Strategic Focus Area
Personalized Health and Related Technologies

SPHN Swiss Personalized Health Network

Pediatric Personalized Research Network Switzerland (SwissPedHealth) – a Joint Pediatric National Data Stream

Main applicants:

Prof. Dr. med. Luregn Schlapbach (University Children's Hospital Zurich)

Prof. Dr. Julia Vogt (ETH Zürich)

NDS Symposium and Monitoring Meeting, 19th September 2023

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ETH zürich

HUG Hôpitaux Universitaires Genève

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The Challenges in Children

Childhood:

- Unique epidemiology, biology, exposure
- Health/disease at the beginning of life
  → impact for 80+ years on the society
- First manifestation of rare diseases
  → prime field for personalized medicine

Challenges:

- Lack of evidence (“little adults”)
- One-size-fits-all approaches
- No intelligent decision-support to enhance learning and management
- Delays to mount research response, delays to implementation (“outdated treatment”)
- Data & research siloes; lack of integration

SwissPedHealth, an NDS for pediatric population

Aim is to make routine data from children's hospitals interoperable, harmonized and quality-controlled using a **modular and scalable approach**

Overarching long-term goal is to enable a learning health system to **improve quality of care**

facilitating **readiness for research** & trials, health-policy creation, and clinical audits

Build infrastructure	Test infrastructure	Enrich infrastructure	Partner with families	Coordinate & oversee
Break disease, discipline, institution silos	Larger numbers of pat.	Smaller numbers of pat.	Focus groups on relevant pediatric aspects	Engage stakeholders
Facilitate access & re-use	Essential pediatric concepts	Detailed biological data (multi omics layers)	Interviews on bioethical aspects	Contribute to cross-fertilization
WP1: Governance & SwissPedData implementation	**WP2: Nested Projects**	**WP3: Lighthouse Project**	**WP4: Ethics & Patient and Public Involvement (PPI)**	**WP5: Management & coordination**
WP Leads: Julia Bielicki, Claudia Kuehni	Claudia Kuehni, Julia Bielicki	Matthias Baumgartner, Jacques Fellay	Klara Posfay- Barbe, Effy Vayena	Luregn Schlapbach, Julia Vogt

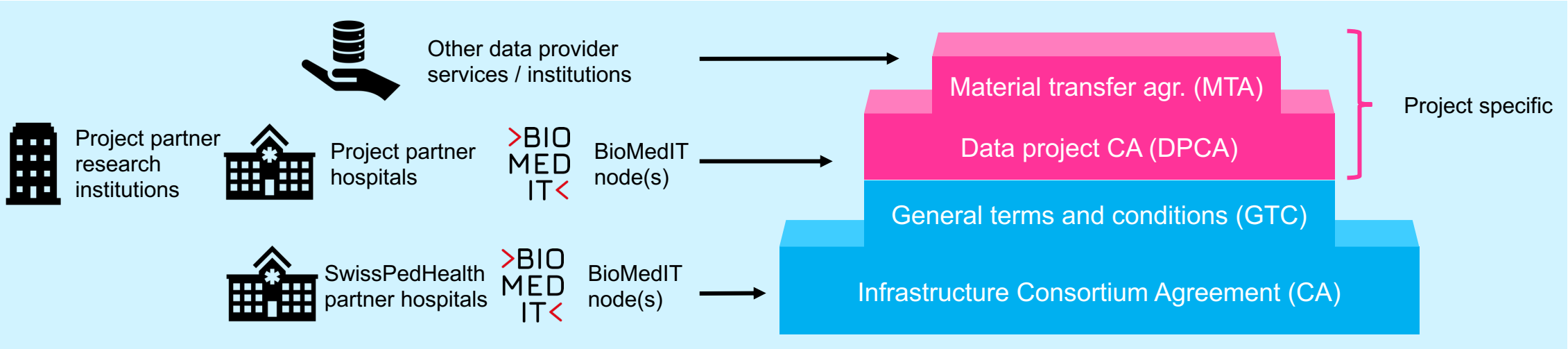
Governance

Agreements:

- Infrastructure CA approved and signed, General Terms and Conditions approved
- Data Project Consortium Agreement (DPCA) & material transfer agreements (MTA) for Lighthouse project approved and signed

Regulatory:

- SwissPedHealth Database regulation approved (“registry like”)



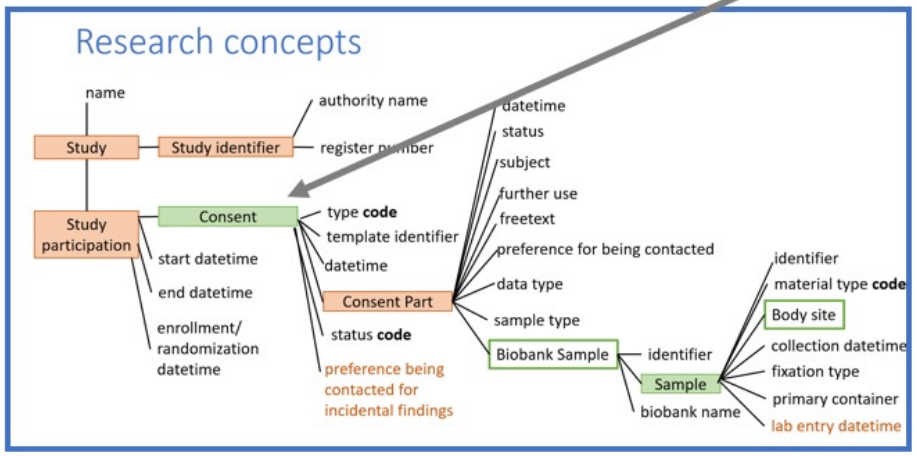
Opportunities & synergies:

