

# Digital Management of Rare Diseases

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**Virtual Symposium**  
**Autoimmunity and the Lung**  
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# Digital management can only benefit RD

## Direct difficulties

- Patient are few
- Knowledge is scarce
- Experts are rare
- Small markets

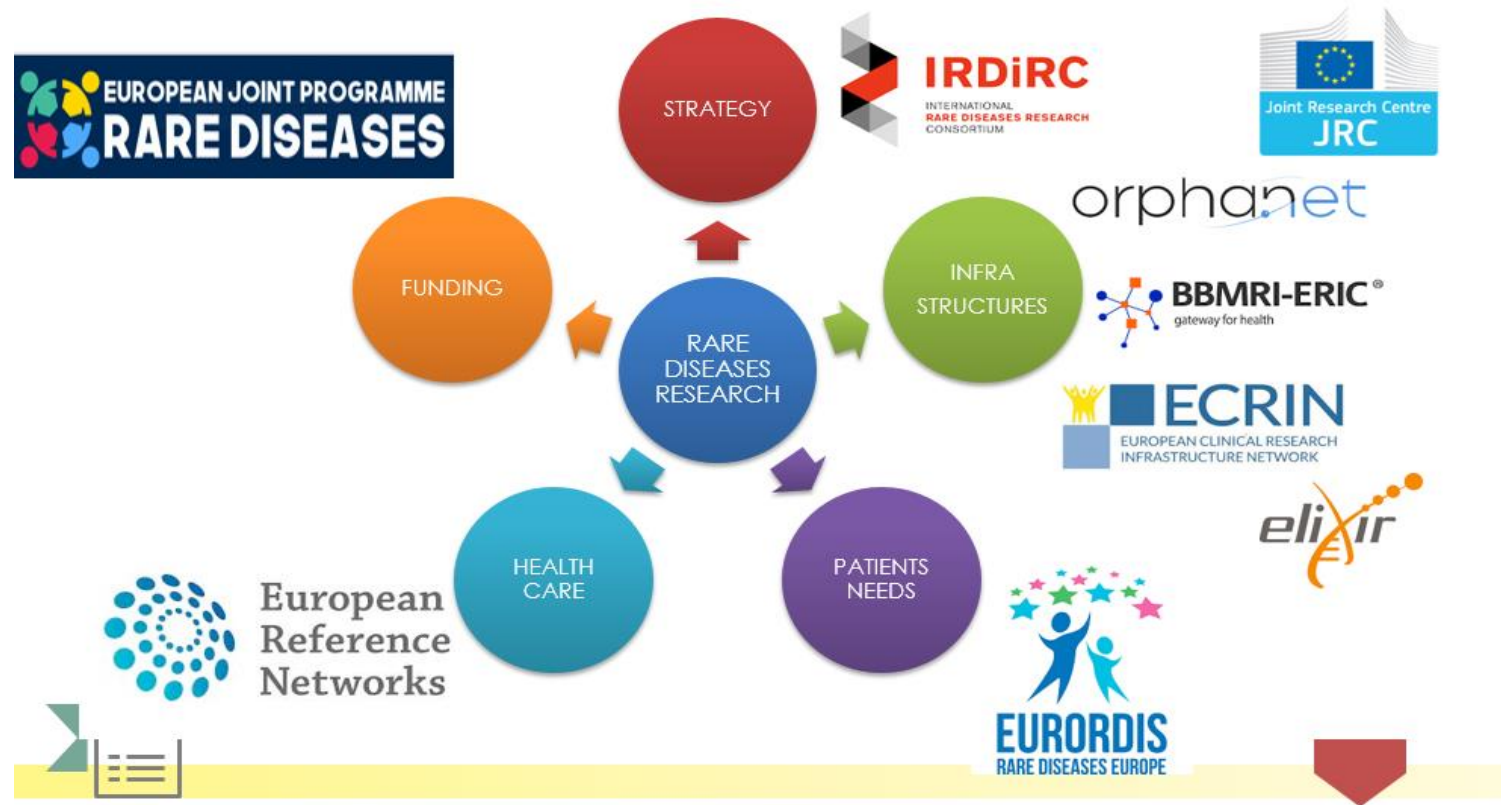
## Derived obstacles

- Transnational collaboration is necessary
- Funding is difficult to obtain

## Targets for action

- Make the most of data and technologies
- Build Stakeholders's forum
- Develop policies

