THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

What's New in Antimicrobial Stewardship

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Disclosures

None

What is Antimicrobial Stewardship?

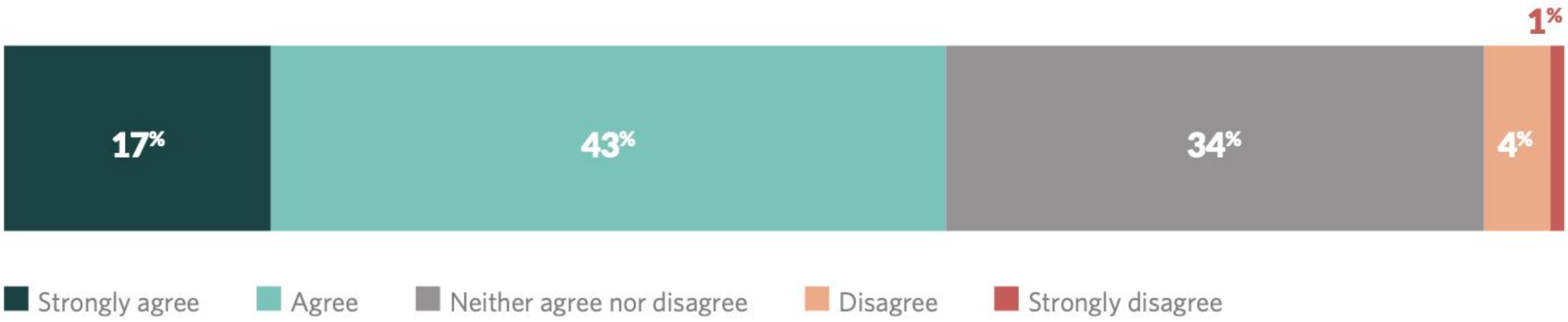
- What are antimicrobial stewardship programs (ASPs)?
  - Antibiotic Police! (unfortunate) - restriction and prevention of use of certain protected antimicrobials
    - Focused on antimicrobial cost and volume
  - More Tools!: Prior Authorization, Prospective Audit and Feedback, Post-prescription review, Antibiotic Time-Outs, Hand-shake Stewardship, etc.

- NEW! - ASPs are designed to ensure that **antibiotics** are given only when necessary and when given are appropriate.
  - Goals: improve patient outcomes, reduce health care costs, minimize the threat of antibiotic resistance
    - Right Outcomes!

Figure 4

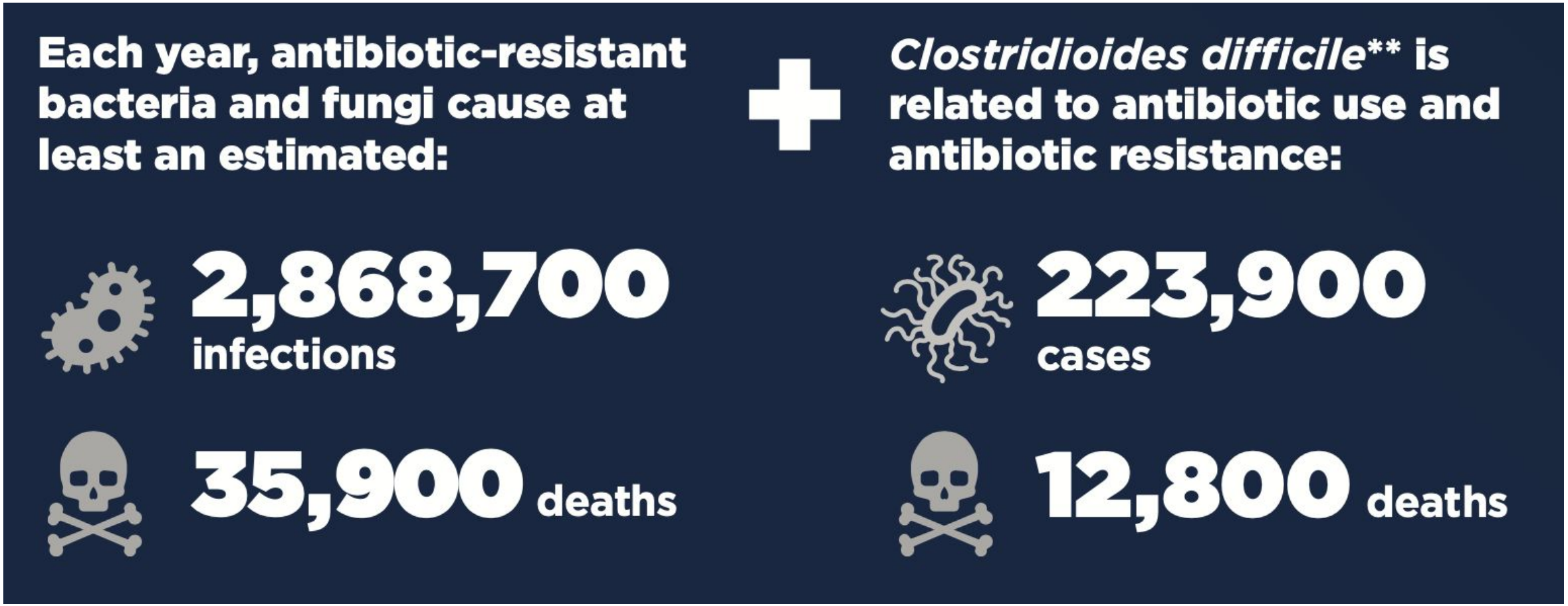
Physicians Feel That They Prescribe Antibiotics More Appropriately Than Their Peers

"I prescribe antibiotics more appropriately than the average rate of my peers."



Pew. 2020

Antibiotics Resistance Threats in the US - 2019



UAB MEDICINE

Antimicrobial Use = Antimicrobial Resistance

Patient/Society Outcomes

Cost and Resistance

Llewelyn, Fitzpatrick et al. 2017

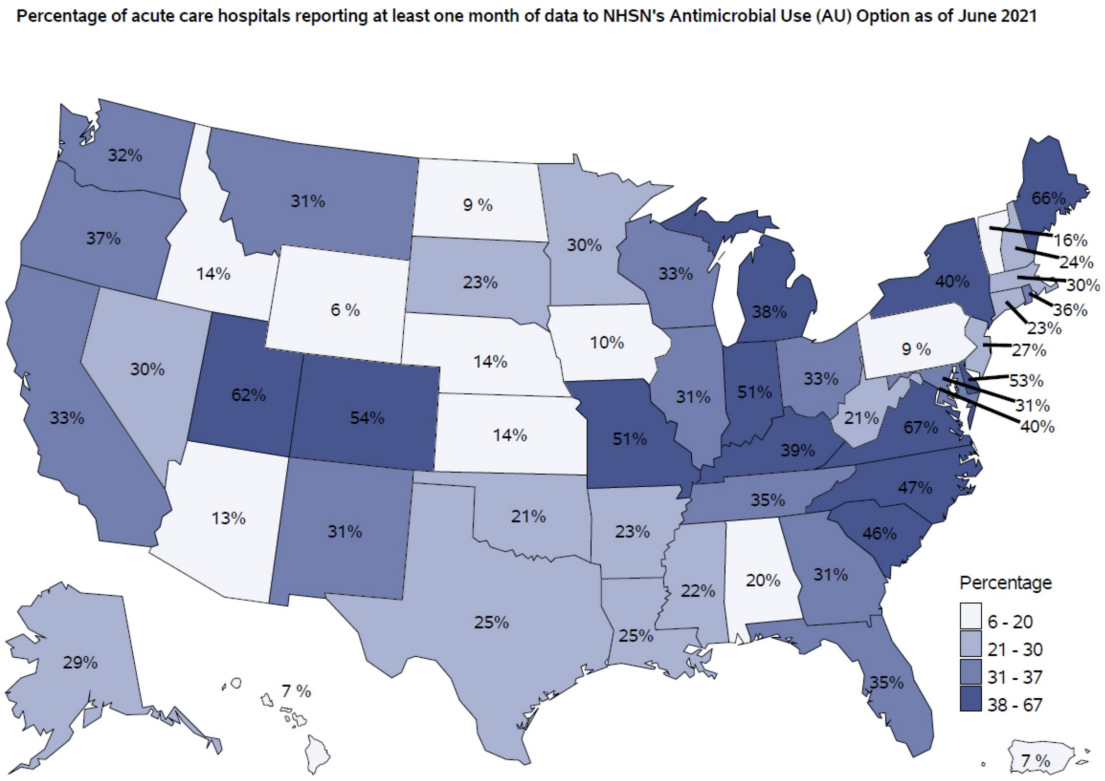
NHSN Antimicrobial Use and Resistance (AUR) Module

- Two modules, Antibiotic Use (AU) and Antimicrobial Resistant (AR)
  - Goal to facilitate risk-adjusted inter- and intra-facility antimicrobial use benchmarking; NHSN and CDC
  - Only inpatient for certain units (MICU/SICU, Med Floor, Neonatal)
- Provides Unit specific antimicrobial use
  - Antimicrobial days per 1000 days present

- **Standardized Antimicrobial Administration Ratio (SAAR)**
  - Dividing Observed vs. Predicted antimicrobial use
  - Generated for each antimicrobial agent category and each location type

NHSN Antimicrobial Use (AU) Option Report - 2020

- Over 1400 acute care hospitals reporting > 9 months of data in 2020
- 3 most commonly used antimicrobial agents:
  - vancomycin, piperacillin-tazobactam and ceftriaxone or cefepime for all SAAR categories
  - piperacillin-tazobactam was the most commonly used agent in ICUs

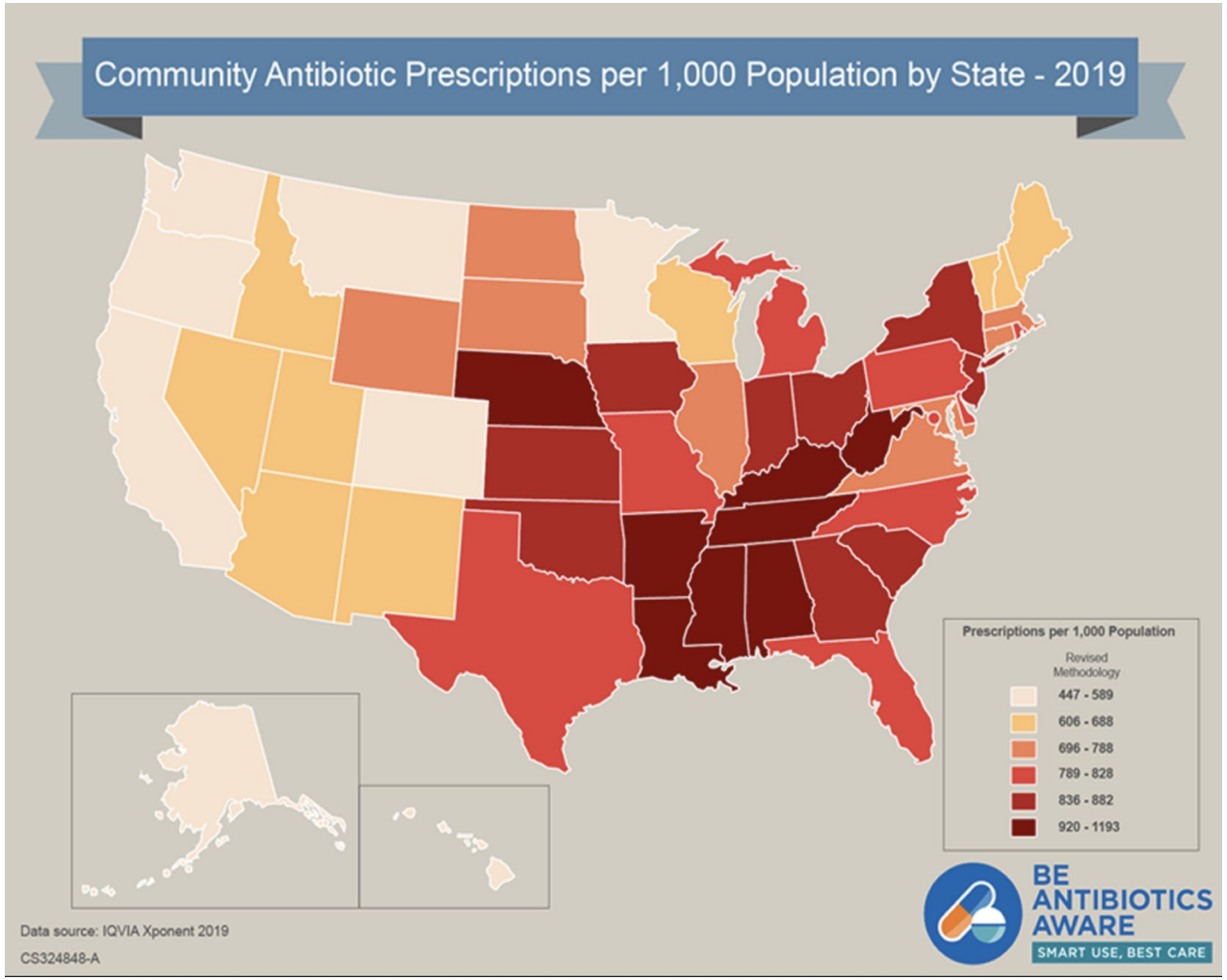


UAB MEDICINE

What about Outpatients?

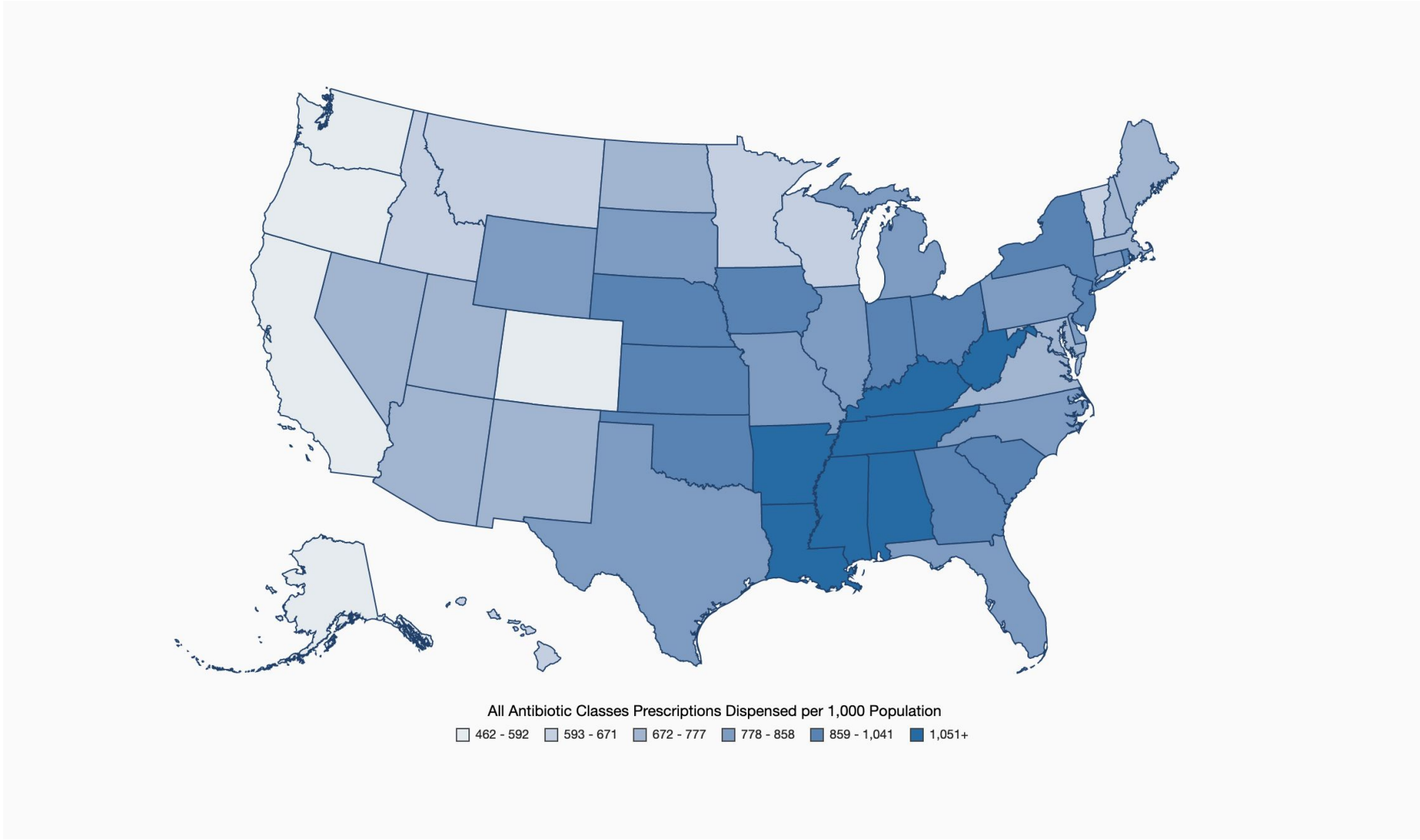
60% of antibiotic expenditures are in outpatient settings

