IICU

Personalized, data-driven prediction and assessment of Infection related outcomes in Swiss ICUs

Prof. Catherine Jutzeler (ETHZ, PhD)
Scientific Coordinator PHRT

Prof. Adrian Egli (UZH, MD PhD)
Scientific Coordinator SPHN

NDS Monitoring meeting, 19.09.2023

Agenda

- Our network
- Overview on WPs
- IICU data flow
- IICU ethical study protocols
- IICU contractual architecture
- PPI activity

Governance – IICU Members

Coordinators

- ~~Prof. Karsten Borgwardt (ETH)~~
- Prof. Catherine Jutzeler (ETH)
- Prof. Adrian Egli (UZH)

IICU Data Manager (PHRT)

- Dr. Nora Toussaint (ETH)

IICU Project Manager (SPHN)

- Dr. Magdalena Lukamowicz-Rajska (CTC, USZ) + further people of the CTC

Executive board members

- ~~Prof. Manuel Battegay (USB)~~
  → ~~Dr. Sabine Kuster (USB)~~
  → Prof. Maja Weisser (USB)
- Prof. Thierry Calandra (CHUV)
- Prof. Jean-Daniel Chiche (CHUV)
- ~~Prof. Hansjakob Furrer (Insel)~~
  → Prof. Christine Thurnheer Zürcher (Insel)
- Prof. Gilbert Greub (CHUV)
- Dr. Andre Kahles (ETH)
- Prof. Laurent Kaiser (HUG)
- Dr. Aitana Neves (SIB)
- Prof. Stephen L. Leib (UniBe)
- Dr. Sylvain Meylan (CHUV)
- Prof. Jerome Pugin (HUG)
  → PD Dr. Filippo Boroli
- ~~Prof. Stephan Jakob (Insel)~~
  → Prof. Yok-Ai Que (Insel)
- Prof. Gunnar Rätsch (ETH)
- Prof. Thierry Roger (CHUV)
- Prof. Reto Schüpbach (USZ)
- Prof. Jacques Schrenzel (HUG)
- Prof. Martin Siegemund (USB)
- Prof. Annelies Zinkernagel (USZ)

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Additional people

- Scientific board
  - Technology and clinical experts from different institutions.
- Data integration managers at each University Hospital
  - Clinical data warehouses
- Clinical trial center of the University Hospital Zurich
- Nexus team at ETH Zurich

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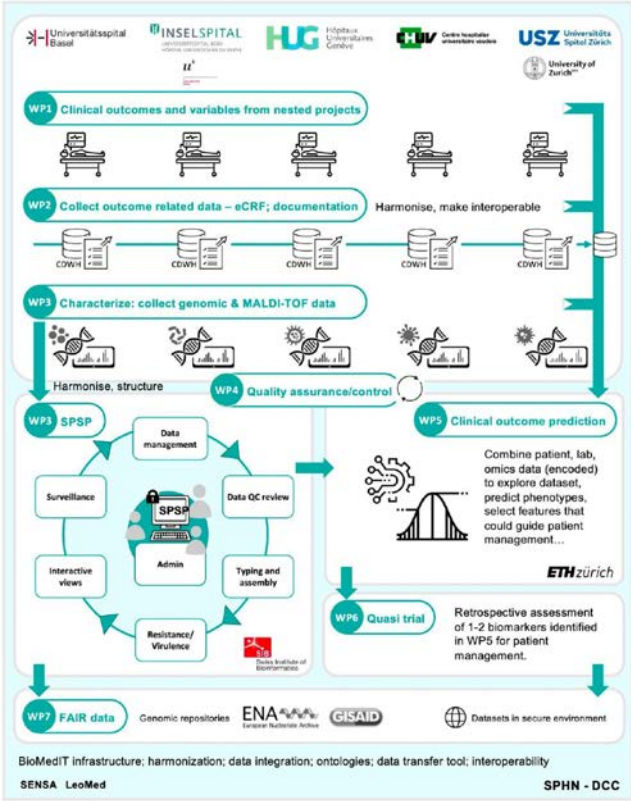
Overview on WPs

