The future of data sharing in EU

ENROL Registry and ENROL Module for the collection of annual counts of RHDs patients (Epiblood)

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European Reference Network
Hematological Diseases (ERN EuroBloodNet)
Funded by the European Union

enrol

European Rare Blood
Disorders Platform

ENROL-
The central registry of the European Reference Network on Rare Hematological Diseases (EuroBloodNet)

European Rare Blood Disorders Platform - ENROL

ERN-EuroBloodNet umbrella for both new and already existing registries on rare hematological disorders (RHD)

Aims to avoid fragmentation of data by promoting the standards for patients registries' interoperability in line with the EU-RD-Platform

ENROL's principle is to maximize public benefit from data on RHD with the only restriction needed to guarantee patient rights and confidentiality, in agreement with EU regulations for cross-border sharing of personal data

➡ possibility to share and pool data

➡ reach critical numbers

➡ analyse KPIs, perform clinical trials & research projects

➡ knowledge generation (evidence)

➡ **better healthcare for RHDs patients**

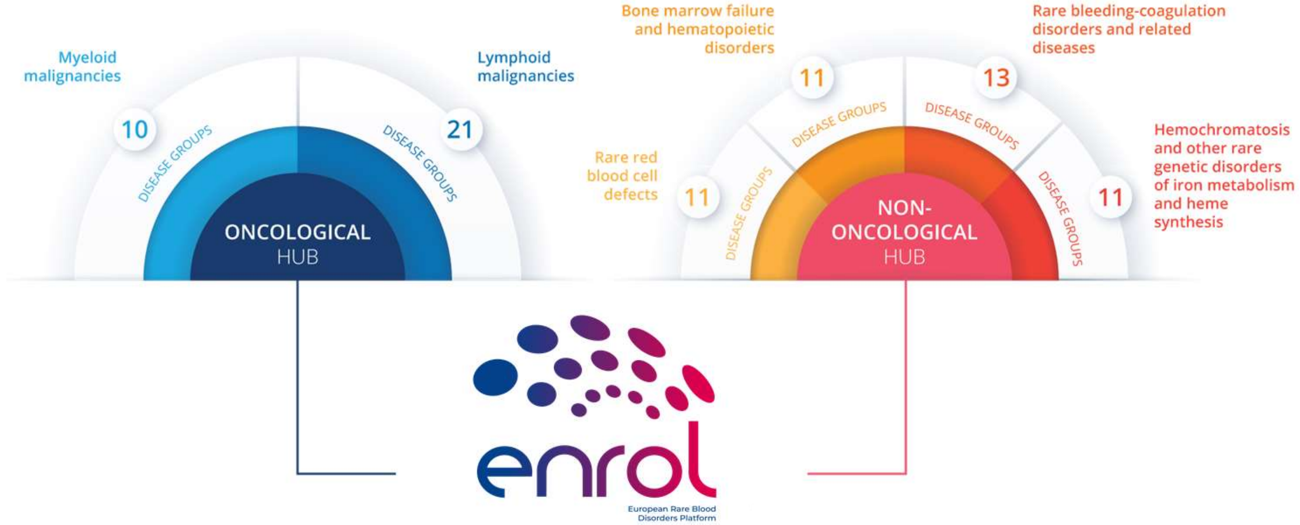
European Rare Blood Disorders Platform - ENROL

Facilitate epidemiological surveillance

Enhance health planning

Enable the identification of patients' cohorts

Promote research & innovative therapies



Myeloid malignancies

10 DISEASE GROUPS

Lymphoid malignancies

21 DISEASE GROUPS

ONCOLOGICAL HUB

Bone marrow failure and hematopoietic disorders

11 DISEASE GROUPS

Rare bleeding-coagulation disorders and related diseases

13 DISEASE GROUPS

Rare red blood cell defects

11 DISEASE GROUPS

Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis

11 DISEASE GROUPS

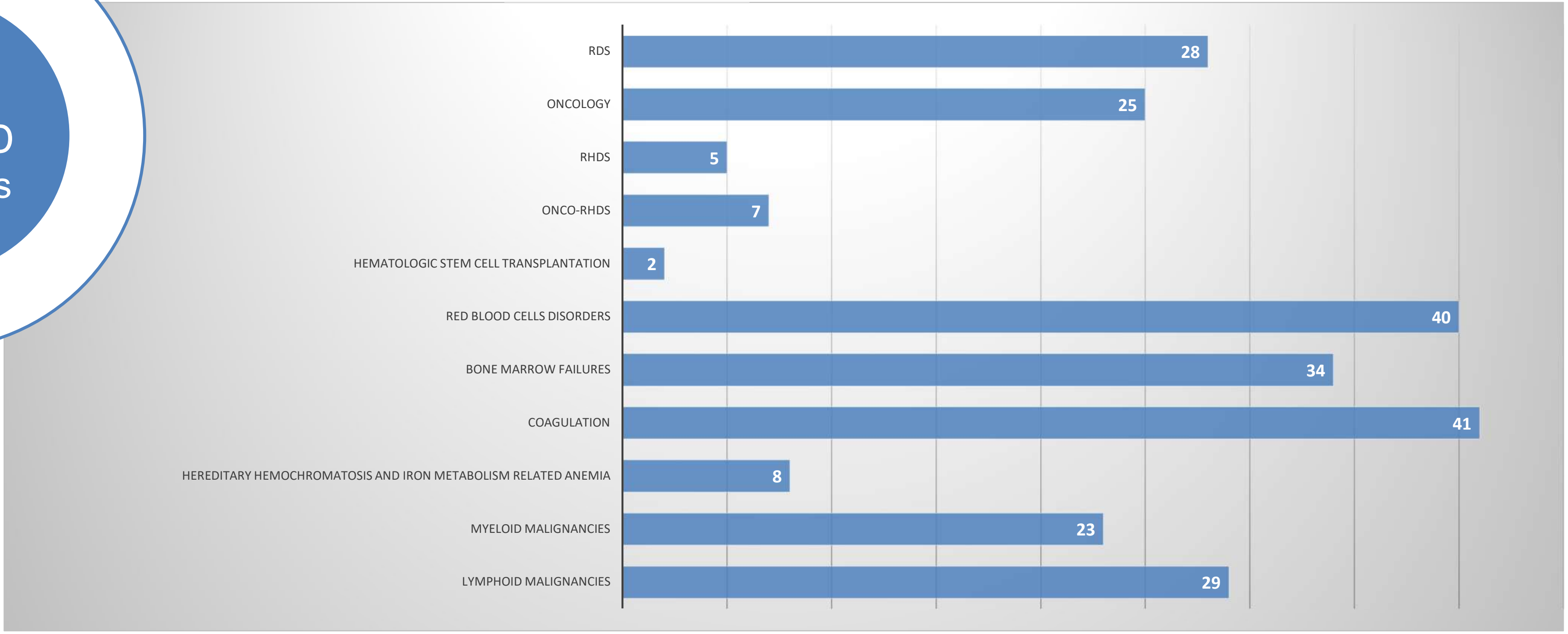
NON-ONCOLOGICAL HUB

enrol

European Rare Blood Disorders Platform

ENROL Directory of Registries in RHD

235
EU RHD
Registries

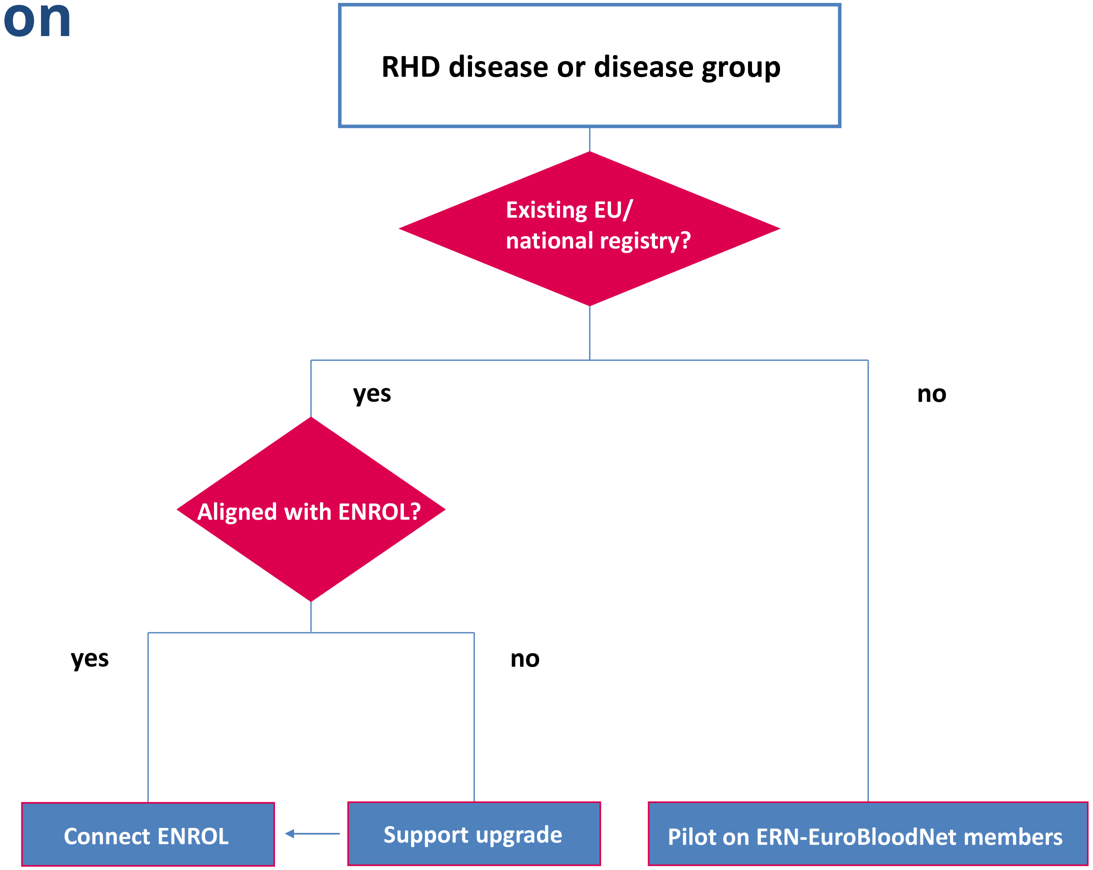


ENROL strategy for data collection

Strategy for data collection includes combination of data sources:

a) Individual sites:
   a) HCPs ERN Members
   b) HCPs non Members

b) Existing/New National/EU registries



RHD disease or disease group

Existing EU/ national registry?

yes

no

Aligned with ENROL?

yes

no

Connect ENROL

Support upgrade

Pilot on ERN-EuroBloodNet members

ENROL Strategy for data collection

European Commission
Joint Research Centre

ERICA
European Rare Disease Research Coordination and Support Action

EU RD PLATFORM

SPIDER

PSEUDONYMISATION TOOL GDPR COMPLIANT

Data providers generate the pseudonym. Keep locally the link between pseudonym and personal data.