- US – 201.9 million outpatient oral antibiotic prescriptions; equaling 613 antibiotic prescriptions per 1000 persons
- South – 698 antibiotic prescriptions per 1000 persons
- Alabama – 922 antibiotic prescriptions per 1000 persons



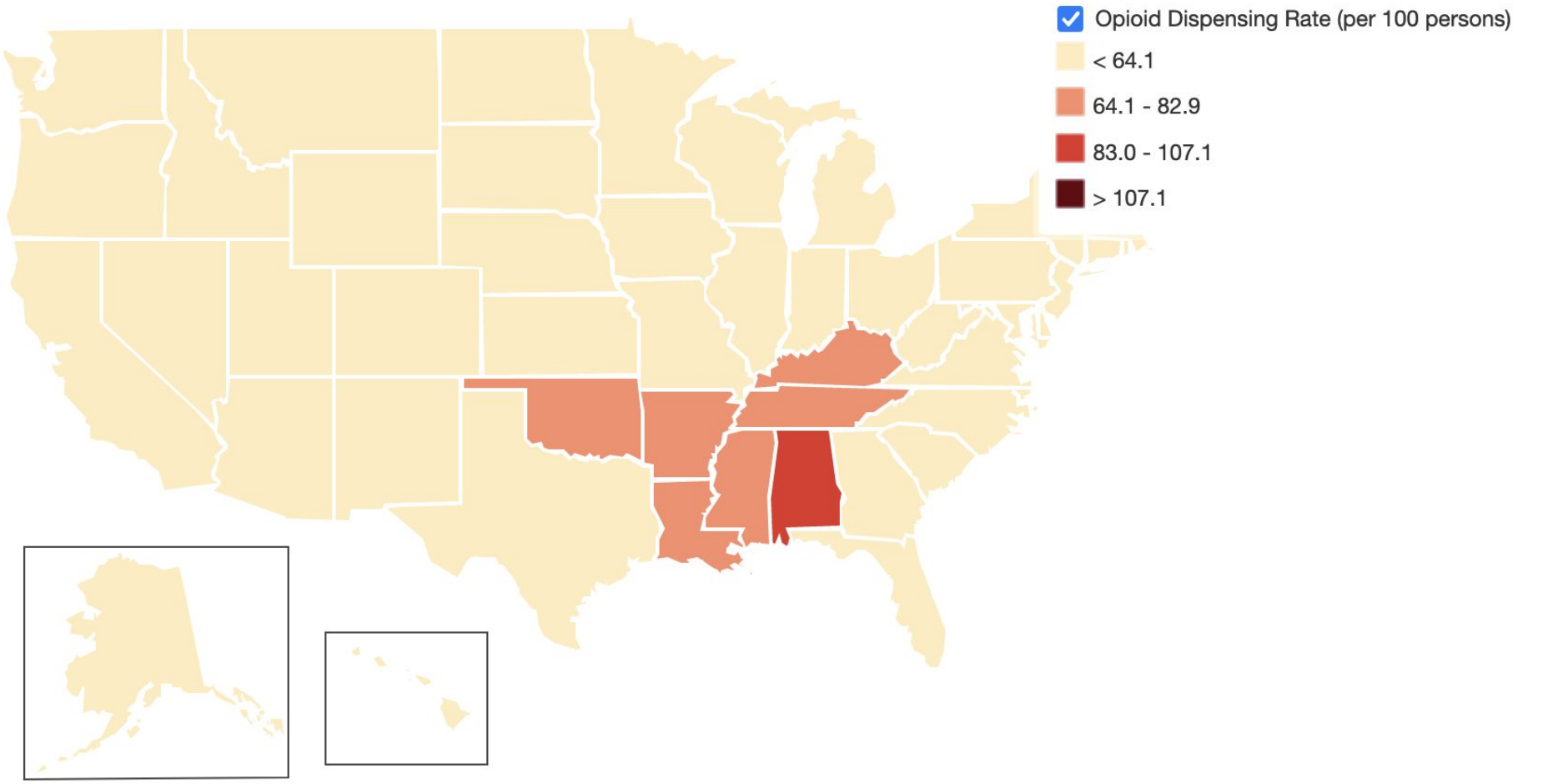
CDC. 2021

Disparities?



https://arpsp.cdc.gov/profile/antibiotic-use/all-classes

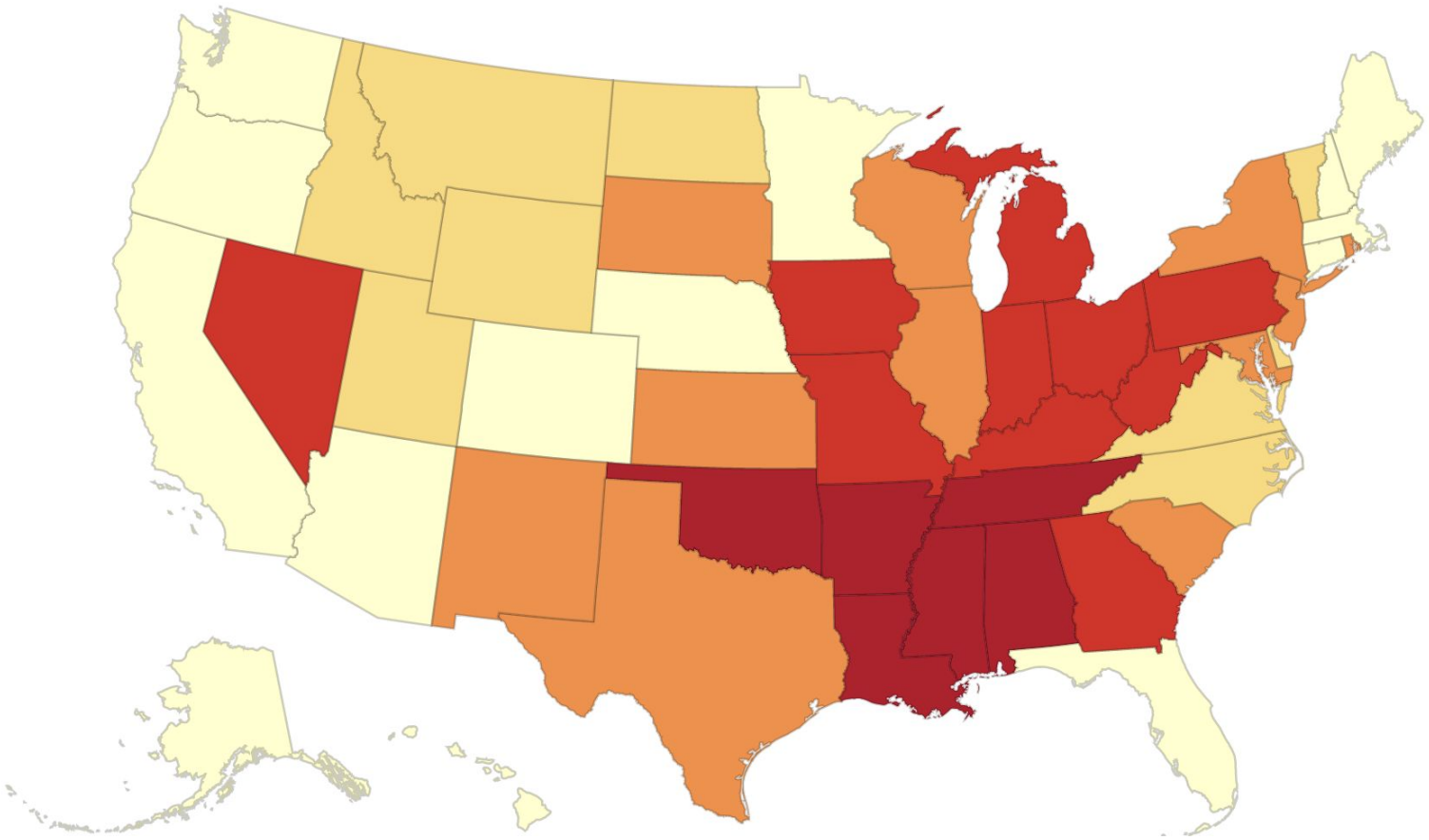
Disparities?



https://www.cdc.gov/drugoverdose/maps/rxstate2019.html

Disparities?

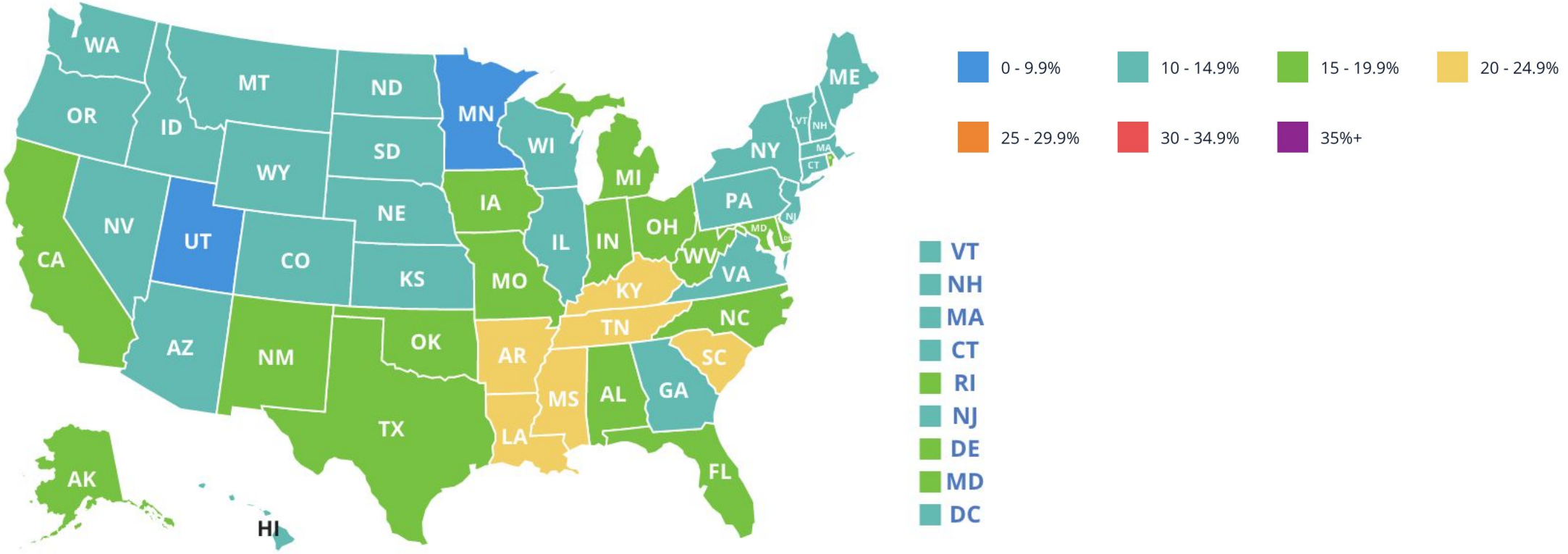
Heart Disease Mortality by State



https://www.cdc.gov/nchs/pressroom/sosmap/heart_disease_mortality/heart_disease.htm

Disparities?

Obesity Rate, Youth Ages 10-17, 2018-19



https://stateofchildhoodobesity.org/children1017/

Report THE PEW CHARITABLE TRUSTS March 2021

Health Experts Establish Targets to Improve Hospital Antibiotic Prescribing

National data shows inappropriate prescribing, opportunities for improvements

Pew. 2021

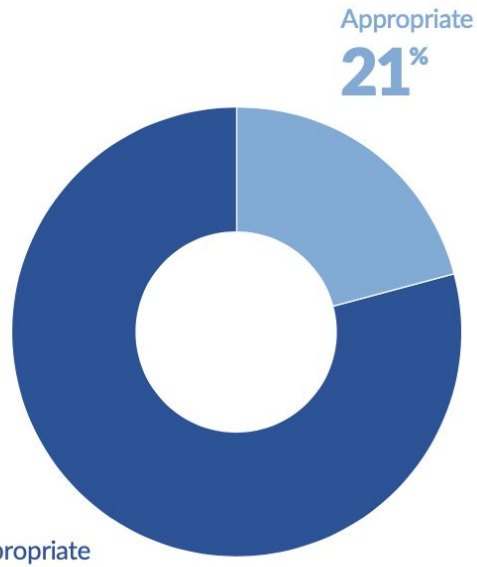
Pew Study - Appropriateness of Inpatient Antibiotics

- Magill, et.al. “Assessment of the Appropriateness of Antimicrobial Use in US Hospitals”
  - 2015 survey; CDC led (10 hospitals total); 12,299 patients; treatment for UTI or CAP or received treatment with fluroquinolones or vancomycin
    - 1,566 patients received antimicrobial quality assessment (AQUA)
  - 219 patient with CAP, 452 with UTI, 550 received FQs, 403 received vancomycin

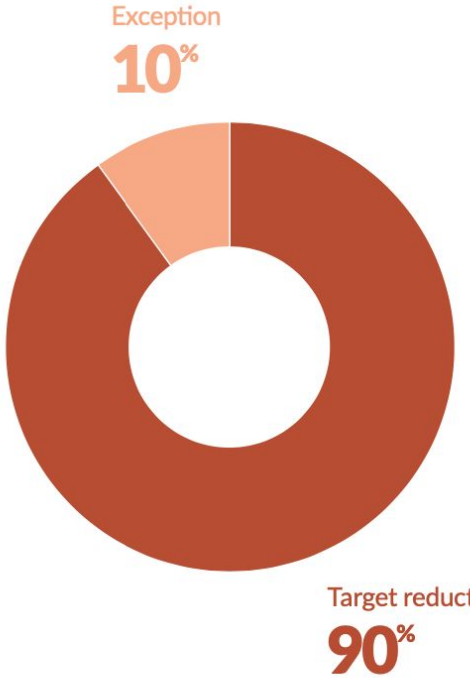
- **Overall treatment was “unsupported” in 55.9% of patients**
  - 79% for CAP, 76% for UTI, 46% with FQs, 27% with vancomycin
  - “Unsupported” treatment due to excessive duration, lack of documented signs or symptoms of infection, continued treatment without microbiologic evidence

Target: Reduce inappropriate antibiotic prescribing for this condition by 90%

Antibiotic prescribing for CAP



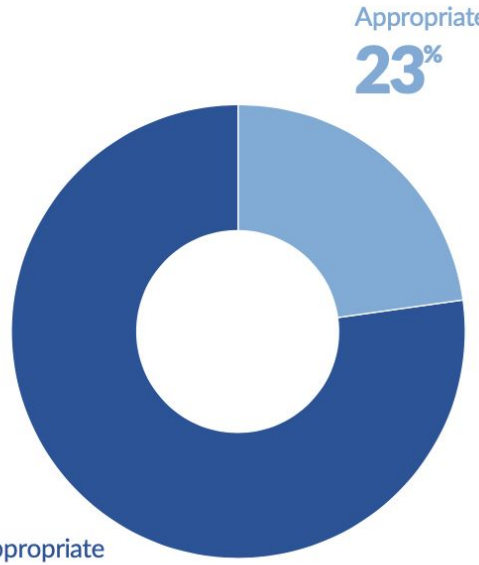
Target to reduce inappropriate prescribing for CAP



