PRO147: MAPPING PROQOLID TO RARE DISEASES: A ON-GOING COLLABORATION BETWEEN MAPI RESEARCH TRUST AND ORPHANET

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Objectives

Patient-Reported Outcome (PRO) assessment is critically needed in clinical research on rare diseases (RD). However, the development of specific PRO measures (PROMs) is an arduous, costly and time-consuming task, and usual strategies to support patient-centric development for Orphan Drugs (OD) fall short. To bridge this gap and help researchers identifying the relevant measures, domains or items, Orphanet and Mapi Research Trust (MRT) have decided a joint effort to connect their databases. Orphanet is an international Consortium of 40 countries across the globe and a reference source of information on RD whose mission is to improve the diagnosis, care and treatment of patients with RD. Orphanet has developed a database describing more than 7000 RD. MRT is a resource and information/documentation centre aiming at helping researchers, clinicians, patients associations, regulators and payors to use Health-Related Quality of Life (HRQoL), PROs and other Clinical Outcomes Assessments in their work and mission. MRT has developed PROQOLID™, a database which describes more than 8000 PROMs in 2019. Our project is to apply Orphanet's approach to code PROQOLID™ PROM, and ultimately to connect the two databases.

Methods

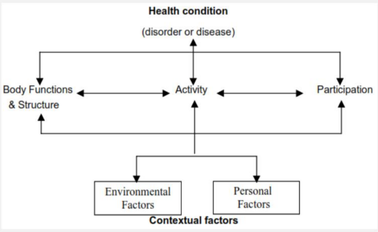
The preliminary steps involved 1) mapping **taxonomies** and 2) performing **inventories**:

- Taxonomies used in PROQOLID™ to qualify RD were reviewed and mapped to Orphanet's
- Inventories involved:

a) **Inventory of functional consequences of Rare Diseases by Orphanet:** Indexing by Orphanet of RD with the adapted International Classification of Functioning, Disability and Health (ICF).
Orphanet adapted the WHO ICF indexing, for a codification of RD impacts on patient's lives into 10 domains. A questionnaire was developed to cover these 10 domains and data were collected from medical experts, disability professionals and/or patient support groups/representatives. Functional consequences are collected by frequency, temporality, severity and loss of ability.

b) **Inventory of PROM claims in Rare Diseases:** Listing all products approved by the FDA and EMA (from 01/2002 to 06/2017) with an orphan drug designation and with a PRO claim).

c) **Inventory in PROQOLID™ of PROM developed in Rare Diseases:** identifying all PROM developed in a specific RD



International Classification of Functioning, Disability and Health, (ICF) developed by WHO in 2001 (WHO website)

Results

a) Inventory of functional consequences of Rare Diseases by Orphanet

Out of the 6200 RD listed in Orphanet, 530 were indexed with the adapted ICF.
The percentage of RD impacting each of the 10 overarching ICF domains range from 35% (Sleep issues) to 72% (Social Life)

Orphanet ICF Domains	Impact in RD (%)*
Social life	72
Daily activities	67
Motor skills	62
Self-care	60
Moving around	58
Interpersonal skills	56
Understanding	53
Communicating with others	49
Temperament and behaviour	46
Sleeping/staying awake	35

** % of number of RD for which item related to the domain is mentioned by the interviewee*

b) Inventory of PROM claims in Rare Diseases

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%).

c) Inventory in PROQOLID™ of PROM developed in Rare Diseases

In PROQOLID™, 64 RD were identified for which 144 PROM were developed. The most frequent RD with PROM were sickle cell anemia, spinal cord injuries, cystic fibrosis, all forms of hemophilia A and B and Duchenne Muscular Dystrophy (see examples in Table 2).

Rare Disease name	Orphanet Code	MESH Code	MESH Term	PROM name described in PROQOLID™
Hemophilia B	98879	D002836	Hemophilia B	Developped in A type: • Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden (Adapted INHIB-QoL) • Patient Perception and Preference for Haemophilia Treatment (HaemoPREF) Developped in A and B types: • Haemo-SYM • Hemophila-specific Quality of Life Questionnaire for Adults (Haemo-QoL-A) • Hemophilia-specific health-related quality of life questionnaire (A36 Hemofilia-QoL®) • Hemophilia Activities List (HAL) • Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment • Questionnaire: Hemophilia Specific (WPAI+CIQ:HS) • Patient Reported Outcomes, Burdens and Experiences (PROBE) • Paediatric Haemophilia Activities List (PedHAL) • Hemophilia Well-Being Index (HWBI) • Haemophilia age group-specific Quality of life questionnaire (QUAL HEMO) • Haemophilia Quality of Life Questionnaire for Children (Haemo-QOL) • Haemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) • Canadian Hemophilia Outcomes - Kids' Life Assessment Tool (CHO-KLAT) • Patient Perception and Preference for Haemophilia Treatment (HaemoPREF) • HemoLatin-QoL
Hemophilia A	98878	D006467	Hemophilia A	
Duchenne muscular dystrophy	98896	D020388	Muscular Dystrophy, Duchenne	• Life Satisfaction Index for Adolescents (LSIA) • Quality of Life in Neurological Disorders (Neuro-QOL) • Work Productivity and Activity Impairment Questionnaire: Duchenne Muscular Dystrophy, Caregiver Version 2.0 (WPAI:DMD-CG) • Pediatric Quality of Life Inventory™ Duchenne Muscular Dystrophy Module (PedsQL™ Duchenne Muscular Dystrophy Module)

Table 2: Examples of PROM developed in RD

Given the complexity of RD classification, a grey area in the indexation remains for PROM developed in diseases with rare forms:
Is a questionnaire developed in a non rare disease appropriate for rare forms of this disease ? Please see below an example in Parkinson disease:

Rare Disease name	Orphanet Code	MESH Code	MESH Term	PROM name described in PROQOLID™
Corticobasal syndrome	454887	D010300	Parkinson Disease	• Parkinson's Disease Questionnaire (PDQ-39) • Parkinson's Disease Quality of Life Scale (PDQUALIF) ➔ **Could the PDQ-39 or PDQALIF be appropriate for rare forms of Parkinson disease?**
Hereditary late-onset Parkinson disease	411602			

Conclusions

The impact of RD on functioning is multiple and frequent, but not reflected in OD labels. Less than 1% of RD have at least one specific PROM capturing its impact on any aspect of the patient's life.
Connecting the Orphanet database describing the functional impact of RD and the MRT database describing the exact functions actually captured by existing PROMs developed for other disease or condition, is highly desirable to facilitate the search of fit-for-purpose measures.
Such connection is also technically feasible with appropriate, systematic coding of both databases based on same coding index; however, the volume of RD in Oprhanet database and PROMs in PROQOLID database necessitate a significant investment to code the full databases.