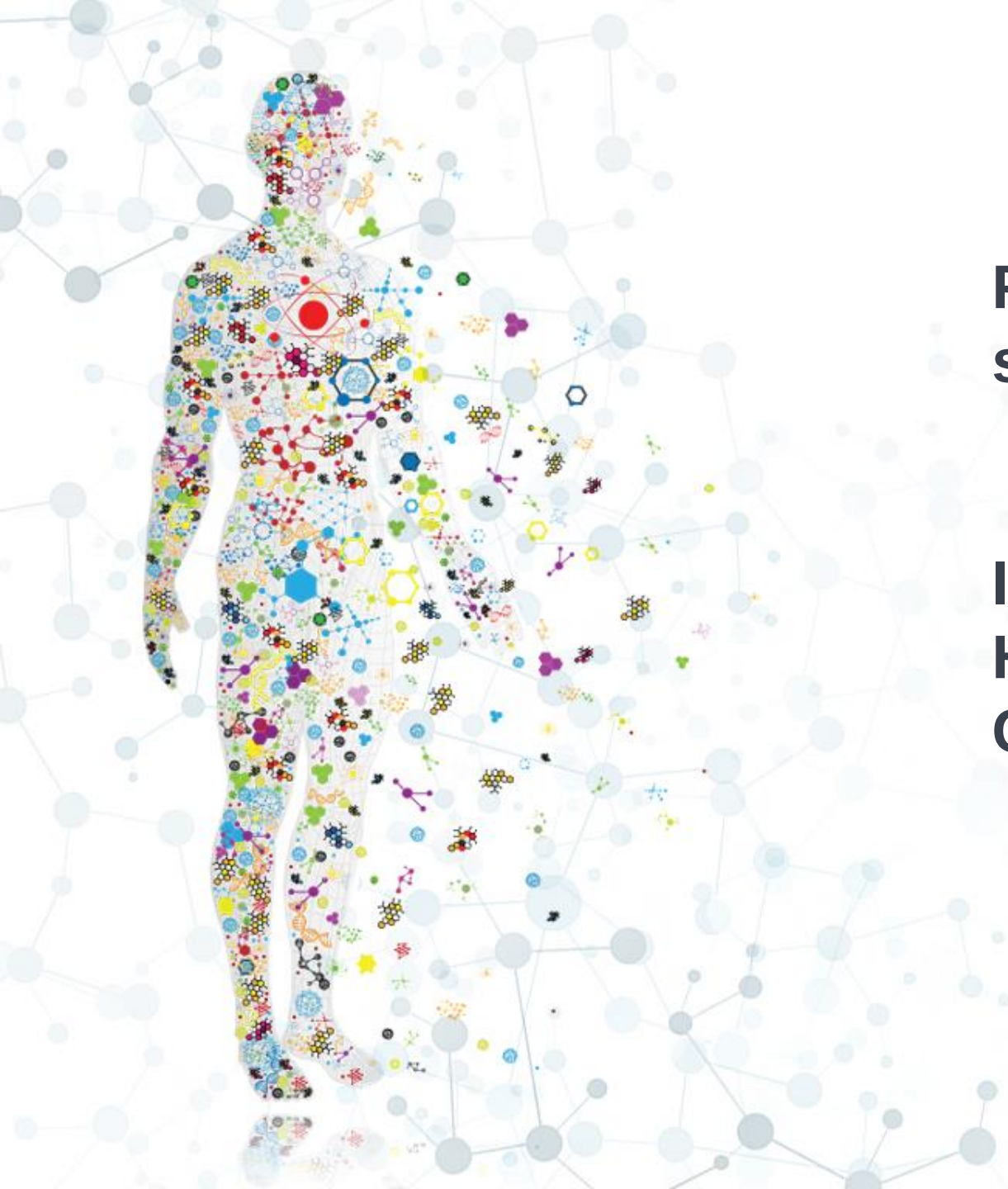


Future development of PBPK science – opportunities and barriers

Iain Gardner PhD
Head of Translational DMPK Science
Certara-Simcyp

Future directions of PBPK Science

- Building confidence for expanded applications in predicting fate of drugs in special populations
- Coupling with detailed quantitative systems pharmacology models to assess impact of PK on pharmacological response
- Integrating with more detailed physical pharmacy models to assist with *in silico* formulation design and workflows
  - IVIVE-guided virtual bioequivalence
- Individualizing dosage regimens via patient avatars as part of personalized medicine initiative
- More robust analytical handling of observed data for reverse-translation
  - Bayesian fitting of models to data in combined PBPK-POP-PK framework

