CONFERENCE

Rare Diseases in the EU: Joint Action shaping the future of ERNs - JARDIN kick-off meeting

8 MARCH 2024

BRUSSELS, EESC, RUE BELLIARD 99, ROOM JDE62

European Commission

European Economic and Social Committee

European Reference Networks

THE ROLE OF PATIENTS' REGISTRIES

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DECLARATION OF CONFLUENT INTERESTS

- I have received unconditional grants and travel honoraria from Actelion, Alexion, Azafaros, BioMarin, Chiesi, DENALI, Sanofi Genzyme, Takeda, Ultragenyx, Paradigm, Orchard, PTC Therapeutics .
- I have no financial or stock market interest in any rare disease product.
- This presentation reflects the presenter's clinical experiences and opinions.

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What is a registry

- A rare disease registry is a systematic and organized database that collects detailed information on individuals affected by a specific rare disease or group of rare diseases. These registries are designed to collect clinical, genetic, epidemiological, and other related data for the purposes of research, clinical management, and decision support.

•Data collection

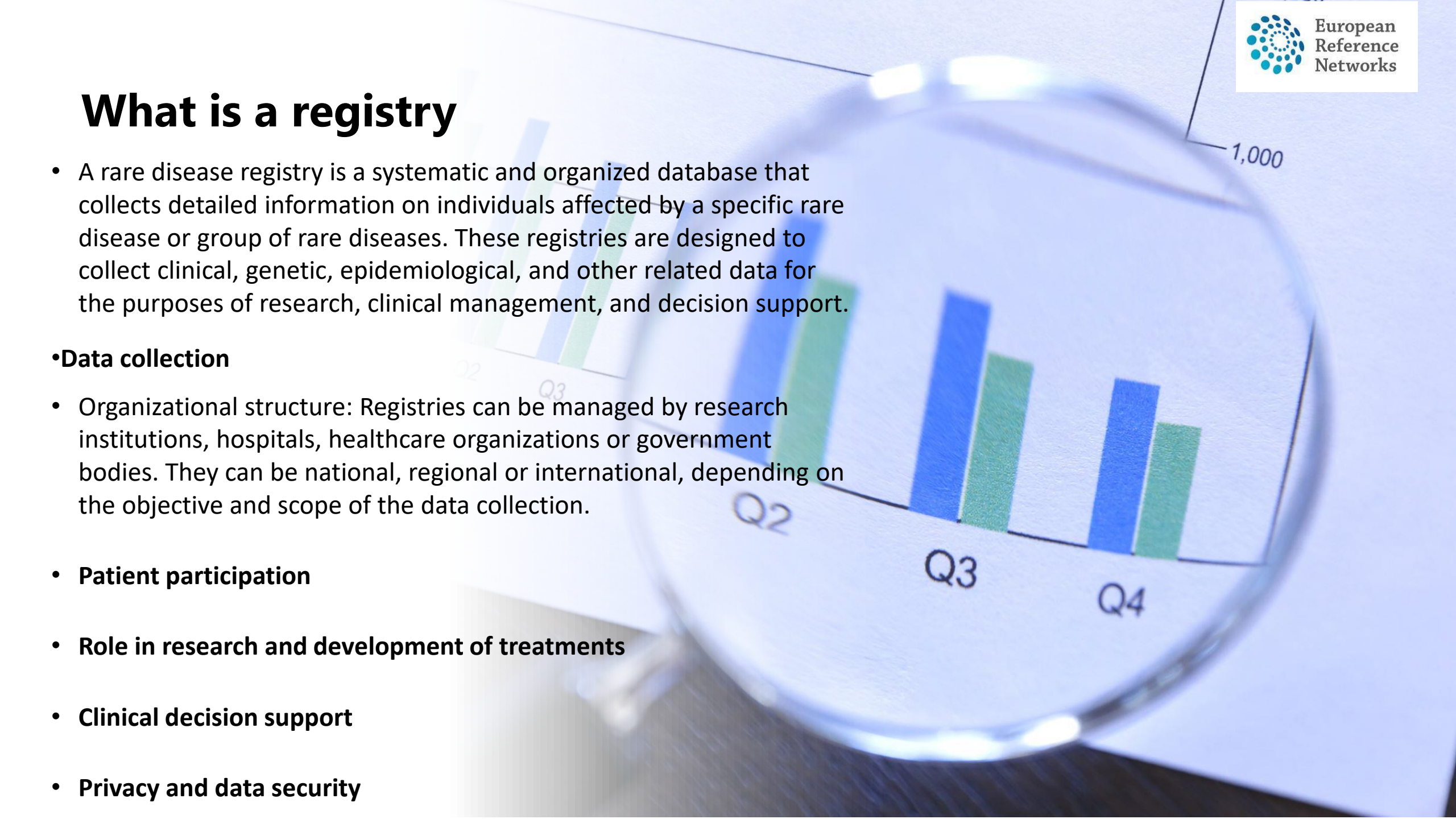
- Organizational structure: Registries can be managed by research institutions, hospitals, healthcare organizations or government bodies. They can be national, regional or international, depending on the objective and scope of the data collection.

