

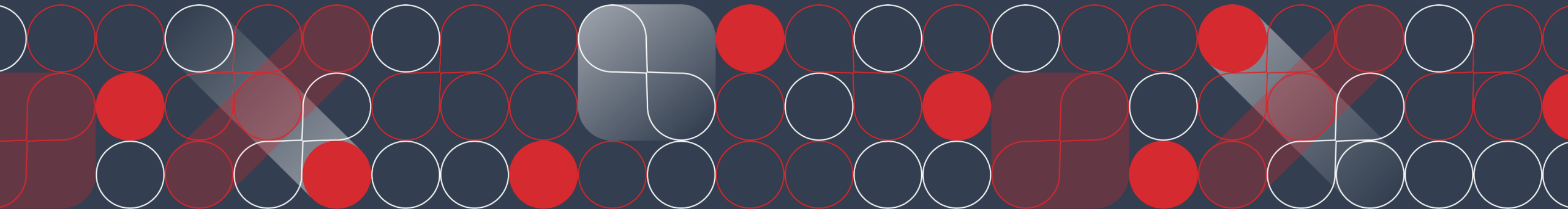


Virtual Human – various approaches, common aim

What PBPK and QSP bring to the table

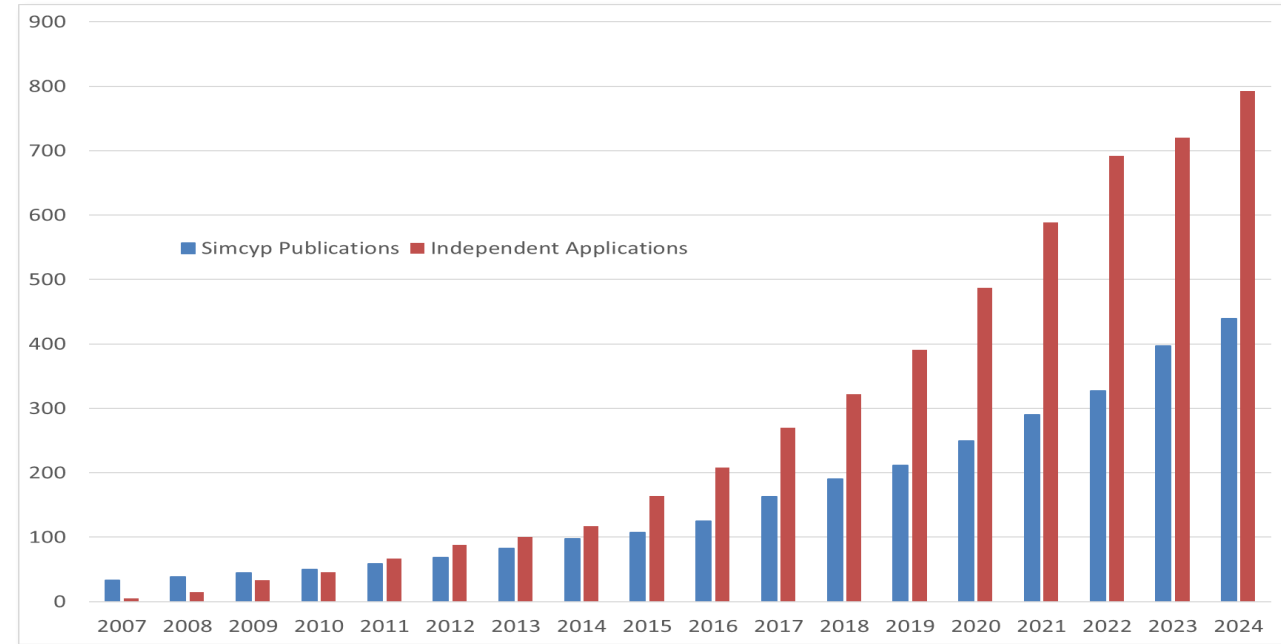
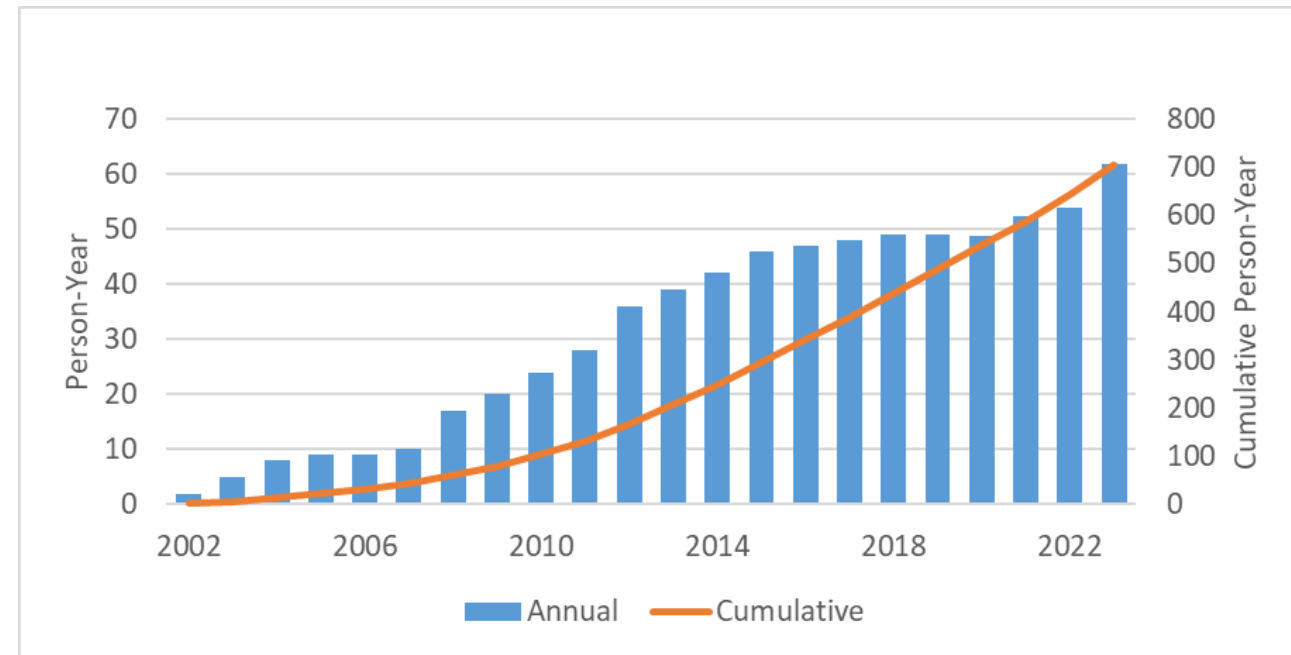
Virtual Human Global Summit II
October 2025, Barcelona/NY