# The European Ecosystem 1997-2020



# Achievements contributing to digital management of RD

# 1- Establishment of National Centres of Expertise

## Based on Quality Criteria

- Competence and experience
- Specific human resources
- Structural and equipment resources
- Appropriate organisation

## Mission

- Expert care / tele-expertise
- Guidelines / training
- Research / registries



## 2- Establishment of Networks of National Centres of Expertise

- Rare Bone Disorders
- Rare craniofacial anomalies and ENT disorders
- Rare Congenital Malformations and Rare Intellectual Disability
- Rare inherited and congenital anomalies
- Rare Endocrine Conditions
- Rare Kidney Diseases
- Rare Neurological Diseases
- Rare Neuromuscular Diseases
- Rare and Complex Epilepsies
- Rare Respiratory Diseases

- Rare Skin Disorders
- Rare Eye Diseases
- Rare Diseases of the Heart
- Rare Hereditary Metabolic Disorders
- Rare Hematological Diseases
- Rare Hepatological Diseases
- Rare Connective Tissue and Musculoskeletal Diseases
- Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases
- Rare Multisystemic Vascular Diseases
- Rare Adult Cancers (solid tumors)
- Paediatric Cancer
- Genetic Tumour Risk Syndromes

# 3- Dissemination of Information

## www.orpha.net

The portal for rare diseases and orphan drugs

*"Rare diseases are **rare**, but rare disease patients are **numerous**"*

Access our Services



Inventory, classification and encyclopaedia of rare diseases, with genes involved



Inventory of orphan drugs



Directory of patient organisations



Directory of professionals and institutions



Directory of expert centres



Directory of medical laboratories providing diagnostic tests



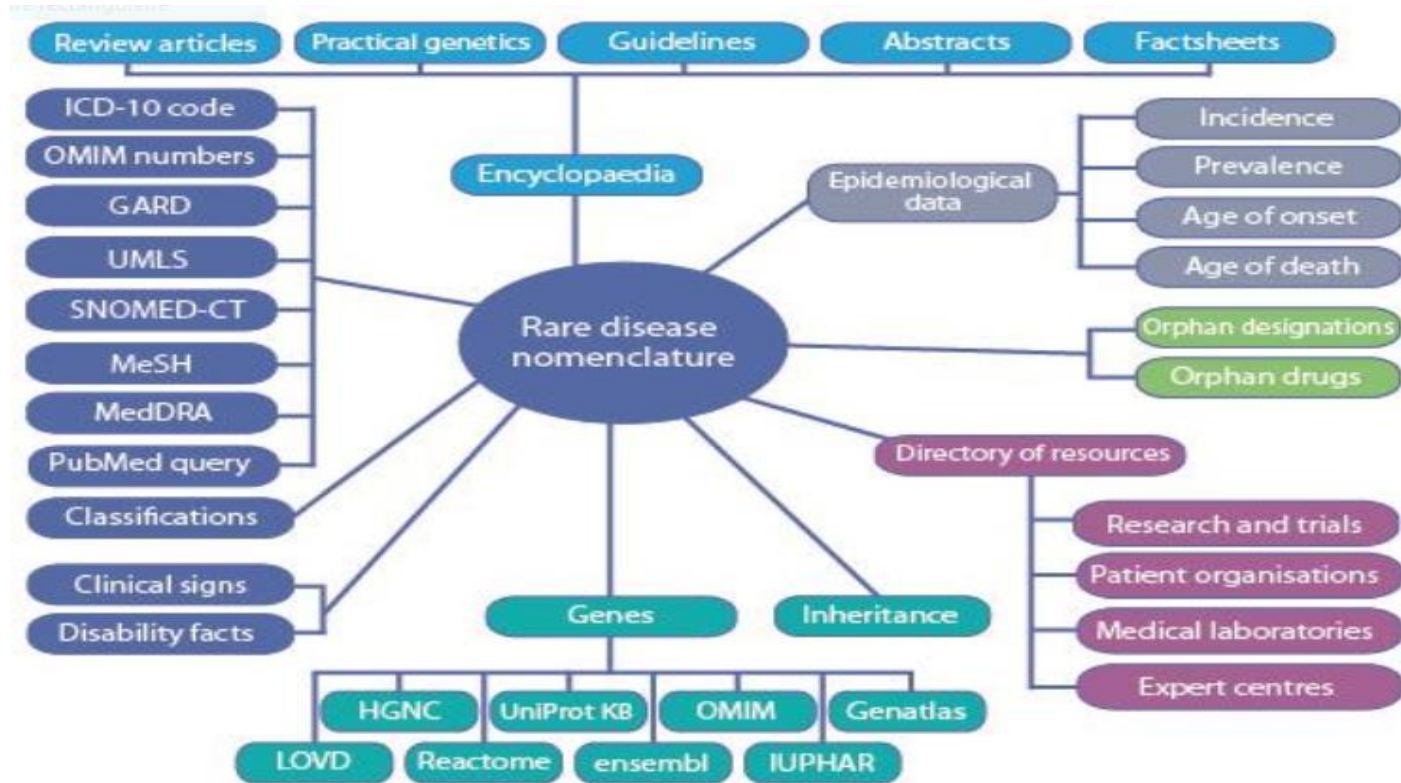
Directory of ongoing research projects, clinical trials, registries and biobanks



