Towards an international definition framework of rare diseases

Ana Rath, Director, Orphanet INSERM
Yann Le Cam, Chief Executive Officer of EURORDIS-Rare Diseases Europe and member of RDI Council
Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database

Stéphanie Ngueang Wakap, Deborah M. Lambert, Annie Olry, Charlotte Rodwell, Charlotte Gueydan, Valérie Lanneau, Daniel Murphy, Yann Le Cam & Ana Rath

European Journal of Human Genetics 28, 165–173(2020) | Cite this article

Abstract

Rare diseases, an emerging global public health priority, require an evidence-based estimate of the global point prevalence to inform public policy. We used the publicly available epidemiological data in the
Almost all of the people with rare disease (>98%) have one of the 390 most prevalent diseases (more common than 1 per 100,000)

Most (89.1%) of rare diseases are very rare (prevalence less than 1 per 100,000)

Sources: Inserm / Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database, (submitted)
Setting strategies based on the more prevalent diseases allows to create the framework of expertise to serve patients with the rarest diseases.

To leave no-one behind.
Most definitions describe the same diseases

Different National Rare Disease definitions...

- Mostly describe the same rare diseases

Sources: Inserm / Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database
Uniform definition would enable comparisons

Different National Rare Disease definitions...

... vary widely in the patients that they include - some definitions exclude 80% of people with rare diseases

➤ a standardized definition would help comparability

Sources: Inserm / Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database
Call to better define rare diseases

How many rare diseases are there?

A lack of robust knowledge of the number of rare diseases and the number of people affected by them limits the development of approaches to ameliorate the substantial cumulative burden of rare diseases. Here, we call for coordinated efforts to more precisely define rare diseases.
How to define a disorder?

- A « disorder » is an object with multiple dimensions
- A « disorder » is an object we isolate within a continuum

« The definition of the disease has exhausted the definers. »
Claude Bernard (1813-1878), *Principes de médecine expérimentale.*
Define a disorder is adopt a point of view …

<table>
<thead>
<tr>
<th>Adopting a clinical point of view</th>
<th>Adopting an etiological point of view</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine disorder</td>
<td>Endocrine disorder</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia</td>
<td>Cholesterol-derived hormone biosynthesis deficiency</td>
</tr>
<tr>
<td>Classic CAH</td>
<td>21-hydroxylase deficiency</td>
</tr>
<tr>
<td>Pure virilizing form</td>
<td>21-hydroxylase complete deficiency</td>
</tr>
<tr>
<td>Salt-wasting form</td>
<td>21-hydroxylase partial deficiency</td>
</tr>
</tbody>
</table>

... then focus on the level of interest for us.
A common definition for what?

To make patients visible in health care systems: need for a common language

For that we need to give a name to each disease and for that we need to define what is a rare disease

Clinical definition = inclusive definition

- what the patient has
  - what the doctor finds
  - what carers can take care of

Best because it applies to every single rare disease regardless of the level of knowledge on the disease, or the cause

Enable to quantify rare diseases = + 6000 in Orphanet database
Give a name to each rare disease

Clinical definition:
- what the patient has
- what the doctor finds
- what carers can take care of

Disorders are clinically homogeneous entities described in at least two independent individuals, confirming that the clinical signs are not associated by fortuity.

Adopting a common definition allows to have a common language
Making patients visible to take action

Integrating a RD-specific codification in health information systems allows for

- Measuring the population burden of RD
- Focusing service delivery on specific patient’ needs
- Commissioning health and social services appropriately
- Identify patients for clinical research

Orphacodes* are being adopted in many places for coding and registries (EU, AU, JP…)
Exist in 9 languages and counting
Mapped to other medical terminologies (interoperability
Specific extensions can be derived to adapt to diverse prevalence-based definitions

Adopting a common language for global and cross-sector interactions

*Orphanet nomenclature of RD. http://www.orphadata.org/cgi-bin/rare_free.html#crossmodal
A definition that is Conceptual & Consensual

Framework of definition needs to be:

- **Evidence-based** with a Public Health objective
- Not prescriptive in terms of prevalence
- **Conceptual:**
  - Recognising that there will be different prevalence thresholds according to national contexts
  - Recognising that diagnostic and therapeutic fields are fast evolving
- **Consensual**
  - Reach agreement between patients, clinicians, geneticists
Towards a framework of an operational description: RDI Action Plan 2020-2021

Objective: RDI and WHO lay down a framework of an operational description of RD and prevalence and incidence figures

Activities 2020:
• Put together an RDI Ad hoc group composed of some Experts Faculty, ICD-11 RD Task Force and RDI Advocacy Committee (under the RDI Council)
• RDI Ad hoc group to define the scope of a paper which provides the operational functional description, terminology and prevalence and incidence figures
• Partner with INSERM, a collaborative centre of WHO for ICD, and Orphanet, leader of ICD-11 RD Task Force
• Bibliographic review and analysis
• State of play in term of definitions, prevalence, incidence, population
• Review and adoption by Ad hoc group
• Consultations with WHO at each step