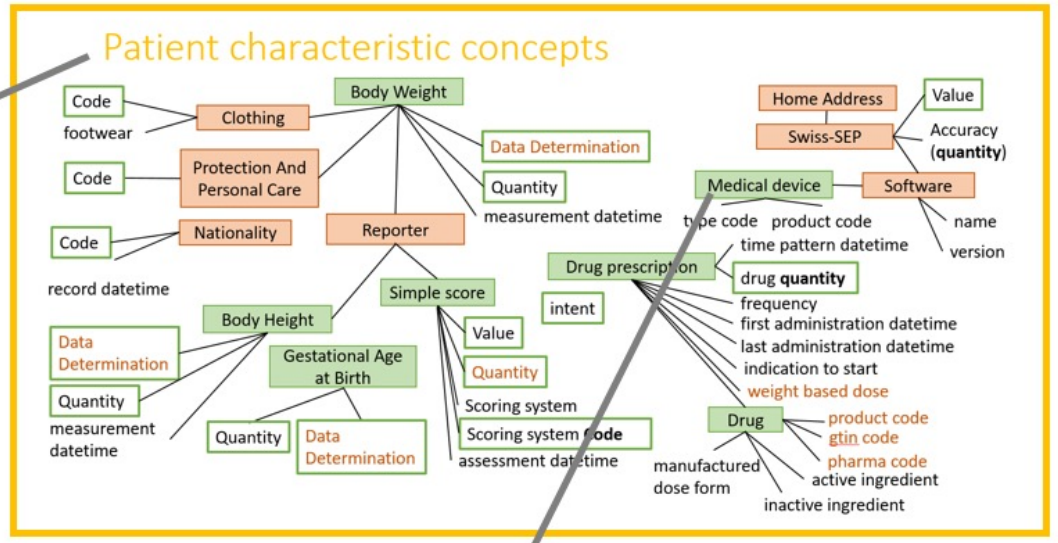
- We can establish sustainable processes for access to NDS data
- For many projects, legal review requirements can be minimized with standardized templates (e.g., DPCA)

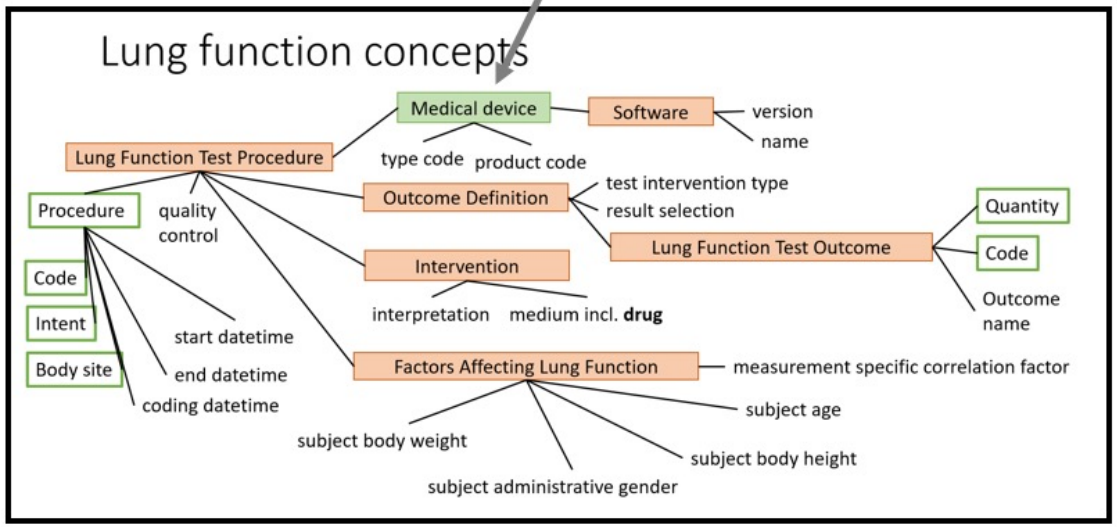
Concepts

SwissPedHealth landscape

- Overview concept infrastructure







Aims:

- Generation of high-quality generic data concepts addressing specific pediatric needs
- Development of (pediatric) research concepts with opportunity of further trial data linkage and re-usability
- Transformation of clinical lung function device data into concepts

Concepts, example

Increasing research data usability: Concepts Study Participation, Consent and Consent Part

- Moving to the future: Combining clinical routine data with “further use trial data” and connecting biobank samples

Study Participation → **Consent** → **Consent Part** → **Biobank sample**

Study Participation

start datetime
11.01.2023

end datetime
11.07.2023

randomization datetime
12.01.2023

Consent

type code
specific

template identifier
SwissPedRECOVERY V1.2

datetime
11.01.2023

status code
accepted

preference being contacted for incidental findings
– *(important for general consent)*

