swiss clinical trial organisation

HRO Lunch Seminar Series

Session 2, 2026

SCTO EDUCATION PLATFORM

Introduction

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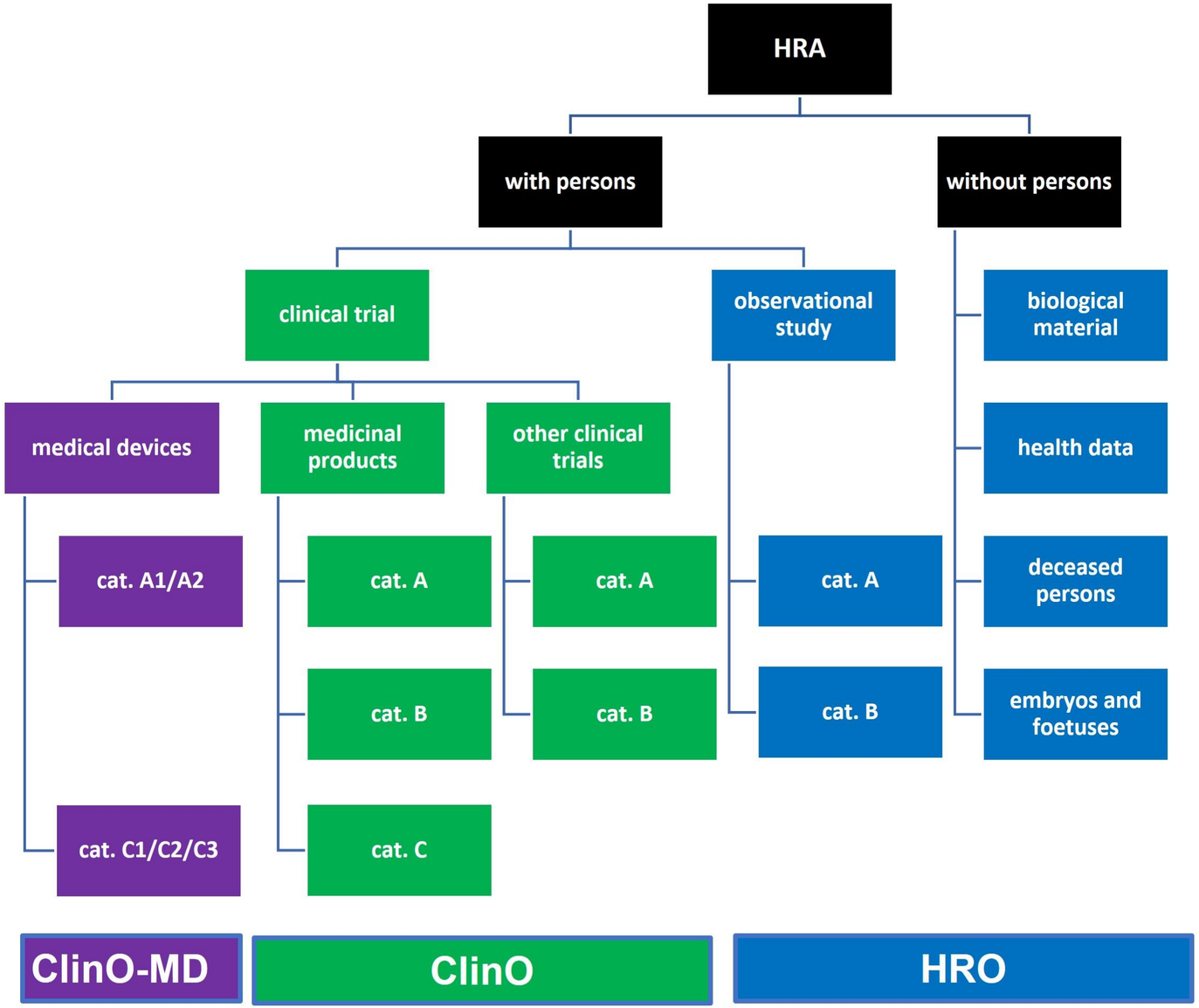
Introduction



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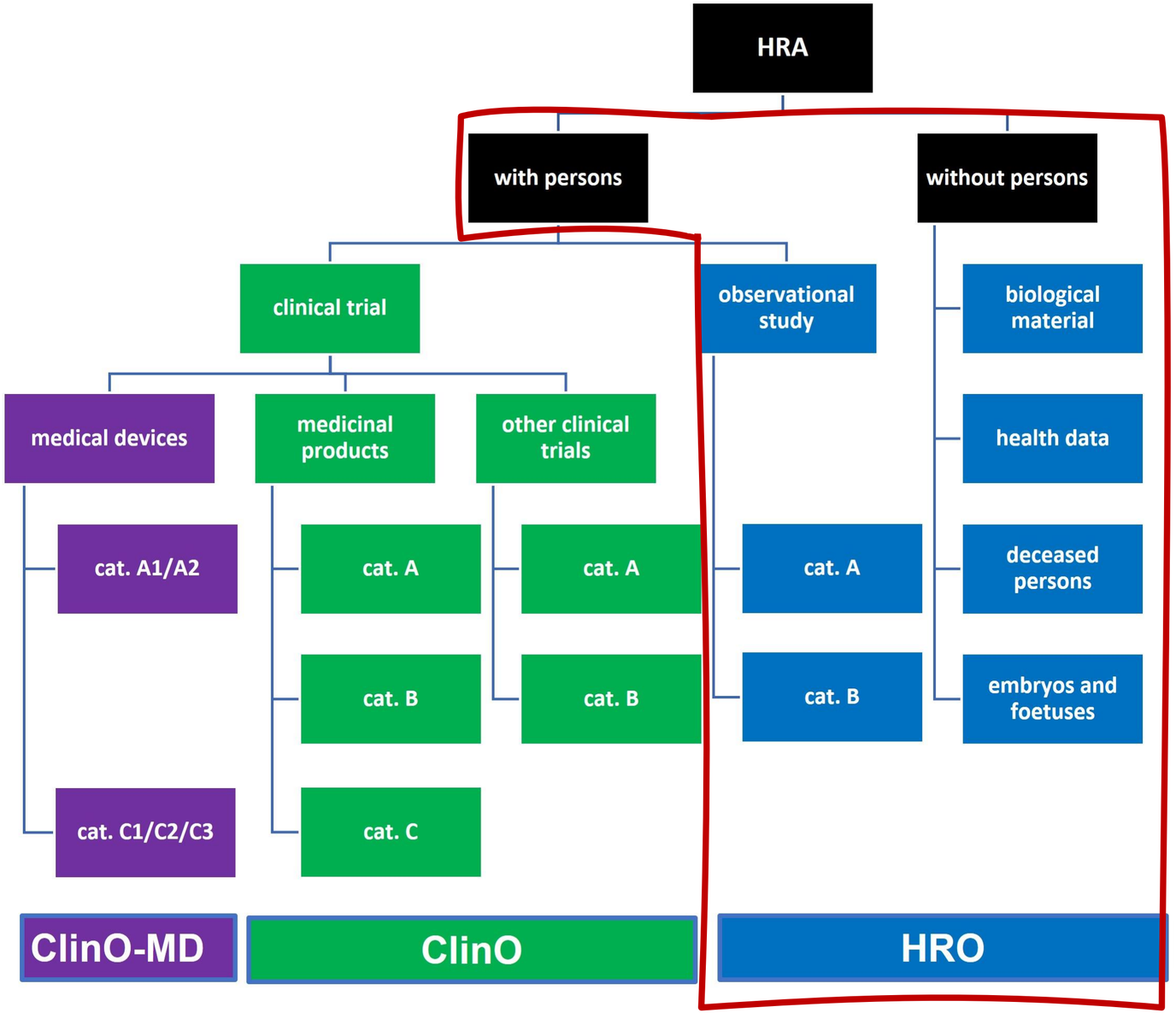
Introduction



General information

- If you require a certificate please login with your correct full name!
- Questions:
  - ➢ during presentation in the chat → for Q&A part at the end
- Presentation recorded
- Video, slides and Q&A document provided after the session on the website
- Feedback poll at end → please fill in!
- HRO lunch project team:
  - Claudia Fila (CTC Zurich)
  - Antoine Poncet (HUG)
  - Stephanie Maissen (SCTO)

Topic, Speakers

PD Dr. Verena Gotta

Head Clinical Pharmacist at Pediatric Pharmacology and Pharmacometrics Research Center of the University Children's Hospital Basel (UKBB), Hub Leader & Senior Researcher at Swiss PedNet

Regina Santoro

Head of Study Coordination at Paediatric Research Centre of the University Children's Hospital Basel (UKBB), Hub Coordinator & Member of Hub Staff Leadership Team at Swiss PedNet

PD Dr. Fabiën Belle-van Sprundel

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Successful paediatric HRO research projects:

