ORAL ANTIBIOTICS FOR SERIOUS INFECTIONS

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DECLARATIONS

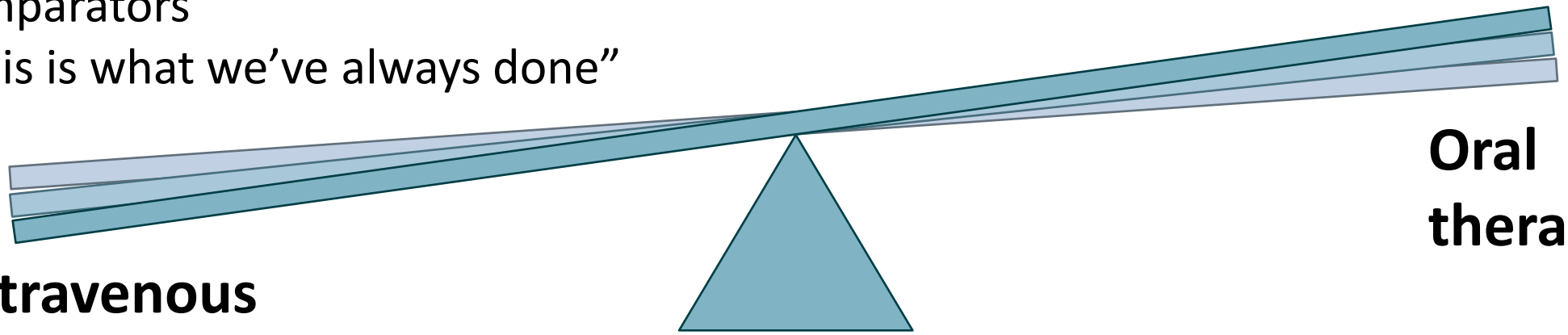
- EKM has served on advisory boards for: Abbvie, Merck, Basilea, Shionogi, Melinta, Ferring, Cidara, Entasis, LabSimply, Pfizer, and GSK, and received speaker honorarium from GSK, Shionogi, and Pfizer.


DURACELL
DURACELL

So it goes…

- Serious infection warrants serious treatment
- Reliable drug exposures
- Historic oral antibiotics as comparators
- “This is what we’ve always done”

- Mentally we’re not here
- Bioavailability (exposures) with beta-lactams
- Toxicities and drug- or disease- interactions (FQs, TMP-SMX)
- “I’ve never done it”



Intravenous Therapy

Oral therapy

MEDICAL PROGRESS

OSTEOMYELITIS: A REVIEW OF CLINICAL FEATURES, THERAPEUTIC CONSIDERATIONS AND UNUSUAL ASPECTS (First of Three Parts)*

FRANCIS A. WALDVOGEL, M.D., GERALD MEDOFF, M.D., AND MORTON N. SWARTZ, M.D.

In our experience, clinically recurrent osteomyelitis is rarely controlled without the combination of careful, complete surgical debridement and prolonged (four to six weeks) parenteral antibiotic therapy at high dosage.

CHEMOTHERAPY AS AN AID IN THE MANAGEMENT OF ACUTE OSTEOMYELITIS

GROVER C. PENBERTHY, M.D.,

AND

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DETROIT, MICH.

FROM THE SURGICAL SERVICES OF THE CHILDREN'S HOSPITAL OF MICHIGAN, HARPER HOSPITAL, AND THE SURGICAL DEPARTMENT, WAYNE UNIVERSITY COLLEGE OF MEDICINE, DETROIT, MICH.

Earliest report of systemic antimicrobial treatment of osteo

high blood levels have been maintained for a number of days. Oral administration of the drug has been possible in nearly all cases. In one patient,

18/19 (95%) received oral therapy
16/19 (84%) achieved clinical cure
0 deaths (!!)

Cortes-Penfield NW, Kulkarni PA. Open Forum Infect Dis. 2019;6(5):ofz181
Penberthy GC, Weller CN. Ann Surg. 1941;114(1):129-46

MEDICAL PROGRESS

TREATMENT OF BACTERIAL ENDOCARDITIS*

MAXWELL FINLAND, M.D.†

BOSTON

DOSAGE AND METHOD OF ADMINISTRATION OF PENICILLIN

Because sufficient and accurate data are not available for a final definition of the optimum dosage forms and methods of administration of penicillin in cases of bacterial endocarditis, it may be of interest to discuss some aspects of this subject.

It is generally agreed that in this disease oral administration is too unreliable and requires excessive amounts so that the use of penicillin in this form has generally been discarded as inadequate. Furthermore, in the dosages required, oral administration may have untoward gastrointestinal effects similar to those resulting from the oral use of the broad-spectrum antibiotics. Nevertheless, this form has undoubtedly been employed by many physicians in the management of patients who turned out to have bacterial endocarditis, particularly when they were treated at home, either entirely, or in the care after recovery, or subsequently, on occasions when prophylactic administration was required. Presumably, the oral route is at times successful, particularly when a very early infection with a highly susceptible organism is being treated with massive doses; it is more likely, however, that such usage is responsible for many therapeutic failures since it may serve as an excuse for the delay in instituting adequate treatment, particularly when there is temporary improvement. However, little of this type of experience is recorded, and therefore this assumption cannot be authenticated.


Woof.

IV to PO – Benefits

- ↓ LOS, facilitate transitions of care[1, 3, 5, 6]
- ↑early ambulation, patient comfort
- ↓ Antibiotic duration[1]
- ↓ 30-day readmission[1]
- ↓ *C. difficile* rates[1]
- ↓ Cost[2, 3, 6, 7]
- ↓ Incidence of line infections[4]
- ↓ Nursing workload

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?

Recommendation

12. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics *(strong recommendation, moderate-quality evidence)*.

Comment: Programs to increase the appropriate use of oral antibiotics can reduce costs and length of hospital stay. IV-to-oral conversion of the same antibiotic is less complicated than other strategies and is applicable to many healthcare settings. The conduct of those programs should be integrated into routine pharmacy activities. ASPs should implement strategies to assess patients who can safely complete therapy with an oral regimen to reduce the need for IV catheters and to avoid outpatient parenteral therapy.

Clin Infect Dis. 2016;62(10):e51–e77

[1] Kurtzhalts KE et al. *Clin Ther* 2016;38:1750-8
[2] Davis SL et al. *Clin Infect Dis* 2005;41:S136-143
[3] Omidvari K et al. *Respir Med* 1998;92:1032-9
[4] Laing RB et al. *J Antimicrob Chemother* 1998;42:107-11
[5] Park SM et al. *Infect Chemother* 2017;31-7
[6] Kuti JL et al. *Am J Health Syst Pharm* 2002;59:2209-15
[7] Paladino JA et al *Am J med*1991;91:462-70

IV to PO – #ECCMID2023 Hot Takes

- Med admin time-and-motion study in UK to assess workforce commitment for IV vs PO
- 22 mins and 5 seconds (IV) vs 80 seconds (PO)
  Three times daily IV medication = 1 hour of nursing time!!!!
- Independent review of IV co-amoxiclav and IV amoxicillin for respiratory infections in Sept 2022; 93 patients
- 75% IV amoxicillin and 25% IV co-amoxiclav inappropriate
  Absolute additional carbon footprint = 5.2361 $kgCO_2e$

Jenkins A, et al. Jabs to tabs: a time and motion study investigating medicines administration. ECCMID 2023 oral abstracts.
Kovacevic G, et al. The impact on the CO2 footprint when inappropriate intravenous antibiotic therapy is used instead of an earlier, clinically appropriate switch to an oral formulation or stopping the therapy entirely in a UK based tertiary hospital.

