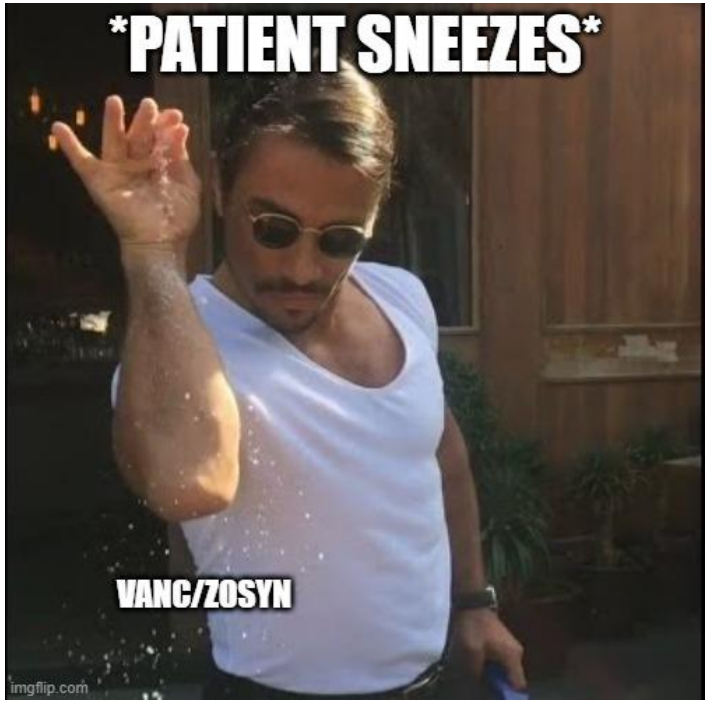
ID Pharmacy Initiatives

Matt Davis, PharmD
Christine Pham, PharmD BCIDP
Meganne Kanatani, PharmD
Ross Pineda, PharmD

Outline

- MRSA Nasal Swab Utility
- Vancomycin AUC-Based Monitoring
- Beta-Lactam Dose Optimization
- Beta-Lactam Allergies
- Antibiotic Ladders
- Re-Evaluate at 48 (hours)



MRSA Nasal Swab Utility

High negative predictive value for ruling out invasive MRSA infections

Clinical Infectious Diseases
MAJOR ARTICLE

The Clinical Utility of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Screening to Rule Out MRSA Pneumonia: A Diagnostic Meta-analysis With Antimicrobial Stewardship Implications

Diane M. Parente,[1] Cheston B. Cunha,[2,3] Eleftherios Mylonakis,[2,3] and Tristan T. Timbrook[4]

- 22 studies (n = 5163)
  - 18 retrospective, 3 prospective, 1 unknown
- MRSA nasal test + culture-confirmed pneumonia
- Pooled prevalence MRSA PNA – **10%***
  - VAP studies – **8%***
- NPV of MRSA nares
  - All – **96.5%**
  - CAP – **98.1%**
  - VAP – **94.8%** (*sensitivity 40%, low prevalence*)
- "Due the low PPV overall positive MRSA nares screens do not have predictive value in the diagnosis of MRSA pneumonia."

**Low prevalence of MRSA PNA could over-estimate NPV of MRSA nares test*

Clinical Infectious Diseases
MAJOR ARTICLE

Determining the Utility of Methicillin-Resistant *Staphylococcus aureus* Nares Screening in Antimicrobial Stewardship

Kari A. Mergenhagen,[1] Kaitlyn E. Starr,[1] Bethany A. Wattengel,[1] Alan J. Lesse,[2,3,4] Zarchi Sumon,[1] and John A. Sellick[2,3]

- National VA Database (2007-2018; n = 245,833)
- MRSA nasal test on admission vs. clinical culture
  - MRSA in cultures – 8.3%; Nares – 22.9%
- Performance: Sensitivity – 67.4%; NPV – **95.5%**
- NPV of MRSA nares by site:
  - Respiratory – **96.1%**
  - Blood – **96.5%**
  - Intra-abdominal – **98.6%** (*40% peritoneal, 23% biliary, 32% unspecified)*

- *"Negative MRSA nares w/in 7 days of clinical culture **can be used to deescalate or avoid empirical [vancomycin]** for many different infection sites for patients who are **not critically ill**."*

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Vancomycin AUC Monitoring

New proposed monitoring system to reduce toxicity while maintaining efficacy

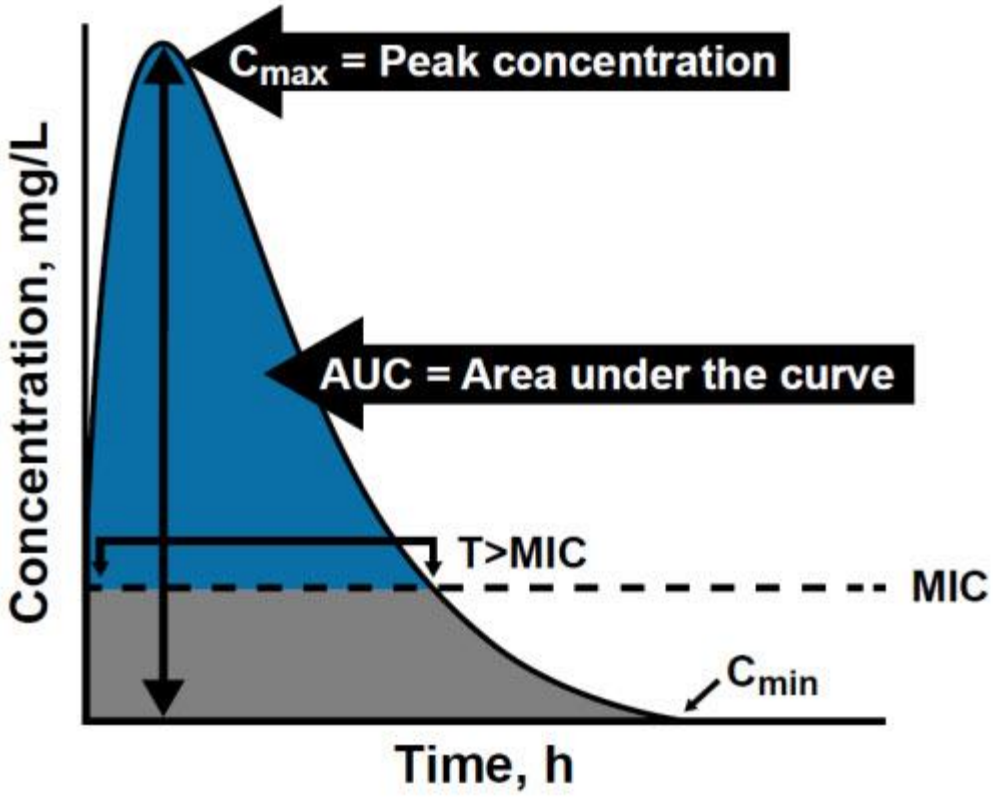
Background - Pharmacokinetics

Antibiotics fall into three major pharmacokinetic categories:

- Peak-dependent (aminoglycosides)
- Time-dependent (beta-lactams)
- AUC-dependent (vancomycin)

Impacts our dosing strategies

- Peak-dependent --> high doses less frequently
- Time-dependent --> low doses more frequently
- AUC-dependent --> total daily exposure



Background - Pharmacokinetics

Antibiotics fall into three major pharmacokinetic categories:

- Peak-dependent (aminoglycosides)
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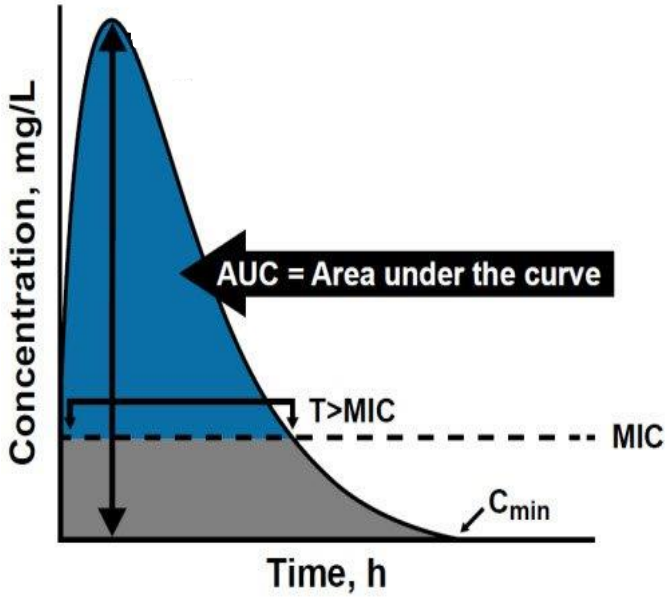
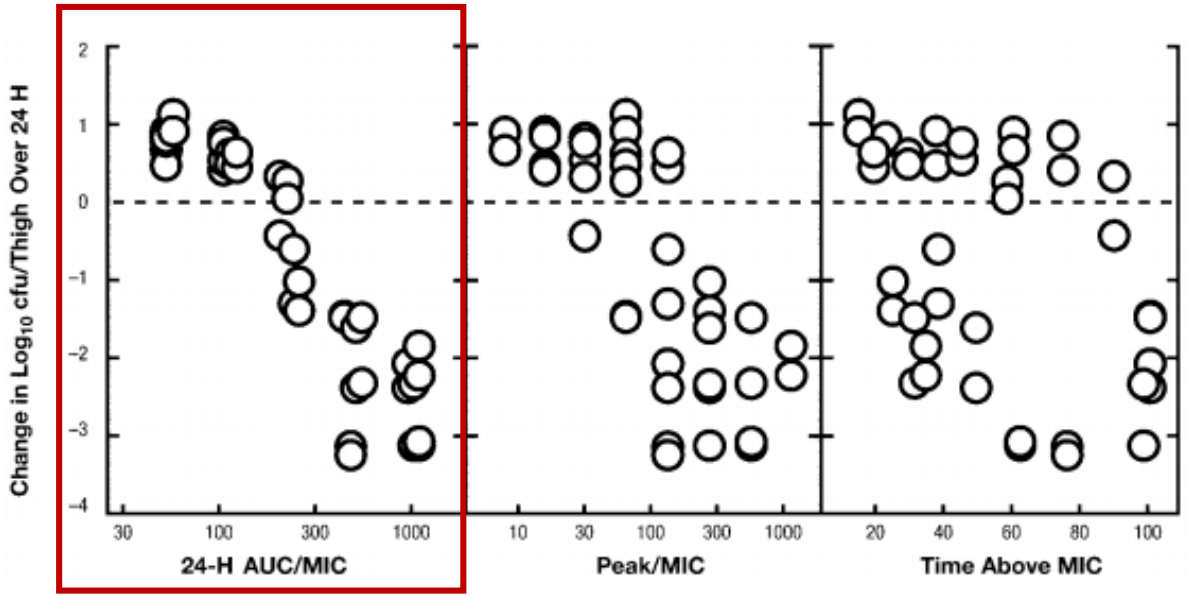
- **AUC-dependent (vancomycin)**





https://www.medscape.org/viewarticle/767071
https://doi.org/10.1086/491712

What's in a Trough? Rationale for Old Targets

- Previous data with improved clinical outcomes for AUC > 400
- Old guidelines recommended trough 15-20 mg/L for severe infections because:
  - "Trough serum vancomycin concentrations [of 15-20 mg/L] should achieve an AUC/MIC of 400"
  - 15-20 mg/L * 24 hrs = 24-hr AUC 360 – 480 mg*h/L
    - Only accounts for the drug concentration at its **lowest point** (i.e. trough)
    - Overshoots AUC toxicity threshold if account for totality of drug exposure (i.e. peak)
- Bottom Line: Trough of 15-20 mg/L **was never the real target** but a surrogate for true target of AUC > 400 mg*hr/L

1. https://doi.org.10.2165/00003088-200443130-00005
2. https://doi.org.10.1093/cid/ciaa1743

New Vancomycin Targets

- Emerging data suggest these targets, particularly >15 mg/L, led to:
  - Unnecessarily high exposure→ toxicity; exposure-toxicity gradient[1]
    - >15 mg/L independently associated with AKI risk in multiple studies
  - Do not definitively correlate to better clinical outcomes
- Over half of patients with a therapeutic AUC, expected to have trough < 15 mg/L[2]
- New guidelines recommend AUC 400-600 mg*h/L[3] instead of troughs
  - There were *minimal to no data on the safety and efficacy of targeted trough concentrations of 15 to 20 mg/L."*
  - Two-levels (peak/random + trough)→pharmacokinetic calculation
  - **Bayesian Modeling software (preferred; 1-2 levels, at least 1 trough)**