- WP1: Clinical outcomes and variables from nested projects
- WP2: Collect outcome related data – eCRF, documentation
- WP3: Characterize: collect genomic & MALDI-TOF data
- WP4: Quality assurance/control
- WP5: Clinical outcome prediction
- WP6: Quasi trial
- WP7: FAIR data



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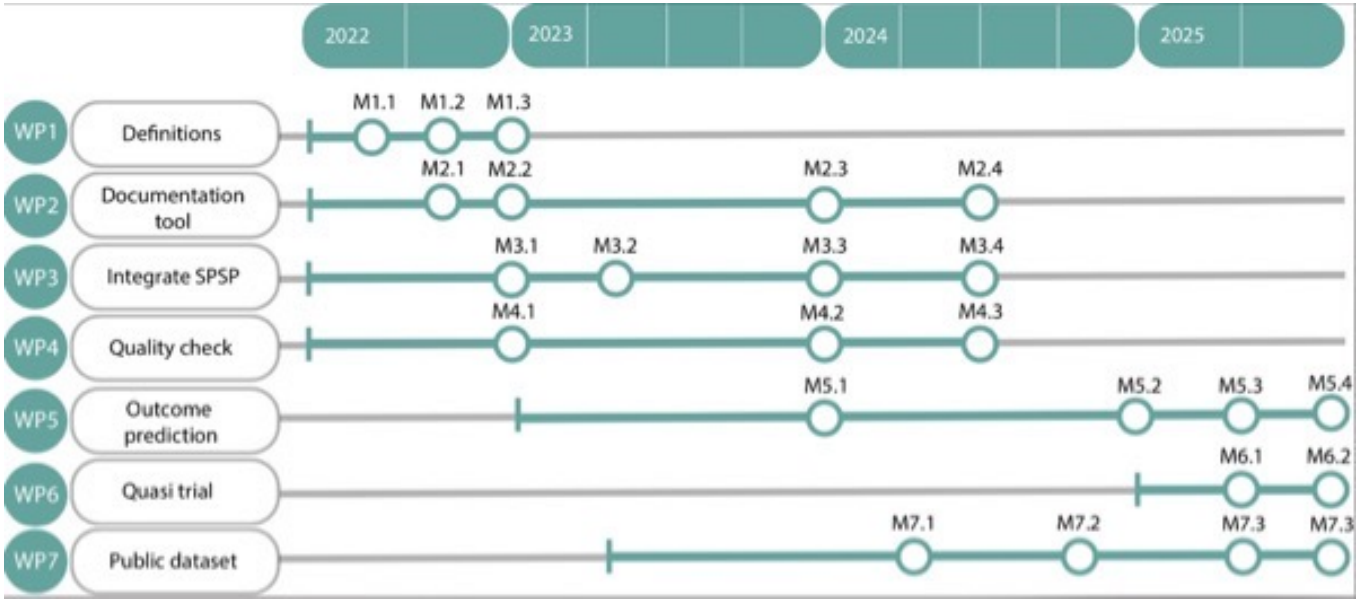
Time plan



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Focus of the NDS IICU

- Maintain the PSSS platform and expand beyond sepsis to other infections, esuring FAIR principles and collaborations.
- Focus on data quality by harmonizing annotation of phenotypes, context, and interpretation with shared standardized definitions and ontologies
- Form a sustainable network between ICUs, infectious diseases, microbiology, and data science. Improving accessibility to data and tools to promote research.
- Develop procedures for rapid and precise assessment of patients exhibiting infection-related phenotypes in-depth and multi-dimensional characterization.
- Generation of a multicentric FAIR public data repository with software packages for phenotype assessment.