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

Li HK, et al. N Engl J Med. 2019;380(5):425-436

OVIVA Results

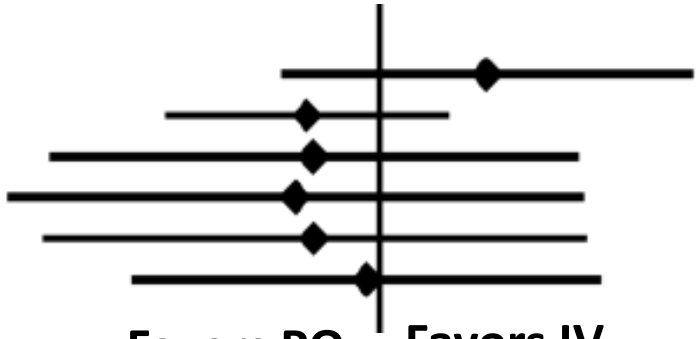
Oral therapy was noninferior even in the "worst-case" scenario

Outcome of interest	IV	PO
Treatment failure within 1 year	14.6%	13.2%
Early discontinuation of treatment Patient preference Possible or probably recurrence	99/523 (18.9%) 3.6% 0.2%	67/523 (12.8%) 0.9% 2.8%
At least one serious adverse event	27.7%	26.2%
Antibiotic-related serious adverse event	13.6%	6.7%
C. difficile infection	1.7%	1%
Duration of therapy (median, days)	78	71
Hospital length of stay (median, days)	14	11
Oxford Knee Score	Improved patient-reported outcome P=0.04 at Day 120 and 365 favoring PO therapy	

What does “PO” mean?

	PO	IV	
4b - Planned PO treatment, heterogeneity p = 0.80			
Penicillins	17/57	9/48	1.59 (0.65, 3.89)
Quinolones	20/189	26/179	0.73 (0.39, 1.35)
Tetracyclines	7/40	7/30	0.75 (0.24, 2.37)
Macrolides / Lincosamides	5/53	6/44	0.69 (0.20, 2.42)
Other single PO antibiotic	8/39	6/22	0.75 (0.23, 2.45)
Combination PO antibiotics	9/63	8/53	0.95 (0.34, 2.62)

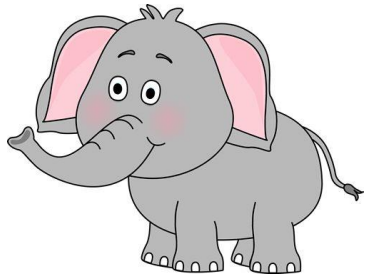
Failure/no failure



- This doesn’t count rifampin
- Dosing not mentioned!
- All tetracyclines = doxycycline
- No oral cephalosporins used
- No linezolid for > 2 weeks
- Minimal SMX/TMP
- 19 different planned oral combinations
  - Cipro + clinda (N=19)
  - Cipro + doxy (N=17)

In this trial, we did not seek to compare specific antibiotic agents or to stipulate which agents should be used. We relied on the expertise of the consulting infectious-disease specialist to select and adjust antibiotic regimens, taking into account factors such as susceptibilities, risk of the emergence of resistance, bioavailability, tissue penetration, side effects, coexisting condi-

Bone penetration….



- Concentration ratio between bone and serum, but…..
  - One sample per (non-infected) patient during surgical procedures is our best data
    - Multiple, steady-state samples unpractical, unethical?
  - Tissue homogenate ≠ distinct tissue compartments
  - Whole tissue concentration ≠ active (free) concentration
  - Conditions of bone not accounted for (calcified, arthritic, density, cysts)
  - Uncertain where pathogens inhabit diseased bone (osteoblasts? matrix?)
  - Time course (of dose, of samples) and intersubject variability is significant
  - PK-PD target for bone infection unknown for most antimicrobials
  - Effect of bone type? Effect of infection on extent and rate of penetration?

Landersdorfer CB, et al. Clin Pharmacokinet. 2009;48(2):89-124
Mouton JW, et al. J Antimicrob Chemother 2008; 61 (2): 235-7

I don’t think you get to give an IV to PO talk without citing Brad Spellberg and “Oral is the New IV”

Oral vs. IV Abx for Osteomyelitis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Greenberg	‘87	30	Ciprofloxacin vs. std IV	50% (7/14) v 65% (11/16)
Gentry	‘90	59	Ciprofloxacin vs. βL+aminoglyc	77% (24/31) v 79% (22/28)
Mader	’90	26	Ciproflox vs. βL/clinda+aminoglyc	79% (11/14) v 83% (10/12)
Gentry	‘91	33	Ofloxacin vs. cephalosporin	74% (14/19) v 86% (12/14)
Gomis	‘99	32	Ofloxacin vs. imipenem	69% (11/16) v 50% (8/16)
Schrenzel	’04	39	Fleroxacin+rifampin v βL/vanco	82% (18/22) v 65% (11/17)
Euba	‘09	48	TMP-SMX+rifampin vs. cloxacillin	81% (17/21) v 77% (21/27)
Li	’19	1054	Std oral vs. std IV	87% (457/527) v 85% (450/527)
Manning	’22	60	PJI/DAIR: IV/Oral vs. IV only	71% (22/31) v 76% (22/29)
Total (N=9 RCTs)		1,381		84% (581/695) v 83% (567/686)

Success = absence of osteo at long term follow up (most studies >1 year); std = standard of care, protocol specified; all RCTs comparing oral to IV-only are in adults, however there are also 9 other adult and 8 pediatric RCTs or quasi-experimental studies comparing mostly oral vs. mostly oral, with high cure rates; refs at https://www.bradspellberg.com/oral-antibiotics

Wald-Dickler N, et al. Oral is the New IV: Challenging Decades of Blood and Bone Infection Dogma: A systematic Review. The American Journal of Medicine. March 2022.

How would you treat this patient?

31yo F with *Prevotella* bacteremia, MRSA and Proteus bilateral LE osteomyelitis

Gram Stain: Few WBCs present; No organisms present
Culture: Rare Proteus mirabilis

PROTEUS MIRABILIS

	MIC (mcg/mL)	MIC Interpretation
Amikacin	<=16	Sensitive
Amp/Sulbactam	<=1/0.5	Sensitive
Ampicillin	<=8	Sensitive
Aztreonam	<=4	Sensitive
Cefazolin	<=2	Sensitive
Cefepime	<=2	Sensitive
Ceftazidime	4	Sensitive
Ceftriaxone	<=1	Sensitive
Cefuroxime	<=4	Sensitive
Ciprofloxacin	<=1	Sensitive
Ertapenem	<=0.5	Sensitive
Gentamicin	2	Sensitive
Levofloxacin	<=0.25	Sensitive
Meropenem	<=1	Sensitive
Piperacillin/Tazobactam	<=4	Sensitive
Sulfa/Trimethoprim	<=2/38	Sensitive
Tetracycline	>8	Resistant
Ticarcillin/Clavulanic Acid	<=8	Sensitive
Tobramycin	2	Sensitive

STAPHYLOCOCCUS AUREUS

	MIC (mcg/mL)	MIC Interpretation
Clindamycin	>4	Resistant
Daptomycin	0.5	Sensitive
Gentamicin	<=1	Sensitive
Linezolid	2	Sensitive
Oxacillin	>2	Resistant

This isolate is Methicillin Resistant Staphylococcus aureus (MRSA), staph are resistant to all beta lactam antibiotics

Sulfa/Trimethoprim	<=0.5/9.5	Sensitive
Synercid	1	Sensitive
Tetracycline	<=1	Sensitive
Vancomycin	1	Sensitive

Gram Stain: ANAEROBIC BOTTLE Gram Negative Rods; 1753 08/27/19
Culture: ANAEROBIC BOTTLE PREVOTELLA SPECIES
AEROBIC BOTTLE No Growth 5 Days

PREVOTELLA SPECIES

	Beta Lactamase
Beta Lactamase	Pos

How would you treat this patient?

