# Healthcare Researcher
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‘Remodeling an existing rare disease registry to be used in regulatory context’

EuRREB
European Registries for Rare
Endocrine and Bone conditions

# Remodeling an existing rare disease registry to be used in regulatory context

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**IRCCS Istituto Ortopedico Rizzoli**

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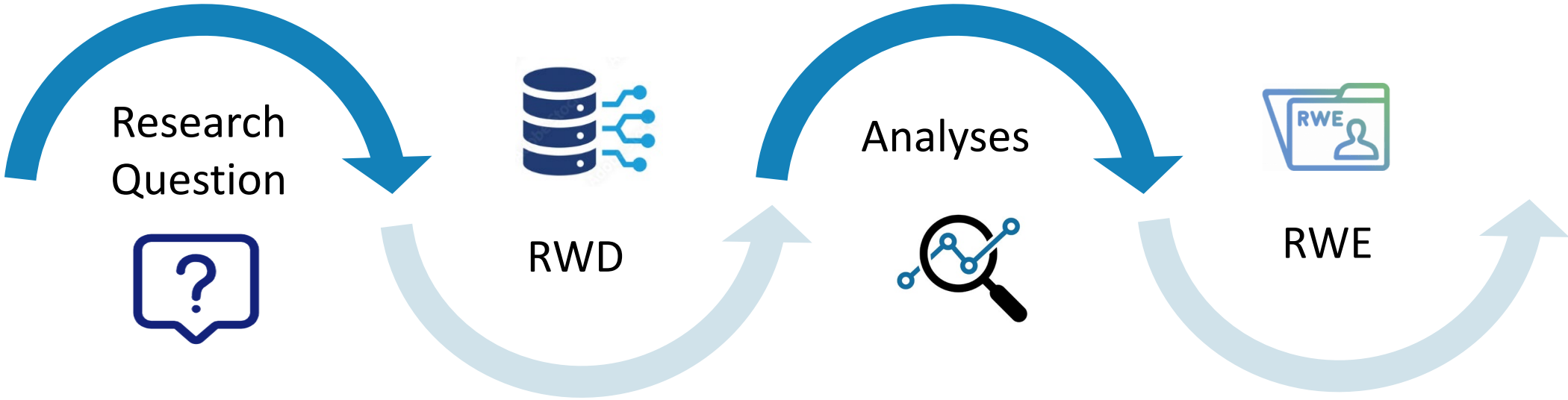
Funded by
the European Union

# RWE & RWD

**Real-World Evidence:** evidence on health and healthcare gathered from several sources. RWEs are the results of the analysis of Real-World Data (RWD)

**Real-World Data:** routinely collected data of a patient's health status or delivery of health care from a variety of sources (EHR, registries, wearable, etc.)




RWD are an intriguing way to explore the rare disease scenario and to investigate orphan drugs

# Registry & RWD

RWDs collected within registries have a key role in increasing the knowledge of RDs:

- ✓Boosting **natural history studies**
- ✓Understanding **disease evolution** and predicting disease severity research
- ✓Promoting **epidemiological investigation**
- ✓Developing **guidelines and recommendations**
- ✓Evaluating the **impact of treatments**

Multi-purpose tool

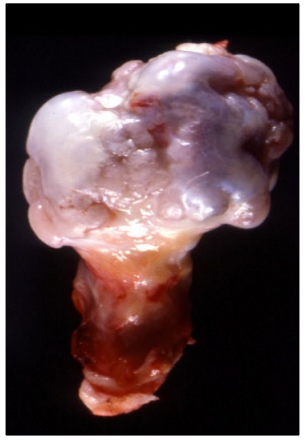
# REM – Registry of Multiple Osteochondromas

REM is a Registry for collection of Multiple Osteochondromas patient data, that relies on a web application, named GeDI

To date, it collects a structured data regarding patient demographics, disease onset, comorbidities, genetic data, family history, and clinical anomalies, with particular attention to treatment details and intermediate outcomes

