European Reference Network
for rare or low prevalence complex diseases

STARTER
STarting an Adult Rare Tumour European Registry

Prospective registries

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

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DECLARATION OF INTERESTS

Annalisa Trama: I have nothing to declare

EURACAN registry

1. Sarcomas
2. Head & neck cancers
3. Rare thoracic cancers

4. Digestive rare cancers
5. Neuroendocrine tumours

6. Endocrine gland tumours
7. Central nervous system tumours
8. Rare female genital cancers
9. Rare urological and male genital tumours
10. Rare skin cancers & non-cutaneous melanoma

EURACAN registry

1. Objectives
2. Data elements
3. Quality assurance
4. Governance

Trama A, et al. The observational clinical registry (cohort design) of the European Reference Network on Rare Adult Solid Cancers: The protocol for the rare head and neck cancers. doi: 10.1371/journal.pone.0283071

ClinicalTrials.gov Identifier: NCT05483374

https://euracan.eu/registries/starter/

Registry objectives

- to help describe the natural history;
- to evaluate factors that influence prognosis (e.g. mortality, survival, progression free survival and treatment response;
- to assess treatments effectiveness (systemic, radiotherapy, surgery, target therapy, immunotherapy and possible combinations);
- to measure indicators of quality of care (diagnostic and staging procedures, treatment strategies, follow-up etc.).

The registry aims to collect information on the storage of biological samples and imaging at the participating centres

Core dataset + ad hoc add on variables study specific

Registry data elements

Common sarcomas

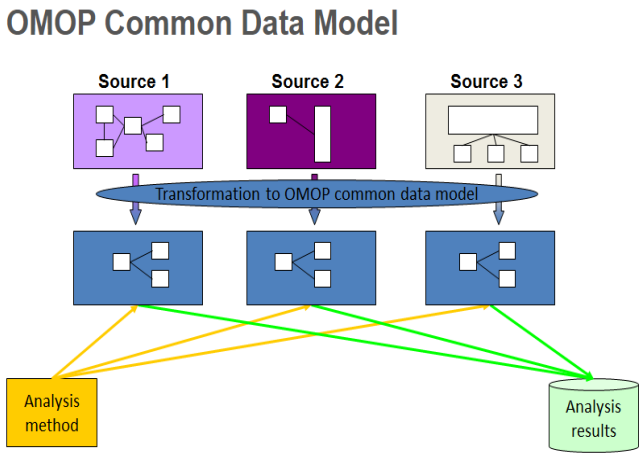
Core data set

International standars

Data dictionaries

Data integration from already available DBs

The Observational Medical Outcomes Partnership (OMOP) Common Data Model



Ultra rare sarcoma (EHE)