Confidential : Iv abx vs oral help

Lenhard, Amanda H
To McCreary, Erin

Reply | Reply All | Forward | [redacted]

Business General

You replied to this message on [redacted]

On swat at Shadyside :

White Team [redacted] Guy with opiate use d/o and foot osteo on IV abx re-presented to hospital after he eloped from SNF where he was getting IV abx for osteo and used opiates during elopement. Plan right now is for him to stay in house for IV abx [redacted] given safety of discharging him with the PICC (and no snf will take him at this point given what happened) and oral option nonideal.

Could you advise on if this patient could go on orals? Or Dalbavancin?

Staying till [redacted] is not ideal.

Thanks for the help.

You'll win the cost conversation

Evaluation of Opportunities for Oral Antibiotic Therapy in Bone and Joint Infections

Hita Bhagat, PharmD[1], Monica K. Sikka, MD[2], Ellie S. Sukerman, MD[2], Jina Makadia, MD[2], James S. Lewis II, PharmD[1,2], and Amber C. Streifel, PharmD[1]

Annals of Pharmacotherapy
2023, Vol. 57(2) 156–162

DOI: 10.1177/10600280221101105
journals.sagepub.com/home/aop
SAGE

Clinical and Economic Impact of Implementing OVIVA Criteria on Patients With Bone and Joint Infections in Outpatient Parenteral Antimicrobial Therapy

Michael Marks,[1,2] Lucy C. K. Bell,[1] Imogen Jones,[1] Tommy Rampling,[1] Katharina Kranzer,[2,3] Stephen Morris-Jones,[3] Sarah Logan,[1] and Gabriele Pollara[1,4]

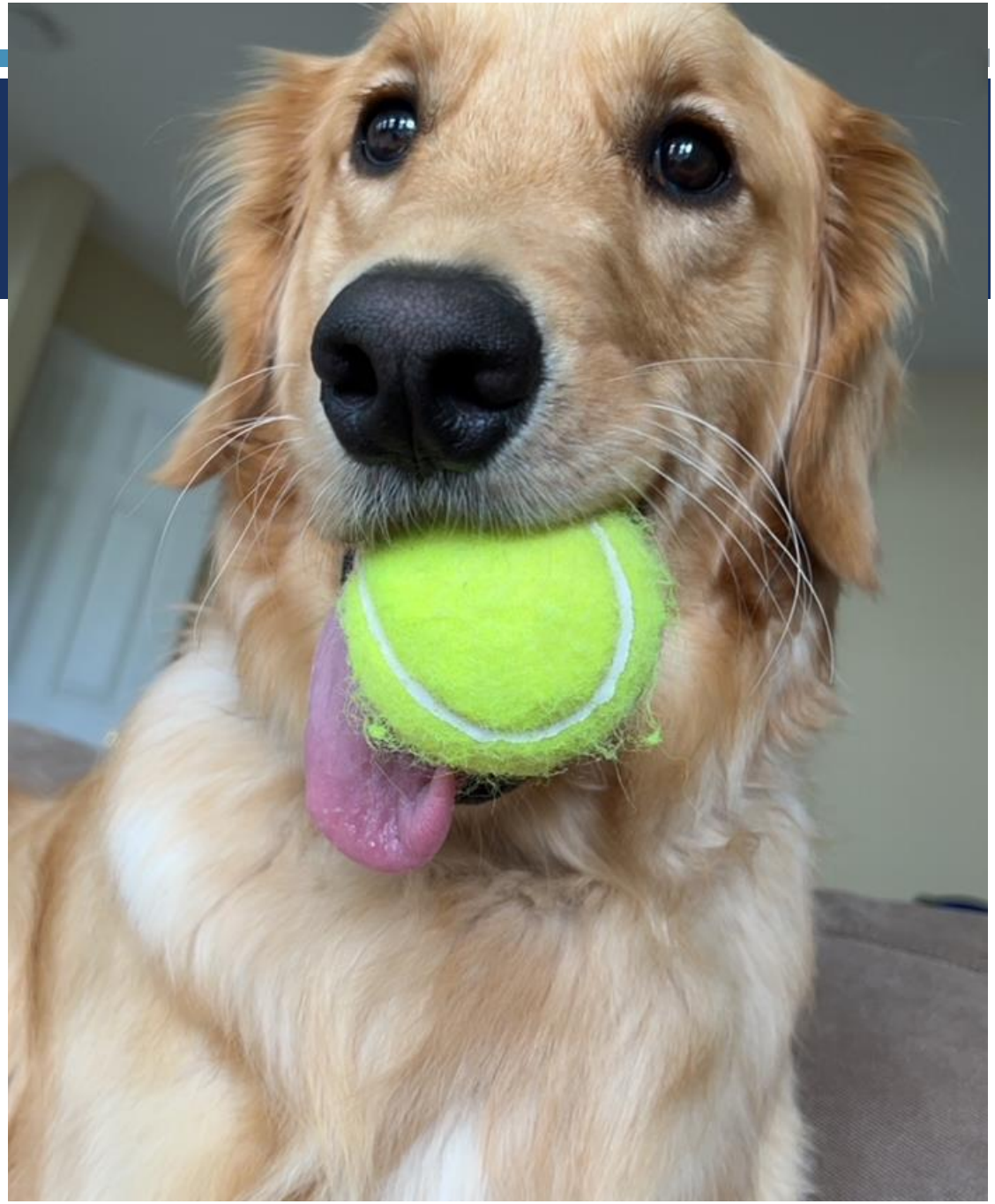
[1]Division of Infection, University College London Hospitals, London, United Kingdom, [2]Clinical Research Department, London School of Hygiene and Tropical Medicine, London, United Kingdom, [3]Department of Clinical Microbiology, University College London Hospitals, London, United Kingdom, and [4]Division of Infection and Immunity, University College London, London United Kingdom

- One UK center estimated 79.7% of OPAT patients eligible for oral ABX, saving median **19.5 IV days and 1234 pounds** per patient
- One USA center estimated cost savings of **$3,270.69 per patient** using PO over IV therapy for bone and joint infections

