BUGS, DRUGS, AND HARM REDUCTION

Skills for Optimizing Antibiotic Therapy in People Who Use Drugs

Ayesha Appa; Kinna Thakarar; Madeline McCrary;
Amanda Roy; Amelia Goff; Kate Roberts

AMERSA 2024

WHY ARE YOU HERE TODAY?

Think about a patient’s story involving antibiotics that didn’t go well.

WHY ARE WE HERE TODAY?

INTRODUCTIONS!

Objectives

1. Demonstrate knowledge of **long-acting injectable antibiotics** in treating serious infections in PWUD.
2. Create a short-list of the **most effective oral antibiotics** for treating serious infections commonly associated with drug use.
3. Collaborate with patients to determine the best antibiotic strategy, use a **shared decision-making** model.

Today's Workshop

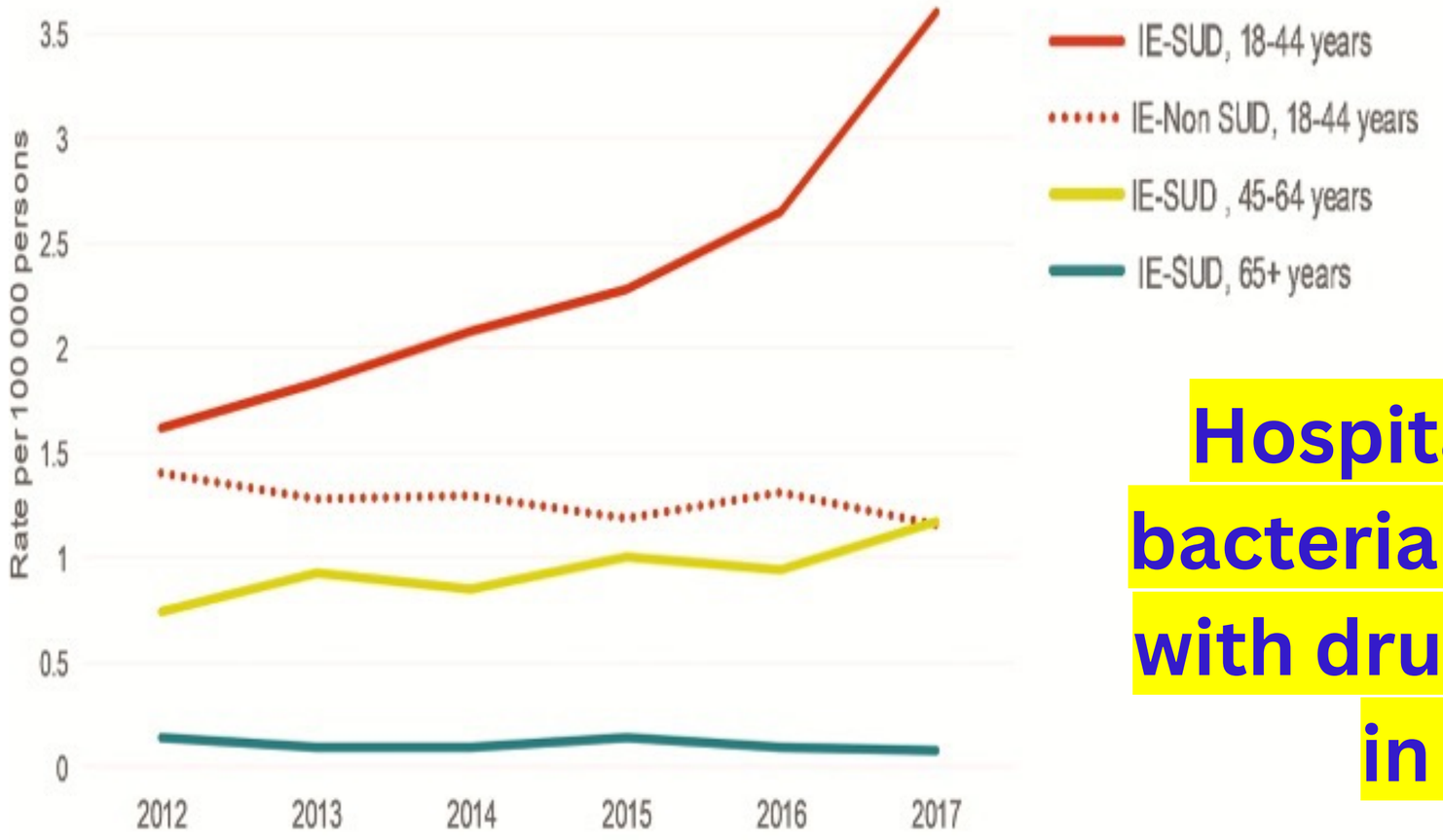
Ground Rules

- **Judgement-free space**
- **Participation > perfection**
- **Respect all voices**
- **Keep it real (world)**

DISCLOSURES

We will be discussing off-label use of antibiotics.

OBLIGATE EPIDEMIOLOGY SLIDE

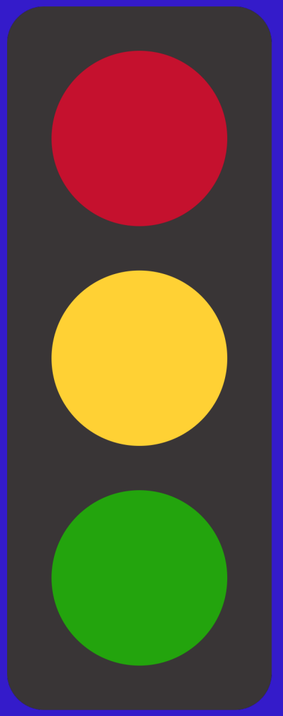


Hospitalizations for serious bacterial infections associated with drug use have risen 2-10X in the last decade.

McCarthy, et al. CID Jan 2020.
Jackson, et al. MMWR June 2018.