→ **All ICU admitted patients** qualify for this study

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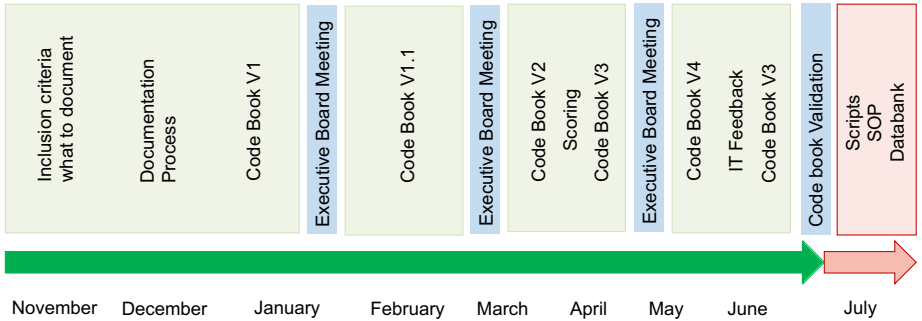
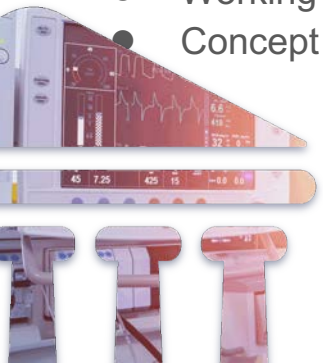
WP1: Clinical outcomes and variables from nested projects



Why?
- The clinical reasoning is not documented in a structured way.
- Detailed documentation of decisions will help later validation of AI algorithms.

- Main goal: Define the data to be collected in a structured way
- Working group established (lead by Prof. Yok-Ai Que, Inselspital)
- Concept of contextual data for an eCRF + Codebook v4.1. (15 page) for harmonized definitions



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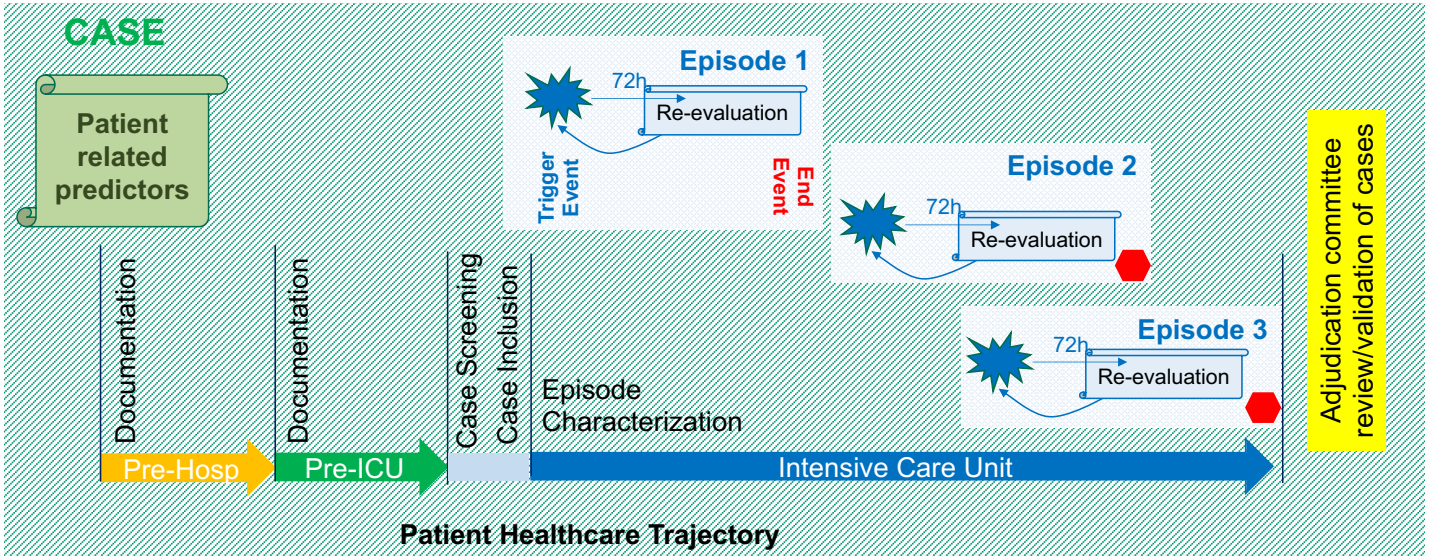
WP1: Clinical outcomes and variables from nested projects