Collection of thematic reports: Orphanet Reports Series



## 4- Free Access to Data [orphadata.org](http://orphadata.org)





# 5- Nomenclature and Ontology

**Ontology Lookup Service**

CLD Home  
Documentation  
Index  
Database Resources  
Database  
Information  
Contact  
About  
Help  
Feedback  
Disclaimer  
Privacy Policy

Orphanet Ontology Browser

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Résoudre les problèmes

## Orphanet Rare Disease Ontology

Summary Classes Notes Mappings Widgets

### Details

ACRONYM	ORDO
VISIBILITY	Public
BIOPORTAL PURL	<a href="http://purl.bioontology.org/ontology/ORDO">http://purl.bioontology.org/ontology/ORDO</a>
DESCRIPTION	<p>The Orphanet Rare Disease ontology (ORDO) is jointly developed by Orphanet and the EBI to provide a structured vocabulary for rare diseases capturing relationships between diseases, genes and other relevant features which will form a useful resource for the computational analysis of rare diseases. It derived from the Orphanet database (<a href="http://www.orpha.net">www.orpha.net</a>), a multilingual database dedicated to rare diseases populated from literature and validated by international experts. It integrates a nosology (classification of rare diseases), relationships (gene-disease relations, epidemiological data) and connections with other terminologies (MeSH, SNOMED CT, UMLS, MedDRA) databases (OMIM, UniProtKB, HGNC, Ensembl, Reactome, IUPHAR, GenAtlas) or classifications (ICD10). The ontology will be maintained by Orphanet and further populated with new data. Orphanet classifications can be browsed in the OLS view. The Orphanet Rare Disease Ontology is updated monthly and follows the OBO guidelines on deprecation of terms. It constitutes the official ontology of rare diseases produced and maintained by Orphanet (INSERM, US14).</p>
STATUS	Production

clinical entity

disease

Lymphangioleiomyomatosis

group of disorders

Rare genetic disease

Rare genetic respiratory disease

Lymphangioleiomyomatosis

Rare respiratory disease

Rare pulmonary disease

Interstitial lung disease

Interstitial lung disease specific to adulthood

Primary interstitial lung disease specific to adulthood

Lymphangioleiomyomatosis

ICD-11

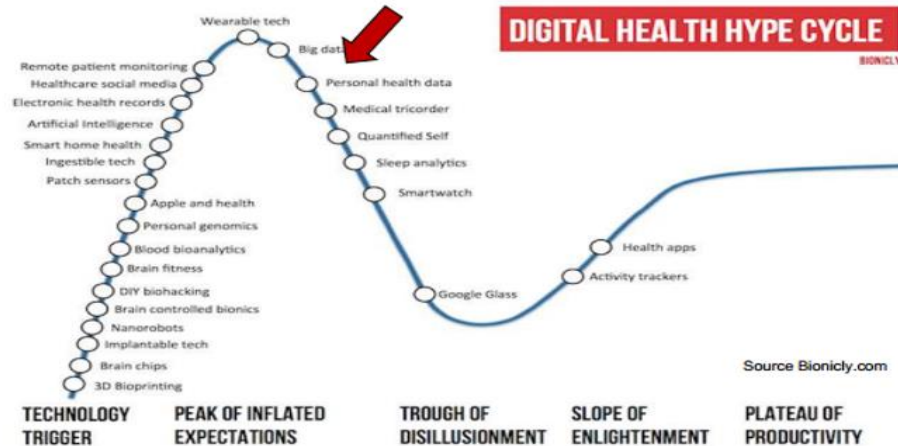
International Classification of Diseases 11th Revision

The global standard for diagnostic health information

# Opportunities thanks to New Trends

## 1- Digital Health Hype Cycle

Big Data: Bubble or not bubble: That's the question!