Consent Part

datetime
11.01.2023

subject
patient

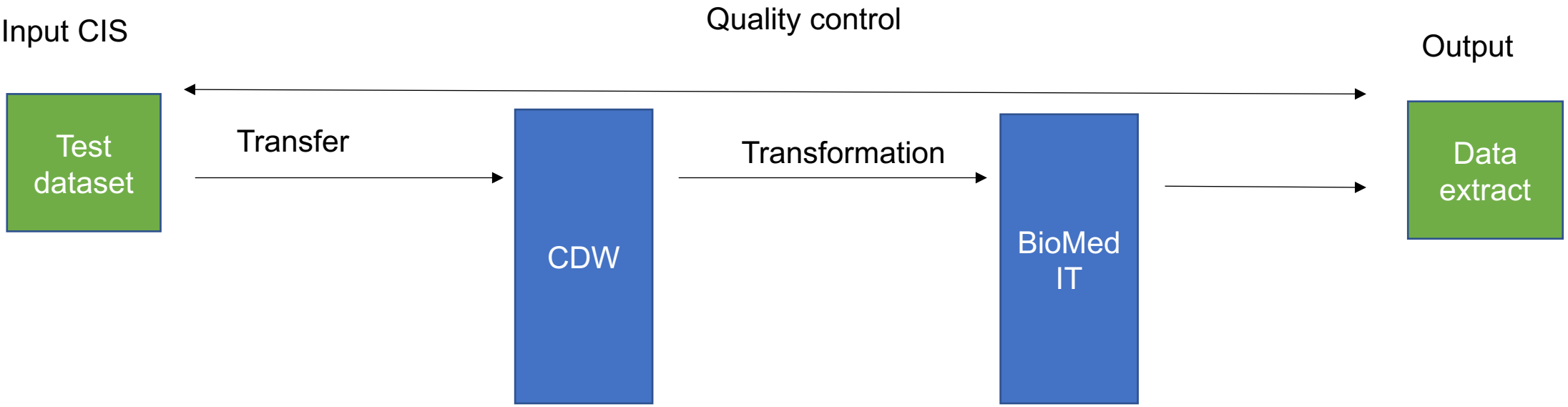
further use
accepted

preference being contacted
– *(relevant for registries, lighthouse project)*

* Note: example is simplified

Data quality check

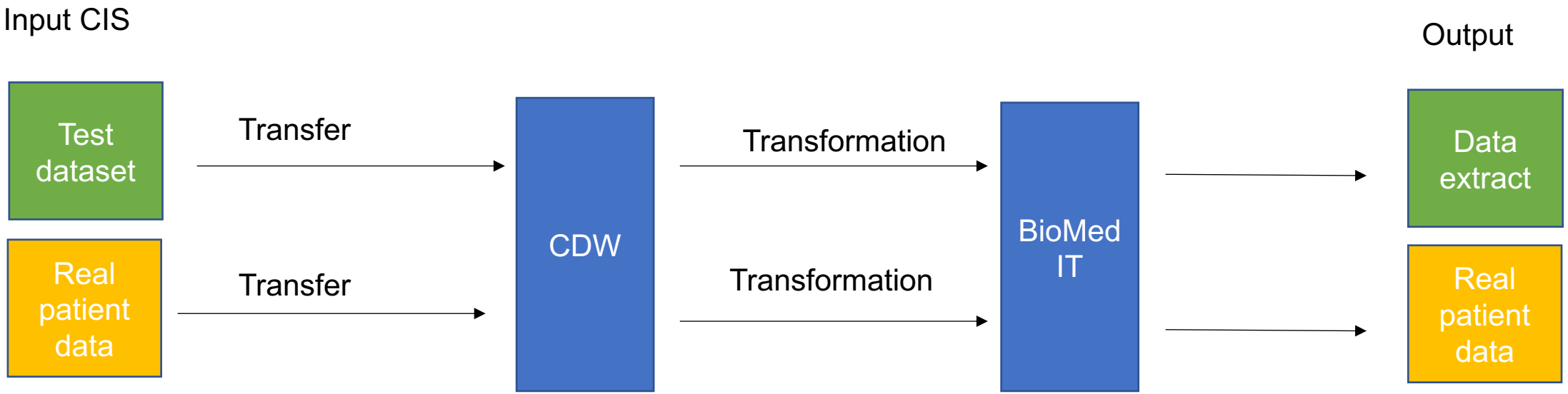
Schema
1) Processing of the test dataset (= pre-defined, de-identified, standardized and structured real-life dataset to ensure data consistency, reproducibility and uniformity within each hospital and between hospitals)



Abbreviation: CIS = Clinical information system; CDW = Clinical Data Warehouse

Data quality check (2)

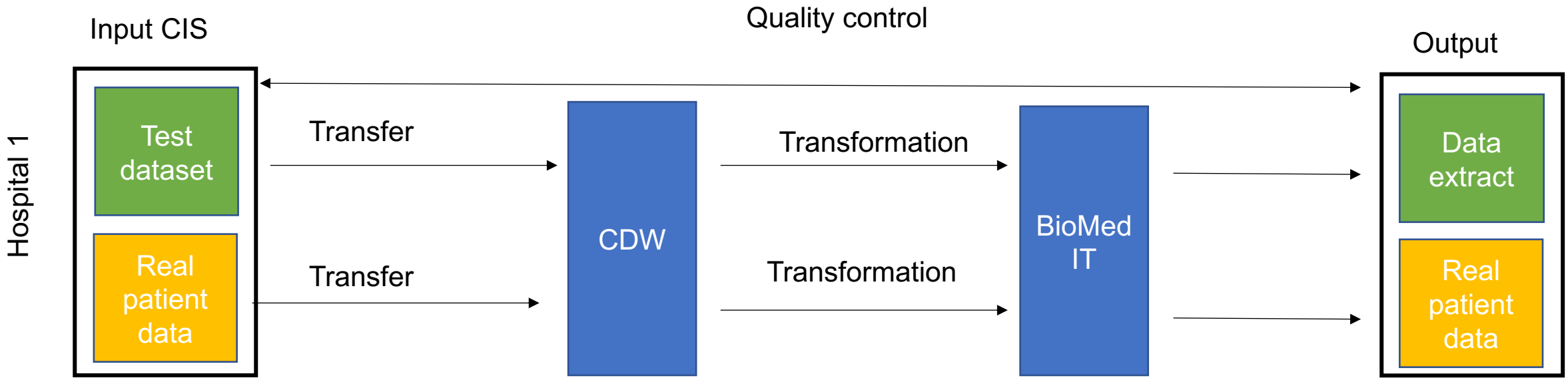
Schema
2) Processing of the real clinical routine data



