

Meeting challenges in evaluating and measuring functioning in rare diseases: a collaboration between Orphanet and Mapi Research Trust

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Background

Rare diseases (RD) often result in a wide spectrum of disabilities, on which information is lacking. There is a need for standardised, curated data on the functional impact of RD to facilitate the identification of relevant Patient Reported/Patient Centered Outcome Measures (PROMs/PCOMs) as well as for the use of validated Quality of Life instruments based on functional outcomes. To address these issues, Orphanet (www.orpha.net) is partnering with Mapi Research Trust (MRT) in order to connect Orphanet to PROQOLID™, MRT's PROMs/PCOMs database through disease codes.

Methodology

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A general lack of information on the disabilities associated with rare diseases and the need for compensation result in a negative impact on social care for persons suffering of a RD. For this reason, the Orphanet Disability/Handicap project documents the functional consequences of rare diseases and their **impact on quality of life** using the [Orphanet Functioning Thesaurus](#), which is derived & adapted from the International Classification of Functioning, Disability and Health – Children and Youth (ICF-CY, WHO 2007).

Telephone interviews

- Highly structured interview to document functional consequences
- Consulted: medical experts, medical sector professionals and patient organisations

Questionnaire

- Questionnaire in 10 themes (in English, French and German) to structure interviews.
- Based on the [Orphanet Functioning Thesaurus](#)

Synthesis

- Interviews are conducted with one medical expert and one patient organisation, separately to assure accurate annotations for each RD analysed
- A synthesis is performed based on all responses provided

Annotation

- During the interviews, functional consequences of rare diseases are annotated according to their **frequency**, **severity** and **temporality**.

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Mapi Research Trust (MRT) is a non-profit organisation dedicated to improving patients' quality of life by facilitating access to Patient-Centered Outcome information. MRT web platform (ePROVIDE™) hosts three databases on Clinical Outcome Assessments (COAs) including PROQOLID™ which provides information on over 2,570+ COAs covering all therapeutic areas updated in collaboration with COA developers and copyright holders.