The future will be digital and biology, but who will lead!  
Google? Watson? alone, or MDs, Physiologists, Biologists "educating" and "mastering" them

# Recognition of the importance of Infrastructures

## Common Good concept

- Big investments
- Sustainability
- Precompetitive tools

## Specific Funding

- Call for proposals
- Example of IMI calls

## Academic recognition

- Articles describing research infrastructures
- Citation of Bioresources in articles
- BRIF BioResource Impact Factor

<http://dx.doi.org/10.1186/s12916-015-0284-9>

# Opportunities thanks to New Trends

## 2- Open Science

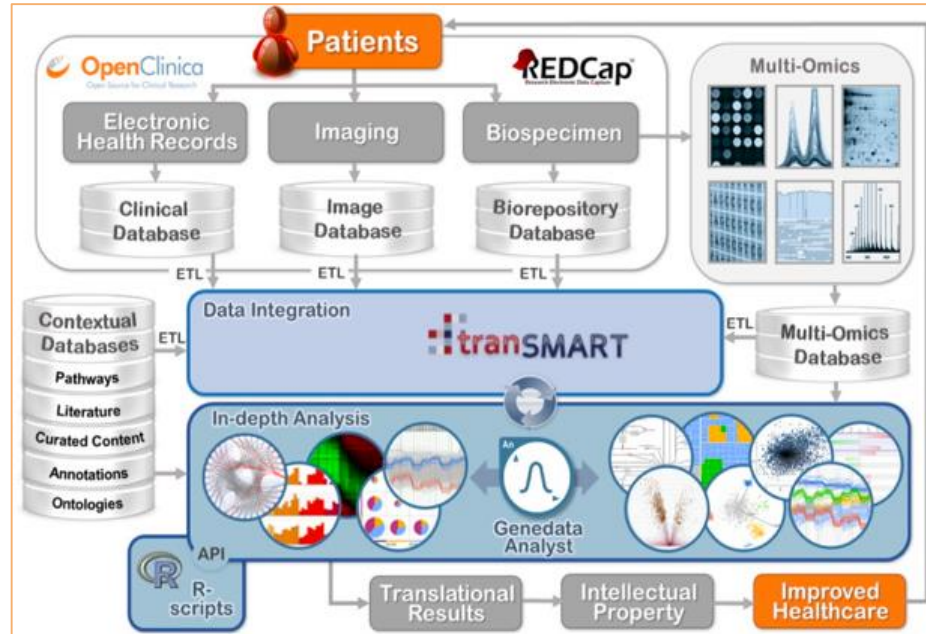


# Open Science Policy

**Open Science does not mean Open Bar**  
As Open as Possible, as Closed as Necessary !