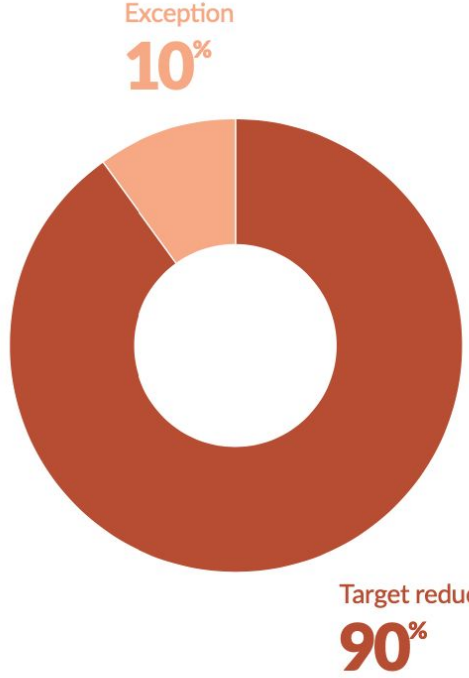
Source: CDC study

Target: Reduce inappropriate antibiotic prescribing for this condition by 90%

Antibiotic prescribing for UTI



Target to reduce inappropriate prescribing for UTI



Source: CDC study

Pew. 2021

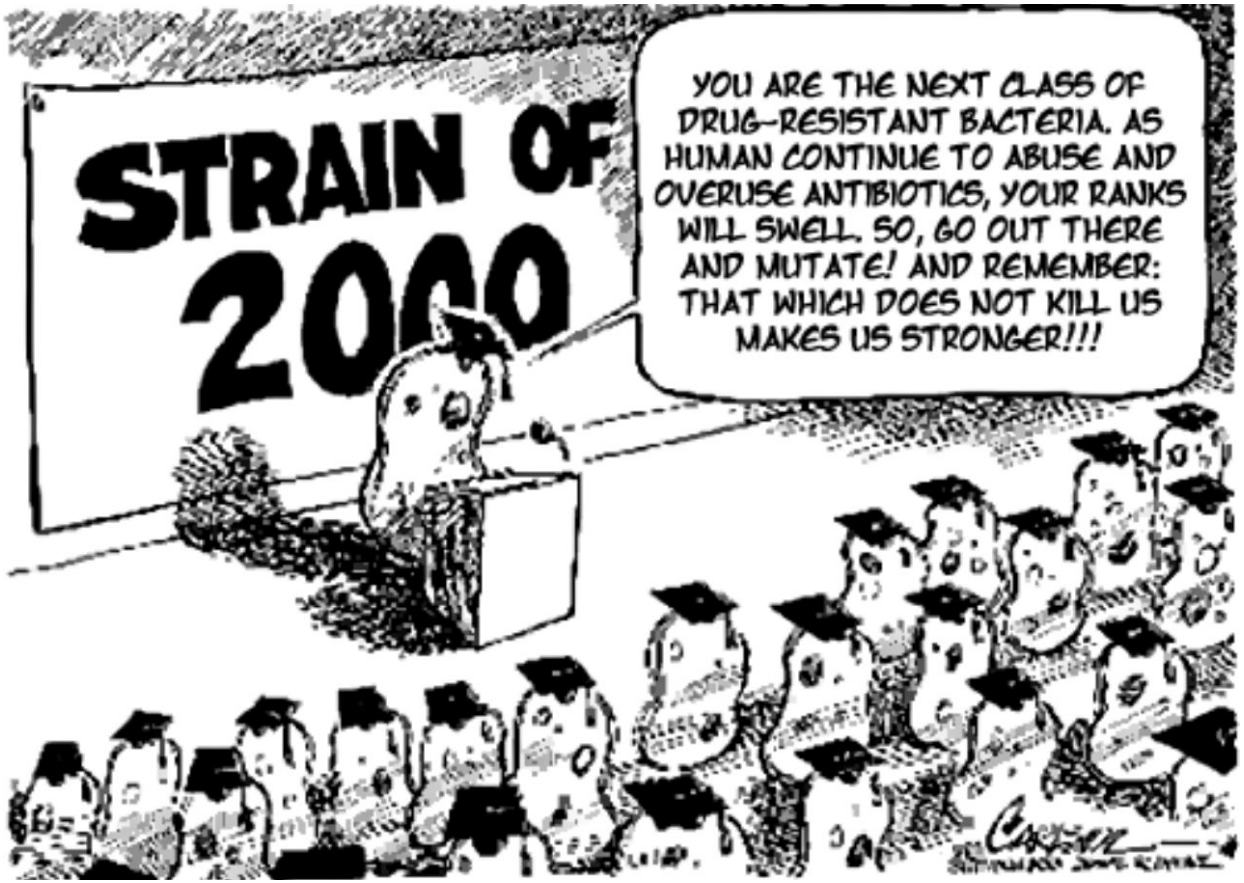
TJC New and Revised Requirements for Antibiotic Stewardship – Released 6/2022

- Effective January 1, 2023 – 12 new and revised elements of performance (EPs)
  - EP 14 – ASPs demonstrate **coordination among all components of the hospital** for antibiotic use and resistance
  - EP 15 – ASPs **document evidence-based use of antibiotics in all departments** and services of the hospital
  - EP 18 – ASPs implement at least **2 evidence-based guidelines to improve antibiotic use** for the most common indications
    - CAP, UIT, SSTI, CDI, Asymptomatic bacteriuria, IV to PO, and surgical prophylaxis
  - EP 19 – ASPs **evaluate adherence** to evidence-based guidelines

STEWARDSHIP INTERVENTIONS **FOR ALL**

5 D's of Antibiotic Prescribing

- Right **D**iagnosis
- Right **D**rug
- Right **D**ose
- Right **D**uration
- **D**e-escalation



4 Moments in Antibiotic Prescribing

1. Does this patient have an infection that requires antibiotics?
2. Have I ordered appropriate cultures before starting antibiotics? What empirical therapy should I initiate
3. A day or more has passed. Can I stop antibiotics? Can I narrow? Can I change IV to PO?
4. What duration of antibiotic therapy is needed for this patient's diagnosis?

Tamma. JAMA. 2019

RIGHT **DIAGNOSIS**

Asymptomatic bacteriuria

Clinical Infectious Diseases

IDSA FEATURES

Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America[a]

Lindsay E. Nicolle,[1] Kalpana Gupta,[2] Suzanne F. Bradley,[3] Richard Colgan,[4] Gregory P. DeMuri,[5] Dimitri Drekonja,[6] Linda O. Eckert,[7] Suzanne E. Geerlings,[8] Béla Köves,[9] Thomas M. Hooton,[10] Manisha Juthani-Mehta,[11] Shandra L. Knight,[12] Sanjay Saint,[13] Anthony J. Schaeffer,[14] Barbara Trautner,[15] Bjorn Wullt,[16] and Reed Siemieniuk[17]

Pyuria + bacteriuria ≠ CAUTI

Review urinalysis, symptoms, and appropriate indications for testing prior to ordering urine culture in catheterized patient

Table 1. Prevalence of Asymptomatic Bacteriuria Reported for Different Populations

Population	Prevalence, %	Reference
Children		
Boys	<1	[7]
Girls	1–2	[8–10]
Healthy women		
Premenopausal	1.0–5.0	[11]
Pregnant	1.9–9.5	[11]
Postmenopausal (age 50–70 y)	2.8–8.6	[11]
Persons with diabetes		
Women	10.8–16	[12]
Men	0.7–11	[12]
Elderly persons in the community (age ≥70 y)		
Women	10.8–16	[13]
Men	3.6–19	[13]
Elderly persons in a long-term care facility		
Women	25–50	[13]
Men	15–50	[13]
Persons with spinal cord injury		
Intermittent catheter use	23–69	[14]
Sphincterotomy/condom catheter	57	[15]
Persons with kidney transplant		
First month posttransplant	23–24	[16, 17]
1 mo–1 y post-transplant	10–17	[16]
>1 y post-transplant	2–9	[16]
Persons with indwelling catheter use		
Short-term	3%–5%/day catheter	[18]
Long-term	100	[19]

UTI AND DELERIUM?

"In older patients with functional and/or cognitive impairment with bacteriuria and delirium (acute mental status change, confusion) and without local genitourinary symptoms or other systemic signs of infection (eg, fever or hemodynamic instability), we recommend assessment for other causes and careful observation rather than antimicrobial treatment."

- This recommendation places a high value on avoiding adverse outcomes of antimicrobial therapy … in the absence of evidence that such treatment is beneficial for this vulnerable population.

Nicolle et al, CID, 2019

NONSPECIFIC SYMPTOMS

Table 1 Prevalence of symptoms and positive urine cultures

		Proportion of positive urine cultures among		
	Prevalence of symptom[1]	Residents with symptom	Residents without symptom	P-value[2]
Fatigue	11% (48/421)	31% (15/48)	32% (120/373)	0.90
Restlessness	5.5% (23/421)	26% (6/23)	32% (129/398)	0.53
Confusion	5.2% (22/421)	14% (3/22)	33% (132/399)	0.057
Aggressiveness	5.0% (21/421)	19% (4/21)	33% (131/400)	0.19
Loss of appetite	5.2% (22/421)	18% (4/22)	33% (131/399)	0.15
Frequent falls	5.2% (22/421)	23% (5/22)	33% (130/399)	0.34
Not being herself/himself	4.3% (18/421)	39% (7/18)	32% (128/403)	0.53
Having any of the above nonspecific symptoms	20% (85/421)	31% (26/85)	32% (109/336)	0.74
Dysuria	2.1% (9/421)	11% (1/9)	33% (134/412)	0.28
Urinary urgency	3.6% (15/421)	33% (5/15)	32% (130/406)	1.0
Urinary frequency	2.4% (10/421)	0% (0/10)	33% (135/411)	**0.035**

[1]Symptoms commencing at any time during the preceding month and still present when sampling urine.
[2]Pearson's chi-square and when appropriate Fisher's exact test comparing proportions of positive urine cultures among those with or without symptoms.

Sundvall, 2014

TREATING FOR IMPROVEMENT

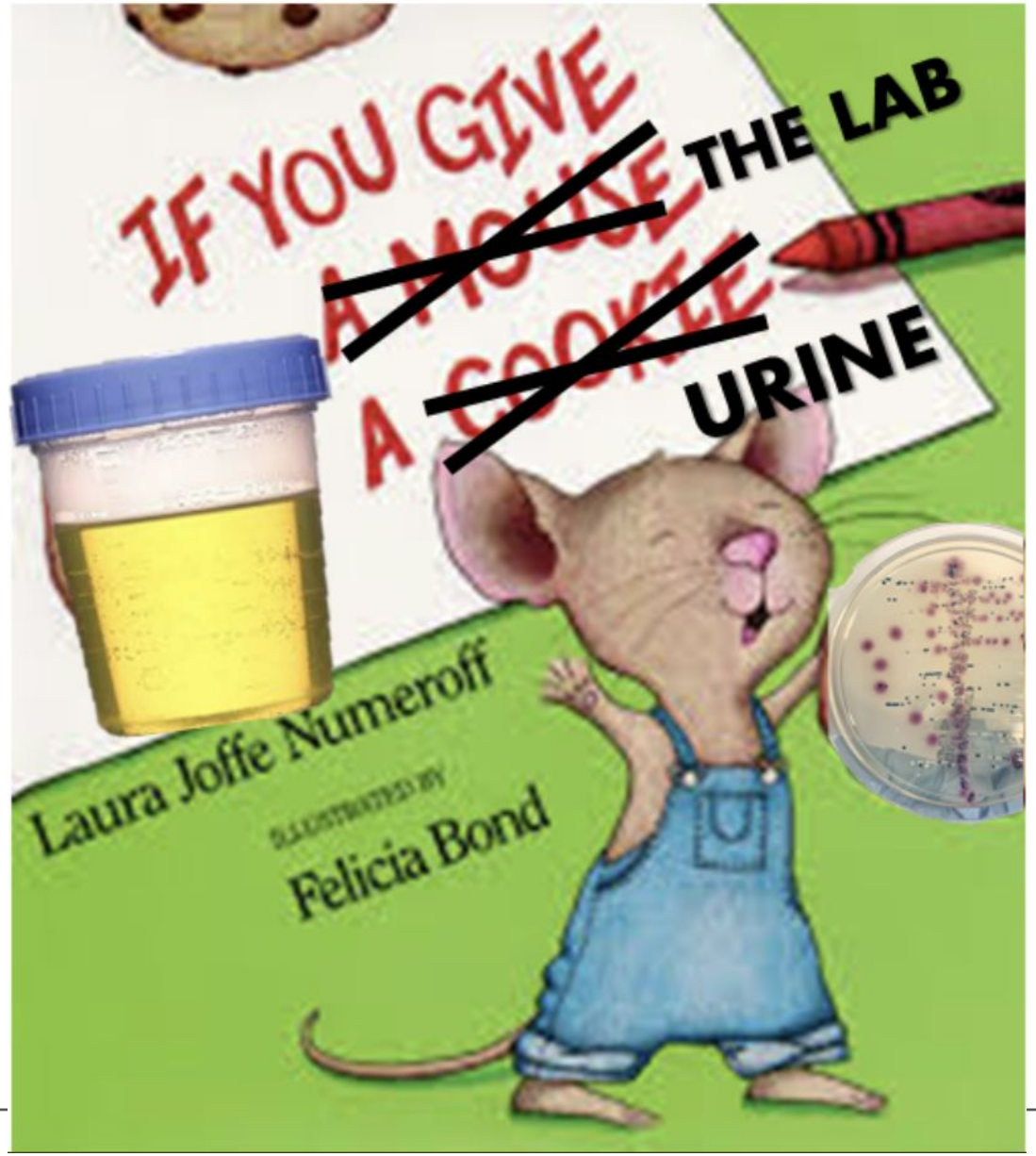
Table 3
Associations between treatment for asymptomatic UTI (or bacteriuria) and functional recovery:.

	Entire sample (n = 343)	Poor recovery (n = 237)	Functional Recovery (n = 106)	P-value
Treated for Asymptomatic UTI	92	76	16	0.005[a]
	Bacteriuric sub-sample:			
	Total (n = 126)	Poor functional recovery (n = 95)	Functional recovery (n = 31)	
Treated with antibiotics for asymptomatic bacteriuria (ASB)	68	58	10	< 0.001[b]
Not treated for ASB (no symptoms/signs)	22	17	5	
Treated for symptomatic UTI	21	11	10	
With symptoms of UTI, infection or sepsis (treated)	15	9	6	

[a] P-value comparing functional decline in those treated for asymptomatic UTI to the remainder of the delirious cohort.
[b] P-value comparing functional decline in individuals treated for ASB to other bacteriuric delirious individuals who were either not treated because of lack of symptoms, or were treated for symptoms of UTI or signs of infection or sepsis.

- 92 delirious patients treated for asymptomatic UTI; improvement in delirium was not observed
  - Higher risk for adverse outcomes; 7.5% vs 3.2% developing CDI

Dasgupta, 2017



If you give the lab a urine from an asymptomatic patient…

…chances are they'll culture it.

If they culture it…

…they might grow bacteria.

If they grow bacteria…

…you may think "It's a UTI!"

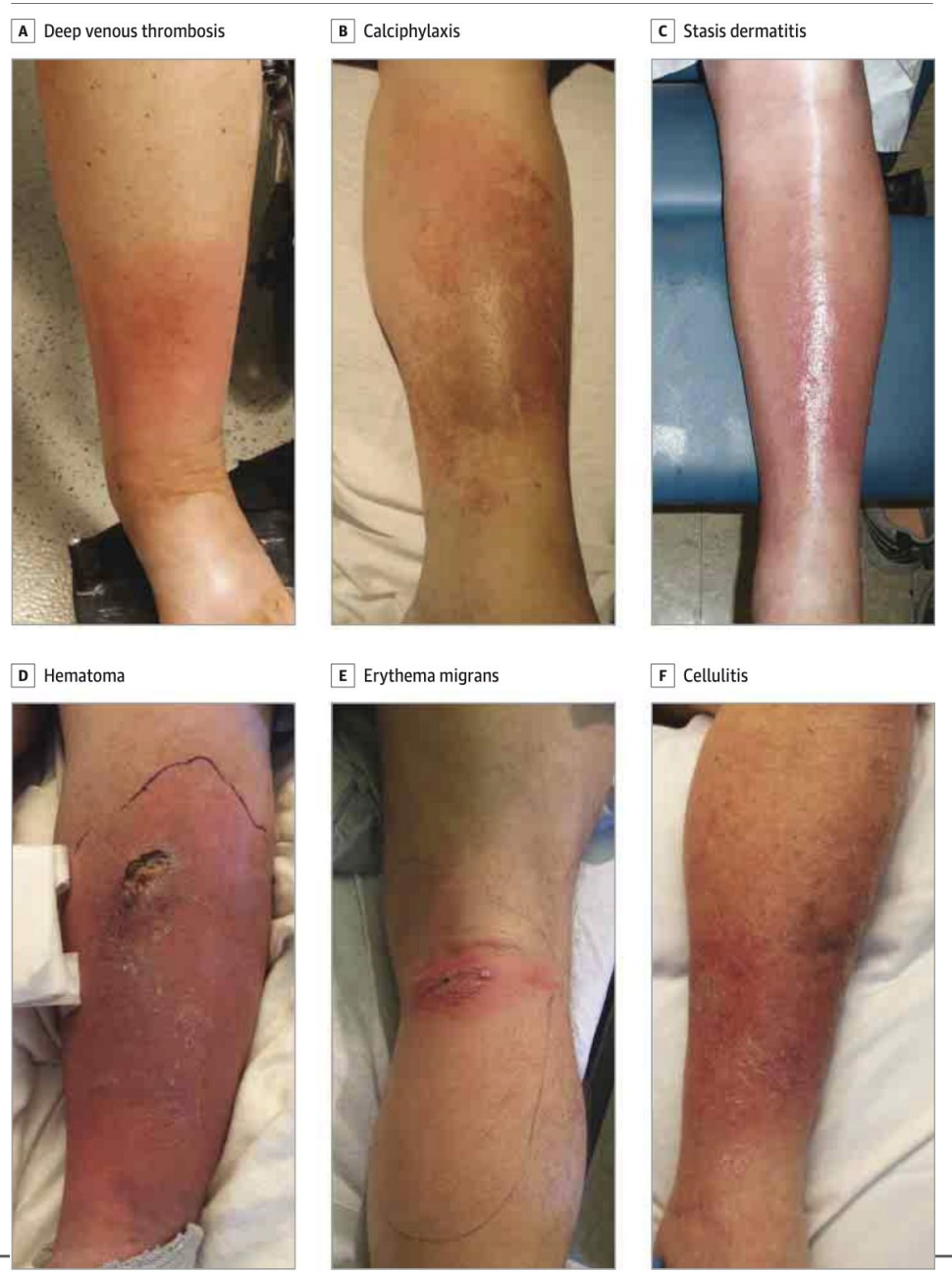
If you think it's a UTI…

…odds are you'll treat with antibiotics.