Abbreviation: CIS Clinical information system; CDW Clinical Datawarehouse

Data quality check (3)

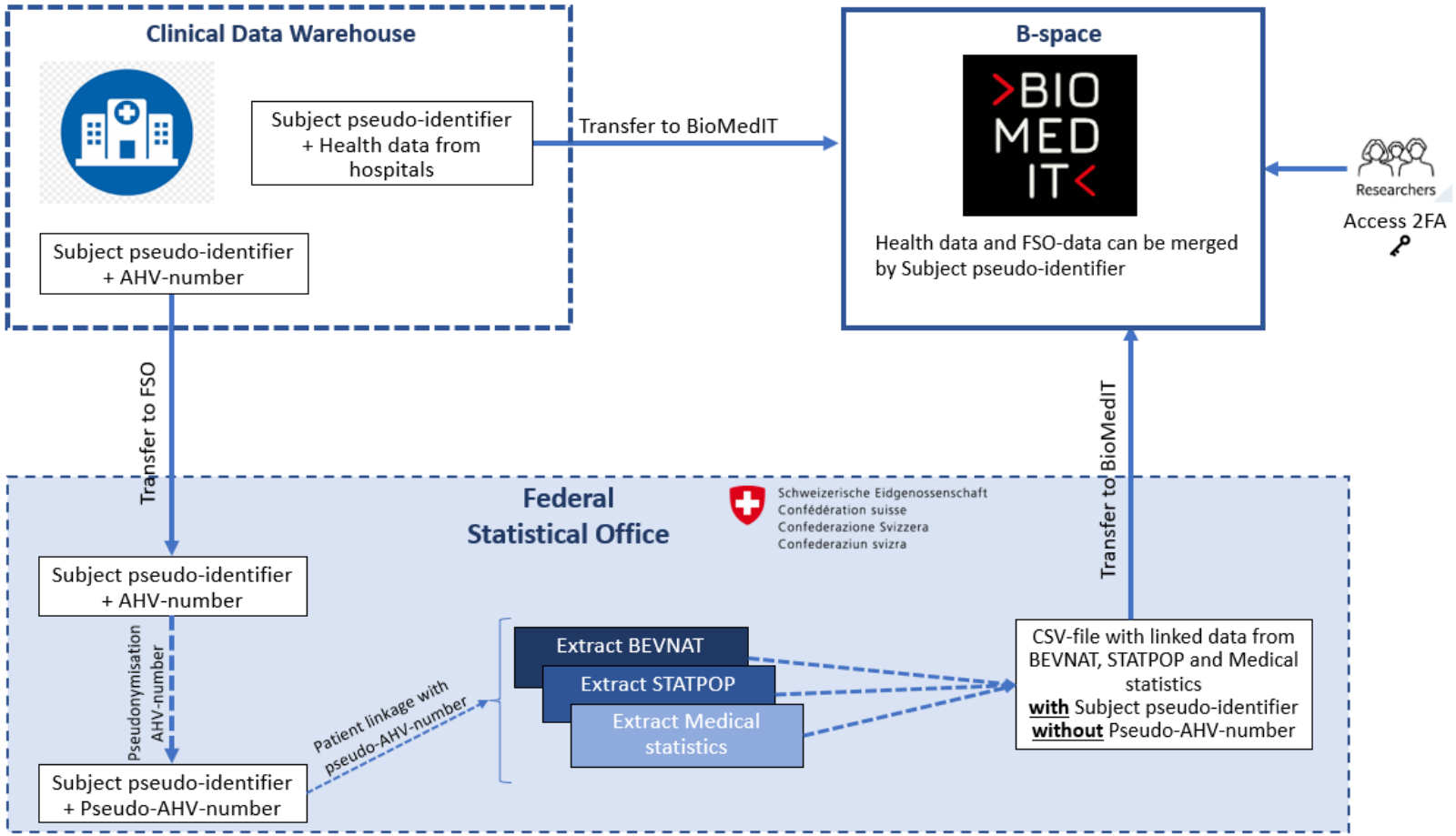
Schema
3) Ensure of high quality data extraction by checking the test dataset output and input



Abbreviation: CIS Clinical information system; CDW Clinical Datawarehouse

NP1: SwissPedGrowth «anthropometrics»