From feasibility to sampling, age-dependent design and data reuse

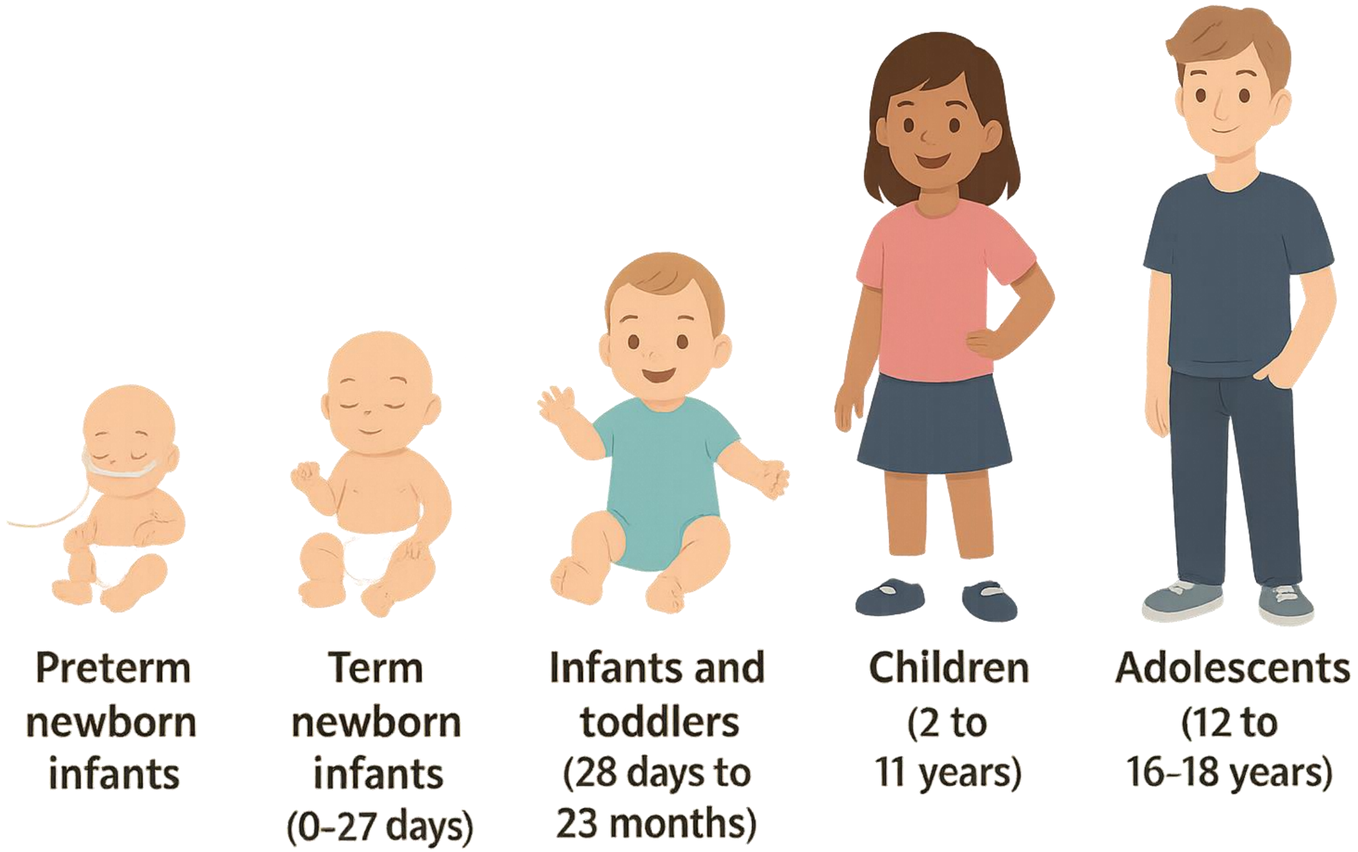
PD Dr. Verena Gotta, Regina Santoro, PD Dr. Fabiën Belle-van Sprundel
Swiss PedNet

HRO Lunch Session 20.05.2026, SCTO Education Platform

Seminar series "Facts and pitfalls of observational studies - How to plan and conduct HRO projects"

Pediatric patients are a heterogenous population

ICH E11 age categories



Addendum to ICH E11: Clinical Investigation of Medicinal Products in the Pediatric Population. Aug 2017
https://database.ich.org/sites/default/files/E11_R1_Addendum.pdf. Picture created with Copilot.

Each age group in itself can be heterogenous

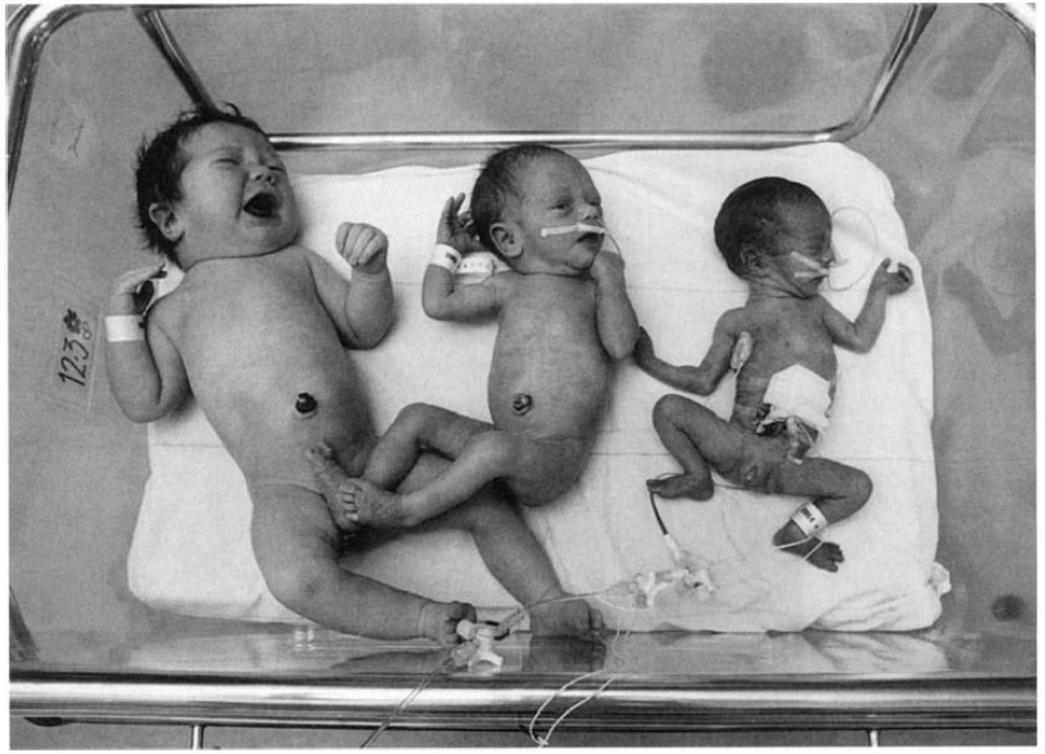
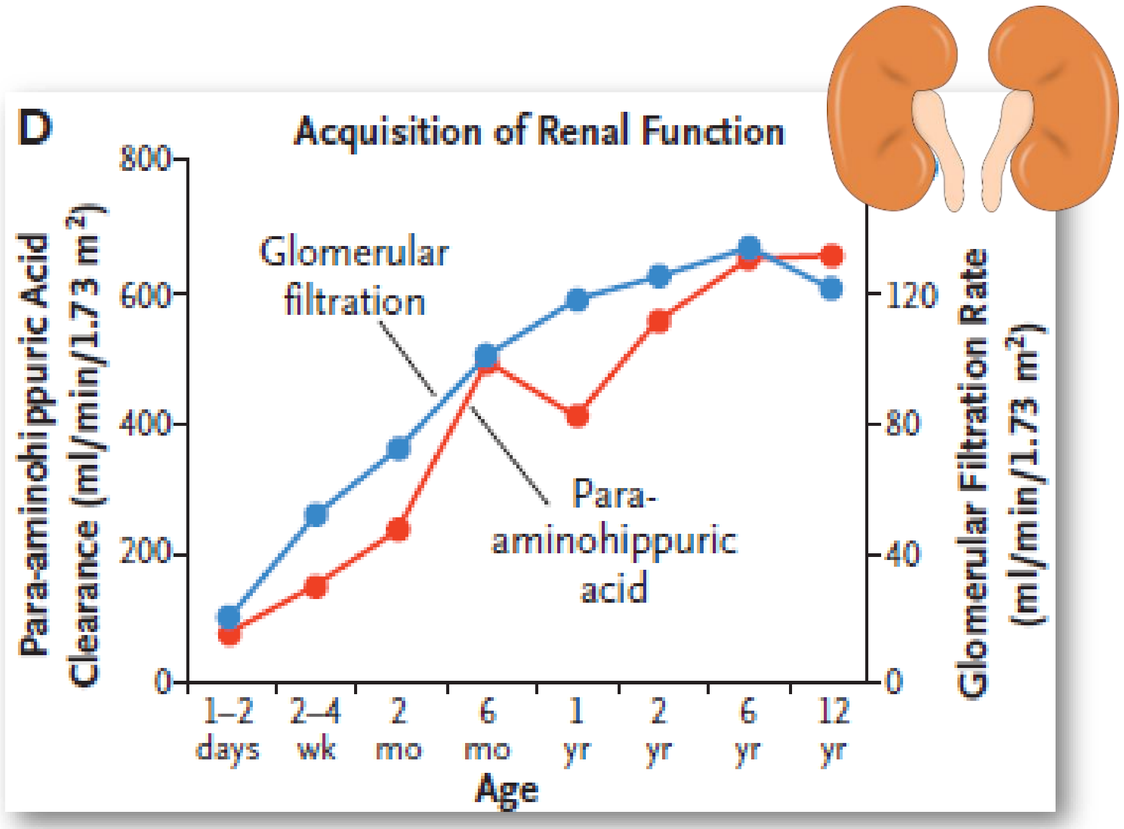


