6	6	100	6	F
White Castle	0	0	6	6	100	6	F

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Company	Beef Policy	Implementation	Transparency	Total Points	Total Possible Points	%-age Total	Grade*
Burger King, Hardee's, Whataburger, Carl's Jr., Five Guys Burgers and Fries, Culver's, Steak 'n Shake, In-N-Out Burger, Checkers Burgers • Fries • Colas, Krystal, smashburger, Freddy's Frozen Custard & Steakburgers, The Habit Burger Grill, Rally's Burgers • Fries • Colas, Fuddruckers, A&W All American Food, Jack's, Farmer Boys	0	0	0	0	100	0	F

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Combating Resistance

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In Closing..

The time may come when penicillin can be bought by anyone in the shops. Then, there is the danger that the ignorant man may easily under-dose himself, and by exposing his microbes to non-lethal quantities of the drug, make them resistant.

Here is a hypothetical illustration…

In Closing..

Mr. X has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci, but enough to educate them to resist penicillin.

He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are not resistant to penicillin, the treatment fails. Mrs. X dies. Who is primarily responsible for Mrs. X's death?

In Closing..

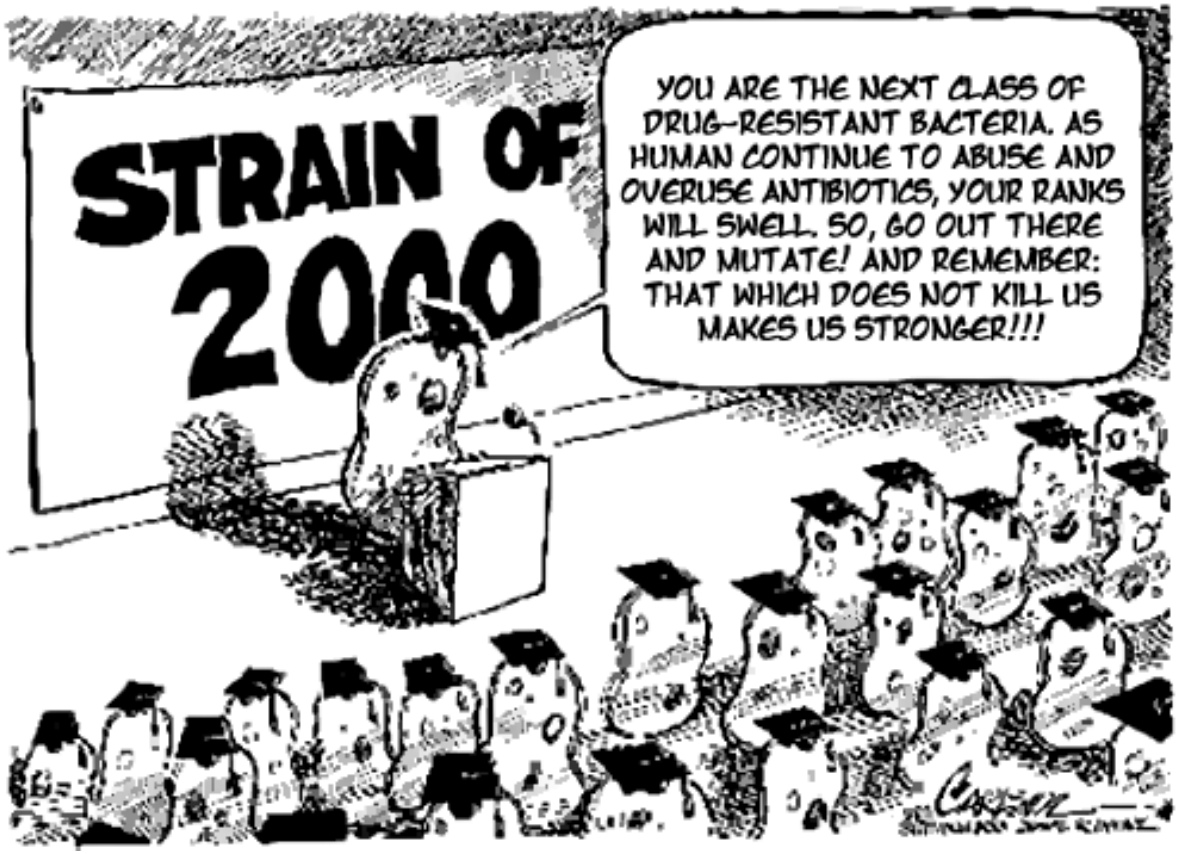
Why..Mr. X, whose negligent use of penicillin changed the nature of the microbe.

Alexander Fleming,

-Nobel Peace Prize Lecture, 1945

Antibiotic Stewardship, Simplified

- Get excited about stewardship
- Identify areas of opportunity
- Stewardship is not about "cutting", "discontinuing", "restricting", it should be about optimizing
- Work together as a team



Antibiotic Stewardship:
Peeling Back the Layers

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