## The FAIR principles

**F**indable  
**A**ccessible  
**I**nteroperable  
**R**eusable



# Funding Open Science is not trivial

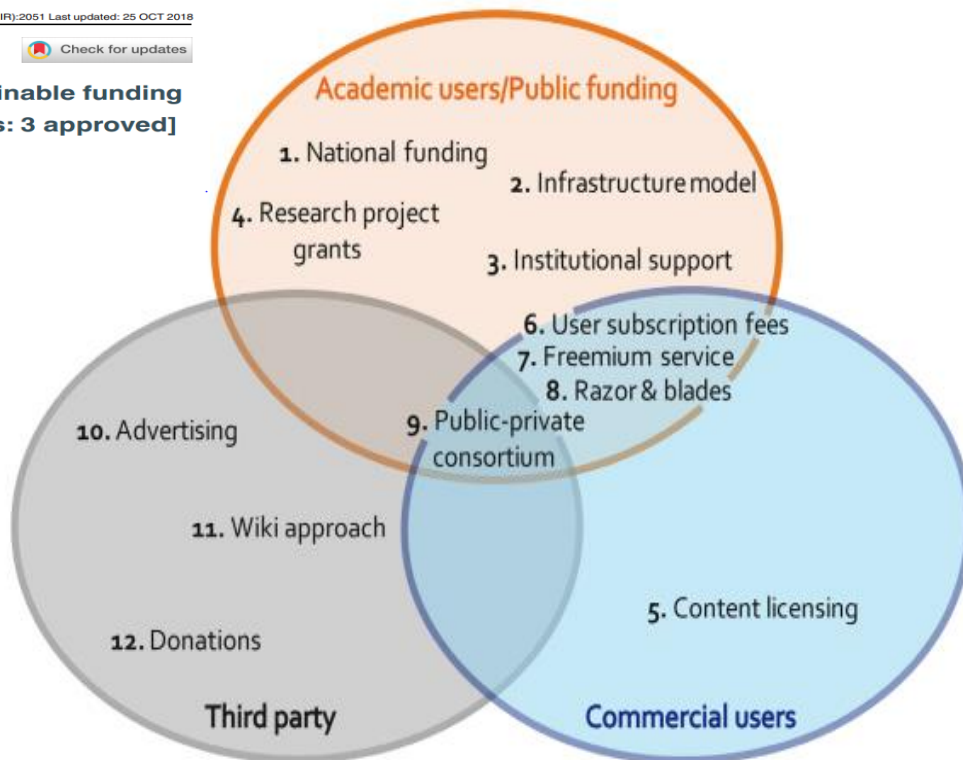


RESEARCH ARTICLE

**REVISED** Funding knowledgebases: Towards a sustainable funding model for the UniProt use case [version 2; referees: 3 approved]

Chiara Gabella , Christine Durinx , Ron Appel

ELIXIR-Switzerland, SIB Swiss Institute of Bioinformatics, Lausanne, 1015, Switzerland



**Figure 1. Funding models sources.** The 12 considered models are represented depending on the origin of the revenues.

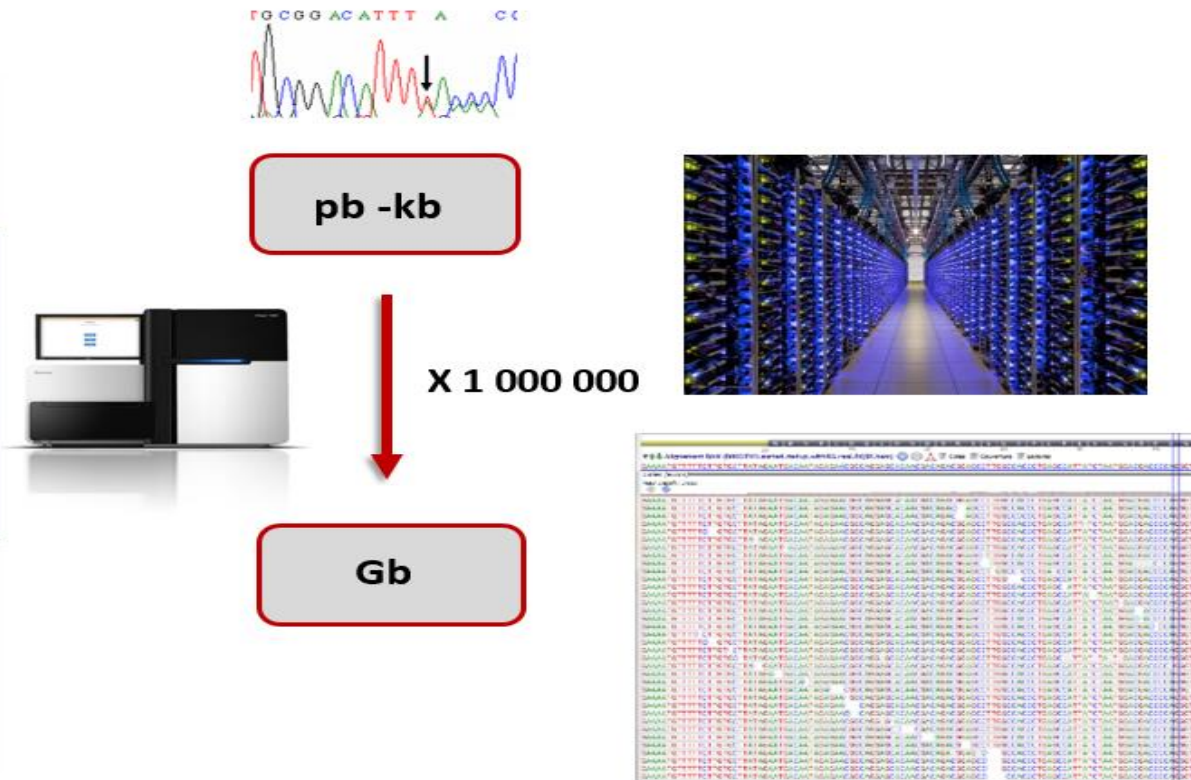
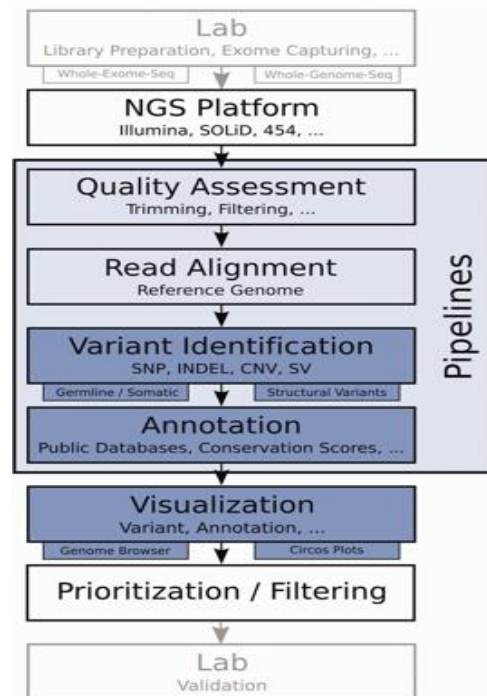
# Opportunities thanks to New Trends