PART 1
LONG-ACTING ANTIBIOTICS

And a case-based traffic light game!



Dalbavancin 101

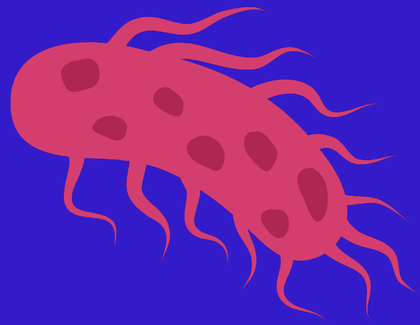
- Spectrum of activity
- Administration pearls/logistics
- Indications – data
- When NOT to use

Case-based practice!

Dalbavancin

- Lipo-glycopeptide
- “long-acting vancomycin”
- FDA approved for skin & skin structure infections in 2014
- Most clinical interest for treatment of *serious gram-positive infections*

True or False?

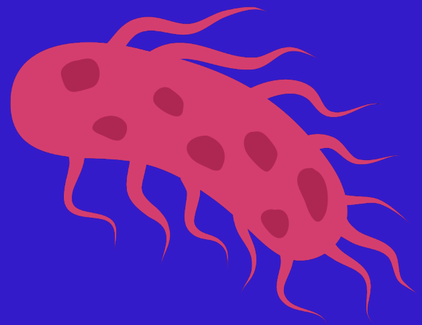


DALBAVANCIN CAN BE USED FOR INFECTIONS CAUSED BY E. COLI

Yell out an answer! Get some candy!

FALSE!

Dalbavancin has a similar spectrum of activity to vancomycin: only gram-positive organisms susceptible to vanco!

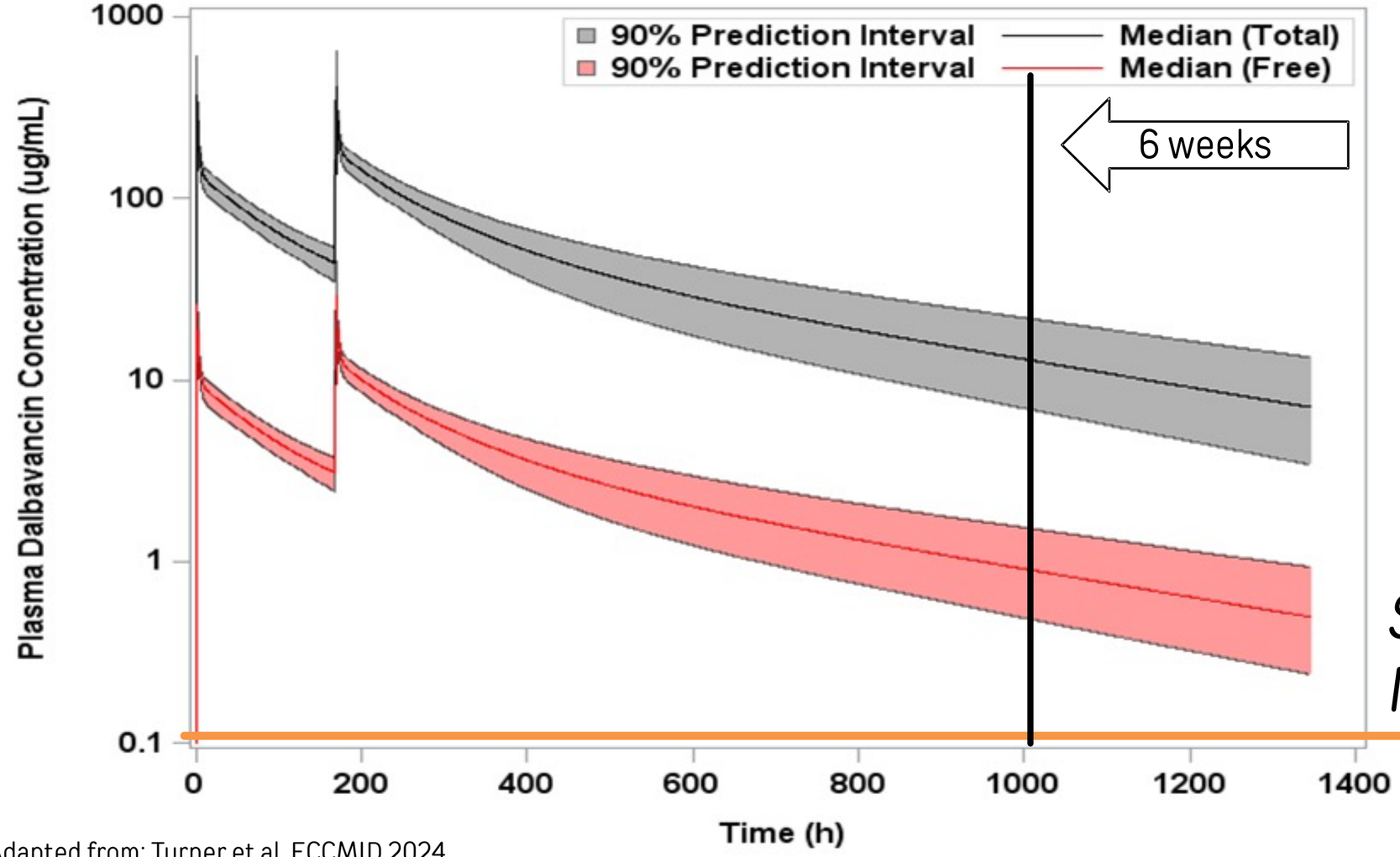


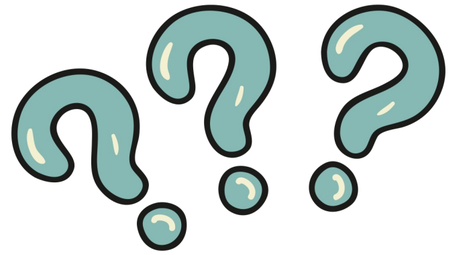
~~DALBAVANCIN CAN BE USED FOR INFECTIONS CAUSED BY E. COLI~~

