



*August 27, 2019*

## **Agenda**

- Didactic: PK/PD
- Case Discussions:  
Spontaneous Bacterial Peritonitis



# UW/TASP

tele-antimicrobial stewardship program

## PK/PD

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August 27, 2019

*This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.*



# Agenda

- **Defining Terms**
- **PK/PD Dosing Principles**
- **Application: Obesity**
- **Application: Prolonged Infusion**



# Defining Terms: Pharmacokinetics

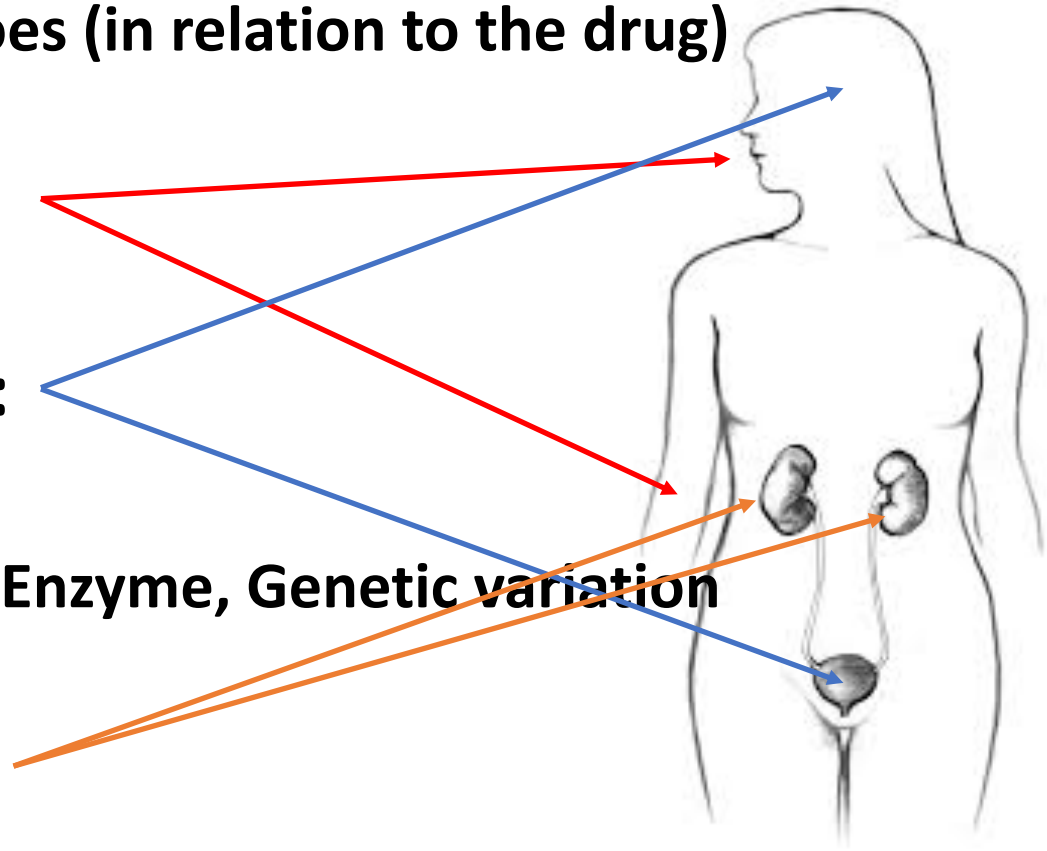
What the body does (in relation to the drug)

**ABSORPTION:**

**DISTRIBUTION:**

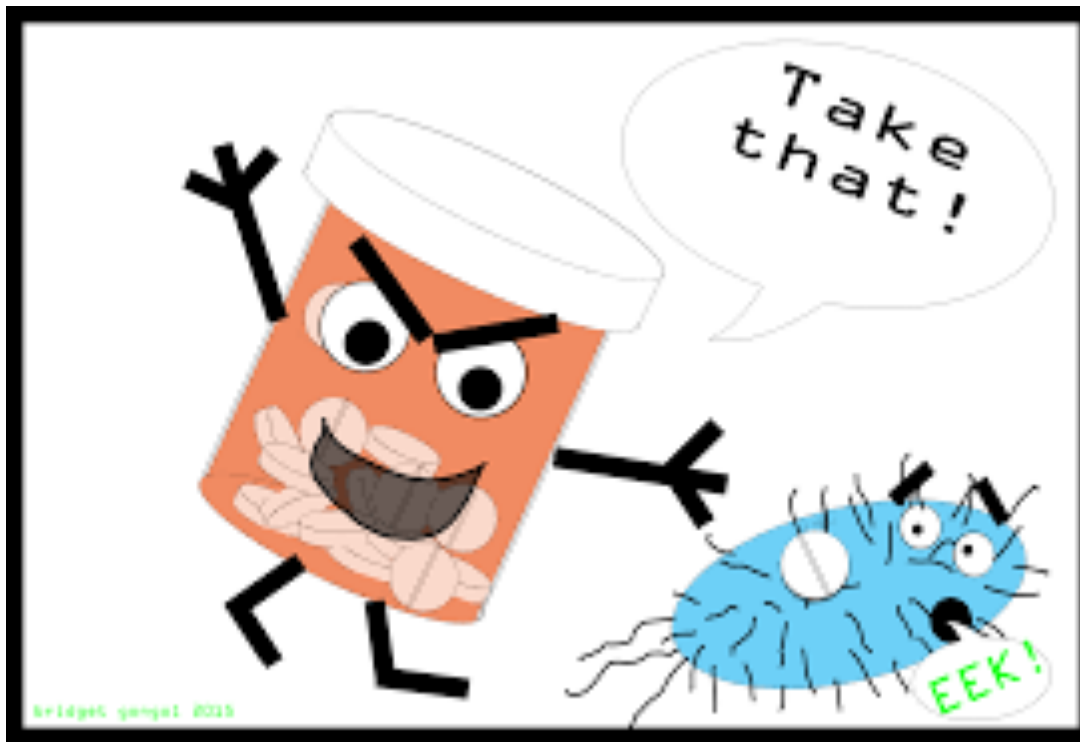
**METABOLISM:** Enzyme, Genetic variation