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WP1: Clinical outcomes and variables from nested projects

Inclusion Criteria — **Case Population**

- Any ICU patient with
  - ✓ At least one microbiological diagnostic procedure within the last 48h

AND

  - ✓ At least one anti-infective prescription

Control Population

- Among all included patients
  - ✓ Patients for which the suspected diagnosis of infection was excluded

Exclusion Criteria

- Patients with expected Length of stay presumably < 24h

N.B Patients transferred from other hospitals will be included whenever they meet criteria

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WP1: Clinical outcomes and variables from nested projects

Once per Case

- Patient related predictors
- Pre ICU Information

For each triggered Episode during Case ICU stay

- Working Hypothesis
- Treatment Evaluation
- Re-evaluation 72h after trigger

Validation

- Adjudication Committee

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WP2: Collect outcome related data – eCRF, documentation

- Main goal: generate the tool to collect the clinical reasoning.

- Working group established (lead: Dr. Pedro David Wendel Garcia and Prof. Reto Schüpbach, USZ).
- eCRF prototype is currently developed (with structure from WP1).
- RedCap database across all centers with harmonized vocabulary from prior sites.

- Prototype testing within the next weeks!
- Roll out before the contractual work is finished to not loose more time.

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WP3: Characterize: collect genomic & MALDI-TOF data

- Main goal: Connect the Swiss Pathogen Surveillance Platform (SPSP) into the NDS IICU.

- Working group established (lead: Dr. Aitana Neves, SIB)

- Data flow and data submission.
- Definition of required metadata.
- Unique identifier to match the data.
- Developing and implementing a bioinformatic pipelines (lead by Dr. Tim Roloff for genomics and Yukino Grütlin for MALDI-TOF MS data).

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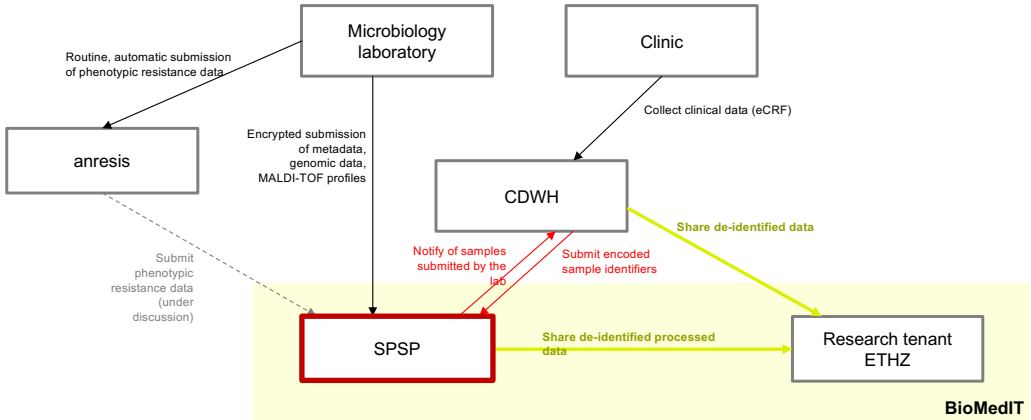
WP3: Characterize: collect genomic & MALDI-TOF data

- Metadata: For resistance data linking with Anresis – is done independent of NDS IICU.
- Open questions: how pseudonymised common identifiers will be shared with SPSP.
- SPSP will use SendCrypt for secure data transfers.