Dalbavancin = long-acting

	Dalbavancin	Vancomycin
Mechanism	Same (inhibits cell wall synthesis)	
Spectrum	**Gram-positive bacteria** (S. aureus, streptococci, enterococci) excluding VRE **No activity vs. gram-negative bacteria**	
Dosing (normal renal function)	1.5 g IV q7–14 days	10–15 mg/kg IV q8h–24h
Half-life	~8 days	8 – 24 hours
Adverse effects	Generally well tolerated; infusion reaction (rare)	Nephrotoxicity, vancomycin infusion reaction
Therapeutic drug monitoring?	Not required	Yes – troughs or AUC
Cost/dose	~$5000	$2-20

Two weekly 1,500 mg doses = sufficient levels for 6+ weeks of therapy





How long does it last?

S. aureus
MIC_{90} (0.06 µg/mL)

Adapted from: Turner et al, ECCMID 2024

Which of the following infections have robust randomized clinical trial data (N > 100 pts) to support use of dalbavancin?

- Osteomyelitis
- Bacteremia
- Meningitis
- Endocarditis
- Cellulitis

Yell out an answer! Get some candy!

CLINICAL TRIAL DATA FOR DALBAVANCIN

Which of the following infections have robust randomized clinical trial data (N > 100 pts) to support use of dalbavancin?

- Osteomyelitis
- Bacteremia
- ~~Meningitis~~
- Endocarditis
- Cellulitis

SUMMARY

Best evidence = bacteremia, SSTIs.

Promising data = endocarditis, osteomyelitis.

Don’t use = meningitis

Dalbavancin: Clinical Data by Indication

SSTI = skin/soft tissue infection
RCT = randomized controlled trial
SOC = standard of care

Indication	Standard of Care (SOC)	Dalbavancin vs. SOC	Level of evidence	Oral Abx vs. SOC
SSTI	Vanco/cefazolin WRITE TO US PO antibiotics	Noninferior	Multiple RCTs	SOC
Bone/joint (osteomyelitis, septic arthritis, prosthetic joint)	Vanc, dapto or linezolid x 3–6 wk	Osteo: Noninferior Other bone/joint: unknown (case series)	Osteo: Phase II RCT (N = 70 dalba, N=10 SOC)	Noninferior –OVIVA (N = 500 in each arm)
S. aureus Bacteremia	IV antibiotic (vancomycin, daptomycin, cefazolin) x 2–6 wk	Noninferior	DOTS RCT (N = 100 each arm)	2nd line/salvage (case series)
Endocarditis (IE)	IV antibiotic (vancomycin, daptomycin, cefazolin) x 4–6 wk	Lack of data	Case series, few RCT data (N = 6 pts with R sided IE in DOTS)	Noninferior: POET (N=200 in each arm)

Rappo et al. *OFID*. 2019;6(1).
Gonzalez et al. *Infect Dis Ther*. 2022;11(1):423–434.

Dalbavancin administration pearls

For counseling patients or when considering use in low-barrier settings

- Must be compounded in sterile environment
- Usually prepared in 500 mL D5W
- Diluted drug is stable for 48 hours
- **Given as 30 min infusion via peripheral IV**
  - Flush line with D5W before/after other IV meds
- Infusion reaction possible --> slow rate
- NO extended monitoring required after dose is given

Evaluating patients for dalbavancin

When to use

- Patient with barriers to standard of care abx
- Indications: SSTI, osteo, complicated bacteremia
- Source control achieved
- Patient can get IV access

When NOT to use

- CNS infections
- Infections due to gram-negatives
- Patient not evaluated/source control not obtained

Dalbavancin 101

- Spectrum of activity
- Administration pearls/logistics
- Indications – data
- When NOT to use

Case-based practice!

TRAFFIC LIGHT GAME!
Practice Case 1

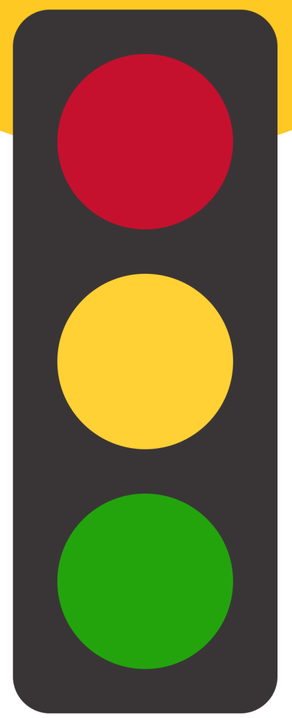
ONE-LINER

35F with OUD on methadone, stimulant use disorder injecting methamphetamine frequently, admitted with complicated Staph Aureus bacteremia.

HOSPITAL COURSE

Has been on vancomycin x 2 weeks.
Needs to leave to get rent check.

IS DALBAVANCIN A GOOD CHOICE?
DISCUSS AT YOUR TABLE FOR 1 MINUTE! HOLD UP A COLOR!



No

Maybe

Yes

CASE 1

ONE-LINER

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HOSPITAL COURSE

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IS DALBAVANCIN A GOOD CHOICE?

CASE 2

ONE-LINER

56M with untreated OUD, stimulant use disorder injecting methamphetamine frequently, presents to ED with back pain, weakness, and murmur.

ED COURSE

CT concerning for epidural abscess.

2/2 blood cultures positive for GPCs in clusters. COWS 12, wants to leave.

IS DALBAVANCIN A GOOD CHOICE?
DISCUSS AT YOUR TABLE - HOLD UP A COLOR

CASE 2

ONE-LINER

56M with untreated OUD, stimulant use disorder injecting methamphetamine frequently, presents to ED with back pain, weakness, and murmur.