Sebastian Polak



Certara UK

- part of international corporation
- scientific software developer (PBPK / QSP)
- users – pharma industry (innovative/generic drugs; small/large molecules), regulatory bodies, scientific institutes, universities
- consultancy services



Simcyp platform PBPK

- >115 Novel Drugs
- 375+ individual label claims
- approved by global regulators using predictions from the Simcyp Simulator in lieu of clinical studies!



ONCOLOGY	Agios Amgen Amgen Ariad Ariad (Takeda) AstraZeneca AstraZeneca AstraZeneca AstraZeneca Beigene BluePrint Medicines BMS Celgene Daiichi Sankyo Daiichi Sankyo Daiichi Sankyo Eisai EMD Serono	Tibsovo (<i>ivosidenib</i>) Blinicyto (<i>blinatumomab</i>) Lumakras (<i>sotorasib</i>) Alunbrig (<i>brigatinib</i>) Iclusig (<i>ponatinib</i>) Calquence (<i>acalabrutinib</i>) Lynparza (<i>olaparib</i>) Tagrisso (<i>osimertinib</i>) Truqap® (<i>capivasertib</i>) Brukinsa (<i>zanubrutinib</i>) Aykakit (<i>avapritinib</i>) Augtyro® (<i>repotrectinib</i>) Inrebic (<i>fedratinib hydrochloride</i>) Turalio (<i>pexidartinib</i>) Ezharmin (<i>valmetostat tosilate</i>) Vanflyta® (<i>quizartinib dihydrochloride</i>) Lenvima (<i>lenvatinib</i>) Tepmetko (<i>tepotinib hydrochloride</i>)	Genentech Genentech Genentech Genentech Genentech Incyte Janssen Janssen Lilly Lilly Loxo Loxo Oncology Menarini/Stemline Mirati Novartis Novartis Novartis Novartis	Alecensa (<i>alectinib</i>) Cotellic (<i>cobimetinib</i>) Gavreto® (<i>pralsetinib</i>) Polivy (<i>polatuzumab vedotin-piiq</i>) Rozlytrek (<i>entrectinib</i>) Pemazyre (<i>pemigatinib</i>) Balversa (<i>pirtobrutinib</i>) Erleada (<i>apalutamide</i>) Retevmo (<i>selpercatinib</i>) Verzenio (<i>abemaciclib</i>) Jaypirca (<i>pirtobrutinib</i>) Vitakvi (<i>larotrectinib</i>) Orserdu (<i>elacestrant</i>) Krazati (<i>adagrasib</i>) Farydak (<i>panobinostat</i>) Kisqali (<i>ribociclib succinate</i>) Scemblix (<i>asciminib</i>) Odomzo (<i>sonidegib</i>)	Novartis Novartis Novartis Novartis Novartis Pfizer Pfizer Pfizer Pharmacyclics Puma Sanofi Seattle Genetics Spectrum Springworks Takeda Takeda Taiho Verastem	Vioice (<i>alpelisib</i>) Rydapt (<i>midostaurin</i>) Tabrecta (<i>capmatinib</i>) Zykadia (<i>ceritinib</i>) Jakavi (<i>ruxolitinib</i>) brance® (<i>palbociclib</i>) Bosulif (<i>bosutinib</i>) Lorbrena (<i>lorlatinib</i>) Imbruvica (<i>ibrutinib</i>) Nerlynx® (<i>neratinib</i>) Jevtana (<i>cabazitaxel</i>) Tukysa (<i>tucatinib</i>) Beleodaq (<i>belinostat</i>) Osgiveo® (<i>nirongacent</i>) Exkivity (<i>mobocertinib</i>) Fruzaqla® (<i>fruquintinib</i>) Lytgobi (<i>futibatinib</i>) Copiktra (<i>duvelisib</i>)
