Rare Disease by the Numbers

Naming, counting, taking action

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orphanet

Inserm
La science pour la santé
From science to health

Who needs rare disease numbers?

Patient advocacy – making the case for people with rare disease

Governments and policy-makers:

- Commissioning health services appropriately
- Focusing service delivery on specific patient needs
- Negotiating cost-efficient orphan drug prices

Researchers:

- Identifying patients and opportunities for clinical research

Orphan drug developers:

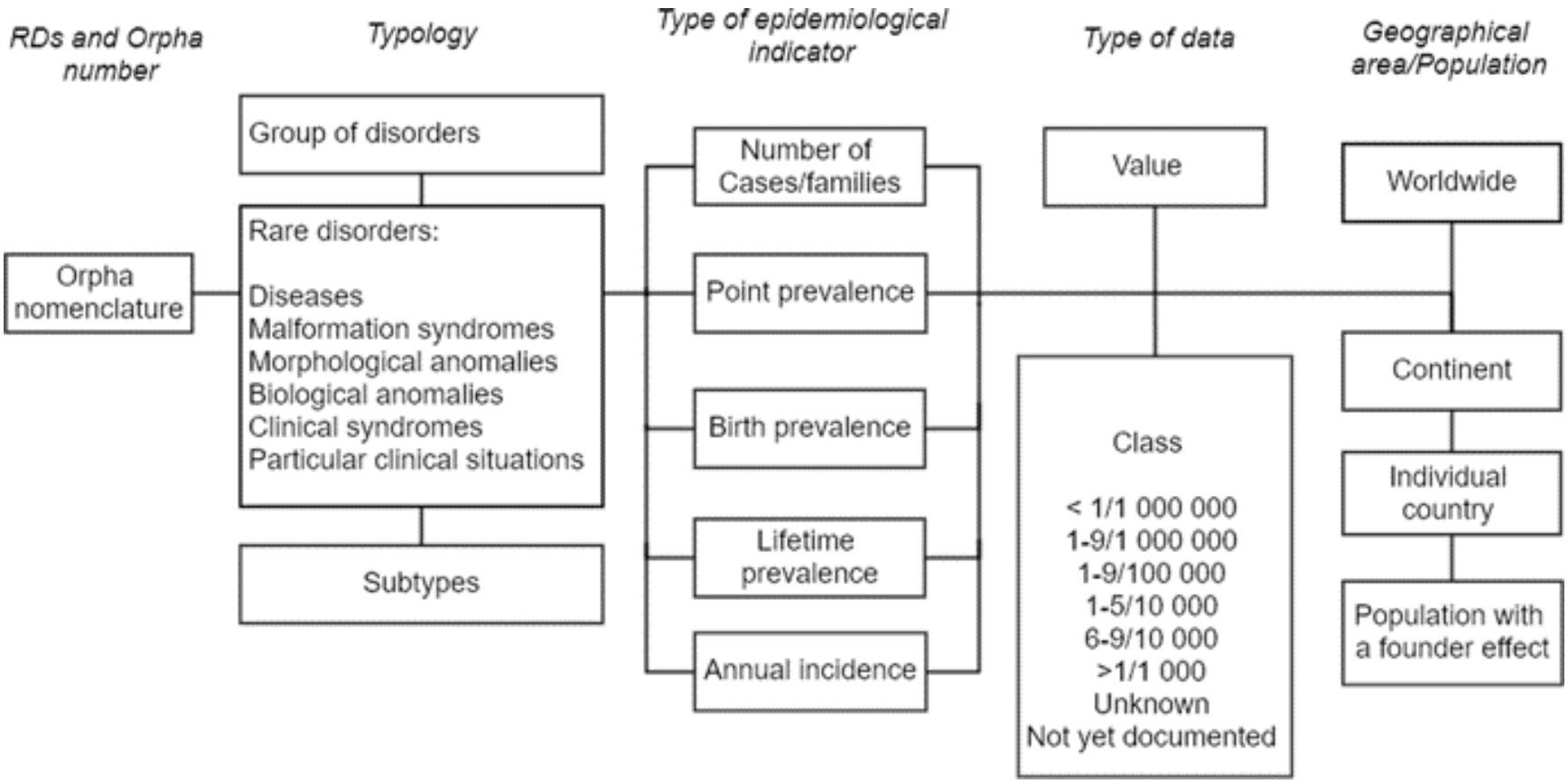
- Identifying rare disease markets
- Planning clinical trials

Why to estimate global RD prevalence?