ED COURSE

CT concerning for epidural abscess.

2/2 blood cultures positive for GPCs in clusters. **COWS 12, wants to leave.**

IS DALBAVANCIN A GOOD CHOICE?
NOT GREAT - WORRY RE: SOURCE CONTROL. LET'S TREAT OPIOID WITHDRAWAL!

CASE 3

ONE-LINER

28F with stimulant use disorder injecting methamphetamine, well-controlled HIV, admitted with septic arthritis due to Group A Strep.

HOSPITAL COURSE

She is 3 weeks into planned 4 weeks of IV penicillin.
Wants to leave because her partner isn't allowed to visit.

IS DALBAVANCIN A GOOD CHOICE?
DISCUSS AT YOUR TABLE - PICK A COLOR

CASE 3

ONE-LINER

28F with stimulant use disorder injecting methamphetamine, well-controlled HIV, admitted with septic arthritis due to Group A Strep.

HOSPITAL COURSE

She is 3 weeks into planned 4 weeks of IV penicillin.
Wants to leave because her partner isn't allowed to visit.

IS DALBAVANCIN A GOOD CHOICE?
DOES SHE NEED DALBA? COULD WE DO ORAL ABX?

Questions?

Find DALBAVANCIN reference slides here.

PART 2

SELECTING OPTIMAL ORAL ANTIBIOTICS

Using 1-2-4-All approach!

CASE 4

ONE-LINER

43F with untreated OUD, housing instability, admitted from jail with **MRSA mitral valve endocarditis** (0.5cm veg on TEE).

HOSPITAL COURSE

Initiates vancomycin, now on 1.5G Q8H.

Bacteremia x 3 days, now cultures clear on vancomycin.

Initiates methadone, now on methadone 50mg s/p 4 weeks in hospital.

She is a single-parent of a 5 year-old child with autism.

THE PATIENT WANTS TO LEAVE, NO DALBA ACCESS. WHAT ORAL ANTIBIOTICS DO YOU REACH FOR?

WHAT IS YOUR APPROACH TO SELECTING THE OPTIMAL ORAL ANTIBIOTIC REGIMEN IN THIS CONTEXT?

1-2-4-ALL

For 1 minute, think about this yourself.

For 2 minutes, talk to your neighbor.

For four minutes, discuss in a group of 4.

Then we'll all come back together!

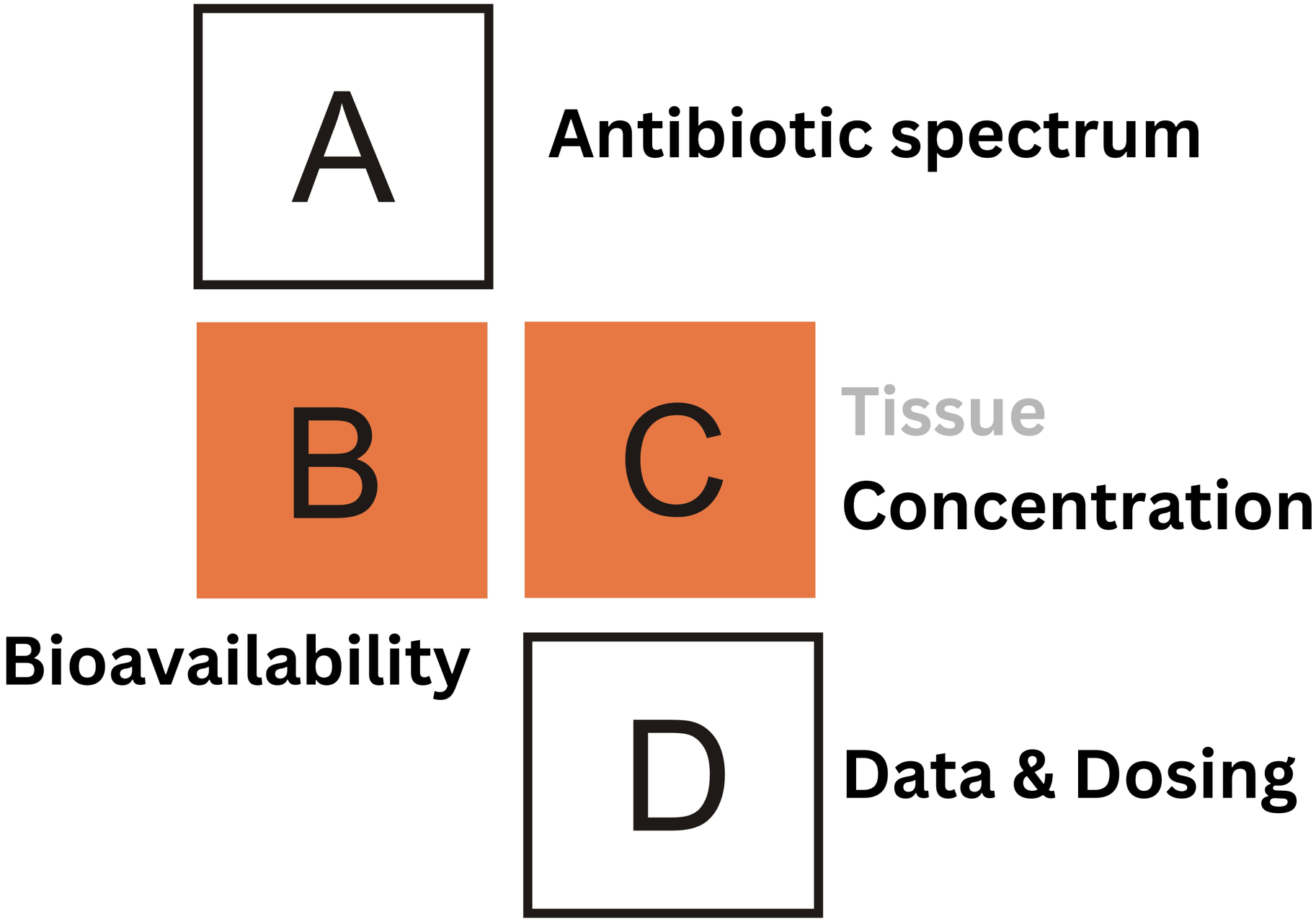
WW Infectious Diseases Do?