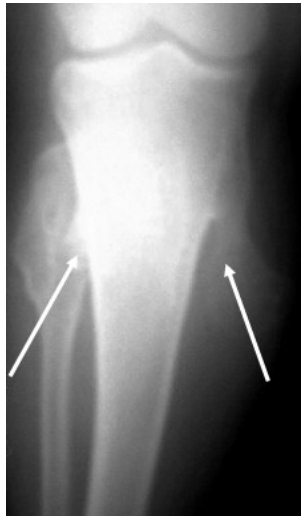
## MULTIPLE OSTECHONDROMAS

> Rare skeletal disorder
> Prevalence: 1-9/100.000
> 2 causative genes (EXT1/EXT2)

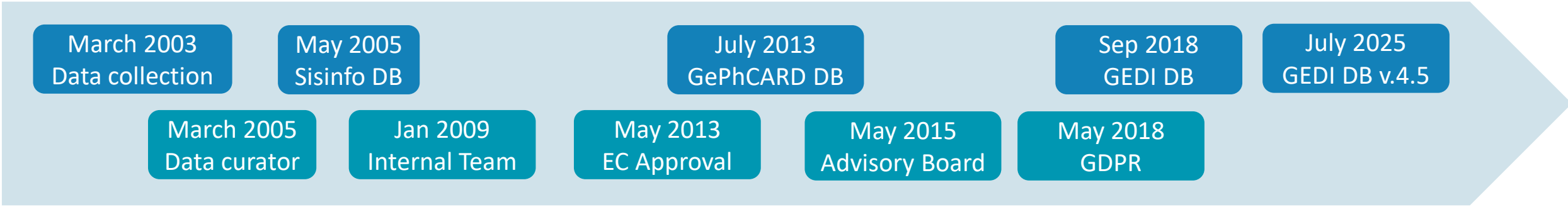


## CLINICAL FEATURES

> Presence of benign bone tumours on long bones, pelvis, and vertebrae
> They grow in number and size during childhood, leading to deformities and limitations
> Ca. 5% risk of malignant transformation



# REM Timeline




- 2003: we started to organize and to structure data
- 2005: a dedicated data curator has been individuated and an IT platform for data collection (SISINFO)
- 2009: an internal team for data management has been established
- 2013: REM registry received Ethical Committee Approval and data was moved to a new platform (GePhCARD)
- 2015: an Advisory Board has been established
- 2018: data was moved to a new platform, named GeDI
- To date: the v4.5 of GeDI has been recently released

# Registries for regulatory assessment

For remodeling the REM as a tool to be used in regulatory context we have evaluated several sources

- The Agency for Healthcare Research and Quality – AHRQ - reference handbook

*This guide has gives advice on a) collaboration with patients (and patients' associations); b) the crucial role of data standards; c) reusing of existing data sources; d) ethical and legal aspects and e) increasing interest in using registries as sources of RWD/RWE for informing decision-making*

- The Patient REgistries iNiTiative - PARENT Joint Action

*This Join Action was intended to help the European countries in developing patient registries and harmonize their development and governance. Within this project has been drafted the "methodological guidelines and recommendations for efficient and rational governance of patient registries," a document providing guidance to set up or remodel a patient registry and oversee it, to increase interoperability and data exchange among registries, and to facilitate analyses of secondary data for public health and research purposes*

# Registries for regulatory assessment

- The FAIR principles

*The FAIR concept has been vastly suggested as a tool for enabling data collection in disease registries and has become a recommended approach, particularly in rare disease scenarios*


- The legal regulations (GDPR)

*The main privacy-preserving set of rules. The GDPR has been implemented, modified, and integrated at the national level, with additional laws and legislations*


- The EMA initiative

*The European Medicine Agency has launched, in 2015, an initiative for patient registries, aiming to discover new ways to increase the role and use of existing disease registries highlighting their potential impact in benefit–risk evaluation of medicinal products. This initiative and subsequent action aim to promote the use of existing registries for collecting information for contributing regulatory assessment (PASS & PAES)*

EMA
EUROPEAN MEDICINES AGENCY

# Recommendations from our experience

**Governance**

- Building an **internal team**
- **Advisory Board** comprised multiple competencies
- Define overall **direction and objectives**, identifying stakeholders, promoting layman and scientific dissemination

**Informed consent**

- Patients **need**
- **Sensitive data** (e.g. genetic info)