F A I R
FINDABLE ACCESSIBLE INTER-OPERABLE REUSABLE

enrol
European Rare Blood Disorders Platform

enrol EpiBlood **Aggregated level data**

Pseudonymised individual patient level data

Data transfer agreement

DATA PROVIDER:

- **Re-use and linkage of clinical data**
- **AI and data driven solutions**

GENOMED4ALL
SYNTHEMA

- **Re-use and linkage of clinical data**
- **Patient Referral system for Clinical trials**

IMPACT-AML
European project on Relapsed/Refractory Acute Myeloid Leukemia

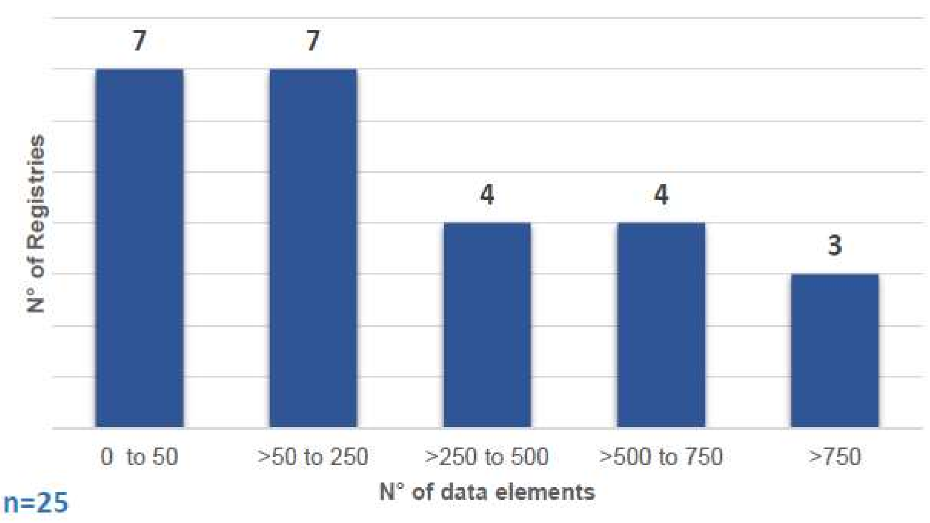
- **Individual sites**
- **Existing/New National/EU registries**

RADeep EUblast **TWIST**

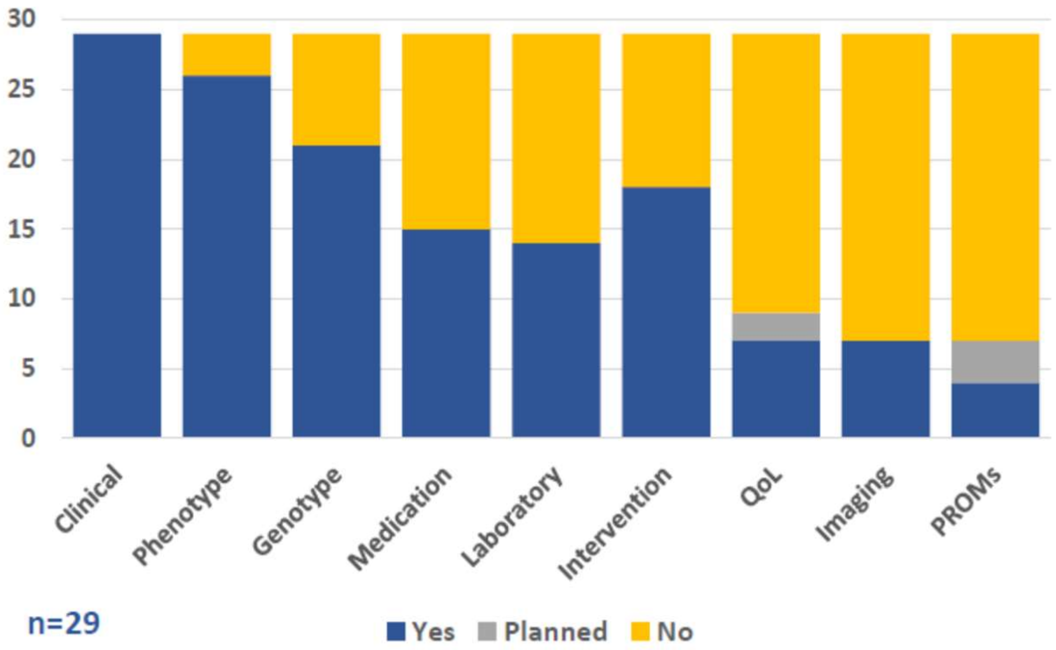
Collection of pseudonymised individual patient-level data

Information Collected by the 29 ERN Registries

Number of Data Elements



Type of Data Elements



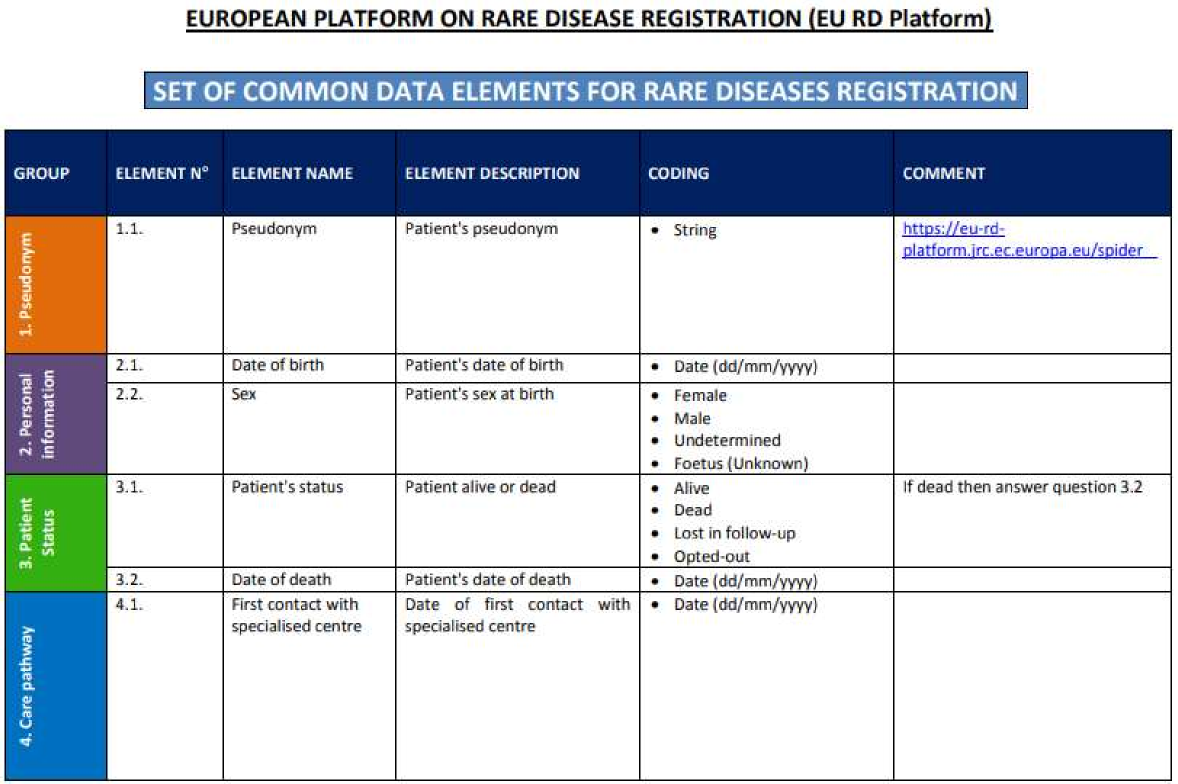
Slide provided by Franz Schaefer (ERNs Coordinators Group)

Collection of pseudonymized individual patient-level data

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE
Directorate F – Health and Food
Unit F.1 – Disease Prevention

EU RD PLATFORM

RD-Common Data Set (RD CDS)



EUROPEAN PLATFORM ON RARE DISEASE REGISTRATION (EU RD Platform)

SET OF COMMON DATA ELEMENTS FOR RARE DISEASES REGISTRATION

GROUP	ELEMENT N°	ELEMENT NAME	ELEMENT DESCRIPTION	CODING	COMMENT
1. Pseudonym	1.1.	Pseudonym	Patient's pseudonym	• String	https://eu-rd-platform.jrc.ec.europa.eu/spider
2. Personal information	2.1.	Date of birth	Patient's date of birth	• Date (dd/mm/yyyy)	
	2.2.	Sex	Patient's sex at birth	• Female • Male • Undetermined • Foetus (Unknown)	
3. Patient Status	3.1.	Patient's status	Patient alive or dead	• Alive • Dead • Lost in follow-up • Opted-out	If dead then answer question 3.2
	3.2.	Date of death	Patient's date of death	• Date (dd/mm/yyyy)	
4. Care pathway	4.1.	First contact with specialised centre	Date of first contact with specialised centre	• Date (dd/mm/yyyy)	

https://eu-rd-platform.jrc.ec.europa.eu/system/files/public/CDS/EU_RD_Platform_CDS_Final.pdf