A

B

C

D


A
Antibiotic spectrum
B
C
Tissue
Concentration
Bioavailability
D
Data & Dosing

A

B

C

D

Antibiotic spectrum

Organism was Staphylococcus aureus, methicillin-resistant

ORAL ANTIBIOTICS WITH MRSA ACTIVITY

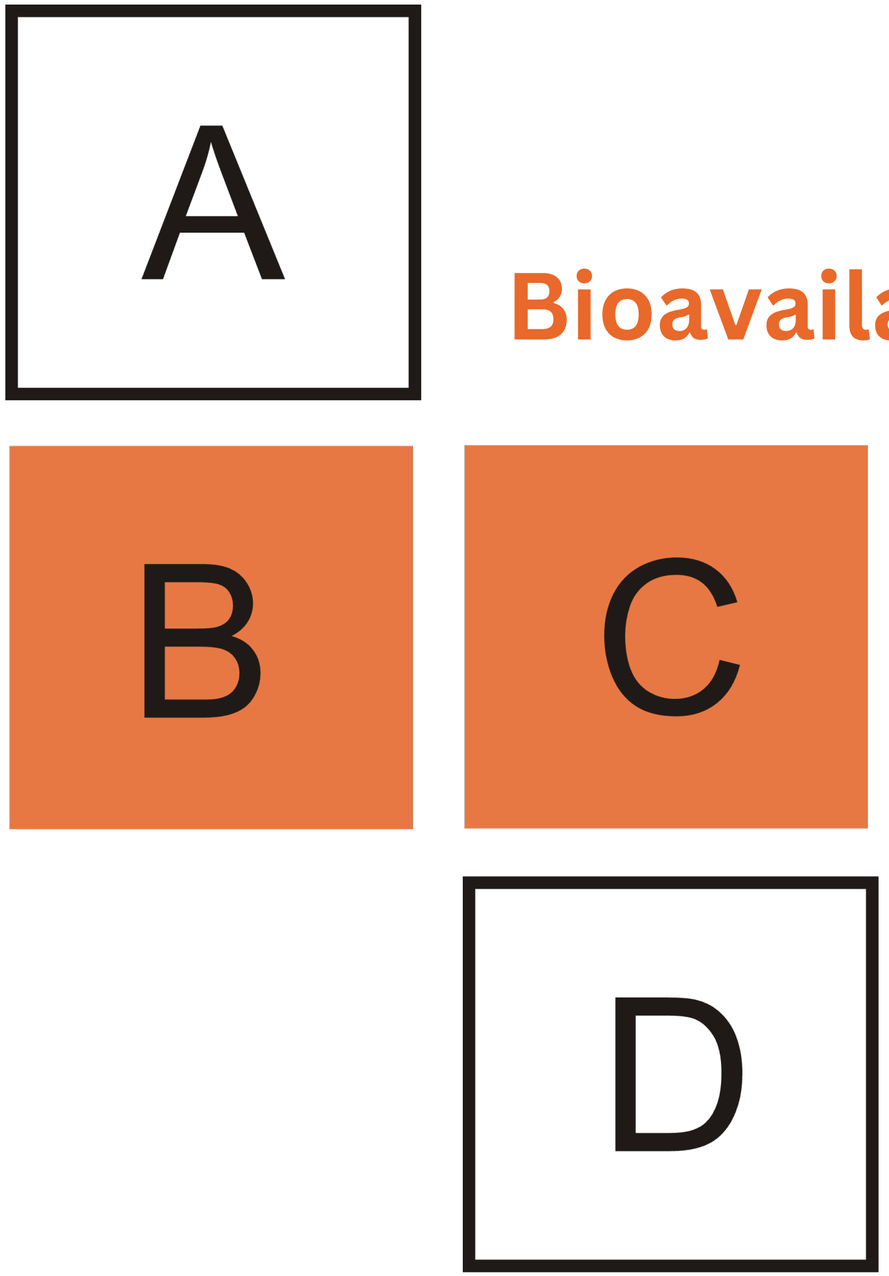
Doxycycline

Linezolid

TMP-SMX

Clindamycin

Ciprofloxacin/Levofloxacin (sometimes)



Bioavailability & Tissue Concentrations

ORAL ANTIBIOTICS WITH MRSA ACTIVITY WITH HIGH BIOAVAILABILITY & GOOD SERUM LEVELS

Linezolid

TMP-SMX

Ciprofloxacin/Levofloxacin

Clindamycin

A

B

C

D

BIOAVAILABLE ORAL ANTIBIOTICS WITH MRSA ACTIVITY WITH BEST CLINICAL DATA FOR ENDOCARDITIS

Linezolid

TMP-SMX

Clindamycin

Doxycycline

Ciprofloxacin/Levofloxacin (would need rifampin)