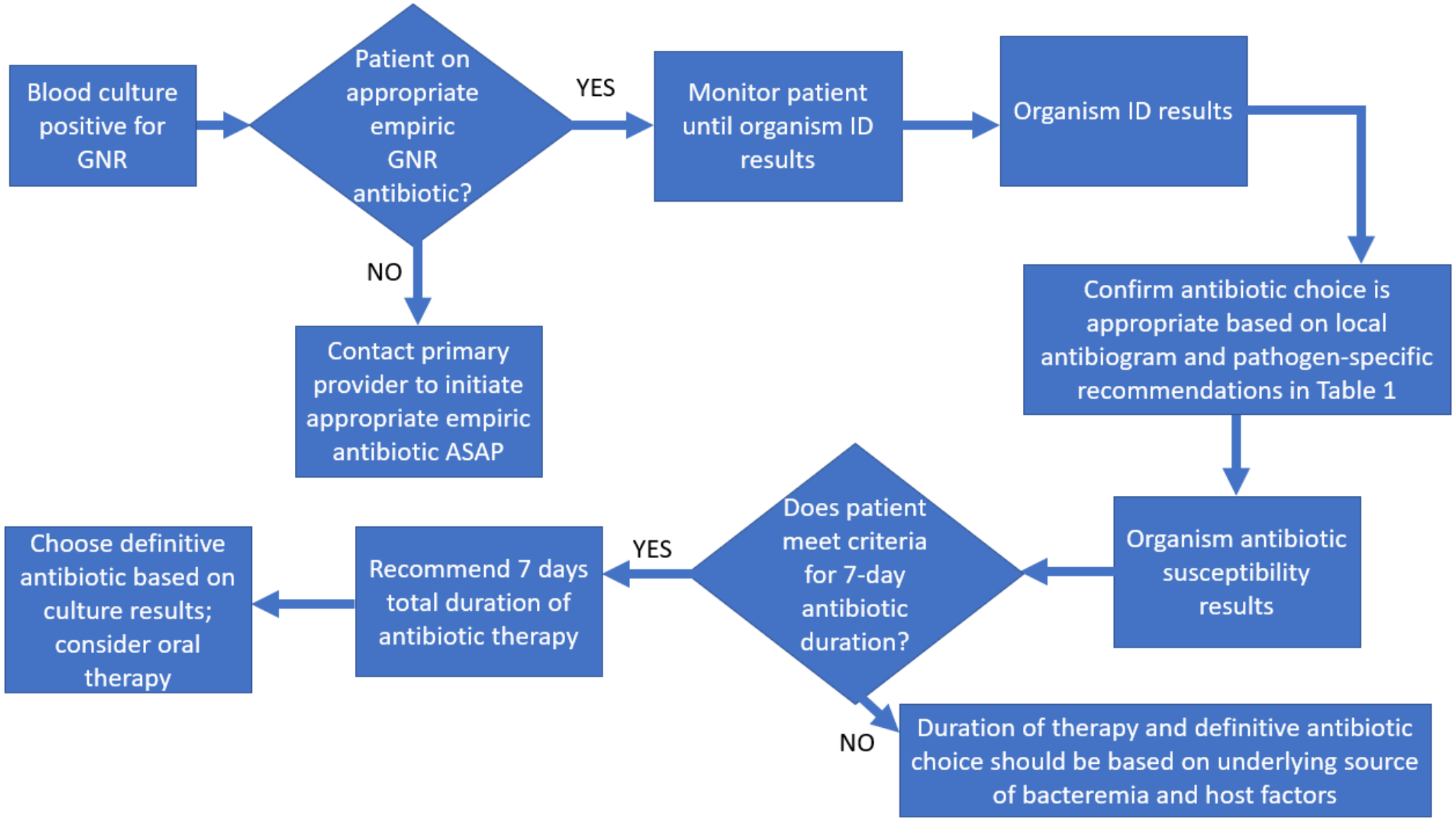
PO for Osteo Summary

- There are more data for oral therapy than IV therapy for the treatment of osteomyelitis
- Oral antibiotics are non-inferior to IV antibiotics for the treatment of (chronic) osteomyelitis
  - No differences in clinical cure
  - Less ADRs and complications with oral therapy
  - Economically advantageous
- Peds guidelines recommend “short course IV followed by oral”
- Vertebral
  - Some data here, TBD, but probably fine (Marconi L, et al. OFID 2022)
  - 72 OVIVA patients
- When using oral antibiotics
  - Make sure you dose them right
  - Make sure you administer them right (food interactions, etc)
  - “Bone penetration” and bioavailability are by no means absolutes

Gram-negative bacteremia



UPMC Pathway



UPMC Criteria

- ✓ Enterobacterales organism (e.g. *E. coli, Klebsiella* spp., *Enterobacter* spp., etc.)
- ✓ Clinical improvement within 72 hours
  - Lack of fever for at least 24 hours
  - SBP > 90 and not requiring vasopressors
  - WBC < 15 thou/µL
- ✓ None of the following medical conditions
  - Current or expected neutropenia (ANC <500 cells/mm^3) within the next two weeks
  - CD4 count < 200 cells/m^3
  - Hematopoietic cell or solid organ transplant within 1 year
- ✓ Source = UTI (cystitis or pyelonephritis), intra-abdominal or biliary, catheter-related/line, pneumonia (without empyema/abscess or cystic fibrosis or bronchiectasis), skin/soft tissue

UPMC Criteria – Source Control

- **Biliary/gallbladder**
  - Adequate drainage of source (surgical, percutaneous, endoscopic)
- **Urinary tract**
  - Stone/obstruction eliminated, no renal abscess, cathether/neph tube exchange or removal
- **Intra-abdominal**
  - Any abscesses/collection drained, necrotic tissues debrided, removal of infected mesh
- **Skin and soft tissue**
  - Incision and drainage of abscess, debridement of the infected/necrotic tissue or amputation
- **Central venous catheter**
  - Removal and exchange of vascular catheter
- **Unknown**
  - No localizing signs or symptoms AND clinically stable and well-looking AND no source identified if imaging was performed

UPMC Criteria

- ✓ Blood cultures positive for < 72 hours
  - Repeat blood cultures after the first positive blood culture are usually not required, but may be beneficial in the following scenarios: (1) patients without an appropriate clinical response within 72 hours, (2) patients with clinical concern for an endovascular infection or endocarditis, (3) patients with recurrent infections (e.g., recurrent UTIs with bacteremia), (4) situations where there is limited or no source control (e.g., central line not removed, abscess not completely drained), (5) reinforce appropriateness of 7-day duration of therapy
  - Short course therapy may not be appropriate if source control was not achieved early in the course (e.g. within 72 hours)

Patient should finish treatment course on the most appropriate, most narrow spectrum antibiotic agent. If patient can absorb and tolerate oral medications and the organism is susceptible to oral options, consider recommending **any*** of the following as oral therapy to complete the course of therapy:

- ✓ Ciprofloxacin 750mg PO twice daily
- ✓ Levofloxacin 750mg PO daily
- ✓ Trimethoprim-sulfamethoxazole 1-2 DS tabs PO twice daily (approximately 5mg/kg every 12 hours)
- ✓ Amoxicillin 1g PO TID
- ✓ Amoxicillin-clavulanate XR 2g PO BID
  - If XR is not covered by insurance, can give:
    - Amoxicillin-clavulanate 875/125mg PO TID
    - Amoxicillin-clavulanate 875/125mg PO BID plus Amoxicillin 1000mg PO BID
- ✓ Cephalexin 1g PO q6h
- ✓ Cefuroxime 500mg PO q8h
  - *Note: To improve bioavailability, counsel patient to take with food. Consider avoiding use if patient is receiving an acid-suppressive medication. Only use for isolates with an MIC ≤ 4 mg/L.*
- ✓ Cefpodoxime 400mg PO BID
  - *Note: Ceftriaxone susceptibility does NOT predict cefpodoxime susceptibility. Robust pharmacokinetic studies have not been completed and benefits should outweigh risks before use.*