Credit Twitter @richdavisphd

Cellulitis

Disease Entity	Antibiotic
Non-purulent SSTI (cellulitis)	Adult dosage
Streptococcal skin infections	Penicillin 2–4 million units every 4–6 h IV Clindamycin 600–900 mg every 8 h IV Nafcillin 1–2 g every 4–6 h IV Cefazolin 1 g every 8 h IV Penicillin VK 250–500 mg every 6 h po Cephalexin 500 mg every 6 h po

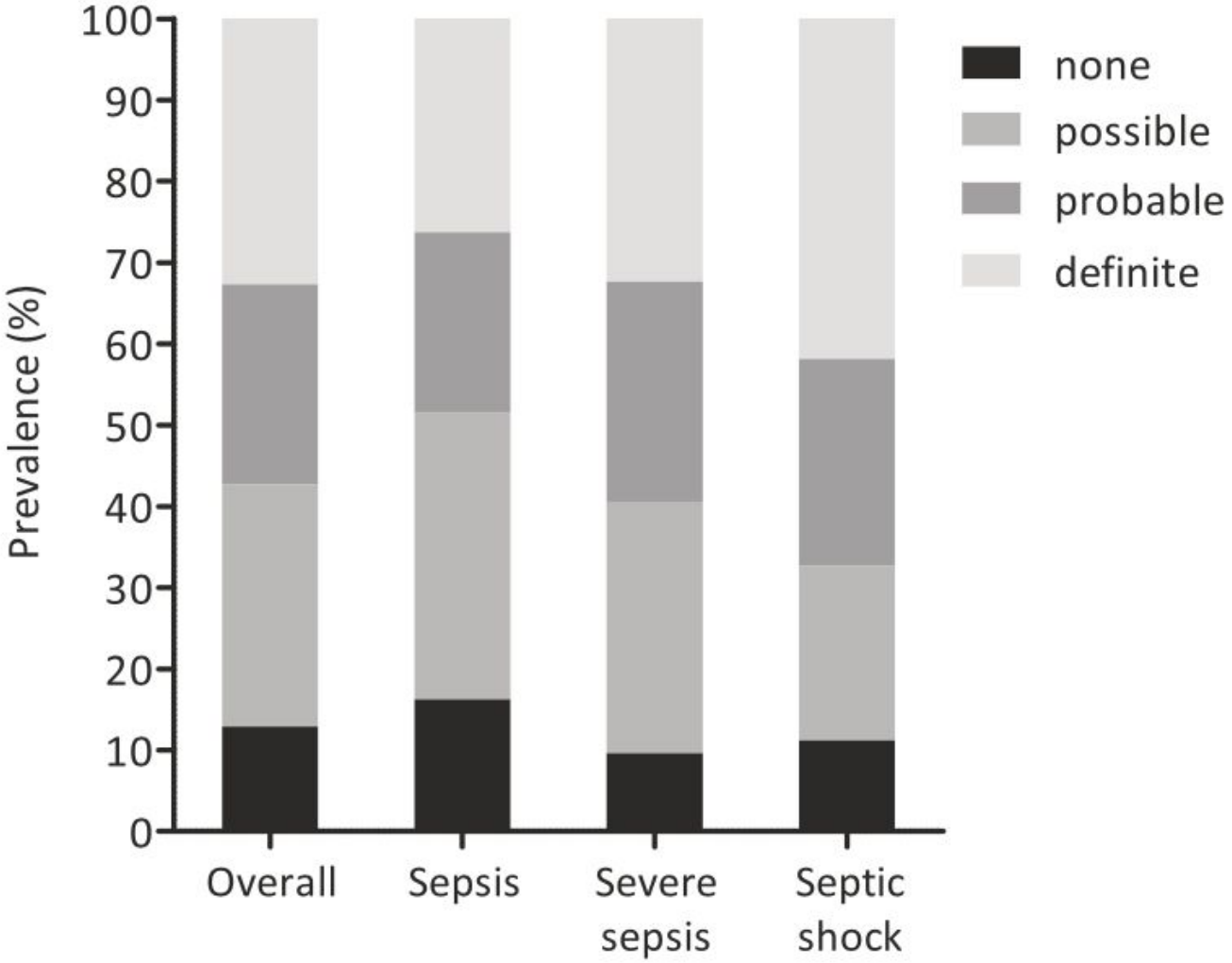


Raff, A.B., Kroshinsky, D., 2016. Cellulitis. JAMA 316, 325.. doi:10.1001/jama.2016.8825

Dennis L. Stevens, et.al., Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, *Clinical Infectious Diseases*, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296

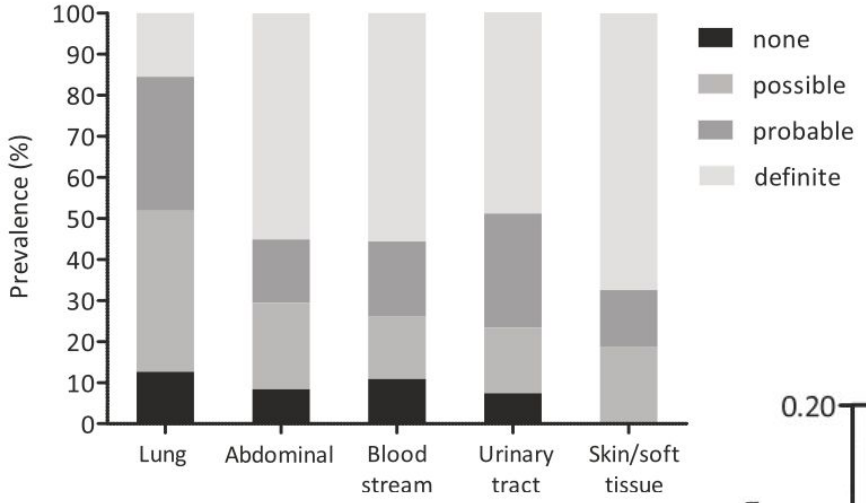
SEPSIS/SIRS ≠ INFECTION

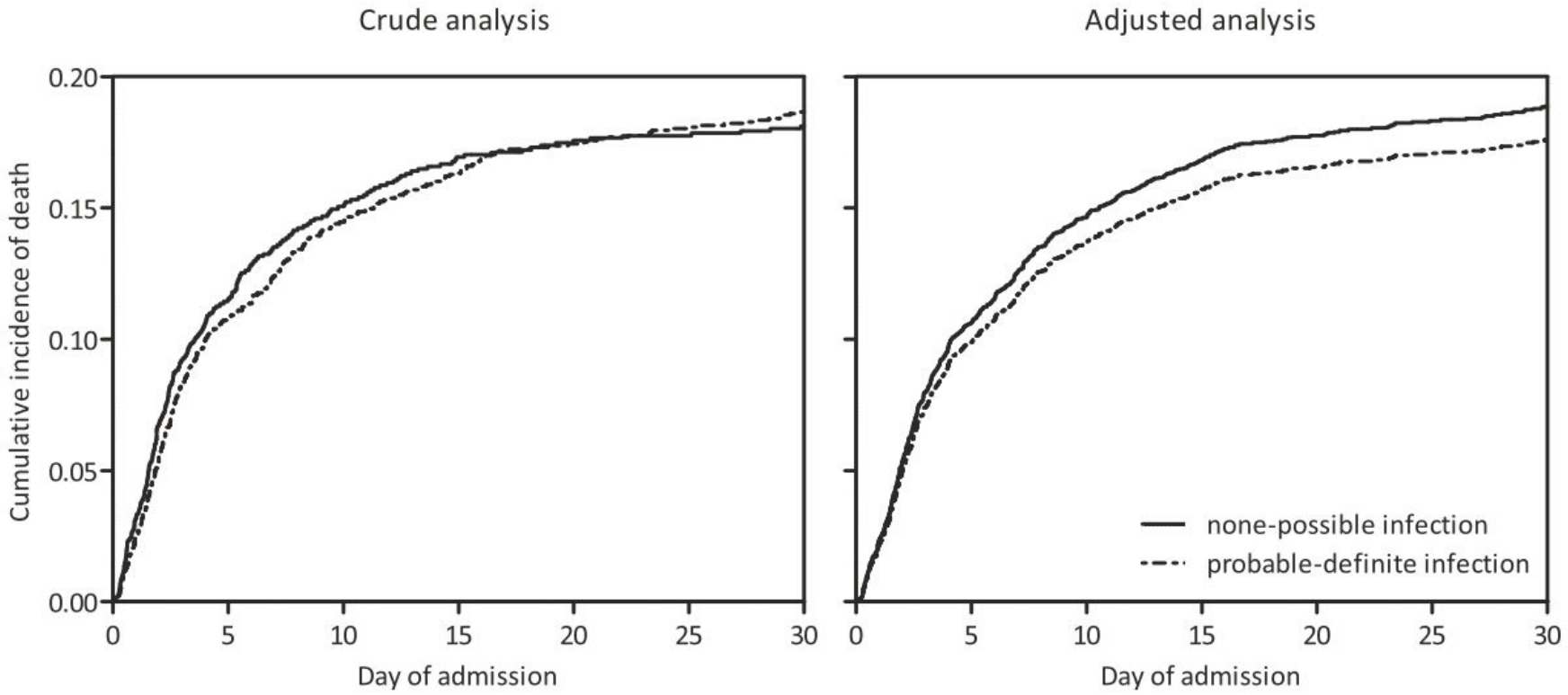
- 2579 patients <u>treated for sepsis</u> (SIRS criteria) and managed according to Surviving Sepsis Guidelines
- Evaluated by post-hoc analysis for infection by CDC/ISF criteria and multidisciplinary review
  - 13% - None
  - 30% - Possible
  - 25% - Probable
  - 33% - Definite



Klein Klowenberg Crit Care 2015

BETTER BY LOCATION? MORTALITY?

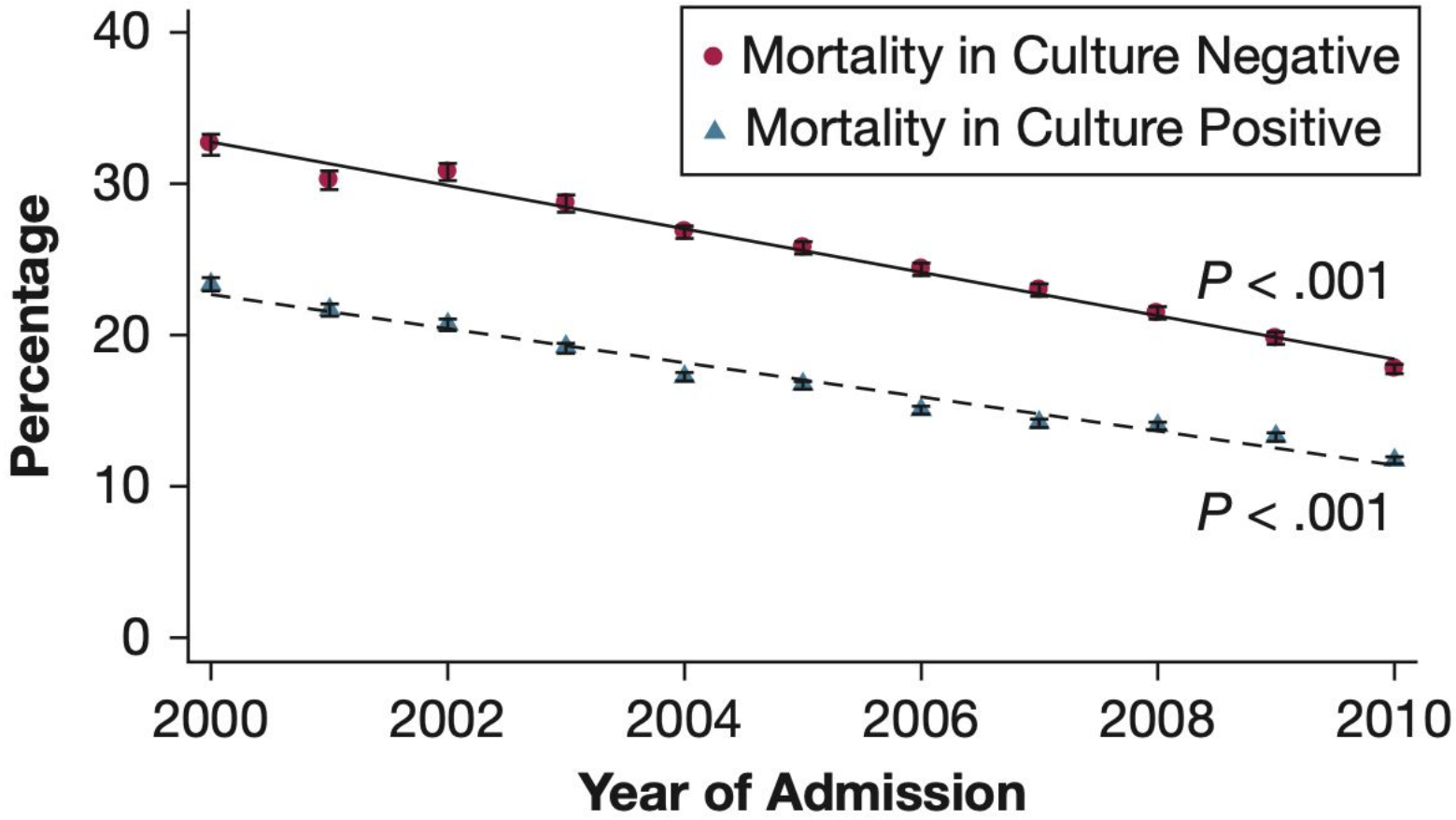




Klein Klowenberg Crit Care 2015

CULTURE NEGATIVE SEVERE SEPSIS

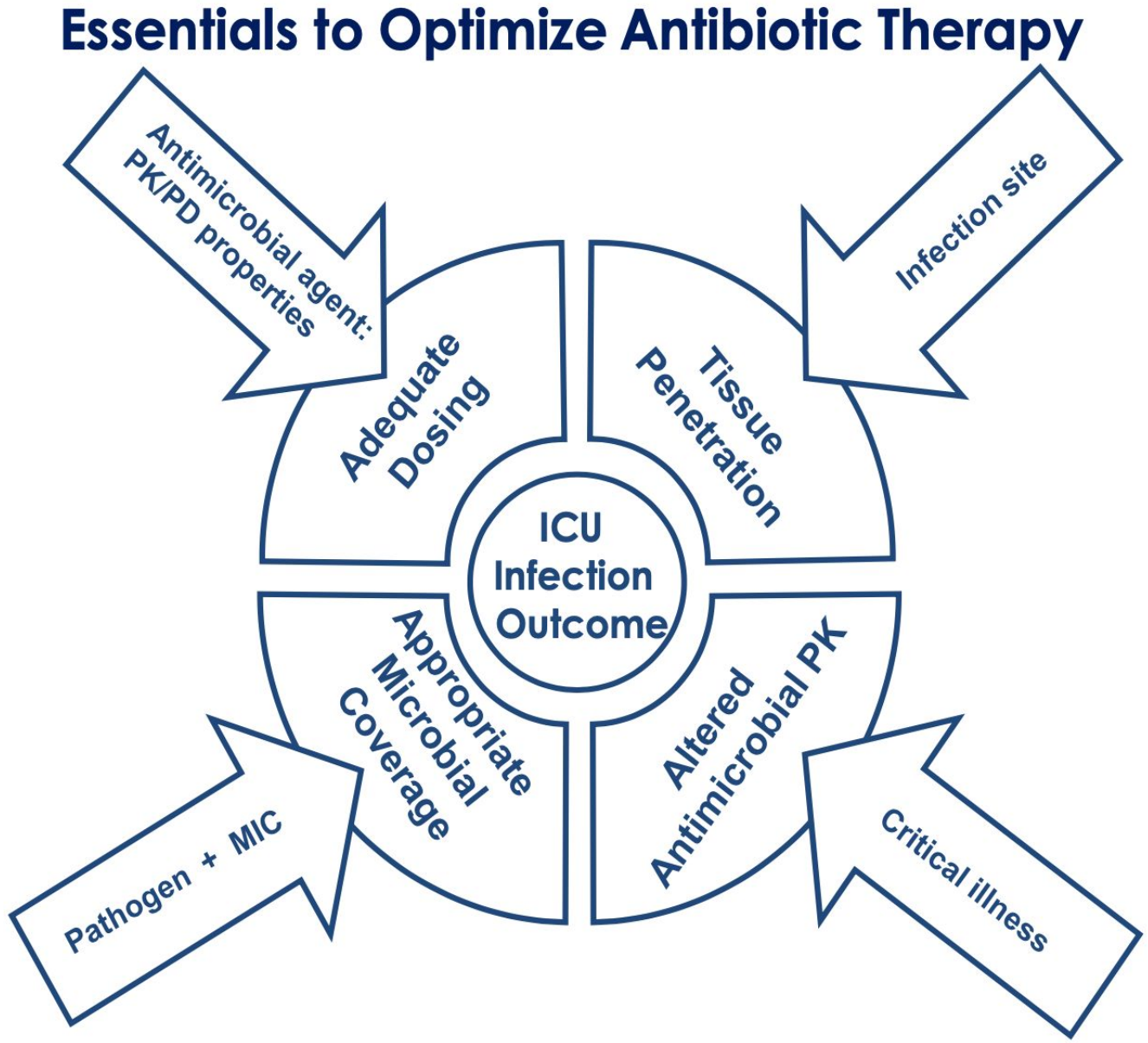
- 6,843,279 admissions of patients with severe sepsis, 3,226,406 (47.1%) had culture-negative results
- CNSS was an independent predictor of mortality (OR, 1.75; 95% CI, 1.72-1.77)