CLINICAL DATA & DOSING

Bug	Examples	Drug & Considerations

Gram positives	Staph, Strep
	NO DDIs with methadone or bupe
		• Linezolid
		  ◦ Check drug interactions; if on >1 other serotonergic agent, counsel patient re serotonin syndrome. Would be very cautious with more than 3 total agents (linezolid + 2 others)
		  ◦ Can cause thrombocytopenia with courses >2 weeks so monitoring q2 wk ideally obtained, can counsel patients on warning signs
		  ◦ **Preferred PO for endocarditis/bacteremia** (in POET trial)
		• TMP/SMX (Bactrim)
		  ◦ If CKD/AKI, watch for high K+ (potassium) particularly if 2 DS BID dosing
		  ◦ **Secondary PO for endocarditis/bacteremia**
		• Doxycycline
		  ◦ Photosensitivity
		  ◦ **Good PO for osteoarticular infections**
		• Cefadroxil (non-MRSA)
		  ◦ BID cephalosporin!
		• Levofloxacin or Moxifloxacin – strep only
		  ◦ Check QTc if also on methadone
		• *Rifampin*
		  ◦ Usually used as adjunct in Staph endocarditis or prosthetic infection once no longer bacteremic
		  ◦ Will **decrease** methadone & bupe levels by upregulating hepatic metabolism – **patients likely need MORE methadone while on rifampin and LESS methadone after stopping**
		  ▪ Induction/de-induction lags by 1-2 wk
		  ◦ If this is going to be destabilizing for patient's OUD, rifampin usually not necessary
		  ◦ Consider **rifabutin** instead for pts on methadone/bupe (interaction possible but much less)

Gram negatives	Pseudomonas, Serratia	• Levofloxacin or Ciprofloxacin
		  ◦ Moxifloxacin – not for Pseudomonas (but once daily)
		  ◦ Check QTc if also on methadone
		• TMP/SMX (Bactrim) – not for Pseudomonas
		  ◦ Only if organism with demonstrated susceptibility

TRYing to keep it simple: an oral antibiotic cheat sheet

Bug	Examples	Drug & Considerations

Gram-positive bacteria	NO DDIs with methadone or bupe
	
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BACK TO THE CASE

ONE-LINER

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HOSPITAL COURSE

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Bacteremia x 3 days, now cultures clear on vancomycin.
Initiates methadone, now on methadone 50mg s/p 4 weeks in hospital.

**THE PATIENT WANTS TO LEAVE, NO DALBA ACCESS.
YOU DISCUSS WHERE HE'LL GO AFTER DISCHARGE, HOW OFTEN HE COULD TAKE ORAL ANTIBIOTICS.
DECIDE TOGETHER ON LINEZOLID BID X 2 WEEKS.**

A

Antibiotic spectrum

B

Bioavailability

C

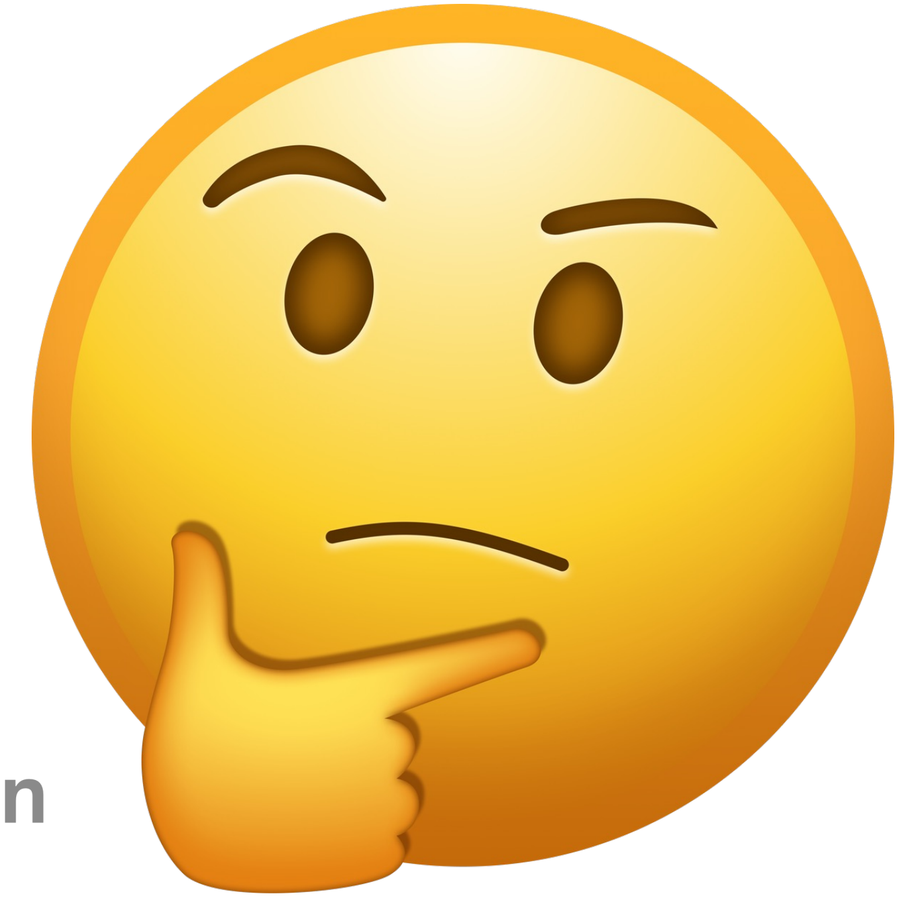
Tissue

Concentration

D

Data &

Dosing



Where does our patient fit in to this?

PART 3
SHARED DECISION-MAKING ABOUT ANTIBIOTICS

Walking through a conversation guide with your neighbor

Shared decision making defined

A collaborative care process that allows patients and their providers to make health care decisions together, taking into account the best available evidence about benefits and harms, as well as patient goals, values, and concerns (preferences).

Sepucha *Health Affairs* 2004

Harm reduction approaches for discharging hospitalized patients

CURBSIDE CONSULT

Can I Safely Discharge a Patient with a Substance Use Disorder Home with a Peripherally Inserted Central Catheter?

Authors: Ayesha Appa, M.D., and Joshua A. Barocas, M.D. Author Info & Affiliations

Published January 25, 2022 | NEJM Evid 2022;1(2) | DOI: 10.1056/EVIDccon2100012 | VOL. 1 NO. 2

Appa et al, *NEJM 2022*, Moore et al, *Therapeutic Infectious Diseases* 2022
Morales, OFID 2022. Baddour *Circulation* 2022 Thakarar et al *Therapeutic Infectious Diseases* 2023

CONVERSATION GUIDE*

A Step-by-Step Guide

SET UP THE CONVERSATION

I'd like to talk to you about treatment options for your infection. Is that OK?

