

Using PROMs in HTA for rare disease treatments

Amanda Whittal¹, Elena Nicod¹, Michela Meragaglia¹, Michael Drummond²

1 – SDA Bocconi School of Management, Milan, Italy

2 – University of York, United Kingdom

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Summary: Developing and administering PROMs for rare disease treatments (RDTs) to be used in health technology assessment (HTA) can be challenging because of RDT specificities. This research aims to identify key factors for stakeholders to consider when using different types of PROMs in HTA for RDTs. A scoping review of scientific and grey literature was conducted, and information was extracted regarding the advantages, challenges, and potential solutions for using different types of PROMs for RDTs. A better understanding of these elements may help HTA stakeholders better manage the challenges in the use of PROMs for RDTs.

Background and purpose

- Patient-reported outcome measures (PROMs) are tools for measuring patient experiences with disease and treatment
- Given the often very severe, disabling and life-threatening nature of rare diseases, considering PROMs allows for deeper understanding of the impact of treatment beyond clinical endpoints¹, a fact increasingly recognised as significant for HTA
- Use of PROMs in RDTs poses unique challenges due to small patient populations, disease heterogeneity, lack of natural history knowledge, and short-term studies²⁻⁴
- This research aims to identify key factors to consider when using different types of PROMs for RDTs in HTA by extracting and synthesising information about the advantages, challenges and potential solutions in using different types of PROMs, and the associated data collection and psychometric property considerations

Methodology

- A scoping review of scientific (PubMed) and grey literature was conducted, with no restrictions on date or publication type
- **Search terms:** *patient reported outcome measure-, patient reported outcome-, prom-, rare disease-, RDT-, orphan medicinal product-, OMP-, challenge-, recommend-* (PubMed) and *patient reported outcome measure, rare disease, health technology assessment* (grey literature)
- **Inclusion criteria:** English language, any insight into PROMs for RDTs in terms of advantages, challenges, and solutions for PROM application, in general and specifically related to HTA. **Exclusion criteria:** not in English, only described application or development of a PROM without relevant description for use with RDTs
- Results were organised into categories considered most important to better ensure successful use of PROMs for RDTs in HTA: 1) data collection/ measurement and psychometric properties, 2) generic PROMs, 3) existing disease-specific PROMs, 4) existing disease-family specific PROMs, 5) creating new disease specific PROMs

Results

- **Included records:** 27 of 66 records identified through PubMed were included, plus five records from the grey literature.
- **Data collection/measurement and psychometric properties**
Challenges: lack of validated PROMs, diversity of use of existing PROMs, difficulties recruiting enough patients for trials, difficult to capture disease manifestation heterogeneity, patients often cannot self report, conventional psychometric analyses require large samples and high quality data. **Solutions:** develop core recommended outcome measures, multi-site/international data collection, proxy measures, use of specific psychometric approaches that can deal with small samples.
- **Generic PROMs (Table 1)**
Advantages: most allow comparison and provide utility data, often preferred by HTA bodies. **Challenges:** may not be sensitive enough to disease specificities. **Solutions:** use generic *and* disease specific PROMs in a complementary way.
- **Existing disease specific PROMs**
Advantages: more sensitive than generic PROMs. **Challenges:** cannot compare patient groups, lack of validated disease specific PROMs. **Solutions:** use generic *and* disease specific PROMs in complementary way.
- **Existing disease-family specific PROMs**
Advantages: more sensitive than generic, more of them exist than disease specific. **Challenges:** may not correspond specifically enough to disease. **Solutions:** use multi attribute questionnaires, concept specific instruments.

Type of PROM	Advantages (A)/ Challenges (C) in RDTs	Potential solutions
Generic PROMS	A	<ul style="list-style-type: none"> • Validated generic PROMs are often preferred by HTA agencies • Preference-based generic measures provide utility data • Generic PROMs allow for comparability across patient populations
	C	<ul style="list-style-type: none"> • Can be unresponsive and miss important information for specific RDTs • Use both a generic <i>and</i> a disease-specific instrument for RDTs in a complementary way • A general RD approach might be to develop a variety of measures with the same basic presentation that include some features of generic measures, but also include the personal and societal context that is appropriate for patients and disease-specific aspects
	C	<ul style="list-style-type: none"> • A generic PROM may be validated, but not necessarily for the population in which it is being used • Selected generic PROMs should ideally be validated for the specific selected population • Benchmarking the range of utility values in diseases with similar characteristics can be useful to validate results of new RD utility studies

Table 1. Example of advantages, challenges and potential solutions for generic PROMs

- **Creating new disease specific PROMs**
Advantages: tailored to disease, can capture meaningful outcomes. **Challenges:** rare disease natural history often poorly understood, effective approaches to PROM creation not always clear. **Solutions:** use all available sources of information to understand disease, take into account any existing guidance

Conclusions and practical application

This study offers the first comprehensive review of the different challenges and potential solutions that may arise for the use of PROMs for RDTs, including the key areas of: data collection/measurement, psychometric properties and types of PROMs (generic, disease specific, disease -family specific, creating new PROMs). The findings are a practical tool for all stakeholders to better understand the potential challenges that may be encountered when using specific types of PROMs for RDTs in HTA, and the potential solutions that may help to overcome them.

References

1. Contesse, M. G., Valentine, J. E., Wall, T. E., & Leffler, M. G. (2019). The case for the use of patient and caregiver perception of change assessments in rare disease clinical trials: a methodologic overview. *Advances in therapy*, 36(5), 997-1010.
2. Acaster, S. (2017). Patient-reported outcome and observer-reported outcome assessment in rare disease trials. *Value in Health*, 20(7), 856-857.
3. Benjamin, K., Vernon, M. K., Patrick, D. L., Perfetto, E., Nestler-Parr, S., & Burke, L. (2017). Patient-reported outcome and observer-reported outcome assessment in rare disease clinical trials: an ISPOR COA emerging good practices task force report. *Value in Health*, 20(7), 838-855.
4. Morel, T., & Cano, S. J. (2017). Measuring what matters to rare disease patients—reflections on the work by the IRDiRC taskforce on patient-centered outcome measures. *Orphanet journal of rare diseases*, 12(1), 171.

Abbreviations
 PROM = patient reported outcome measure
 HTA = health technology assessment
 RDT = rare disease treatment
 OMP = orphan medicinal product