**ELIMINATION:**



# Defining Terms: Pharmacodynamics

What the drug does (in relation to the body)

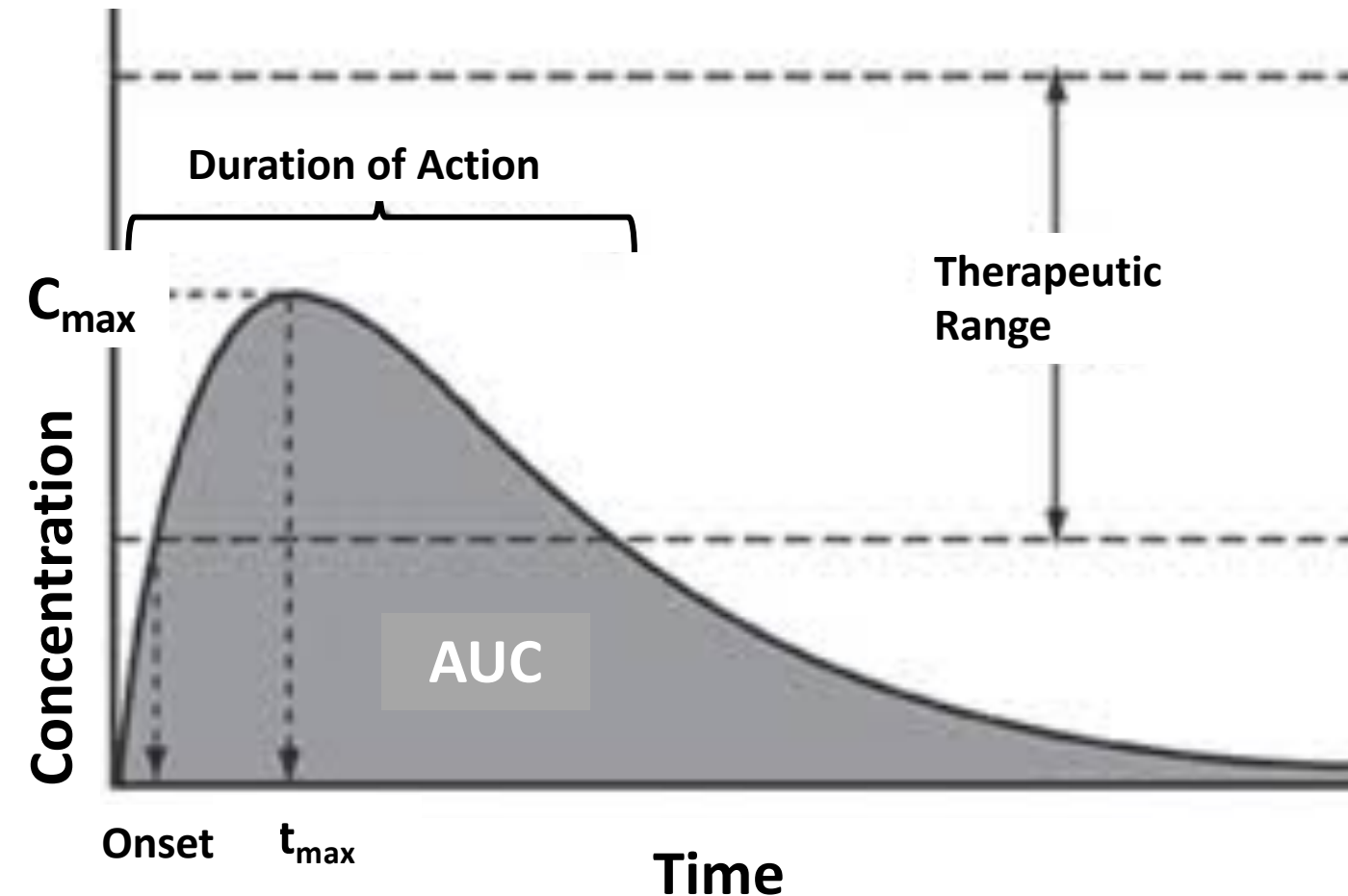


**Efficacy of Antibiotics  
is directly related to  
how we dose them**



# Defining Terms: Pharmacodynamics

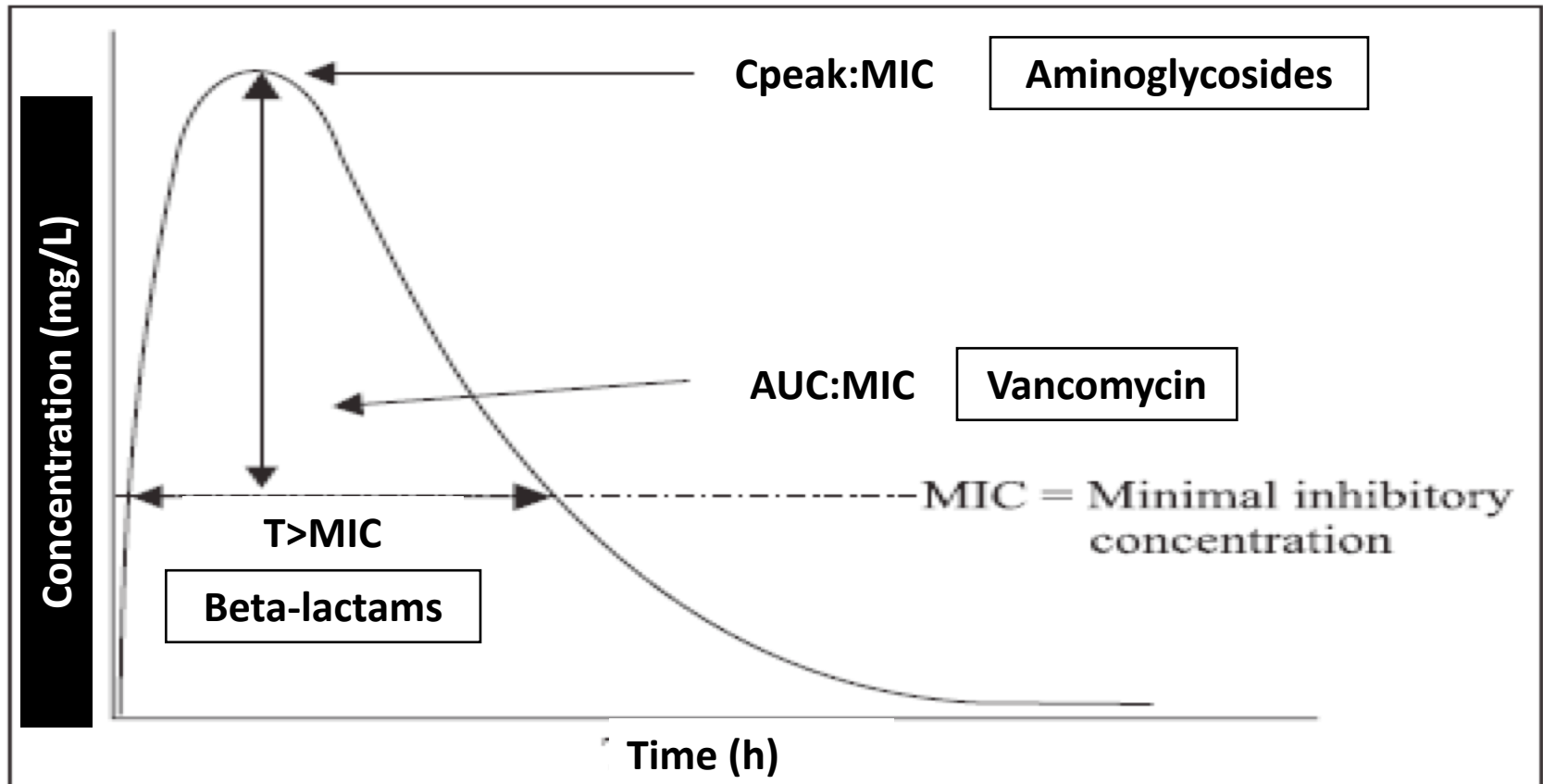
What the drug does (in relation to the body)



# PK/PD Dosing Principles:

## Managing antibiotic dose in relation to bacteria

What the drug does (in relation to the body)



AUC = Area under the curve, MIC = Minimal inhibitory concentration, T = Time

Santos Filho L et al. Braz J Microbiol. 2007 Apr/June;38(2):183-193.

Meagher AK et al. Antimicrob Agents Chemother. 2007 Jun;51(6):1939-45.