RARE DISEASE	Agios Akarx (Eisai) AstraZeneca Aurinia Genentech Genentech Global Blood Therapeutics	Pyrkynd (<i>mitapivat</i>) Doptelet (<i>avatrombopag maleate</i>) Koselugo (<i>selumetinib</i>) Lupkynis (<i>voclosporin</i>) Enspryng (<i>satralizumab</i>) Erysdi (<i>risdiplam</i>) Oxbryta (<i>voxelotor</i>)	Intercept Ipsen Kadmon Merck Mirum Mitsubishi Tanabe Novartis	Ocaliva (<i>obeticholic acid</i>) Sohonus® (<i>palovarotene</i>) Rezurock (<i>belumosudil</i>) Welireg (<i>belzutifan</i>) Livmarli (<i>maralixibat</i>) Dysval (<i>Valbenazine</i>) Isturisa (<i>osilodrostat</i>)	Peloton/Merck PTC Therapeutics Sanofi Genzyme Traverse Vertex Vertex	Welireg (<i>belzutifan</i>) Emflaza (<i>deflazacort</i>) Cerdelga (<i>eliglustat tartrate</i>) Filspari (<i>sparsentan</i>) Symdeko (<i>tezacaftor/ivacaftor</i>) Trikafta (<i>elexacaftor/ivacaftor/tezacaftor</i>)
CENTRAL NERVOUS SYSTEM	AbbVie AbbVie Alkermes Alkermes	Rinvoq (<i>upadacitinib</i>) Qulipta (<i>atogepant</i>) Aristada (<i>aripiprazole lauroxil</i>) Lybalvi (<i>olanzapine/samidorphan</i>)	Eisai Idorsia Janssen Kyowa Kirin	Dayvigo (<i>lemborexant</i>) Quviviq (<i>daridorexant</i>) Ponvory (<i>ponesimod</i>) Nourianz (<i>istradefylline</i>)	Lilly Novartis Pfizer UCB	Reyvow (<i>lasmiditan succinate</i>) Mayzent (<i>siponimod fumaric acid</i>) Zavzpret (<i>zavegepant</i>) Briviact (<i>brivaracetam</i>)
INFECTIOUS DISEASE	Gilead Janssen Merck	Veklury (<i>remdesivir</i>) Olysio (<i>simeprevir</i>) Pifeltro (<i>doravirine</i>)	Merck Nabiva Novartis	Prevymis (<i>letermovir</i>) Xenleta (<i>lefamulin acetate</i>) Egaten (<i>trilabendazole</i>)	Pfizer Tibotec ViiV	Paxlovid® (<i>nirmatrelvir, ritonavir</i>) Eduvant (<i>rilpivirine</i>) Cabenuva Kit (<i>cabotegravir/rilpivirine</i>)
GASTROENTEROLOGY	AstraZeneca Helsinn	Movantik (<i>naloxegol</i>) Akynzeo (<i>fosnetupitant/palonosetron</i>)	Phathom Shionogi	Voquezna TriplePak (<i>vonoprazan/amoxicillin/clarithromycin</i>) Symproic (<i>naldemedine</i>)	Shire	Motegrity (<i>prucalopride</i>)
CARDIOVASCULAR	Actelion (J & J) Bayer (and Merck)	Opsumit (<i>macitentan</i>) Verquvo (<i>vericiguat</i>)	BMS Johnson & Johnson	Camzyos (<i>mavacamten</i>) Xarelto (<i>rivaroxaban</i>)	Pfizer	Revatio (<i>sildenafil</i>)
ENDOCRINE	AbbVie Astellas	Orilissa (<i>elagolix</i>) Veozah® (<i>fezolinetant</i>)	Janssen Lilly	Invokana (<i>canagliflozin</i>) Olumiant (<i>baricitinib</i>)	Lilly Merck	Mounjaro (<i>tirzepatide</i>) Steglatro (<i>ertugliflozin</i>)
OTHER	Galderma	Aklief (<i>trifarotene</i>)	Takeda	Livtency (<i>maribavir</i>)		