Gupta Chest 2016

RIGHT **DOSE**

COMPLEXITY OF DOSING

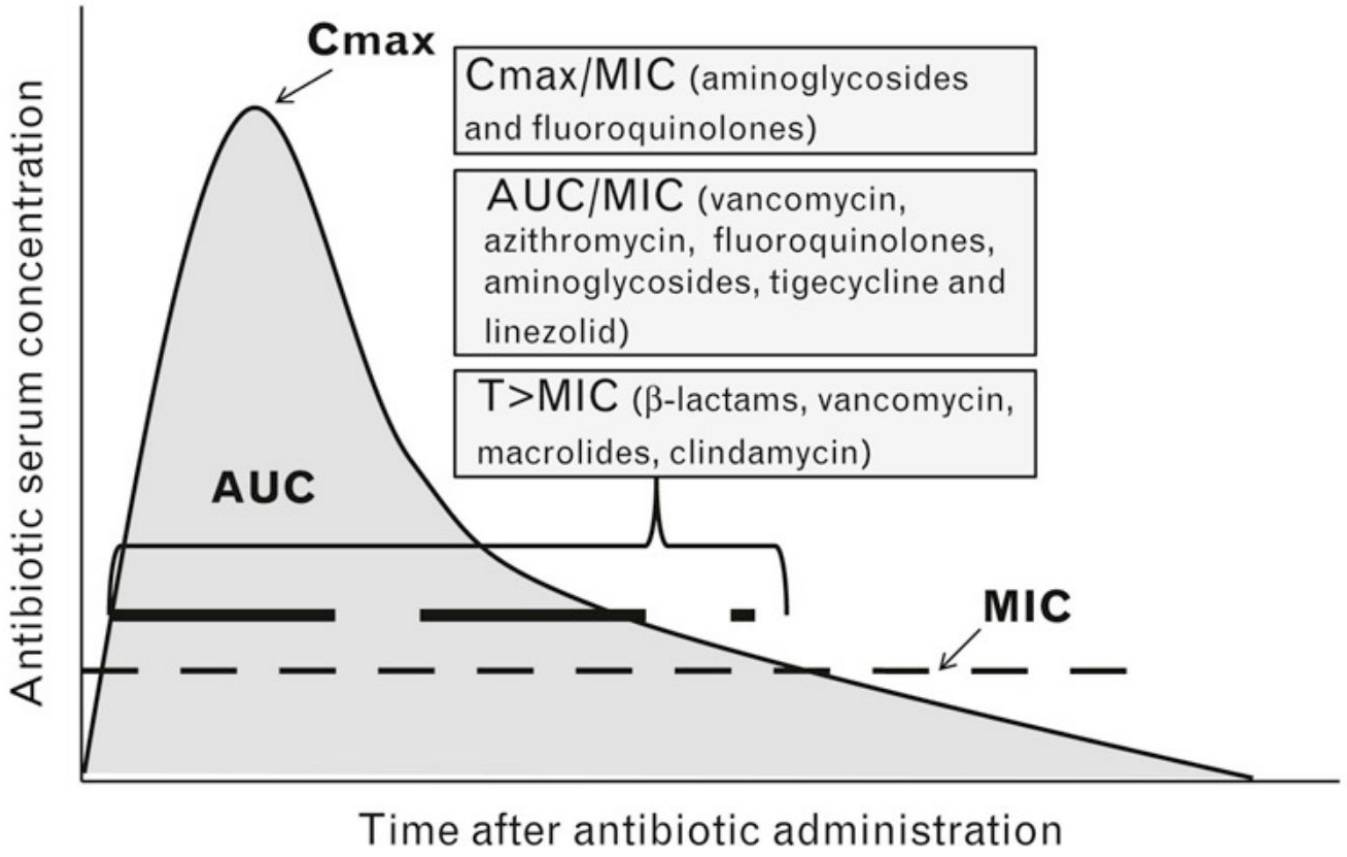


Kollef Inten Care Med 2017

AUC/MIC DOSING - VANCOMYCIN

Vancomycin Therapeutic Guidelines: A Summary of Consensus Recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists

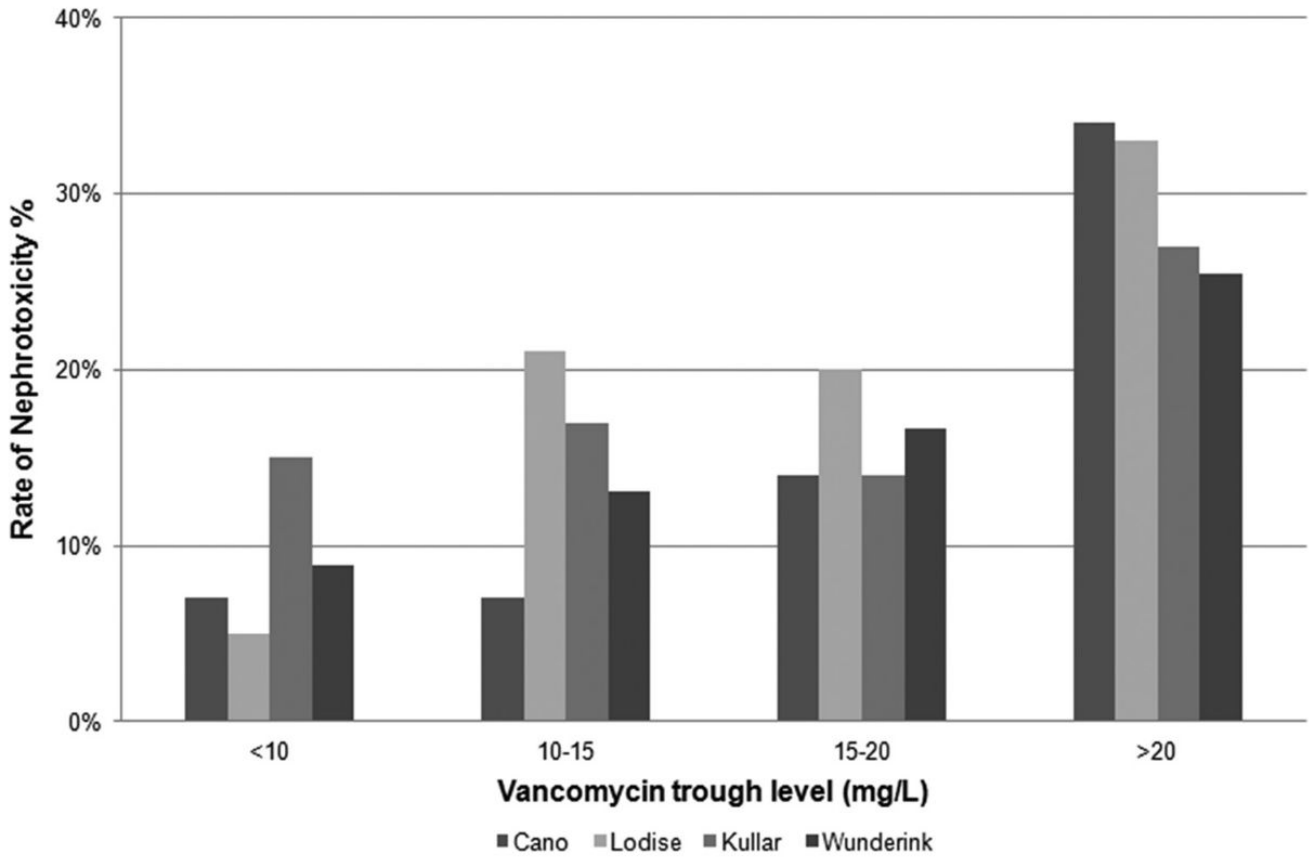
- "On the basis of in vitro, animal, and limited human data, an AUC/MIC value of 400 has been established as the pharmacokinetic-pharmaco-dynamic target [for vancomycin]."



Ryback CID 2009

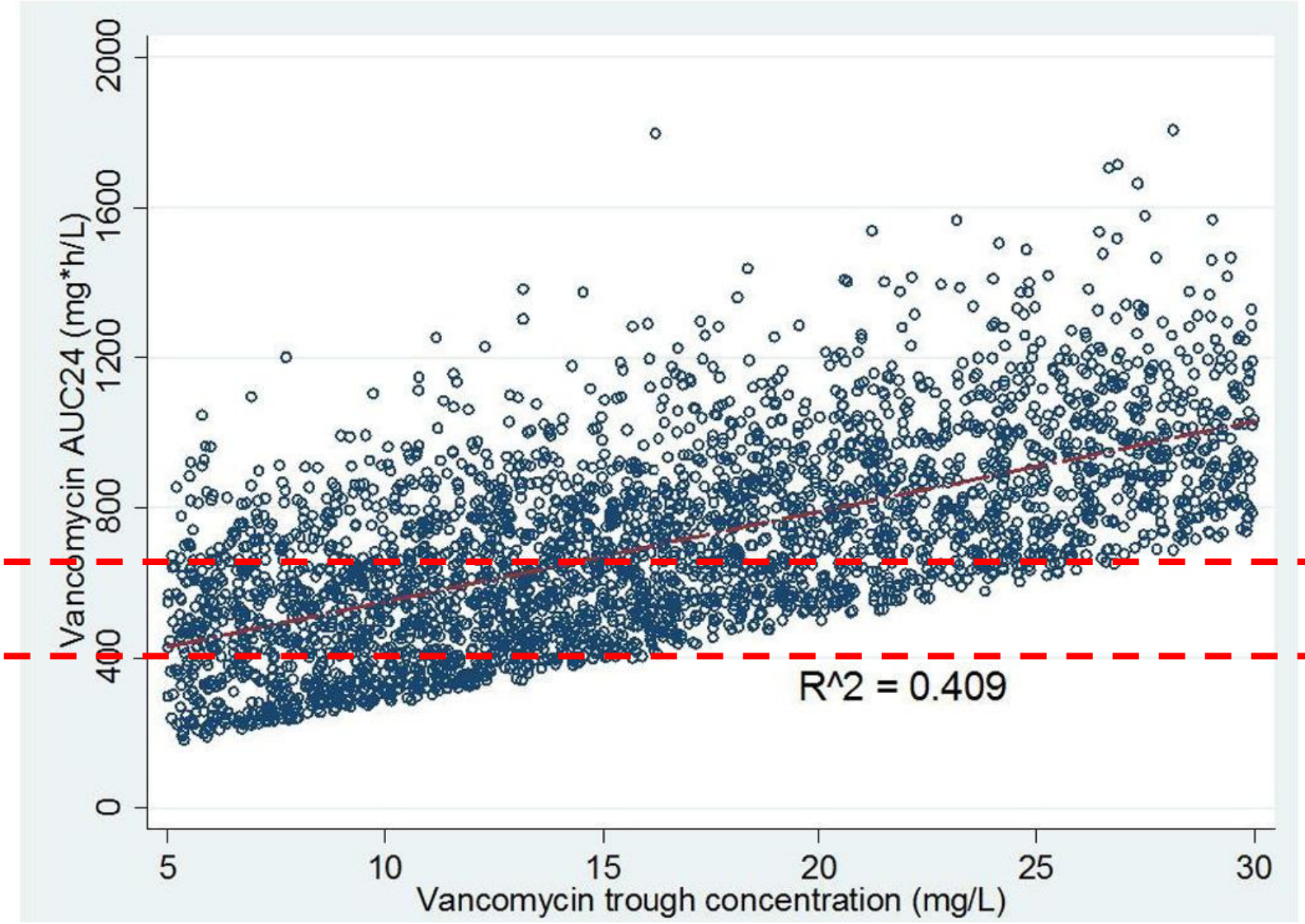
AKI RISK BY VANCOMYCIN TROUGH LEVEL

- The relationship between troughs of>15 mg/liter and nephrotoxicity persisted after adjustment for covariates known to independently increase the risk of a nephrotoxicity event.
- An incremental increase in nephrotoxicity was also observed with longer durations of vancomycin administration.