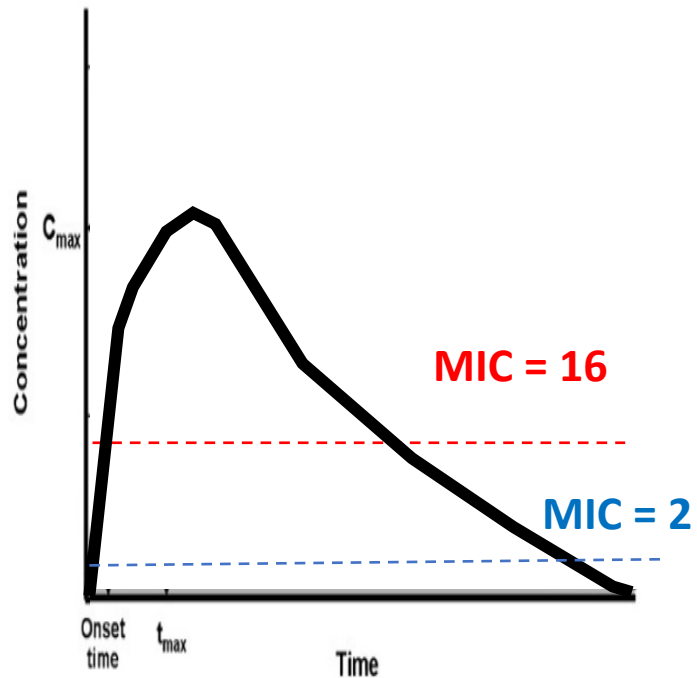
Craig WA. Infect Dis Clin North Am. 2003 Sep;17(3):479-501.



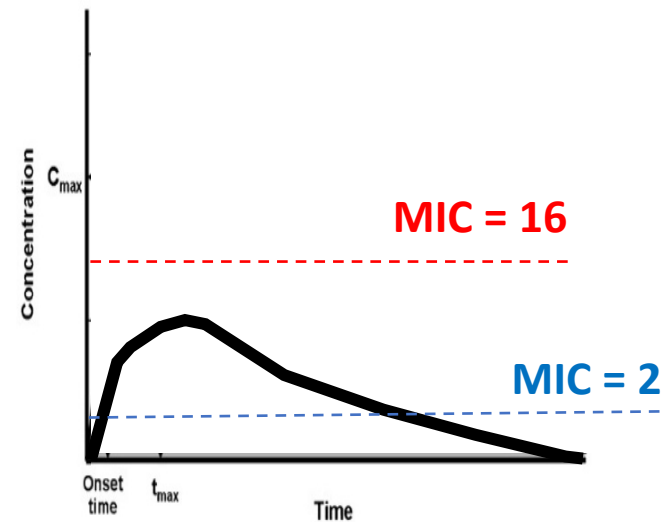
# PK Practical Applications:

## Cefazolin concentration in blood vs. urine

### URINE Concentrations of Cefazolin



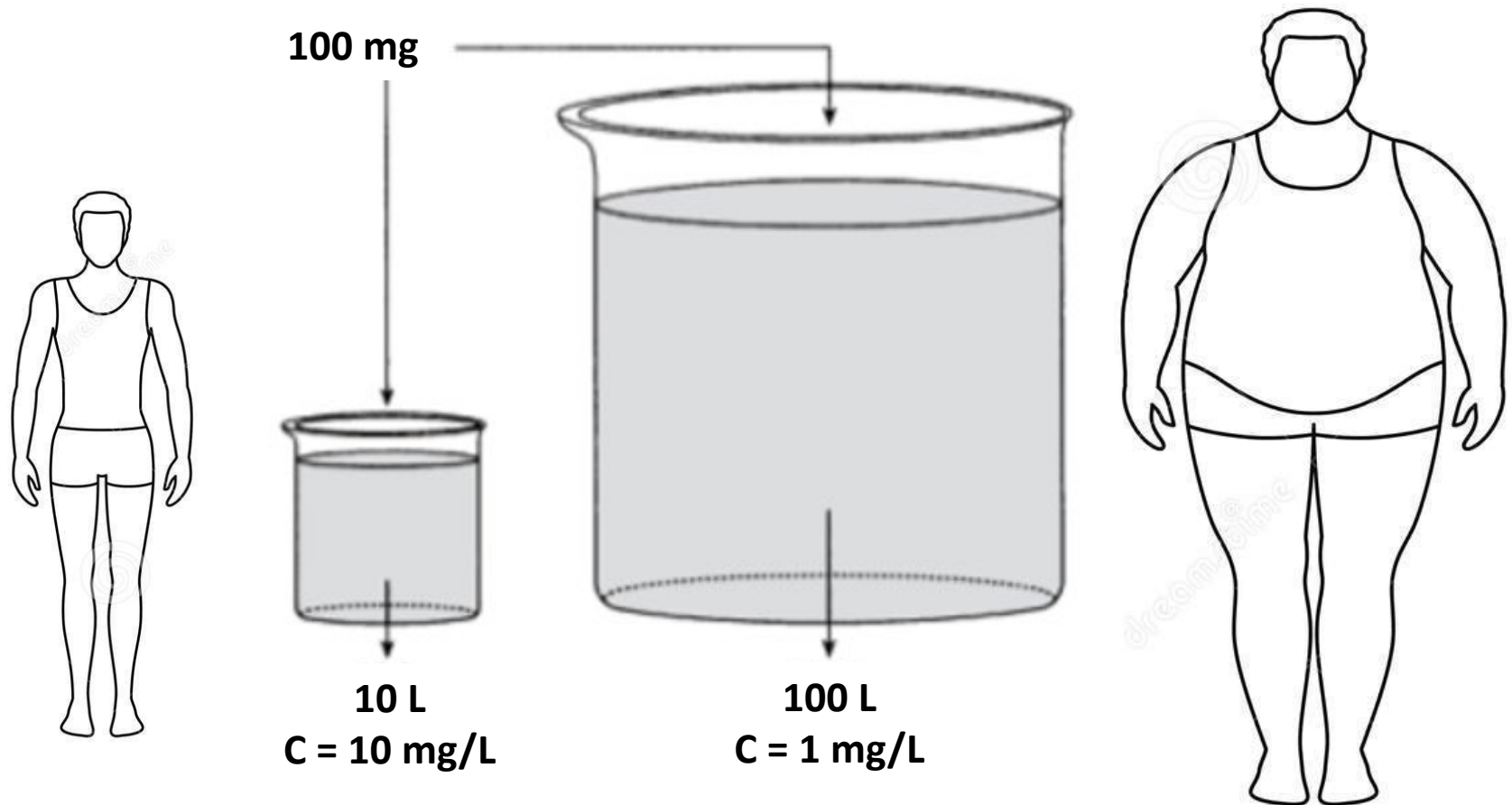
### BLOOD Concentrations of Cefazolin





# PK Practical Applications:

## Dosing in Obese Patients



# PK Practical Applications:

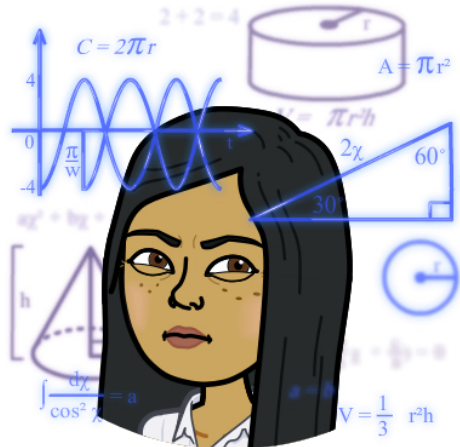
