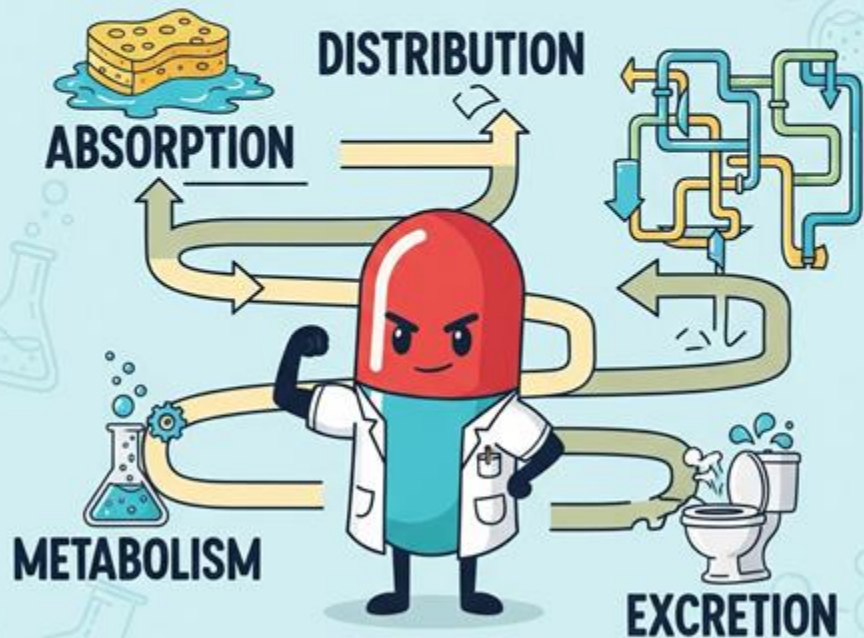


PHARMACOKINETICS

is Simple Sometimes



Pharmacokinetics is Simple ... Sometimes

DH 05
PHUSE EU CONNECT

Vincent Buchheit

November 2025

Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



Data Inconsistencies and Missing Data



Exposure Response



Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



Data Inconsistencies and Missing Data



Exposure Response



50% of Package Insert is provided by Pharmacokinetic Data Analysis (e.g. Invirase®)

Warning

PK: ADME

Special Populations

Drug Interactions

Contra-indications

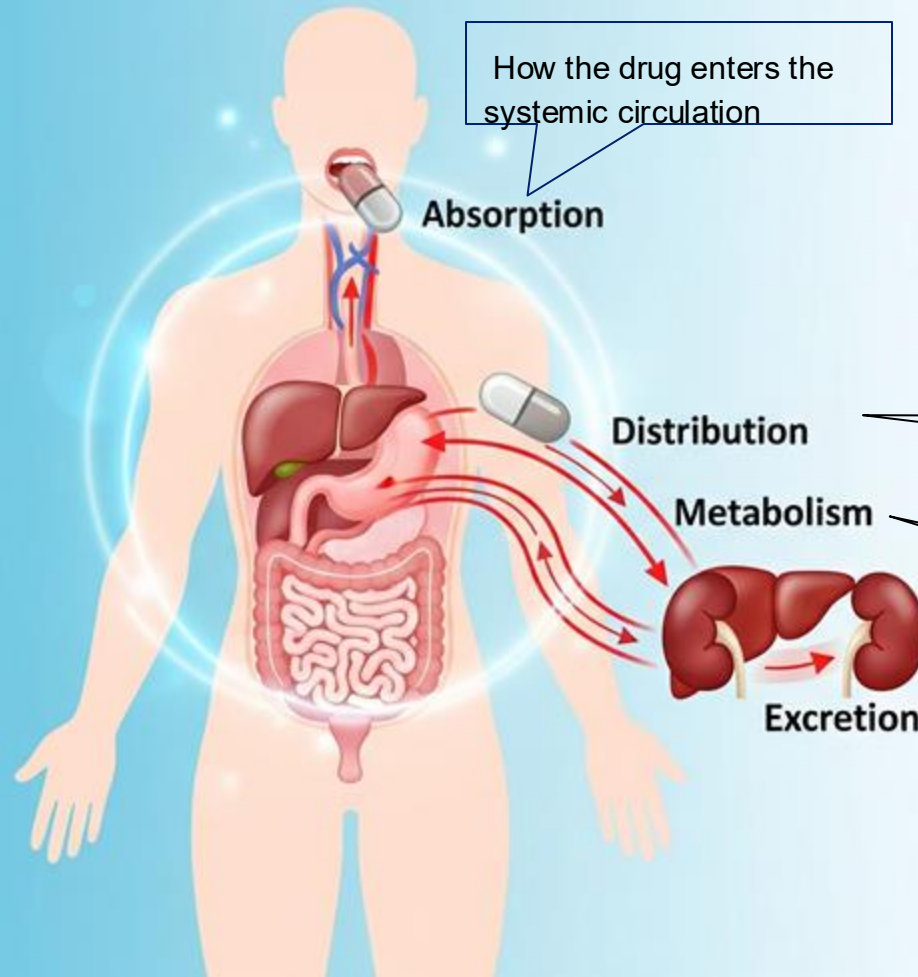
Warnings

Precautions

Drug Interactions

Adverse Reactions

Dosage and Administration



Pharmacokinetic (PK) =

What the body does to the drug

How the drug spreads throughout the body

How the body modifies the drug into metabolites

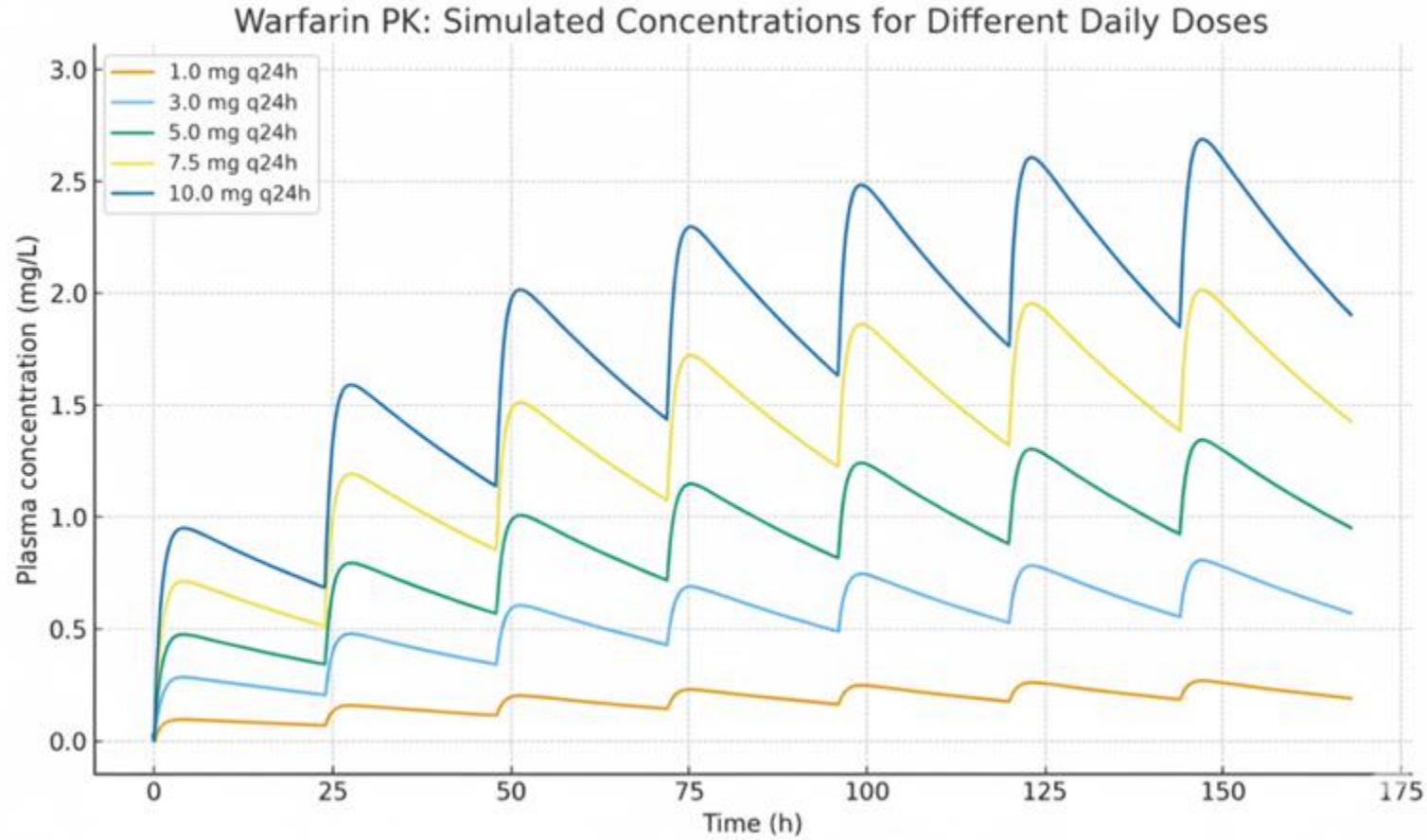
How the drug and its metabolites are eliminated from the body

Why do we collect Pharmacokinetic (PK) data?