Collection of pseudonymized individual patient-level data

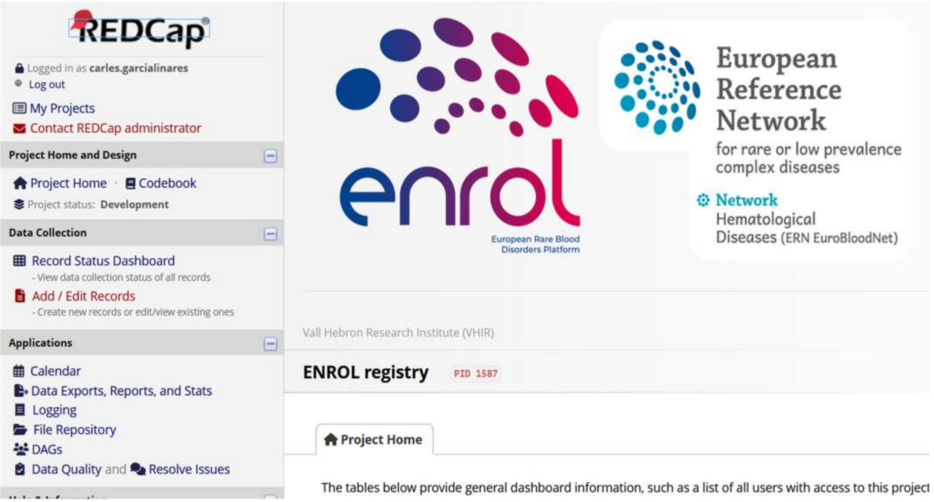
RD-
Common
Data Set
(RD CDS)

5. Disease history	5.1.	Age at onset	Age at which symptoms/signs first appeared	• Antenatal • At birth • Date (dd/mm/yyyy) • Undetermined	
	5.2.	Age at diagnosis	Age at which diagnosis was made	• Antenatal • At birth • Date (dd/mm/yyyy) • Undetermined	
6 Diagnosis	6.1.	Diagnosis of the rare disease	Diagnosis retained by the specialised centre	Orpha code (strongly recommended – see link) / Alpha code/ ICD-9 code/ ICD-9-CM code / ICD-10 code	http://www.orphadata.org/cgi-bin/inc/product1.inc.php
	6.2.	Genetic diagnosis	Genetic diagnosis retained by the specialised centre	International classification of mutations (HGVS) (strongly recommended – see link) / HGNC / OMIM code	http://www.hgvs.org
	6.3	Undiagnosed case	How the undiagnosed case is defined	• Phenotype (HPO) • Genotype (HGVS)	
7. Research	7.1.	Agreement to be contacted for research purposes	Patient's permission exists for being contacted for research purposes	• YES • NO	
	7.2.	Consent to the reuse of data	Patient's consent exists for his/her data to be reused for other research purposes	• YES • NO	
	7.3.	Biological sample	Patient's biological sample available for research	• YES • NO	If YES answer question 7.4
	7.4.	Link to a biobank	Biological sample stored in a biobank	• YES (if appropriate use link) • NO	https://directory.bbmri-eric.eu
8.Disability	8.1.	Classification of functioning/disability	Patient's disability profile according to International Classification of Functioning and Disability (ICF)	• Disability profile / Score	http://www.who.int/classifications/icf/whodasii/en/

https://eu-rd-platform.jrc.ec.europa.eu/system/files/public/CDS/EU_RD_Platform_CDS_Final.pdf

ENROL REDCap

- Secure web application for building and managing databases, supporting regulatory compliance (21 CFR Part 11, FISMA, HIPAA, GDPR).
- It enables rapid development/implementation of changes, with a user-friendly interface for data collection and analysis.
- It ensures data integrity and confidentiality through validation tools and role-based access control.



Logged in as **carles.garcialinares**

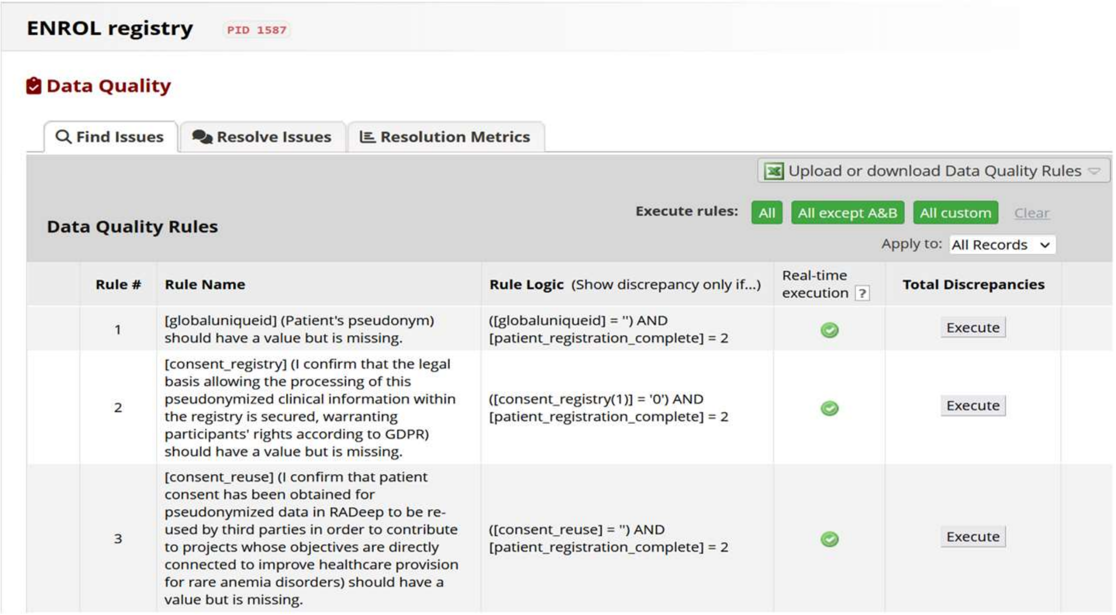
Project status: **Development**

Vall Hebron Research Institute (VHIR)

ENROL registry

The tables below provide general dashboard information, such as a list of all users with access to this project

- Mandatory Common Data Elements



ENROL registry

Data Quality

Data Quality Rules

Rule #	Rule Name	Rule Logic (Show discrepancy only if...)	Real-time execution ?	Total Discrepancies
1	[globaluniqueid] (Patient's pseudonym) should have a value but is missing.	([globaluniqueid] = '') AND [patient_registration_complete] = 2	✓	Execute
2	[consent_registry] (I confirm that the legal basis allowing the processing of this pseudonymized clinical information within the registry is secured, warranting participants' rights according to GDPR) should have a value but is missing.	([consent_registry(1)] = '0') AND [patient_registration_complete] = 2	✓	Execute
3	[consent_reuse] (I confirm that patient consent has been obtained for pseudonymized data in RADeep to be re-used by third parties in order to contribute to projects whose objectives are directly connected to improve healthcare provision for rare anemia disorders) should have a value but is missing.	([consent_reuse] = '') AND [patient_registration_complete] = 2	✓	Execute

EpiData questions

Demographics & Disability

- Global survival
- Total/new number of patients by age/sex/country/genotype
- Number of deaths by age/sex/country/genotype
- Main cause of death by age/sex/genotype
- % Patients presenting disability profile

Diagnosis

- Distribution (number) by method of diagnosis/age at diagnosis/age at onset
- Time taken for diagnosis/genetic diagnosis/from first symptoms to medical diagnosis
- % Patients confirmed by a genetic screening/with certain mutation
- % of undiagnosed patients
- Time from referral to medical diagnosis

European Reference Network
Hematological Diseases (ERN EuroBloodNet)
Funded by the European Union

ERN Members Monitoring Indicators - Registry

Name	Definition & key criteria	Reported by
Number of new patients referred to the Health Care Providers of the ERN, with the diagnosis of a disease or condition that falls within the scope of the ERN	The number of patients attending the ERNs' Health Care Providers for the first time during the reporting period, whose disease or condition falls within the scope of the ERN, whatever their age. Includes visits to outpatient's clinics, hospital discharges and emergencies, coming from national and international referrals.	Members → Without stratification!! EpiBlood → Collect structured EpiData on 72 Disease Groups
Number of new patients uploaded to the ERN registry	The number of new unique patients uploaded to the ERN managed registry or registries. This number must be equal or greater than the number of new patients of the ERN having signed the informed consent agreement. Each new patient entry must contain the minimum dataset.	ENROL/ EpiBlood
Percentage of the total ERN patients that are uploaded to the registry	Percentage of the total ERN patients that are uploaded to the ERN managed registry or registries.	ENROL / EpiBlood
Use of Orphacodes to code/classify patient cases	Acknowledgement that a clinical centre uses orphacodes to code/classify patient cases in case the use of orphacodes is a relevant goal for the ERN.	Members

Registries indicators

Name	Definition & key criteria	Reported by
Mapping of the registries/data sources in all the clinical units constituting each ERN	Mapping of the registries/data sources in all the clinical units constituting each ERN (i.e., provide a list of the existing patient data sources in the clinical units of the ERN that are relevant for the ERN work on registries). By 2024	ENROL
ERDRI .dor and .mdr registration	Metadata of the registries/data sources provided to the Directory of Registries and Central Metadata Repository of the Joint Research Centre. 50% of registries/ data sources constituting the ERN uploaded metadata by 2024; 100% by 2025	ENROL
Practical technical model to connect and make registries interoperable	Design, proposition and implementation of a practical technical model to connect and make registries interoperable (using the European Rare Diseases Registry Infrastructure, tools and services). Respecting European Health Data Space and Joint Research Centre/EU RD Platform guidelines and guidance. By 2026.	ENROL
Implementation of pseudonymization data linkage and data transfer services in line with JRC recommendation (SPIDER)	SPIDER is fully ready to be used, has the data processor record, and does not collect any personal data. ERNs will aim at an ambitious % of registries' data sources using SPIDER by 2026. ERN's central registry by 2026; % of registries' data sources in the clinical units using SPIDER by 2026.	ENROL – Pilot lead by Vall d'Hebron

Interoperability indicators according to 2023 EU4Health Programme | Direct grants to European Reference Networks (ERNs)