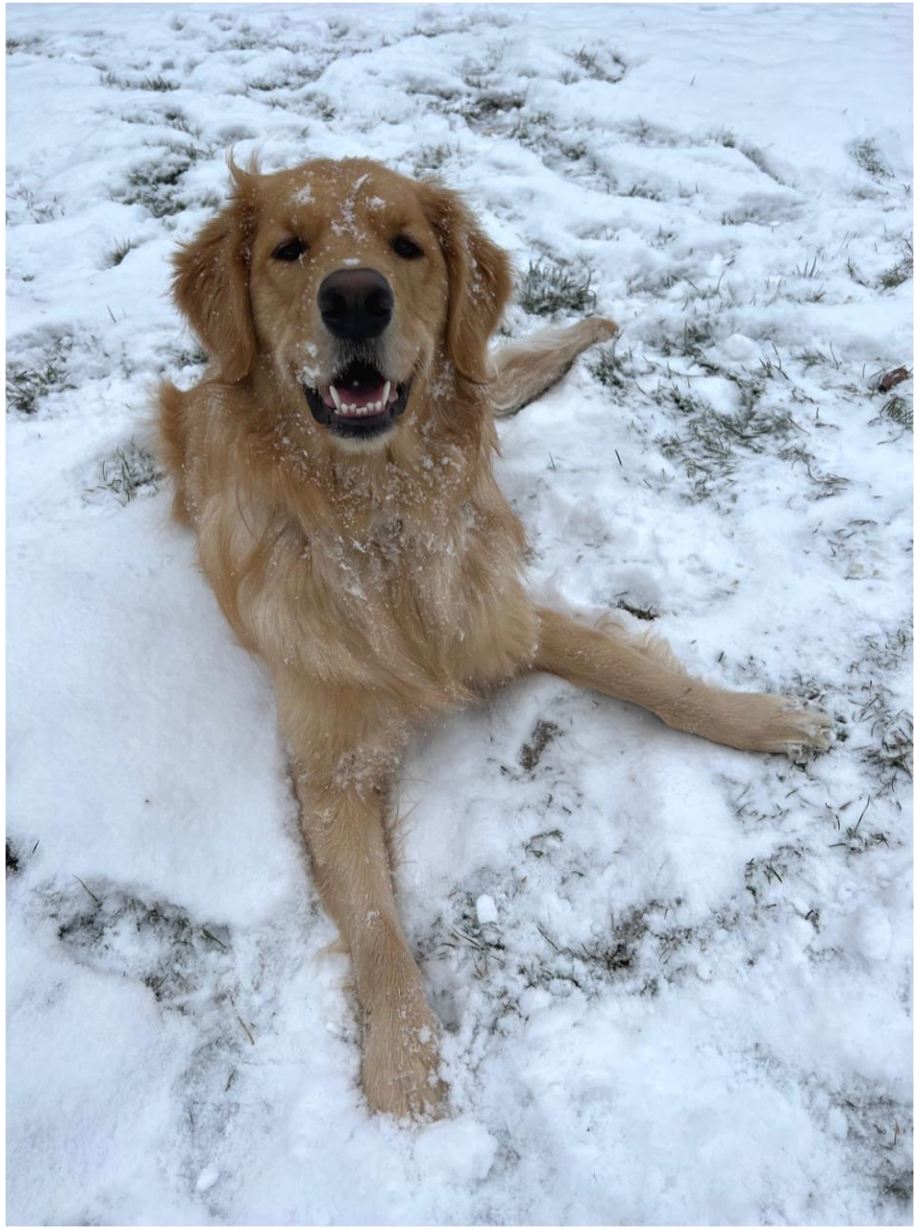
***X** Cefadroxil is not recommended due to inadequate data for dosing for gram-negative bacteremia*

***X** Cefdinir is not recommended due to poor pharmacokinetics/pharmacodynamics*

Available literature suggests there may be a higher incidence of recurrent bacteremia when PO beta-lactams are used, but this may be because of suboptimal dosing of oral beta-lactams in previous studies. The higher doses recommended above are based on expert opinion, if an oral beta-lactam is selected for definitive therapy.

RCT data coming soon!

- "What is the safest and most effective treatment approach for adults with Gram-negative bloodstream infections?“
- Adult patients
- 8 US hospitals
- IV vs early oral RX of gram-negative bloodstream infections



Tamma PD, Cosgrove SE. CMI. 2023.
https://www.pcori.org/research-results/2022/optimizing-outcomes-adults-gram-negative-bloodstream-infections

Endocarditis

Antibiotic regimens recommended for IE vary widely and often require ≥4 weeks of therapy, generally given by the intravenous route. Absorption of orally administered antimicrobial agents may be unreliable, and such a strategy is generally not recommended as sole therapy for IE. Several other aspects of

Baddour LM, et al. Circulation. 2015 Oct 13;132(15):1435-86.

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

- Multicenter RCT in Denmark (400 patients)
- All patients received IV therapy for 10 days
  - 199 continue IV
  - 201 switch to oral
- Outcome: composite of all cause mortality, unplanned cardiac surgery, relapsed bacteremia, embolic events (follow-up 6 months after treatment)
- Micro: Streptococcus 49%, Enterococcus 22%, MSSA 22%, Other 7% (NO MRSA)
- **Results: 24 (12.1%) IV group vs 18 (9.0%) oral group (95% CI, −3.4 to 9.6; P=0.40)**

Iversen K, et al. N Engl J Med. 2018.

POET Antibiotic Regimens

Infecting pathogen	All patients received 2 antibiotics from the list
PSSA/E and MSSA/E	Amoxicillin 1g four times daily, Fusidic acid 750mg BID, Linezolid 600mg BID, Rifampin 600mg BID
MSSA/E	Dicloxacillin 1g four times daily, Fusidic acid 750mg BID, Linezolid 600mg BID, Rifampin 600mg BID
MRSE	Linezolid 600mg BID, Fusidic acid 750mg BID, Rifampin 600mg BID
E. Faecalis, Streptococci with PCN MIC < 1 mg/L	Amoxicillin 1g four times daily Moxifloxacin 400mg daily Linezolid 600mg BID Rifampin 600mg BID
Streptococci with PCN MIC ≥ 1 mg/L	Moxifloxacin 400mg daily Linezolid 600mg BID Rifampin 600mg BID Clindamycin 600mg TID