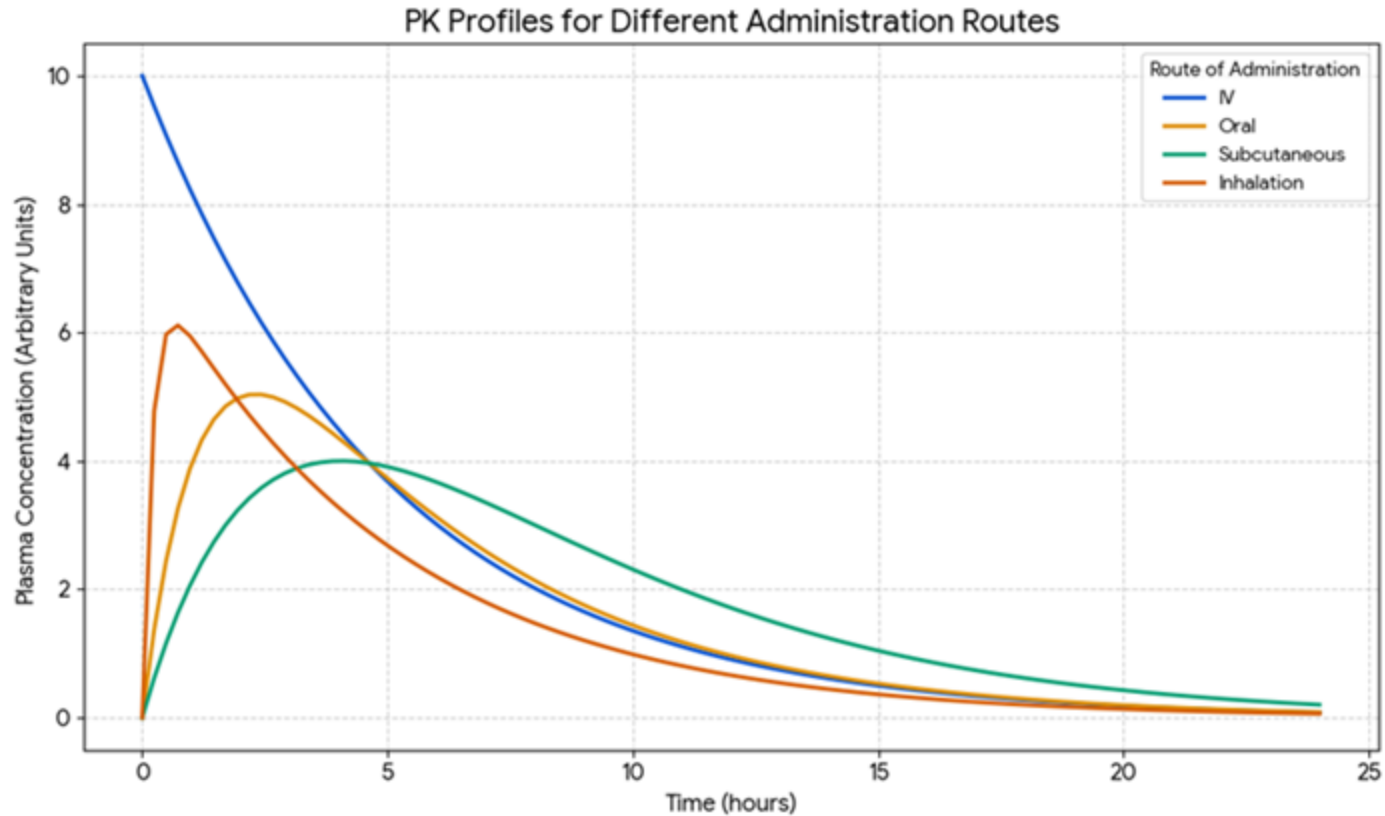


- Understand drug concentration-time profile
- Determine appropriate dose and dose frequency to achieve desired therapeutic effects while minimizing adverse events