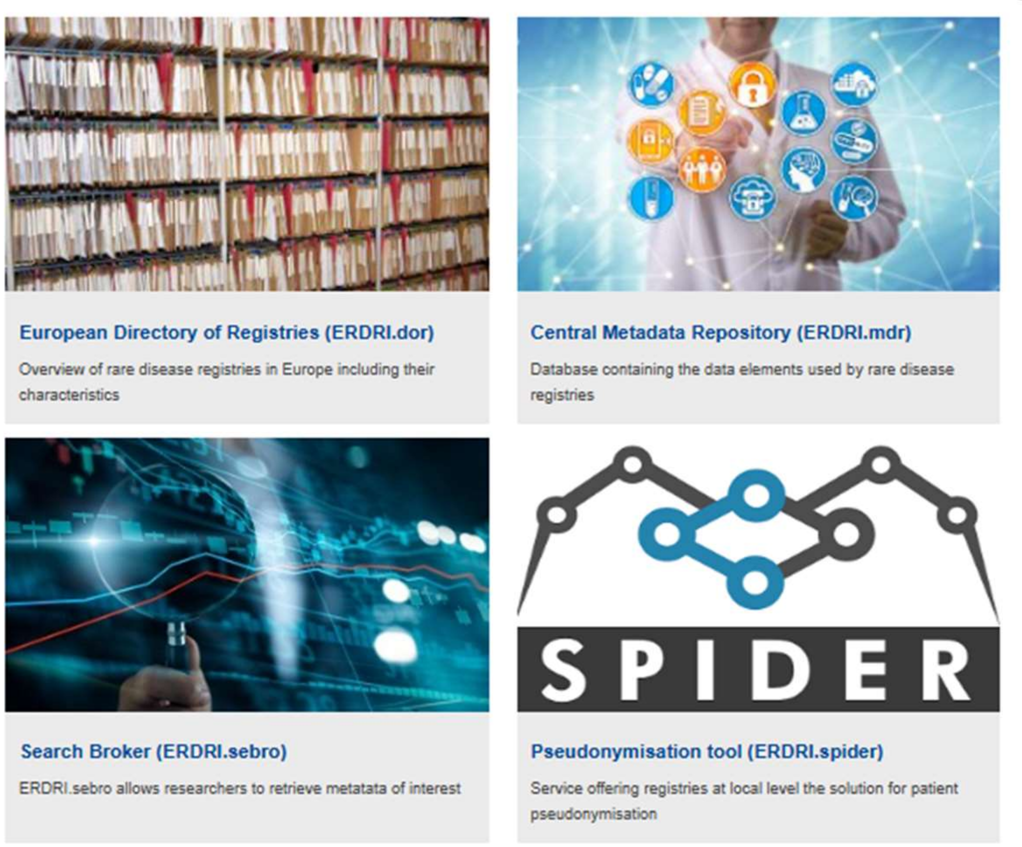
WP5, Registries, data management and analysis | Area : Interoperability

13 Metadata of the registries/data sources provided to the **Directory of Registries – ERDRI.dor** and the **Central Metadata Repository – ERDRI.mdr** of the Joint Research Centre EU RD Platform

14 Design, proposition and implementation of a practical technical model to connect and make registries interoperable (using the European Rare Diseases Registry Infrastructure, tools and services)

15 Implementation of pseudonymisation, data linkage and data transfer services in line with JRC recommendation (**ERDRI. SPIDER**)

EUROPEAN RARE DISEASE REGISTRY INFRASTRUCTURE



European Directory of Registries (ERDRI.dor)

Overview of rare disease registries in Europe including their characteristics

Central Metadata Repository (ERDRI.mdr)

Database containing the data elements used by rare disease registries

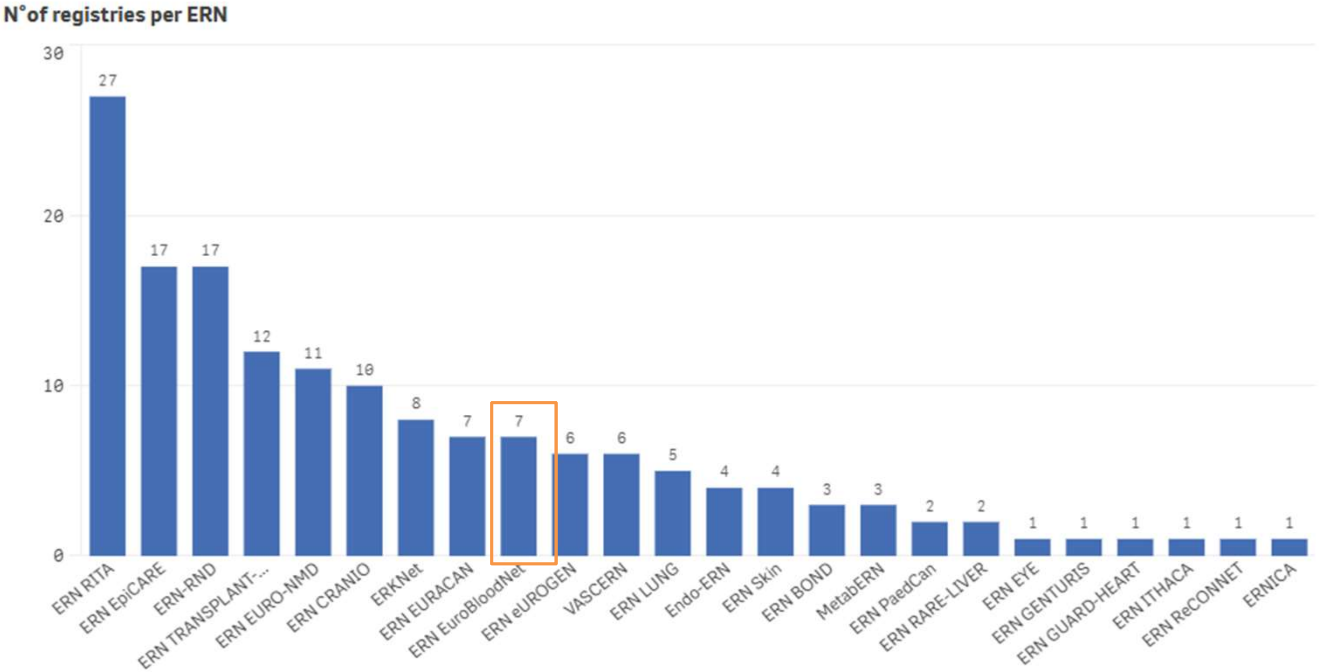
Search Broker (ERDRI.sebro)

ERDRI.sebro allows researchers to retrieve metatata of interest

Pseudonymisation tool (ERDRI.spider)

Service offering registries at local level the solution for patient pseudonymisation

ERN registries/HCPs presence in ERDRI.dor



1. Rare Anaemia Disorders European Epidemiological Platform
2. Utrecht Rhino Registry and Utrecht Rhino Biobank
3. Severe Chronic Neutropenia International Registry
4. Master Framework for R-R AML
5. GPOH/DGHO DBA registry
6. European Rare Blood Disorders Platform
7. Cyprus Haemoglobinopathy Patient Registry

How to enter your Registry in ERDRI.dor?

FIRST, become an ERDRI ‘verified user’ by sending to ERDRI office the Verification Form.

Resources: ERDRI webpage

Manuals and instruction videos

ERDRI User access guide | PDF

ERDRI.dor User documentation | PDF

Specify its association to ERN-EuroBloodNet

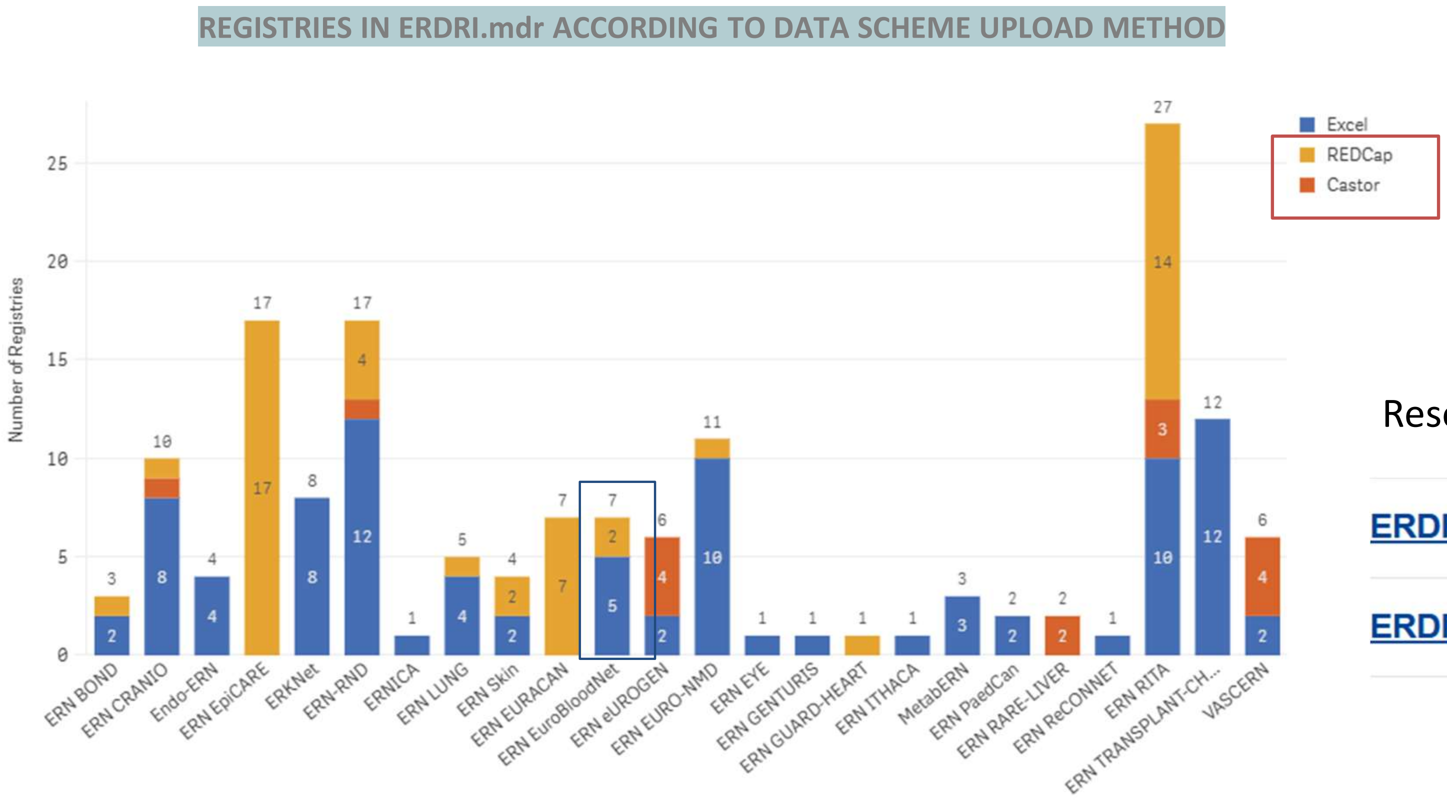
Example: RADeep Registry in ERDRI.dor

Rare Anaemia Disorders European Epidemiological Platform

General information of the registry

Acronym/Short name	RADeep
Medical area	Rare Anaemia Disorders
Type	Epidemiology, Clinical, Basic Research, Patient driven, Healthcare planning
Data provider	University hospital, Non university hospital , Physician, Research Institution
Other	Existing national/regional registries
Description	RADeep is a joint venture conceived in the core of ERN-EuroBloodNet, the European reference network for rare haematological disorders, as an umbrella for both new and already existing European patients' registries in rare anaemias (RAs). RADeep's Principle is to maximize public benefit from data on RAs opened-up through the platform with the only restriction needed to guarantee patient's rights and confidentially in agreement with EU regulations for cross-border sharing of clinical data.
Is member of:	ERN EuroBloodNet
Is member of Eurocat?	No
Website	https://www.radeepnetwork.eu
Sponsors	