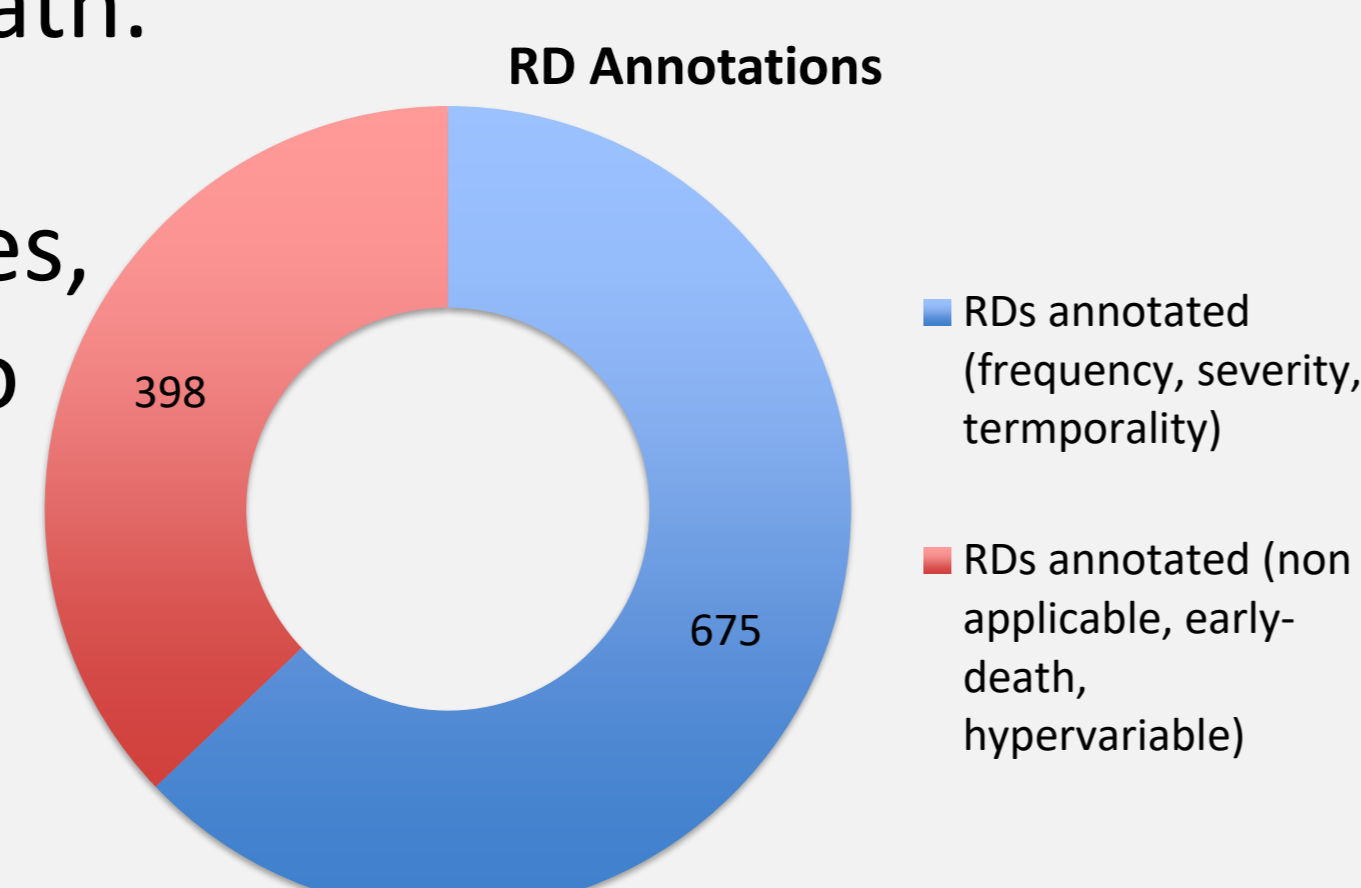
In order to link PROQOLID™ data with Orphanet disability data, the taxonomy used to qualify RDs in PROQOLID™ was reviewed and mapped to Orphanet's. All PROMs developed for RDs were identified, and all products approved by the FDA and EMA from 2002 to 2017 with an orphan drug designation (ODD) and a PRO claim were listed.

Results

• The Orphanet knowledge database contains over 6 000 rare diseases of which 1073 RD have been assessed for their functional consequences and are available online.

• Of those 1073 RD, **675** have been annotated using the functional consequences questionnaire based on their severity, frequency and temporality. The remaining **398** RD were annotated, after discussions with medical experts, as either being highly variable, non applicable or resulting in early-death.

• Of the 390 most prevalent rare diseases, **156** have been annotated according to their functional consequences.



PROMS developed in RD

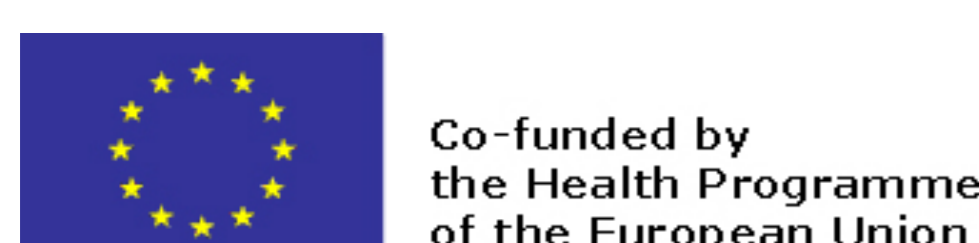
In PROQOLID™, 64 RD were identified to date for which 144 PROM were developed. The RD with the most PROM were sickle cell anemia, spinal cord injuries, cystic fibrosis, all forms of hemophilia A and B and Duchenne Muscular Dystrophy.

Regulators' perspective on PROMS in RD

The EMA and FDA labels review showed that 17.4 % of the orphan drugs included a PROM claim. PROM used in labels were primarily focusing on symptoms (100%), rarely on functioning (4%) or health-related quality of life (12%).

Conclusion

Linking these two databases, and providing standardised, curated data, will enable the community to identify PROMs/PCOMs for RD, and is the first step towards validated Quality of Life instruments based on functional outcomes.



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