



# Registries for Rare Diseases: State of art in Europe

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# Context and Rationale

- Very small number of patients affected by a specific rare disease: need to collect data at international level
- Promising achievements but research and development gaps and bottlenecks
  - Limited knowledge on natural history
  - Early market authorisations for Orphan Drugs
- Availability of information technology
  - Easier to store and retrieve data
  - Online solutions for collaborative efforts

# Context and Rationale (2)



- Many patient “registries” already in place
- Funding at national and EU level
- Registries for research purpose
  - mainly run by physicians and biologists with no training in epidemiology
  - Discontinuity of funding after completion of the research project
- Registries run by companies
  - Independence of clinicians and researchers ?
  - Rules unclear
- More and more legal constraints

# Specificities of RD patient registries

- most RD are genetic in origin and a large proportion of them are familial, which implies that family related cases have to be identifiable;
- The scarcity of cases imposes a large geographical coverage of the data collection which implies multiple collaborations and exchanges of data, ideally transnational; language barriers

# Specificities of RD patient registries

- The cost of establishing and maintaining a PR is nearly equal for a prevalent disease as it is for a RD, although budgets are more difficult to obtain for the latter. Legacies are less frequent.
- Intrinsic high motivation of clinicians and researchers
- Active patients organisations as partners to set up the registry and to contribute to awareness and acceptance



# Issue 1

Typology of data collections  
Importance to select the right type

# Clinical research: the tools



- Patient information management systems
- Repository of cases
- Ad hoc observational studies:
  - Transversal studies
  - Longitudinal studies: Cohorts
- Registries

# Patient information management systems



- Already in place: no cost to collect the data but cost to access them
- Death certificates, hospital discharges, prescribing, drug consumption, disability certificates
- Not designed for research but for management
- Have to be used knowing the limitations of the data
- Better use as one source among others for capture/recapture studies
- Prerequisite for use should be made easier
- Encourage use of electronic data collection systems and the interoperability of the systems

# Ad Hoc observational case studies

- Designed to serve specific purposes
- Clear protocol adapted to analysis
- Prospective and retrospective
- Limited in time
- Less expensive
- Very powerful / +++research
- Necessity of a repository of data

# Hospital based registries

- Catalog of cases and of data
- Most common type of registration for RD
- No systematic outreach of additional cases
- Not adapted to establish incidence and prevalence
- Adapted to study the natural history of diseases with the limit due to selection biases: mild cases are missed / poor/ early stages
- Permanent registration
- Lower cost than population registries

# Population based Registries

- Permanent collection of cases and of data
- population defined capture area
  - Excludes hospital-based collections of cases
  - Complete ascertainment of cases
- Defined protocol
- Ready to use or basis for complementary ad hoc studies
- Very expensive

# Clinical research: goals/tools



- Incidence and prevalence
- Course of the disease
- Ad hoc study design
- Population registries
- Cohorts
- Registries with repeated data collection
- Ad hoc studies with retrospective data



# Issue 2

Points to consider for establishing  
a data collection or funding it

# Goal and tools

- Justification for the systematic permanent collection of data vs ad hoc study
- Case definition well documented
- Clinical objectives
  - Research questions
- Design
  - Study population, study in time
  - Method of case ascertainment, data sources
  - Voluntary or mandatory
- List of variables

# Definition of data

- Agreement between experts / health authorities / patients organisations
- Foresee the use when defining the data
- Minimum data set vs maximum data set
- Temptation to collect every thing
  - Time and money consuming
  - Discourage participation
- Difficulties of data definitions
  - Diagnostic criteria
  - Qualitative variables /scores/ quantitative
  - To be adapted to future analysis

# Handling of familial cases / genetic data

- Possibility to link cases within a family
- Need to identify individuals recorded several times at different places and within centres (in general)
- Mechanism:
  - family ID
  - Link between individuals
  - pedigree
- Complexity of representation of genetic data

# Collection of data



- Data Format
  - Ready to use for statistical analysis
  - Problems of missing data
  - Validation process (good practice)
- Data Support
  - Paper files / questionnaires
  - Computerized database (PC)
  - Shared database: on-line access

# Pooling of data

- Model 1: minimum investment
  - Paper files are sent to a unique place
- Model 2: easier for legal reasons and not dependent on Internet connection
  - Data are computerised and stored locally
  - Data are transmitted to a central place from time to time as flat files (Eurocat)
- Model 3: expensive to establish/legal issues
  - Data are stored centrally and collected online

# Collection of data



- Data collection: responsible person
  - Clinician in charge of the patient at clinics
  - Research assistant if based on hospital files
  - Patients organisation
- Registrar scope of responsibilities
  - Quality control, safety, reporting, controlling access to data, documenting changes, archiving
- Data storage level
  - By the clinician in direct contact with the patient
  - By a national coordinator: anonymized data
  - By an International coordinator

# Softwares

- Need for a software for database management
  - Several commercial products for off line databases
  - Online systems have to be developed
  - To be customised easily
  - Storage of data
  - Management of the storage process
    - Restricted access
    - Data security
    - Logical verification
    - User friendly
- Need for a software for data analysis
  - Any software is usable as the data can be extracted

# Conclusion



- Ethical imperative to promote access and exchange of information
- Provided that confidentiality is protected
- Implementation of security mechanisms to ensure
  - Security
  - Long term conservation
  - Long term funding

# Conclusion



- Mechanisms in place before start of data collection
- Written protocol describing the rights and obligations of all parties
- Policy statement about collaborative research
- Appropriate funding