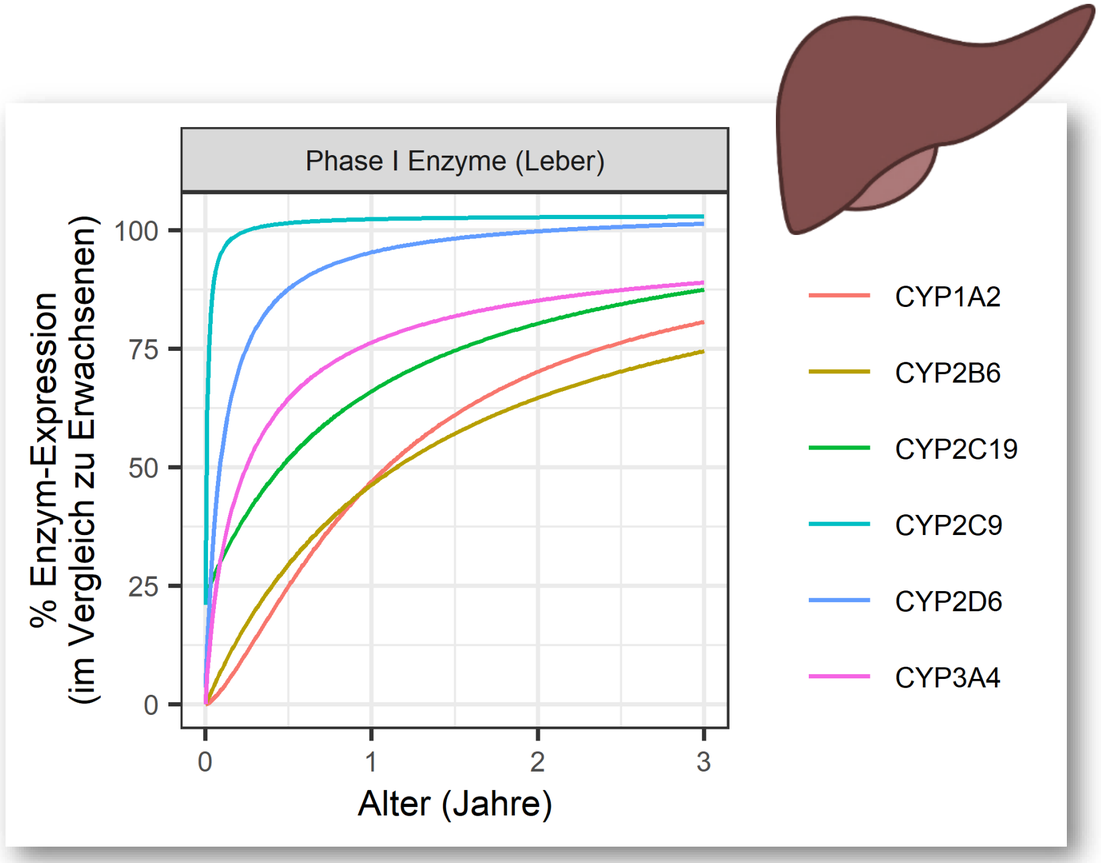
Abb. 1.1. 3 Neugeborene. Links ein normalgewichtiges Kind, das am Termin geboren wurde. In der Mitte ein untergewichtiges, am Termin geborenes Kind und rechts eine Frühgeburt.

F. Frei et al., *Kinderanästhesie*

Hetergenous age-dependent physiology

Example renal and hepatic function maturation during childhood



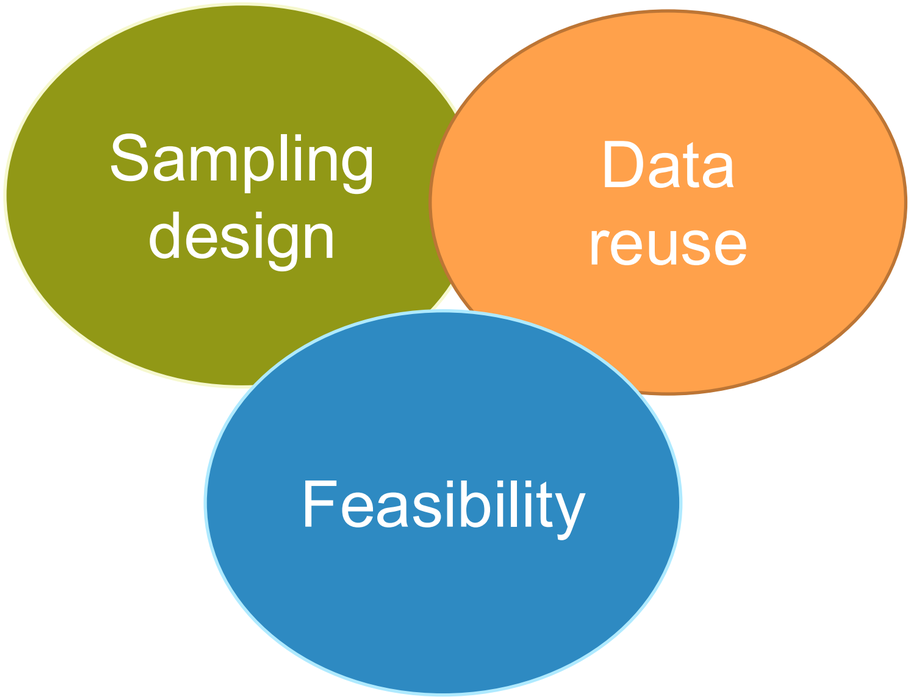


Kearns GL et al. *Developmental pharmacology--drug disposition, action, and therapy in infants and children.* N Engl J Med. 2003 Sep 18;349(12):1157-67

Gotta V & Timmermann M. *Besonderheiten der klinischen Pharmakologie in der Pädiatrie.* Kinder-und Jugendärzt*in 56. Jg. (2025) Artikel #6981
Reifungsgeschwindigkeit gemäss Johnson TN et al. Clin Pharmacokinet 2006

Implications for a pediatric HRO research project

Challenges with respect to:



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University Children's Hospital Basel

Sampling design considerations in pediatric HRO projects

PD Dr. Verena Gotta
Lead Clinical Pharmacist, Pediatric Pharmacology and Pharmacometrics,
University Children's Hospital Basel (UKBB)
Hub Leader & Senior Researcher at Swiss PedNet

Topics covered

Research Involving Sampling & Collection / Further Use of Data/Samples:

- The challenge of age-dependent physiology

Research Involving Sampling & Collection

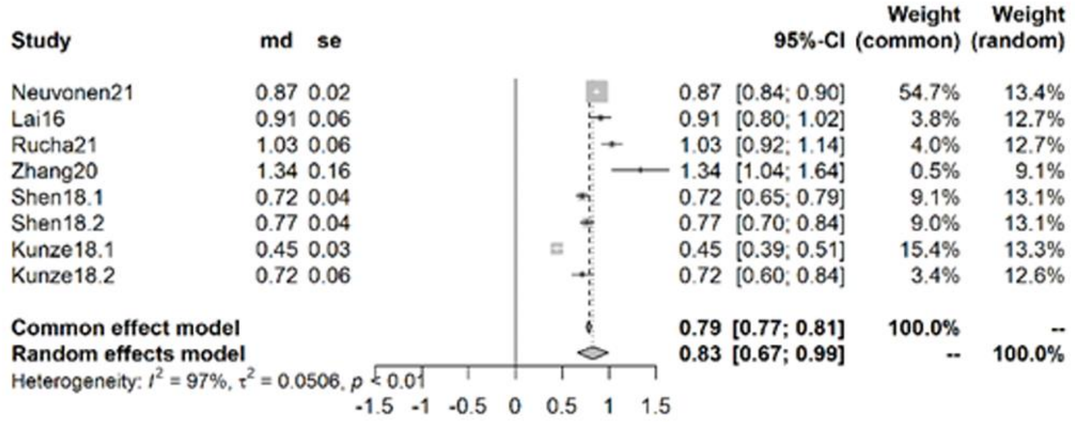
- Justification of sampling procedure and blood volume in pediatric HRO studies
- Considerations for non-invasive biomarker measurement

The challenge of age-dependent physiology

Example: sample size determination for novel biomarker (healthy children)

1. Adult reference value?

-> meta-analysis mean and SD



2. Define pediatric age groups of interest

- infants (<24 months)
- pre-school children (2-6 years)
- school children (>6-12 years)
- adolescents (>12-18 years of age)

☹ healthy neonates (0-28 days)
impossible to include with minimal risk
-> cord blood (day 0)

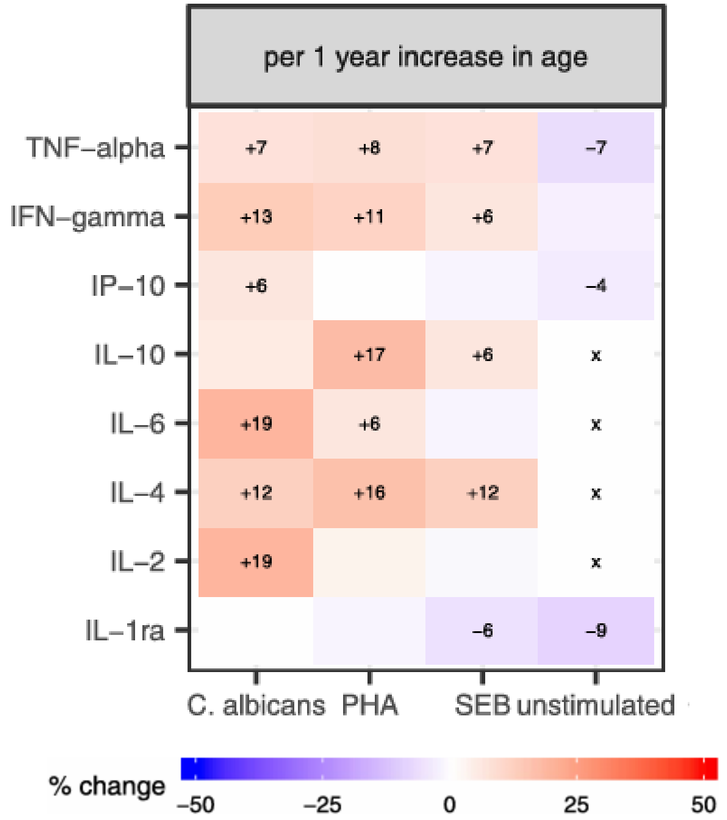
-> compare mean with adult reference

-> multiple testing!