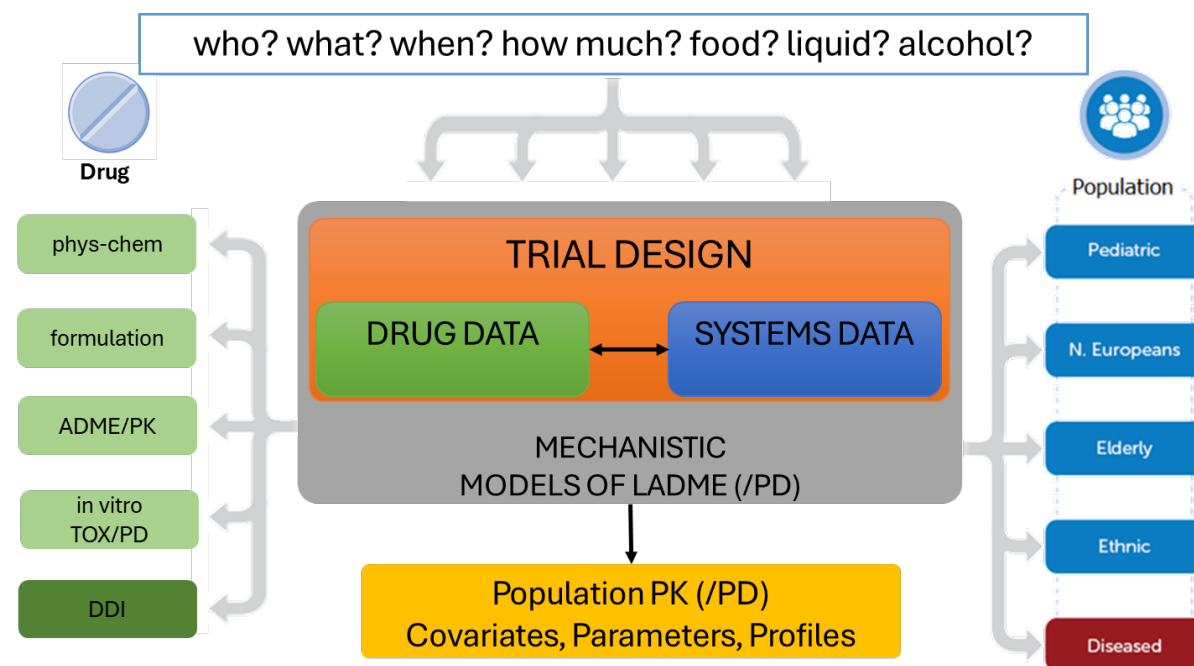
PBPK & QSP

PBPK

Physiologically based pharmacokinetic (PBPK) modeling is a mathematical mechanistic modeling technique for describing, predicting the absorption, distribution, metabolism and excretion (ADME) of xenobiotics in humans (animal species).

QSP/QSTS

Quantitative systems pharmacology (QSP) is a discipline utilizing various mathematical models to characterize biological systems, disease processes and progression, and drug pharmacology.



Virtual Human

MAIN AIM

to help – at individual level with the benefit for population

- prevention
- treatment
 - medical procedures (surgery)
 - drugs
 - efficacy
 - safety
 - pharmacodynamics/tox-safety – QSP/QSTS
 - pharmacokinetics – PBPK

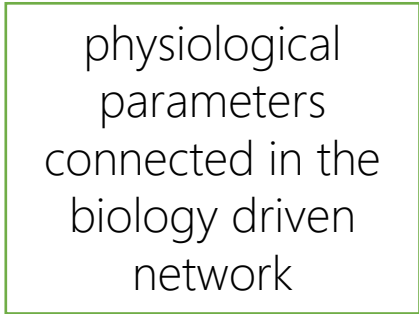
PRACTICAL UTILIZATION

IVIVE of ADME --> Metabolism



$$CL_{int} \left[\frac{L}{h} \right] = \left[\sum_{j=1}^n \left(\sum_{i=1}^n \frac{V_{max} (rhCYP_j)_i \times CYP_j \text{abundance}}{K_m (rhCYP_j)_i} \right) \right] \times MPPGL \times \text{Liver Weight}$$