ERN registries in ERDRI.mdr


REGISTRIES IN ERDRI.mdr ACCORDING TO DATA SCHEME UPLOAD METHOD

You can use directly REDCap/Castor data dictionary

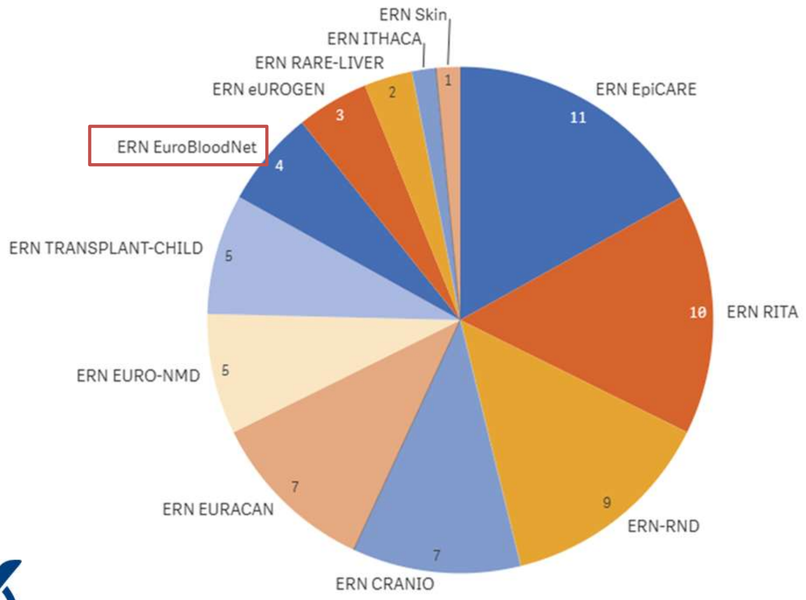
Resources: [ERDRI webpage]()

[ERDRI.mdr User documentation]() | PDF

[ERDRI.mdr Video tutorial]()

R,SI4

SPIDER ready ERN registries/HCPs



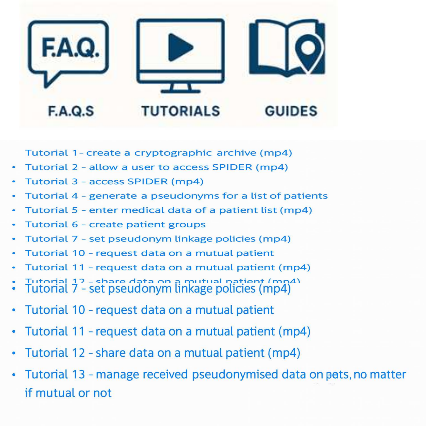
Pseudonym ***GENERATION***

Pseudonym ***LINKAGE***

Encrypted pseudonymised data ***TRANSFER***

SPIDER

Spider Share Network



Tutorial 1 – create a cryptographic archive (mp4)
- Tutorial 2 – allow a user to access SPIDER (mp4)
- Tutorial 3 – access SPIDER (mp4)
- Tutorial 4 – generate a pseudonyms for a list of patients
- Tutorial 5 – enter medical data of a patient list (mp4)
- Tutorial 6 – create patient groups
- Tutorial 7 – set pseudonym linkage policies (mp4)
- Tutorial 10 – request data on a mutual patient
- Tutorial 11 – request data on a mutual patient (mp4)
- Tutorial 12 – share data on a mutual patient (mp4)

- Tutorial 7 – set pseudonym linkage policies (mp4)
- Tutorial 10 – request data on a mutual patient
- Tutorial 11 – request data on a mutual patient (mp4)
- Tutorial 12 – share data on a mutual patient (mp4)
- Tutorial 13 – manage received pseudonymised data on pats, no matter if mutual or not

- Being a verified user in ERDRI
- HCP/ Registry entered in ERDRI.dor
- Metadata in ERDRI.mdr
- Generate a criptographic archived file and a password (only the Registry owner can do it)
- Specify the allowed users in your HCP/ Registry
- These people will be the ones authorized to create SPIDER pseudonyms in your HCP/ Registry

A pilot will be lead by VHIR in 2/3 HCPs in 2026

Slide 19

R,SI4 Confirmar con Nuria
Reidel , Sara Isabel, 02/11/2025

ENROL Data Transfer from RADeep

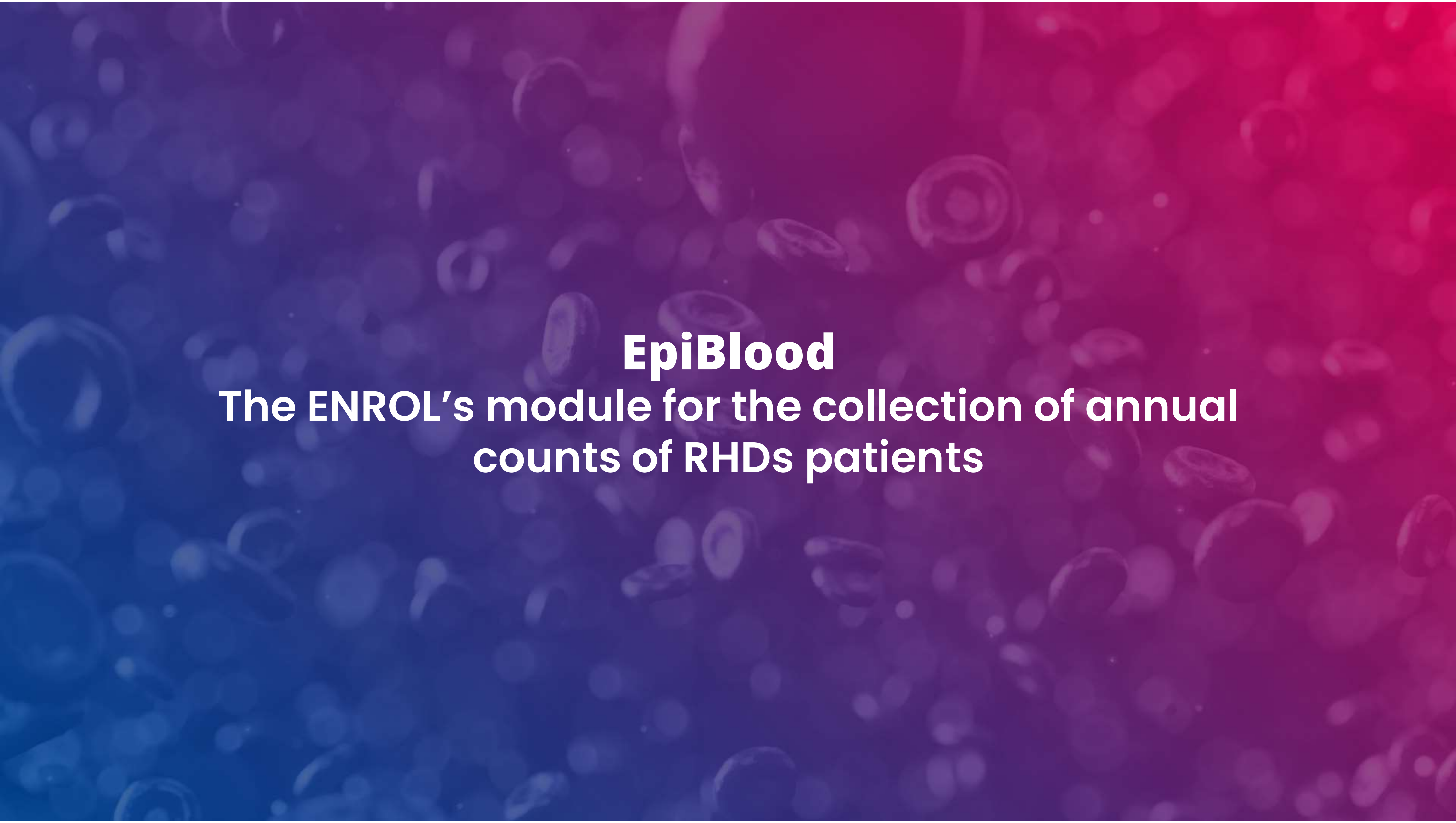
Country	Nº of patients
Belgium	887
Cyprus	166
Denmark	123
France	932
Greece	117
Italy	1100
Spain	987
The Netherlands	373
Total	**4.685**

138 Centres contributing to RADeep
44 ERN Members are already meeting indicator criteria

Objective 5: To reinforce clinical research in the field of rare and complex conditions and diseases by collecting data and carrying out research activities.