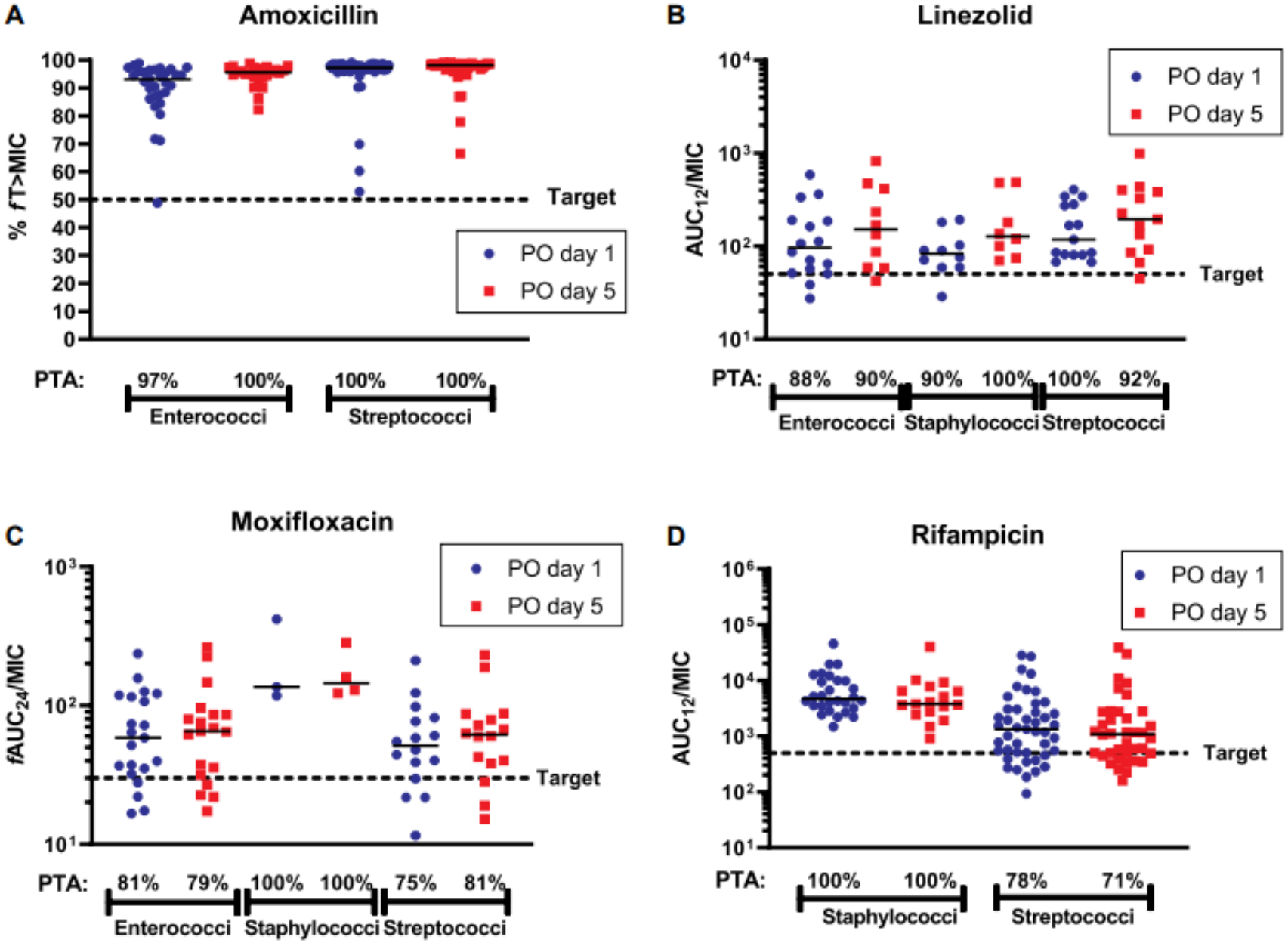
Iversen K, et al. N Engl J Med. Supplementary Materials.

POET TDM 😍

Table 1. Clinical Breakpoints and Pharmacokinetic/Pharmacodynamic Targets

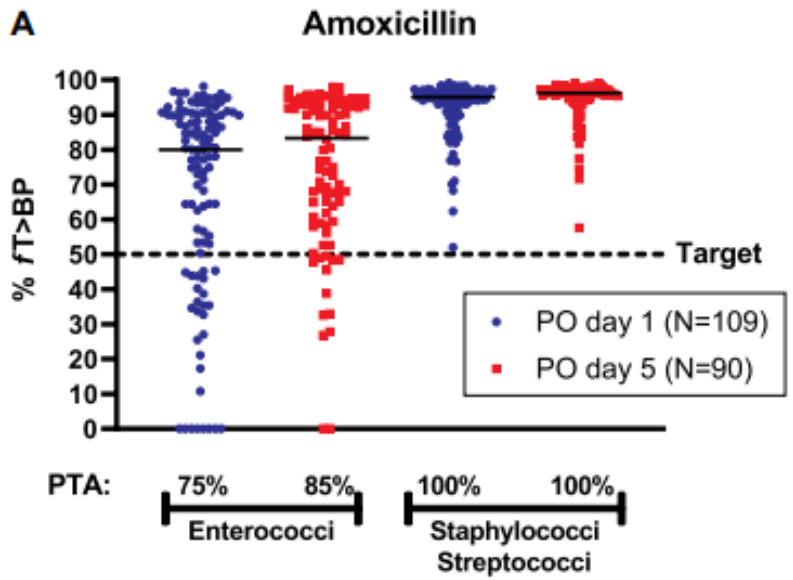
Drug	Dose	Approximate Unbound Fraction (%)	Bacterial Species	Clinical Breakpoint (mg/L)	Pharmacokinetic/ Pharmacodynamic Target
Amoxicillin	PO: 1000 mg q6 h	80	Enterococci	4	*f*T > BP or *f*T > MIC more than 50% of dosing interval[b]
			Staphylococci Streptococci	0.5[a]	
Dicloxacillin	PO: 1000 mg q6 h	3	Staphylococci	0.5[c]	*f*T >BP more than 50% of dosing interval[b]
	IV: 3000 mg q6 h				
Linezolid	PO or IV: 600 mg q12 h	Not used	Enterococci Staphylococci	4	AUC_{12}/BP >50 or AUC_{12}/MIC >50
			Streptococci	2[d]	
Moxifloxacin	PO or IV: 400 mg q24 h	50	Enterococci Streptococci	0.5[e]	*f*AUC_{24}/BP >30 or *f*AUC_{24}/MIC >30[b]
			Staphylococci	0.25	
Rifampicin[f]	PO: 600 mg q12 h	Not used	Staphylococci Streptococci	0.064	AUC_{12}/BP >500 or AUC_{12}/MIC >500

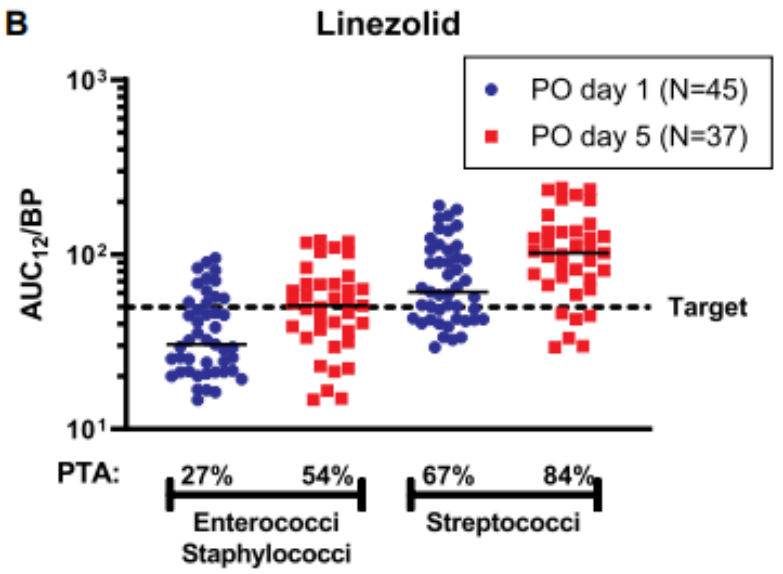
Bock M, et al. CID. 2023.