Impact of Dose Level



Impact of Route of Administration



Patient Variability

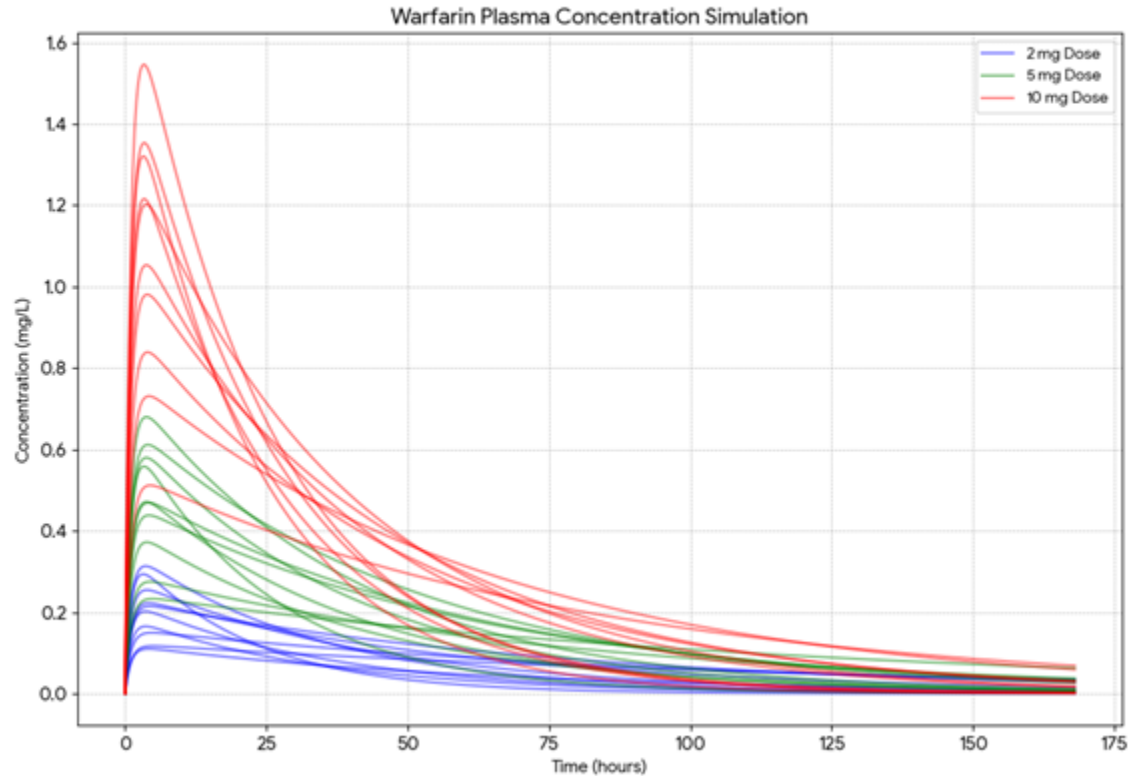


Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



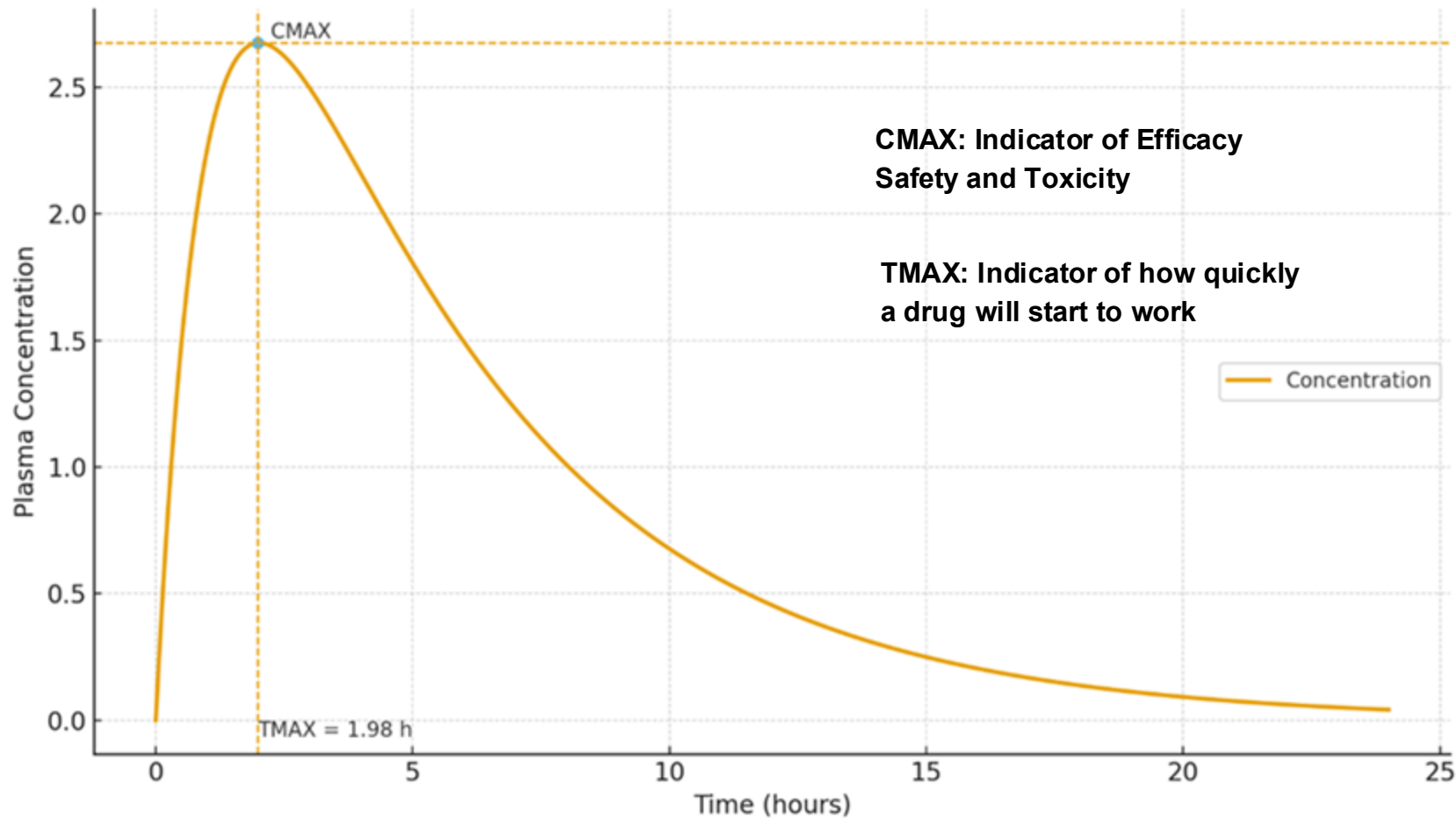
Data Inconsistencies and Missing Data



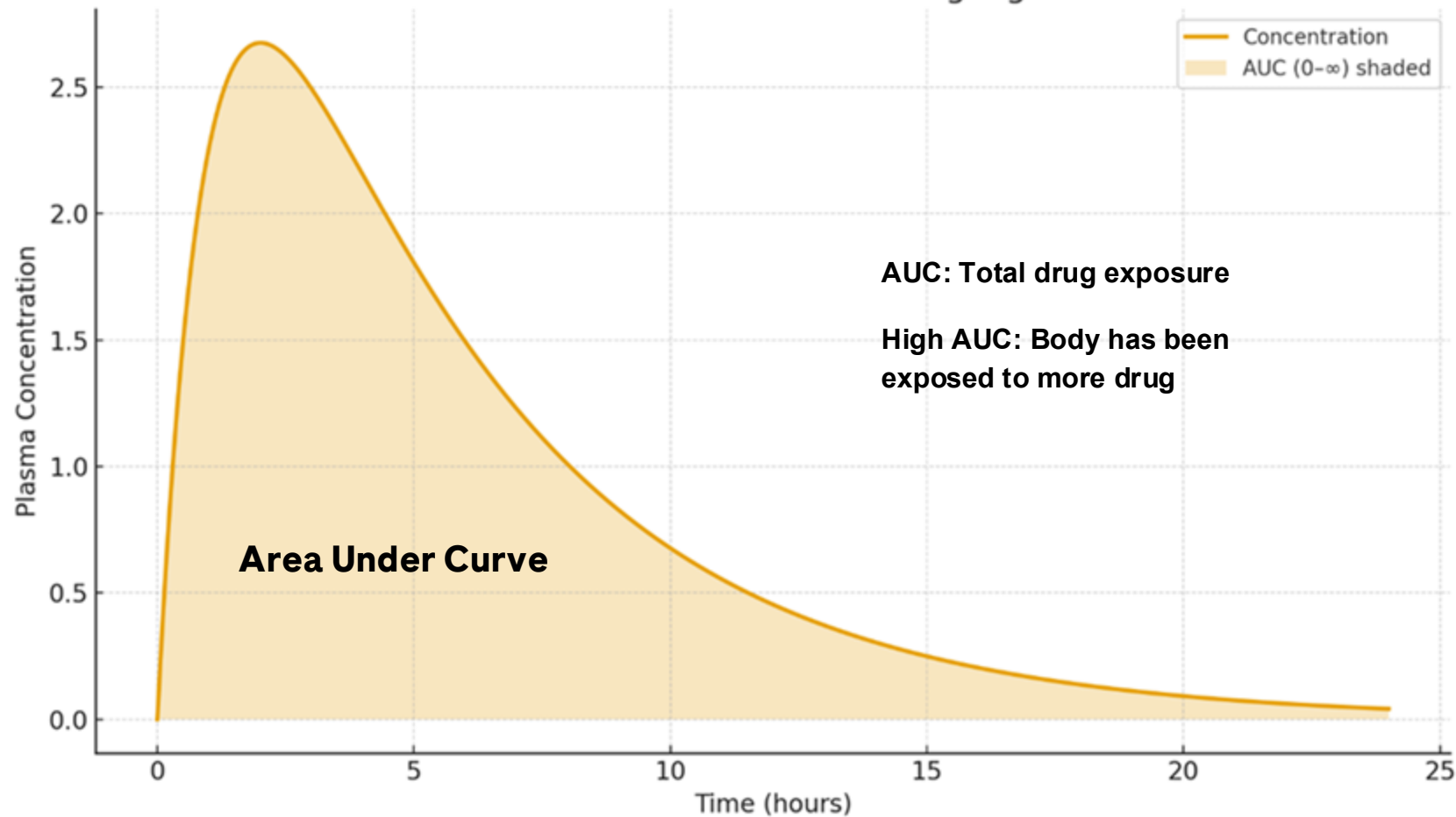
Exposure Response



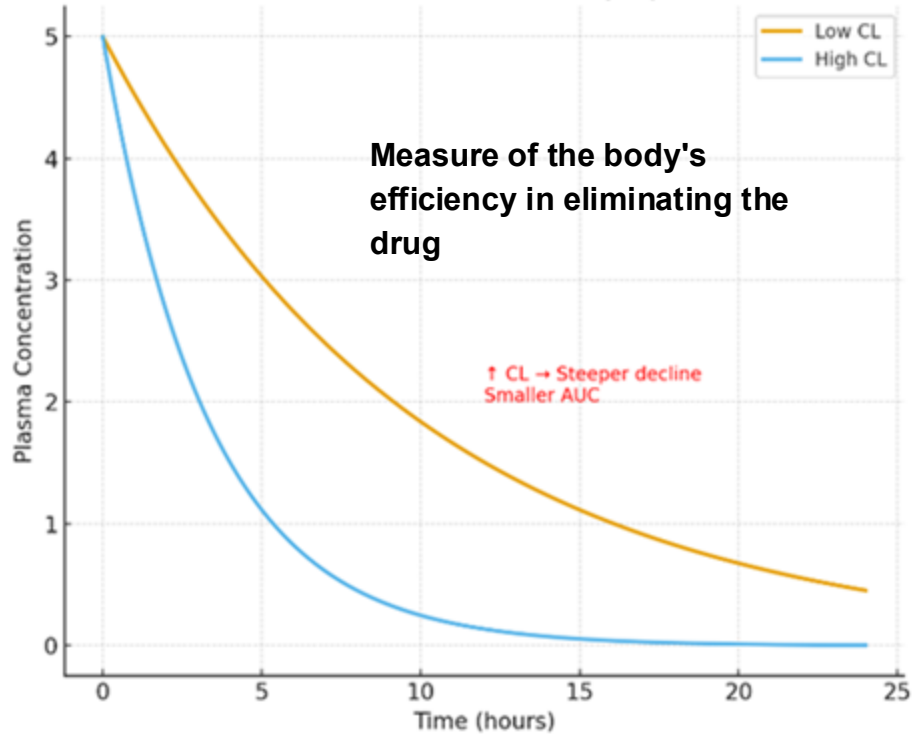
Simulated PK Profile — CMAX & TMAX



Simulated PK Profile — AUC Highlighted