Indicator 5.3. Number of new patients uploaded to the ERN registry
Indicator 5.4. Percentage of the total ERN patients that are uploaded to the registry
Indicator 5.5. Use of orphacodes in clinical centres

Funded by the European Union

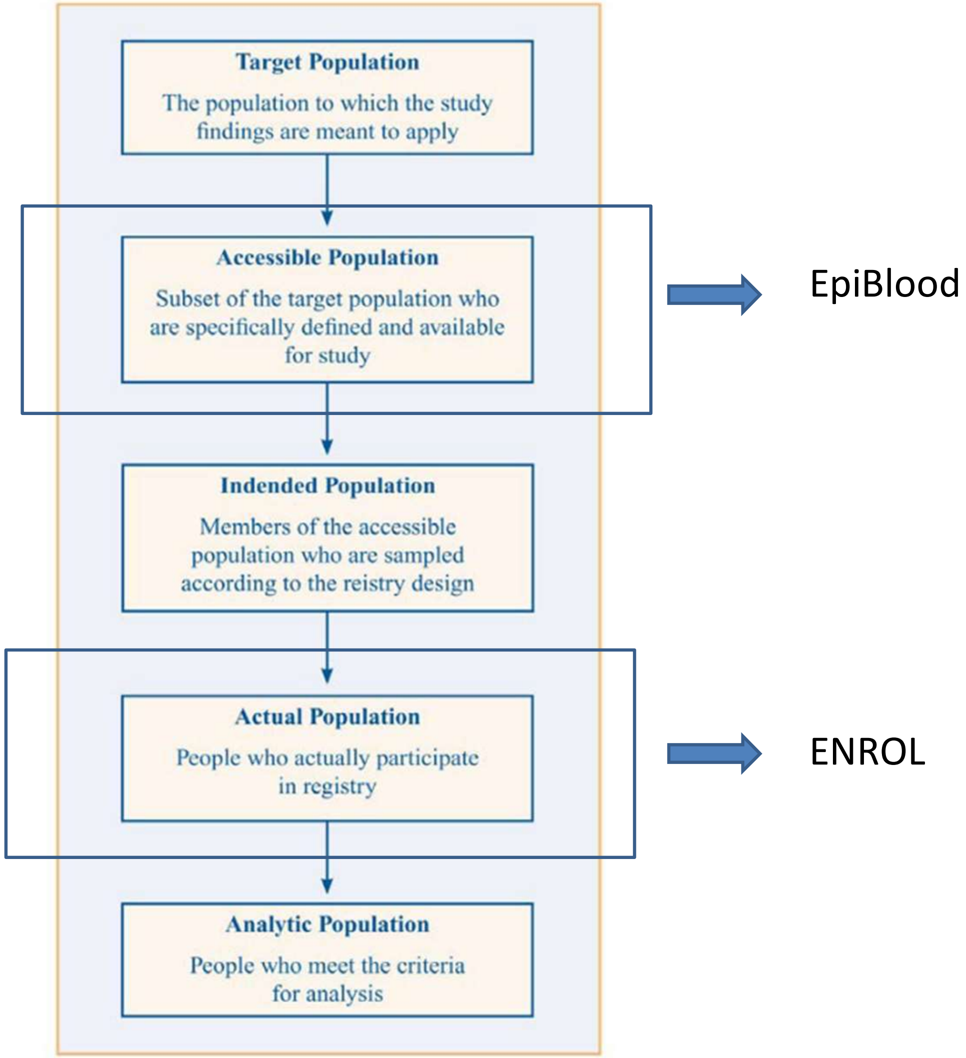


EpiBlood

The ENROL’s module for the collection of annual counts of RHDs patients

Patient population

- The purpose of registry-based research is to provide information about a specific patient population to which all study results are meant to apply.
- To determine how well the study results apply to the target population, five populations, each of which is a subset of the preceding population, need to be considered
- Also how well each population **represents** the preceding population.



Target Population
The population to which the study findings are meant to apply

Accessible Population
Subset of the target population who are specifically defined and available for study

Indended Population
Members of the accessible population who are sampled according to the reistry design

Actual Population
People who actually participate in registry

Analytic Population
People who meet the criteria for analysis

EpiBlood

ENROL

ENROL disease baselines

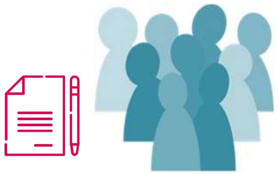
Registry Population

Number of patients enrolled in ENROL

Disease Population

Number of patients in follow-up in the centres that are diagnosed with any rare hematological disease

ENROL disease baselines



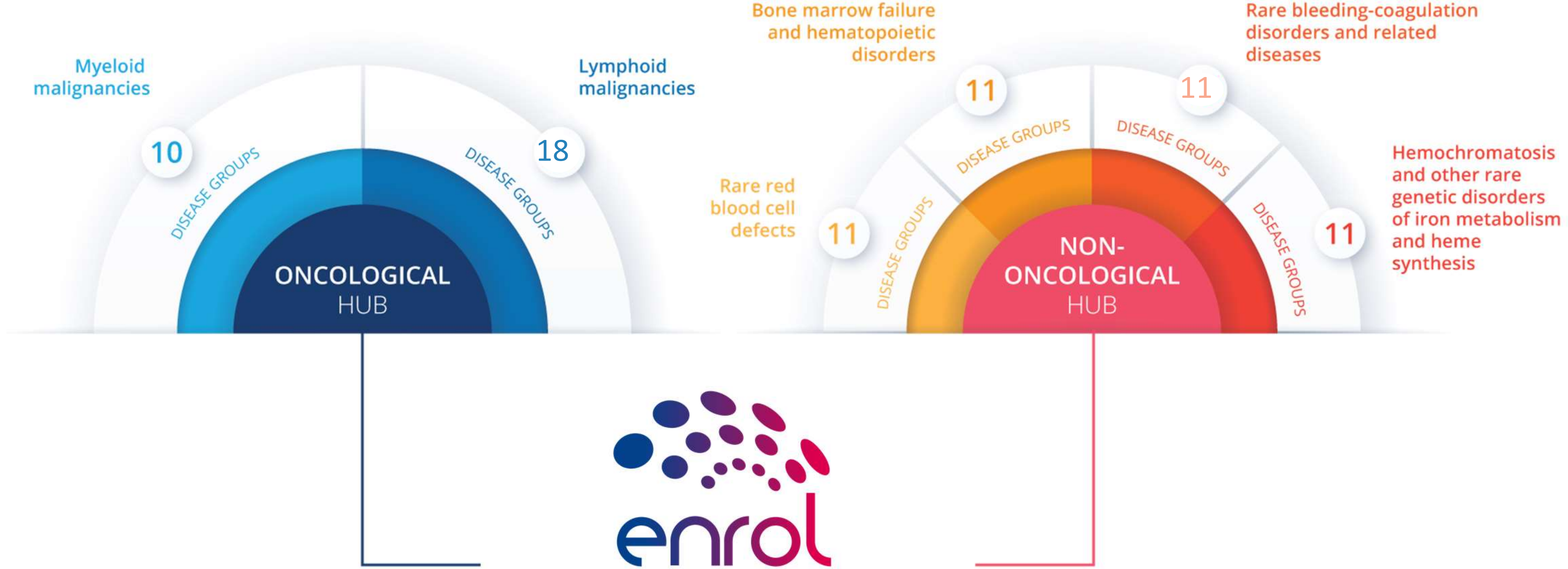
Registry Population

= REPRESENTATIVENESS

Disease Population

- Registry data is representative for epidemiological surveillance
- Identify source of bias
- Registry’s data is reliable

Disese groups for data gathering



Myeloid malignancies

10 DISEASE GROUPS

Lymphoid malignancies

18 DISEASE GROUPS

ONCOLOGICAL HUB

Bone marrow failure and hematopoietic disorders

11 DISEASE GROUPS

Rare bleeding-coagulation disorders and related diseases

11 DISEASE GROUPS

Rare red blood cell defects

11 DISEASE GROUPS

Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis

11 DISEASE GROUPS

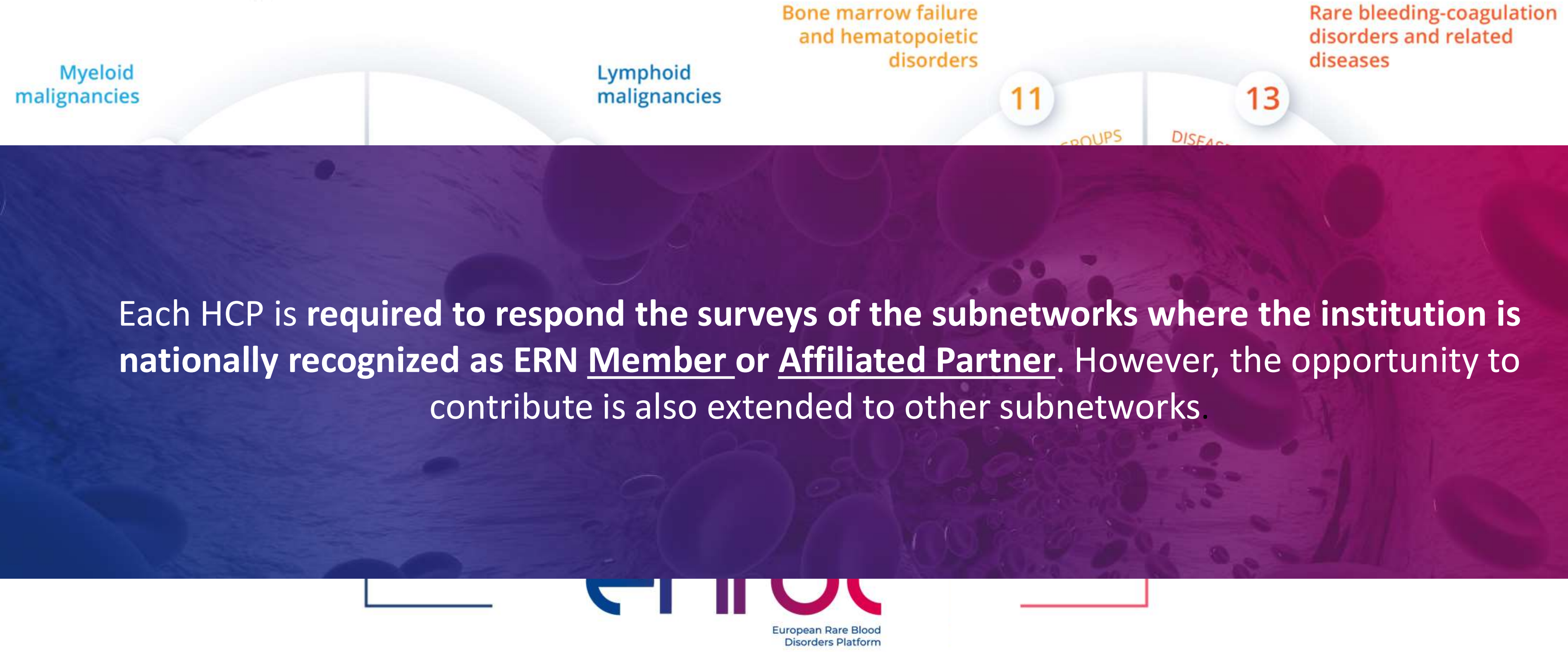
NON-ONCOLOGICAL HUB

enrol

European Rare Blood Disorders Platform

Funded by the European Union

ENROL EpiBlood – Disease Groups



Each HCP is **required to respond the surveys of the subnetworks where the institution is nationally recognized as ERN <u>Member</u> or <u>Affiliated Partner</u>**. However, the opportunity to contribute is also extended to other subnetworks.