Nephrotoxicity vs. Exposure

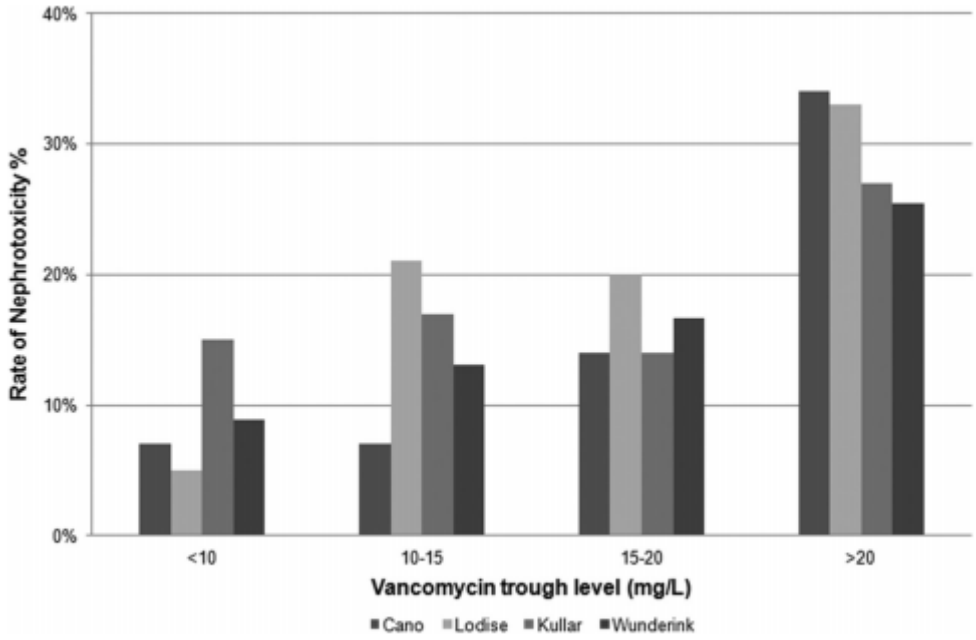
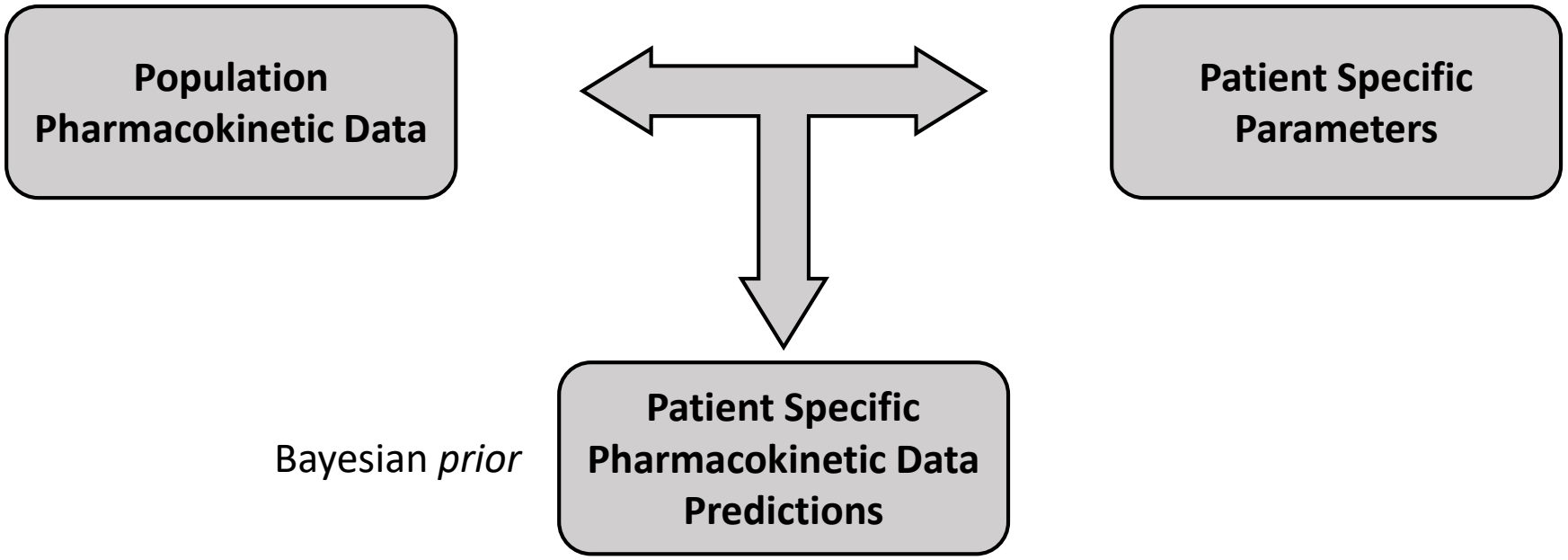


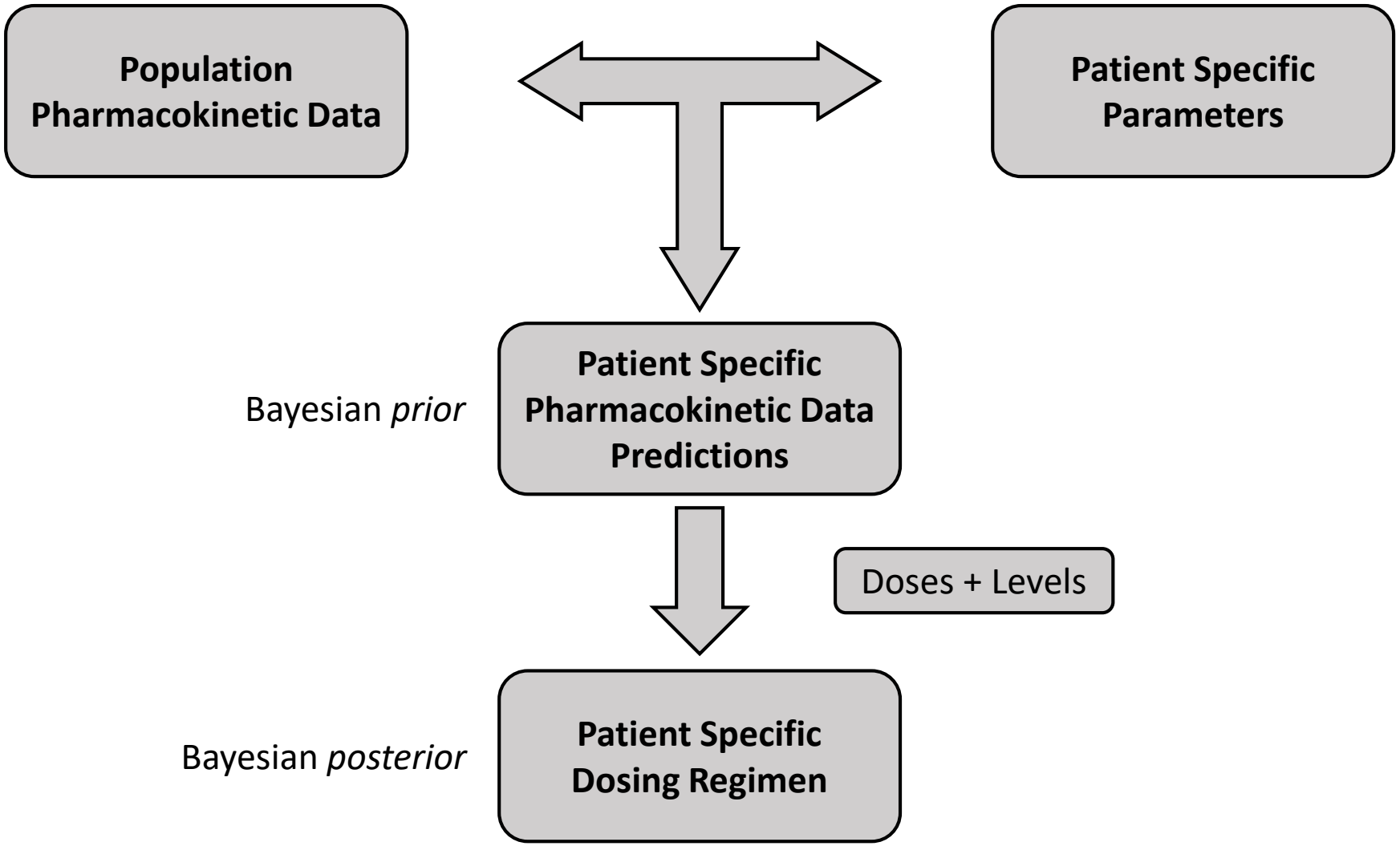
FIG 3 Incidence of vancomycin nephrotoxicity with rising trough levels (8, 22, 36, 50).

1. https://doi.org/10.1128/AAC.01568-12
2. https://doi.org/10.1128/AAC.01653-13
3. https://doi.org/10.1093/ajhp/zxaa036