ASSESS UNDERSTANDING

- What have you heard from your medical team about why you are on antibiotics?
- How serious is the infection?
- How long do you need to be on antibiotics?
- What would happen if you didn't take the antibiotics or stopped them sooner than recommended?

SHARE PROGNOSIS

- As you know, you have a serious infection. My hope is that we can treat your infection successfully, but I worry that the infection could come back if we don't give you **(ROUTE)** of antibiotics for **(XX amount of time).**
- If the infection came back, this would mean you could possibly end up back in the hospital with a worse infection, the infection could be harder to treat, or you could die.

EXPLORE KEY TOPICS

The reason I want to have this conversation is because there are a few different options for your treatment. I'd like to be able to talk with you about how these treatments differ in terms of how well they work. I'd also like to consider with you how these choices might fit in with your life.

- First, can you tell me a little about what matters to you most when you think about your infection.
- Are there any things in your life that might make it hard for you to get this treatment for your infection?
- What sorts of things have brought you strength in the past when you have had to get through difficult times?
- What would be hardest about staying in the hospital for **XX** amount of time?
- What would be hardest if you were to be discharged to finish your treatment?

Now I'd like to ask you a little bit about drug use. I am not here to judge you; I

Conversation guide as a harm reduction-based approach

“It makes me feel **safer going home and have a better control of my health…when you get to be…part of the decision**,…it’s control. I have a say in my life, because a lot of times in situations like this, you don’t.”
Patient

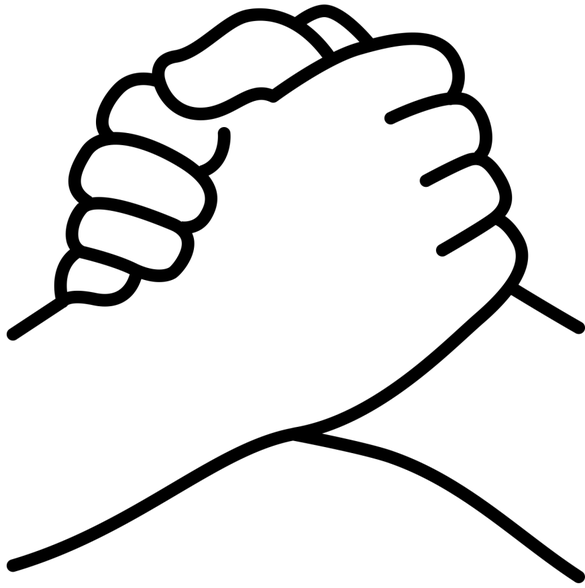
”…it's still important to have open discussions with people, understand their goals, worries, strengths and weaknesses. And I think the guide helps do that."
Health Care Professional

Thakarar et al, *Thera Adv Infect Dis* 2022

WHAT DOES THIS LOOK LIKE IN PRACTICE?

Scan QR code and work through a script with your neighbor for next 5-10 minutes!

Other innovative ways to incorporate harm reduction into antibiotic discharge planning?



Multidisciplinary Interprofessional Care Conference

- "OPTIONS-DC" est 2018 at OHSU
- Identify treatment options agreeable to both patients and clinical team
  - Harm reduction
  - Patient-centered care
- Primary team, ID physician, ACS (medical provider, SW, peer), CM
- Led by OPAT RN
- Improve cross-team communication and care coordination decisions
- Standardized conference tool

Sikka et al, BMC Infect Dis 2021.

OPTIONS DC: Standardized Conference Tool

Figure 1: OPTIONS DC Conference Format

Introductory Script: "Thank you for taking time to attend this conference. OPTIONS-DC is a structured multidisciplinary conference with a goal to review all aspects of OPAT and discuss the best and safest options for this patient to receive treatment for their infection. I will ask each discipline to weigh in on specific questions. It is vital that we consider patient preferences in discharge planning and treatment decisions. As we proceed, I ask that everyone approach this discussion with the following ethical principles in mind:

- How much is paternalism playing a role in this decision-making process?
- What is beneficent in this patient's situation?
- What is non-maleficent in this patient's situation?
- What autonomy does this patient have in the current situation?"

Because the language we use when talking about addiction can reduce stigma and improve care, we want to take an opportunity to remind people to use person-first, non-stigmatizing language (for example, avoiding the term "abuse"). Folks are encouraged to gently remind one another about this as we are all learning."

Topic (responsible participant)	Specific considerations for review
1. Infection type and management (ID)	Therapeutic options (Drug, dose, route, frequency)
	Recommended duration of therapy
2. Antibiotic Administration and Setting Safety (OPAT, ID, CM) • Which route (IV, long acting, PO)? • What setting (hospital, home infusion, infusion center, SNF)?	Living environment: *Access to running water, refrigeration, heat in winter, non-abusive/safe environment*
	Provider ability to reach patient after discharge: *Working personal cell phone, available emergency contact*
	Patient ability to self-manage care; social supports
	Insurance coverage in outpatient settings
	Transportation
3. Substance use history (ACS)	Substance, severity, use practices
	Engagement with ACS in hospital
	Medication treatment for SUD
	Peer support and engagement
	Potential use triggers, including PICC line
4. Patient goals and preferences (all; commonly ACS peer provides unique insights)	Understanding of seriousness of infection and possibility of progression if not fully treated
	Other patient-identified priorities (e.g. parenting, work)
5. Stability for discharge (primary team)	Skilled Nursing needs
	Physical or occupational therapy needs
	Wound care needs
6. Access to outpatient care (primary team, ID, ACS)	Established primary care provider
	Plan for continuing SUD care after discharge
	Ongoing additional mental health needs and follow up
	Plan for ID follow-up including imaging needs

Sikka et al, BMC Infect Dis 2021.