## Obese Patients: PK Altered due to Extra Adipose Tissue

Total  
Body Weight

Ideal  
Body Weight

### Hydrophilic Drug

Adipose is 30-40% water  
Ex: Gentamicin



### Hydrophobic Drug

(Lipophilic)  
Drug accumulation  
Ex: Amphotericin B

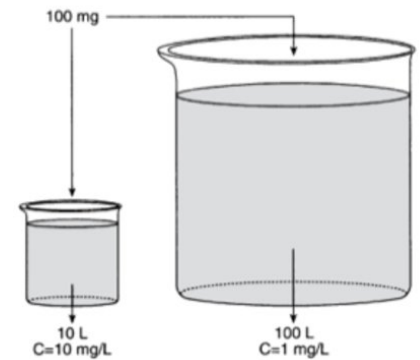
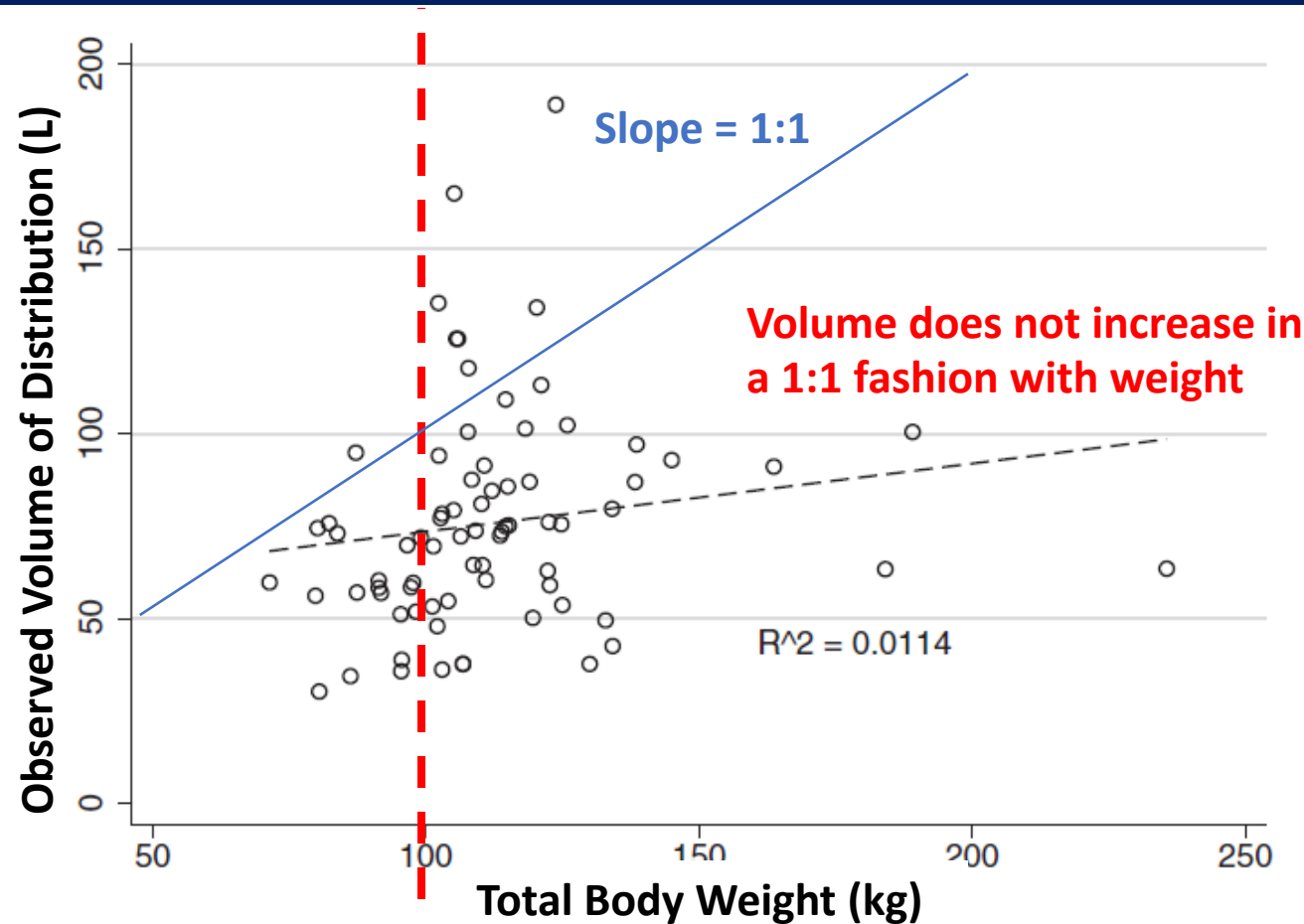