Effect of Clearance (CL)



Effect of Volume of Distribution (Vd)

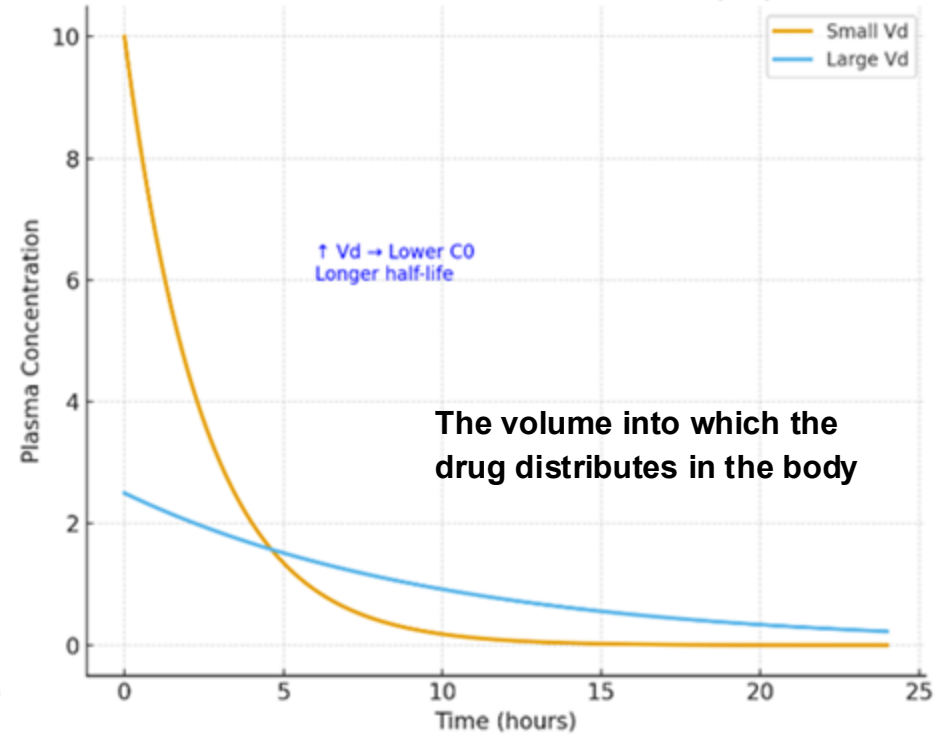


Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



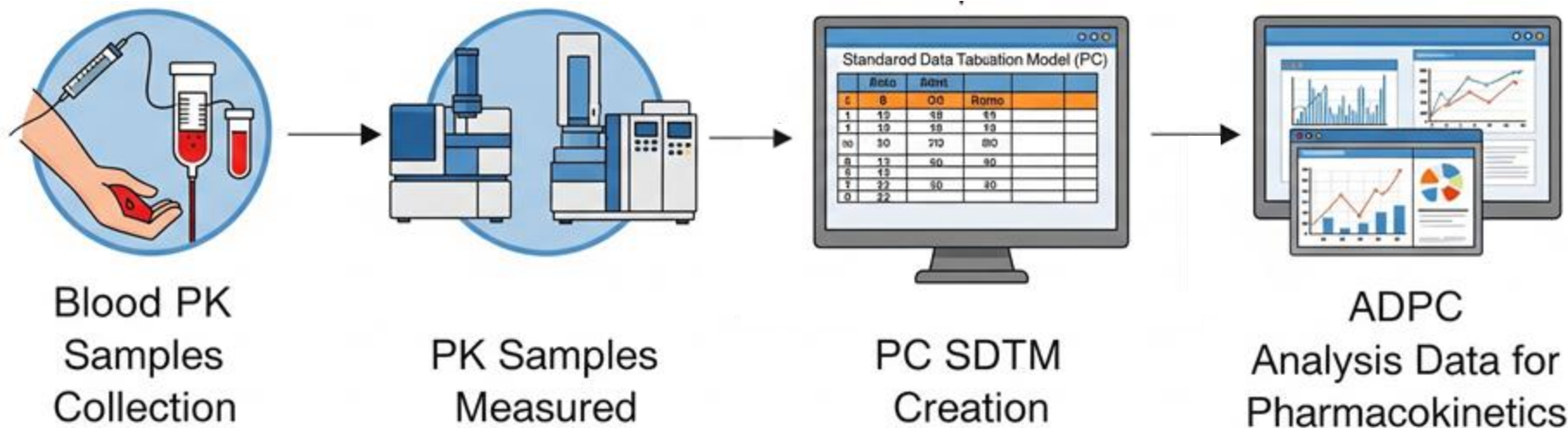
Data Inconsistencies and Missing Data



Exposure Response



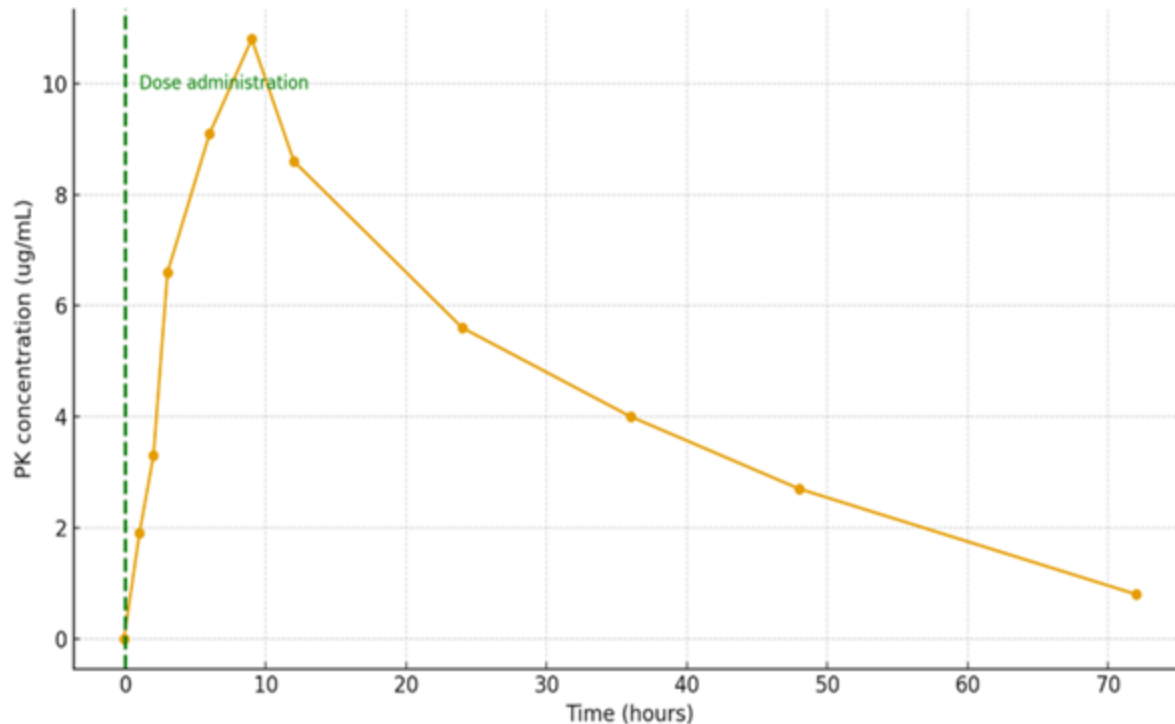
PK data flow: From PK samples to ADPC



PK data flow: From ADPC to TLGs



Non Compartmental Analysis (NCA)