- NP1 ethics (2023-00022) approved Apr. 2023
- External data linkage FSO

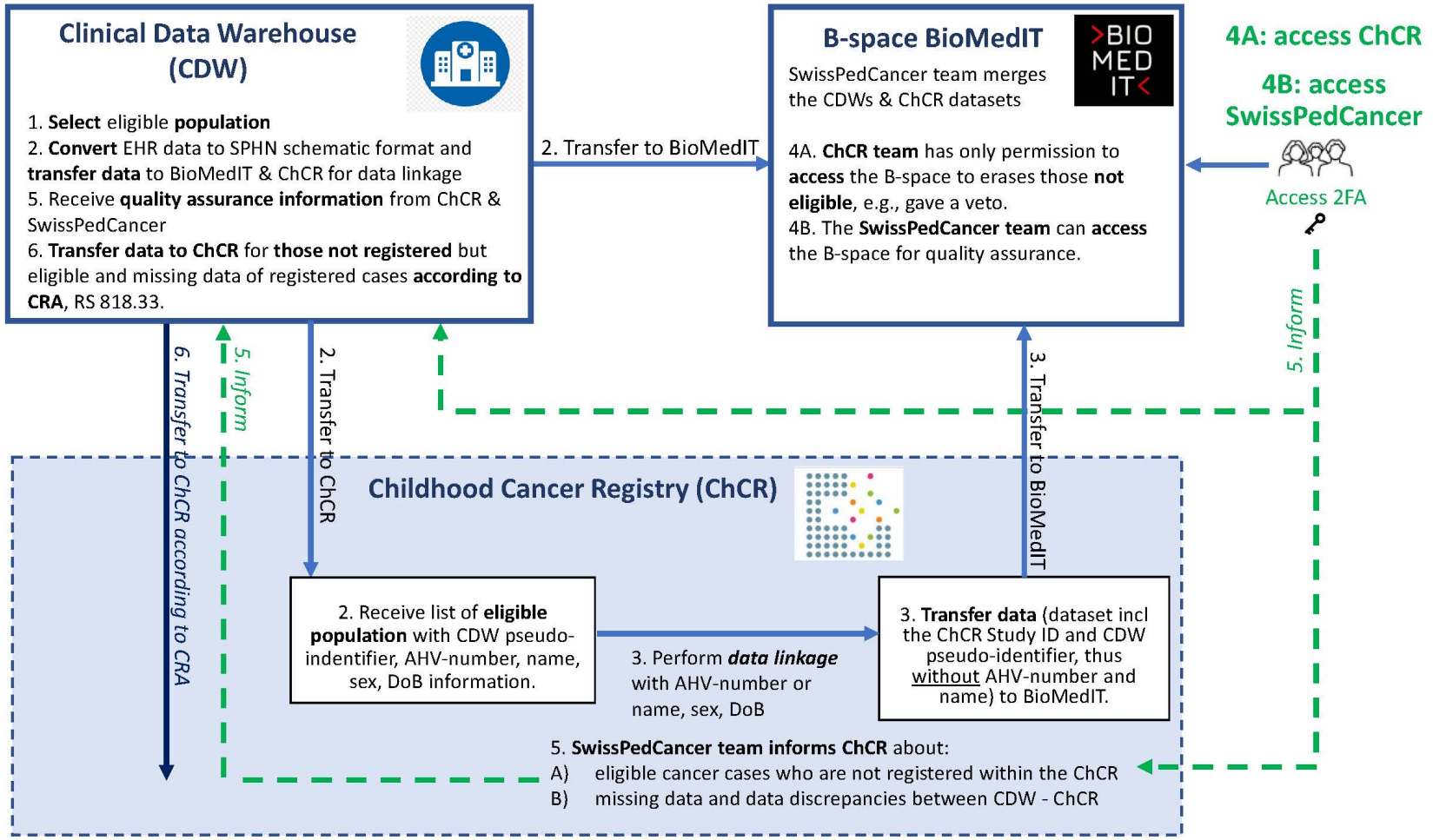


Opportunities & synergies:

- Collaborations initiated with US (PEDSNet) and Portugal
- Ethics template for other projects (nested, demonstrator, etc.)

NP2: SwissPedCancer «childhood cancer»

- NP2 ethics: request for Clarification of Responsibility submitted (Req-2023-01081)
- ChCR: data access + exploration

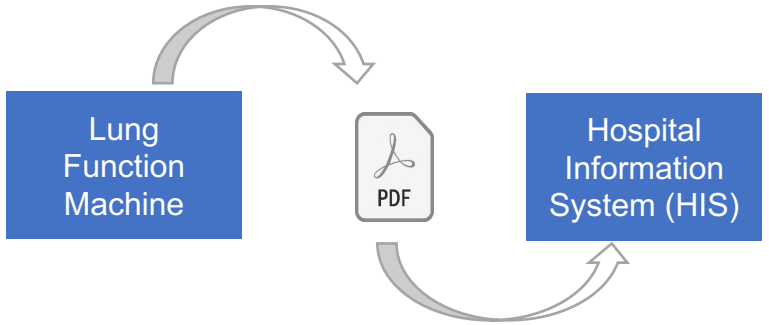


Opportunities & synergies:

- Facilitates bidirectional data flows with registries

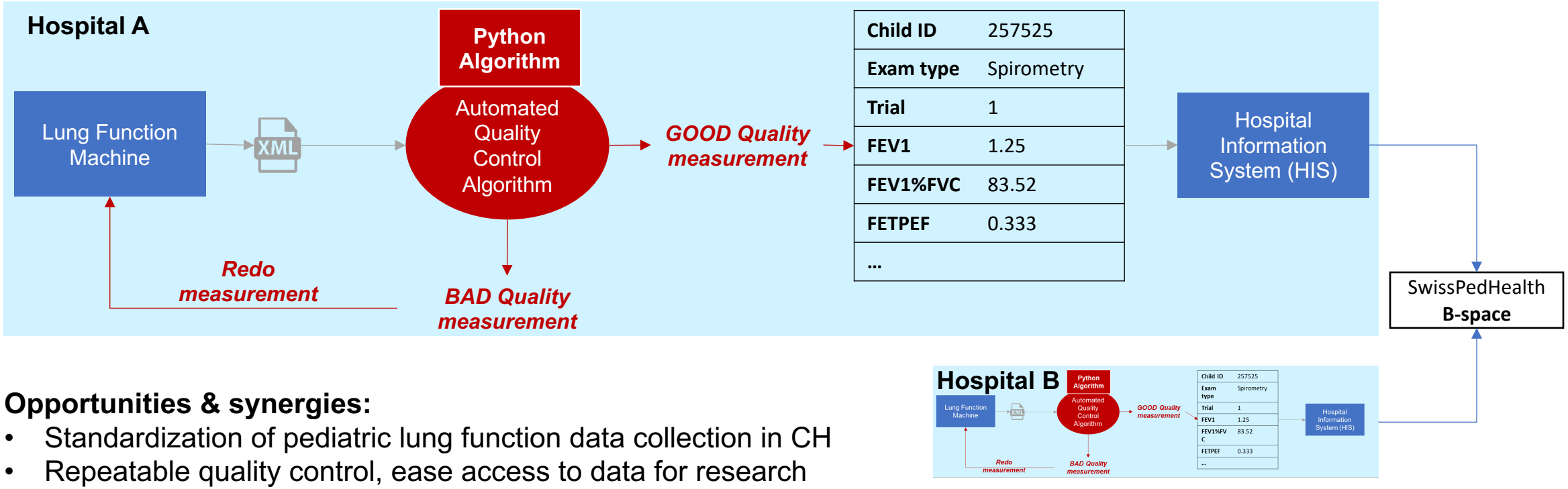
NP3: Standardization of lung function

- Current data pipeline:



Problem: hard to use/access data when stored in a PDF

- New data pipeline:

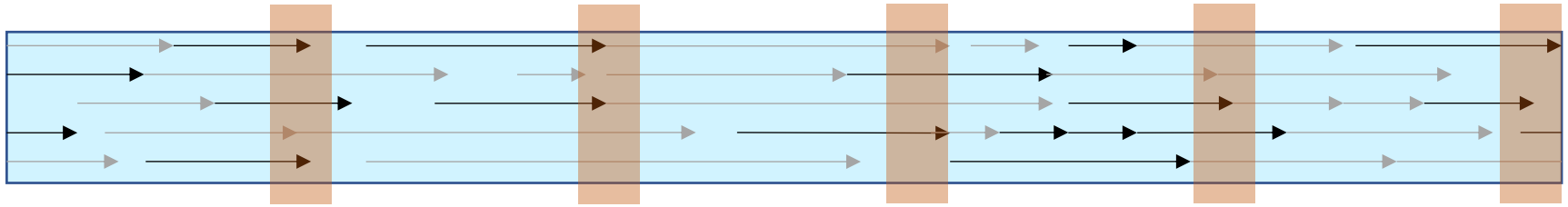


Opportunities & synergies:

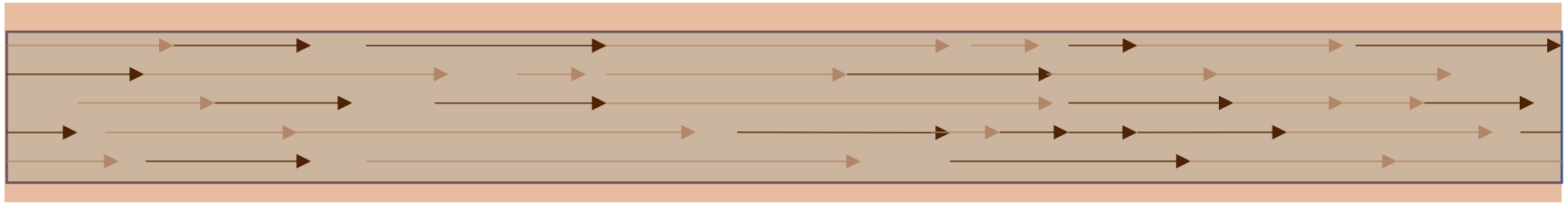
- Standardization of pediatric lung function data collection in CH
- Repeatable quality control, ease access to data for research

NP4: SwissPedAB «antibiotics»

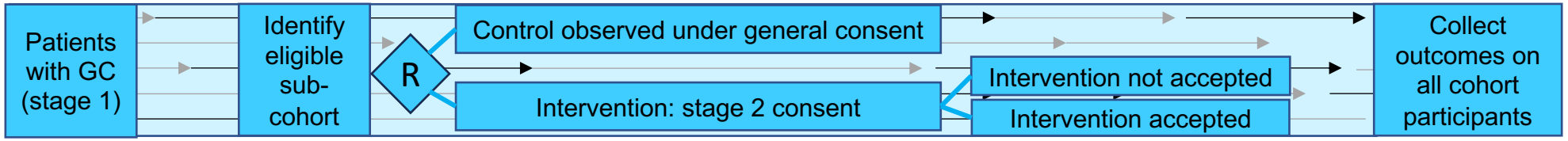
- Antibiotics are among the most commonly used pharmacological agents in pediatrics
- Tracking longitudinal exposure to antibiotics in hospital is currently not feasible
- This hampers quality improvement initiatives and research



Current state of the art = PPS (i.e. cross-sectional assessments through point prevalence surveys)



SwissPedAB = longitudinal assessment in all relevant dimensions (e.g dose, duration)



Preparation for innovative TwiCs designs (TwiCs = trials within cohorts)

Opportunities & synergies:

- Will allow research to improve pharmacological management in inpatient pediatric care

Multi-omics for rare diseases diagnosis

Phase 1: PHRT study

Proof of concept

- Successfully completed

DOI: 10.1038/s42255-022-00720-8

Phase 2: Retrospective cohort study

Re-use of samples from patients with life threatening-phenotypes (n=250)