Comprehensive data set

International standars

Data dictionaries

An ad hoc e-CRF

REDCap

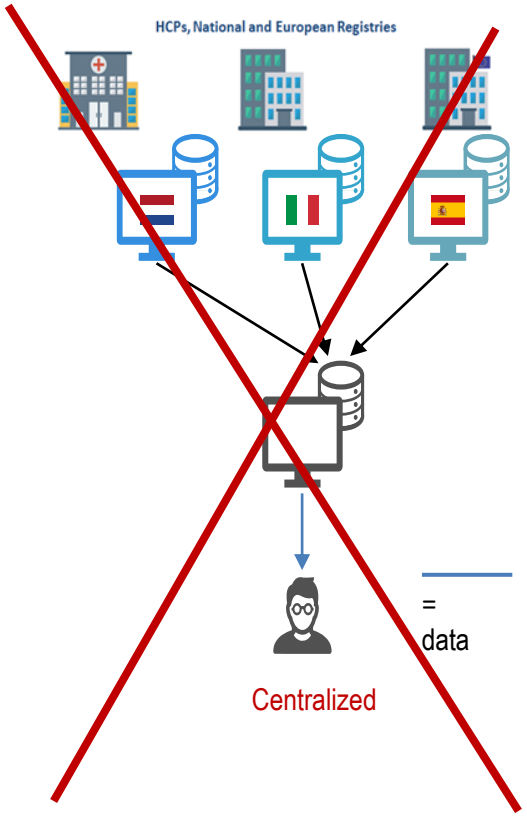
G1 Sarcoma

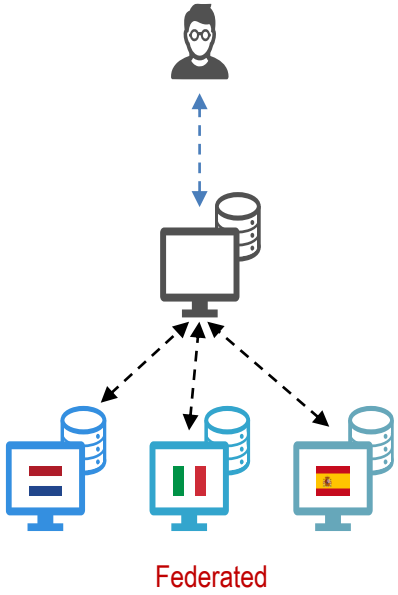
Registry data elements

Registry quality assurance

- Conformance
  - the data should be recorded in agreement with the correct formats (e.g. range of values, date formats);
- Completeness
  - the data should not have missing values or data records;
- Plausibility
  - the data should be believable (e.g. internal consistency; temporal and atemporal comparison);

Registry quality assurance





Registry quality assurance

- Health care provider level
  - Automated data quality checks are in place at data entry
  - Data quality checks can be run by users
  - Training
  - Guidelines

- Central level
  - Centralised data manager monitoring (data quality reports issued, contact with data providers)
  - Routine meetings discussing data quality (including data retrieval and data sources)
  - Bench mark
  - Data checked and accessible for the analyses yearly

Registry Governance

- The governance of the Registry is set in a public document clarifying the rules and procedures to access and manage the Registry

  - Drafted by CLB and INT
  - Reviewed with e-PAGS (4 ad hoc meetings dedicated)
  - Shared with the EURACAN SC and board
  - Shared with participating centres
  - Centrally managed

Data access rules

Data remain the property of the contributing HCPs or registries

Each HCP or national registry is free to access and use its own data for research purposes

Who can use the registry data (upon the presentation of a study protocol)

- each HCP or national registry including data in the EURACAN Registry
- **third parties** (e.g., pharmaceutical companies, patient organisations, competent authorities etc.)
- **commercial companies, depending on the study, may be asked to contribute funding**. **Data do not move from the HCPs or national registries and the commercial companies will not access the EURACAN registry federated database**.

Review of the study protocol

- domain registry working group (RWG), made up of 3 to 5 members including an ePAG, to review the study protocols presented for the domain. Additional expertise may be brought in as required.

HCP/registries agreement

- once a study on a specific domain is approved by the SC, the scientific secretariat will inform the relevant HCP or national registry by email requesting to express its willingness to share its data for the approved study.
- **the PI of the proposed study will be responsible for arranging a preliminary ethical review that will be shared with the participating centres**.