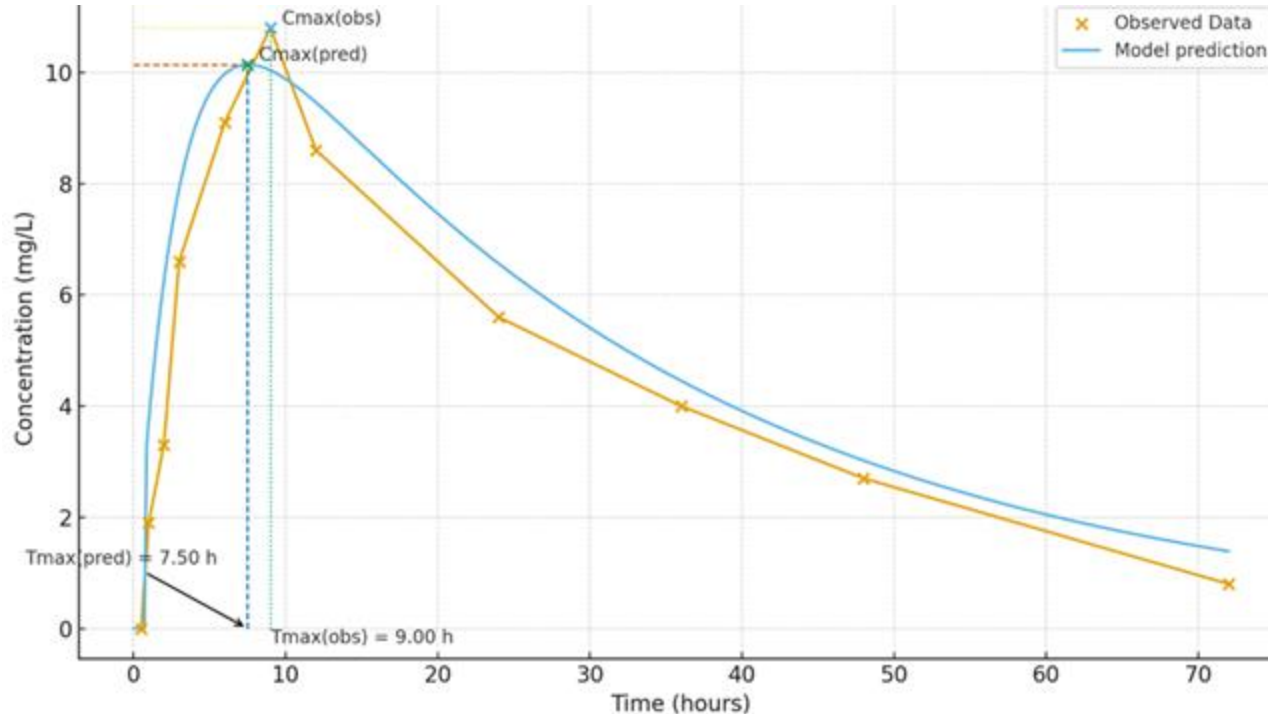


When people say, "Pharmacokinetics is simple," they're often referring to **Non-Compartmental Analysis (NCA)**.

NCA is a widely used and relatively straightforward method for determining key PK parameters directly from observed drug concentration-time data.

We also call it "Join the dots" approach".

PK Modeling or Population PK modeling (POPPK)



PK Model: curve that best fits the data as a whole

PopPK investigates covariates (patient characteristics like age, weight, renal function) which impact PK data

NCA vs. Modeling

Non Compartmental Analysis (NCA)	Population PK (POPPK)
Simple and fast to perform	Time consuming (several weeks)
Requires rich sampling	Works with sparse data
Only descriptive	Simulate scenarios not yet tested in clinical studies

Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



Data Inconsistencies and Missing Data



Exposure Response



The “SOMETIMES” COMPLEXITIES

Missing data

PK sampling date time	Scheduled timepoint	Dose date time	Imputed PK sampling date time
05 Feb 2025 - ????	pre-dose	05 Feb 2025 - 10:30	05 Feb 2025 -
05 Feb 2025 - ????	2hrs post-dose	05 Feb 2025 - 10:30	05 Feb 2025 -

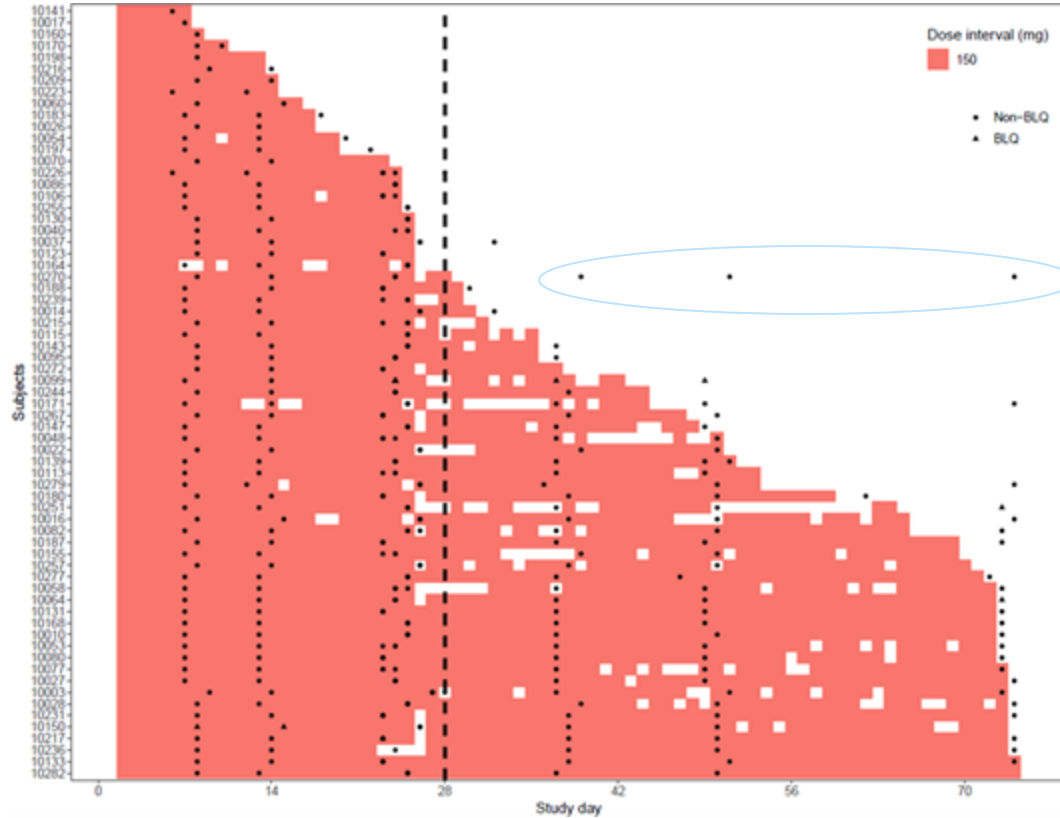
The “SOMETIMES” COMPLEXITIES

Data inconsistency

PK sampling date time	Scheduled timepoint	Dose date time	Time After Dose (hrs)
05 Feb 2025 - 10:15	pre-dose	05 Feb 2025 - 10:30	-0.25
05 Feb 2025 - 12:25	2 hrs post-dose	05 Feb 2025 - 10:30	1.917
05 Feb 2025 - 14:45	4 hrs post-dose	05 Feb 2025 - 10:30	4.25
05 Feb 2025 - 18:27	8 hrs post-dose	05 Feb 2025 - 10:30	7.95
05 Feb 2025 - 00:15	12 hrs post-dose	05 Feb 2025 - 10:30	-10.25