- **Patient participation**

- **Role in research and development of treatments**

- **Clinical decision support**

- **Privacy and data security**



Relevance of rare disease registries

- Understanding incidence and prevalence
- Facilitate scientific research
- Improve diagnosis and management of the disease
- Support the development of drugs and therapies
- Optimize the allocation of healthcare resources
- Promote awareness and education

- **Types of registers**
- **National registers vs. international.**
- **Patient registries vs. clinical data registers.**
- **Estimated number of registers in EU: approximately 700**

What are rare disease registries for

Rare disease registries function as organized collections of data about individuals with rare conditions. Here's an overview of how they generally operate:

Data Collection

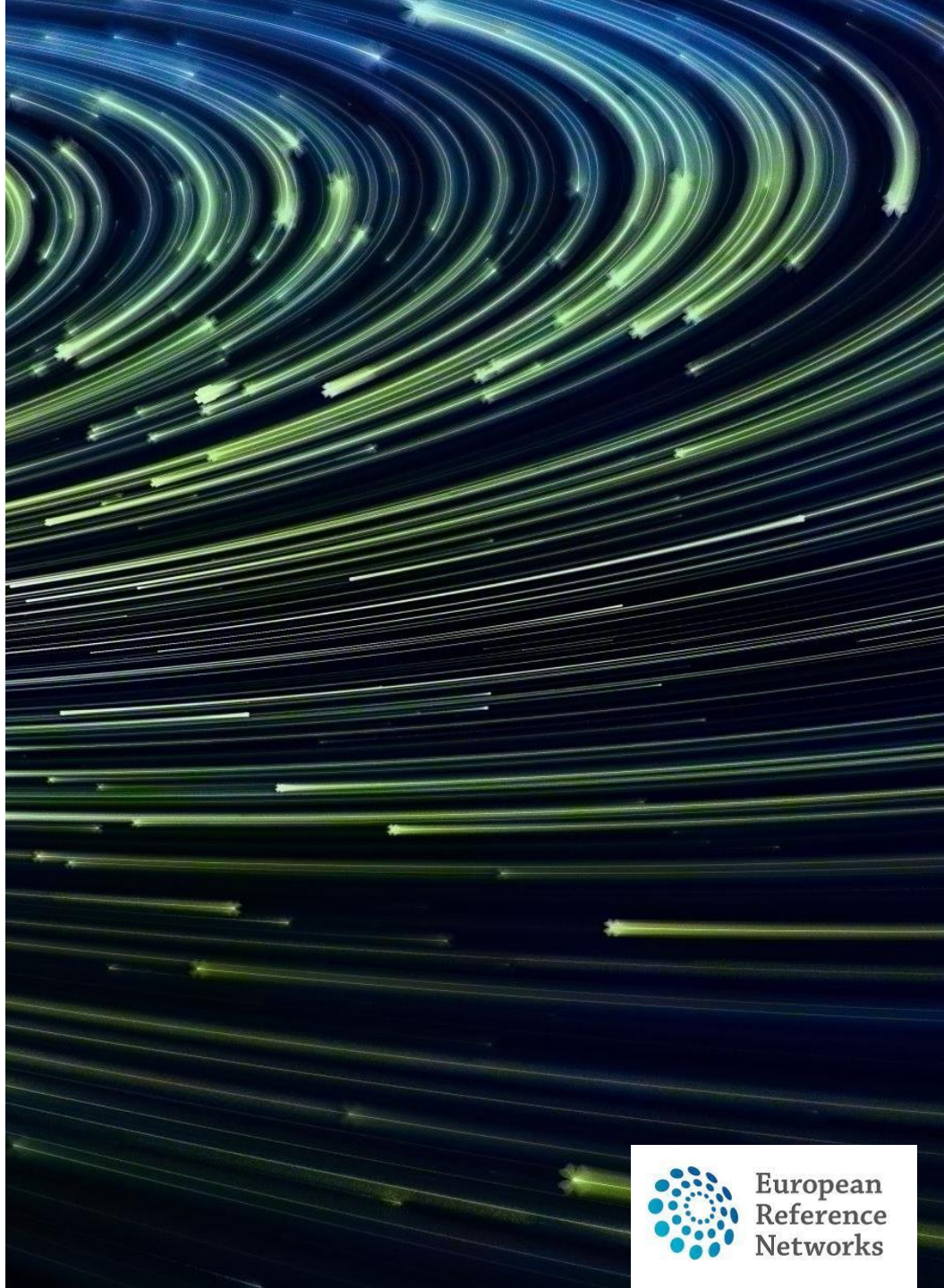
Patient Partecipations

Organization and management of data

Data Usage

Collaboration and sharing of data

Evaluation of efficacy



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European Platform on Rare Disease Registration