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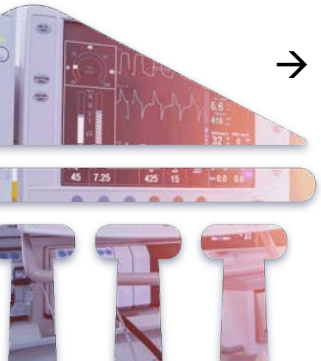
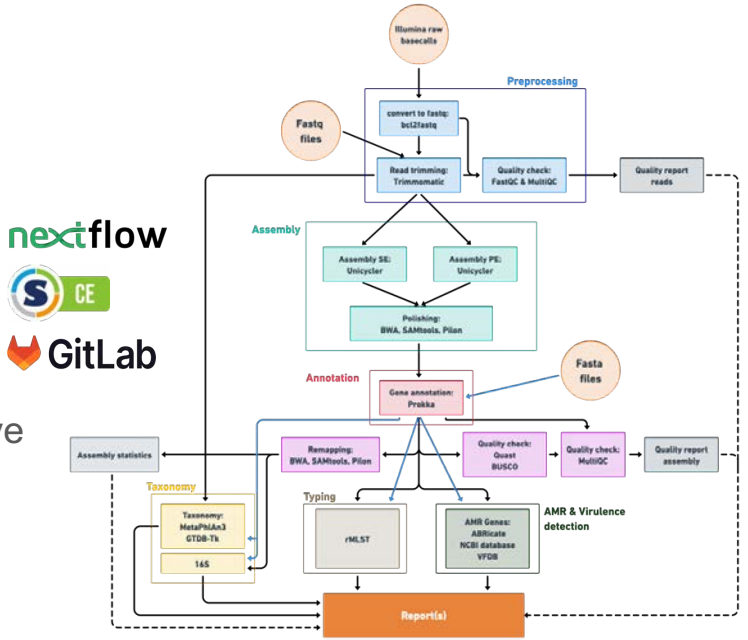
WP3: Bioinformatic pipeline

- Main goal: Standardized analysis
- Clinical bioinformaticians agreed on QC indicators and cutoffs, with pathogen-specific values.
- Code will be available on GitHub sib-swiss for a collaborative effort (UZH currently investigating under which license).

- Flexible input: bcl, fastq, or fasta files
- Nextflow workflow & code available on GitLab
- Build on singularity containers & Modular with thorough QC



→ Sequencing of all positive blood culture from ICU patients



nextflow

CE

GitLab

ridom BIOINFORMATICS

CLC Genomics Workbench

SPSP
Swiss Pathogen Surveillance Platform

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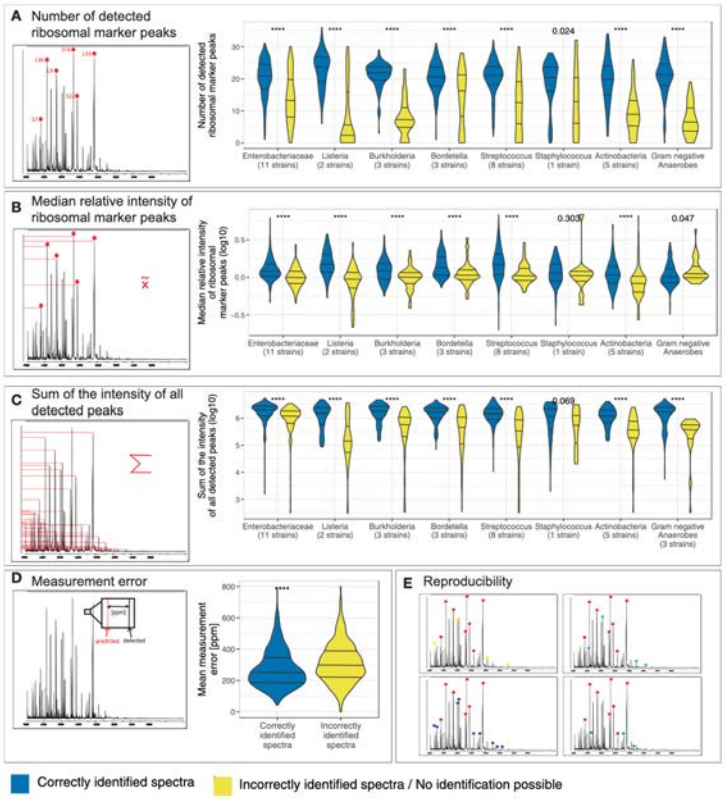
WP3: MALDI-TOF MS