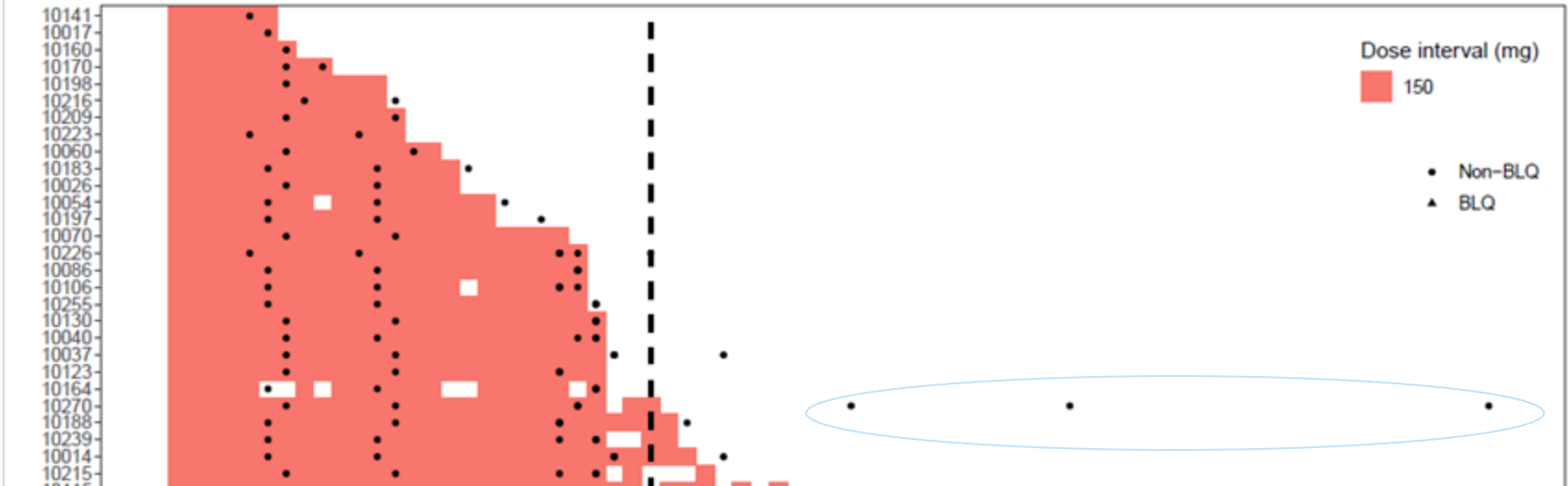
The “SOMETIMES” COMPLEXITIES

Data inconsistency



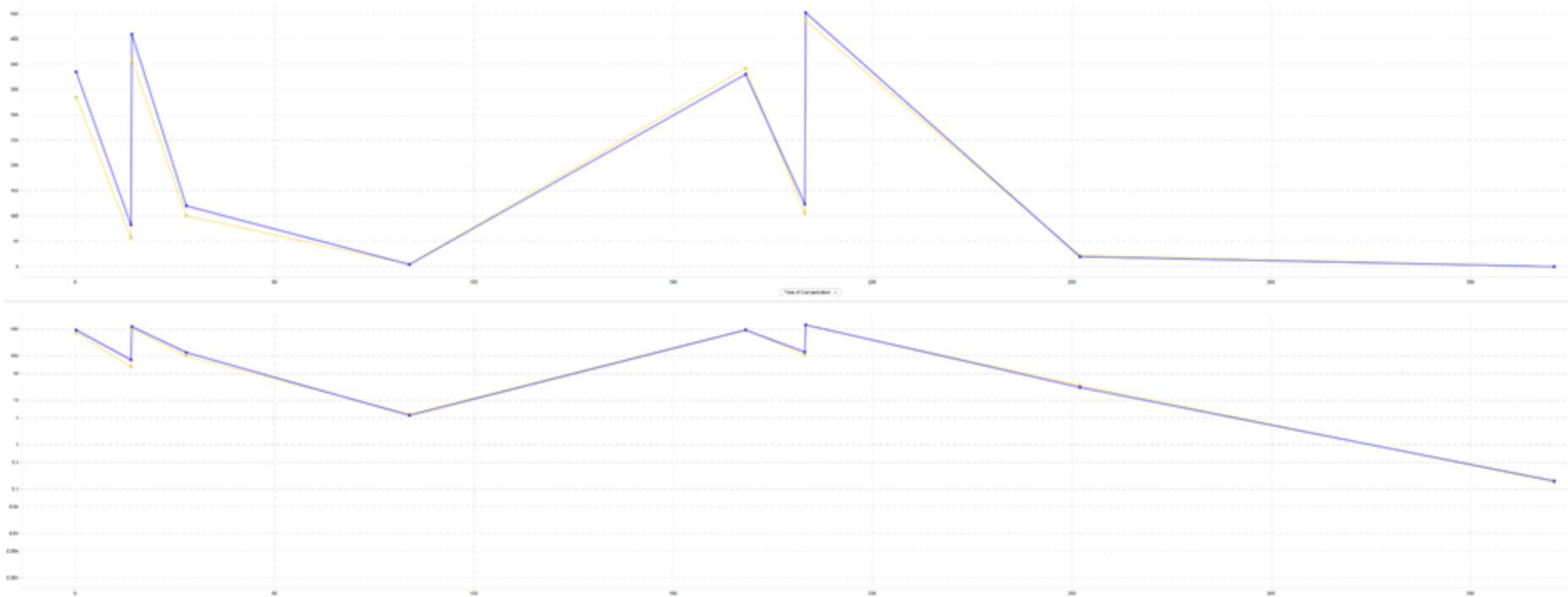
The “SOMETIMES” COMPLEXITIES

Data inconsistency



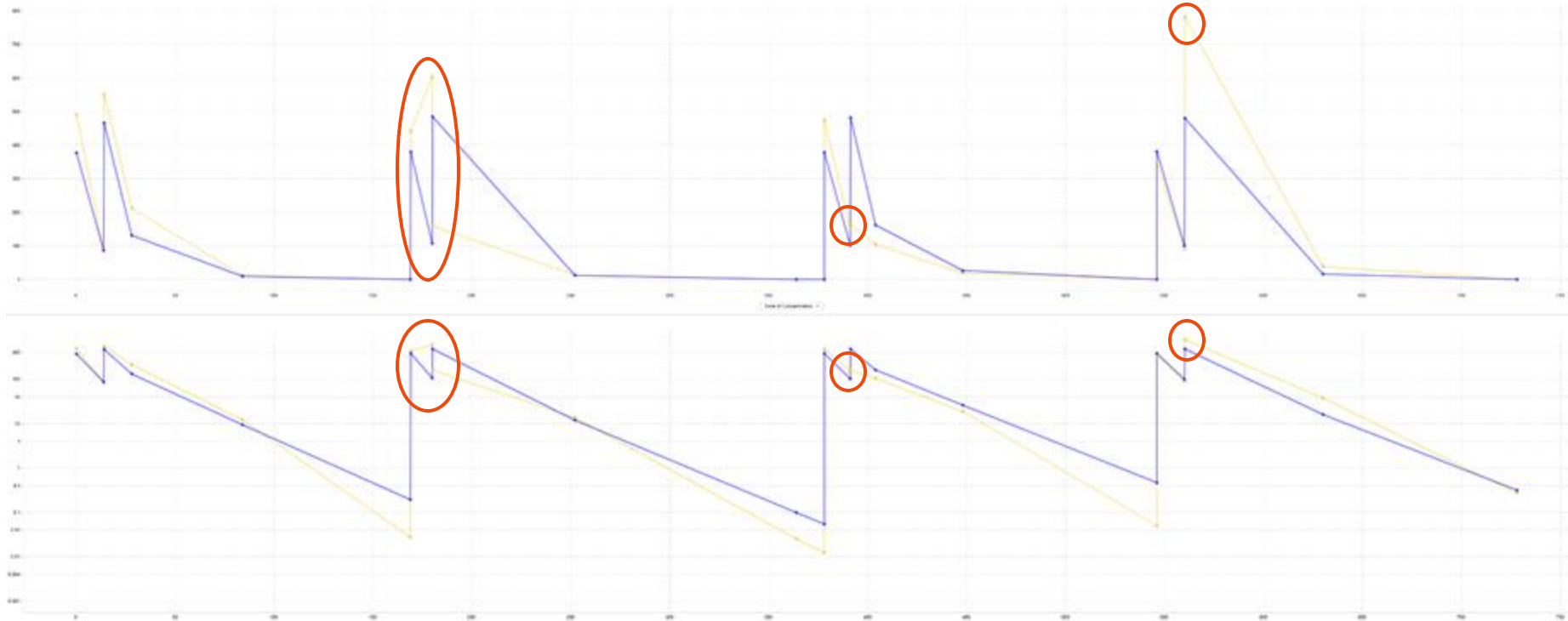
The “SOMETIMES” COMPLEXITIES

Leverage PK model for outliers detection



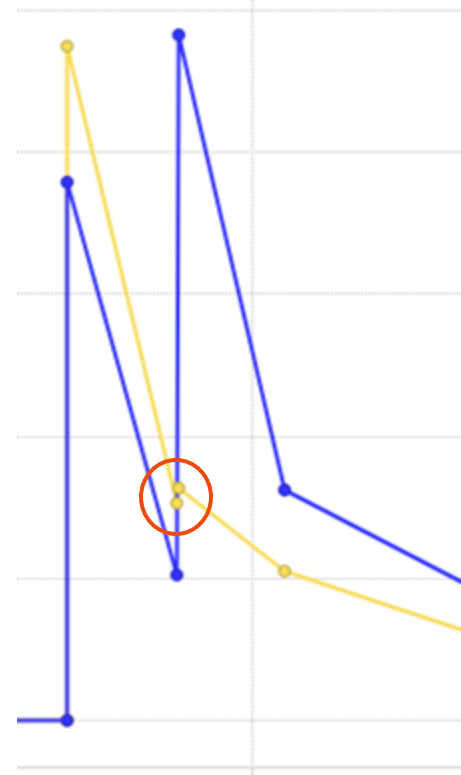
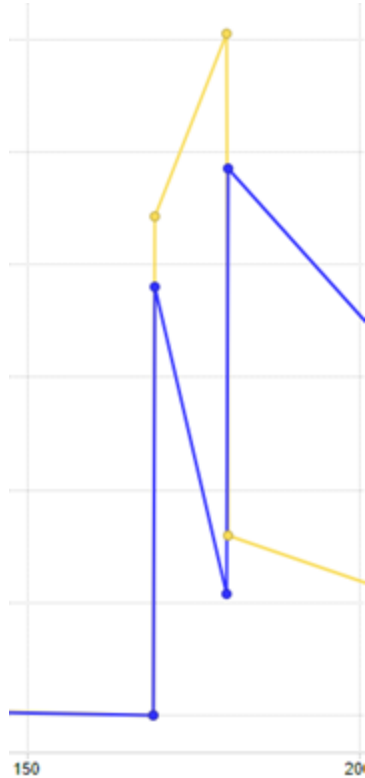
The “SOMETIMES” COMPLEXITIES

Leverage PK model for outliers detection



The “SOMETIMES” COMPLEXITIES

Leverage PK model for outliers detection



Why data quality matters

- Scientists derive pharmacometric parameters (e.g., C_{max} , C_{avg} , AUC) from collected data
- These parameters are then integrated with pharmacodynamic data for exposure-response analyses