EUROPEAN PLATFORM ON RARE DISEASES 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	The JRC is working on providing a pseudonymisation tool to the registries
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/eurocat/eurocat-network/jrc-eurocat-central-registry_en

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GROUP	ELEMENT N°	ELEMENT NAME	ELEMENT DESCRIPTION	CODING	COMMENT
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/eurocat/eurocat-network/jrc-eurocat-central-registry_en

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European Platform on Rare Disease Registration

Makes RD patient data FAIR

ERDRI provides the infrastructure and tools to make registries' data

F FINDABLE
A ACCESSIBLE
I INTEROPERABLE
R REUSABLE

https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-network/jrc-eurocat-central-registry_en

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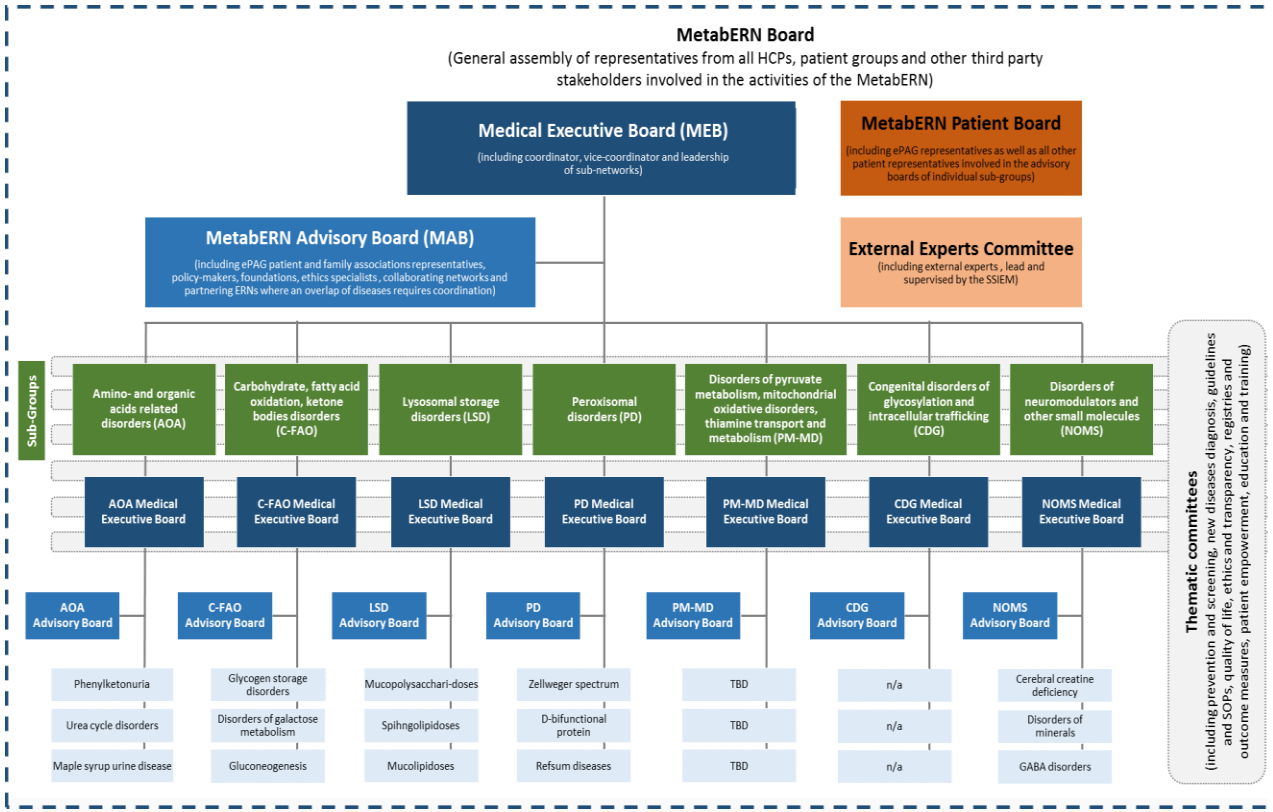
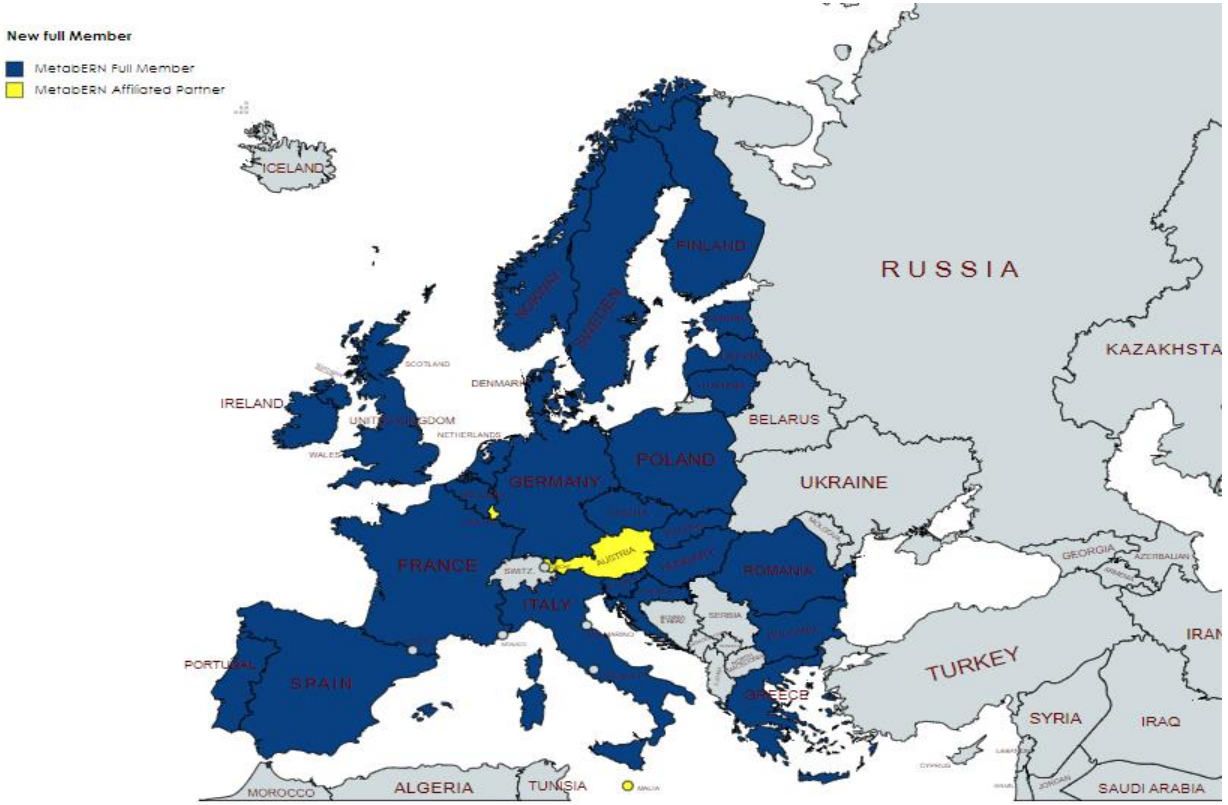
MetabERN MEMBERS

