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A QALY is NOT a QALY when it comes to Health Technology Appraisals of Paediatric Rare Diseases

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BACKGROUND

- The phrase “a QALY is a QALY is a QALY” is often quoted to emphasise that all QALYs are equal regardless of the patient population accruing benefit.
- Consequently, the ICER threshold remains consistent irrespective of the population. However, is a ‘one size fits all’ approach appropriate when appraising paediatric rare diseases?
- Aside from highly specialised technology (HST) appraisals, NICE does not differ its methods and processes depending on the population, meaning paediatric rare populations (where the paediatric indication is the first or only indication to launch) are evaluated equivalently to adult populations.
- As such, there is limited guidance on how to assess paediatric rare populations in health technology appraisals, specifically capturing clinical benefit, patient and carer quality of life, and societal preferences.

OBJECTIVE

- This conceptual poster discusses different approaches to assessing the impact of treatments for paediatric rare diseases on quality of life in children and how to appropriately assess rare conditions via the NICE single technology appraisal (STA) process.

ASSESSING THE IMPACT OF TREATMENTS FOR RARE DISEASES ON QUALITY OF LIFE IN CHILDREN

- The updated NICE manual does not recommend specific measures of health-related quality of life (HRQoL) in children and young people. This poses a number of challenges as outlined below:

Box 1: Challenges for assessing quality of life in children

- NICE recommends the use of a generic measure with good psychometric performance, with the EQ-5D questionnaire preferred despite this not being intended for use in children.
- The usefulness of generic tools for assessing the impact on rare disease is limited since these will not robustly reflect all relevant aspects of the disease.
- A number of instruments exist for measuring HRQoL in children but these commonly rely on proxy-reported data.
- A lack of a UK value set for paediatric HRQoL instruments makes it challenging to generate utility values for economic evaluations of treatments for paediatric rare diseases.

- It was acknowledged in the NICE appraisal of risdiplam for the treatment of spinal muscular atrophy (SMA) (TA755) that there is not an ideal source of utilities that robustly reflects the differences in HRQoL between motor milestones in people with SMA.
- This is being addressed during the period of managed access for risdiplam - the approach being taken for collecting appropriate health state utility values (Figure 1) can serve as a conceptual framework for generating HRQoL evidence for paediatric rare diseases.

Figure 1. Conceptual framework for generating HRQoL evidence for paediatric rare diseases

1. Identify relevant domains of HRQoL for the disease in question

- ❑ Identify which HRQoL domains are of potential relevance, crosschecking instruments for similar disease types as necessary.
- ❑ Validate identified domains and revise according to patient and clinical expert opinion to produce a disease specific framework for capturing the impact on HRQoL by adding, simplifying, disaggregating and deprioritising domains as necessary.
- ❑ Assess which domains impact HRQoL in a way that is relevant for paediatric rare diseases – exclude any domains deemed to be not relevant.

2. Evaluate existing tools

- ❑ Evaluate which existing tools (both generic and disease-specific) could measure the relevant domains.
- ❑ Highlight the limitations of EQ-5D questionnaire, including an assessment on its validity, responsiveness and reliability to reflect paediatric HRQoL.
- ❑ Determine the appropriateness of each tool based on:
  - Published guidance supporting its use in the given population/condition;
  - The existence of a UK value set or mapping algorithm;
  - The ability to match domains in each tool to the domains in the disease specific framework.

3. Selection of tools

- ❑ Assess the content validity of possible tools to determine whether the range of items and response levels are sufficient to demonstrate a change in HRQoL between health states.

- The HRQoL framework in SMA generated by this development process consisted of 13 domains (Table 1), all of which were considered to relevant to at least one of the relevant patient age groups, while seven domains were deemed relevant to caregivers.
- This framework was validated for its development methodology and relevance to the disease by experts in utility collection and a patient advocacy group; feedback from these stakeholders was used to revise and refine the framework.