## 3- Genomics



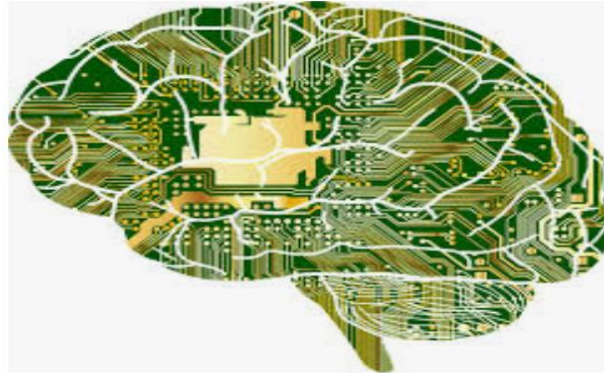


# Enormous production of data

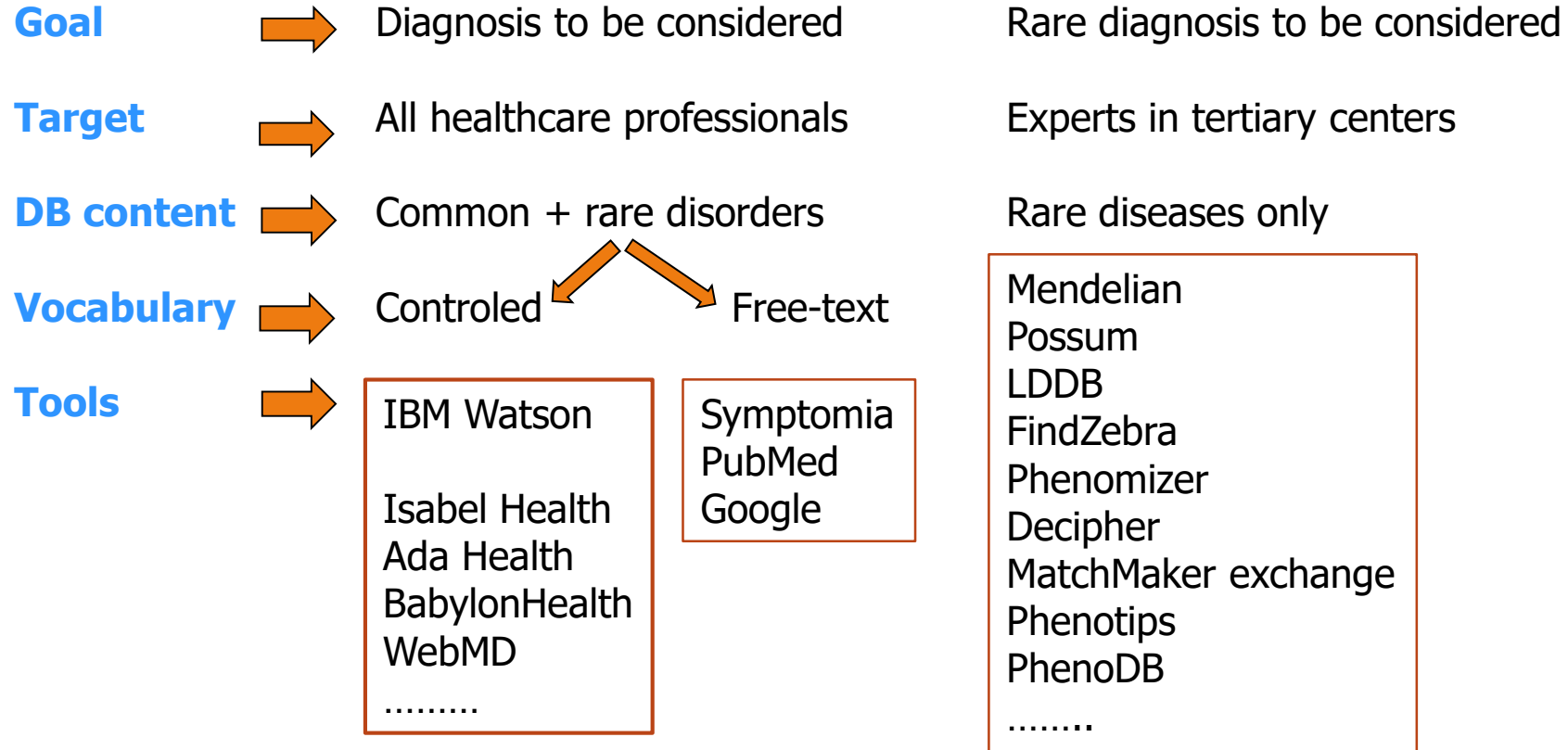


# Opportunities thanks to New Trends

## 3- Artificial Intelligence



# 1st opportunity: Clinical Decision Support Systems



# Sources of Data used by CDSS

- Data from Publications
  - Scientific articles – Half open
  - Abstracts - open
- Data from Open public infrastructure
  - Orphanet
  - OMIM
  - ClinVar
- Real World Data from organized private sources
  - Electronic health records
  - Registries, cohorts
- Real World Data from unorganized sources
  - Internet
  - Social media

## Recommendations

- ✓ Use standardized metrics to facilitate evaluation and comparison
- ✓ Validate the findings on external datasets and real patient cases
- ✓ Use standardized terminologies to enhance interoperability – HPO
- ✓ Combine expert and data knowledge to enhance explicability
- ✓ Provide robust methods dealing with the imbalance and data volume issues
- ✓ Make training sets accessible

# 2nd opportunity: Generation of new Knowledge

- Data from primary sources
  - Omics data
  - Imaging data
  - Ex vivo data
  - Clinical data from EHR
  - Telesurveillance data
- Methods
  - Deep Phenotyping
  - Supervised or unsupervised methods
- Challenges from rarity
  - Lack of large datasets to train algorithms
  - Need for harmonization of heterogeneous data
  - Few data standards / Common data elements
  - Stratification of diseases by their underlying mechanism