Special populations

Commentary

ACCP

A Proposal for Scientific Framework Enabling Specific Population Drug Dosing Recommendations

The Journal of Clinical Pharmacology
2015, XX(XX) 1–6

DOI: 10.1002/jcph.579

Pravin R. Jadhav, PhD, MPH[1], Jack Cook, PhD[2], Vikram Sinha, PhD[3], Ping Zhao, PhD[3], Amin Rostami-Hodjegan, PharmD, PhD[4], Vaishali Sahasrabudhe, PhD[2], Norman Stockbridge, MD, PhD[5], and J. Robert Powell, PharmD[6]

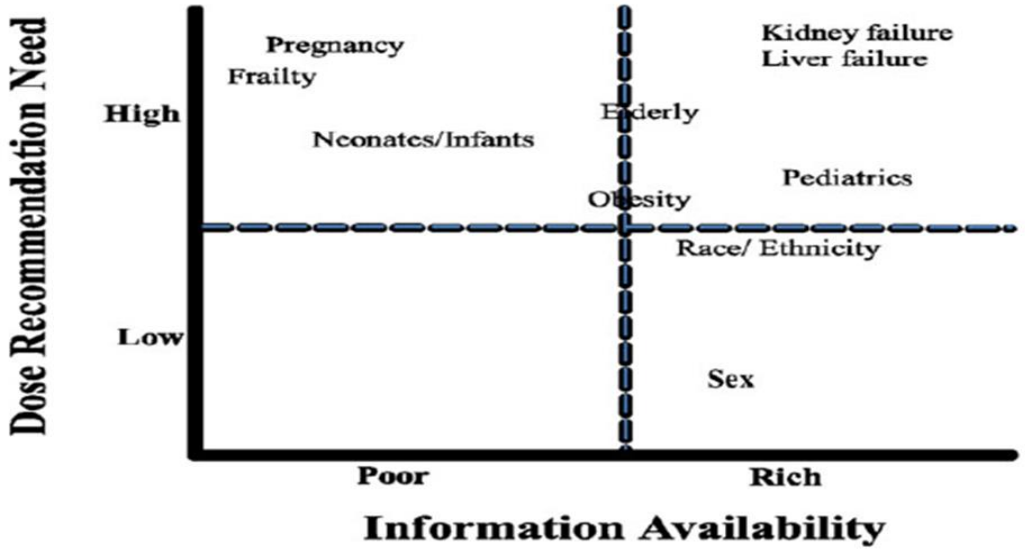


Figure 1. Conceptual distribution of data availability vs dose recommendation need for specific populations.

