Recommendations for better use of quality of life evidence in HTA for rare diseases

Elena Nicod, PhD, Director

Dolon Ltd

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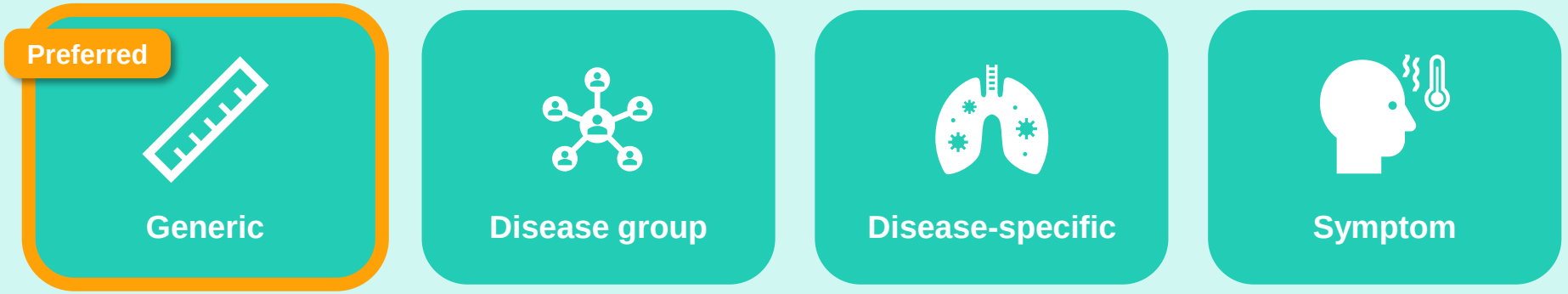
PROMs and considerations for their use in HTA

4 types of PROMS



	Added benefit assessment	Cost effectiveness assessment
How is it used?	Directly in assessment	To derive health state utility values (HSUVs) for use within economic models from: ✓ PROMs (e.g. directly, mapping) ✓ Patient responses (e.g. visual analogue scale, standard gamble) ✗ Experts (often not accepted) HSUVs are numerical values measuring quality of life in a given health state (1 = full quality of life; 0 = “dead”)

Improving interpretation of evidence relating to quality of life in health technology assessment of rare disease treatments[6]

Five recommendations derived from the following research:

What is known in the literature

- *Scoping review of use of PROMs in rare diseases*[1]
- *Systematic review on use of mapping in rare diseases*[2]
- *Use of HSUV techniques in rare diseases: challenges and opportunities* [3]

Use in practice and learnings

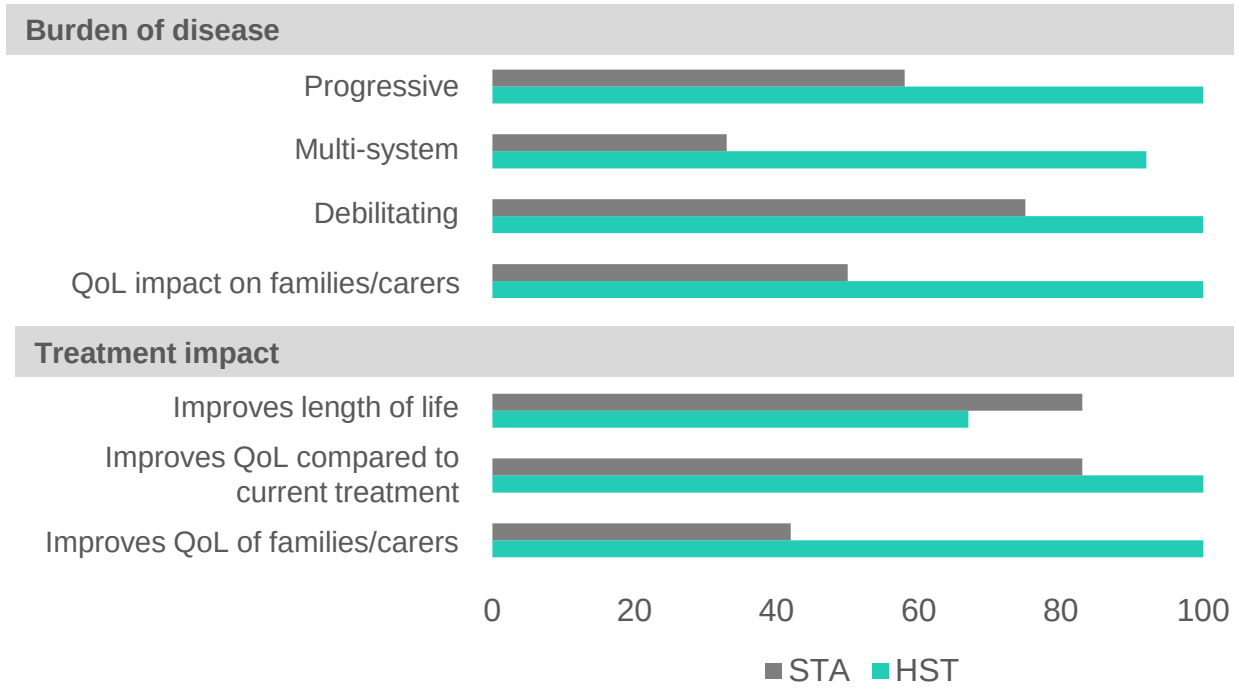
- *Consideration of QoL in the HTA of rare disease treatments*[4]
- *Participant observation of technology appraisal committees*[5]