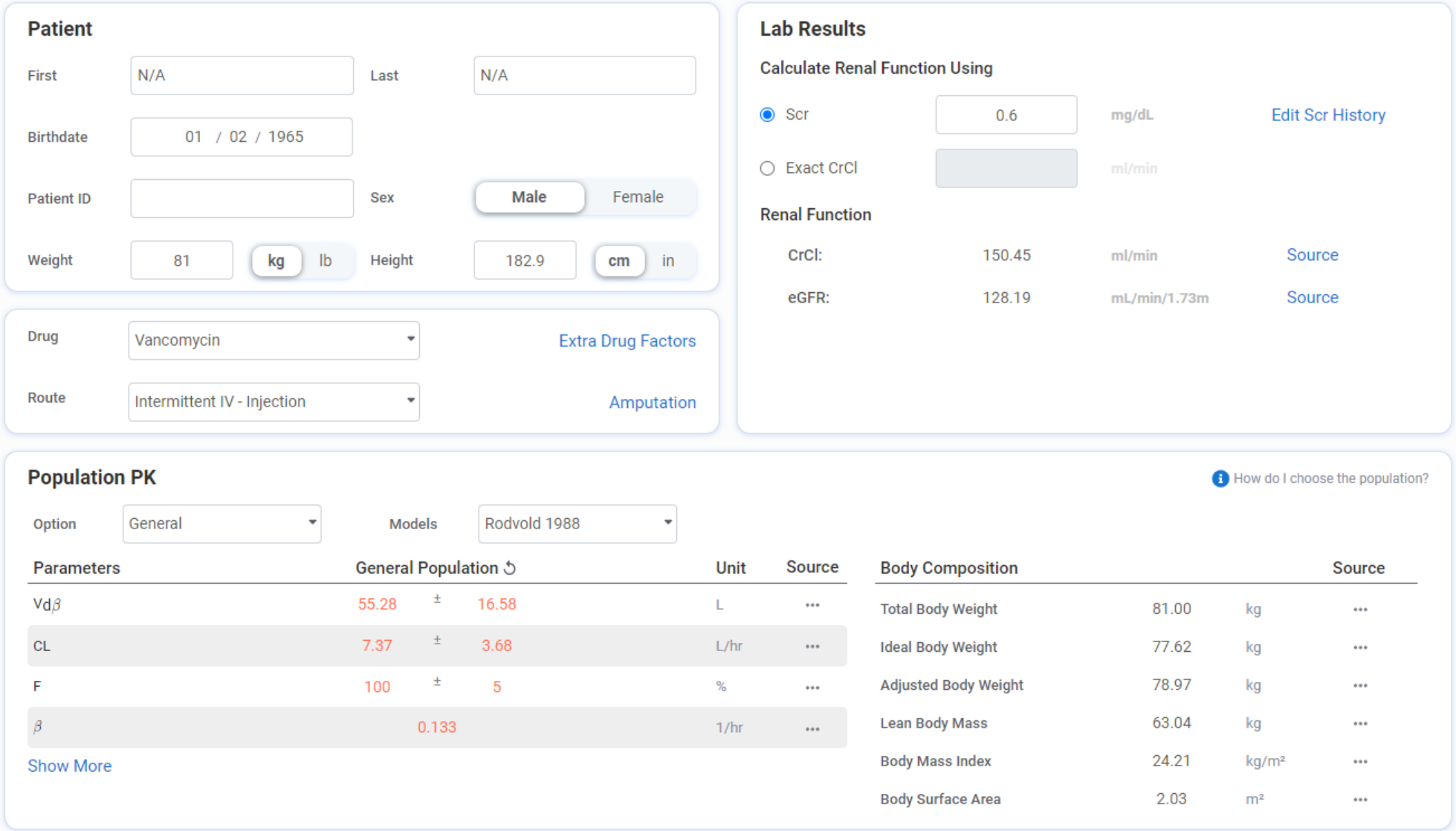
Bayesian Software



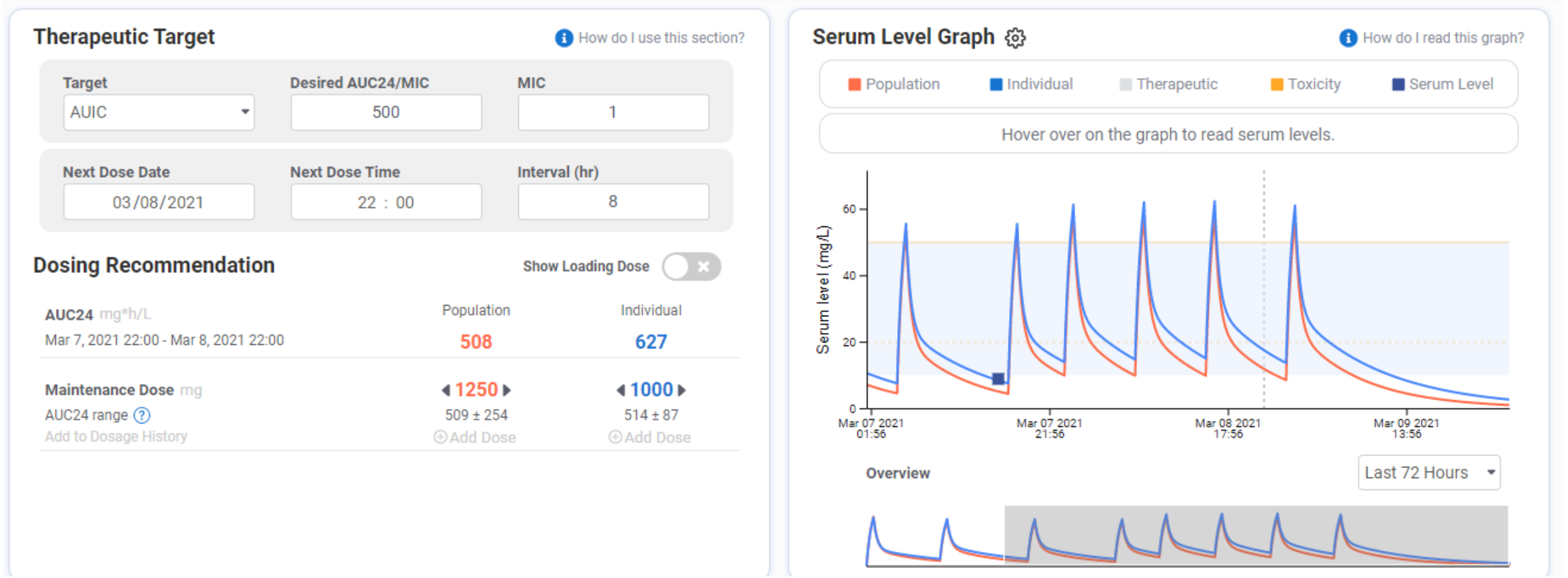
Bayesian Software



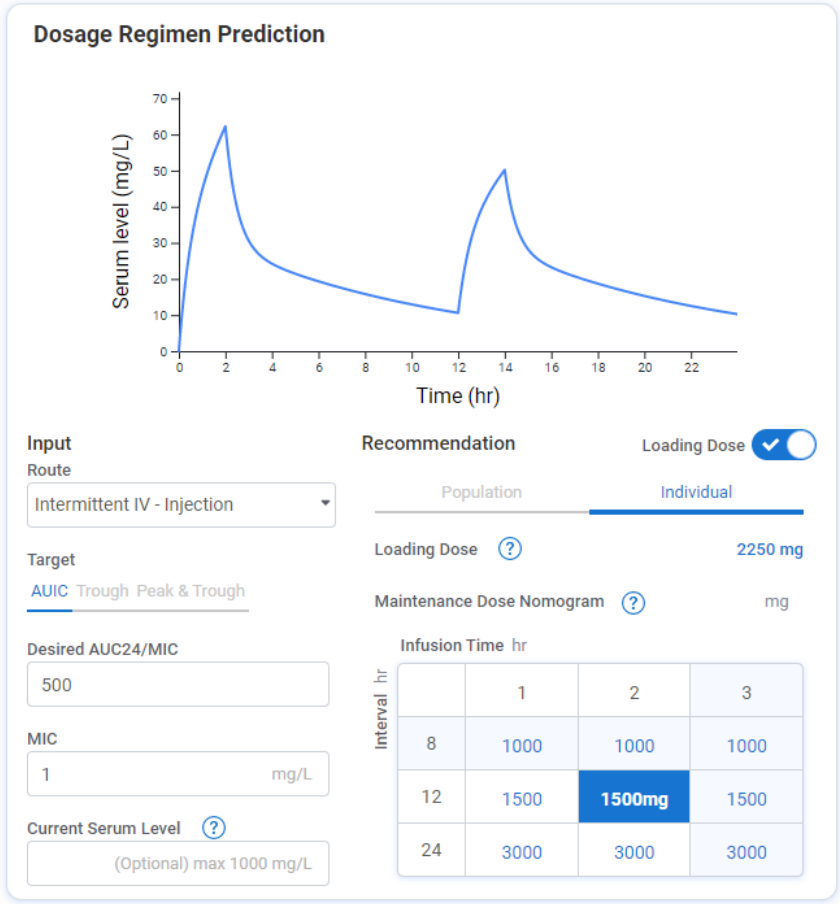
Bayesian Software Example



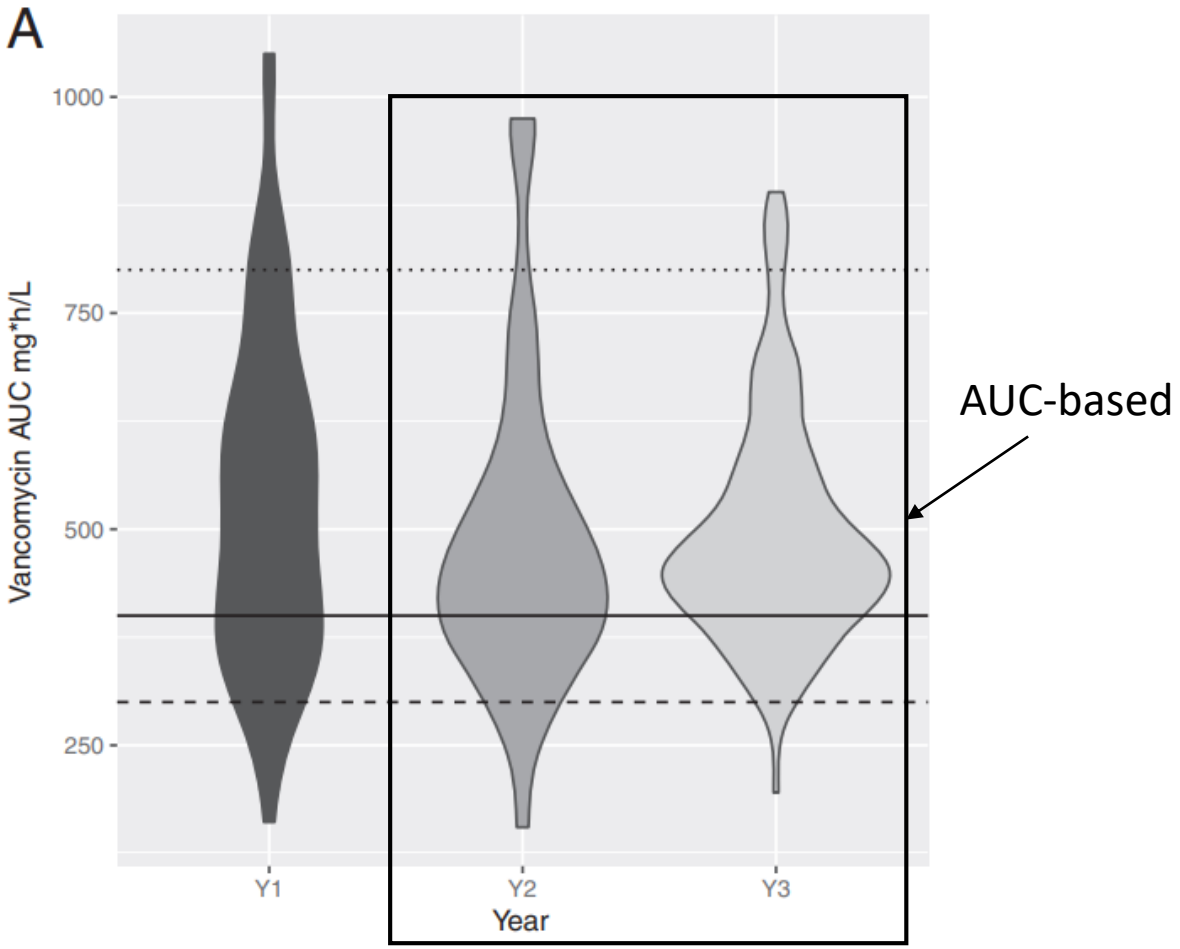
Bayesian Software Example

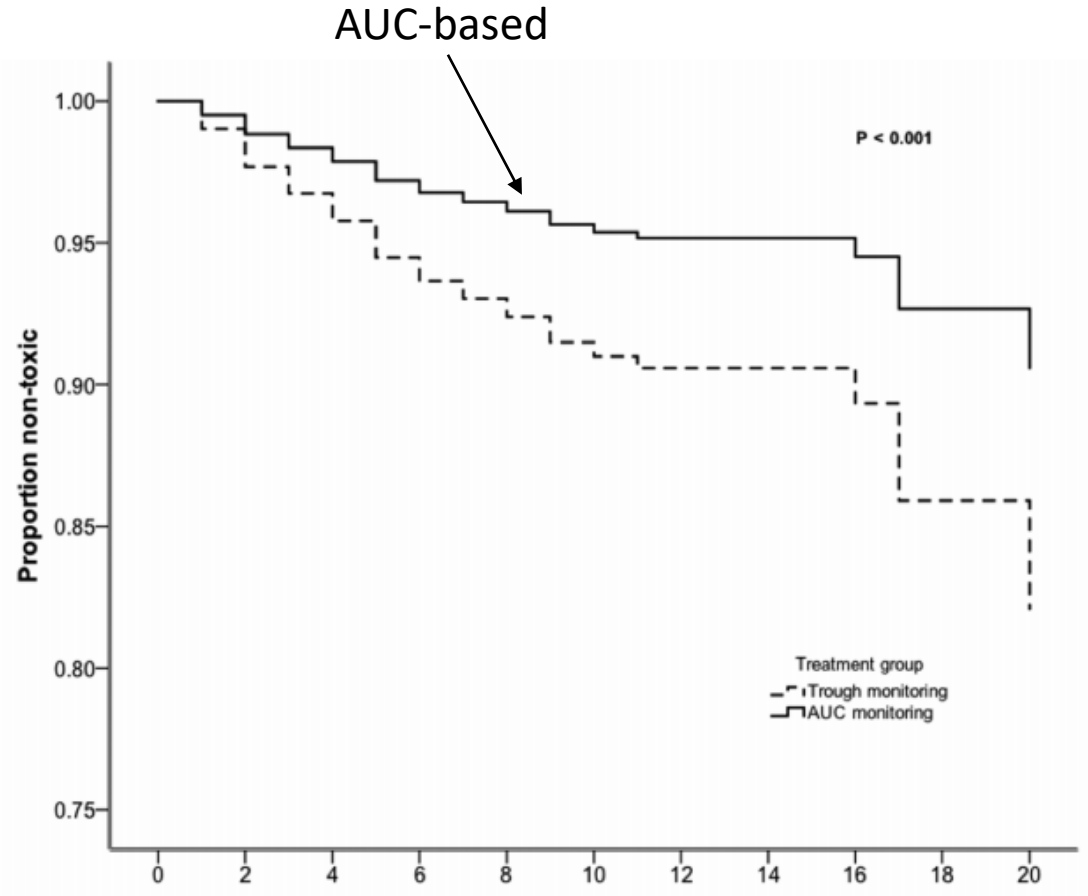


Bayesian Software Example



A Focus on Patient Safety

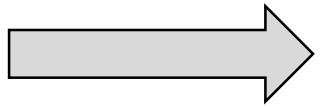




https://doi.org/10.1128/AAC.01293-17
https://doi.org/10.1093/cid/ciz460

New Targets

VANCOMYCIN GOAL TROUGH LEVELS	
Goal Trough 10-15 mg/L	**Goal Trough 15-20 mg/L**
• Skin and soft tissue infections • Urinary tract infections • Febrile neutropenia (empiric) • Coagulase-negative staphylococci (e.g. *S.epidermidis, S. hominis, etc.*) ◦ Excluding sites with limited drug penetration (CNS, osteomyelitis, endocarditis)	**Serious** infections caused by ***S. aureus*** **(MRSA)** • Central nervous system (CNS) • Bloodstream infection • Endovascular (endocarditis) • Pneumonia (health-care associated) • Osteomyelitis • Septic joint (+prosthetic joints)



VANCOMYCIN GOAL TROUGH LEVELS	
Goal AUC 400-600	
• Skin and soft tissue infections • Urinary tract infections • Febrile neutropenia (empiric) • Coagulase-negative staphylococci (e.g. *S.epidermidis, S. hominis, etc.*) ◦ Excluding sites with limited drug penetration (CNS, osteomyelitis, endocarditis)	**Serious** infections caused by ***S. aureus*** **(MRSA)** • Central nervous system (CNS) • Bloodstream infection • Endovascular (endocarditis) • Pneumonia (health-care associated) • Osteomyelitis • Septic joint (+prosthetic joints)

Exceptions to AUC-based monitoring:

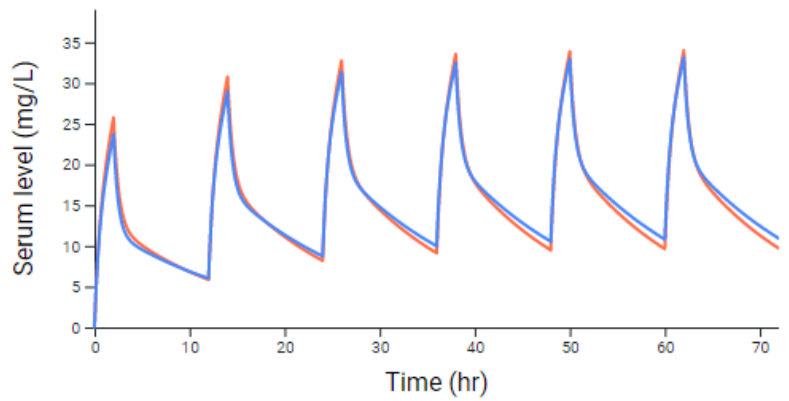
- Unstable renal function
- Hemodialysis

Transitioning to Outpatient

- Situation/Background:
  - Inpatient monitoring will be AUC-based, but home health companies might not universally have access to AUC-based dosing
- Assessment:
  - An integrative approach should be used to bridge traditional monitoring targets to AUC-based targets for discharge plans
- Recommendation:
  - Patient-specific trough targets (which correlate to target AUCs) can be generated via Bayesian calculator prior to discharge for instruction to home health
  - ID pharmacy/rounding pharmacy can help facilitate this if contacted prior to discharge