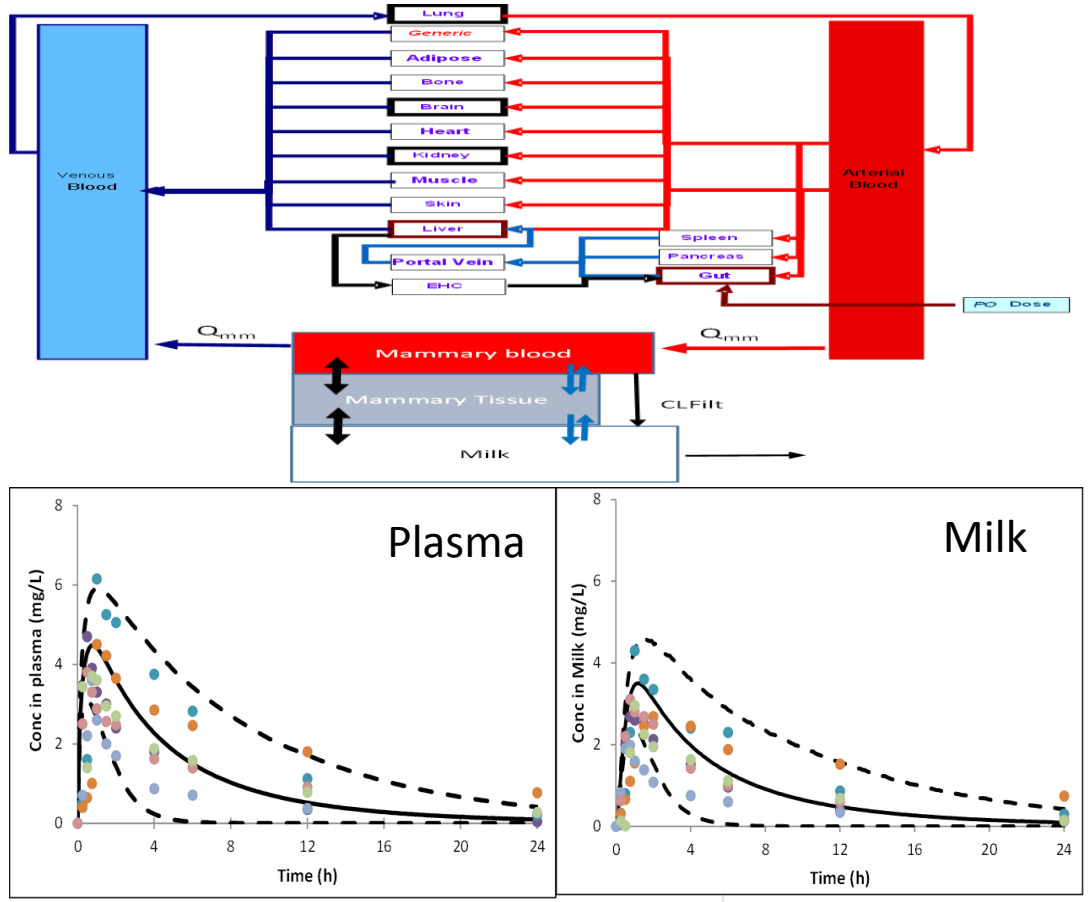
CPT: Pharmacometrics & Systems Pharmacology

Review | Open Access

Drug Dosing in Pregnant Women: Challenges and Opportunities in Using Physiologically Based Pharmacokinetic Modeling and Simulations

Alice Ban Ke, Rick Greupink, Khaled Abduljalil

First published: 19 January 2018 | https://doi.org/10.1002/psp4.12274 | Cited by: 8