**Data Security**

- Measure to **maintain privacy**
- **GDPR**

# Recommendations from our experience

## Data Safety

- Hosted on a **secure datacenter**
- **Encrypted data** and connection
- **Separate databases** (DMZ zone)

## Data quality and reliability

- **Consistency:** uniformity of format and data
- **Accuracy:** correct representation of patients' data
- **Completeness**: minimum dataset
- Data capturing is carried out by **expert registry staff**
- Collect information derived from **health records**, reports, and clinical documentation
- **Double-check** for captured data

# Recommendations from our experience

**The semantic interoperability**

- Set of **Common Data Elements** for RDs Registration [JRC]
- Implemented with **ontologies**: ORDO (Orphanet), HGVS, HPO, ICF, MedDRA, etc.

**Safety Analysis**

- Reporting of **safety**
- Monitoring of **adverse events**
- Aggregate **analyses**

# Fuel for thought

> Define the purposes

> Choose data, platform & go by regulation

> Individuate proper ontology and standards for your data and your aims

> Organize the governance, considering all the stakeholders

# Fuel for thought

## PROs & CONs

- Registry as source of information for clinical protocols, RRCT, PASS and PAES
- Incorporate ontology & standards for your data and your aims
- Increase visibility, opening new opportunities
- Increased stakeholders' engagement

- Time consuming effort for data collection and training
- Impact on economic sustainability
- Hardship of tailoring a multi-aim registry (flexibility vs rigidity)
- Time and effort in keep the registry up-to-date (new scientific findings)

# References


**AHQR GUIDELINES**

- Registries for Evaluating Patient Outcomes: A User's Guide: 4th Edition
  https://effectivehealthcare.ahrq.gov/products/registries-guide-4th-edition/users-guide

**EMA INIZIATIVE ON PATIENT REGISTRIES**

- EMA publication: https://link.springer.com/article/10.1007/s40264-019-00848-9
- EMA website: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/patient-registries

**FAIR PRINCIPLES**

- Publication: https://www.nature.com/articles/sdata201618

**JRC SET OF COMMON DATA ELEMENTS FOR RARE DISEASES**

- Download: https://eu-rd-platform.jrc.ec.europa.eu/sites/default/files/CDS/EU_RD_Platform_CDS_Final.pdf

**PARENT PROJECT**

- Download:
https://ec.europa.eu/health/sites/health/files/ehealth/docs/patient_registries_guidelines_en.pdf

**RD-CODE**

- Project websie: http://www.rd-code.eu/

# Thank you

## Ways to contact us:

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drop-in sessions via Zoom

European Registries for Rare Endocrine and Bone Conditions

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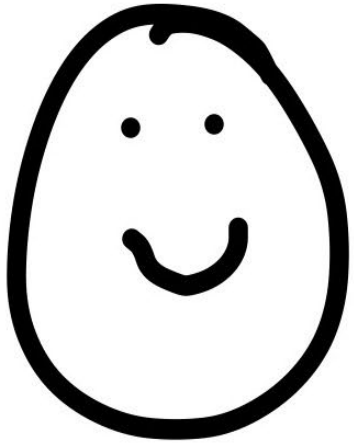
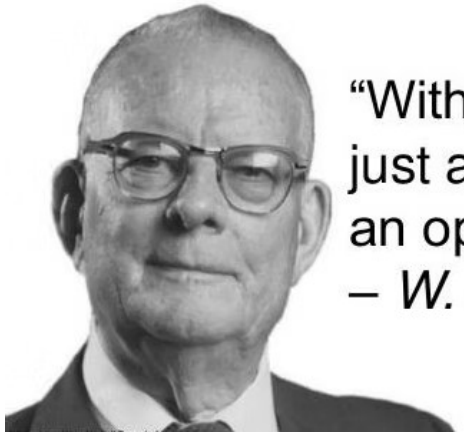
Endo-ERN
European Reference Network on Rare Endocrine Conditions

ERN BOND
EUROPEAN REFERENCE NETWORK ON RARE BONE DISEASES



# Do you have any Questions?



"Without data you're just another person with an opinion."
– *W. Edwards Deming*