Real Patient Example

Serum Concentration Prediction



Input

Route: Intermittent IV - Injection

Dose: 750 mg

Interval: 12 hr

Infusion Time: 2 hr

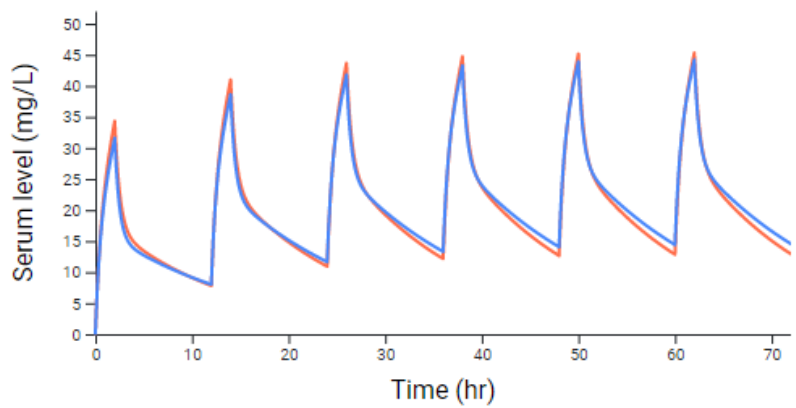
MIC: 1 mg/L

Prediction

	Population	Individual
Peak (?) mg/L	21.05	21.28
Trough mg/L	9.73	11.01
Average Concentration mg/L	17.00	17.72
AUC24 hr*mg/L	407.94	425.17
AUC24/MIC	407.94	425.17

Show More

Serum Concentration Prediction



Input

Route: Intermittent IV - Injection

Dose: 1000 mg

Interval: 12 hr

Infusion Time: 2 hr

MIC: 1 mg/L

Prediction

	Population	Individual
Peak (?) mg/L	28.07	28.37
Trough mg/L	12.97	14.67
Average Concentration mg/L	22.66	23.62
AUC24 hr*mg/L	543.92	566.89
AUC24/MIC	543.92	566.89

Show More

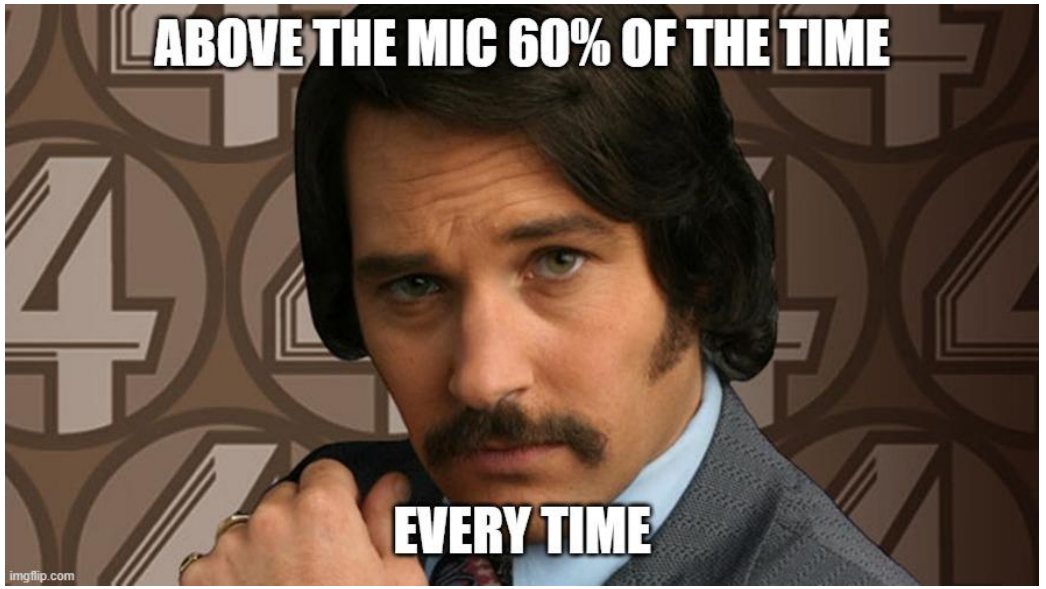
Vancomycin AUC Summary

- Transition to AUC-based monitoring via Bayesian software will:
  - Provide lower vancomycin exposure → lower toxicity risk
  - Maintain therapeutic targets (AUC/MIC 400-600 mg*h/L)
  - Decrease time to effective monitoring/dose-adjustment

Go-Live:

Anticipated Q3 2021

Currently performing on a case-by-case basis



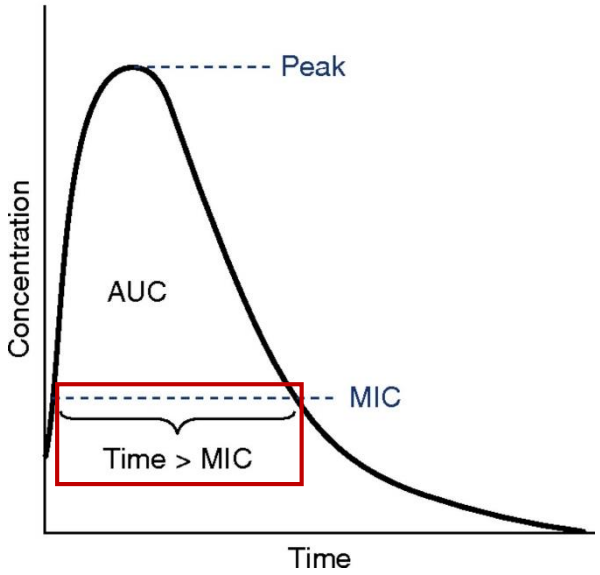
Beta-Lactam Dose Optimization

Strategies to improve pharmacodynamics effects of beta-lactams and clinical outcomes

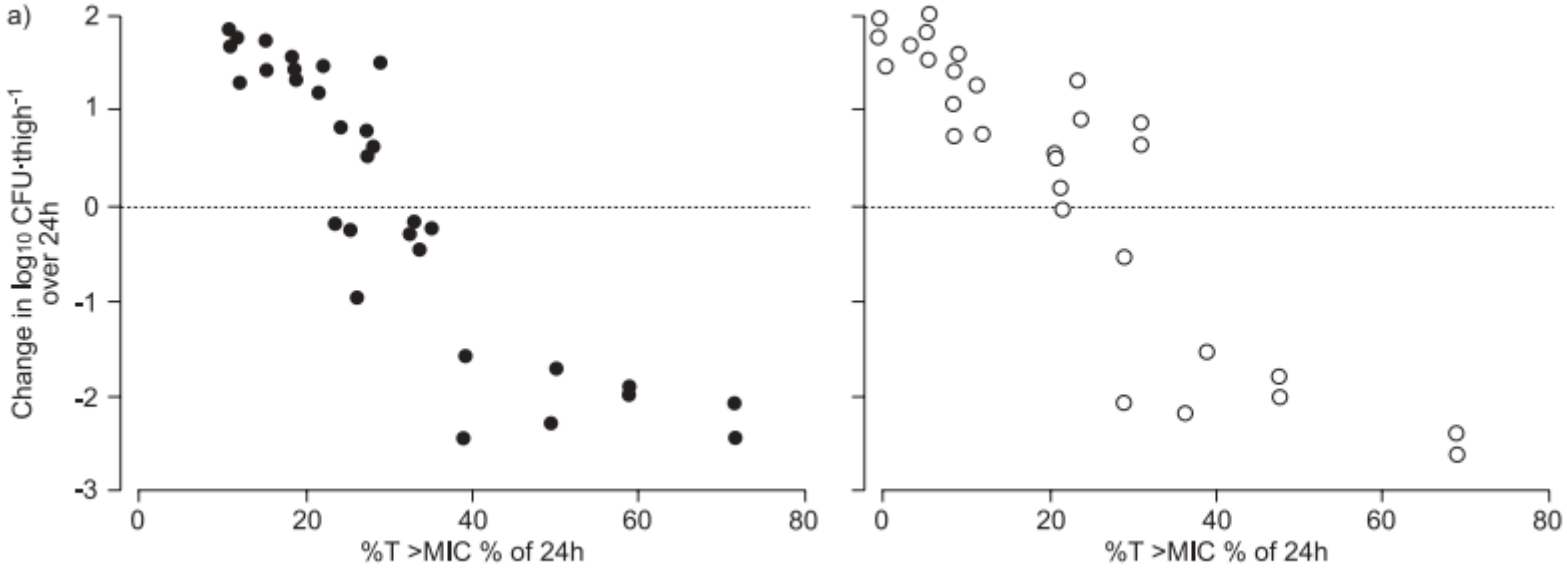
Background – Pharmacokinetics Part 2

Antibiotics fall into three major pharmacokinetic categories:

- Peak-dependent (aminoglycosides)
- **Time-dependent (beta-lactams)**
- AUC-dependent (vancomycin)



E. coli ***Pseudomonas aeruginosa***



*Data shown for piperacillin-tazobactam

https://cjasn.asnjournals.org/content/14/7/1080/tab-figures-data
https://doi.org/10.1183/09059180.00010304

Dose Optimization for Beta-Lactams

- Problem: Resistance rates high at UCLA
  - ICU ESBL – 29.5%; *Pseudomonas* 1st-line resistance ~30%
- Solution:
  - Increase dosing to packaged labeled dosing + PK/PD based dosing
  - **Prolonged infusions->mortality benefit in sepsis/critically ill**
    - Already doing this for piperacillin-tazobactam!
- Order panels currently being built – Go-live = Mid-April
- Upcoming educational talks

https://doi.org/10.1016/S1473-3099(17)30615-1
https://doi.org/10.1093/cid/cis857
https://doi.org/10.1086/510590

Clinical Outcomes Data

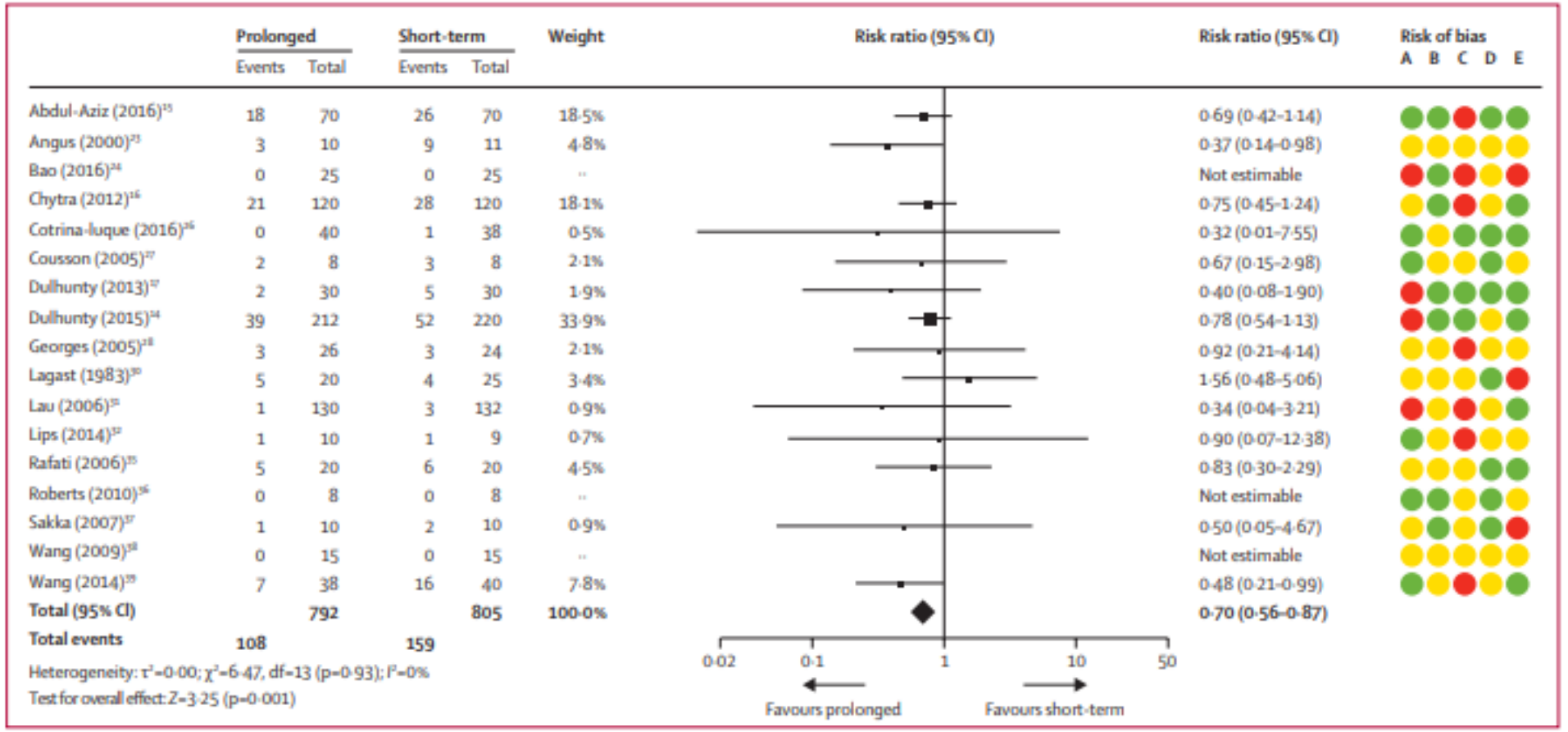


Figure 2: **Forest plot of mortality among patients treated with prolonged versus short-term infusion of antipseudomonal antibiotics**
The areas of squares are proportional to the weight given to each study. Risk ratios are the centres of each square. df=degrees of freedom.