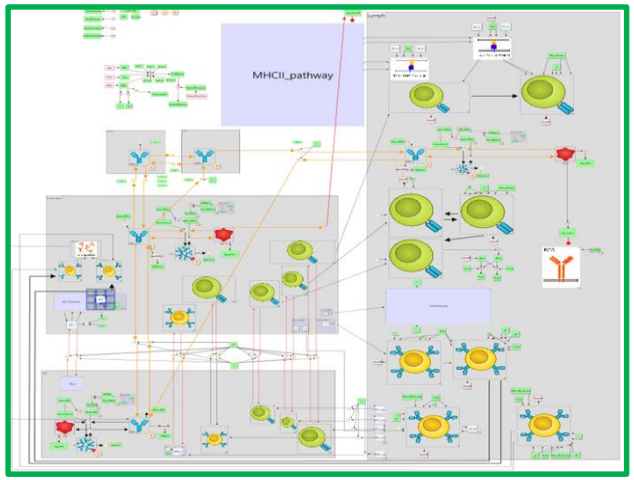
Abduljalil *et al.*, ACoP, 2017

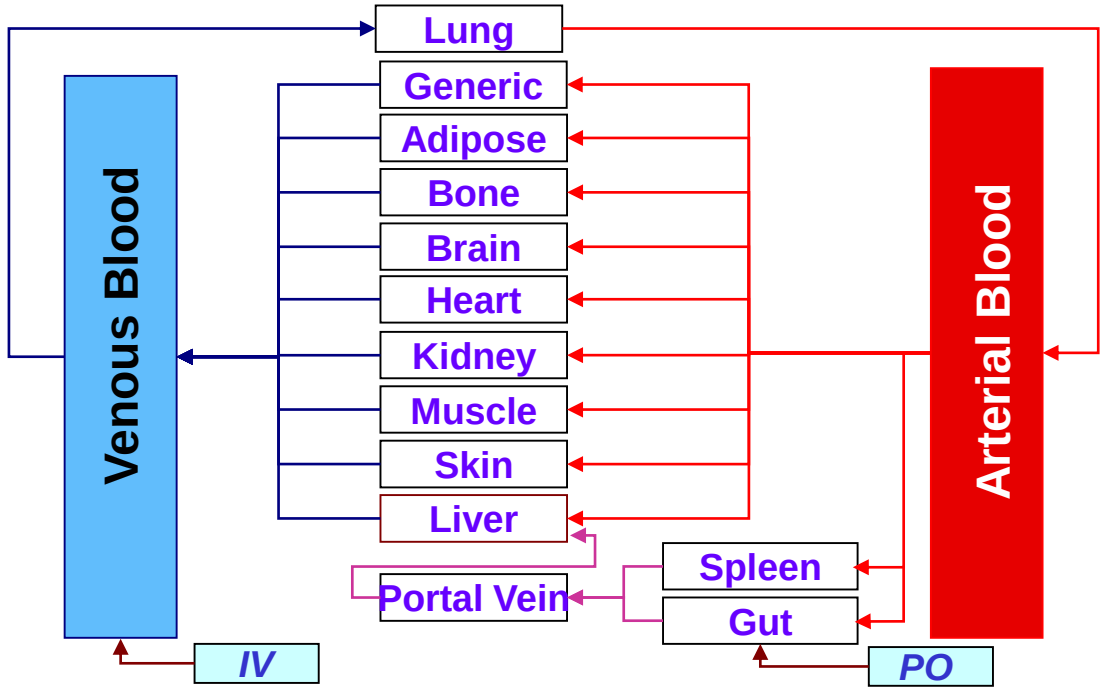
CERTARA

Dynamically Coupled PBPK-QSP/TS models

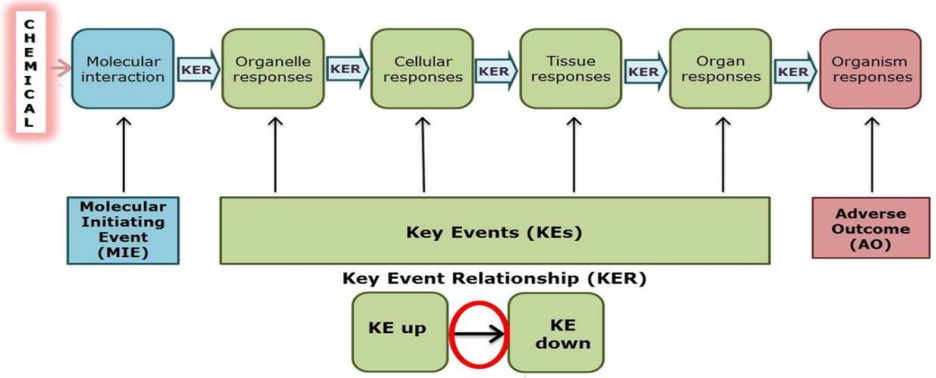
- Technology challenges to combine PBPK and systems biology approaches largely overcome
  - applications already being published

