Is there enough focus on capturing data from pediatric patients and their caregivers in non-oncology indications?

Jan McKendrick, Reece Grindley, Sudesh Basra
Avalere Health, London, UK

PCR31

Background

The EU Pediatric Regulation 2006 encourages research and development of new medicines to include pediatric populations by, for example, requiring a Pediatric Investigational Plan (PIP).[1] Additionally, the importance of patient involvement in healthcare decisions is also recognized in the National Institute for Health and Care Excellence (NICE) guideline on experience of healthcare for babies, children, and young people.[2]

Quantifying how conditions and treatments affect children's daily lives and overall quality of life (QoL) can be used to help guide healthcare decisions; it is also important to consider the financial, emotional, and even physical burden for caregivers of pediatric patients.

However, it is unclear to what extent quantitative and qualitative data are collected from pediatric patients and their caregivers for new treatments, and how data are being used to influence health technology assessment (HTA) outcomes.

Methods

Assessments of pharmaceutical treatments for non-oncology pediatric populations (non-oncology indications constitute 93% of all PIPs[2]) conducted by NICE from January 2021 to June 2024 were identified. Instruments capturing pediatric patient reported outcome (PRO) data and caregiver burden/QoL data for the treatment were identified, along with any associated commentary from NICE. Additional data and/or discussion around patient or caregiver burden were also captured.

Results

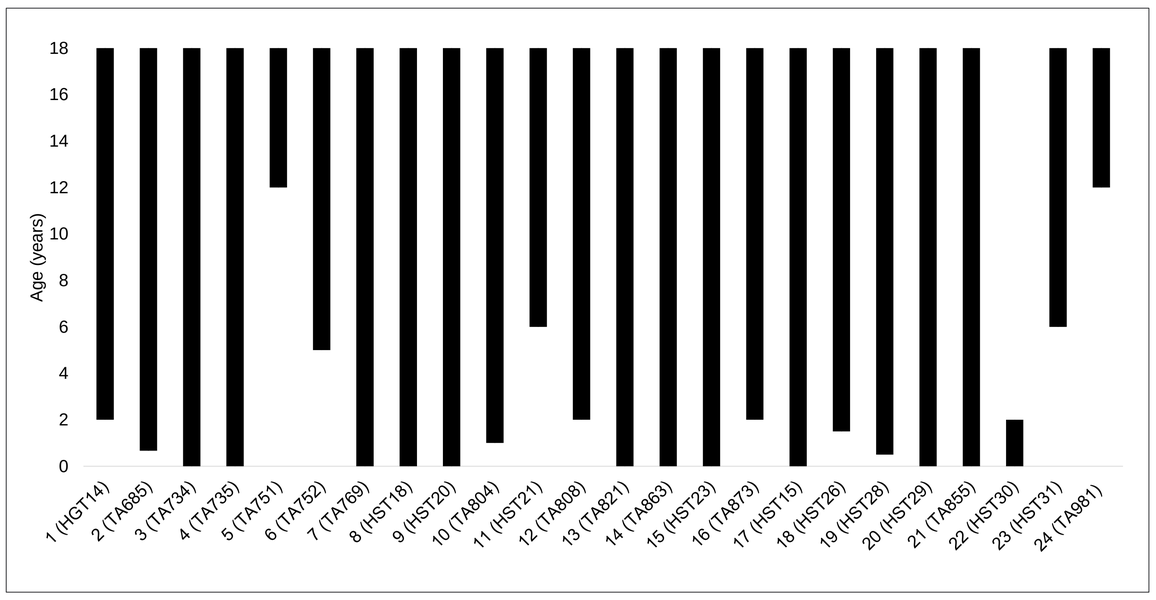
Between January 2021 and June 2024, 37 technology appraisals or highly specialized technology (HST) guidance documents for pediatric populations were published, with 24 in non-oncology populations (Table 1).