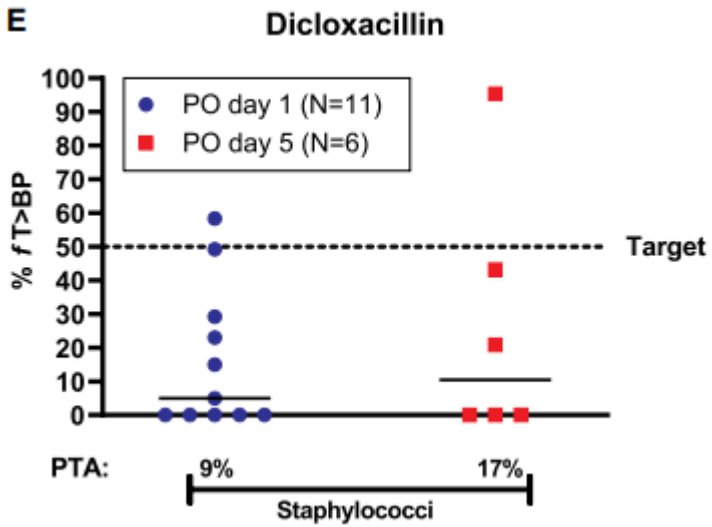


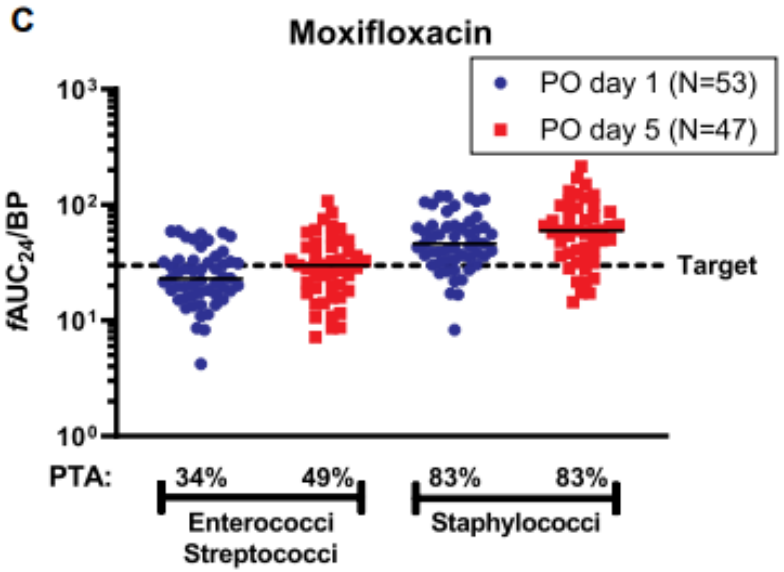
POET TDM

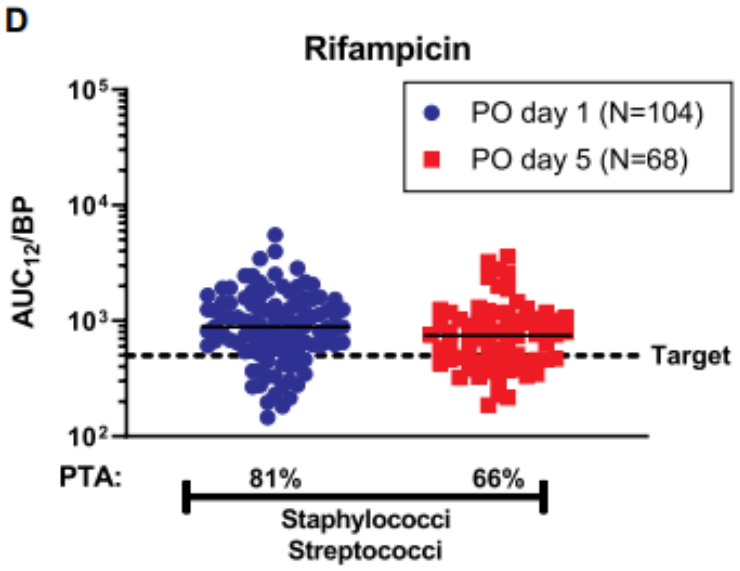
Bock M, et al. CID. 2023.











POET TDM

Bock M, et al. CID. 2023.

POET – 5 years (!!) later

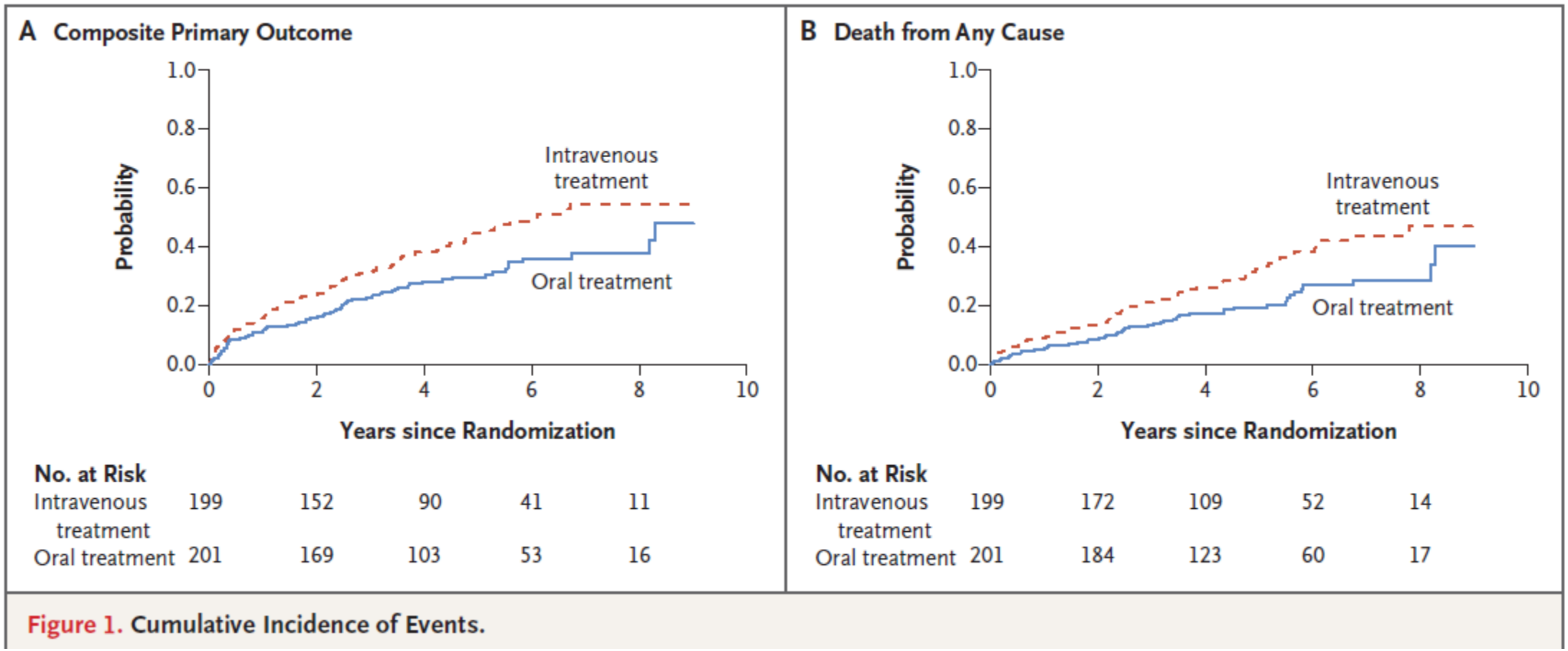


Figure 1. Cumulative Incidence of Events.