78 HCPs from 23 countries

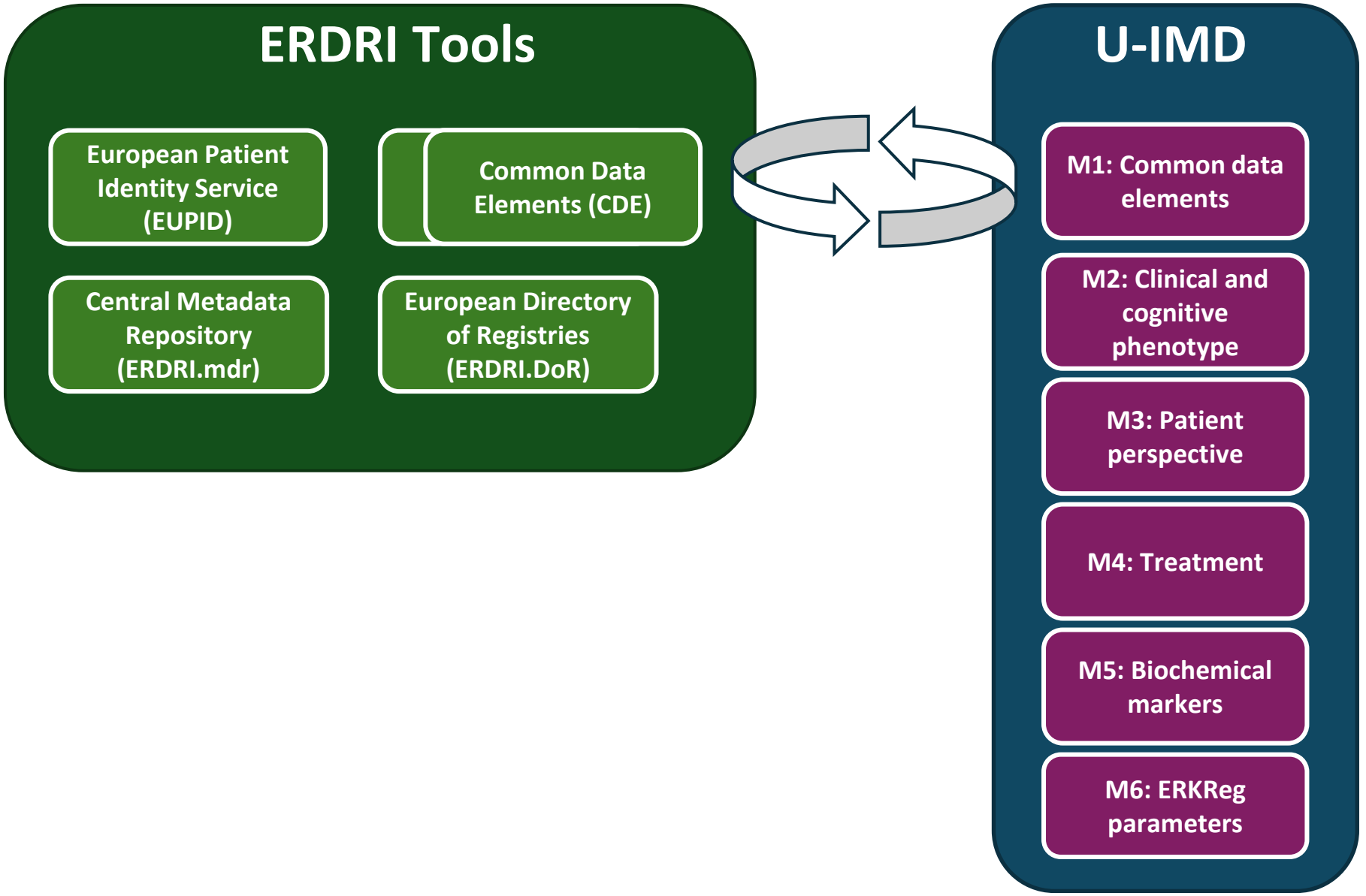
101 HCPs from 27 countries with the inclusion of the new full Members in January 2022)





Advertisements

U-IMD and ERDRI



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Modular design of the U-IMD registry

Module 1
Common data elements

- **Set of CDE for RD registration** (JRC)
- New nosology for 1,000+ IMDs according to **IEMbase**
- Mapped to **Orphanet** and **OMIM**

Module 2
Clinical and cognitive phenotype

- **Human Phenotype Ontology (HPO)**
- Results of **standard IQ tests**

Module 3
Patient perspective

- Pediatric Quality of Life Inventory (**PedsQL**)
- World Health Organization Quality of Life (**WHOQOL**)

Module 4
Treatment

- **WHO ATC classification system** as standardized vocabulary for pharmacotherapy

Module 5
Biochemical markers

- Selection of biochemical markers established by the **IEMbase**.
- Mapped to **Human Metabolome Database (HMDB)**.

Module 6
ERKReg parameters

- **Full panel of disease progression parameters** of the ERK-REG.

Module 7
NEWBORN SCREENING

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Find us at: https://www.u-imd-registry.org

UIMD
Unified Registry for Inherited Metabolic Disorders

REGISTRY

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U-IMD Homepage
Participating centers
Contact

About U-IMD

U-IMD is the acronym for the Unified European Registry for Inherited Metabolic Disorders. The overall aim of this project is to promote health for children, adolescents and adults affected by rare Inherited Metabolic Disorders (IMDs). The project has three major activities:

1. Establishing the U-IMD patient registry as a tool of the European Reference Network for Hereditary Metabolic Disorders (MetabERN).
   U-IMD will fully implement the common data elements of the European Platform on Rare Disease Registration (EU RD Platform) and will be integrated into the European Rare Disease Registry Infrastructure (ERDRI). U-IMD will be the first unified European registry that encompasses all IMDs.
2. Upgrading already existing IMD registries to the standard of U-IMD, starting with the registry of the International Working Group on Neurotransmitter Related Disorders (iNTD).
3. Developing a standard for minimal core data sets shared by the MetabERN and the European Rare Kidney Disease Reference Network (ERKNet).

Diseases in U-IMD

All IMDs, with no exclusion, are of interest to MetabERN. Considering the complexity of more than 1000 known IMDs rare IMDs are structured in 7 subnetworks by MetabERN.

The U-IMD registry will cover all IMD subgroups specified by MetabERN.