1. Whittal A, Meregaglia M, Nicod E. The use of patient-reported outcome measures in rare diseases and implications for health technology assessment. The Patient. 2021 Jan
2. Meregaglia M, Whittal A, Nicod E, Drummond M. 'Mapping' health state utility values from non-preference-based measures: a systematic literature review in rare diseases. Pharmacoeconomics. 2020 Jun;38(6):557-574
3. Meregaglia M, Nicod E, Drummond M. The estimation of health state utility values in rare diseases: overview of existing techniques. Int J Technol Assess Health Care. 2020 Oct;36(5):469-473
4. Nicod, E., Meregaglia, M., Whittal, A. et al. Consideration of quality of life in the health technology assessments of rare disease treatments. Eur J Health Econ 23, 645–669
5. Facey et al. Preliminary results from participant observation of appraisal committee meetings
6. Nicod E, Lloyd AJ, Morel T, Meregaglia M, Upadhyaya S, Whittal A, Facey K, Drummond M. Improving Interpretation of Evidence Relating to Quality of Life in Health Technology Assessments of Rare Disease Treatments. The Patient-Patient-Centered Outcomes Research. 2023 Jan;16(1):7-17.

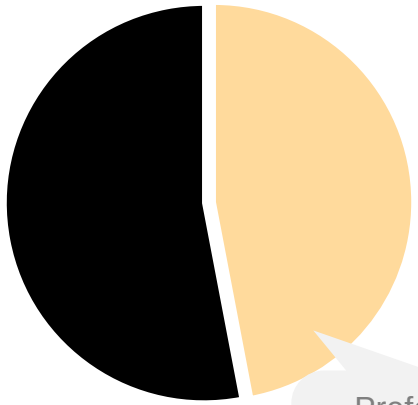
1 Given the complexity, severity and lack of clinical knowledge associated with many rare diseases, it is essential to evaluate the impacts of the condition, and the impacts of treatments, on the QoL of patients and carers

NICE

Burden of disease and treatment impact of medicines approved through NICE's HST pathway versus standard technology appraisal[1]



...but only 47% of HTA bodies require PRO evidence[2]



Preference for routinely collected data from generic/ validated PROMs

1. Nicod E, Meregaglia M, Whittal A, Upadhyaya S, Facey K, Drummond M. Consideration of quality of life in the health technology assessments of rare disease treatments. EU J Health Economics. 2022 Jun 1:1-25.
2. Nicod E, Lloyd AJ, Morel T, Meregaglia M, Upadhyaya S, Whittal A, Facey K, Drummond M. Improving Interpretation of Evidence Relating to Quality of Life in Health Technology Assessments of Rare Disease Treatments. The Patient-Patient-Centered Outcomes Research. 2023 Jan;16(1):7-17.

2 When critically assessing evidence, challenges related to development and administration of patient-reported outcome measures in rare diseases should be taken into account

1

Challenges in selecting appropriate PROMs or developing new PROMs

(e.g., due to lack of disease knowledge, complexity of condition)

2

Challenges to collecting PRO data

(e.g., due to young and cognitively impaired populations, high rates of missing data)

3

Challenges related to poor or inconclusive PRO results

(e.g., due to response shift phenomenon; poor psychometric properties, floor / ceiling effects)

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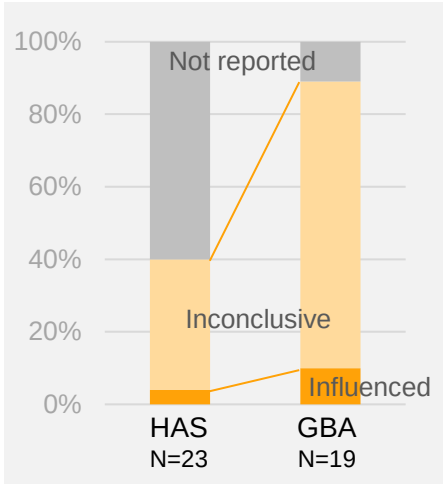
3 During the appraisal, interpretation of evidence from patient reported outcome measures and health state utility values should recognize that lack of significant effect does not necessarily imply lack of benefit on QoL[2]