Lodise. AAC. 2013

RELATIONSHIP BETWEEN TROUGH AND AUC

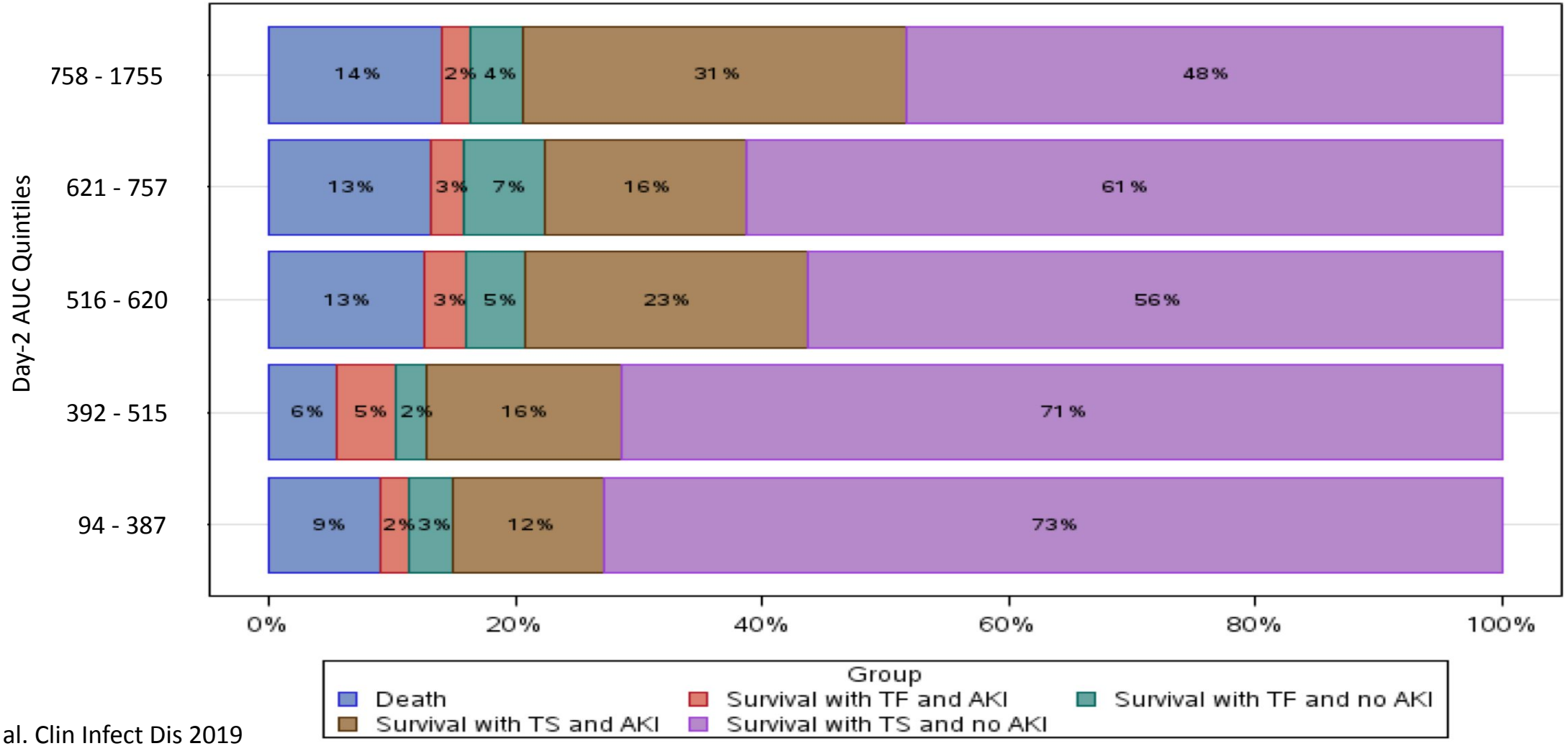


400-600

Slide Courtesy of Matt Brown

OUTCOMES ASSOCIATED WITH AUC

- PROVIDE – MRSA bacteremia



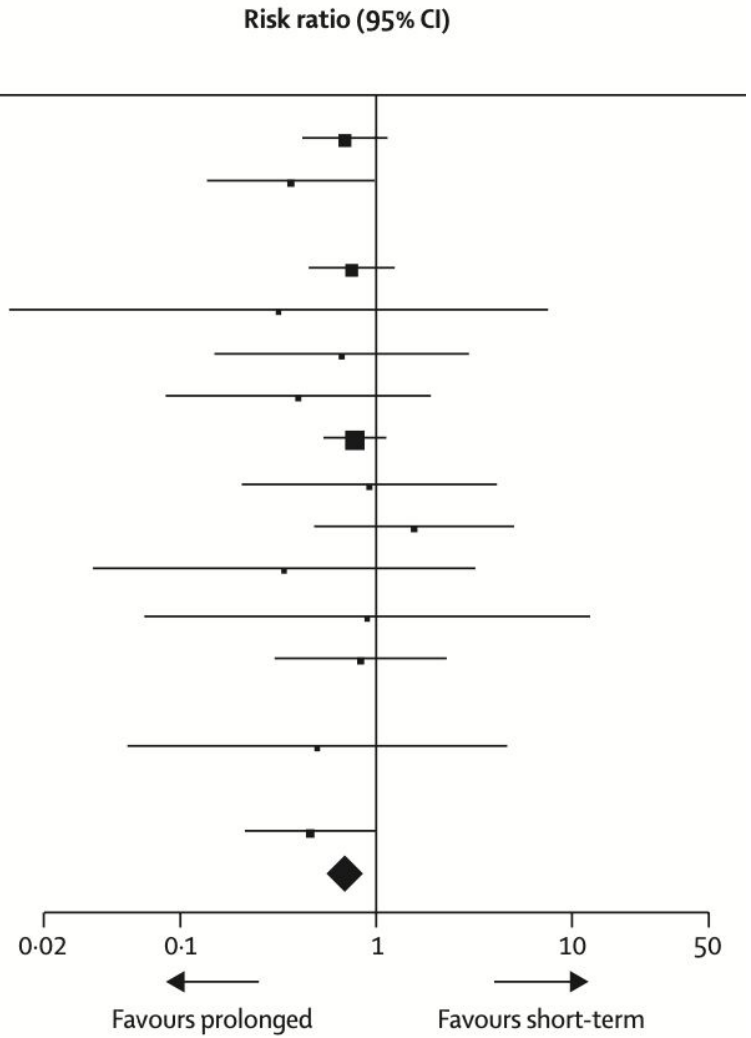
Lodise TP, et al. Clin Infect Dis 2019

EXTENDED INFUSIONS BETA LACTAMS

- Risk of death in patients with sepsis treated with prolonged infusion of antipseudomonal β-lactams was 30% lower compared to short-term infusion
  - Carbapenems, piperacillin-tazobactam, ceftazidime, cefepime

	Prolonged		Short-term		Weight
	Events	Total	Events	Total	
Abdul-Aziz (2016)[15]	18	70	26	70	18·5%
Angus (2000)[23]	3	10	9	11	4·8%
Bao (2016)[24]	0	25	0	25	..
Chytra (2012)[16]	21	120	28	120	18·1%
Cotrina-luque (2016)[26]	0	40	1	38	0·5%
Cousson (2005)[27]	2	8	3	8	2·1%
Dulhunty (2013)[17]	2	30	5	30	1·9%
Dulhunty (2015)[14]	39	212	52	220	33·9%
Georges (2005)[28]	3	26	3	24	2·1%
Lagast (1983)[30]	5	20	4	25	3·4%
Lau (2006)[31]	1	130	3	132	0·9%
Lips (2014)[32]	1	10	1	9	0·7%
Rafati (2006)[35]	5	20	6	20	4·5%
Roberts (2010)[36]	0	8	0	8	..
Sakka (2007)[37]	1	10	2	10	0·9%
Wang (2009)[38]	0	15	0	15	..
Wang (2014)[39]	7	38	16	40	7·8%
Total (95% CI)		**792**		**805**	**100·0%**
Total events	**108**		**159**		

Heterogeneity: τ^2=0·00; χ^2=6·47, df=13 (p=0·93); I^2=0%
Test for overall effect: Z=3·25 (p=0·001)

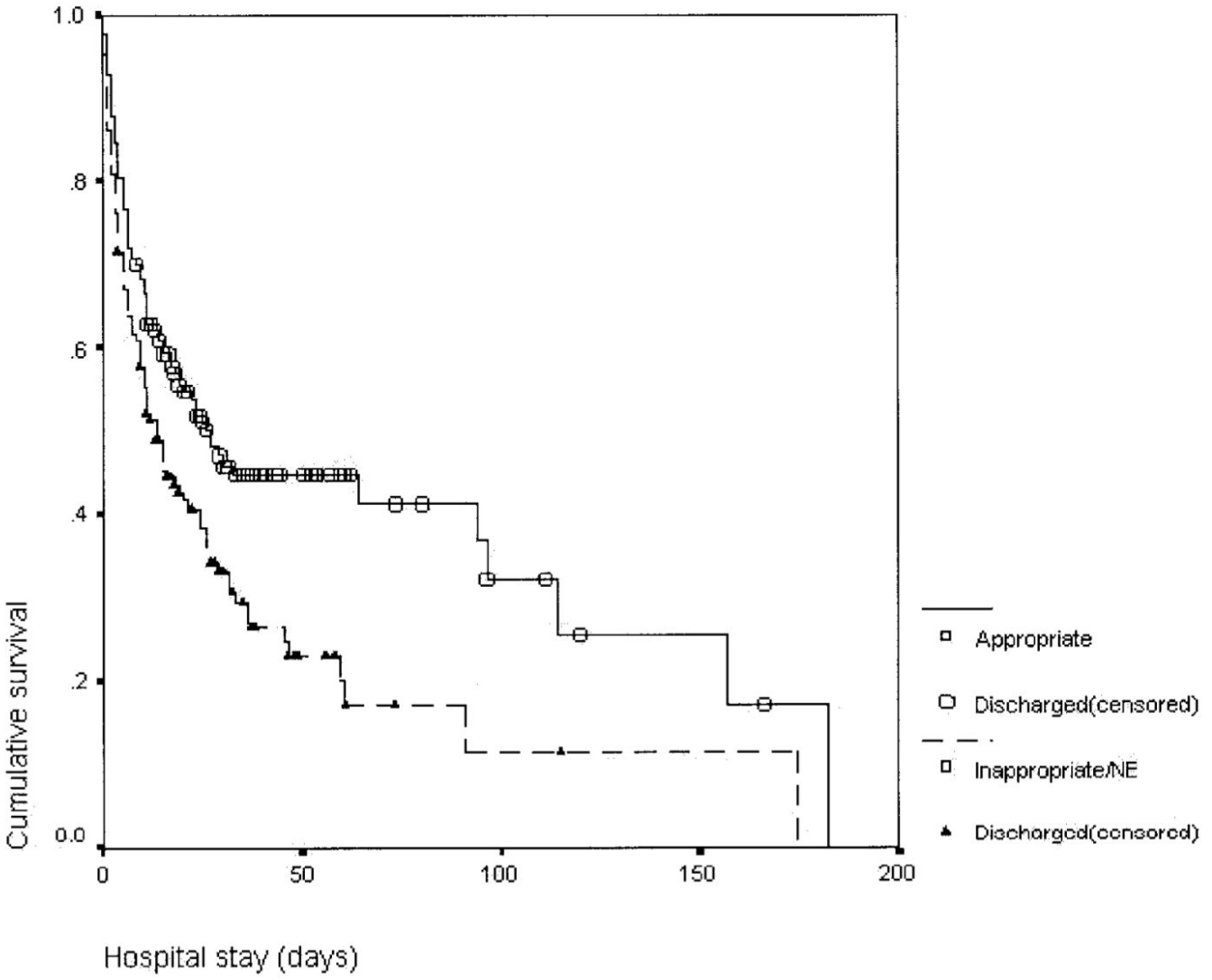


Vardakas Lancet ID 2018

RIGHT **DRUG**

APPROPRIATE "COVERAGE"

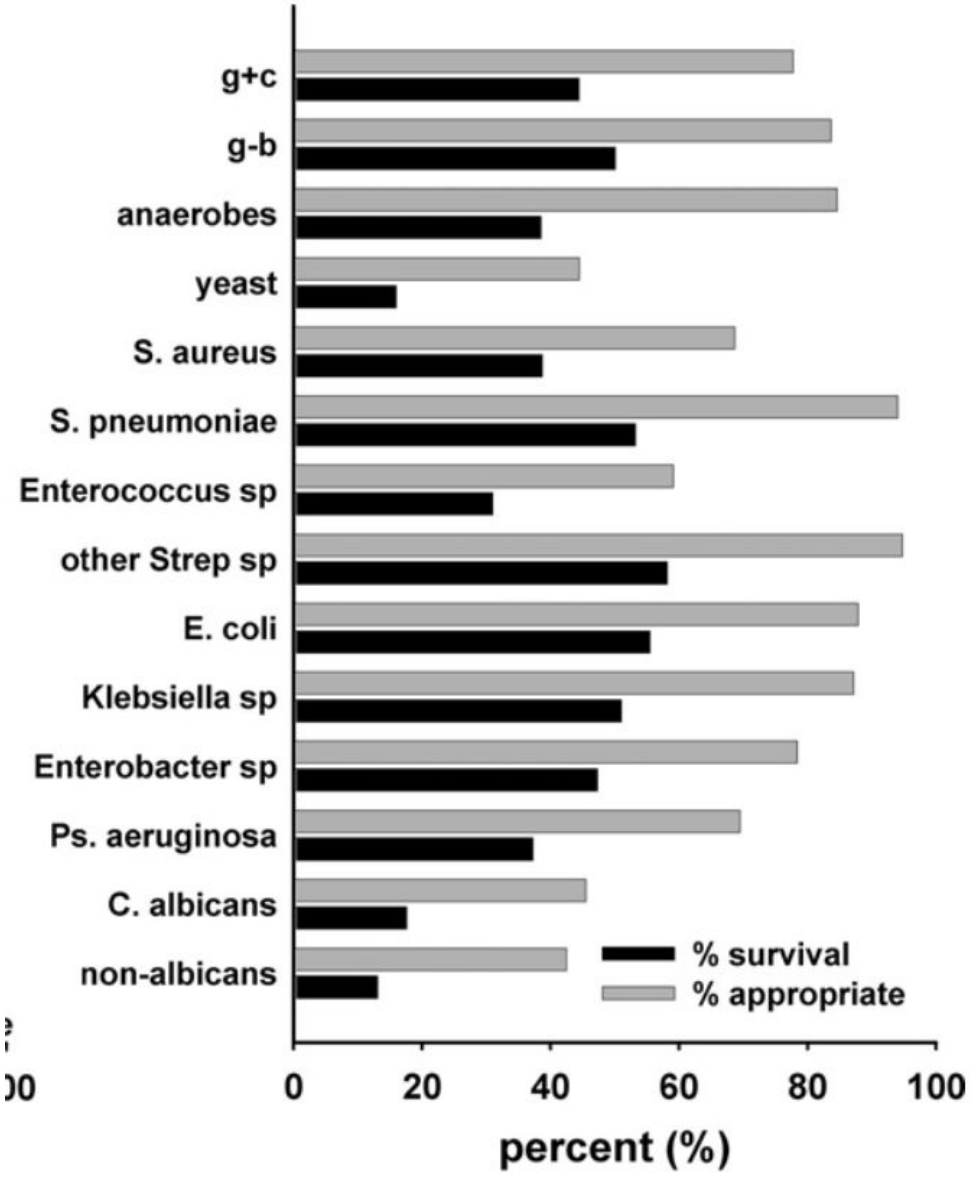
- 406 patients in a tertiary ICU; 67% with microbiologic documentation
  - sepsis in 105 (25.9%)
  - severe sepsis in 116 (28.6%)
  - septic shock in 185 (45.6%)
- Fungal infection and prior antibiotics were independent variables leading to inappropriate empiric antibiotics



Garrnacho-Montero CCM 2003

RISK OF INAPPROPRIATE EMPIRICS

- 5,715 patients with septic shock, retrospective evaluation; overall survival 43.7%
- Survival rates after appropriate initial therapy, 52%, and inappropriate initial therapy 10.3%
  - Appropriate antibiotics in 80% of cases
- After adjustment, inappropriateness of initial antimicrobial therapy remained most highly associated with risk of death (OR, 8.99; 95% CI, 6.60-12.23)



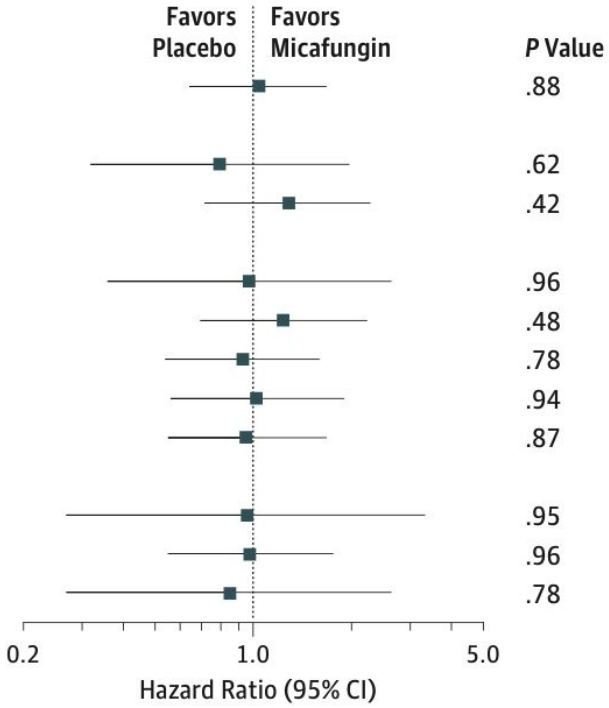
Kumar Chest 2009

EMPIRICUS TRIAL

- Empiric micafungin for 14d vs. placebo
- 260 patients (128 in micafungin group and 123 in placebo group)
  - inclusion criteria required one site of candida colonization, unresolved sepsis, organ dysfunction; exclusion non-neutropenic, transplant

Figure 3. Comparison of Survival at Day 28 in the Modified Intent-to-Treat Population and in Predefined Subgroups

	Micafungin		Placebo			
	Survived at Day 28, No.	Total No.	Survived at Day 28, No.	Total No.	Hazard Ratio (95% CI)	*P* Value
All patients	90	128	86	123	1.04 (0.64-1.67)	.88
SOFA score						
≤8	53	66	58	68	0.79 (0.32-1.96)	.62
>8	37	62	28	55	1.28 (0.71-2.27)	.42
Admission category						
Surgical	23	34	23	31	0.97 (0.36-2.63)	.96
Medical	67	94	63	92	1.23 (0.69-2.22)	.48
Colonization index ≥0.5[a]	70	101	70	99	0.93 (0.54-1.59)	.78
Corrected colonization index ≥0.4[b]	54	76	56	80	1.02 (0.56-1.89)	.94
Candida score ≥3	66	96	58	85	0.95 (0.55-1.67)	.87
(1-3)-ß-D-glucan, pg/mL[c]						
>250	14	21	17	25	0.96 (0.27-3.33)	.95
>80	61	91	58	84	0.98 (0.55-1.75)	.96
≤80	29	37	28	39	0.85 (0.27-2.63)	.78



Timsit JAMA 2016

COVERING RESISTANCE

MORTALITY RISK FACTORS WITH CARBAPENEM-RESISTANT BACTEREMIA: A FOCUS ON EARLY VS DELAYED ANTIBIOTICS

Stephanie Bass[1], Elizabeth Neuner[1], Seth Bauer[1], Simon Lam[1]; [1]Cleveland Clinic, Cleveland, OH

- Adult patients admitted to an ICU with sepsis due to gram-negative bacteremia resistant to a carbapenem were included
  - Exclusion criteria included polymicrobial, recurrent, or breakthrough infections, or patients who expired before appropriate antibiotics were initiated.
- 115 patients; 69 (60%) survivors and 46 (40%) non-survivors at day 30
- Early appropriate antibiotics was not associated with mortality
  - Older age and higher SOFA score were independent risk factors for 30-day mortality

Bass CCM Poster 2013

IDSA GUIDELINES FOR IAI

- Empiric coverage of *Enterococcus* is not necessary in patients with community-acquired intra-abdominal infection
  - Specific treatment not indicated unless recovered form the blood or only isolate in culture from infected site
- Empiric therapy directed against vancomycin-resistant *Enterococcus faecium* is not recommended unless high risk
- Completion of the antimicrobial course with PO forms is acceptable in patients able to tolerate an oral diet and in patients in whom susceptibility studies do not demonstrate resistance
  - moxifloxacin, ciprofloxacin plus metronidazole, levofloxacin plus metronidazole, an oral cephalosporin with metronidazole, or amoxicillin-clavulanic acid

Solomkin, CID, 2010

SINGLE DOSE AMINOGLYCOSIDES

A Systematic Review of Single-Dose Aminoglycoside Therapy for Urinary Tract Infection: Is It Time To Resurrect an Old Strategy?