ENROL EpiBlood– Agreggated data variables

- The variables to be collected for onco-surveys:

Number of new patients referred to the Health Care Providers participating in the ERN diagnosed with this disease group (≥18 years

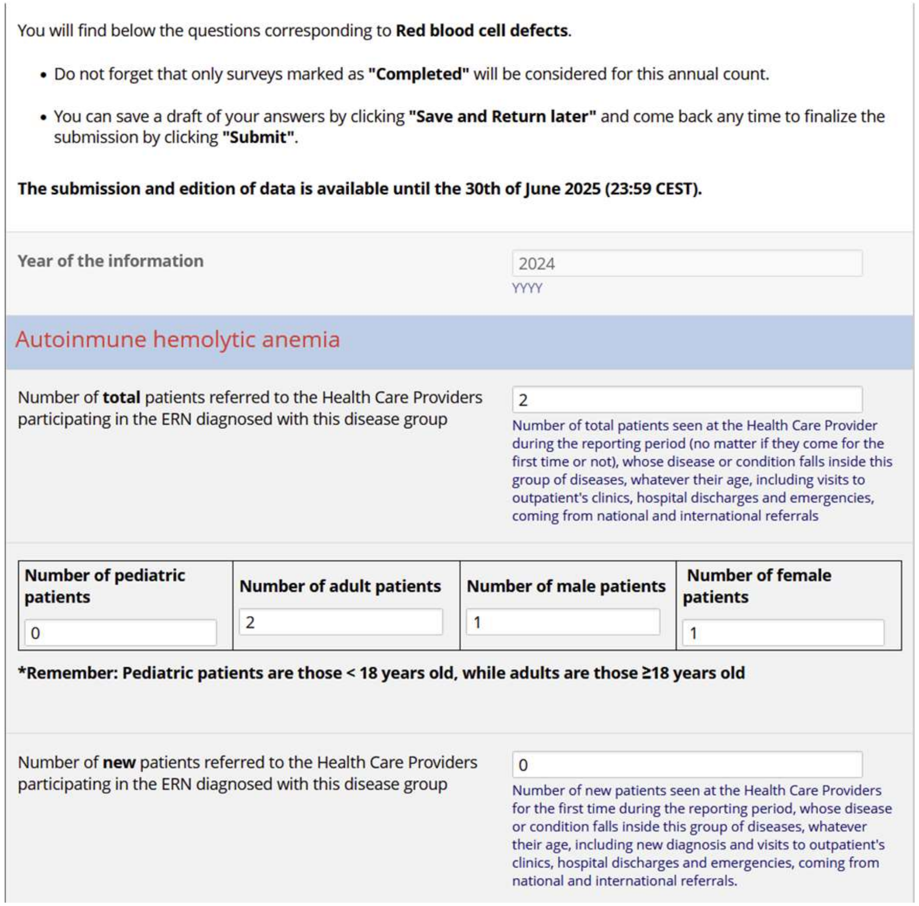
  - Number of new female adult patients (≥18 years)
  - Number of new male adult patients (≥18 years)

- The variables to be collected for non-onco-surveys:

- Number of total patients referred to the Health Care Providers participating in the ERN diagnosed with this disease group
  - Number of total pediatric patients (<18 years)
  - Number of total adult patients (≥18 years)
  - Number of total female patients
  - Number of total male patients

- Number of new patients referred to the Health Care Providers participating in the ERN diagnosed with this disease group
  - Number of new pediatric patients (<18 years)
  - Number of new adult patients (≥18 years)
  - Number of new female patients
  - Number of new male patients

EpiBlood- REDCap survey



You will find below the questions corresponding to **Red blood cell defects**.

- Do not forget that only surveys marked as **"Completed"** will be considered for this annual count.
- You can save a draft of your answers by clicking **"Save and Return later"** and come back any time to finalize the submission by clicking **"Submit"**.

The submission and edition of data is available until the 30th of June 2025 (23:59 CEST).

Year of the information: 2024 (YYYY)

Autoinmune hemolytic anemia

Number of **total** patients referred to the Health Care Providers participating in the ERN diagnosed with this disease group: 2

Number of total patients seen at the Health Care Provider during the reporting period (no matter if they come for the first time or not), whose disease or condition falls inside this group of diseases, whatever their age, including visits to outpatient's clinics, hospital discharges and emergencies, coming from national and international referrals

Number of pediatric patients	Number of adult patients	Number of male patients	Number of female patients
0	2	1	1

***Remember: Pediatric patients are those < 18 years old, while adults are those ≥18 years old**

Number of **new** patients referred to the Health Care Providers participating in the ERN diagnosed with this disease group: 0

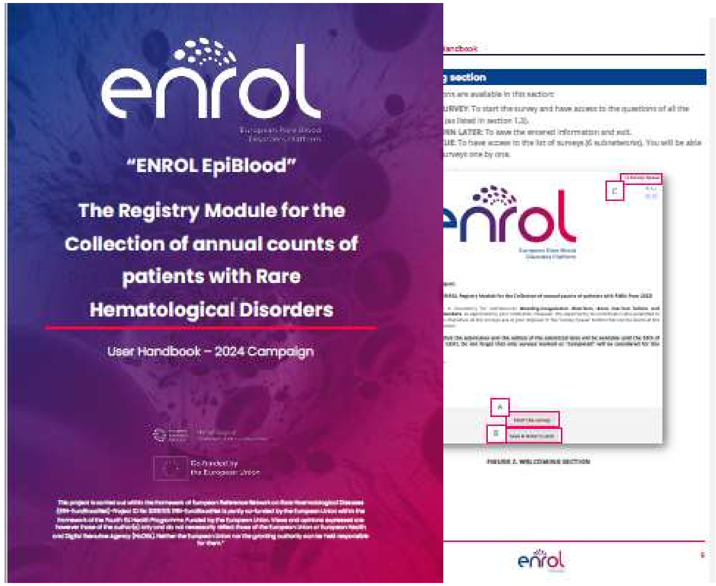
Number of new patients seen at the Health Care Providers for the first time during the reporting period, whose disease or condition falls inside this group of diseases, whatever their age, including new diagnosis and visits to outpatient's clinics, hospital discharges and emergencies, coming from national and international referrals.

Data monitoring:

- Syncrhronic alerts and warnings
- Asyncrhonic emails from ENROL data monitor

ENROL EpiBlood– Support material

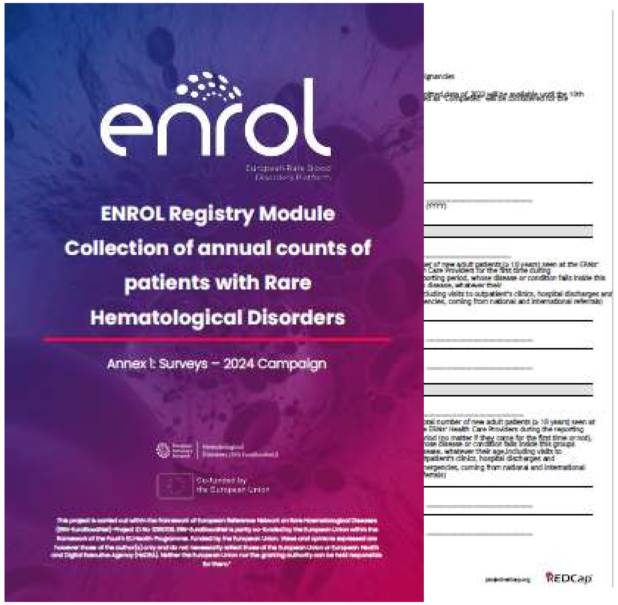
- Handbook & PDF template



“ENROL EpiBlood”

The Registry Module for the Collection of annual counts of patients with Rare Hematological Disorders

User Handbook – 2024 Campaign



ENROL Registry Module Collection of annual counts of patients with Rare Hematological Disorders