The challenge of age-dependent physiology

Example cytokines as promising diagnostic biomarkers

Both **baseline** and **dynamic response** (*in vitro*) may be age-dependent (healthy children)



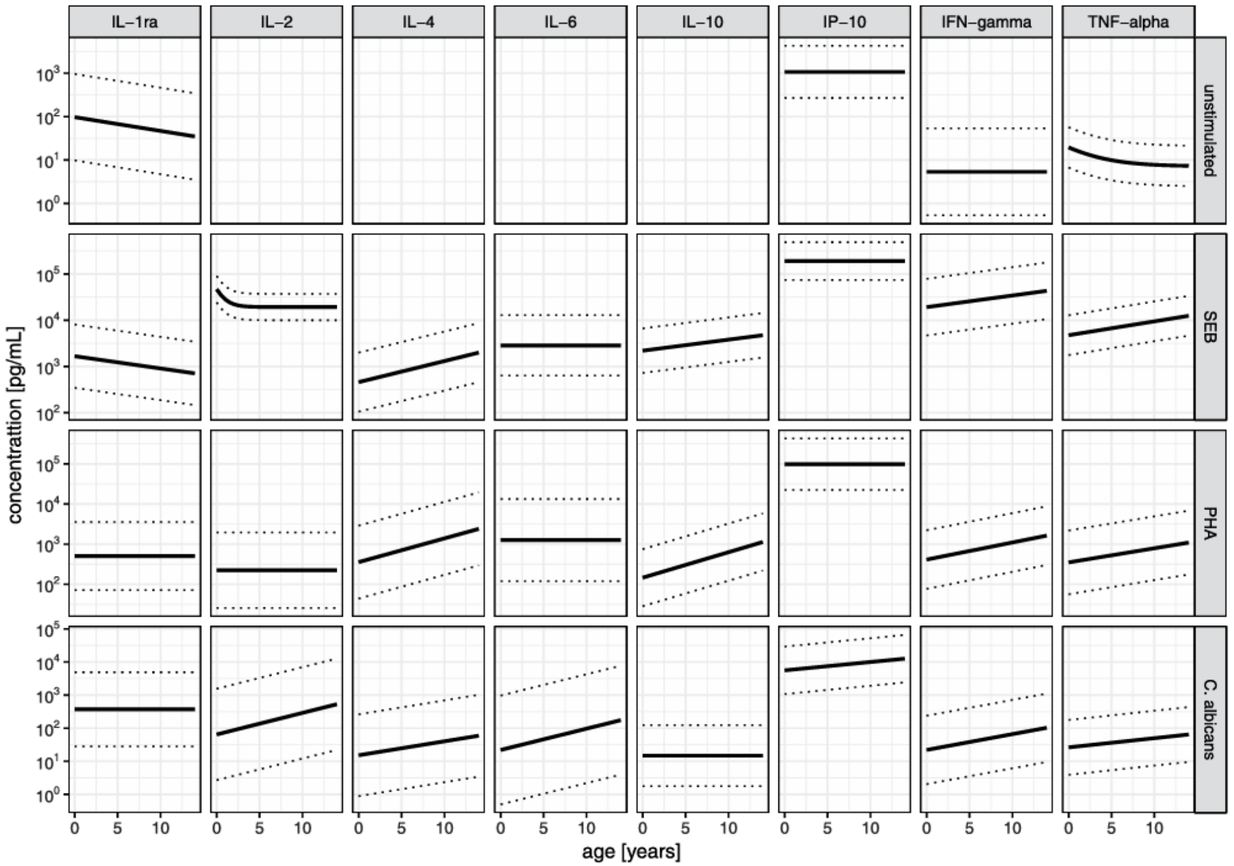
Decker ML, Gotta V, Wellmann S, Ritz N. Cytokine profiling in healthy children shows association of age with cytokine concentrations. Sci Rep. 2017 Dec 19;7(1):17842. doi: 10.1038/s41598-017-17865-2.

The challenge of age-dependent physiology

Example cytokines as promising diagnostic biomarkers

University Children's Hospital Basel

Use of **statistical modeling** to support age-appropriate normal & dynamic reference ranges



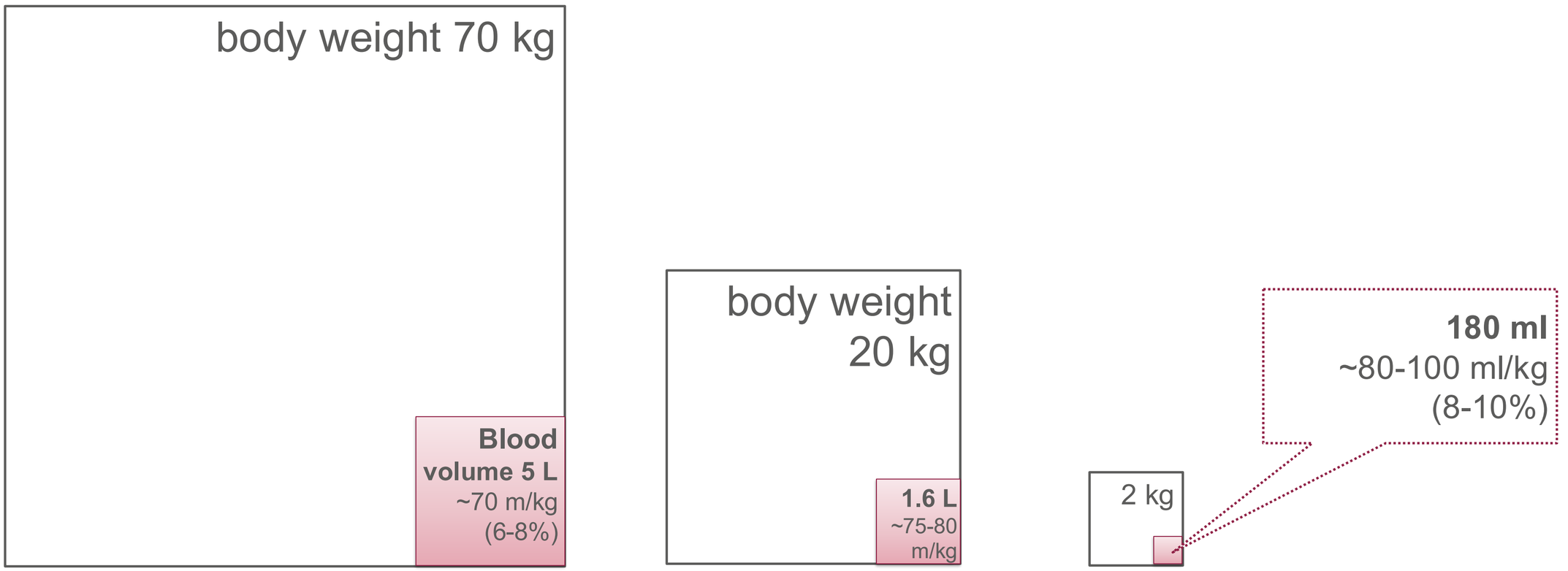
Decker ML, Gotta V, Wellmann S, Ritz N. Cytokine profiling in healthy children shows association of age with cytokine concentrations. Sci Rep. 2017 Dec 19;7(1):17842. doi: 10.1038/s41598-017-17865-2.

The challenge of age-dependent physiology

-> Considerations for pediatric HRO projects:

- Carefully select and balance age-groups
- Use of statistical modeling to evaluate age-dependencies

Blood volume in children



Howie SRC. Blood sample volumes in child health research: review of safe limits. Bull World Health Organ 2011;89:46–53

What is «minimal risk»?