$$CL_H = \frac{Q_H \times fu_B \times CL_{int}}{Q_H + fu_B \times CL_{int}}$$



Random sampling
from data driven
distributions

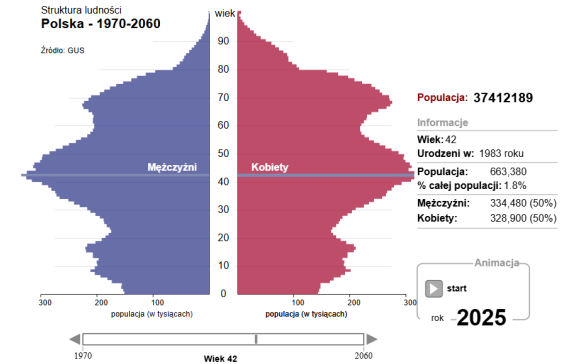
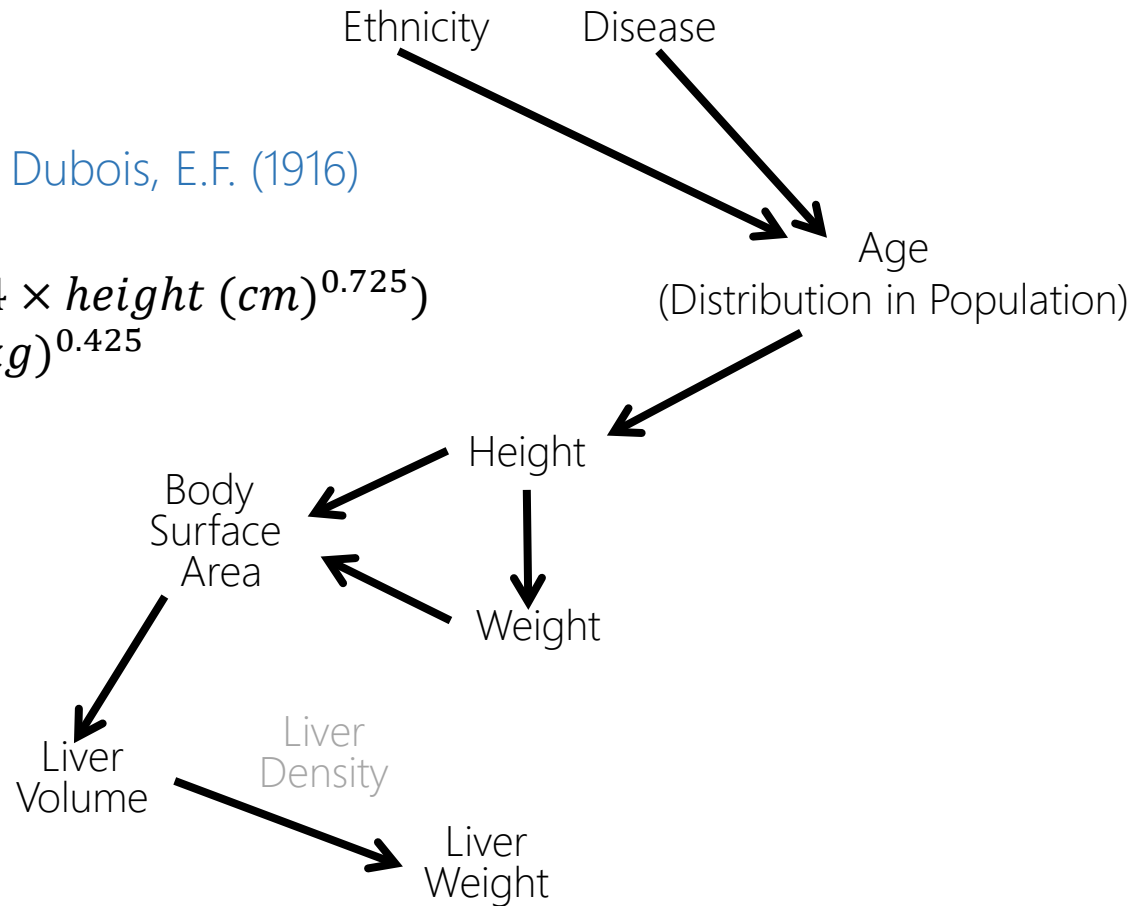
VARIABILITY!

IVIVE of ADME --> Metabolism

Dubois, D. / Dubois, E.F. (1916)

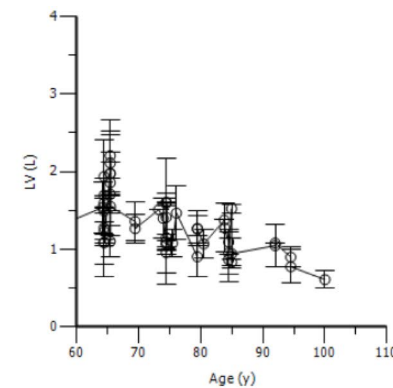
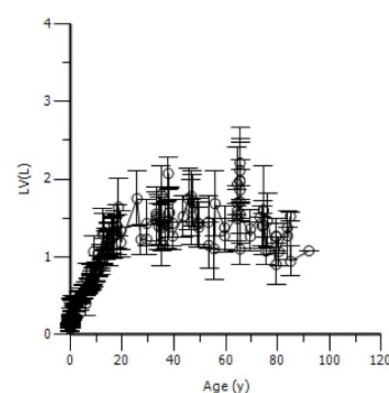
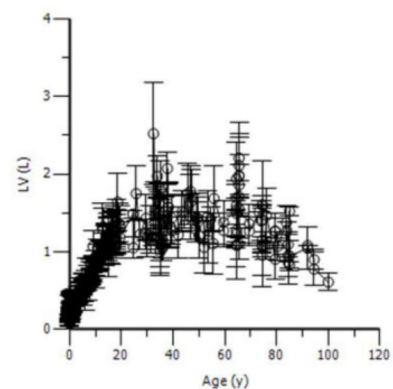
$$BSA(m^2) = 0.007184 \times height(cm)^{0.725} \times weight(kg)^{0.425}$$