- Amino and organic acids-related disorders (AOA)
- Pyruvate metabolism mitochondrial oxidative phosphorylation disorders, krebs cycle defects, disorders of thiamine transport and metabolism (PM-MD)
- Carbohydrate, fatty acid oxidation and ketone bodies disorders (C-FAO)
- Lysosomal storage disorders (LSD)
- Peroxisomal disorders (PD)
- Congenital disorders of glycosylation and disorders of intracellular trafficking (CDG)
- Disorders of neuromodulators and other small molecules including porphyrias (NOMPS)

Who can participate in U-IMD

U-IMD will be available for all Members of MetabERN as well as for voluntarily collaborating health care providers (hospitals) outside of MetabERN. U-IMD is intended to be used by physicians treating patients with rare inherited metabolic disorders.

How to join U-IMD / How to submit patient data

- Contact the Registry Coordinator with the expression of interest by email; your application will be evaluated by the U-IMD Steering Committee.
- Sign the U-IMD letter of agreement
- Using the template approved by IRB in University Hospital in Heidelberg, prepare and submit ethics application for U-IMD to your local IRB (respecting national/local standards).
- Receive personalized usernames and passwords and start data entry.

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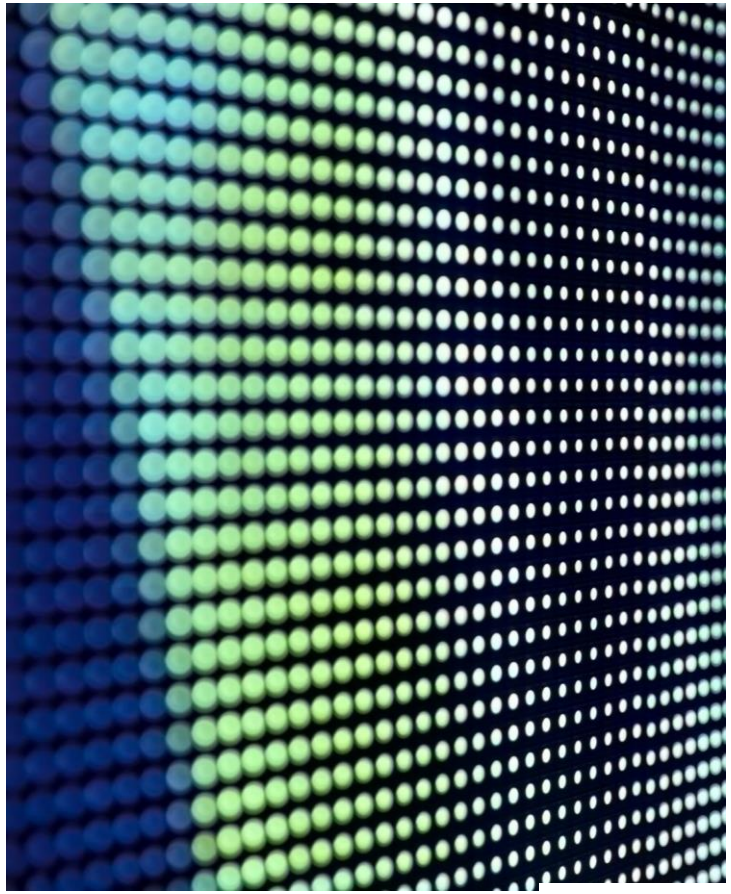
Benefit of patient registry

- Better understanding of thediseas
- Access to information and resources
- Better diagnosis and treatment
- Partecipation to research
- Psycological and social support
- Possibility to participate to clinical studies
- Better disease management



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Research-based on registries

•Registry-based research and development for rare diseases is a key pillar in advancing the understanding and improving the management of these conditions. Here's how registries can impact research and development:

- **Patient identification for clinical trials**
- **Characterization of the natural history of the disease**
- **Validation of biomarkers and endpoints for clinical trials**
- **Evaluation of the effectiveness of treatments**
- **Identification of emerging trends and needs**
- **Support for the evaluation of orphan drugs and innovative therapies**

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Challenged related to rare disease registries

•The challenges associated with rare disease registries can be varied and include several aspects, including:

- **Low prevalence and fragmentation**
- **Difficulty in data collection**
- **Data access problems**
- **Financial sustainability**
- **Differences in the definition and classification of rare diseases**
- **Patient involvement**
- **Ethical and regulatory challenges**

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Patient involvement

•Patient involvement in rare disease registries is crucial and can lead to numerous benefits. Here's how patients are involved:

- **Active participation**
- **Awareness and education**
- **Allow sharing of experiences**
- **Provide feedback and input**
- **Participation in governance**
- **Empowerment**

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Registry Impact on public health

•Rare disease registries have a significant impact on health policy in several ways:

- **Information and awareness**
- **Orientation of health policies**
- **Support for drug research and development**
- **Promotion of collaboration and assistance network**
- **Influence on the financing of health initiatives**
- **Monitoring the effectiveness of policies**