Kellie J. Goodlet,[a] Fatima Z. Benhalima,[a] Michael D. Nailor[b]

- Gentamycin 5mg/kg x 1 dose
  - Other aminoglycosides have also been studied

TABLE 2 Provider considerations for evaluating the appropriateness of single-dose AG therapy for UTI[a]

Single-dose AG therapy may be appropriate
Lower tract infection (cystitis)
Local endemicity of organisms resistant to first-line UTI agents
Inpatient admission may be averted
Questionable patient adherence to oral therapy
Patient preference over oral therapy
Otherwise healthy individual
Alternative therapy recommended
Urosepsis/bacteremia
Previous infection with AG-resistant organism
High risk of *Enterococcus* sp. infection
Chronic renal insufficiency
Patient history of significant AG-mediated adverse drug event

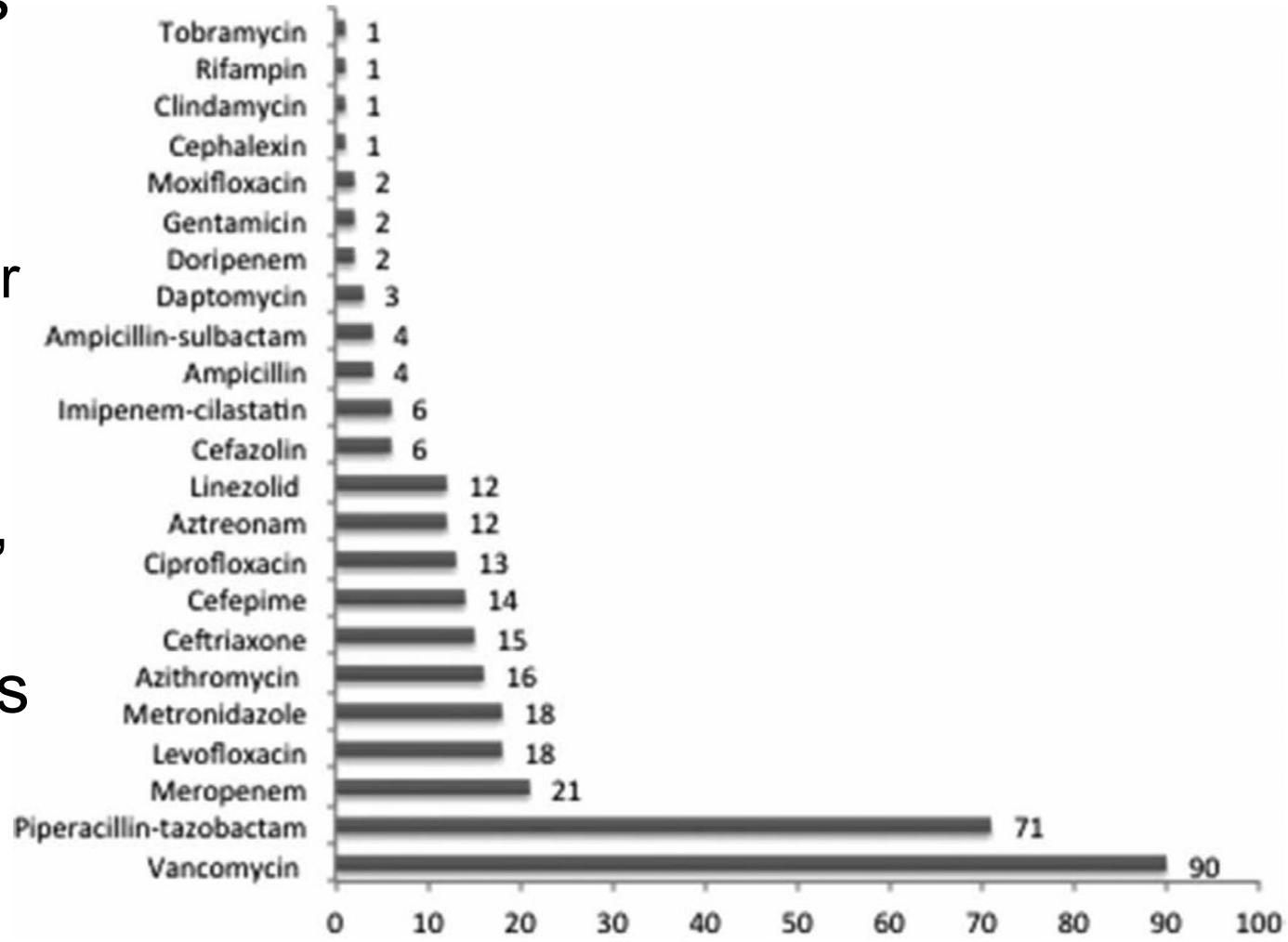
[a]AG, aminoglycoside; UTI, urinary tract infection.

Goodlet, 2018

DE-ESCALATION

PROLONGED EMPIRIC ANTIBIOTIC THERAPY

- 76 ICUs from 32 US hospitals
- PEAT (Prolonged Empiric Antibiotic Therapy)
  - empiric antibiotics continued for greater than 72 hours without indication
- Out of 660 empiric antibiotics, 333 antibiotics (50%) were continued for at least 72 hours where CDC infection criteria were not met



Thomas CCM 2015

ICU STEWARDSHIP ROUNDS

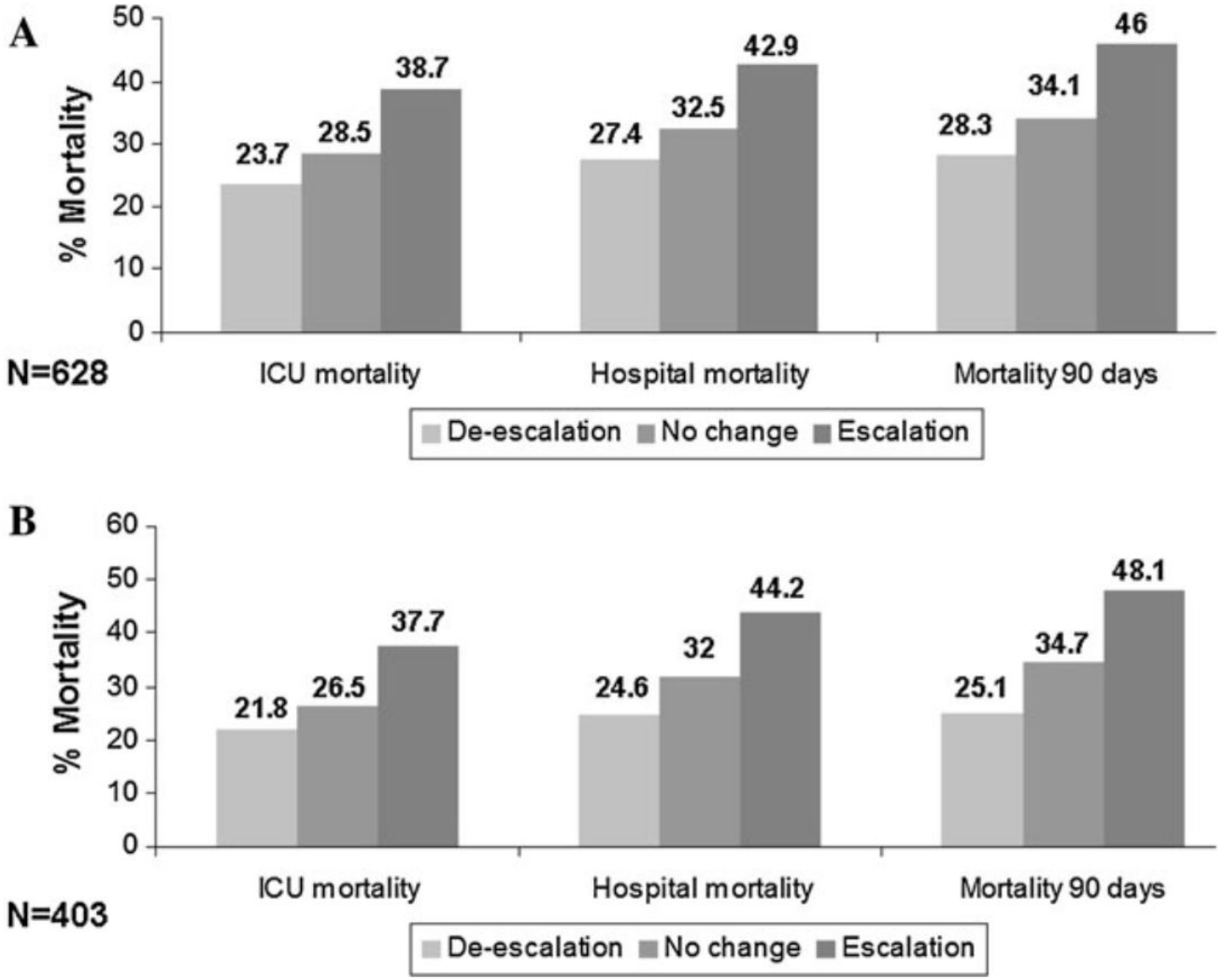
EMR *"virtual round"*

Pre ICU-AMS ward

Recommendations (n = 412)	Recommendations, No. (%)	Acceptance of Recommendations, No. (%)
Moment 1. Escalation (including initiation)	63 (15.3)	57 (90.5)
Moment 2. De-escalation	63 (15.3)	54 (85.7)
Moment 3. Discontinuation	173 (42)	145 (83.8)
Moment 4. Switch	49 (11.9)	44 (89.9)
Moment 5. Optimization	64 (15.5)	55 (85.9)

DE-ESCALATION = BETTER MORTALITY

- Prospective, observational; 712 patients admitted with severe sepsis or septic shock receiving broad spectrum antibiotics
- 34.9% had de-escalation of antibiotics
- De-escalation was a protective factor in 90d mortality



Garnacho-Montero Inten Care Med 2014

EARLY DE-ESCALATION OF ANTIFUNGALS

- Multicenter post-hoc study; 235 cases of candidemia evaluating impact of early de-escalation (ED) within 5 days to fluconazole
  - Candidemia caused by fluconazole-susceptible strains with controlled source and hemodynamic stability
  - 54 cases classified as ED, 181 as non-ED cases

- In the ED and non-ED groups, 30-day mortality was 11.1% and 29.8% (P = .006), respectively.
  - ED had no significant impact on mortality (OR, 0.50; 95% CI, 0.16–1.53).

5.RIGHT **DURATION**

Appropriate Durations

- "Constantine Units" – 7, 14, 21 days
  - arbitrary decisions regarding appropriate duration, in most cases
- Patients are put at unnecessary risk for antibiotic resistance when treatment is given for longer than necessary, not when it is stopped early
- Patients may respond differently to the same antibiotic, depending on diverse patient and disease factors
  - Longer durations needed? Possibly.

(Llewelyn, Fitzpatrick et al. 2017) (Wald-Dickler, Spellberg, 2019)

EDITORIAL

The New Antibiotic Mantra—"Shorter Is Better"

Brad Spellberg, MD

Table. Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

Disease	Treatment, Days	
	Short	Long
Community-acquired pneumonia[1-3]	3-5	7-10
Nosocomial pneumonia[6,7]	≤8	10-15
Pyelonephritis[10]	5-7	10-14
Intraabdominal infection[11]	4	10
Acute exacerbation of chronic bronchitis and COPD[12]	≤5	≥7
Acute bacterial sinusitis[13]	5	10
Cellulitis[14]	5-6	10
Chronic osteomyelitis[15]	42	84

Abbreviation: COPD, chronic obstructive pulmonary disease.

Spellberg. JAMA. 2016

ACP American College of Physicians® Leading Internal Medicine, Improving Lives

CLINICAL GUIDELINE

Appropriate Use of Short-Course Antibiotics in Common Infections: Best Practice Advice From the American College of Physicians

Rachael A. Lee, MD, MSPH; Robert M. Centor, MD; Linda L. Humphrey, MD, MPH; Janet A. Jokela, MD, MPH; Rebecca Andrews, MS, MD; and Amir Qaseem, MD, PhD, MHA; for the Scientific Medical Policy Committee of the American College of Physicians*

- Best Practice Advice 1:
  - limit antibiotic treatment duration to 5d days in patients with COPD exacerbations and acute uncomplicated bronchitis
- Best Practice Advice 2:
  - antibiotics for CAP for a minimum of 5d
- Best Practice Advice 3:
  - Women with UTI: NFT for 5d, TMP-SMX for 3d, fosfomycin single dose
  - Men and women with acute pyelonephritis: 5-7d FQ and 14d TMP-SMX
- Best Practice Advice 4:
  - nonpurulent cellulitis; 5-6d course of antibiotics active against streptococci

(Lee, Centor et al. 2021)

ULTRA-SHORT-COURSE FOR VAP

- 1290 patients; started on antibiotics for possible VAP with daily minimum PEEP of ≤5 cm H2O and FiO2 ≤40% for at least 3 days
- Very short antibiotic courses (1–3 days) were associated with outcomes similar to longer courses (>3 days) in patients with suspected VAP but minimal and stable ventilator settings.

Table 3. Competing Risk Analyses of Outcomes Among Patients Prescribed 1–3 Days Versus >3 Days of Antibiotics

		Time to Extubation Alive		Ventilator Death		Time to Hospital Discharge Alive		Hospital Death	
Patient Population	No.	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
All patients	1290	1.16 (.98–1.36)	.08	0.82 (.55–1.22)	.32	1.07 (.91–1.26)	.43	0.99 (.75–1.31)	.96
Propensity-matched population	514	1.15 (.97–1.38)	.12	0.89 (.57–1.38)	.60	1.08 (.88–1.32)	.45	0.92 (.67–1.27)	.62
Patients with VAP diagnosis codes (propensity-matched population)	104	1.27 (.86–1.88)	.24	0.69 (.26–1.79)	.44	0.94 (.59–1.51)	.80	1.24 (.66–2.34)	.51
Patients with ≥25 neutrophils per low-power field and positive cultures for potentially pathogenic organisms (propensity-matched population)	100	1.00 (.67–1.49)	.98	0.85 (.29–2.50)	.77	1.33 (.85–2.07)	.21	0.60 (.27–1.31)	.20

Klompas. CID. 2017

URINARY TRACT INFECTIONS IN MEN

- Afebrile men with suspected UTI treated with 7 days was noninferior to 14 days of ciprofloxacin or trimethoprim/sulfamethoxazole treatment

Table 3. Primary and Secondary Outcomes

Characteristic	No./total No. (%)		
Resolution of UTI symptoms 14 days after stopping active antimicrobials	**7-Day antimicrobial + 7-day placebo group**	**14-Day antimicrobial group**	**Absolute difference, % (1-sided 97.5% CI)[a]**
As-treated population (primary analysis)	122/131 (93.1)	111/123 (90.2)	2.9 (-5.2 to ∞)
As-randomized population	125/136 (91.9)	123/136 (90.4)	1.5 (-5.8 to ∞)
Recurrence of UTI symptoms within 28 days of stopping study medication (secondary outcome)	**7-Day antimicrobial + 7-day placebo group**	**14-Day antimicrobial group**	**Absolute difference, % (2-sided 95% CI)[b]**
As-treated population	13/131 (9.9)	15/123 (12.9)	-3.0 (-10.8 to 6.2)
As-randomized population	14/136 (10.3)	23/136 (16.9)	-6.6 (-15.5 to 2.2)

Abbreviation: UTI, urinary tract infection.