- *Prevalence*: the proportion of a population who have a specific disease at a given time. **Definitions of RD are based on prevalence.**
- Definitions of how many people have RDs varies between countries
- The original '6-8% of people have a rare disease' estimate was not evidence-based "… not accompanied by analysis or substantive citation of sources"
- Governments and policy-makers, researchers, patient advocates, and orphan-drug developers need the data
- Orphanet maintains a DB of epidemiological data for RD

Can we derive an estimate of prevalence of RDs from all the epidemiological data in Orphanet?

Orphanet epidemiology DB



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Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database

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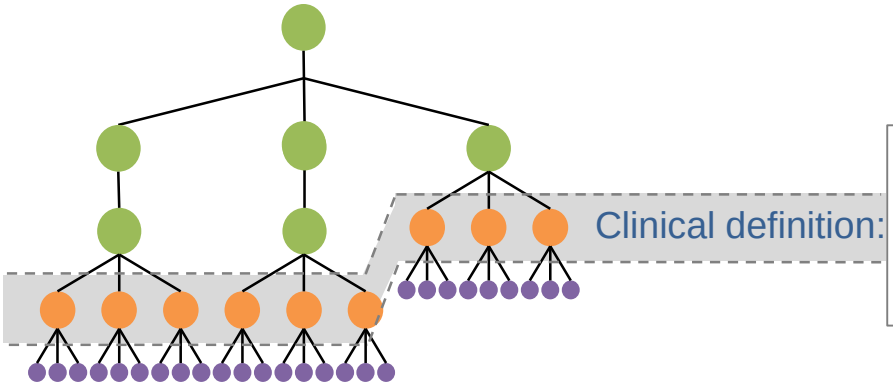
1. Adopting a conceptual definition for rare diseases

« The definition of the disease has exhausted the definers. »

Claude Bernard *(1813-1878), Principes de médecine expérimentale*.

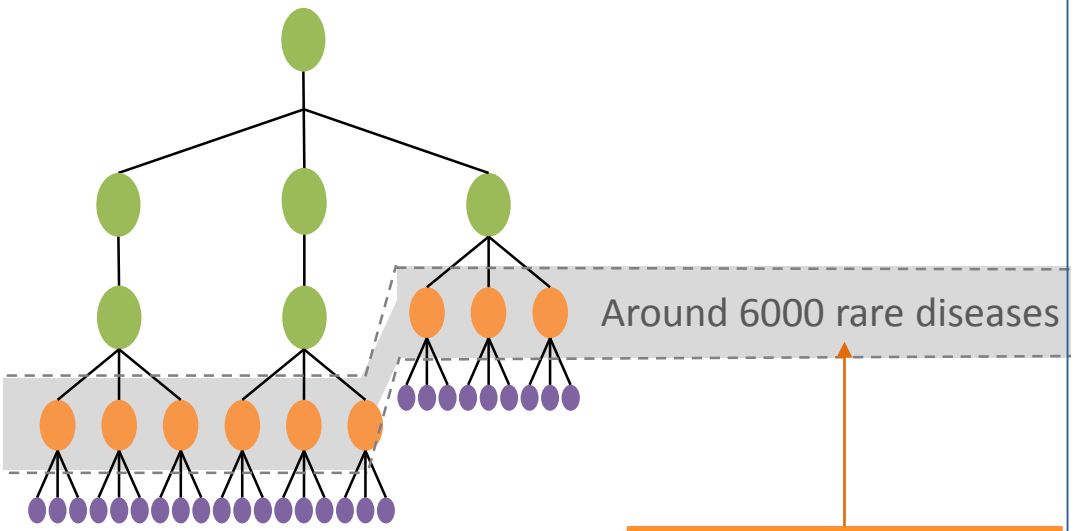


Disorders are clinically homogeneous entities described in at least two independent individuals, confirming that the clinical signs are not associated by fortuity.