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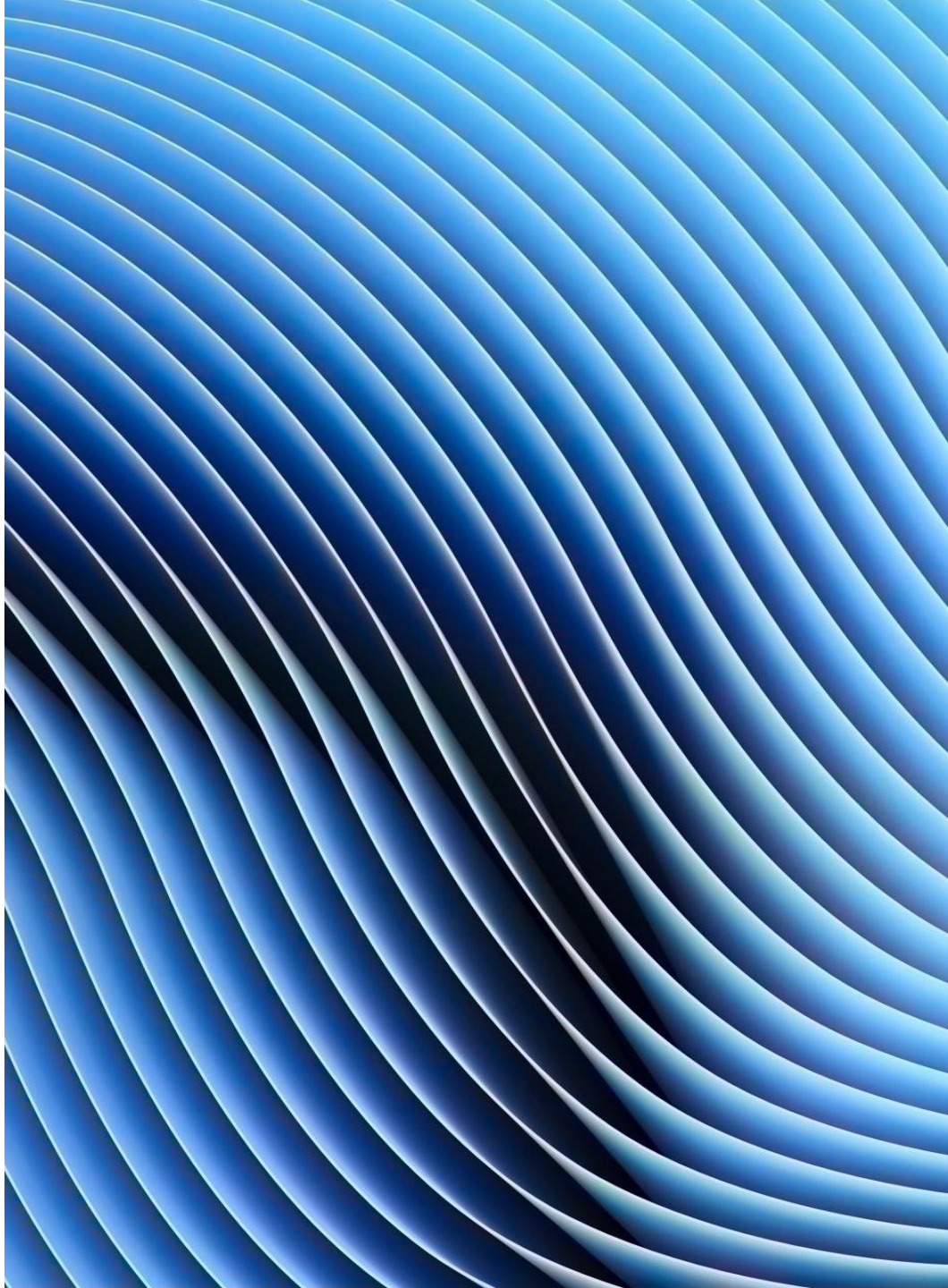
Future of rare disease registries

•The future of rare disease registries is promising and presents several interesting perspectives:

- **Integration and interoperability**
- **Innovative technologies**
- **Patient involvement**
- **Focus on access and equity**
- **Collaborative initiatives**
- **Emphasis on ethics and privacy**
- **Long-term monitoring and results**
- **Valuable source of data for A.I. applications**



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Collaborations and partnerships

•Collaborations and partnerships in rare disease registries play a crucial and beneficial role for several reasons:

•More complete and representative data collection

•Sharing best practices.