Adjusted  
Body Weight



# PK Practical Applications:

## Total Body Weight Overestimates Vanco Dose in Obese Patients



Bauer LA, Applied Clinical Pharmacokinetics 2nd Edition

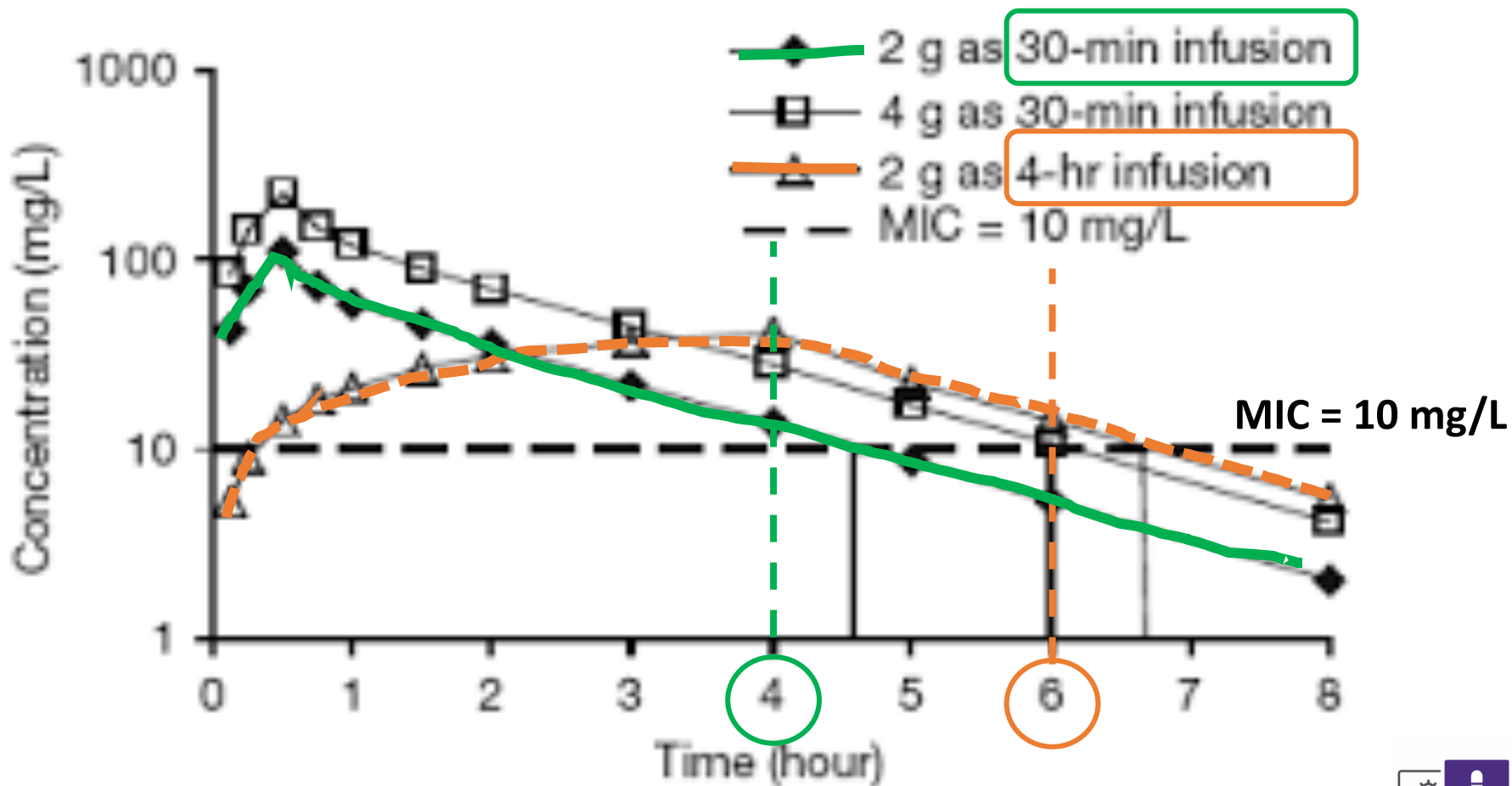
Figure 2. Scatterplot and linear fit plot of the observed vancomycin volume of distribution based on two-sample estimation compared to total body weight.