Immune response model





QSTS

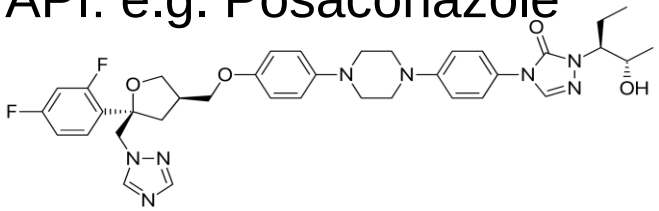


Kierzek et al, CPT:PSP, 2019

CERTARA

A Virtual Workbench for Formulation Design: IVIVE guided VBE

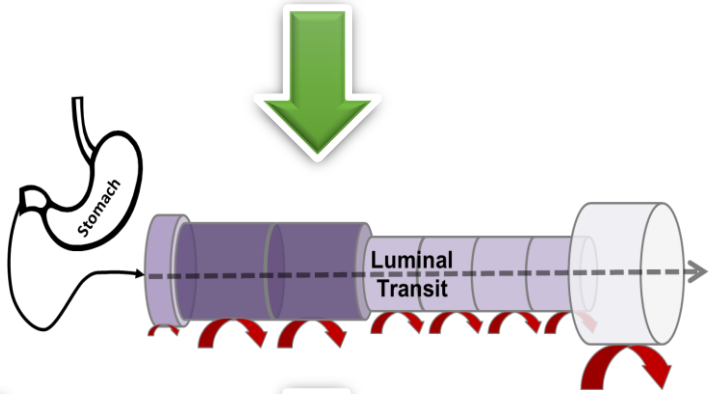
API: e.g. Posaconazole

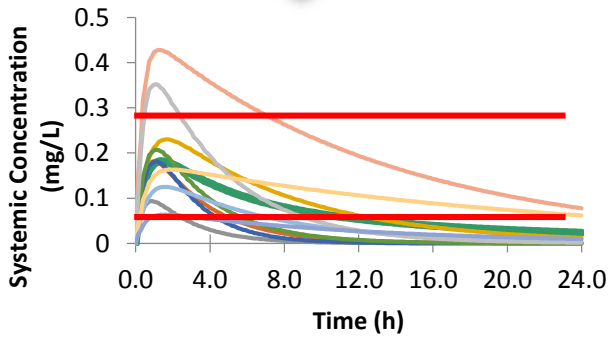


Surfactant
Excipients
Buffers
etc

Target Populations, Healthy vs Patients, between and within subject variability

In vitro experiments





Optimisation/ Virtual BE

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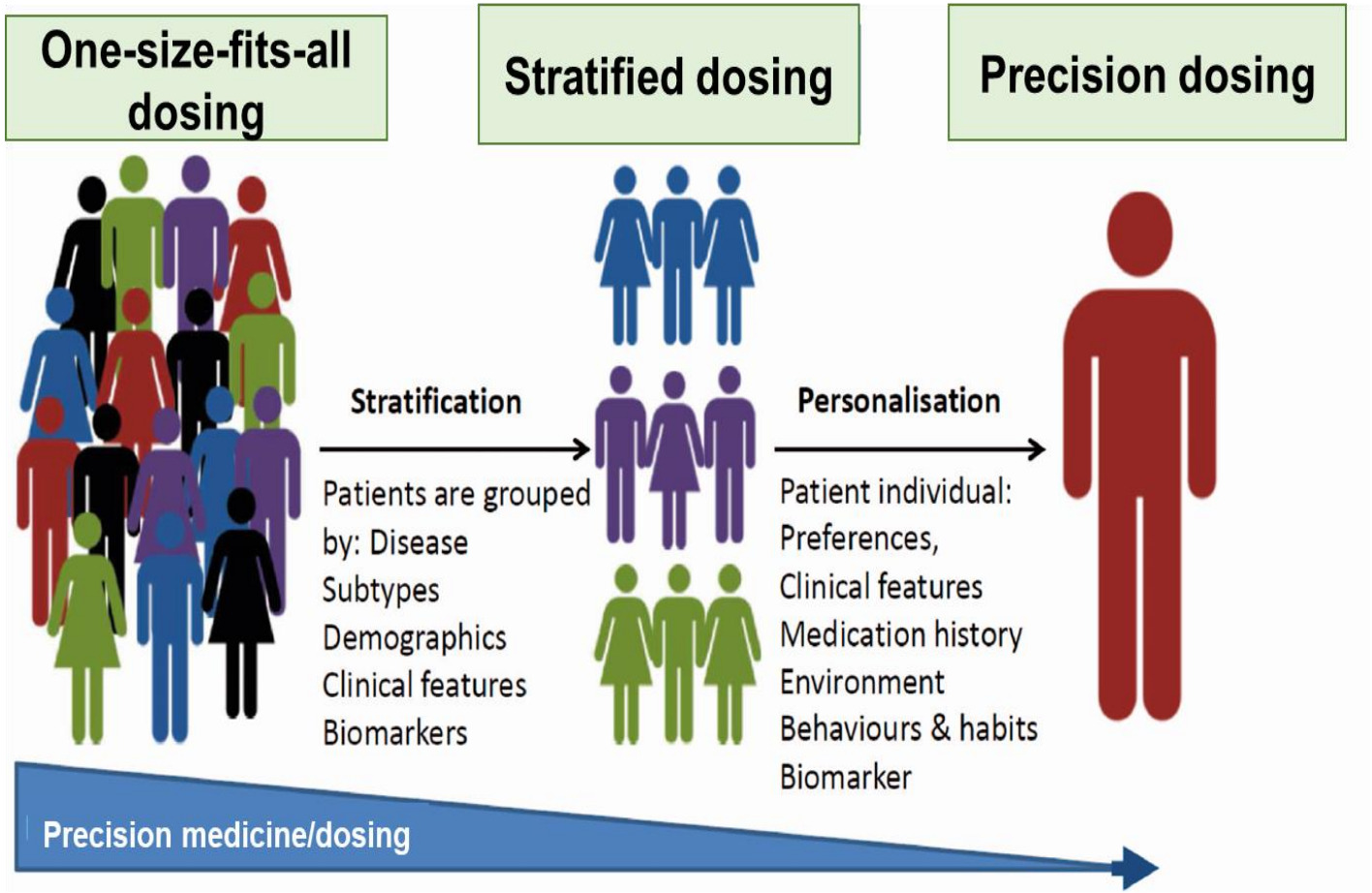
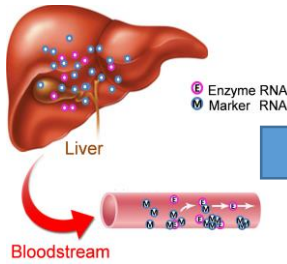
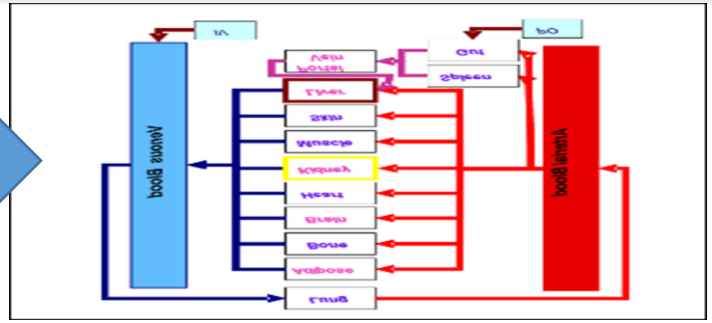
Virtual twin and just-in-time dispensing







'**The virtual-twin**' in action
Individualised dose prediction.
DDI screening with AI directed alternatives

PBPK + Liquid Biopsy

CERTARA

Barriers

- Further verification and qualification of models needed
  - Sometimes lack of quality data in public domain
- Scientific and technological advances still needed
  - Pharmaceutical workbench
  - Virtual twin
  - Transporter abundance and scaling and DDI prediction
    - Progress being made with PET data and *in vitro* modelling approaches
- Recognition of open science approach to PBPK platform development
  - Models/data should be published in peer reviewed journals
    - For complex models line by line code review is not practical
- Effort needed to collate and curate and analyze quality data for PBPK models is still under appreciated