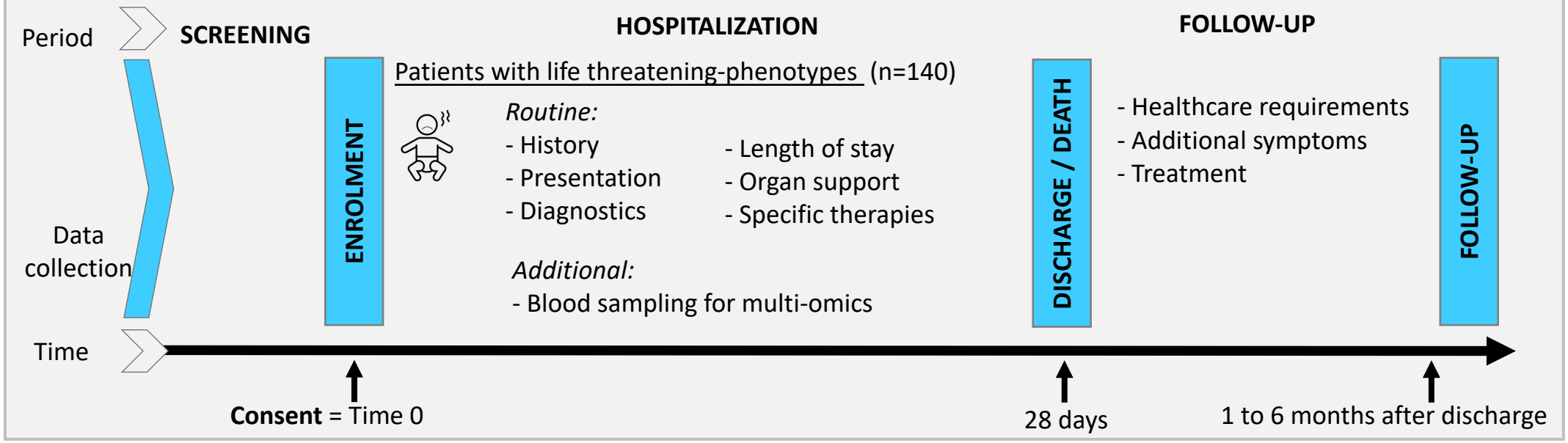
Generation and integration of multi-omics data
Machine learning workflow