# PD Practical Applications:

## Prolonged infusion of Piperacillin/Tazobactam

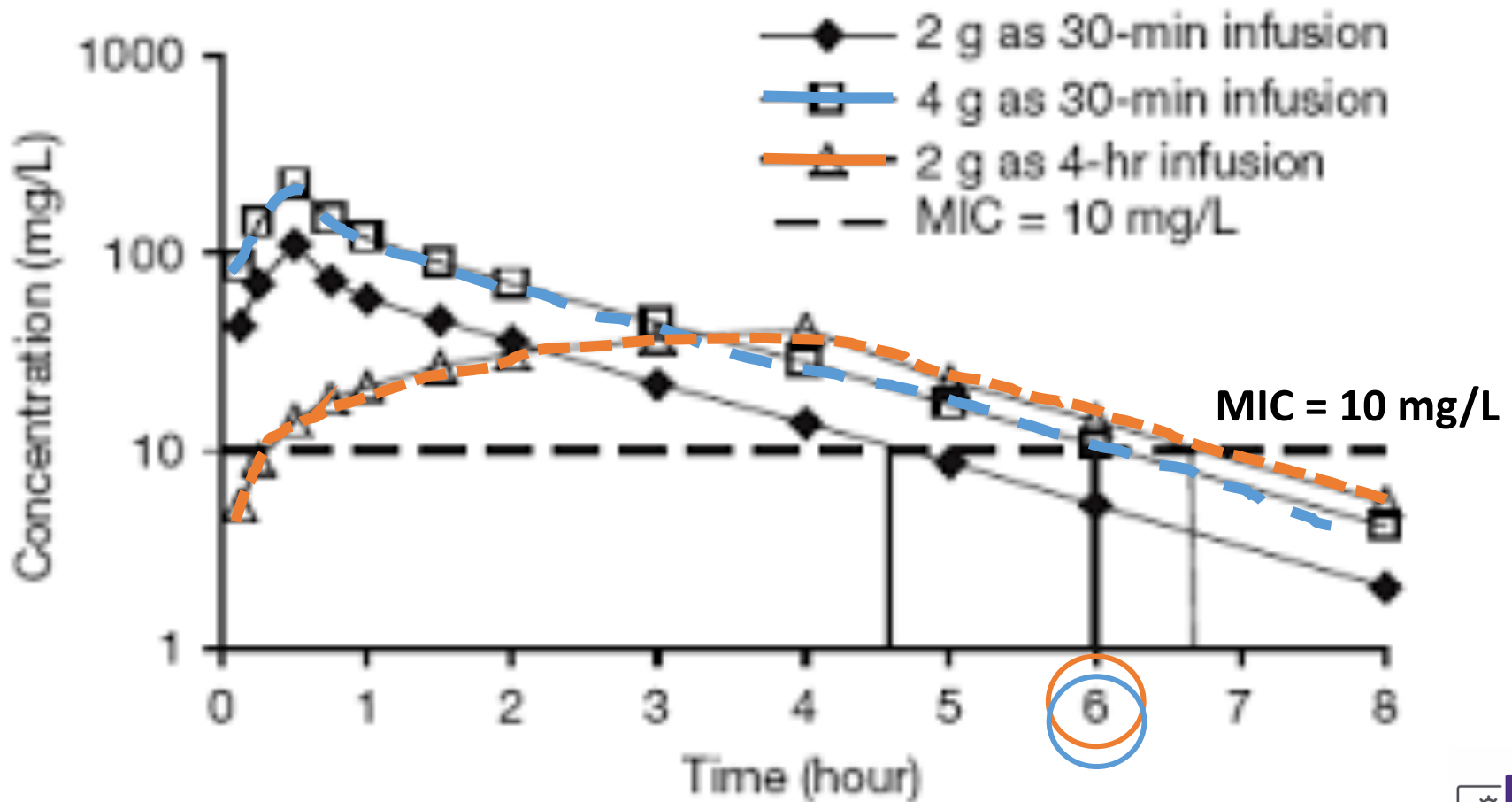
Dosing goal: Drug concentration > MIC for as long as possible