Sampling of max. 1-5% of total blood volume (TBV) over 24h*

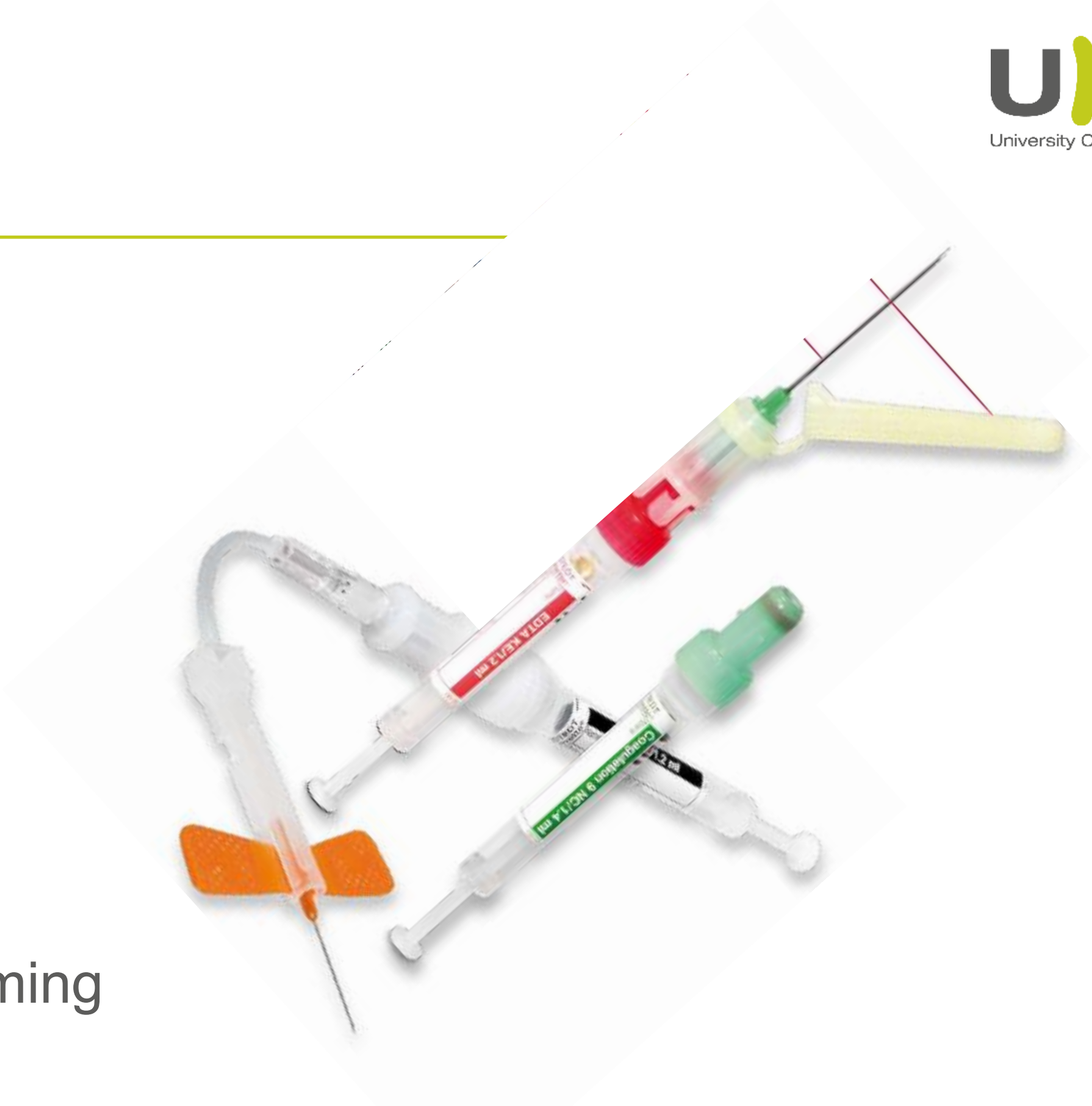
	body weight (kg)	TBV (ml)	1% ml blood	3% ml blood	5% ml blood
TBV ~ 90 ml/kg	**0.5**	**45**	0.45	1.35	2.25
	1	**90**	0.9	2.7	4.5
	3	**270**	2.7	8.1	13.5
TBV ~ 80 ml/kg	5	400	4	12	20
	10	800	8	24	40
	15	1200	12	36	60
	20	1600	16	48	80
TBV ~ 70 ml/kg	40	2800	28	84	140
	80	5600	56	168	280

*up to 10% of TVB over 8 weeks

Howie SRC. Blood sample volumes in child health research: review of safe limits. Bull World Health Organ 2011;89:46–53
Peplow C, et al. Blood draws up to 3% of blood volume in clinical trials are safe in children. Acta Pædiatrica 2019 108, pp. 940–944
Heidmets LT, et al. Blood loss related to participation in pharmacokinetic study in preterm neonates. Neonatology 2011;100:111–115

Sampling technique

+ Small sample volume
- Pain-/stressful, potentially time-consuming



- larger sample volume
+ *if catheter already in place*: not painful & efficient

Opportunistic sampling design

Example of pharmacokinetic study (HRO project, minimal risk)

1. Practical considerations (4 fixed sampling times for opportunistic sampling in pediatric hematopoietic cell transplant (HCT) recipients

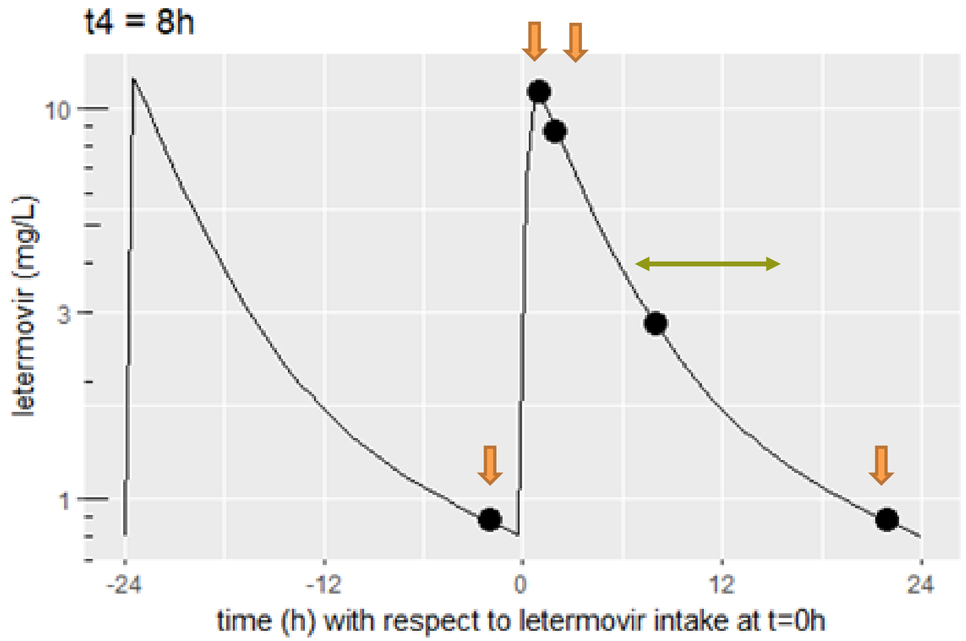
Letermovir blood sampling schedule*	**Time with respect to letermovir administration** (approximate)	**Comment**
6h00 (t_1)	-2h	*Opportunistic sampling:* Time of daily routine blood draws
		Expected administration of letermovir at 8h00 (IV), and between 8h-9h for PO.
9h00 (t_2)	+1h	*Opportunistic sampling:* Temporary disconnection of catheter for showering, end of IV letermovir infusion
10h00 (t_3)	+2h	*Opportunistic sampling:* Reconnection of catheter, routine blood draw for determination of immunosuppression (CSA, TAC) level; immunosuppression administration at 10h00
16h00 (t_4) (16h-20h)	+8h (Range +8h to +12h)	Timing with routine additional blood draw, in case scheduled
6h00 (day +1) (t_5)	+22h	*Opportunistic sampling:* Time of daily routine blood draws

*in patients <10kg only the t_1 sample will be drawn.

Opportunistic sampling design

Example of pharmacokinetic study (HRO project, minimal risk)

1. Practical considerations (4 fixed sampling times for opportunistic sampling)
2. **Optimal design evaluation** for 1 additional blood sample, based on published PopPK model



→ **good precision** (relative standard error ≤ 10-20% in clearance, ≤ 30% in the central volume of distribution) **can be obtained for a timing of this t_4 sample between +8h and +12h**

Characteristics of an ideal pediatric biomarker

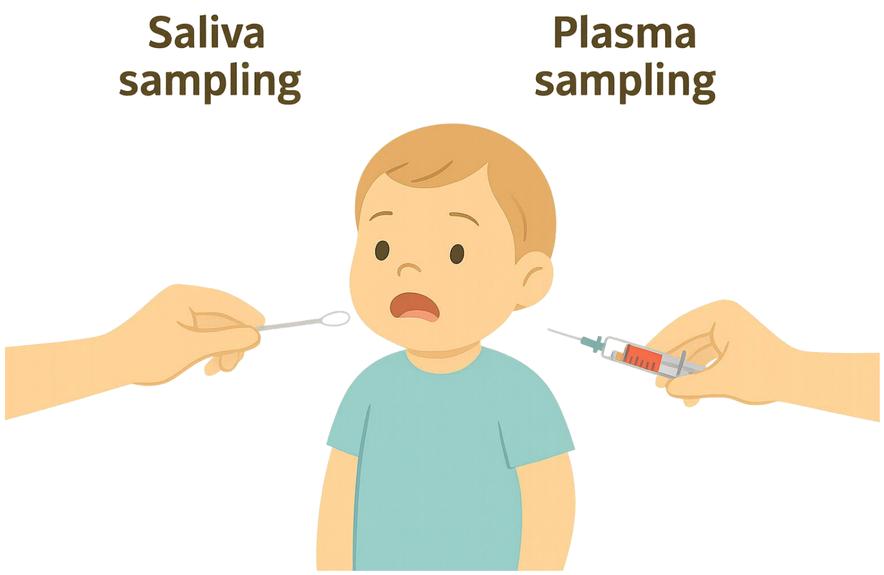
- **Noninvasive**
- Well-established «normal» values in children
- Age-dependent physiologic and dynamic changes understood
- Applicable to pediatric-specific diseases – e.g. scaling necessary?
- Cost-effective