$$Liver\ Volume\ (L) = 0.722 \times BSA\ (m^2)^{1.176}$$

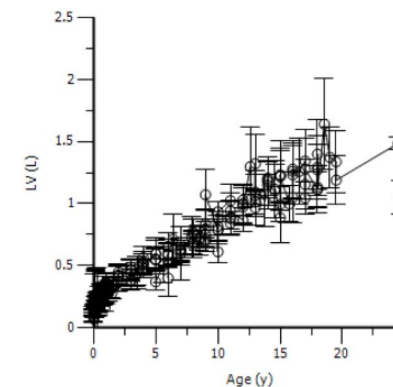
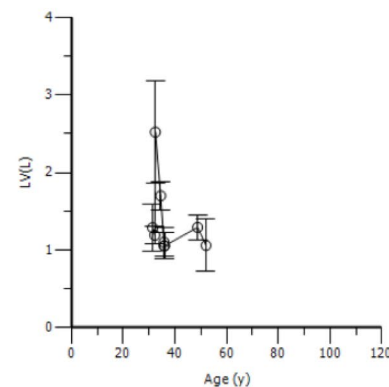
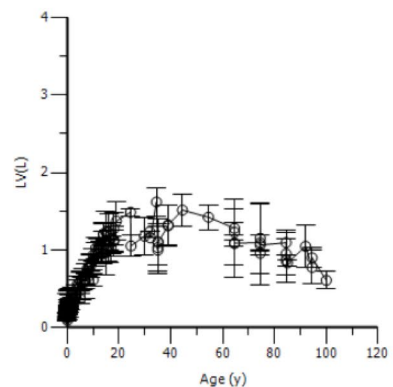


EXAMPLE OF BETWEEN POPULATION DIFFERENCES

IVIVE of ADME --> Metabolism



$$\text{Liver Volume (L)} \\ = 0.722 \times \text{BSA (m}^2\text{)}^{1.176}$$



QUALITY!

Verification – Validation – Qualification



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Opinions and letters of support on the qualification of novel methodologies for medicine development

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The European Medicines Agency (EMA) publishes opinions on the qualification of innovative development methods and letters of support for novel methodologies that have been shown to be promising in the context of research and development into pharmaceuticals.

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Page contents

Simcyp Simulator

Artificial intelligence-based measurement of non-alcoholic steatohepatitis histology

Centiloid measure of Amyloid PET to quantify brain amyloid deposition

GFR slope as a Validated Surrogate Endpoint for RCT in CKD

The opinions are given by EMA's [Committee for Medicinal Products for Human Use \(CHMP\)](#) on the basis of recommendations by the [Scientific Advice Working Party](#).

For more information and guidance on the qualification of novel methodologies, see [Qualification of novel methodologies for medicine development](#).

Simcyp Simulator



Qualification opinion for Simcyp Simulator

Adopted

Reference Number: EMADOC-1700519818-2006369

Discussing further qualification of Simcyp use cases with EMA, including:

- Expanded DDI use cases
- Paediatrics
- Pregnancy / Lactation
- Bioequivalence assessment

Qualification process took
2.5 Years

CERTARA



Virtual Human – various approaches, common aim

What PBPK and QSP bring to the table

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THANK YOU