- Main goal: Improve data quality & standardize
- Folder structure, with the .fid file: raw data.
- Sample identifier from the LIS, with the .jason file.
- Identified species, with the .mxml file

- QC for MALDI-TOF MS: number of detected ribosomal marker peaks, median relative intensity of ribosomal marker peaks, sum of the intensity of all detected peaks, measurement error, reproducibility.

→ Includes all spectra from patients (also before and after the ICU)



Cuénod A, et al. Front Cell Infect Micro 2021

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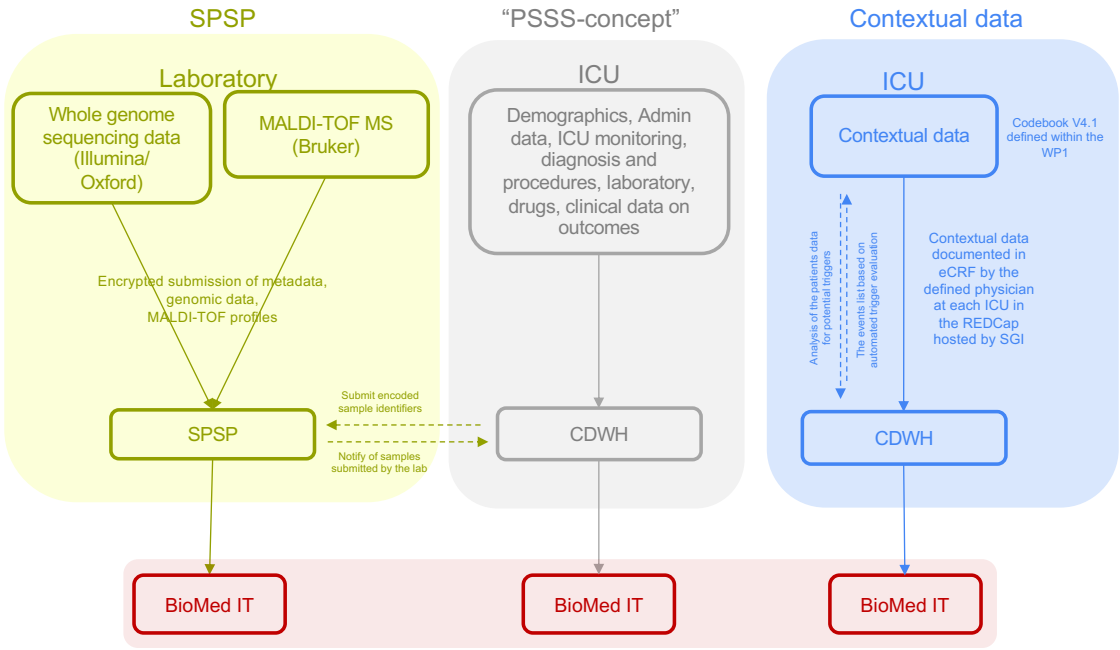
NDS IICU Dataflow

- The data collection, process and delivery to the respective project stakeholders have been define within the IICU “data registry” protocol (submitted to EC for approval on 18.08.2023)
- The data workflow for the IICU project could be divided in three main sections.