Table 1. Survey outline and tools utilised for risdiplam HRQoL data collection

Group	Baseline	Tools utilised			
1 – Person with SMA aged 7	Completion of description questions	DMD-QOL-8D self report			-
2 – Person with SMA aged 8–12					PedsQL child report
3 – Person with SMA aged 13–18					Teen report
4 – Person with SMA aged 19–25					Young adult report
5 – Person with SMA aged 26+					Adult report
6 – Caregiver (pwSMA aged 0–1)	Completion of description questions about person cared for	DMD-QL-8D proxy report	EQ-5D	Supplementary caregiver questions	-
7 – Caregiver (pwSMA aged 2–4)					Parent report for toddlers
8 – Caregiver (pwSMA aged 5–7)					Parent report for young children
9 – Caregiver (pwSMA aged 8–12)					Parent report for children
10 – Caregiver (pwSMA aged 13–18)					Parent report for teens
11 – Caregiver (pwSMA aged 19–25)					Parent report young adults
12 – Caregiver (pwSMA aged 26+)					Parent report for adults
13 – Caregiver (pwSMA aged 7–26+)		-			-

Abbreviations: pwSMA, person with spinal muscular atrophy; ; SMA, spinal muscular atrophy

APPROPRIATE CONSIDERATION OF THE RARITY OF CONDITIONS DURING THE NICE STA PROCESS

- NICE currently evaluates treatments for very rare conditions (considered to be those with a prevalence of ≤1 in 50,000 patients) via the HST programme, with a willingness to pay threshold in excess of £100,000 per QALY gained.
- However, the majority of treatments for rare diseases (≤5 in 10,000 people affected) do not qualify for this and are subsequently appraised via the STA route and the standard £20,000-30,000 threshold.
- NICE adopted the severity modifier in order to fairer represent societal preferences of severe conditions; however, not all treatments for paediatric rare diseases would qualify for a greater QALY weighting given the substantial length of life that would be factored into calculations.
- Treatments for paediatric rare diseases are therefore disadvantaged due to challenges in evidence generation in small patient populations and high treatment costs.
  - A recent review concluded that treatments for rare diseases face more committee meetings and longer appraisal times compared to non-orphan medicines in the STA process[1].
- The QALY alone is insufficient to capture the value of treatments for paediatric rare diseases, therefore it is critical that all value elements associated with rare conditions are factored in during decision making for an STA appraisal.
- Considerations for the appropriate assessment of rare diseases via this route are presented below:

Box 2: Considerations for appraising treatments for paediatric patients with rare diseases via the NICE STA process

Rarity modifier for paediatric patients to align with other HTA bodies

- NICE previously dismissed incorporating a rarity modifier in its methods review as it was concluded that rarity was not valued highly by society; however, would society value rarity differently in the context of paediatric diseases?
- This could be addressed by automatically assigning a greater QALY weighting, similar to the severity modifier NICE currently use, for treatments indicated for paediatric rare diseases that are granted orphan drug designation by the MHRA.
  - This would align with other HTA bodies globally (e.g. Norway, Sweden, Australia) as well as ensuring consistency across the UK since the SMC accepts a greater level of uncertainty in the economic evaluation of treatments with orphan designation while also allowing for patient and clinician engagement.

Framework for greater acceptance of uncertainty and consistency in decision making

- The revised NICE manual highlights that committees may be able to accept a higher degree of uncertainty for conditions where evidence generation is challenging, such as rare diseases.
- There is a need for transparent guidance on how committees will assess uncertainty in order to apply a greater flexibility in its decision making so manufacturers can address this in their submissions.
- Treatments for paediatric rare diseases being appraised via the STA route should be reviewed by the HST committee to ensure consistency in decision making.

Societal and ethical values

- Align with recommendations from the UK Rare Disease Framework[2] to minimise delays and improve access to specialist care treatments and drugs considering:
  - The time taken for patients to be accurately diagnosed with a rare disease;
  - The urgency for these patients to receive treatment.

CONCLUSIONS

- A QALY is not a QALY when appraising treatments for paediatric rare diseases via the usual NICE STA process – this places such technologies at a disadvantage and results in an inequity in access to orphan designated treatments in the UK and compared to other countries.
- The modular approach to reviewing its methods allows NICE to pilot new approaches and/or update its guidance to reflect new recommendations – the considerations outlined herein will help to ensure that decisions on reimbursing treatments for paediatric rare diseases truly reflect the benefit offered to these patients.

DISCLOSURES

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REFERENCES

1. Clarke, S., et al. J. Orphanet J Rare Dis 2021;16,:218;