Table 1: Details of assessments of non-oncology pediatric indications

	Assessment	Published date	Generic PRO	Disease-specific PRO	Caregiver instrument
1	Metreleptin for treating lipodystrophy (HST14)	24-Feb-21			
2	Anakinra for treating Still's disease (TA685)	31-Mar-21			
3	Secukinumab for treating moderate to severe plaque psoriasis in children and young people (TA734)	7-Oct-21		✓	
4	Tofacitinib for treating juvenile idiopathic arthritis (TA735)	20-Oct-21	✓	✓	
5	Dupilumab for treating severe asthma with type 2 inflammation (TA751)	8-Dec-21			
6	Belimumab for treating active autoantibody-positive systemic lupus erythematosus (TA752)	15-Dec-21	✓	✓	
7	Palforzia for treating peanut allergy in children and young people (TA769)	2-Feb-22		✓	
8	Atidarsagene autotemcel for treating metachromatic leukodystrophy (HST18)	28-Mar-22			
9	Selumetinib for treating symptomatic and inoperable plexiform neurofibromas (HST20)	5-May-22	✓		
10	Teduglutide for treating short bowel syndrome (TA804)	30-Jun-22			
11	Setmelanotide for treating obesity caused by LEPR or POMC deficiency (HST21)	6-Jul-22	✓		
12	Fenfluramine for treating seizures associated with Dravet syndrome (TA808)	8-Jul-22	✓		
13	Avalglucosidase alfa for treating Pompe disease (TA821)	24-Aug-22	✓	✓	
14	Somatrogon for treating growth disturbance in children and young people aged 3 years and over (TA863)	1-Feb-23	✓	✓	✓
15	Asfotase alfa for treating paediatric-onset hypophosphatasia (HST23)	1-Mar-23	✓		
16	Cannabidiol for treating seizures caused by tuberous sclerosis complex (TA873)	1-Mar-23	✓	✓	
17	Onasemnogene abeparvovec for treating spinal muscular atrophy (HST15)	19-Apr-23			
18	Eladocagene exuparvovec for treating aromatic L-amino acid decarboxylase deficiency (HST26)	19-Apr-23			
19	Birch bark extract for treating epidermolysis bullosa (HST28)	20-Sep-23			
20	Velmanase alfa for treating alpha-mannosidosis (HST29)	13-Dec-23	✓	✓	
21	Risdiplam for treating spinal muscular atrophy (TA755)	15-Dec-23	✓	✓	✓
22	Sebelipase alfa for treating Wolman disease (HST30)	10-Jan-24			
23	Setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome (HST31)	22-May-24	✓	✓	
24	Voxelotor for treating haemolytic anaemia caused by sickle cell disease (TA981)	12-Jun-24	✓		

Ages of patients included in the studies varied widely (Figure 1).

Figure 1: Age ranges included within the licensed indication



As per the European Medicines Agency's guidance, it was assumed that the indication "children" included all children under 18 years of age. "Babies" was assumed to include children of 0-2 years of age.

Nine assessments did not include PRO instruments for pediatric patients in the pivotal clinical study, and of the remaining 15 assessments (Figure 2):

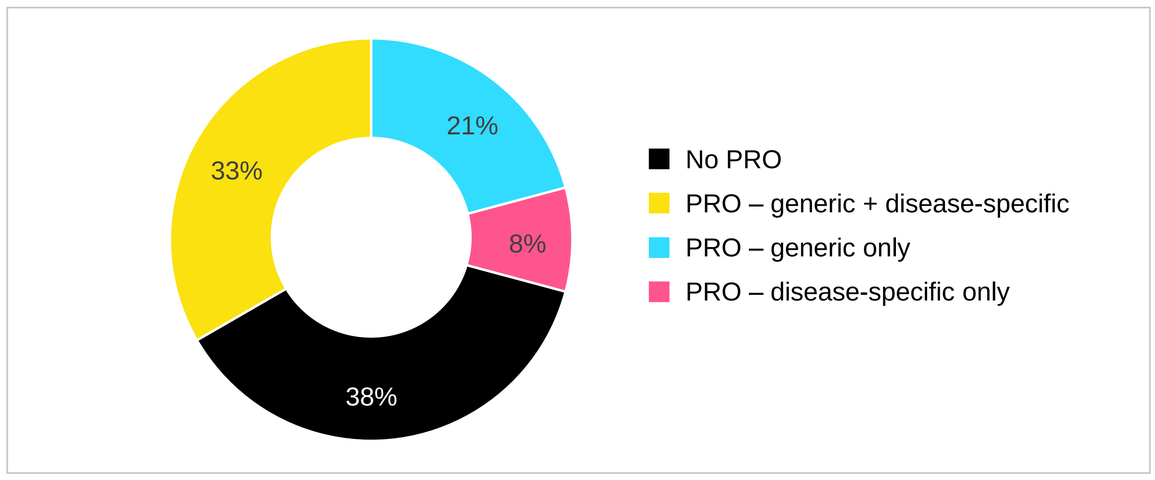
- 13 included ≥1 generic PRO instrument
- 10 included ≥1 disease-specific PRO instrument
- 8 included both