Care conference model not possible?

When care conference not held… Consider an essentials checklist!

- Patient preference
- Follow up (working phone, transitional care support, PCP, transport)
- Insurance considerations
- Documentation in chart & patient AVS
- Based on system, consider who/what roles completing tasks

Shared decision-making study acknowledgements

Study participants
Study team:
MaineHealth: Michael Kohut, PhD, Henry Stoddard MPH, Deb Burris RN, Frank Chessa, PhD, Rebecca Hutchinson, MD, MPH, Kathleen M. Fairfield MD, DrPH, MPH.
Tufts University: Tom Stopka, PhD. Baystate: Peter Friedmann, MD.
Dartmouth Hitchcock: Colleen Kershaw, MD.
Brigham and Women's: Daniel Solomon, MD.
University of Alabama; Ellen Eaton, MD.
OHSU: Monica Sikka, MD, Alyse Douglass, RN, Kathleen Young, RN, CARN, Heather Mayer, RN, Liz Parkes-Perret, Celine Jo, MD/MPH candidate,
Tufts University School of Medicine Rebecca Hutchinson, MD, MPH, MaineHealth/Tufts University School of Medicine,
Funders: Tufts CTSI, National Center for Advancing Translational Sciences, National Institutes of Health, Award No. UL1TR002544.

WHY ARE YOU HERE TODAY?

Think about the patient's story you started this session with -
what is one thing you'll take with you? or one thing you might do differently now?

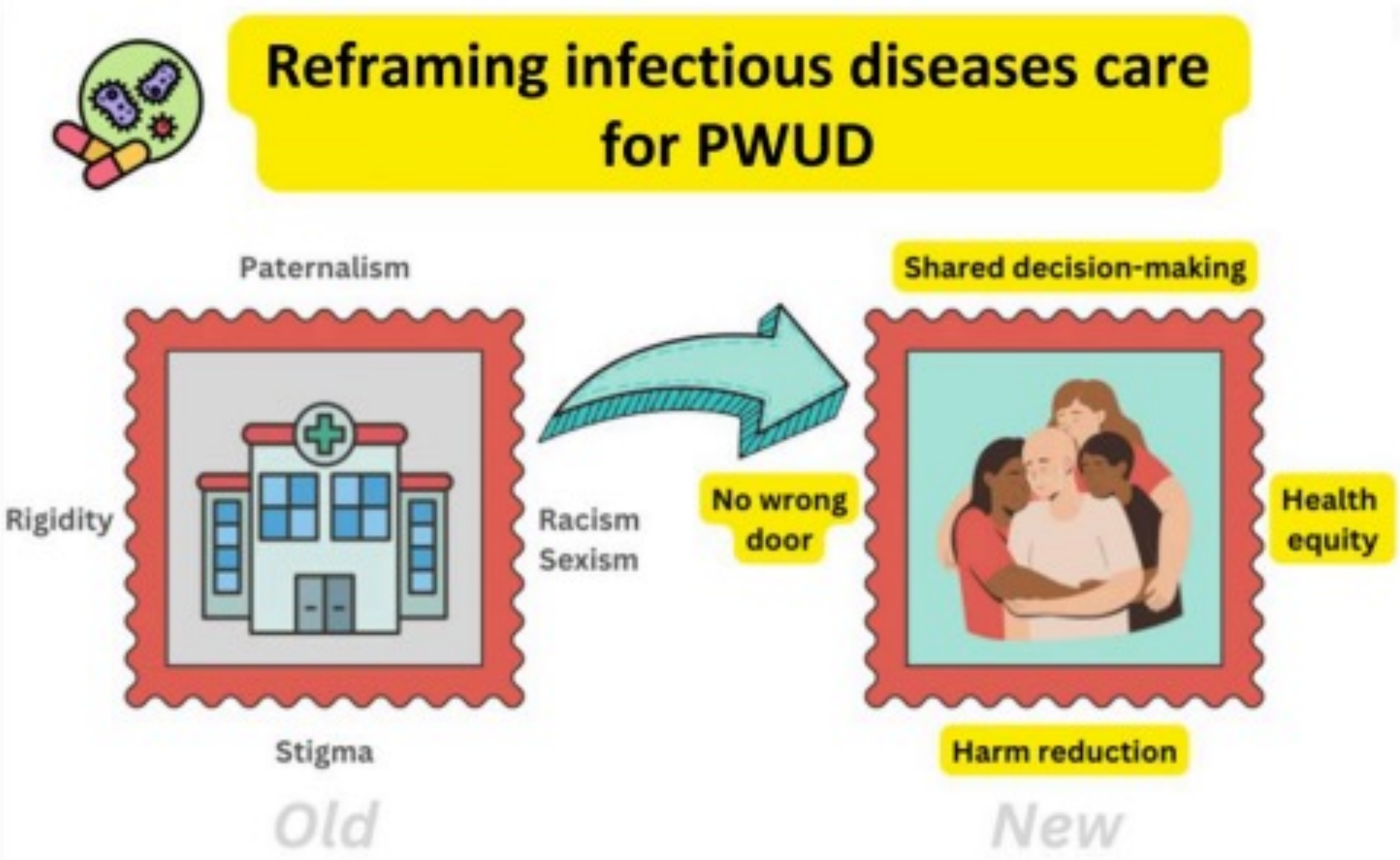


Figure 1. Key tenets of improving infectious diseases care of PWUD include reframing our clinical decisions around principles of shared decision making, health equity, and harm reduction and ensuring that all doors remain open to engagement in infection and/or substance use disorder treatment. Abbreviation: PWUD, people who use drugs.

Thakarar K, Appa A, Abdul Mutakabbir JA, et al. *Clinical Infectious Diseases*, Volume 78, Issue 2, 15 February 2024, Pages e12–e26, https://doi.org/10.1093/cid/ciad664

THANK YOU!

Questions, thoughts, concerns?

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