Annex I: Surveys – 2024 Campaign

https://eurobloodnet.eu/enrol/enrol-epiblood/documents/

Outcomes: Occurrence & Concentration of patients

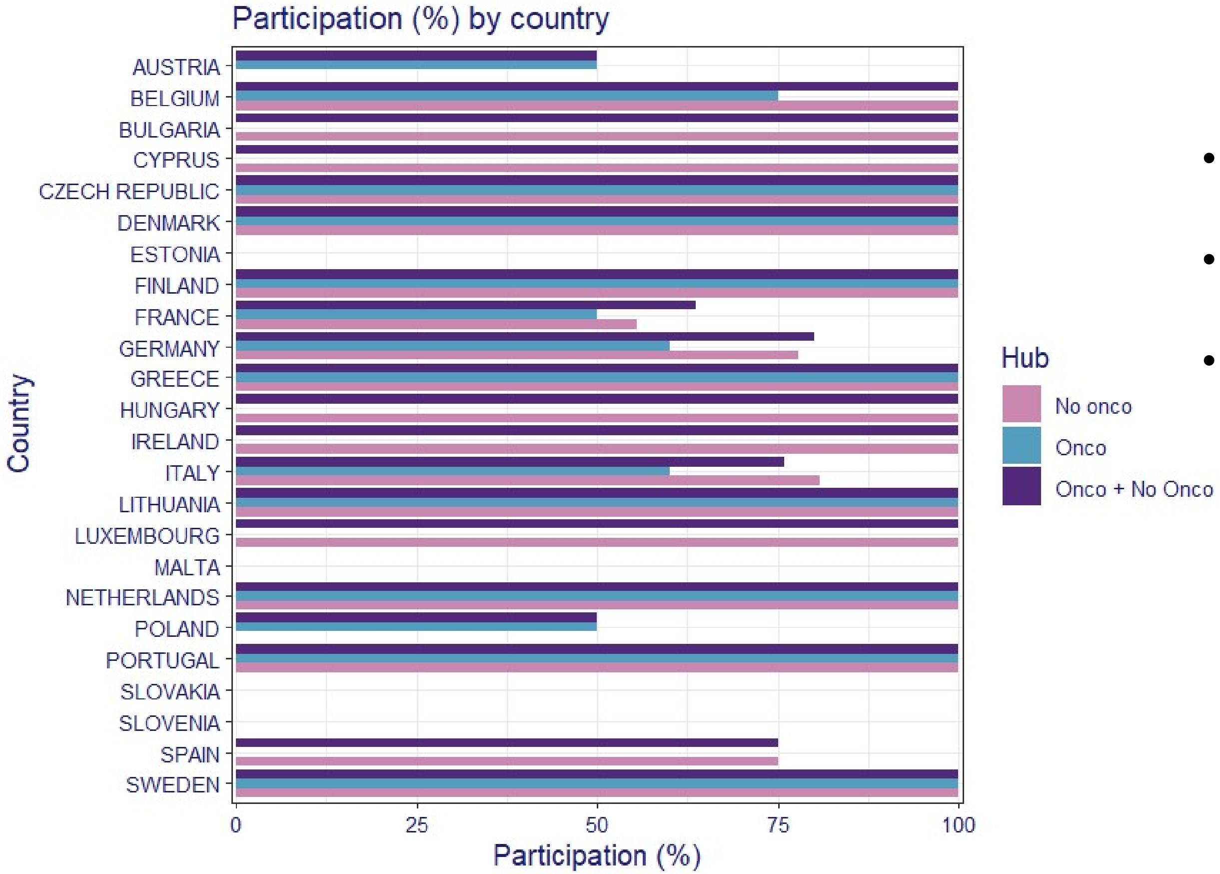
- **RHDs occurrence was evaluated through the estimation of prevalence and cumulative incidence:**
  - Prevalence (Patients/Inhabitants) was estimated as total number of patients diagnosed with a RHDs in 2022 divided by the number of residents in EU in the same year
  - Annual cumulative incidence per 100,000 inhabitants (New patients/Inhabitants) was calculated as the total number of newly diagnosed patients with a RHDs during a calendar year since 2013 to 2022 divided by the number of residents in EU at the same years. Average annual cumulative incidence was then estimated.

- **RHDs patients' coverage at the national level and concentration per HCP** was evaluated through:
  - Ratio HCP/inhabitants: The number of HCP sharing information on number of total RHDs patients, RHDs new patients or both, in some year over 100,000 inhabitants.
  - Ratio Patients/HCP: Expressed as the mean of RHDs patients per 100,000 inhabitants by HCP

Occurrence & Concentration of patients

↑ N Patients	Efficient system for patients concentration
↓ HCP/Inhabitants	An optimum strategy for RD management would concentrate high number of patients in a few HCP acting as reference center at the national level.
↑ Patients/HCP	We would expect for this to be the case in countries with fewer member HCP, which would have a low member-to-population ratio and higher patient-to-member ratios.
↑ N Patients	Coverage of patients is good, but efficiency of the health system in terms of concentration in reference centers is low
↑ HCP/Inhabitants	
↓ Patients/HCP	This low efficiency could be derived from a low reporting, or from a gap in the diagnostic procedures for such diseases.
↓ N Patients	Dispersion of patients across the EU MS
↓ HCP/Inhabitants	
↓ Patients/HCP	Need to increase the recognition of Members for the subnetwork to improve patients coverage.

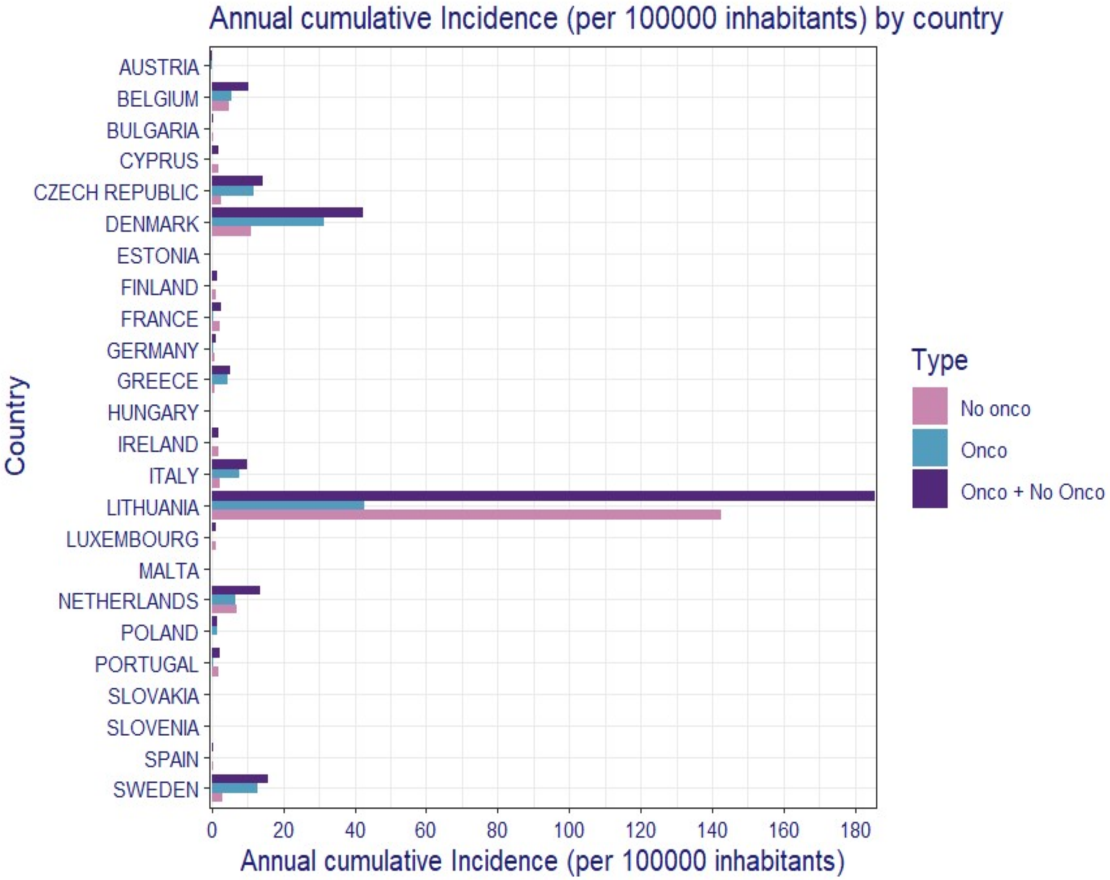
First results- participation by country

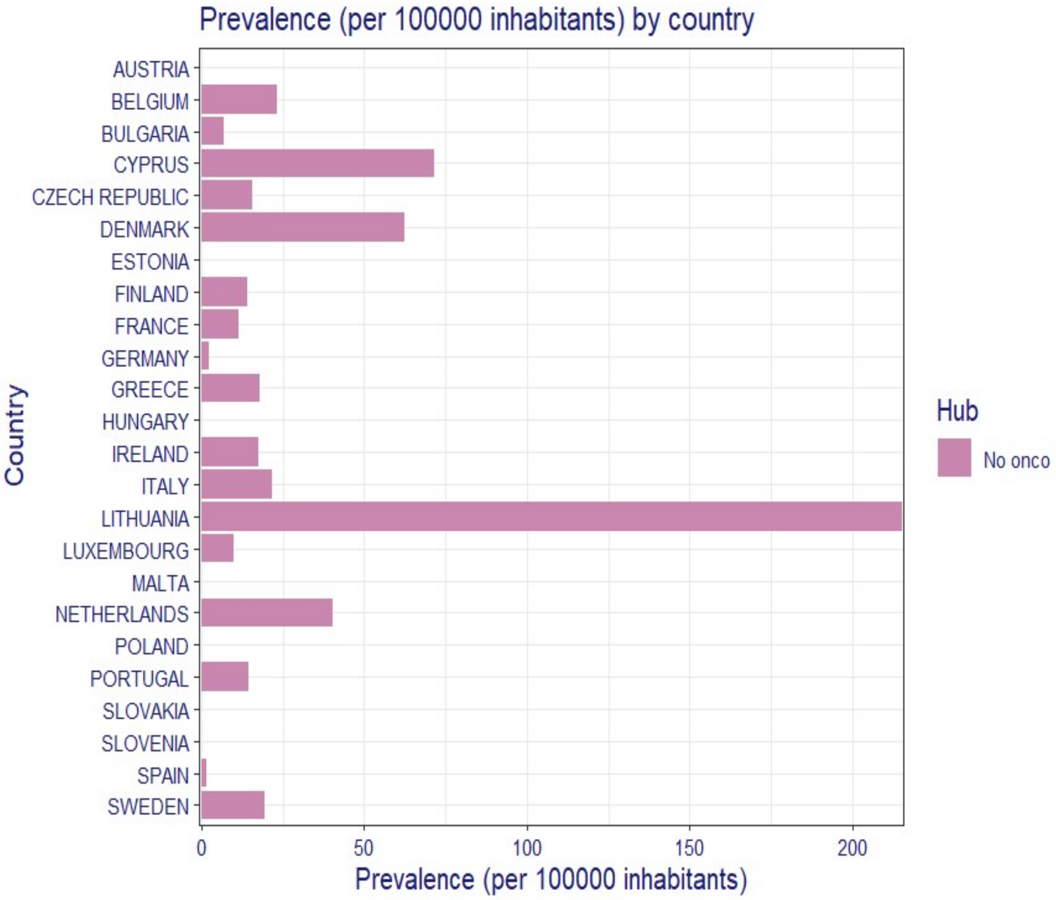


- Mean total participation: 78,4%
- Mean Onco participation: 63,8%
- Mean No-onco participation: 80,0%

Preliminary results- confidence intervals not yet estimated

First results- participation by country





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Next steps: key dates

- **11-12/2025**: Compilation of lessons learned from 2024 edition→ **survey improvements**
- **12/2025:** You will receive the contact list **to confirm who will be the person entering the numbers in the survey. (!) <u>One link per representative</u>**
- **12/2025**: You will receive a PDF showing the questions and the user manual for the survey → **! start preparing 2025 numbers**
- **03/2026: EpiBlood 2025 edition launch**
- **05/2026: EpiBlood 2025 edition closure**

Thank you!

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