Meta-analysis of 14 RCTs (n= 1,597); Anti-pseudomonal beta-lactams in patients with sepsis

"Prolonged infusion was associated with lower all-cause mortality than short-term infusion **(RR 0·70, 95% CI 0·56–0·87)**."

https://doi.org/10.1016/S1473-3099(17)30615-1

Piperacillin-tazobactam

Indication	Old Dose	New Dose	Reference
CF	LD, 4.5g IV Q6 over 3h OR 18g continuous infusion	No change	https://doi.org/10.1093/jac/dkt300
Obesity	LD, 4.5 IV Q8 over 4h	No change	https://doi.org/10.1002/phar.1324
Neutropenic fever, critically ill/ICU, *PSEUDOMONAS*	LD, 3.375g IV Q8 over 4h	**LD, 4.5g IV Q8 over 4h**	https://doi.org/10.3390/antibiotics4040643 https://doi.org/10.1177/0897190016684453
Non-severe infections	LD, 3.375 IV Q8 over 4h	No change	https://doi.org/10.1086/510590
Renal Impairment			
CrCl ≤20	LD, 3.375 IV Q12 over 4h	LD, 3.375-4.5g* IV Q12 over 4h	https://doi.org/10.1177/0897190016684453
IHD	LD, 3.375 IV Q12 over 4h	LD, 3.375-4.5g* IV Q12 over 4h	https://doi.org/10.1177/0897190016684453
CVVHD	LD, 3.375 IV Q8 over 4h	Flow Rate 1-4 L/hr: LD, 4.5g IV Q8 over 4h Flow Rate>4L/hr: Call ID Pharmacy; TDM Suggested	https://doi.org/10.2215/CJN.10260915 Uptodate

*Higher dose is recommended for obesity, severe infections (critically ill or neutropenic fever), or MIC > 8
LD = loading dose

Meropenem

Indication	Old Dose	New Dose	Reference
CNS, Cystic Fibrosis, MIC ≥ 2	2g IV Q8	LD 2g over 30min, then 2g IV Q8 **infused over 4h**	https://doi.org/10.1016/j.jcf.2016.04.002 https://doi.org/10.1016/S1473-3099(17)30615-1
All other indications	1g IV Q8	LD 1g over 30min, then 1g IV Q8 **infused over 4h**	https://doi.org/10.1186/s40560-020-00442-7 https://doi.org/10.3390/antibiotics4040643 https://doi.org/10.1128/aac.49.1.461-463.2005
		Renal Impairment	
>25 CrCl ≤50 ml/min	1-2g IV Q8	LD 1-2g* over 30min, then 1-2g* IV Q12 **infused over 4h**	https://doi.org/10.10mrdav16/S1473-3099(17)30615-1
10 ≤CrCl ≤ 25 mL/min	0.5-1g IV Q12	LD 0.5-1g* over 30min, then 0.5-1g* IV Q12 **infused over 4h**	https://doi.org/10.1016/S1473-3099(17)30615-1
CrCl <10 ml/min	0.5-1g IV Q24	LD 0.5-1g* over 30min, then 0.5-1g* IV Q24 **infused over 4h**	https://doi.org/10.1016/S1473-3099(17)30615-1
IHD	0.5g IV Q24	LD 0.5-1g* over 30min, then 0.5-1g* IV Q24 **infused over 4h**	UptoDate https://doi.org/10.1016/S1473-3099(17)30615-1
CVVHD	1-2g IV Q8-12 (Q8 is recommended for rates exceeding 2L/H)	Flow Rate ≤ 2L/H: LD 1-2g* over 30min, then 1-2g* IV Q12 **over 4h** Flow Rate 2-4L/H: LD 1-2g* over 30min, then 1-2g* IV Q8h **over 4h** Flow Rate >4L/H: Call ID Pharmacy; TDM Suggested	

*Higher dose is recommended for CNS, cystic fibrosis, and MIC 2 or greater
LD = Loading dose

Cefepime

Indication	Old Dose	New Dose	Reference
CNS, critically ill, neutropenic fever, *Pseudomonas, Enterobacterales* MIC > 2,	2g IV Q8	LD 2g over 30min, then 2g IV Q8 **infused over 4h**	https://doi.org/10.1016/S1473-3099(17)30615-1 https://doi.org/10.1093/cid/cis916
All other indications	1g IV Q8	LD 1g over 30min, then 1g IV Q8 **infused over 4h**[++]	https://doi.org/10.1016/S1473-3099(17)30615-1
Renal Impairment			
>30 CrCl ≤, ml/min	1-2g IV Q8	LD 1-2g* over 30min, then 1-2g* IV Q12 **infused over 4h**	UptoDate https://doi.org/10.1016/S1473-3099(17)30615-1
11 ≤CrCl ≤ 29 mL/min	1-2g IV Q12-Q24	LD 0.5-1g* over 30min, then 0.5-1g* IV Q12 **infused over 4h**	
CrCl <11 ml/min	0.5-1g IV Q24	LD 0.5-1g* over 30min, then 0.5-1g* IV Q24 **infused over 4h**	
IHD	1g IV Q24	LD 0.5-1g* over 30min, then 0.5-1g* IV Q24 **infused over 4h**	UptoDate https://doi.org/10.1016/S1473-3099(17)30615-1
CVVHD	1-2g IV Q8-12 (Q8 is recommended for rates exceeding 2L/H)	Flow Rate ≤ 2L/H: LD 2g over 30min, then 2g IV Q12 **over 4h** Flow Rate 2-4L/H: LD 2g over 30min, then 2g IV Q8h **over 4h** Flow Rate >4L/H: Call ID Pharmacy; TDM Suggested	

*Higher dosing for CNS, Enterobacterales MIC > 2, critically ill, neutropenia *Pseudomonas*
[++]Can consider 2g Q12h for dosing convenience
LD = Loading dose

Considerations

- Line access
- Patient preference
- Y-site Compatibility
  - Call pharmacy

IV (Y-site) Incompatibility Data	
Known Incompatible Agents	
AVOID administering with cefepime	
Acyclovir	Magnesium sulfate
Liposomal amphotericin B	Metoclopramide HCl
Caspofungin	Midazolam HCl
Chlorpromazine HCl	Ondansetron HCl
Ciprofloxacin	Pantoprazole sodium
Diazepam	Promethazine HCl
Diltiazem HCl	Tacrolimus
Diphenhydramine HCl	Voriconazole
Famotidine	Dobutamine HCl**
Ganciclovir	Dopamine HCl**
Hydroxyzine HCl	Mycophenolate mofetil HCl**
Hydroxyzine Hcl	Nicardipine HCl**
Isavuconazonium sulfate	Propofol**
Labetolol	Vancomycin HCl**

**Uncertain compatibility, depends on concentration and formulation. For additional information or clarification, call pharmacy.

IV (Y-site) Incompatibility Data	
Known Incompatible Agents	
AVOID administering with meropenem	
Amiodarone HCl	Nicardipine HCl
Clindamycin	Phenytoin sodium
Ciprofloxacin	Acyclovir
Diazepam	Liposomal amphotericin B**
Hydralazine HCl	Doxycycline hyclate**
Isavuconazonium sulfate	Ondansetron**
Ketamine	Pantoprazole**
Mycophenolate mofetil HCl	Propofol**

**Uncertain compatibility, depends on concentration and formulation. For additional information or clarification, call pharmacy.

Prolonged Infusion Summary

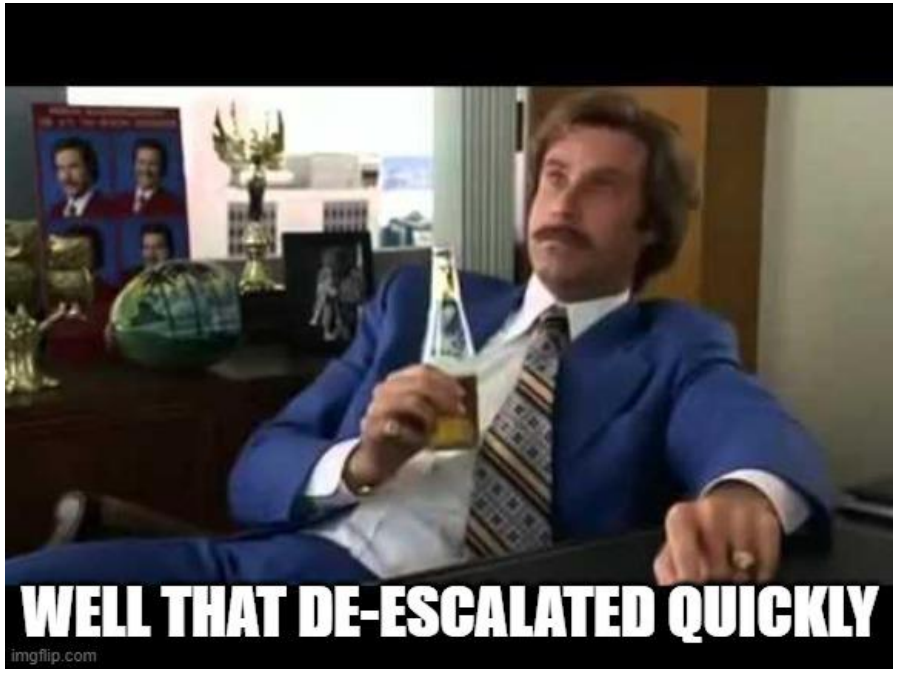
- Lower all-cause mortality in sepsis has been observed with extended infusion beta-lactams
  - Biologically plausible (pharmacodynamics)
  - 4-hr infusion will be the new standard at UCLA
- Can be ordered via order panels (similar to piperacillin-tazobactam)
- Consider
  - Line access of patient and concomitant medications
  - Ask a pharmacist!

Go-Live:

4/19/2021 meropenem

5/3/2021 pip-tazo, cefepime

Currently performing on a case-by-case basis



Antibiotic Ladders

To guide escalation and de-escalation of antibiotics

2/7/2021 12:36 PM

Specimen Information: Clean Catch, Midstream; Urine

Bacterial Culture >100,000 CFU/mL Escherichia coli !
Urine Susceptibility Setup Date: 02/06/2021

Susceptibility

	Escherichia coli MIC (MCG/ML)	
Ampicillin	>=32	**Resistant**
Ceftriaxone	>=64	**Resistant**
Ciprofloxacin	>=4	**Resistant**
Ertapenem	<=0.12	**Susceptible**
Gentamicin	<=1	**Susceptible**
Nitrofurantoin	<=16	**Susceptible**
Oral Cephalosporins	R	**Resistant**
Piperacillin + Tazobactam	64	**Intermediate**
Trimethoprim/Sulfamethoxazole	>=320	**Resistant**

2/8/2021 10:52 AM

Specimen Information: Peripheral Vein; Blood

Bacterial Culture **Klebsiella pneumoniae !!**
Blood Susceptibility Setup Date

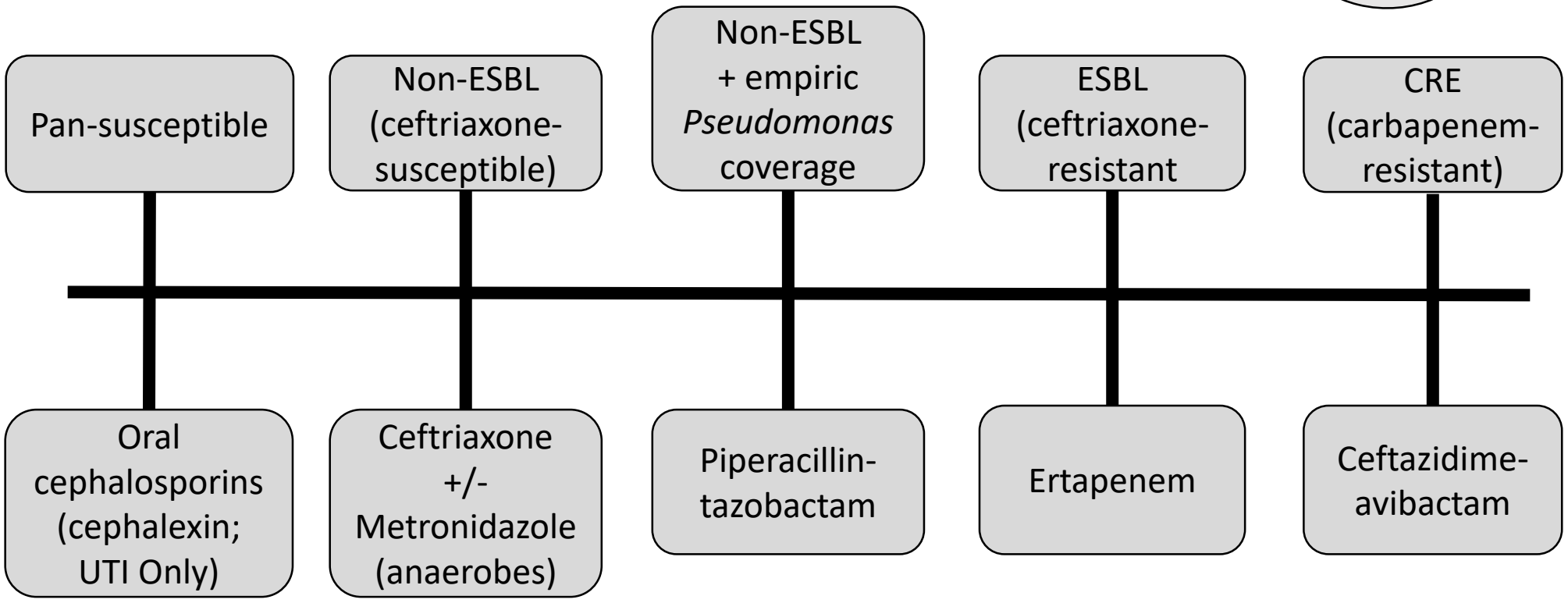
Susceptibility

	Klebsiella pneumoniae MIC (MCG/ML)	
Ceftriaxone	<=1	**Susceptible**
Ciprofloxacin	<=0.25	**Susceptible**
Gentamicin	<=1	**Susceptible**
Piperacillin + Tazobactam	<=8	**Susceptible**
Trimethoprim/Sulfamethoxazole	<=1/20	**Susceptible**

The Antibiotic Ladders

Gram-Negative Enteric organisms:
E. coli
Klebsiella pneumonia
Proteus mirabilis
Common infections:
GI, UTI

ESBL Rates
(*E. coli* + *K. pneumoniae*)
Outpatient/ED – **19%**
Wards – **24%**
ICU – **29.5%**