Median follow 5.4 years (IQR 4-6.9)

Primary outcome: 32.8% (oral) vs 45.2% (IV), HR 0.65; 95%CI (0.47-0.90)

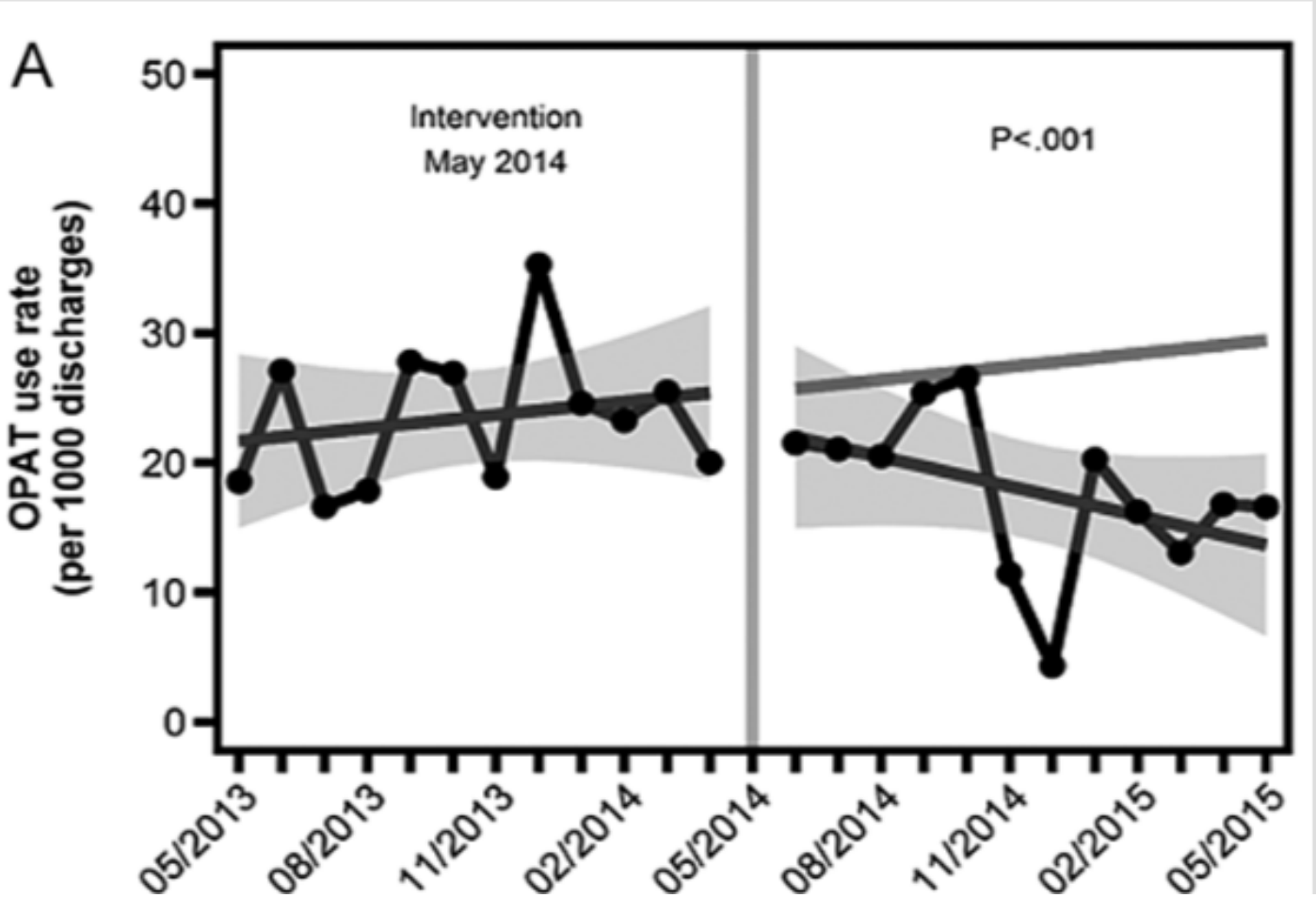
Pries-Heje MM, et al. NEJM. Feb 2022.

Some final thoughts

There are patients who cannot take oral

- **Clinically unfit for PO**
  - No active oral agent for infection
  - Hemodynamically instability
  - Severe vomiting or diarrhea within past 24 hours
  - Non-functional GI tract (obstruction, malabsorption, short gut, etc.)
  - Mucositis
  - Aspiration risk (altered mental status, impaired swallowing, etc.)
  - Not tolerating at least a clear liquid diet or tube feeds
  - Medication cannot be administered through feeding tube
- **Patient specific factors**
  - Major drug interactions
  - Allergies
  - Intolerances or toxicities (role of TDM?)
  - Refusal

This is hard to do, but it is possible



- Osteoarticular
  - 9.3 to 4.4 per 1000 discharges
- Surgical Site
  - 5.7 to 3 per 1000 discharges
- Respiratory
  - 5.5 to 1.2 per 1000 discharges

Hersh AL et al JPIDS 2018

Tipping the scales

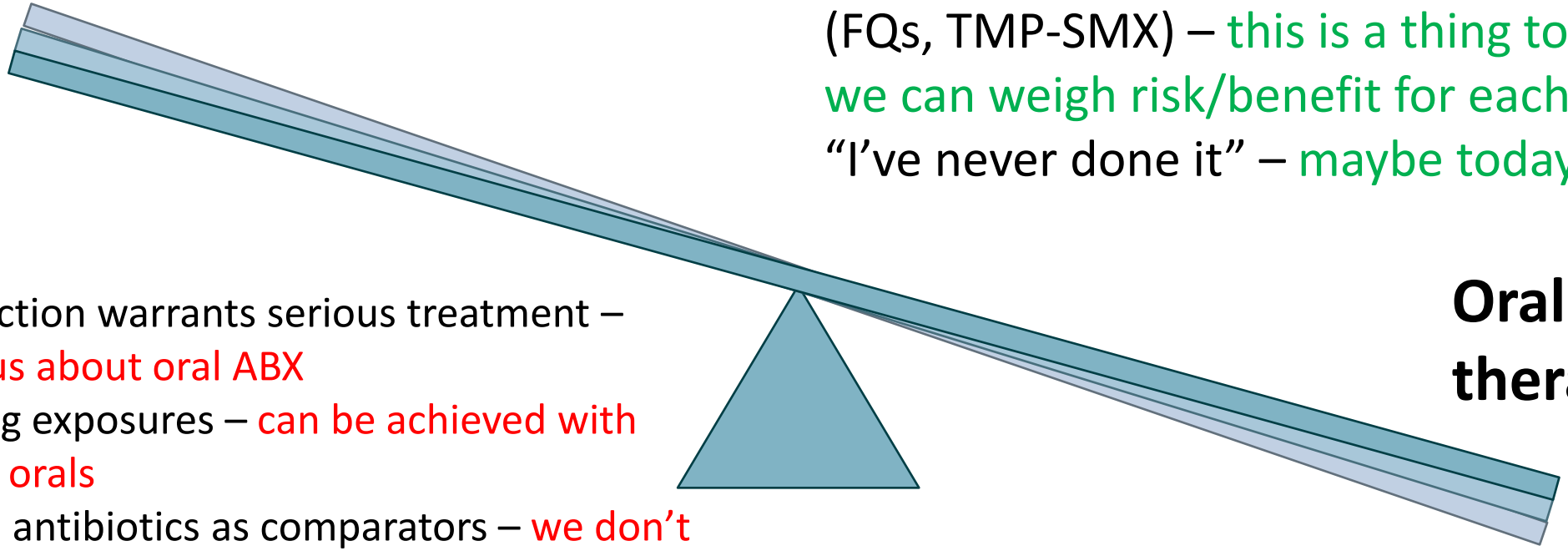
Intravenous Therapy

Mentally we're not here – hopefully it's a little better now

Bioavailability (exposures) with beta-lactams – it's not not an issue, but it's also not insurrmountable for all BLs

Toxicities and drug- or disease- interactions (FQs, TMP-SMX) – this is a thing to consider, we can weigh risk/benefit for each patient

"I've never done it" – maybe today's the day!



Oral therapy

Serious infection warrants serious treatment – we're serious about oral ABX

Reliable drug exposures – can be achieved with appropriate orals

Historic oral antibiotics as comparators – we don't use these drugs

"This is what we've always done" – it's a new day

ORAL ANTIBIOTICS FOR SERIOUS INFECTIONS

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