Legal basis: country specific

General Data Protection Regulation

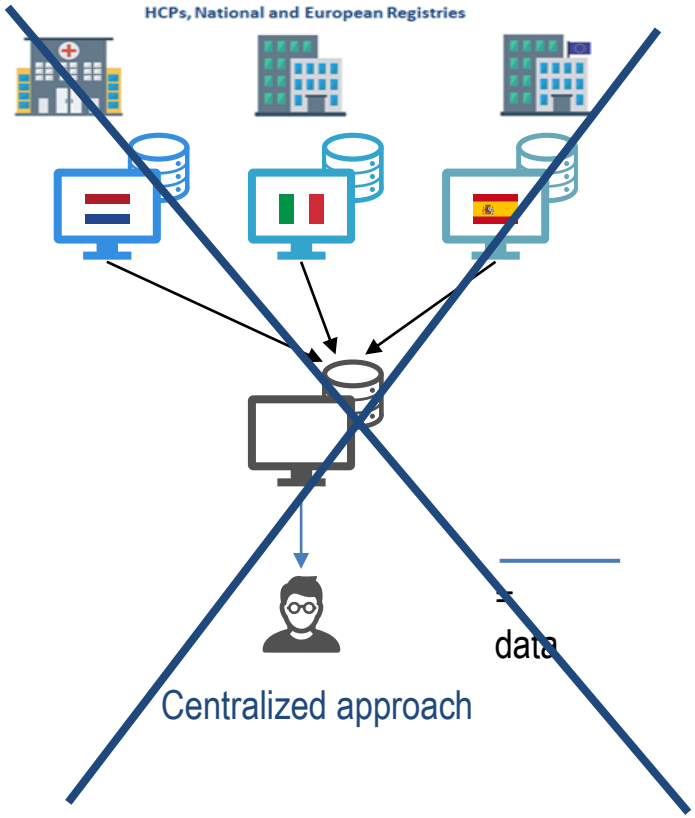
Under Article 9(2) of the GDPR, lawful processing of personal data for scientific research entails:

- the consent of data subjects,
- the pursuing of a substantial public interest,
- the pursuing of a scientific research purpose.

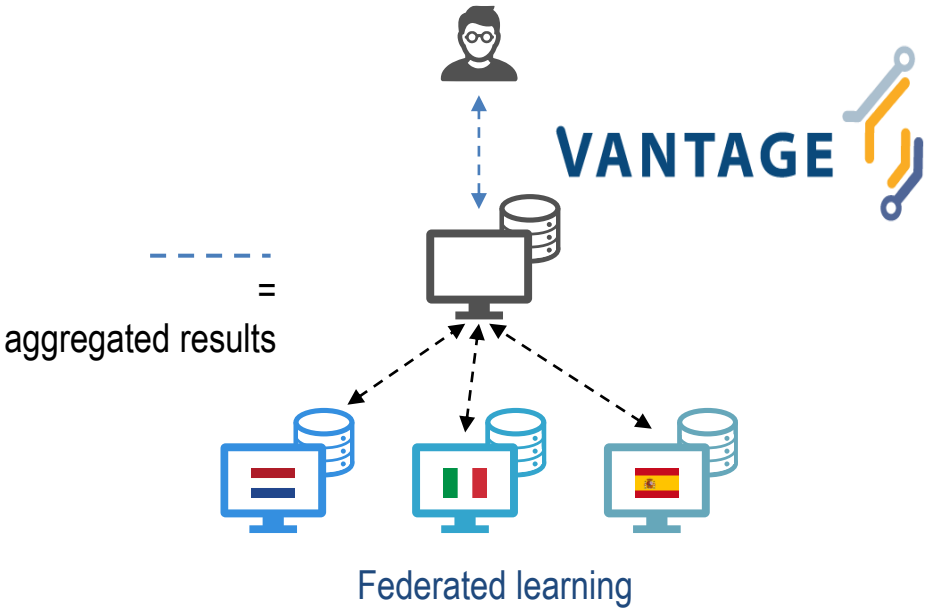
Institutional consent already collecting the consent of the patients for using their data for future research can be used (verify the possibility of sharing data internationally)

Ad hoc registry consent (template available in english)

Privacy preserving solutions



Performing an analysis across multiple decentralized data sources, without exchanging their data.