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

Adopting a common definition allows to have a common language

2. Counting rare diseases



Epidemiological study

6172 RD*

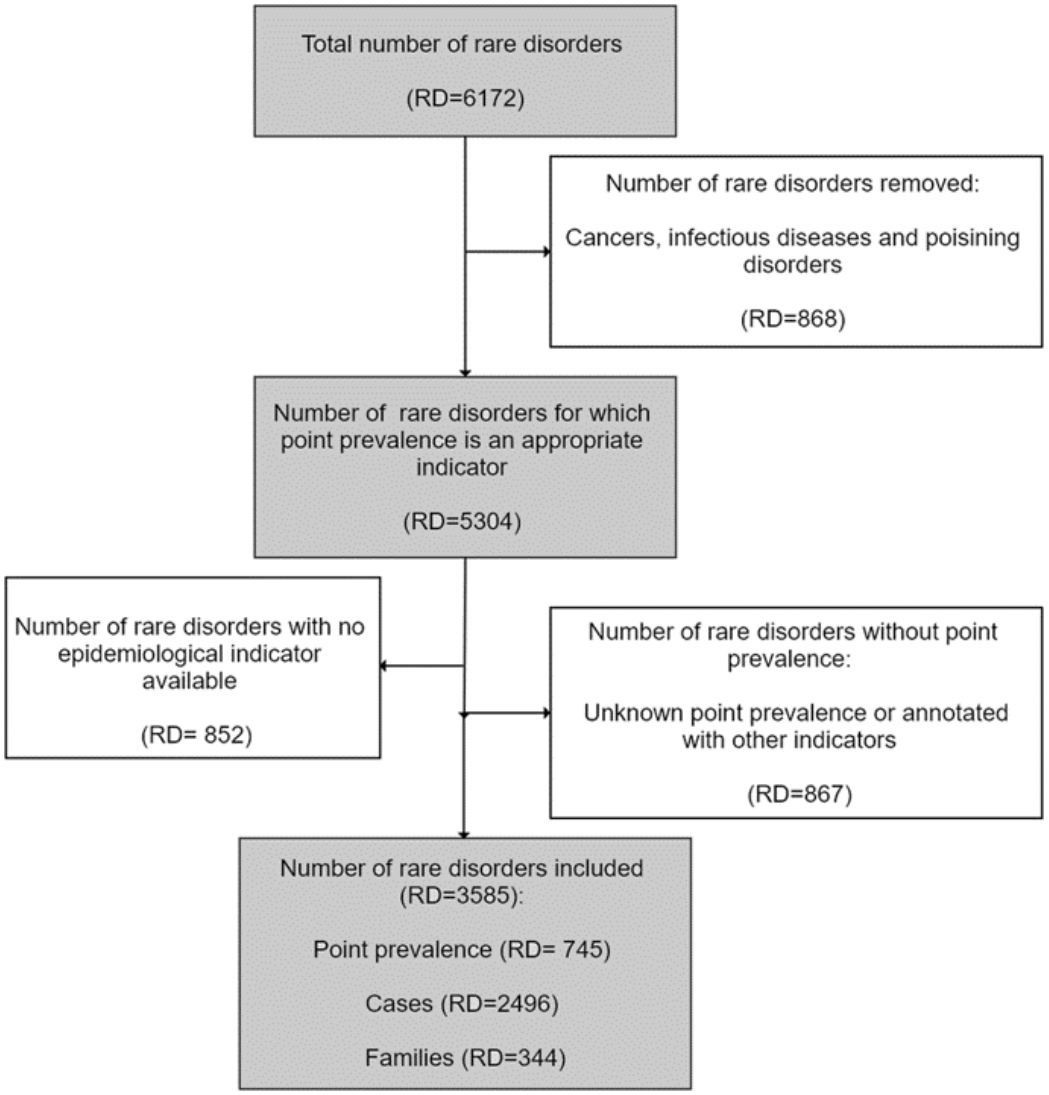
- 70% exclusively pediatric
- 12% exclusively adult
- 18% both pediatric & adult

