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 everything
  - 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 developped
  – 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