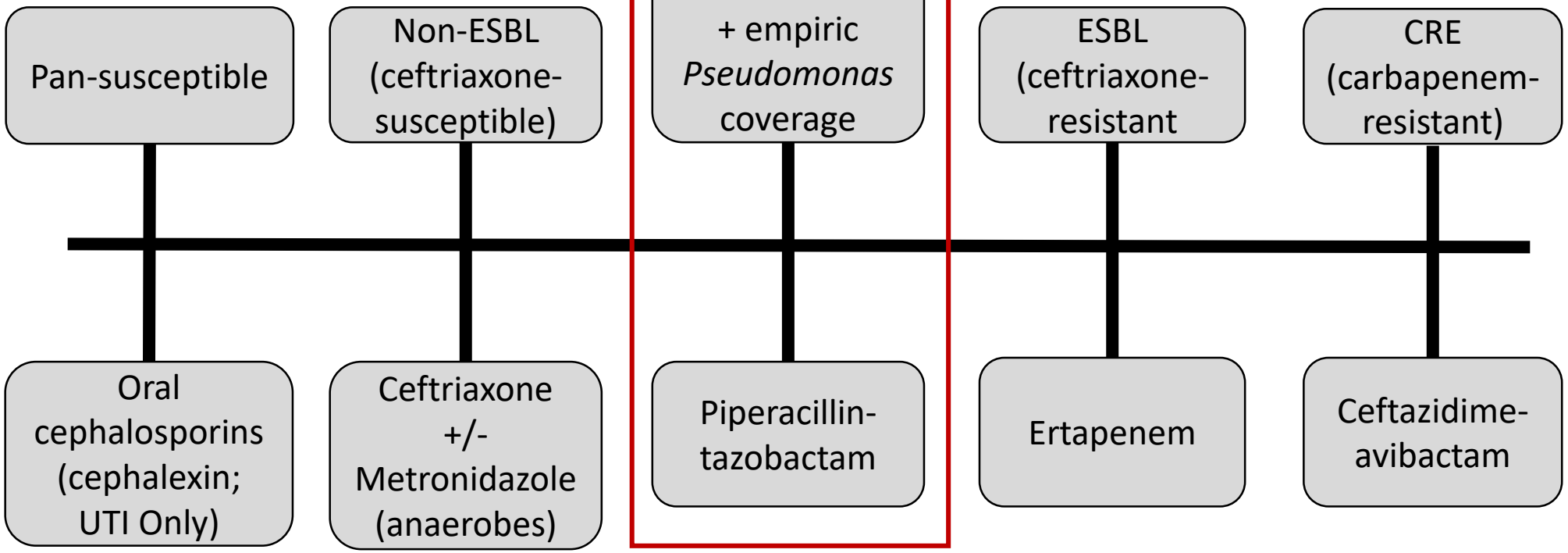


The Antibiotic Ladders

Gram-Negative Enteric organisms:
E. coli
Klebsiella pneumonia
Proteus mirabilis
Common infections:
GI, UTI

Don't get stuck here!
No *Pseudomonas*?
No need for pip-tazo

ESBL Rates
(*E. coli* + *K. pneumoniae*)
Outpatient/ED – **19%**
Wards – **24%**
ICU – **29.5%**

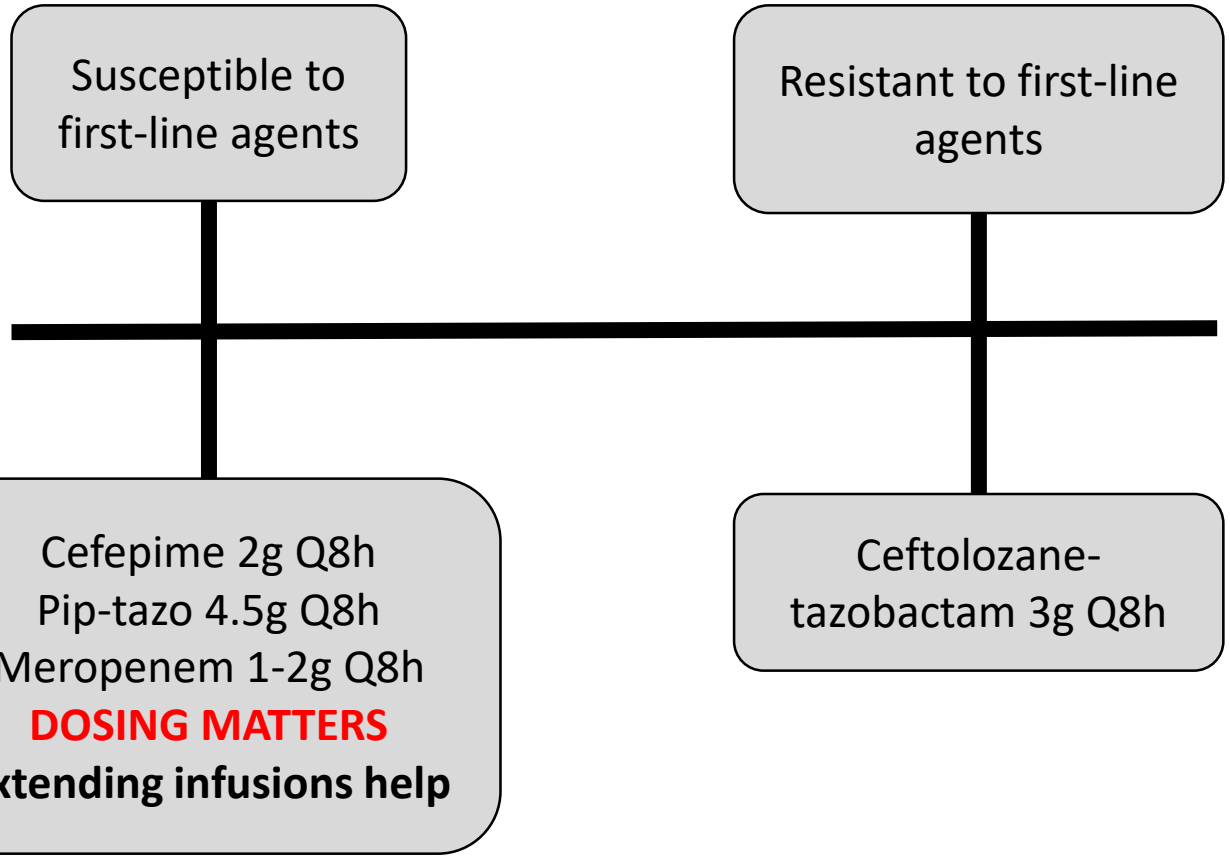


The Antibiotic Ladders

Pseudomonas aeruginosa

Common Infections:
HAP/VAP, CLABSI, hospital-acquired

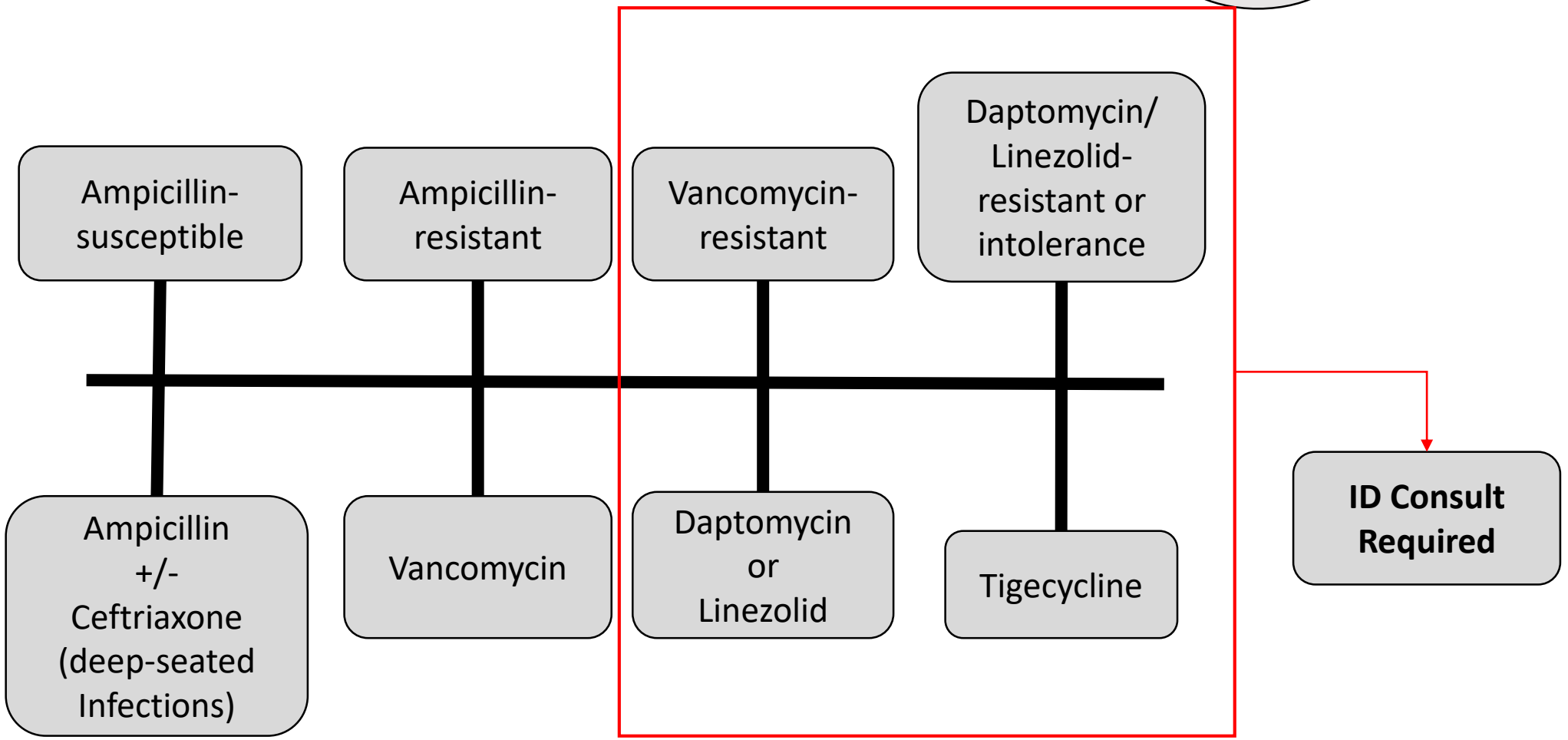
***Pseudomonas* susceptibility (ICU):**
Cefepime – 71%
Pip-tazo – 66%
Meropenem – 69%



The Antibiotic Ladders

Enterococcus faecalis
***Enterococcus faecium* (more resistant)**
Common infections:
Hepatobiliary, GI, CLABSI