❖ 72% are genetic in origin

- 86% of RD are prevalent diseases
- 14% of RD are incident diseases

Orphanet database, October 2018

3. Estimating how common are rare diseases?



3 situations:

- Point prevalence figure
- Prevalence class only:
  - Max value
  - Min value
- Nb of Cases-families:

$$= \frac{\textit{Indirect point prevalence } \sum \textit{ of cases and families reported}}{\textit{Global population size}}$$

How many patients suffering from RD?

Orphanet study * calculates best minimum estimate of the global prevalence of rare diseases:

3.5 - 5.9% of the population (263 - 446 Million people) worldwide

- Based on literature data for 68% of prevalent rare diseases
- Using EU definition (prevalence of less than 5 per 10,000).

Must also factor in additional contribution of incident diseases:

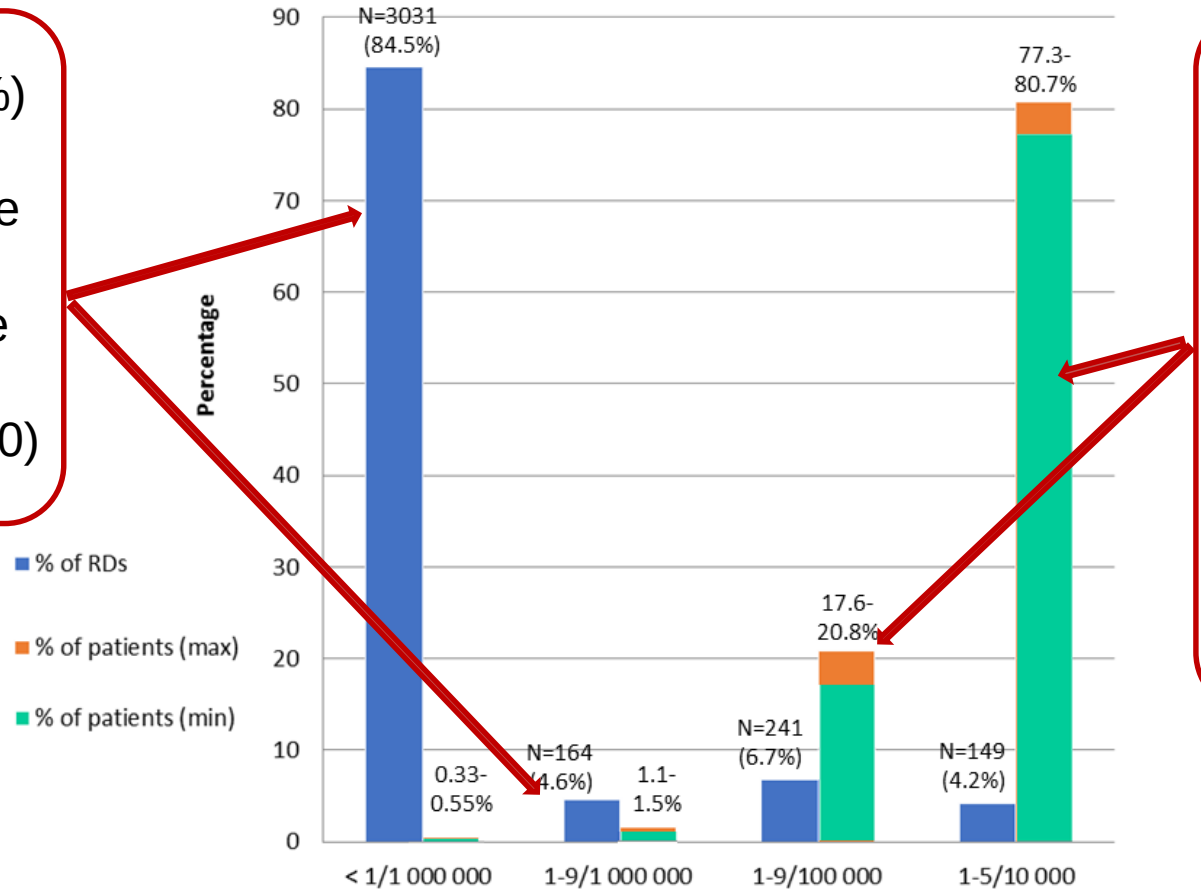
- Rare cancers: <6/100,000 annual incidence
  - 4,300,000 estimated total cases in Europe #
- Rare infectious diseases:
  - Global rare epidemic threats - hemorrhagic fevers (Ebola)
  - Rare in some regions and common in others - Malaria, Tuberculosis

** Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database,EJHG*

 # Gatta G, van der Zwanb AM, Casali PG et al. Rare cancers are not so rare: The rare cancer burden in Europe. Eur J Cancer. 2011 Nov;47(17):2493-511.

How many patients suffering from RD?

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



Almost all of the people with rare disease (>98%) have one of the 390 most prevalent diseases (more common than 1 per 100,000)

3.5 - 5.9% of the population (263 - 446 Million people) worldwide

*Based on 68% of prevalent RD based on EU definition (<50/100,000), data from literature.

Different RD definitions over the world

Country / Continent	RD Prevalence definition per 100,000	<1 /1,000,000	1-9 / 1,000,000	1-9/ 100,000	1-5 / 10,000
Korea [10]	5	✓	✓	+/-	-
Australia [11]	10	✓	✓	✓	-
Taiwan [12]	10	✓	✓	✓	-
Japan [13]	40	✓	✓	✓	✓
EU [4]	50	✓	✓	✓	✓
China [14]	76	✓	✓	✓	✓
USA [9]	80	✓	✓	✓	✓

- Cover a largely overlapping list of diseases
- Cover a very different RD patient population

Examples of the most common rare diseases - worldwide prevalences of 1-5 per 10,000

Recessive X-linked ichthyosis	Alpha-1-antitrypsin deficiency	Cystinuria
Steinert myotonic dystrophy	Non-acquired isolated growth hormone deficiency	Hereditary hemorrhagic telangiectasia
Alpha-thalassemia	Mucopolysaccharidosis type 2	Partial chromosome Y deletion
Turner syndrome	Stargardt disease	Distal arthrogryposis type 1
Fabry disease	Sickle cell anemia	Omphalocele
Phenylketonuria	Osteogenesis imperfecta	Retinitis pigmentosa
Marfan syndrome	Fragile X syndrome	Neuralgic amyotrophy

How can we routinely collect accurate and standardized rare disease information?

Where do we go next?

Making patients visible to take action

Counting people with rare diseases and their use of health care system needs to be implemented systematically in electronic records for useful data and combining of datasets

Adopting a common language globally across sectors

- Clinical: health and social sectors
- Research: registries and data repositories

Promoting large-scale disease registries

Making patients visible to take action

Integrating rare disease-specific coding in health systems is a challenge, but necessary

- ICD and other health coding systems do not capture all rare diseases
    - ICD used to capture reason for admission, not underlying chronic disease

- Implement ORPHAcodes*
    - Being implemented in Europe, Australia, Japan…
    - Interoperable with other international nomenclatures
    - Captures all rare disease data

RDCODE: EU collaborative grant for implementation of Orphacoding in clinical systems in 4 countries (2019-2021)

- helpdesk, nomenclature pack and tools

*Orphanet nomenclature of RD. http://www.orphadata.org/cgi-bin/rare_free.html#crossmodal

Open the discussion on …

- Agree on a common, comprehensive definition for prevalent RD worldwide?
- Agree on a different definition for incident diseases?

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Thank you!