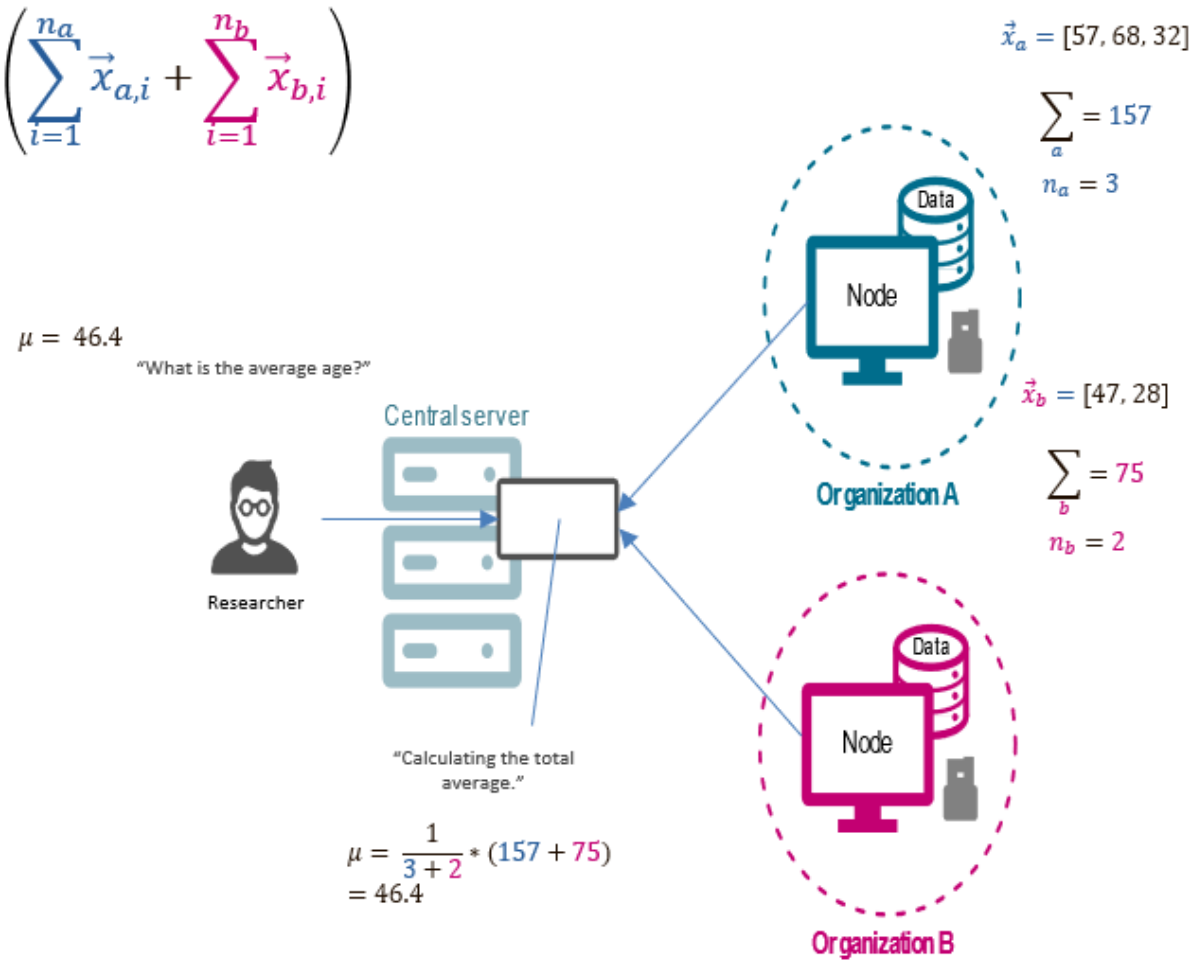


…in words

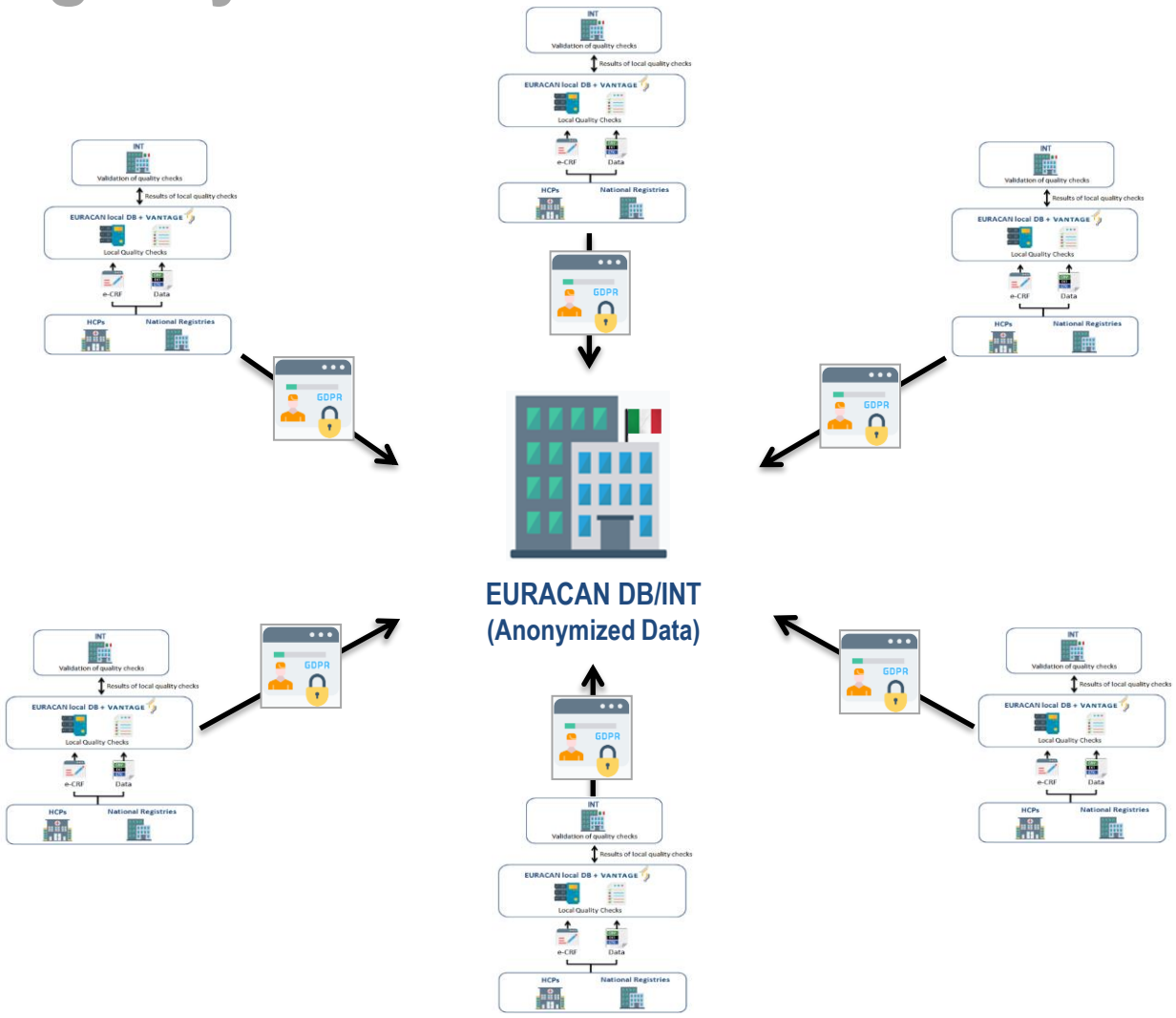
Federated learning is a machine learning technique that trains an algorithm across multiple decentralized devices or servers holding local data samples, without exchanging them

Federated average

$$\mu = \frac{1}{n_a + n_b}\left(\sum_{i=1}^{n_a} \vec{x}_{a,i} + \sum_{i=1}^{n_b} \vec{x}_{b,i}\right)$$



EHE registry



Open-source process

- Join the collaborative
- Propose a study to the open collaborative
- Write protocol
  - http://www.ohdsi.org/web/wiki/doku.php?id=research:studies
- Code it, run it locally, debug it (minimize others' work)
- Publish it: https://github.com/ohdsi
- Each node voluntarily executes on their CDM
- Centrally share results
- Collaboratively explore results and jointly publish findings

Question

How could data from registries complement studies such as those conducted in PUSH-IT and play a role in the regulatory assessment?