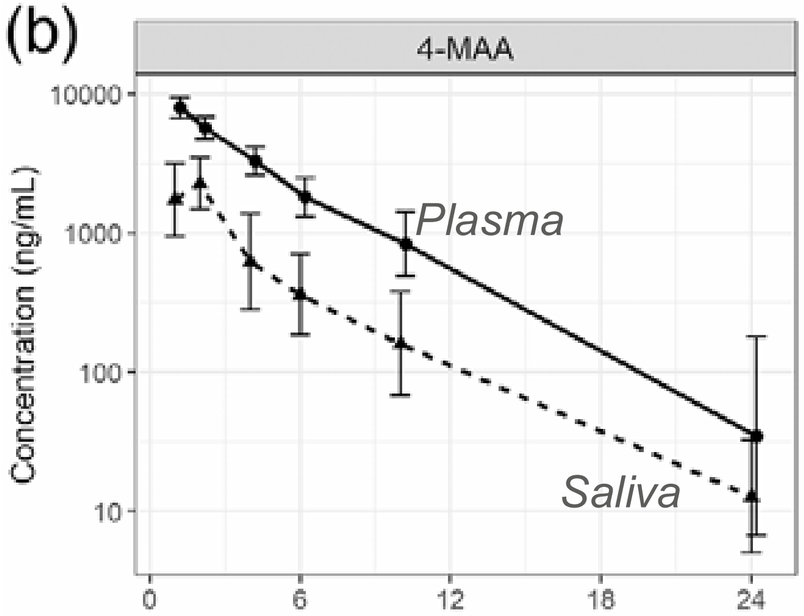
Goldman J, et al. Development of biomarkers to optimize pediatric patient management: what makes children different? Biomark Med. 2011 Dec; 5(6): 781–794. doi: 10.2217/bmm.11.96
Kelly LE, et al. Useful pharmacodynamic endpoints in children: selection, measurement, and next steps. Pediatr Res. 2018 Jun;83(6):1095-1103. doi:10.1038/pr.2018.38

Consider non-invasive biomarker alternatives

Example: Pharmacokinetic (PK) study in saliva and plasma

Rich saliva PK sampling may complement sparse plasma PK sampling…





Anliker-Ort M, et al. Pharmacokinetics-Based Pediatric Dose Evaluation and Optimization Using Saliva - A Case Study. J Clin Pharmacol. 2024 Mar 18. doi: 10.1002/jcph.2428.

Consider non-invasive biomarker alternatives

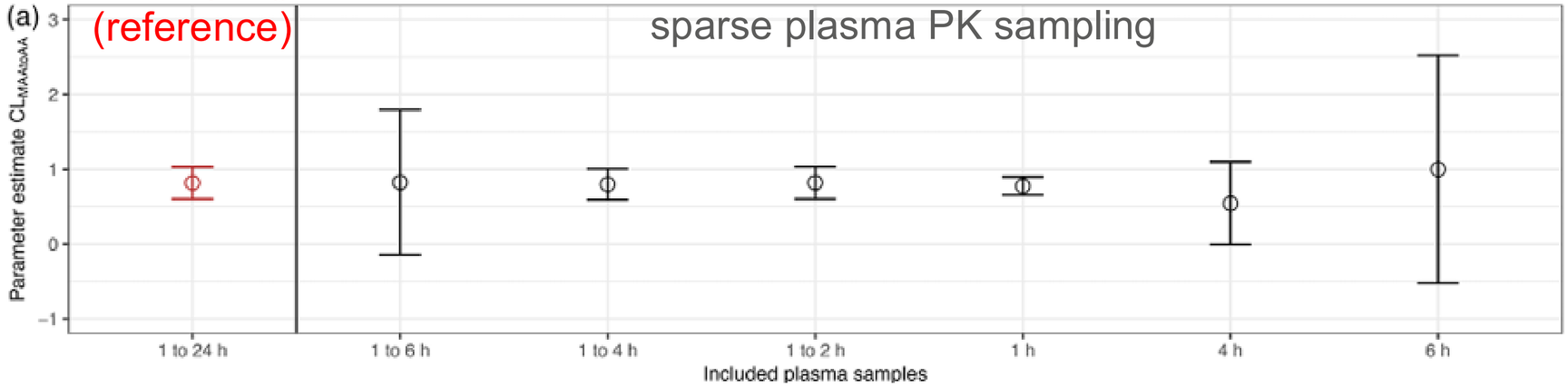
Example: Pharmacokinetic (PK) study in saliva and plasma

Rich saliva PK sampling may complement sparse plasma PK sampling **in future studies**

… when combined with population PK (mixed-effect) modeling

rich plasma PK sampling (reference)

→ non-biased PK parameter estimates from sparse plasma PK sampling



Anliker-Ort M, et al. Pharmacokinetics-Based Pediatric Dose Evaluation and Optimization Using Saliva - A Case Study. J Clin Pharmacol. 2024 Mar 18. doi: 10.1002/jcph.2428.

Non-invasive biomarker measurements

- Saliva
- Transcutaneous
- Urine
- Breath
- Wearables
- …

- left-over plasma samples (biobanking)

Research Involving Sampling & Collection

-> Considerations for pediatric HRO projects:

- Carefully assess blood volume, optimal sampling technique, opportunistic sampling
- Consider complementary non-invasive alternatives (may require «validation»)
- Use of statistical modeling to analyse sparse data

Topic, Speakers

PD Dr. Verena Gotta

Head Clinical Pharmacist at Pediatric Pharmacology and Pharmacometrics Research Center of the University Children's Hospital Basel (UKBB), Hub Leader & Senior Researcher at Swiss PedNet

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Feasibily of pediatric HRO projects

Regina Santoro

Head of Study Coordination, Paediatric Research Centre (PRC), University Children's Hospital Basel (UKBB)

Hub Coordinator & Member of Hub Staff Leadership Team at Swiss PedNet

«Feasiblity»


Operational resources
Site capability
Recruitment Feasibility
FEASIBILITY
Regulatory Feasibility
Financial Feasibility

Challenge «Involving Children»

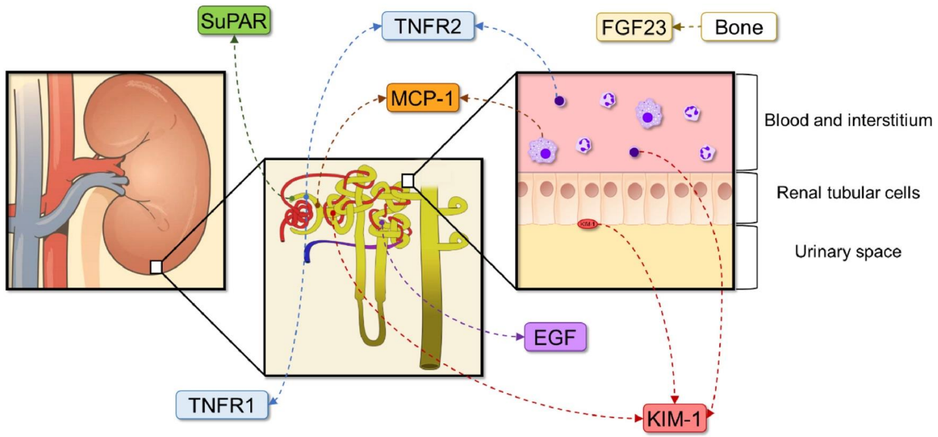
Consent & Ethics - Children cannot legally give consent on their own

Time and organizational demands - Visit planning

The unpredictability of children's behavior - Children are children

Generalizability - Small sample sizes, selective participation

A practical example «KIDNEY CHECK»



Evaluation of Novel Biomarkers for Early Detection of Renal Injury in children at increased risk to develop CKD; a prospective study; P.I. Alexandra Goischke

Background: Assessment of kidney function using serum creatinine

Plasma and Urine Biomarkers of CKD: A Review of Findings in the CKiD Study;*Originally published at https://doi.org/10.1016/j.semnephrol.2021.09.003*

A practical example «KIDNEY CHECK»

Objectives:

1. To detect early kidney dysfunction with new biomarkers in high-risk populations for developing chronic kidney disease

2. To establish age-appropriate reference ranges for these biomarkers in a healthy pediatric population

Procedure:

Combined biomarker measurements in blood and urine

Sample Processing:

Blood processing within 30 minutes of collection

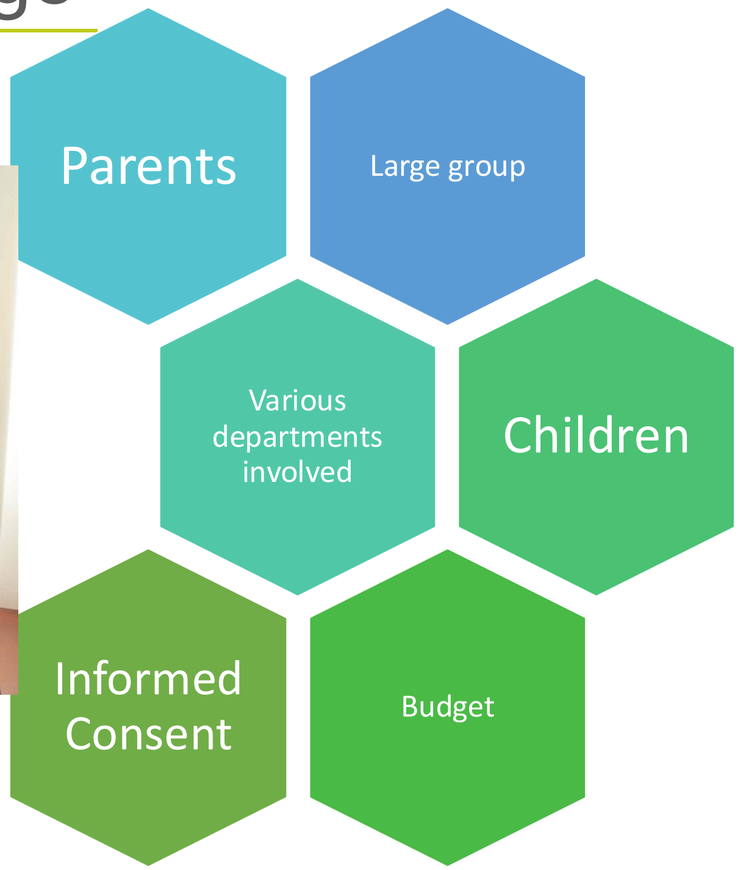
(Blood can only be used if urine is also present! And vice versa)

Population of Interest

Total over 400 Children, in 3 groups:

1. Healthy Control group → Where to find? Preoperative Anesthesia Consultation / n=100
2. Confirmed CKD-Group → Nephrology consultations at the polyclinic / n=38
3. CKD-Risk-Group → Endocrinology, Nephrology, Rheumatology / n=280

The Feasiblity-Challenge



PRC Paediatric Research Centre

UKBB kompetent & menschlich

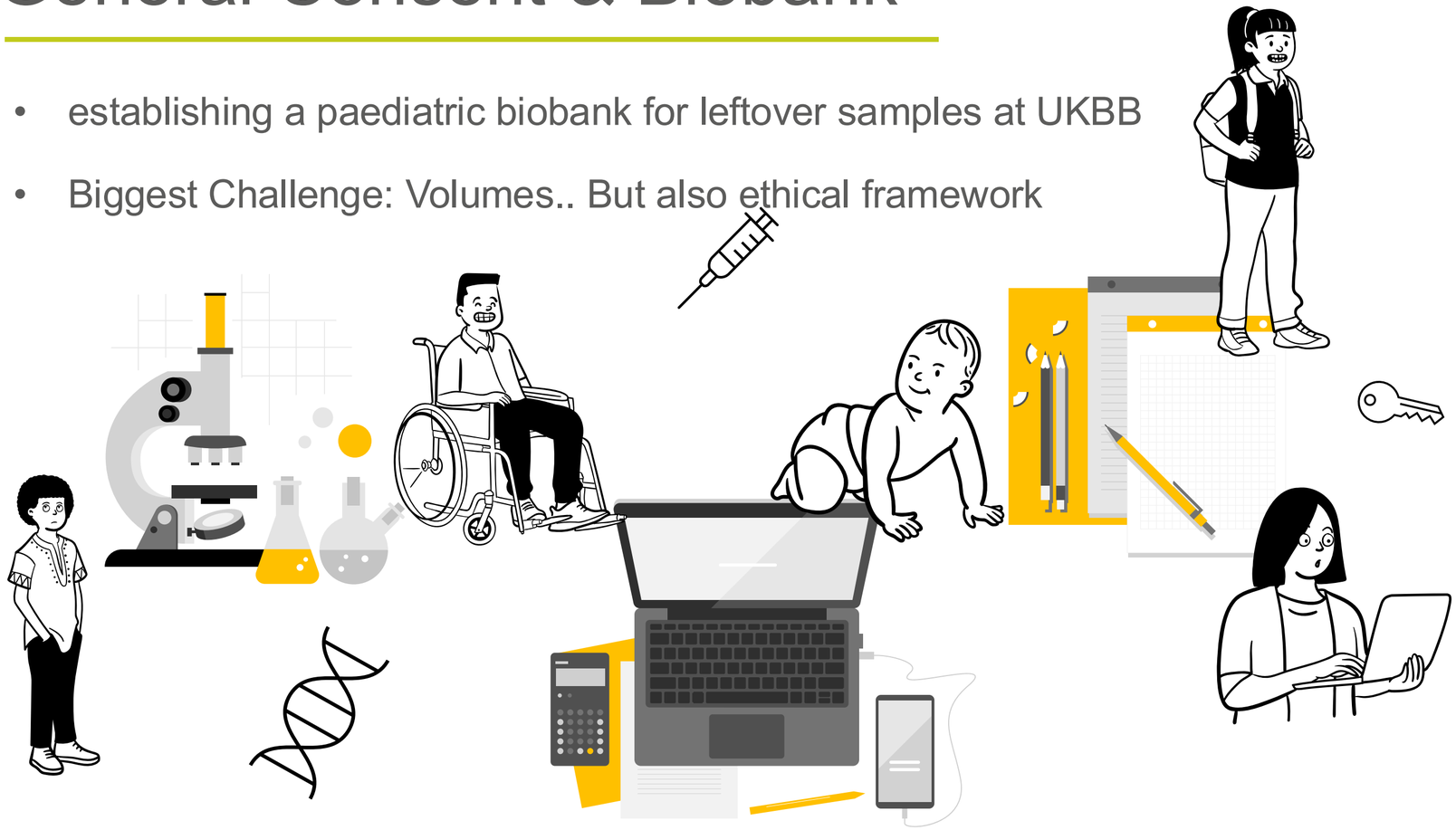
Children

Children and their Parents

Generated by AI using ChatGPT

General Consent & Biobank

- establishing a paediatric biobank for leftover samples at UKBB
- Biggest Challenge: Volumes.. But also ethical framework



https://pixabay.com/

How can it work?

https://pixabay.com/

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UNIVERSITÄT BERN

Data reuse: ethical & legal challenges

PD Dr. Fabiën Belle

Research Team Leader Paediatric Routine Data, Institute of Social and Preventive Medicine (ISPM), University of Bern,

Research Team Leader / Senior Researcher at Swiss PedNet

Often (paediatric) studies don’t get delayed because of resources—but because of ethical approval and legal agreements

Some potential hurdles/ pitfalls…

- **Study design** appropriate for children (sampling, pain, anxiety, etc.)
- **Risk-benefit** (stress assessment, what do parents consider acceptable?)
- **Age-specific** consent & patient information (multiple versions, signature patient + legal rep, re-consent)
- **Misclassification** (research vs. quality control)

191223_abgrenzung-qualitatssicherung-von-forschung_finalisierte-version_de_en.pdf

- Overly **vague** study protocols
- **What if** we want to do XX in the future? >> Amendment!
- General **consent**: informed vs accepted
- **Legal agreements**

Quick fixes

Ask around…

- IC understandable? Ask children!
- Protocol clear?
- What worked for others, what not?, etc.

Use examples / templates

(if available)

Legal Agreement Templates (DTUA) – SPHN

Call your ethical committee

pre-consult, during the process

Choose your EC wisely - *if possible*

Example data reuse in paediatric NDS

Swiss Ped Health
A Pediatric National Data Stream

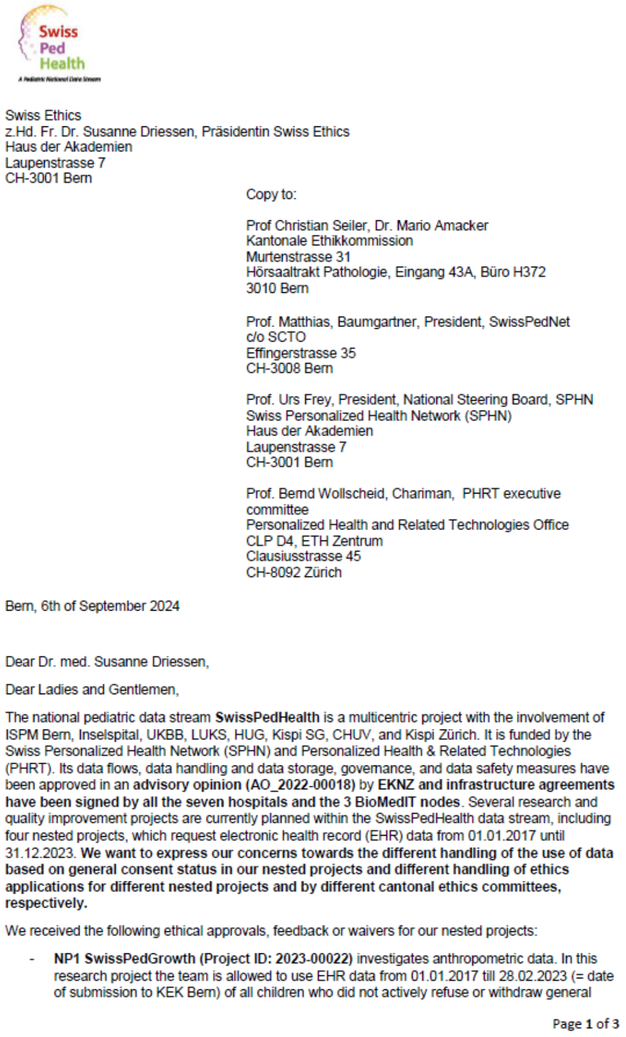
- 4 nested projects
- **Health database regulation - Advisory opinion**: data flows, data handling and data storage, agreements, governance, and data safety measures
- 1st nested project - **Ethical application template**
  - All children who did not actively refused or withdraw GC (Art. 34 HFG, Art. 37-40 HFV)
  - No distinction between sites
- 2nd project: waiver – huge legal challenges ~ 1 yr!