Vancomycin-resistance:
E. faecium – **65%**
E. faecalis – **6%**

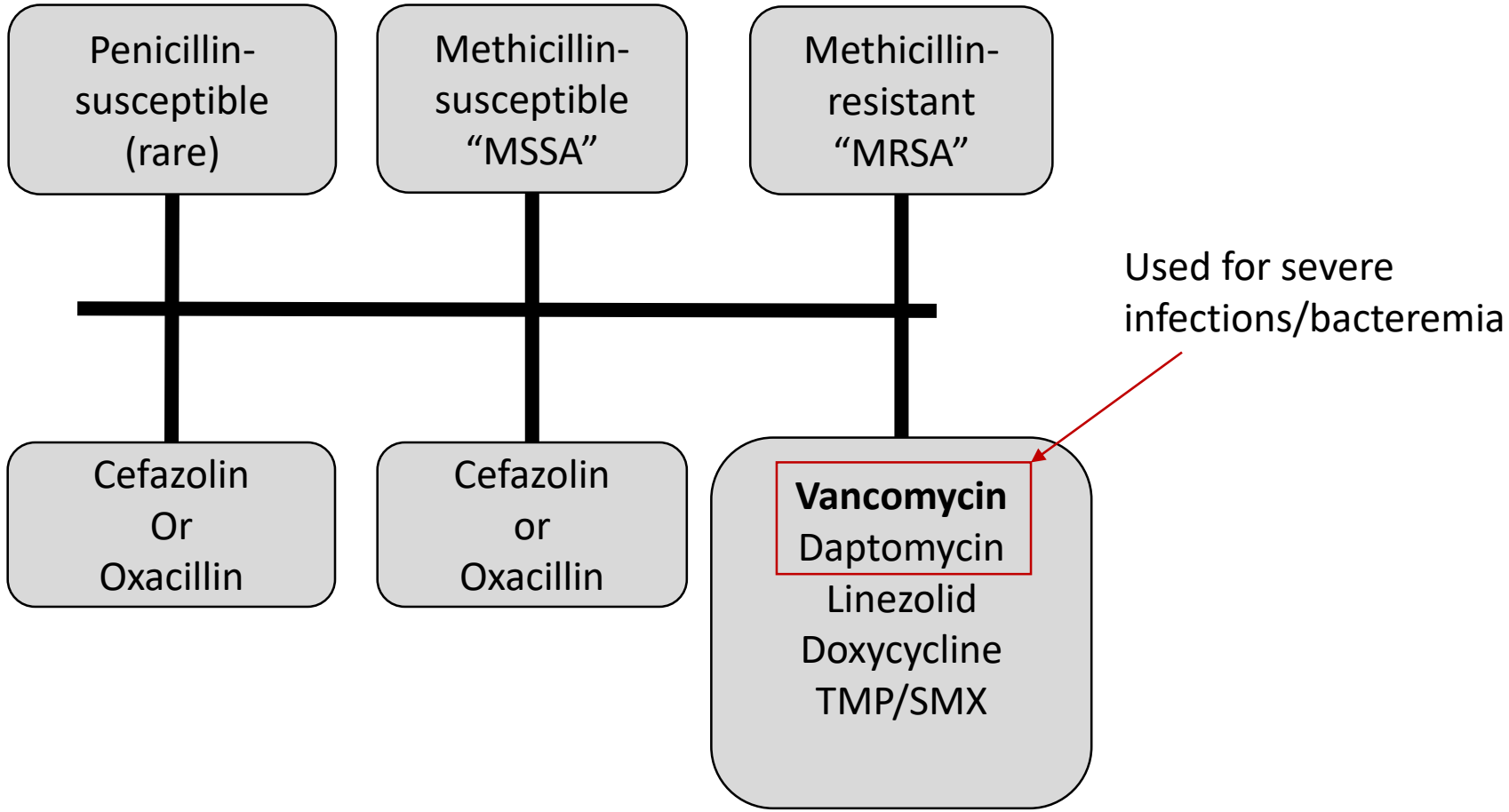


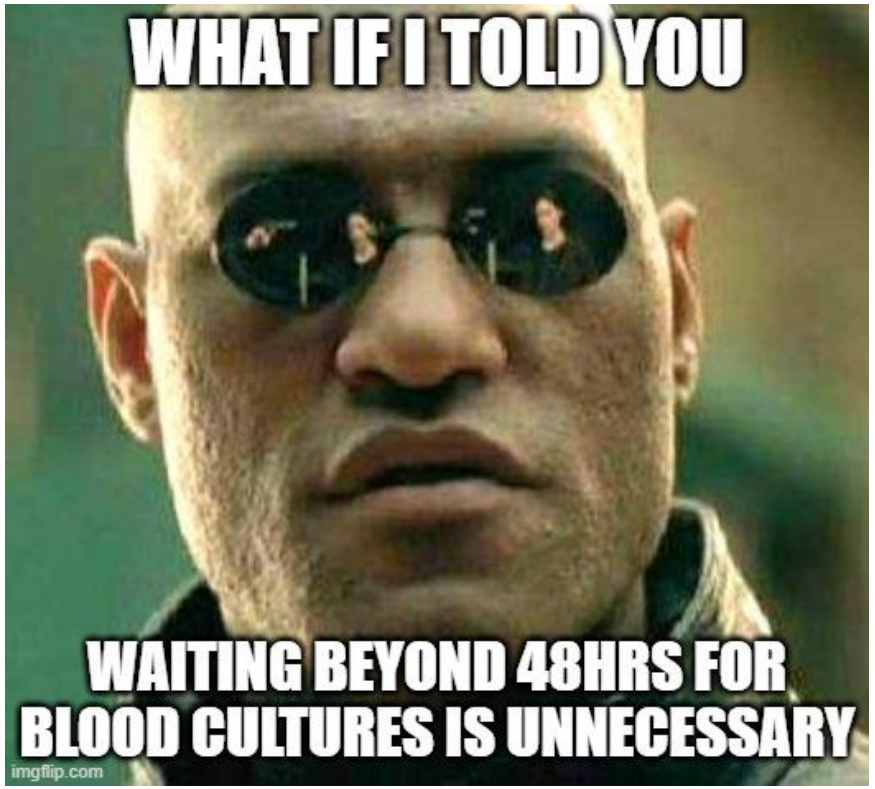
The Antibiotic Ladders

Staphylococcus aureus

Common infections:
Skin/soft tissue, CLABSI, implanted hardware

Methicillin-Resistance:
All – 25%
Ward – 26.3%
ICU – 26.4%





Re-Evaluate at 48 (hours)

Minimal information gained from blood cultures beyond 48 hours

Re-Evaluate at 48 (hours)

"Clinicians should be aware ***that little information is gained from blood cultures by waiting beyond the 48-hour period."***

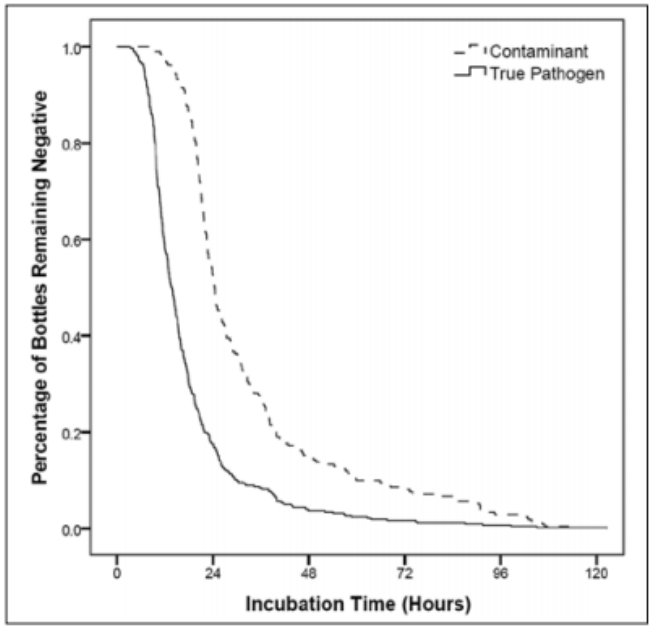


Figure 1. Kaplan-Meier plot of cultures positive for true pathogens and contaminants.

By 48 hours, 98% of aerobic Gram-positive and Gram-negative BSIs and 74% of anaerobic BSIs were detected.

NPV of 48h BCx = 99.8%

DOI: 10.1177/1060028013511229

Re-Evaluate at 48 (hours)

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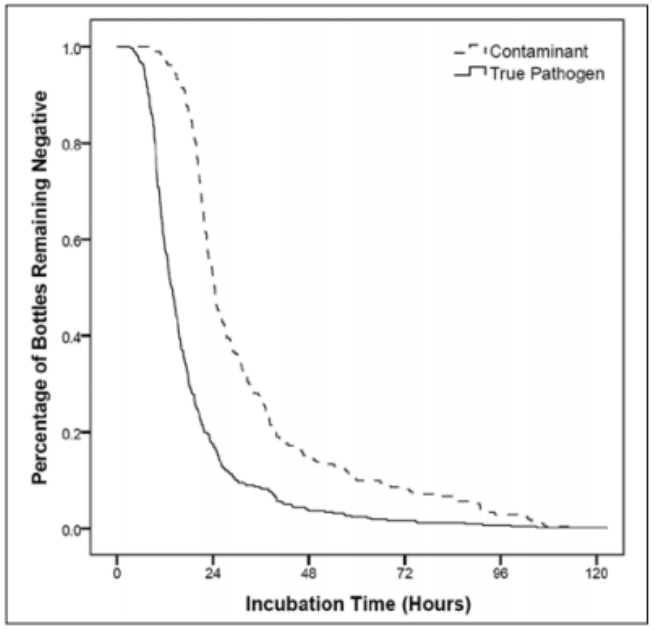
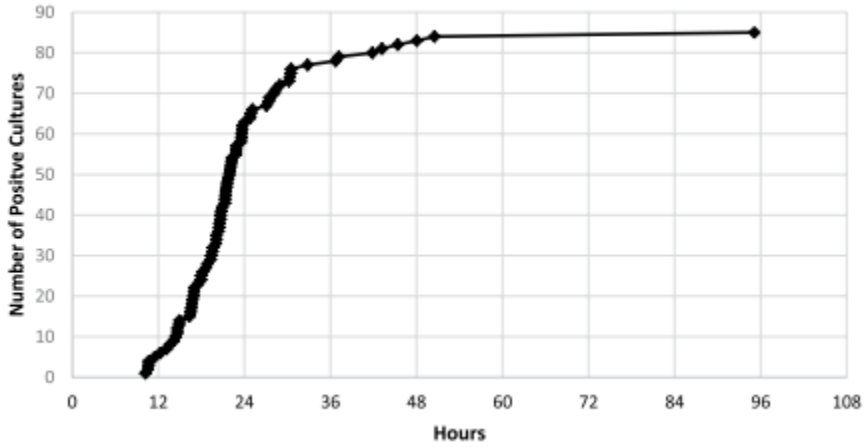


Figure 1. Kaplan-Meier plot of cultures positive for true pathogens and contaminants.



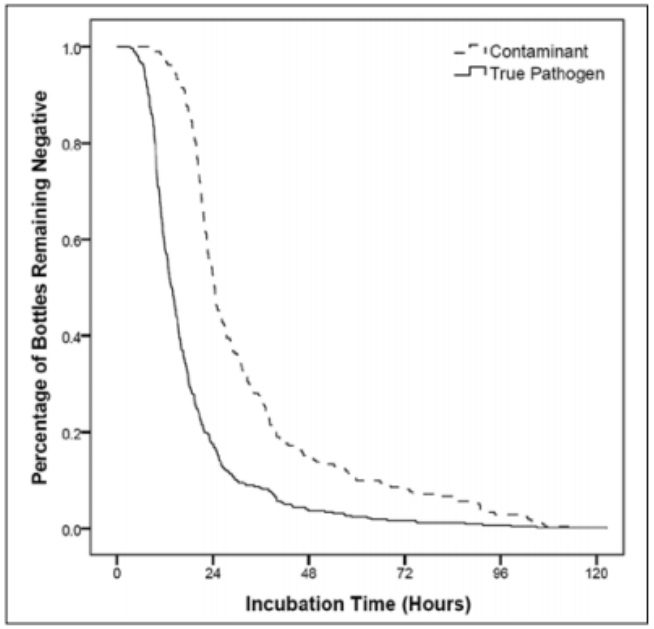
Gram-positive cocci were identified within 48 hours in 97.6% of cases of MRSA bacteremia.

These findings may inform the timing of discontinuation of empirical vancomycin among critically ill adults**.**

DOI: 10.1177/1060028019877937

Re-Evaluate at 48 (hours)

"Clinicians should be aware ***that little information is gained from blood cultures by waiting beyond the 48-hour period."***



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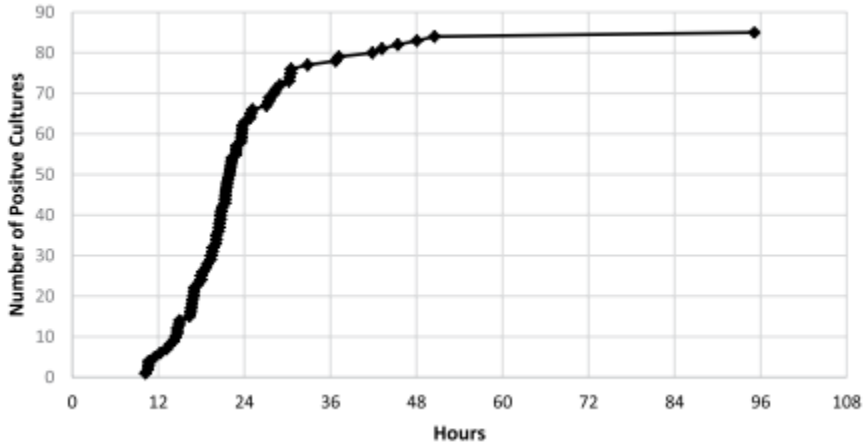
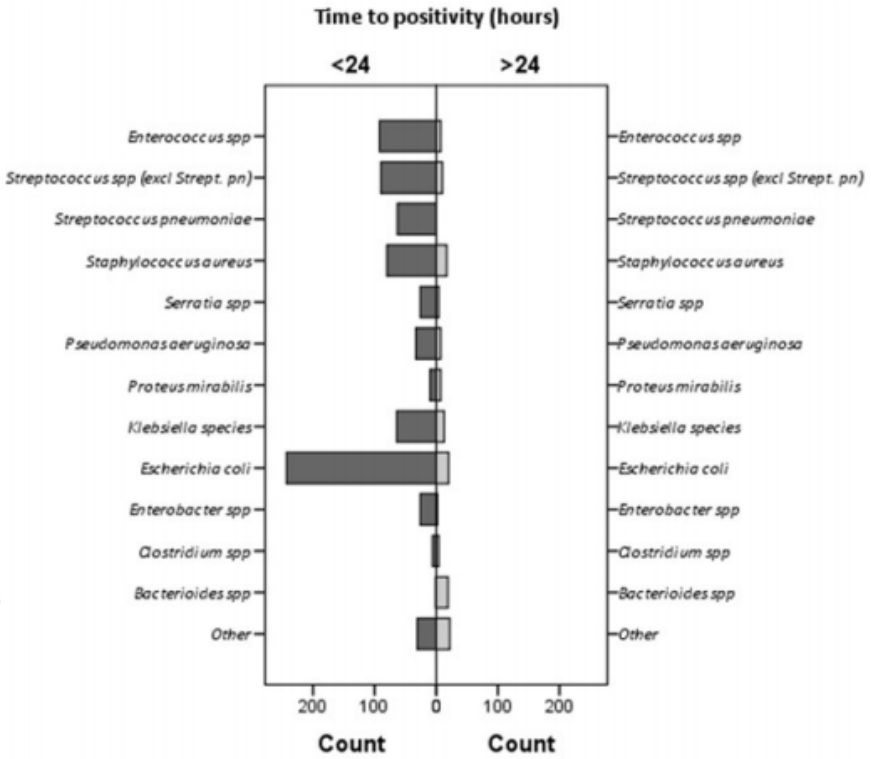




The probability of positivity when blood cultures are negative after 24 hours is very low. Postponing reevaluation of the differential diagnosis, solely for pending blood culture results, is not rational at this time point. **The source of infection was not a predictor of short versus prolonged TTP.**

This probability is further decreased after 48 hours.