# PD Practical Applications:

## Prolonged infusion of Piperacillin/Tazobactam

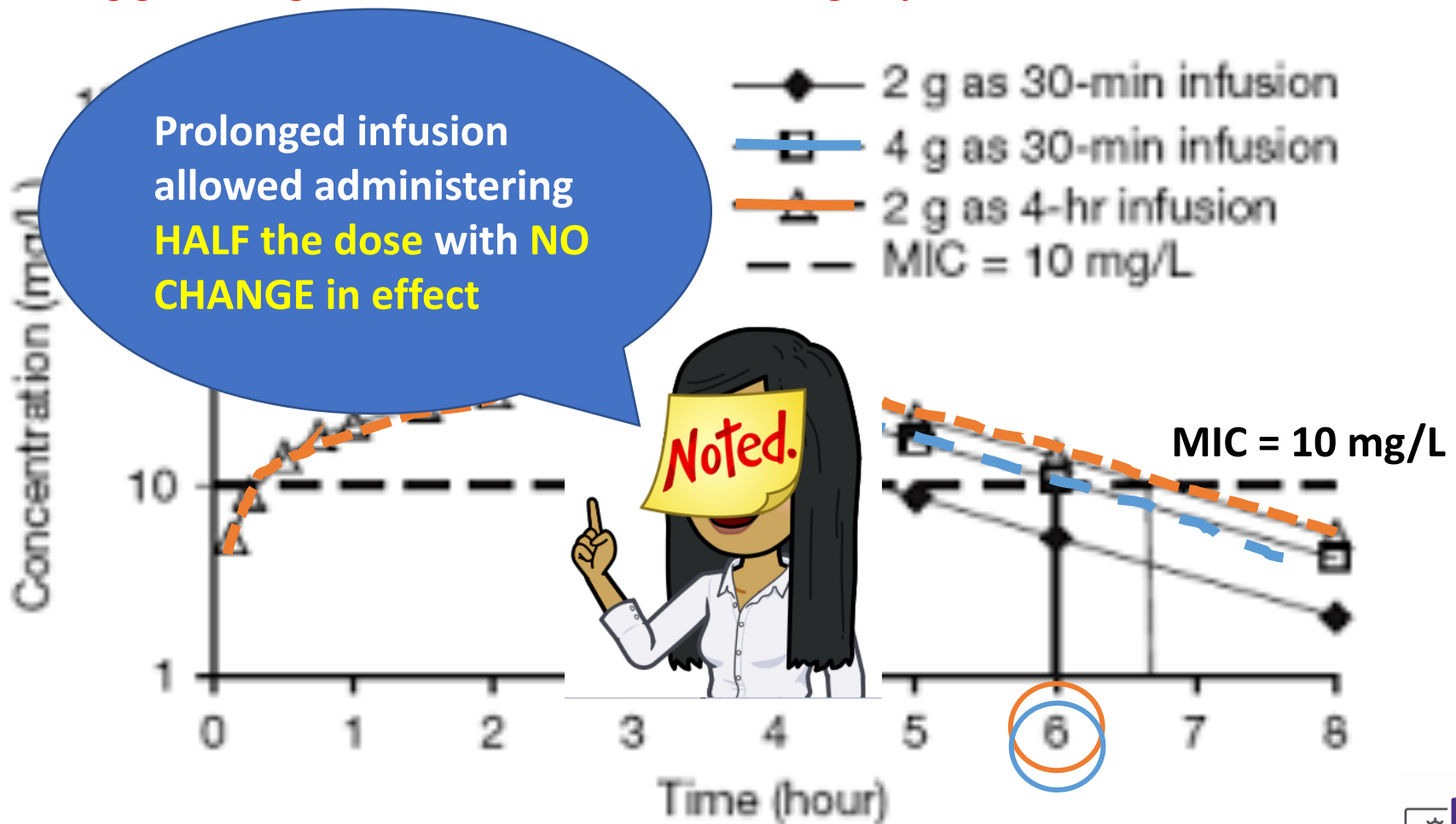
Dosing goal: Drug concentration  $>$  MIC for as long as possible



# PD Practical Applications:

## Prolonged infusion of Piperacillin/Tazobactam

Dosing goal: Drug concentration  $>$  MIC for as long as possible



# Summary

## **PK/PD Dosing Principles**



To optimize antibiotic activity (i.e. pick a dose) consider

- How the body acts on the drug (PK)
- How the drug acts on the body/bacteria (PD).

## **Application: Obesity**



Drug concentration does not always increase linearly with weight.  
Hydrophilic vs hydrophobic drugs will accumulate differently

## **Application: Prolonged Infusion**



For Pip/Tazo, giving less drug over a prolonged infusion allows reduction in total dosage used without compromising efficacy