- Poor data quality (incorrectly recorded dose times, incorrectly recorded dose amounts, swapped sample concentrations....) at this stage can affect patient-level predictions and, if not addressed, can compromise exposure-efficacy and exposure-safety analyses

Table of Contents



Fundamental Principles



PK Parameters



NCA Modeling



Data Inconsistencies and Missing Data



Exposure Response



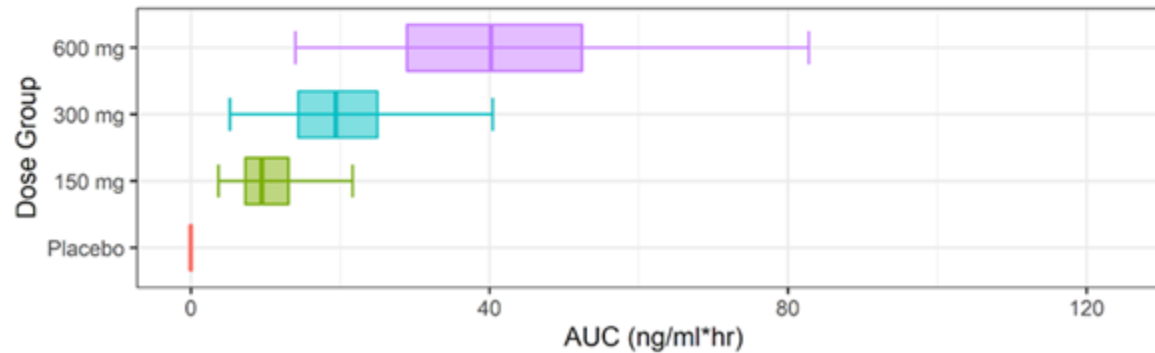
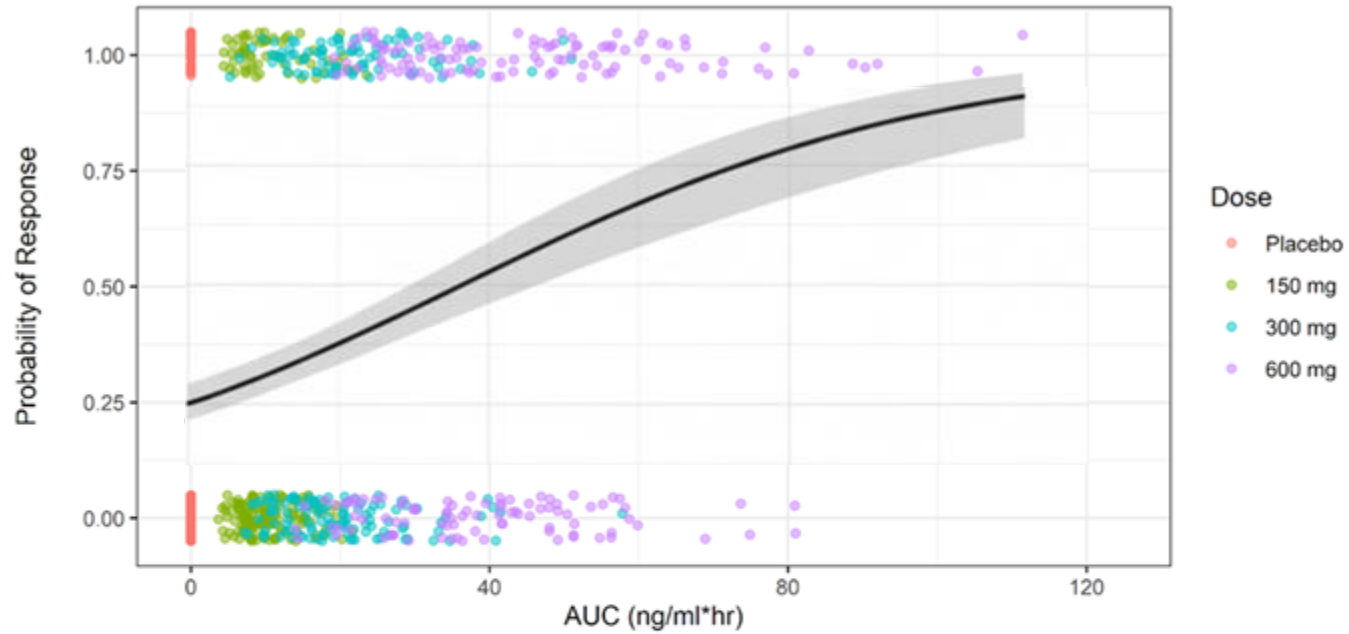
Exposure Response



link the drug's exposure (AUC, C_{max}...) to its observed pharmacological effects (PD)

Key benefits

Determining the **dose or exposure range** that **maximizes efficacy while minimizing toxicity**