# IA used in the field of RD

- Data from primary sources
  - Omics data
  - Imaging data
  - Ex vivo data
  - Clinical data from EHR
  - Telesurveillance
- Methods
  - Deep Phenotyping
  - Transfer Learning
- Challenges from rarity
  - Lack of large datasets to train algorithms
  - Need for harmonization of heterogeneous data
  - Few data standards / Common data elements
  - Stratification of diseases by their underlying mechanism



100



# Remaining challenges

- Digital data readiness is insufficient in most countries /heterogeneous solutions
- Social/Psychological/cultural challenges rather than technical
- Shortage of data experts / data managers / data analysts
- Legal obligations security / privacy: Pseudonymization
- Still archaic system of rewards for data management teams
- Short funding cycles of infrastructures not fit for purpose
- ? Right level of multilateral cooperation, given political tensions and general competition

# Personal view

- Establish networks of controlled-access data that can be searched
- Specialized shared data collections with patient organisations
  - Common Data Elements
  - Ontologies, Metadata
  - Standard tools (eHR, Xnat, Omero...)
  - Governance requiring some investment from hosting institutions
- No central DB, but a federated network of data providers
- Open data as much as possible
- Maximize collaborations

# The ecosystem matters

## Is it in place for your Rare Diseases ?

*A community*



*Computational tools*



*Data sets*



*An ecosystem*