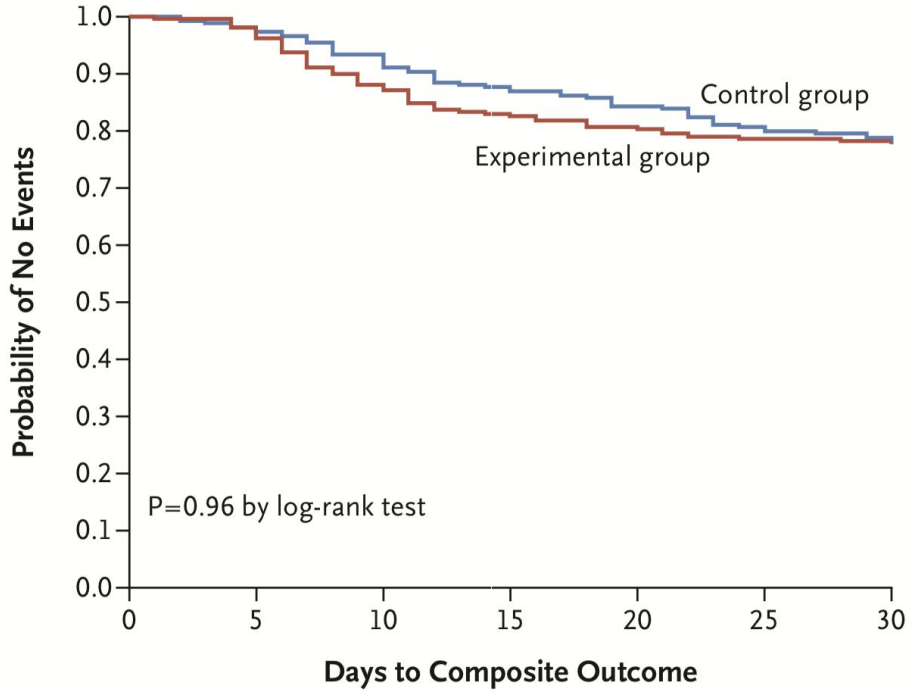
[a] The primary analysis used a 1-sided 97.5% CI for noninferiority, which was established if the lower bound of the 1-sided 97.5% CI did not cross the noninferiority margin of −10% difference in symptom resolution.

[b] The secondary outcome was analyzed using a 2-tailed superiority hypothesis test of differences in proportions (2-sample test for equality of proportions with continuity correction) with α = .05 and with 2-sided 95% CIs.

Drekonja. JAMA. 2021

STOP-IT

- 518 patients with complicated intraabdominal infection and adequate source control
  - Randomized to 4 days of antibiotics from source control and 2d following resolution of SIRS; experimental mean 4 days, control mean 8 days
  - No difference in recurrent infection or death



Source control procedure – no. (%)		
Percutaneous drainage	86 (33.1)	86 (33.3)
Resection and anastomosis or closure	69 (26.5)	64 (24.8)
Surgical drainage only	55 (21.1)	54 (20.9)
Resection and proximal diversion	27 (10.4)	37 (14.3)
Simple closure	20 (7.7)	12 (4.7)
Surgical drainage and diversion	3 (1.2)	4 (1.6)

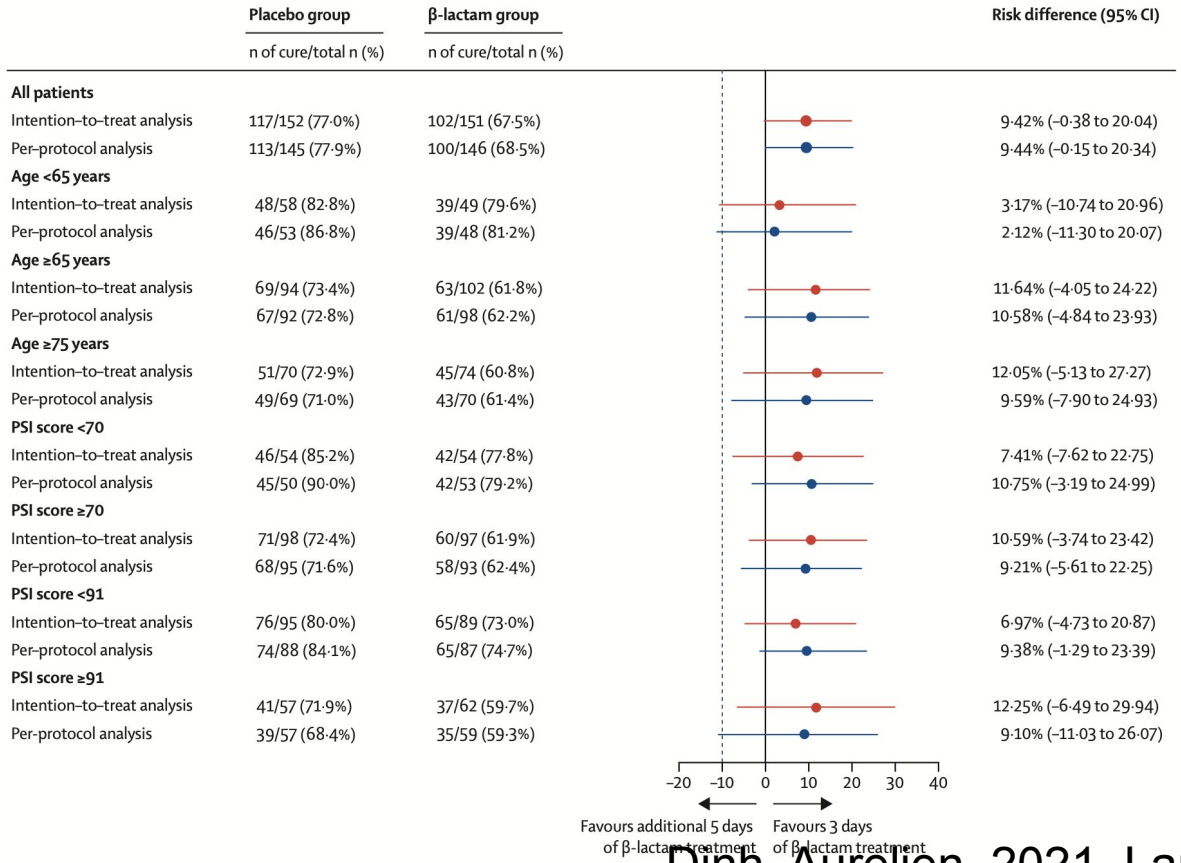
Sawyer, NEJM, 2018

SHORT COURSES FOR CAP

- Pneumonia Short Treatment (PCT); DB, RCT, placebo controlled
  - France; 301 hospitalized pts randomized at day 3 after clinical stability
    - High dose Augmentin TID for additional 5d or placebo

	Placebo group	β-lactam group	Difference	p value
Cure at day 30				
ITT analysis	109/152 (72%)	109/151 (72%)	−0·47 (−11·31 to 9·98)	>0·99
Per-protocol analysis	105/141 (74%)	107/141 (76%)	−1·42 (−12·08 to 9·20)	0·89
Mortality at day 30	3/152 (2%)	2/151 (1%)	0·60 (−3·50 to 4·40)	>0·99
Patients with at least one adverse event related to treatment	22/152 (14%)	29/151 (19%)	−4·70 (−7·08 to 2·31)	0·29
Patients with at least one serious adverse event related to treatment	1/152 (1%)	1/151 (1%)	0·00 (0·00 to 0·99)	>0·99
Length of hospital stay, days,	5·00 (4·00 to 9·00)	6·00 (4·00 to 9·00)	−1·00 (−1·00 to 1·00)	0·74
Recovery time, days	15·00 (9·00 to 21·50)	15·50 (7·00 to 20·00)	−0·50 (−4·00 to 5·50)	0·33

Data are n/N (%), median (IQR) or between-group difference in percentage points, with 95% CI in parentheses. Unless otherwise stated, analyses are in the ITT population. χ^2 test was used to compare the distributions of categorical variables and Student's *t* tests to compare the distributions of quantitative continuous variables. ITT=intention-to-treat.



Dinh, Aurelien. 2021. Lancet

DEVELOPING AN "EXPECTED PRACTICE"

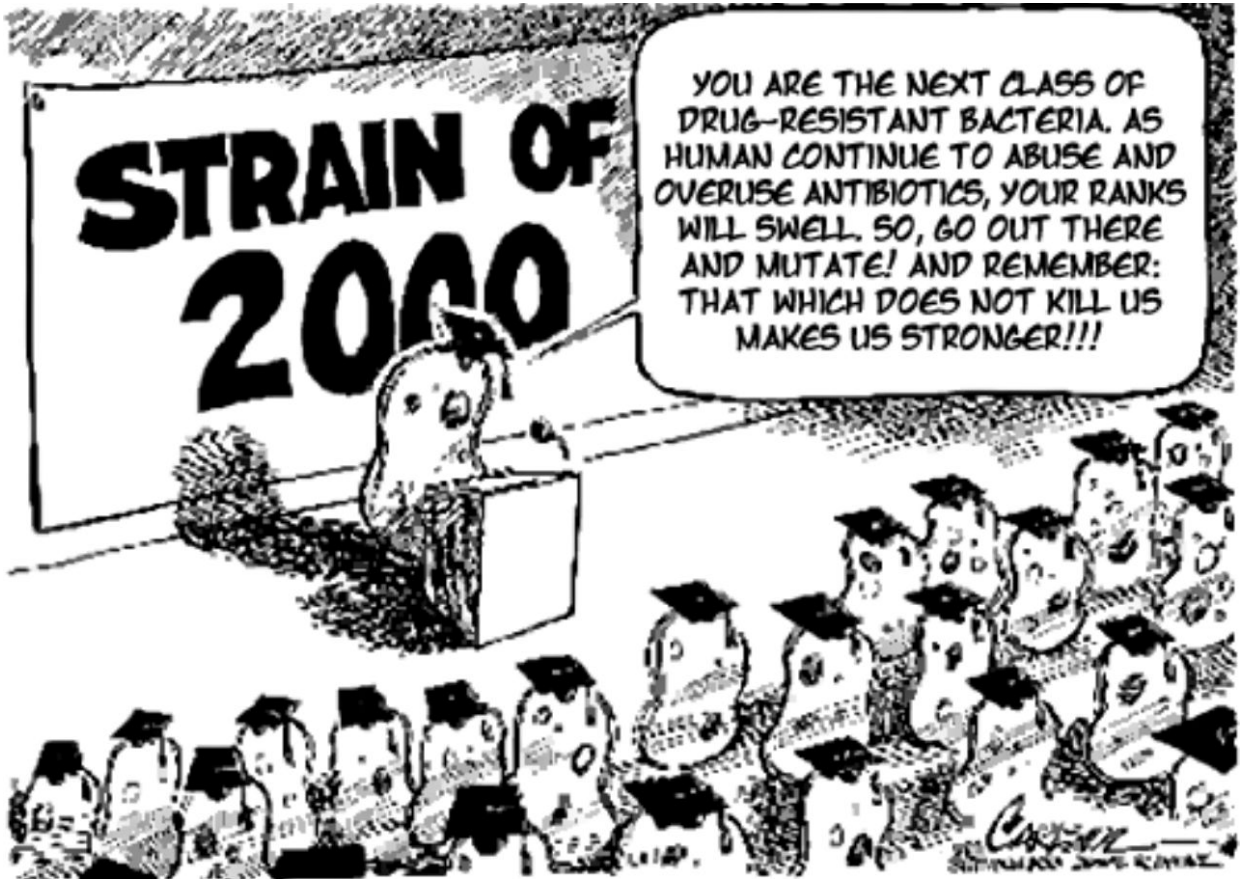
"…expected practice has alleviated concerns by our providers regarding both what the evidentiary basis of the practice is and the knowledge that they are acting in compliance with practice standards our institution has set."

Variable	Baseline	Postintervention	Difference, *P* Value
Mean EP antibiotic DOT (IQR), d			
UTI	14.3 (13.7 to 15.0)	12.9 (12.4 to 13.5)	–1.4 (–2.3 to –0.6); $P = .001$
SSTI	20.0 (19.2 to 20.9)	17.9 (17.1 to 18.7)	–2.2 (–3.3 to –1.0); $P < .001$
PNA	18.0 (17.2 to 18.8)	16.0 (15.3 to 16.7)	–2.0 (–3.2 to –0.9); $P = .001$
VAP	36.1 (31.5 to 40.8)	26.5 (23.6 to 29.4)	–9.6 (–16.0 to –3.3); $P = .003$

(Yadav, 2019)

5 D'S OF ANTIBIOTIC PRESCRIBING

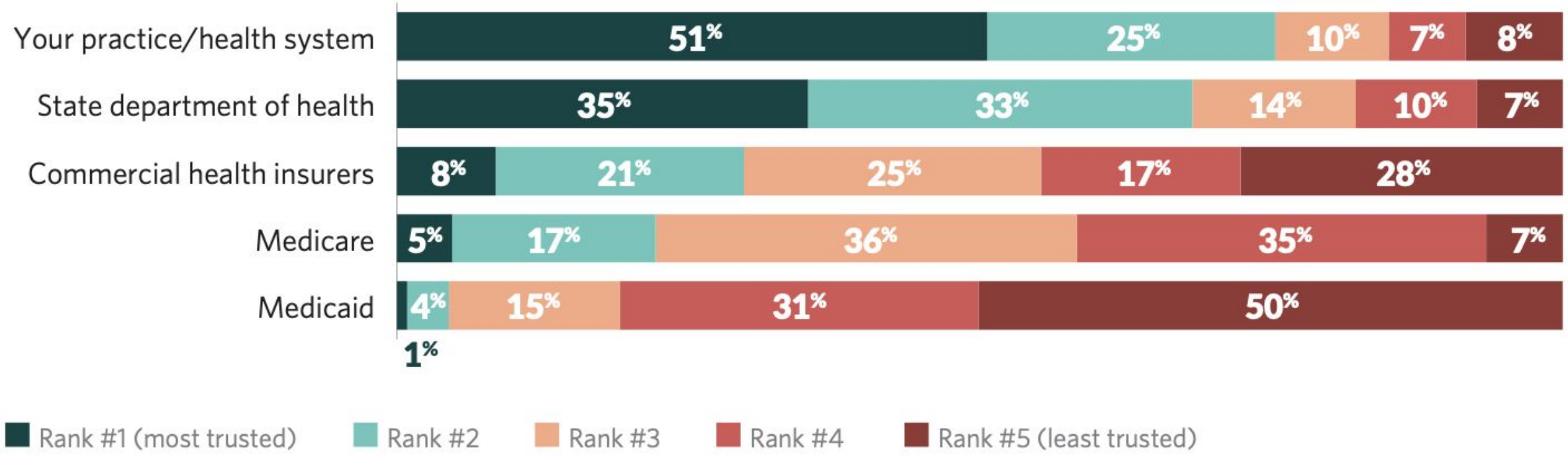
- Right **D**iagnosis
- Right **D**rug
- Right **D**ose
- Right **D**uration
- **D**e-escalation



A Physician's Own Practice or Health System Is the Most Trusted Organization to Provide Prescribing Feedback

"Which of the following organizations would you have the most confidence in to provide you with accurate feedback on your antibiotic prescribing practices?"

Internal medicine and family medicine physicians



Pew. 2020

Take Aways

- There are national programs now monitoring antimicrobial use
  - Future goal to move from volume and closer to appropriateness
  - New TJC recommendations
- Remember the 5Ds when prescribing antimicrobials
  - We can be successful, though we must challenge dogma
  - Disparities exist in antimicrobial prescribing, as with other issues
- Institutional guidelines developed by “all” are the best mechanism to improve and evaluate antimicrobial use appropriateness aiming for better overall outccomes

Questions?

- Feel free to email me at jstripling@uabmc.edu

Thank you for the opportunity and your time!