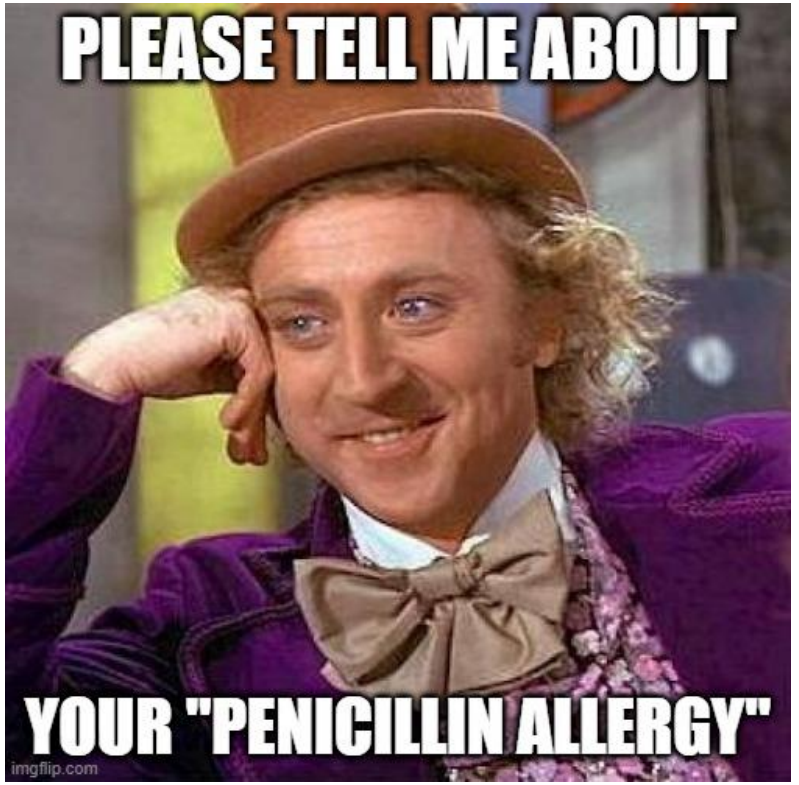
DOI: 10.1371/journal.pone.0208819

Re-Evaluate at 48 (hours) – Take Home

- Blood cultures that are negative at 48h are highly likely to remain negative
- Empiric anti-MRSA antibiotics (e.g. vancomycin) can be discontinued if no MRSA isolated if suspicion is low in clinically stable patients
  - For pneumonia, MRSA nares has high negative predictive value
- **If no resistant organisms are recovered, de-escalation should be considered in clinically stable patients**
  - See antibiotic ladders for appropriate de-escalation choices

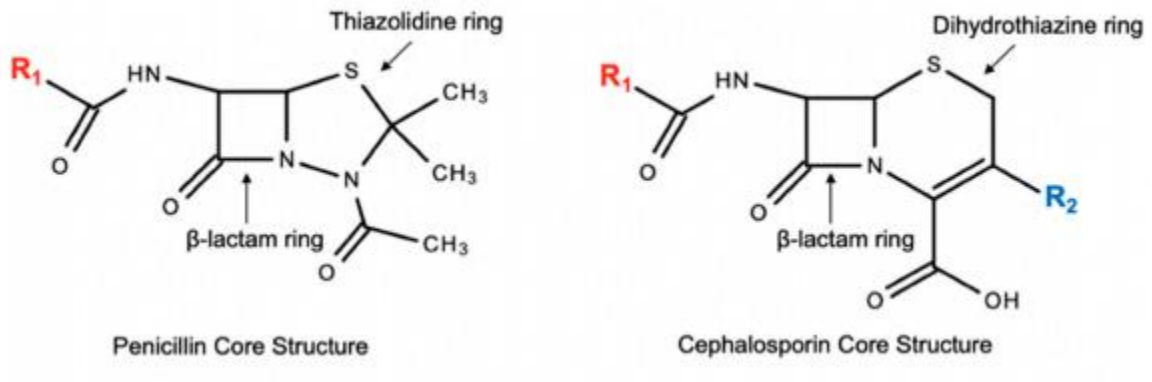
Beta-Lactam Allergies

Incidence and cross-reactivity mitigation



Background – Beta-Lactam Allergies

- 8% of U.S. population has a reported penicillin allergy
  - Only 1 in 20 patients with a reported penicillin allergy have an acute reaction to an oral challenge test (gold standard)
- 1% carries history of cephalosporin allergy
  - Previous belief of high cross-reactivity of cephalosporin and penicillin allergies
  - Now known to be side-chain driven



https://doi.org/10.1007/s11882-014-0476-y
https://doi.org/10.3390/pharmacy7030103

Side Chain Similarities

Beta-lactam Antibiotic Cross-Allergy Chart

Beta-lactams	AMOXICILLIN*	AMPICILLIN	CLOXACILLIN	PENICILLIN	PIPERACILLIN*	CEFADROXIL	CEFAZOLIN	CEPHALEXIN	CEFOXITIN	CEFPROZIL	CEFUROXIME	CEFIXIME	CEFOTAXIME	CEFTAZIDIME	CEFTRIAXONE	CEFEPIME	ERTAPENEM	IMIPENEM	MEROPENEM
AMOXICILLIN*		X^1	X^5	X^4	X^3	X^1	✓	X^1	✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓	✓
AMPICILLIN	X^1		X^5	X^4	X^3	X^2	✓	X^2	✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓	✓
CLOXACILLIN	X^5	X^5		X^5	X^5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X^4	X^4	X^5		X^5	✓	✓	✓	X^3	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X^3	X^3	X^5	X^5		X^3	✓	X^3	✓	X^3	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X^1	X^2	✓	✓	X^3		✓	X^1	✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X^1	X^2	✓	✓	X^3	X^1	✓		✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFOXITIN	✓	✓	✓	X^3	✓	✓	✓	✓		✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓
CEFPROZIL	X^2	X^2	✓	✓	X^3	X^2	✓	X^2	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	✓	✓	X^2	✓		X^3	X^1	X^3	X^1	X^2	✓	✓	✓
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^3		X^3	X^3	X^3	X^3	✓	✓	✓
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^1	X^3		X^3	X^1	X^1	✓	✓	✓
CEFTAZIDIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^3	X^3	X^3		X^3	X^3	✓	✓	✓
CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^1	X^3	X^1	X^3		X^1	✓	✓	✓
CEFEPIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^2	X^3	X^1	X^3	X^1		✓	✓	✓
ERTAPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		X^5	X^5
IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^5		X^5
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^5	X^5	

* Also applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)

AVOID ALL beta-lactam antibiotics if:

- ICU admission related to allergy
- Delayed beta-lactam antibiotic allergy causing:
  - interstitial nephritis
  - hepatitis
  - hemolytic anemia
- Delayed severe skin allergic reactions:
  - Stevens-Johnson syndrome
  - toxic epidermal necrolysis
  - exfoliative dermatitis
  - acute generalized exanthematous pustulosis (AGEP)
  - drug reaction with eosinophilia and systemic symptoms (DRESS)

LEGEND:	
Penicillins	
1st Generation Cephalosporins	
2nd Generation Cephalosporins	
3rd Generation Cephalosporins	
4th Generation Cephalosporins	
Carbapenems	
✓	Different structure. CONSIDERED SAFE TO PRESCRIBE
Reaction likely based on side chain:	
X^1	Same side chain - clinical evidence of cross reaction. DO NOT PRESCRIBE
X^2	Same side chain - Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE
X^3	Similar side chain - Potential for cross reaction. DO NOT PRESCRIBE
Reaction likely based on Beta-lactam ring	
X^4	Clinical evidence of cross reaction. DO NOT PRESCRIBE
X^5	Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE

https://www.bcpharmacists.org/readlinks/guest-post-beta-lactam-allergy-benefits-de-labeling-can-be-achieved-safely

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CLOXACILLIN	X^5	X^5		X^5	X^5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PENICILLIN	X^4	X^4	X^5		X^5	✓	✓	✓	X^3	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
PIPERACILLIN*	X^3	X^3	X^5	X^5		X^3	✓	X^3	✓	X^3	✓	✓	✓	✓	✓	✓	✓	✓	✓
CEFADROXIL	X^1	X^2	✓	✓	X^3		✓	X^1	✓	X^2	✓	✓	✓	✓	✓	✓	✓	✓	✓
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CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^3		X^3	X^3	X^3	X^3	✓	✓	✓
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CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^1	X^3	X^1	X^3		X^1	✓	✓	✓
CEFEPIME	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^2	X^3	X^1	X^3	X^1		✓	✓	✓
ERTAPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		X^5	X^5
IMIPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^5		X^5
MEROPENEM	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	X^5	X^5	

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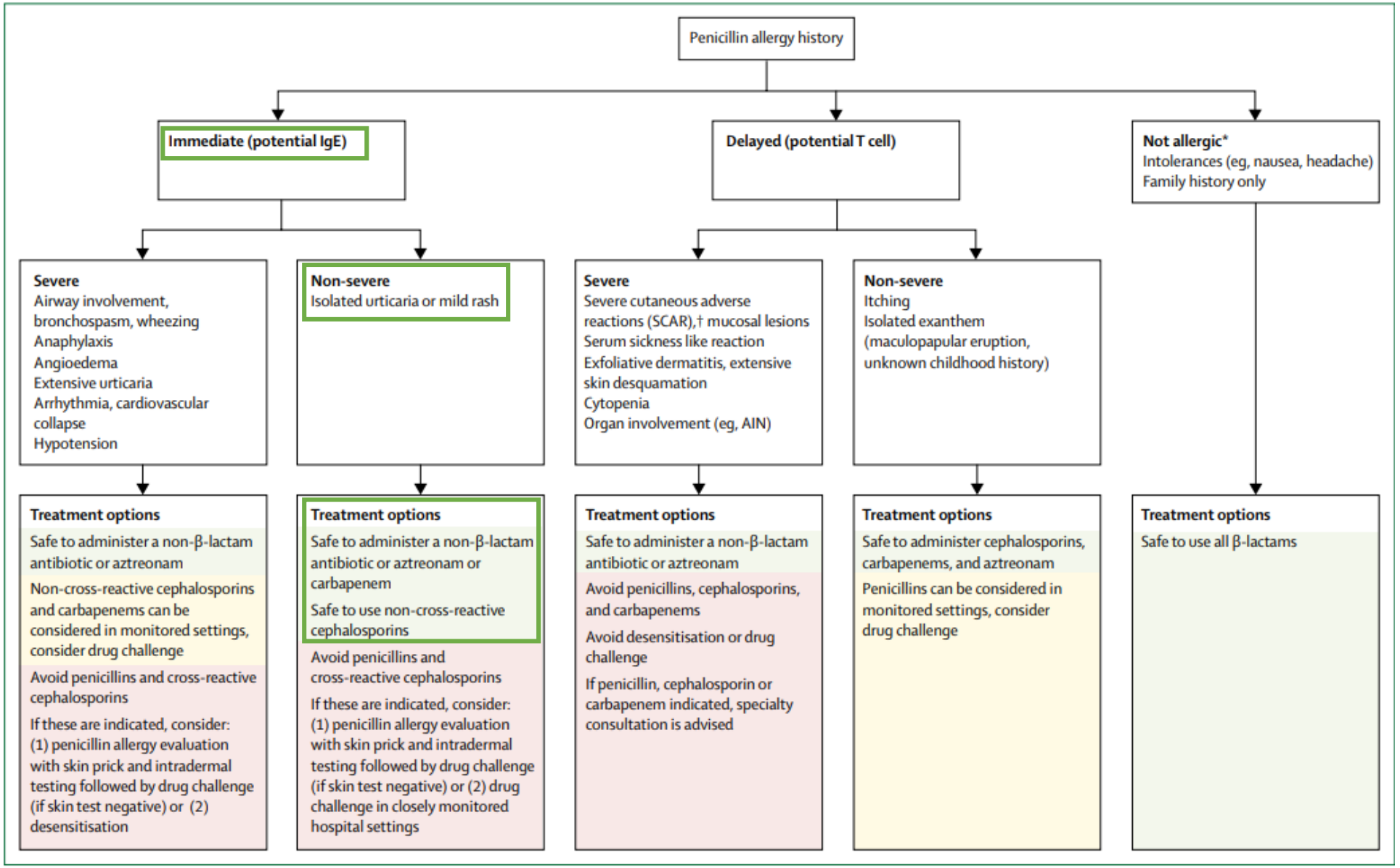
X^5	Theoretical risk of cross reaction, no clinical studies. DO NOT PRESCRIBE

Cefazolin doesn't cross-react with any other beta-lactam!

https://www.bcpharmacists.org/readlinks/guest-post-beta-lactam-allergy-benefits-de-labeling-can-be-achieved-safely

Penicillin Allergy Decision Algorithm



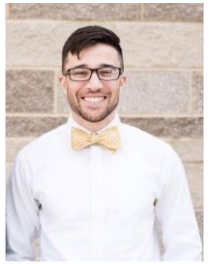
https://doi.org/10.1016/S0140-6736(18)32218-9

Final Thoughts

- **<u>Most vancomycin is unnecessary</u>**
  - Where needed, we can optimize dosing
  - MRSA nares helpful in ruling out MRSA pneumonia
- Extended infusions for beta-lactams improve clinical outcomes
- Majority of penicillin allergies are either false or no longer relevant
- Diminishing utility beyond 48hr on blood cultures
  - De-escalation benefits your current (and future) patients!

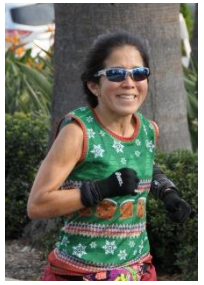
When to Call ID Pharmacy

- **<u>Dosing</u>**
- Antibiotic allergies (cross-reactivity, alternatives)
- Microbiology (new bugs, odd resistance)
- Renal (dys)function/AKI, CVVHD, IHD
- Antimicrobial toxicity concerns
- Nerd out about antibiotics



RRMC - Adults
Extension: x71423
Pager: p99917
CC Chat: Matthew Davis
Hours: M-F 0730-1600

SMH – Adults
Extension: x77567
Pager: p61029
CC Chat: Christine Pham
Hours: M-F



RRMC – Adults/Peds
Extension: x78510
Pager: p92528
CC Chat: Meganne Kanatani
Hours: MWF 9-1730, TTh 10-1830