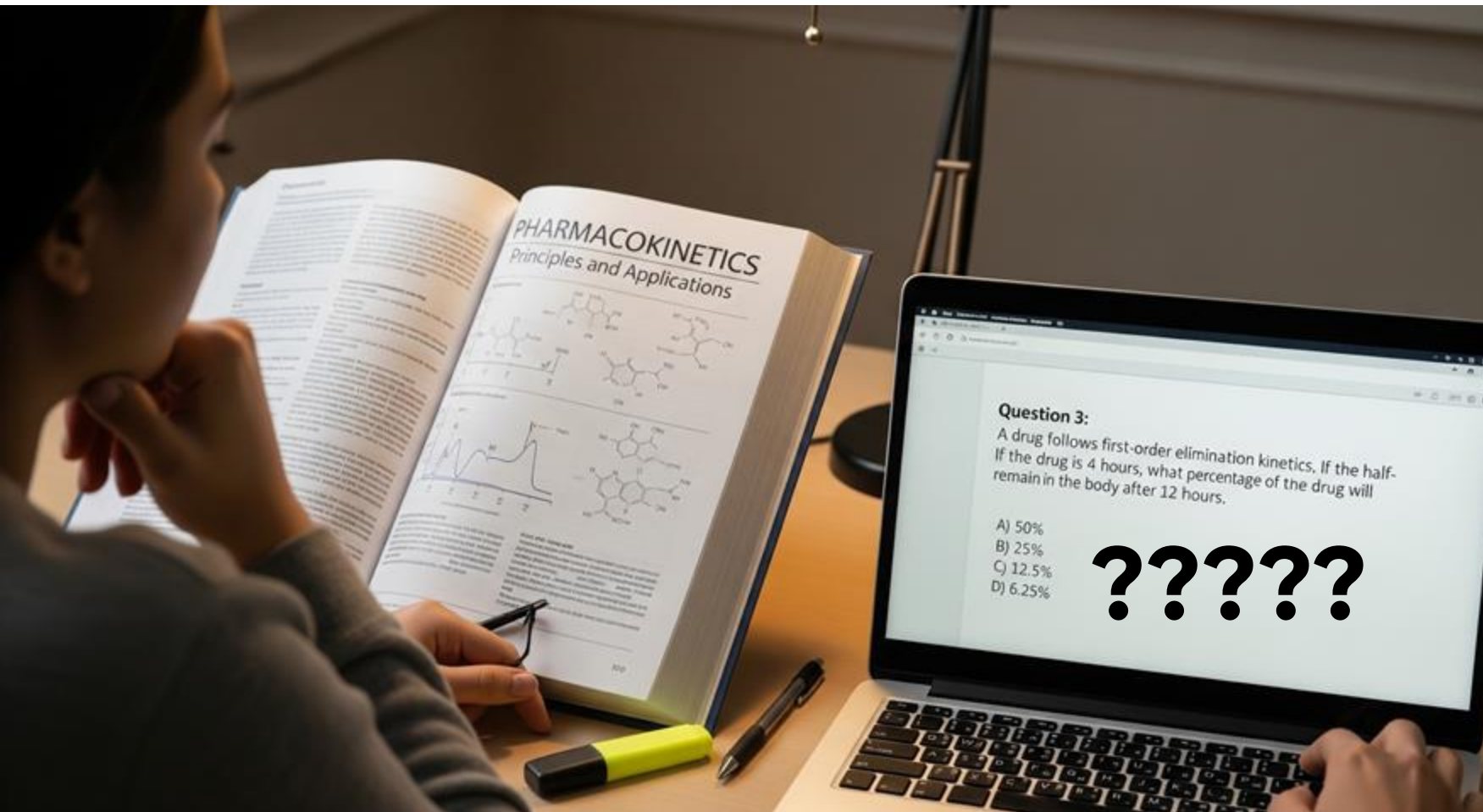
**ACKNOWLEDGMENTS
TO MY COLLEAGUES**

Contact Details

 +41 79 87 78 267

 Vincent.buchheit@roche.com

 <https://www.linkedin.com/in/vincent-buchheit-b4a2991a/>



PHARMACOKINETICS

Principles and Applications



Question 3:

A drug follows first-order elimination kinetics. If the half-life of the drug is 4 hours, what percentage of the drug will remain in the body after 12 hours.

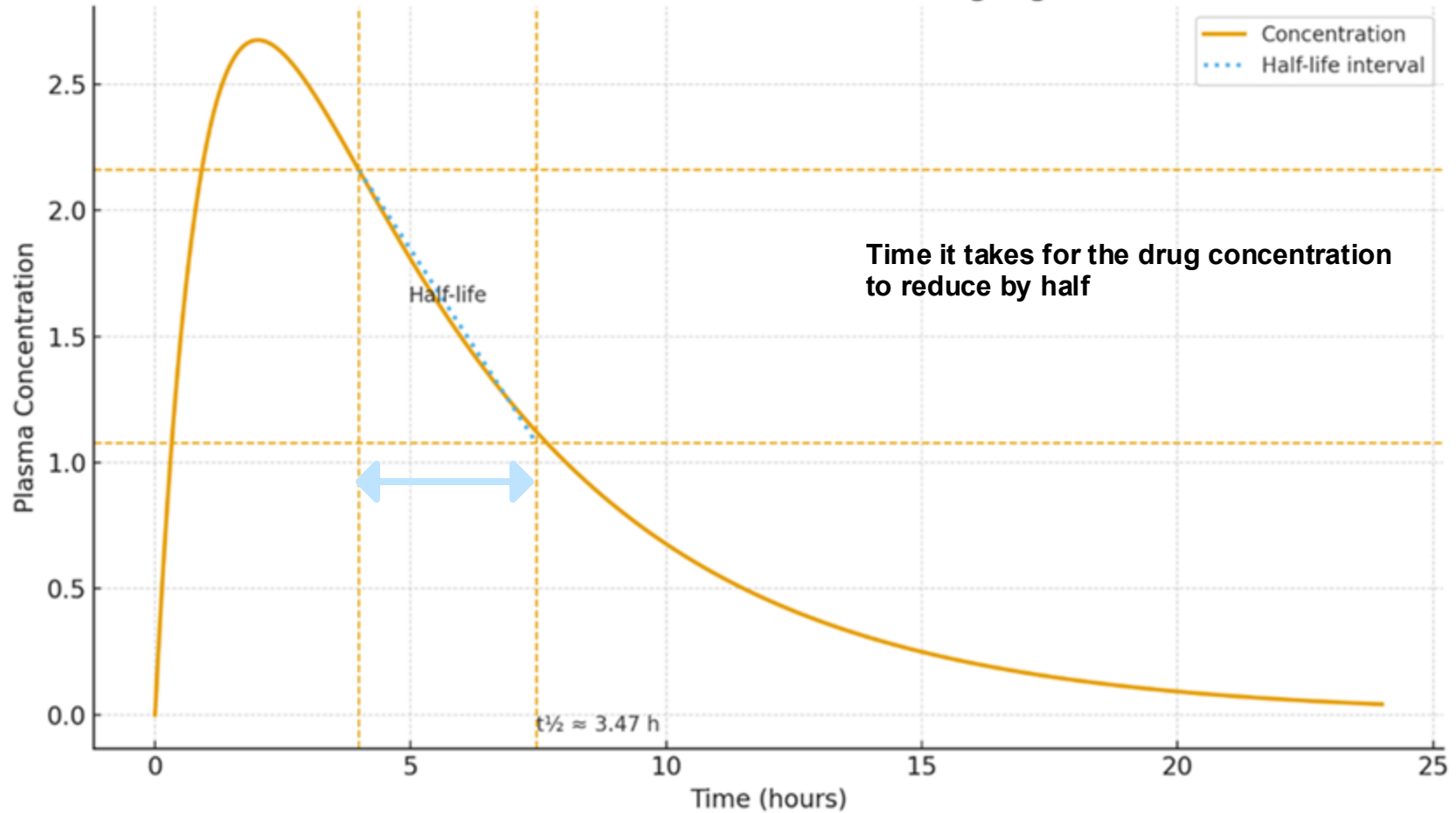
- A) 50%
- B) 25%
- C) 12.5%
- D) 6.25%

?????

Doing now what patients need next

BACK UP

Simulated PK Profile — Half-life Highlighted



ADA

Anti-Drug Antibodies