- 190 samples processed
- Integration and machine learning pipeline development

Phase 3: Prospective cohort study

"n of 1" diagnostic protocol

- 7 patients enrolled
- Enrollment acceleration and expansion to multicenter



Generation and integration of multi-omics data

Extreme phenotypes

Data collection

Statistical approach

Clinical decision support

Raw data

Multi-omics

Clinical features

Metabolites & Proteins

RNA

DNA

to RDF

Metadata to RDF

Integrative processing

Clinical features

DNA

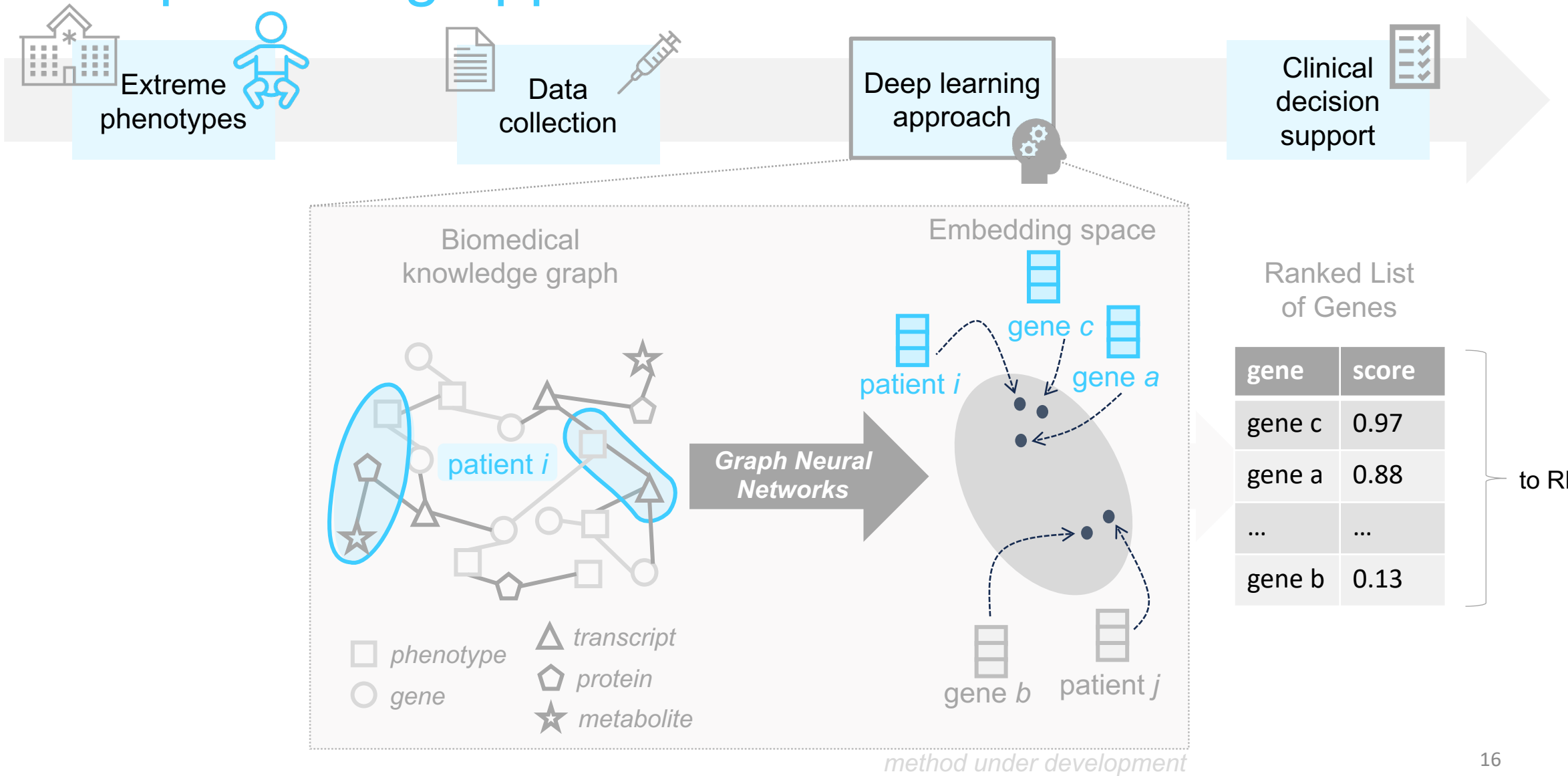
RNA

Proteins

Metabolites

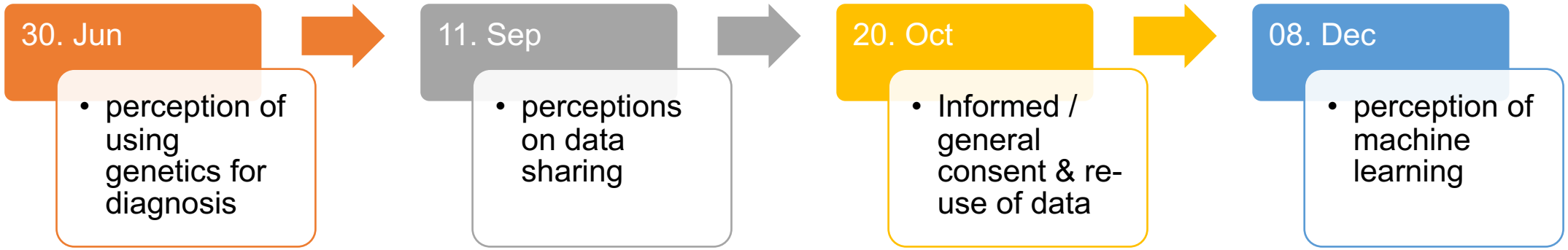
Results to RDF

Deep learning approach



Patient and public involvement

- Contact with Geneva Partner-REC hub for identification of an interested PPI group
- Meetings with other WP leaders & 2 PPI representatives in Steering Committee to identify needs
- The dates scheduled in Geneva & the topics for these focus groups are:



- We also involved our partner patients to review study documents, e.g., flyer for the lighthouse project, the invitation to the focus group, etc.

Opportunities & synergies:

- Establishment of new links with other groups working on PPI projects
- Bringing the PPI data to the ethics interview study

Lessons learned from first focus groups

Parents extremely happy to be asked about their opinion. They have many constructive ideas.

Focus group 1: Use of genetic data for diagnosis

- Genetic testing is wanted and even expected by parents
- Perception of the omnipotence and usefulness of genetic testing ambivalent
- Need for parental consent for genetic testing ambivalent
- Parents tended to be in favor of extending testing to family and siblings
- Supporting the child and explaining the genetic tests is necessary

Focus group 2: Sharing of medical data for clinical purpose and research

- Importance of data sharing for clinical purposes but also research recognized
- Use of anonymized data for research can be altruistic
- All medical data could be shared
- Children should be told about sharing of data as soon as capable of understanding and should be consented when possible
- Little knowledge on how data is used and shared now

Bioethics

WP4: Ethics & Patient and Public Involvement (PPI)

- **Interviews will be conducted** with ~25 medical / laboratory providers and ~25 parents / caregivers from Lighthouse project phase 3
- **Scoping literature review** - Most of the literature is from the US, Canada, Autralia and UK, with limited information from other European countries
- **Ethics protocol** submitted to cover both interview studies
- **Interview guide** drafted (October: get feedback from Lighthouse team, PPI members and to include input from Geneva focus groups
- **Timeline** - conduct provider interviews as soon as Ethics approval (fall 23/winter 24) and start with parent interviews (winter/spring 24), offered in French, German or English

Opportunities & synergies:

- ‘test’ what we learn from PPI focus groups
- Provide input back to Lighthouse on how participants might hypothetically desire future results

Expected benefits for children

Patients:

- Data collected →learning →improved care
  - Research
  - Quality control

- Patient and Public Involvement

Swiss-wide:

- Harmonized data for joint research and quality control

- Platforms for more efficient trials

- Support for next generation of researchers

- Enhance data science excellence hospital - ETH domain

- Excellence in rare diseases

- National research network

SwissPedHealth consortium

Expertise in pediatrics, rare diseases and omics, epidemiology, governance, PPI, computer science and engineering to improve children's health care.

Main applicants

- Schlapbach, Luregn
- Vogt, Julia

SPHN co-applicants

- Kuehni, Claudia
- Bielicki, Julia
- Posfay-Barbe, Klara
- Baumgartner, Matthias
- Latzin, Philipp
- Giannoni, Eric

PHRT co-applicants

- Fellay, Jacques
- Borgwardt, Karsten
- Vayena, Effy

Associated applicants

- Ormond, Kelly
- Stocker, Martin
- Lauener Roger
- Schulzke, Sven
- Froese, Sean
- Goetze, Sandra
- Pedrioli, Patrick
- Pachlopnik Schmid, Jana
- Zamboni, Nicola
- Rauch, Anita
- Spycher, Ben
- Forrest, Christopher

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SwissPedHealth consortium (2)

WP1 Governance & Data implementation
Tatjana Welzel
Edén Sorolla
Allesandra Pellitelli
Oliver Brupbacher

WP2 Nested Projects
Fabiën Belle
Anna Hartung
Léa Ho Dac
Lorenz Leuenberger
Manon Jaboyedoff
Varvara Dimopoulou
Xenia Bovermann
Yara Shoman

WP3 Lighthouse Project
David Scherrer
Daphné Chopard
Dylan Lawless
Emanuele Palumbo
Ioannis Xenarios
Johannes Trück
Katrin Männik
Keith Harshman
Mariam Ait Oumelloul
Thomas Sutter
Vito Zanotelli

WP4 PPI & Bioethics
Chloé Caruso
Aurélie Martin Necker
Katrin Hofmann

WP5 Management
Project : Rebeca Mozun
Data: Julia Ruppel
Andrea Agostini

Scientific advisory board
Michael Levin
Marshall Summar
Nelson Sánchez-Pinto