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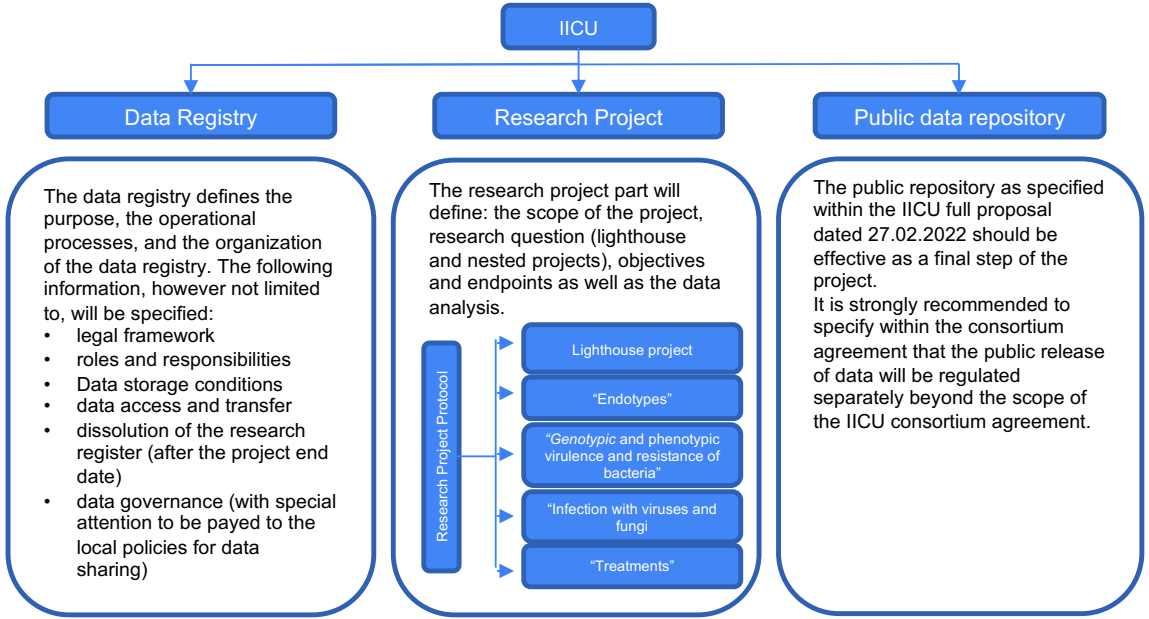
IICU study protocol development

- three main sections: data registry, research project(s) and public data repository.
- Data registry is submitted to ethics and almost 30 days under review.
- Research project with Lighthouse is currently written and will be submitted before the end of the year.



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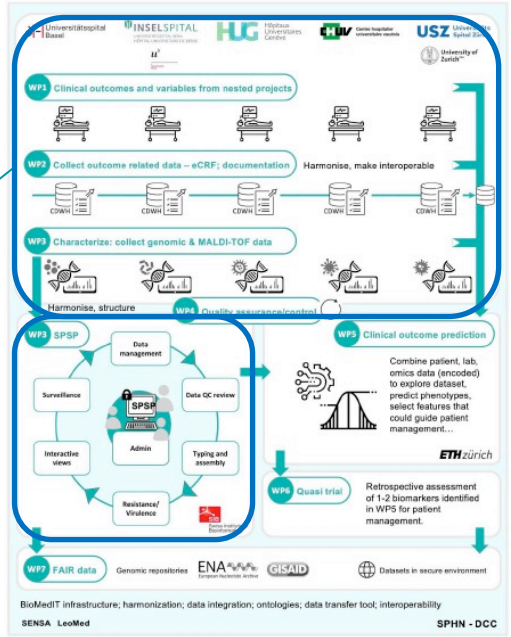
IICU study protocol: data registry

Data Registry

The following information are specified:

- legal framework
- roles and responsibilities
- data storage conditions
- data access and transfer
- dissolution of the research register (after project end date)
- data governance (special attention to local policies for data sharing)

WP1
WP2
WP3
WP4



Protocol V1.0 dated 29.06.2023 shared with the IICU members on 03.08.2023 has been submitted to the lead Zurich Ethics Committee (EC) on 18.03.2023