•Data harmonization

•Maximum use of resources

•Promotion of research and development of treatments

•Influence on health policies

•Stakeholder involvement

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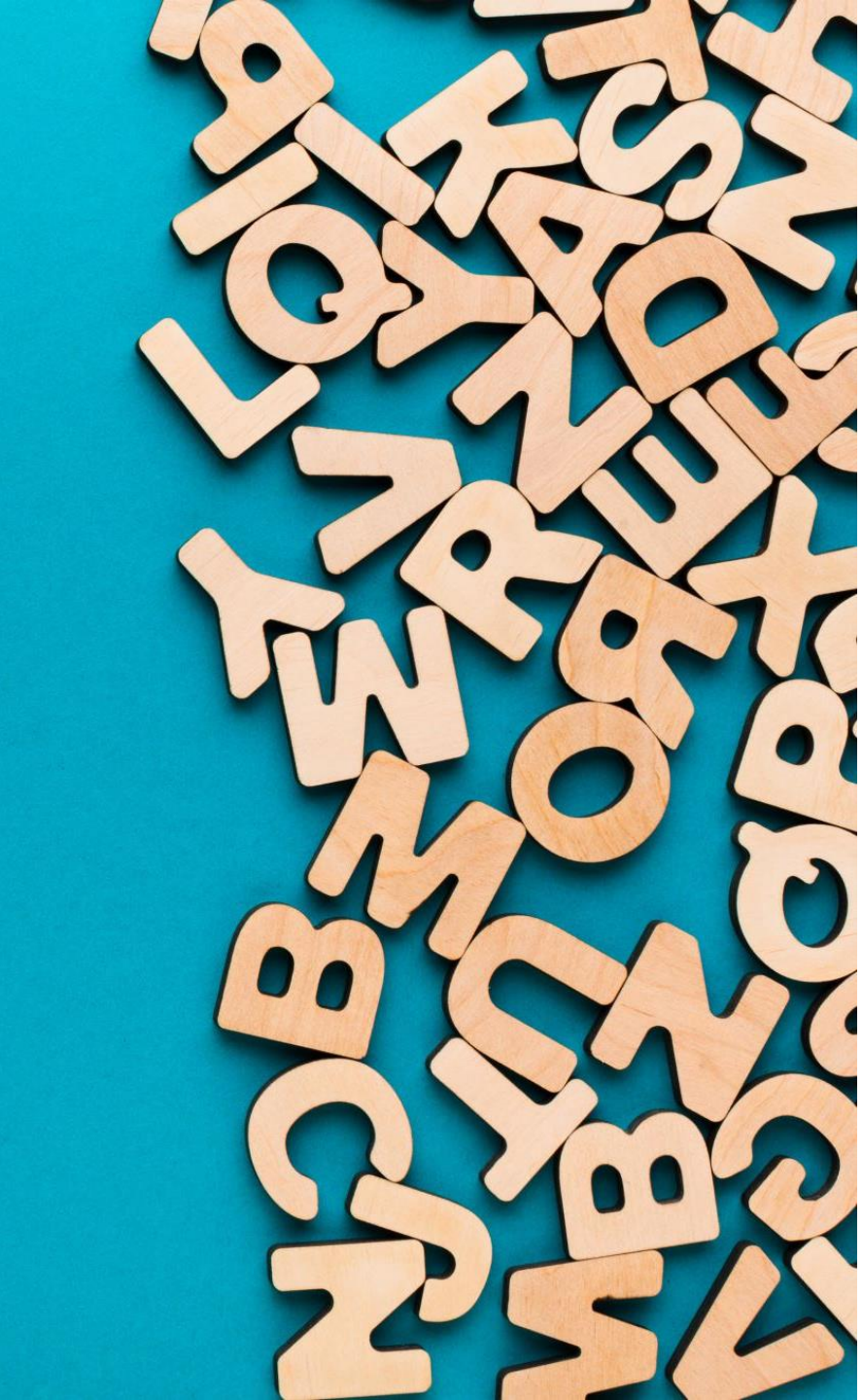
Take home messages

- Proper collection of data into ERN-based registries is crucial today to:
  - Describe natural histories of the diseases
  - Identify patients to be enrolled in clinical trials and monitor the CT outcome
  - Study safety and efficacy of innovative drugs
  - Quantify patients unmet needs
- ERN-based Registries are an important tool integrated into the NHS since they represent:
  - A pretious source for clinicians for the patient management
  - A pretious source of data to shorten the diagnostic gap by secondary data usage
  - A pretious sorce for the knowledge generation and awareness of rare diseases
  - A pretious source for the creation of health programmes aimed at a quick diagnosis, a more efficient management and a sustainable planning of orphan therapies
- Some problems still remains:
  - There are at the moment different legislation in MS ruling registries and data management
  - Privacy concept is not the same in all MS
  - Interoperability still remains a major obstacle
  - EHDS is expected to help MS in having a regulation for sharing data
  - A.I. is requiring a regulation for the secondary use of data, however, there is inequality in its use among MS
  - The Joint Action JARDIN is expected to analyze the situation and suggest solutions to integrate ERNs into the NHS also for data management



- *THANKS FOR THE ATTENTION*