	Added benefit assessment	Cost effectiveness assessment
QoL in HTA	PRO results qualitatively examined	Utility values used to quantify QoL for each health state in economic model
Impact of evidence[1] *(Non-cancer orphan medicines)*	**HAS** **GBA** **Limited impact** • Not clinically relevant or significant endpoint ≠ *country evidentiary requirements* • Not accounted for 	**NICE** **65% of utilities derived from conventional approaches were uncertain** • Benefits / long-term effects not captured • Insensitive to change / ceiling effects • Implausible health states **ZIN** **100% uncertain (2/2)**

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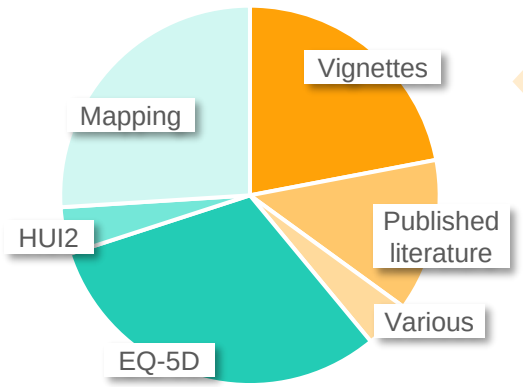
4 Other forms of evidence, including non-conventional approaches to QoL and patient and clinical input and evidence, should be considered to enable a fuller appreciation of the impact of a rare disease treatment on QoL[3]

Non-conventional techniques to HSUVs

NICE Mostly in HST appraisals



Reasons[1,2]

- No trial QoL data
- Missing HSUV for model health states
- Mapping algorithm on healthy population
- Trial QoL not used

There is a lack of clarity on acceptability and robustness of methodological approach

Patient-based evidence

NICE Mostly to support interpretation of EQ-5D

1 Patient evidence

Surveys, stories, submissions

- Interpretation of uncertainty
- Patient perspectives (e.g., administration)
- Survey deriving EQ-5D into HSUV

2 Patient input

- Interpretation of uncertainty
- Dimensions not captured in model
- Patient perspectives (e.g., tolerability)

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5 It is important to consider QoL impacts on the family and carers to better capture the added benefit of a medicine[2]

Nature of rare diseases

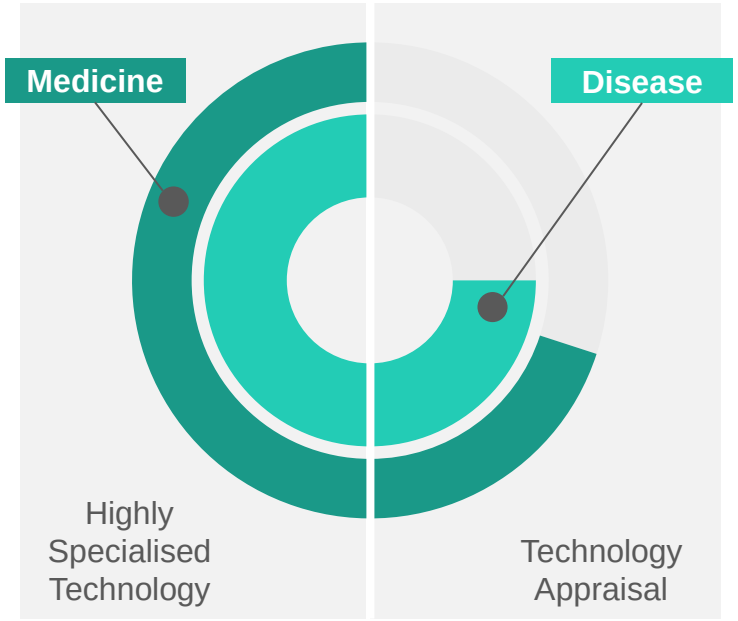
- **80%** affect children
- Genetic
- Life-threatening and debilitating
- Multi-system
- Require supportive care

Impact on carers

- Heavy time burden
- Reduced professional activity
- Financial burden
- Deteriorated mental health
- Burden of care
- Difficulties in daily tasks

NICE

Carer impact on QoL of NICE non-cancer orphan medicines[1]



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Five recommendations for PROMs in rare diseases

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2	When critically assessing evidence, challenges related to development and administration of patient reported outcome measures in rare diseases should be taken into account
3	During the appraisal, interpretation of evidence from patient reported outcome measures and health state utility values should recognize that lack of significant effect does not necessarily imply lack of benefit on quality of life
4	Other forms of evidence, including non-conventional approaches to quality of life and patient and clinical input and evidence, should be considered to enable a fuller appreciation of the impact of a rare disease treatment on quality of life
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