3rd project - Different views cantonal ECs

- **CER-VD:** “the application of Art 34 HRA is accepted for contactable persons as well as for contactable persons **6 weeks after** the reminder has been sent, according to the procedure in force”

- **KEK Zurich**: “From May 2015, a signed GK must be available from the data at the Children's Hospital Zurich so that the data can be used further. (**No GK available is equivalent to a rejection** of the GK)”

- **KEK Bern**: “Patients who have been treated since 01.01.2016 and for whom no status quo on the general consent is available must be contacted and informed of the right to object by means of a general consent. If there is no response in the form of consent or refusal **within 30 days**, it can be assumed that the patient is not exercising their right to object. Encrypted non-genetic data may then continue to be used (Art. 33 HRA para. 2). For patients who cannot be reached or who are deceased, an exemption may be requested in accordance with Art. 34 HRA”



Swiss Ethics
z.Hd. Fr. Dr. Susanne Driessen, Präsidentin Swiss Ethics
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Murtenstrasse 31
Hörsaaltrakt Pathologie, Eingang 43A, Büro H372
3010 Bern

Prof. Matthias, Baumgartner, President, SwissPedNet
c/o SCTO
Effingerstrasse 35
CH-3008 Bern

Prof. Urs Frey, President, National Steering Board, SPHN
Swiss Personalized Health Network (SPHN)
Haus der Akademien
Laupenstrasse 7
CH-3001 Bern

Prof. Bernd Wollscheid, Chariman, PHRT executive committee
Personalized Health and Related Technologies Office
CLP D4, ETH Zentrum
Clausiusstrasse 45
CH-8092 Zürich

Bern, 6th of September 2024

Dear Dr. med. Susanne Driessen,

Dear Ladies and Gentlemen,

The national pediatric data stream **SwissPedHealth** is a multicentric project with the involvement of ISPM Bern, Inselspital, UKBB, LUKS, HUG, Kispi SG, CHUV, and Kispi Zürich. It is funded by the Swiss Personalized Health Network (SPHN) and Personalized Health & Related Technologies (PHRT). Its data flows, data handling and data storage, governance, and data safety measures have been approved in an **advisory opinion (AO_2022-00018)** by **EKNZ and infrastructure agreements have been signed by all the seven hospitals and the 3 BioMedIT nodes**. Several research and quality improvement projects are currently planned within the SwissPedHealth data stream, including four nested projects, which request electronic health record (EHR) data from 01.01.2017 until 31.12.2023. **We want to express our concerns towards the different handling of the use of data based on general consent status in our nested projects and different handling of ethics applications for different nested projects and by different cantonal ethics committees, respectively.**

We received the following ethical approvals, feedback or waivers for our nested projects:

- **NP1 SwissPedGrowth (Project ID: 2023-00022)** investigates anthropometric data. In this research project the team is allowed to use EHR data from 01.01.2017 till 28.02.2023 (= date of submission to KEK Bern) of all children who did not actively refuse or withdraw general

Page 1 of 3

Bias 1: Different timing GC introduction

Example: number of families to be contacted for NP3 without Article 34

Center	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	Approximated number of lung function tests per year	GC introduction date
Bern	~17'500 (44%)							~22'500 (56%)									~2500/year	1.2017
Basel	~9'000 (56%)									~7'000 (44%)							~1000/year	6.2018
Luzern	~21'000 (88%)														~3'000 (12%)		~1500/year	9.2023
Zurich	~15'000 (31%)							~33'000 (69%)									~3000/year	4.2015
Geneva	~7'000 (44%)							~9'000 (56%)									~1000/year	5.2017
Lausanne	~14'000 (88%)														~2'000 (12%)		~1000/year	5.2024

Before GC introduction
After GC introduction

Bias 2: Different ECs treatment within the same ‘umbrella’ project

Ethical committees	NP1	NP2	NP3	NP4
KEK Bern	*01.01.2027 -28.02.2023* Permits the use of EHR data for all children **who have not actively refused or withdrawn** their general consent. (Art. 34 HFG, Art. 37-40 HFV). *Till 01.03.2023*, The research team may only use data from children for whom a GC form has been signed and approved.	Waiver Quality Control Project	Art. 34 accepted **30 days after no reponse**	Waiver Quality Control Project
CER-VD			Art. 34 accepted **6 weeks after reminder**	
KEK Zurich			**Failure to sign** the GC is deemed to be a **rejection** of the GC	

Bias 3: Unequal treatment of patients whose GC status is unclear (informed)

Ethical committees	NP1	NP2	NP3	NP4
KEK Bern	*01.01.2027 -28.02.2023* Permits the use of EHR data for all children **who have not actively refused or withdrawn** their general consent. (Art. 34 HFG, Art. 37-40 HFV). *Till 01.03.2023*, The research team may only use data from children for whom a GC form has been signed and approved.	Waiver Quality Control Project	Art. 34 accepted **30 days after no reponse**	Waiver Quality Control Project
CER-VD			Art. 34 accepted **6 weeks after reminder**	
KEK Zurich			**Failure to sign** the GC is deemed to be a **rejection** of the GC	

Administrati blem / dilemma:

Local ethics co tional level;

The approval p ds of sick children and t

This is alrea methods?

Wir werden klinische Routinedaten (z. B. Geburtsdatum, Geschlecht, Größe, Gewicht) sowie Informationen aus der Diagnose des Patienten verwenden. Wir werden auch die Daten von Lungentests verwenden, die zwischen dem 01.01.2017 und dem 31.12.2023 durchgeführt wurden.

Kispi ZH: Art. 34 HFG ist nicht zutreffend. Es können nur Patienten ab Einführung des Generalkonsents eingeschlossen werden, welche den Generalkonsent unterschrieben haben.

CHUV: Art. 34 HFG gilt für:
- Daten von Patienten, die laut CHUV als nicht kontaktierbar gelten (verloren zur Nachuntersuchung oder verstorben),
- Daten von Personen, die nach dem festgelegten Verfahren kontaktiert werden/wurden und innerhalb von sechs Wochen nach Kontaktierung nicht geantwortet haben.

Alle anderen Zentren: Art. 34 HFG gilt für den Zeitraum 01.01.2017 – 31.12.2023 für Patienten, von denen kein unterschriebener Generalkonsent vorliegt bzw. von

18 months later!

Successful data reuse

Talk/call/read

NOTE: data provider requirements can be different from ECs

Ask an «outsider» to read through

Choose wisely

Is it worth the «battle»?

Gain vs Pain

Q&A part – Questions?

Verena Gotta

Regina Santoro

Fabiën Belle

Thank you for participating!

Further questions to:

Verena.Gotta@ukbb.ch

Regina.Santoro@ukbb.ch

fabien.belle@unibe.ch

HRO lunch session 3

- 23 September 2026 –

Speaker: Swiss Biobanking

Registration possible soon under:

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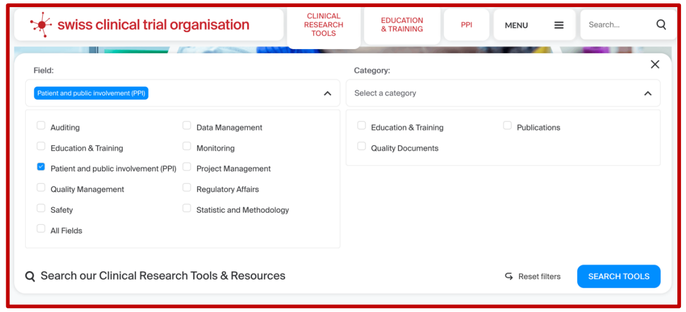

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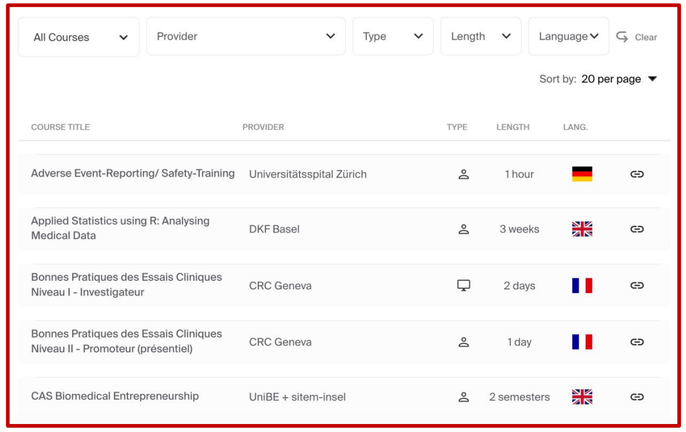

Thank you!

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