The submission completeness has been confirmed by the EC on 25.08.2023

Expected EC Feedback on 25.09.2023

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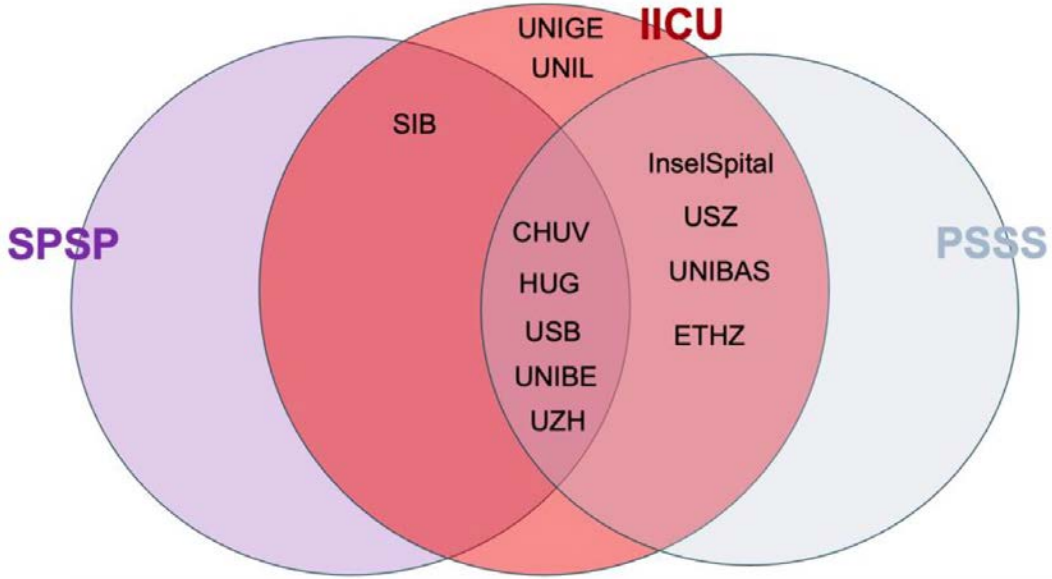
IICU contractual architecture

- Many stakeholders (n = 12 institutions).
- Complex relationsships.

- Some challenge:
  - No clear legal leader.
  - Perception of data has changed since the last driver project.
  - Change of people.



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IICU contractual architecture

- Many meetings with SPHN (Julia Maurer), SIB (Mathilde Heusghem & Frederic Erard), and UZH (Nora Lipp, Magdalena Lukamowicz-Rajska)
- Three contracts where generated based on previously accepted documents:
  - NDS IICU: CONSORTIUM AGREEMENT INCLUDING DATA TRANSFER AND USE AGREEMENT, DATA TRANSFER AND PROCESSING AGREEMENT AND MATERIAL TRANSFER AGREEMENT
  - IICU-PSSS Collaboration Agreement
  - IICU-SPSP Collaboration Agreement

- Shared on the 7th of July 2023 & feedback until 31st of August 2023
- Feedback from all most all legal institutions with 113, 19, and 20 = 152 comments

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IICU PPI activity

- Discussion with Chantal Britt

- Prof. Reto Schüpbach plans a patient day with sepsis survivors and relatives

- Website expansion of www.sepsis-network.ch with “lay communication”: frequently asked question
- Citizen science project on sequencing of bacteria with a school class: Prof. Egli
    - Students will use social media (Instagram, Tiktok, etc) to communicate science.

- Participation on Scientifica 2023 with Prof. Schüpbach and Prof. Egli
    - Two presentation: Antimicrobial resistance and Sepsis
    - Well-attended: around 50 people

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What are our next steps

- Finalize the different legal contracts.
- Submit the remaining ethical protocols.

- WP2: role out the prototype.
- WP3: test pipelines with each center to ensure data exchange.

- PPI: Update on patient day and citizen science project with school class.
- Transfer data to Leonhard Med so WP5 and WP6 can start from ETH colleagues.
- Make a workshop with all stakeholders how and where to share the data (WP7).

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Thank you for your attention!

A special thanks to
- Dr. Nora Toussaint (IICU data managerin)
- Dr. Magdalena Lukamowicz-Rajska (SPHN coordinator)
- all the working group heads and members