Seven different generic PROs were included within those studies, although several instruments were not pediatric-specific.

- EQ-5D (seven)
- PedsQL (six)
- SF-36 (three)
- Child Health Questionnaire, Patient Global Impression of Change, Patient Life Interference, Infant and Toddler Quality of Life Questionnaire (SF-47) (one each)

In some cases, instruments were only used in age-based subgroups of the overall population; this was not always clear in the submission documentation.

Figure 2: PRO instruments included in the clinical studies of the new treatment (n=24 assessments)



As expected, a range of disease-specific measures were used, and in 80% of the studies with a disease-specific PRO, this was in addition to at least one generic instrument.

Only two (8%) studies collected data on caregiver burden/QoL instruments using two different instruments:

- Generic: Caregiver Life Interference (including Family Life Interference)
- Disease specific: caregiver-reported Spinal Muscular Atrophy Independence Scale

Additional uses of pediatric PRO/caregiver data

Quantitative data (generated via specific instruments) were often used to describe and characterize the disease from the patient perspective, and to provide inputs to cost-effectiveness models (eg, utility values).

Caregiver burden was also described and, sometimes, also quantified: four specific caregiver instruments were cited (once each): Caregiver Life Interference including Family Life Interference, Zarit Burden Interview, Work Productivity & Activity Impairment—General Health, and Hospital Anxiety and Depression Scale.

Key HTA commentary

- NICE criticized the use of both generic and disease-specific PRO instruments to capture treatment impact in these pediatric indication:
  - Generic instruments lack sensitivity to capture the full effect of disease-specific symptoms (HST31).
  - Disease-specific instruments lack data about patient experience/symptoms following treatment and the relationship to overall health-related quality of life (HRQoL) (HST14).
- NICE committee discussions benefited from, and often relied upon expert input from clinicians, patients, and families/caregivers to supplement and contextualize clinical data.
- Deriving utility estimates for cost-effectiveness models was challenging—reliance on published estimates required assumptions to be made and justified.
- Limitations around data collection, particularly for younger pediatric populations, were recognized:
  - Instruments may not be appropriate and/or validated for all ages within a study making data analysis and interpretation challenging.
  - Proxy respondents for pediatric PROs may have been required and may vary by age group—assessments were often unclear about if/how a proxy was used and rarely considered the extent to which proxy reporting reflected pediatric patient experience.
- The impact of caregiver perspectives on economic model outcomes varied with only one submission stating that caregiver utility values was a driver of the Incremental Cost-Effectiveness Ratio.

Discussion

The extent and nature of data use around patient and caregiver burden of illness, and HRQoL outcomes, varied significantly between the HTA submissions.

- Pediatric patients' burden of illness was well-described but often not followed by comprehensive reporting of the impact of treatment on patient PROs.
- Where treatment-related symptom reduction was reported, the extent to which it impacted HRQoL was not explicit.

Although caregiver QoL can be affected significantly when caring for a pediatric patient, the impact on caregivers is not frequently assessed.

- Aside from describing burden, caregiver data were mainly used to define an acceptable disutility value within the economic model.
- NICE increasingly suggests that these data are valuable, especially when the condition necessitates that the patient is highly dependent on the caregiver (common for pediatric indications).

Conclusions

Despite the importance of delivering patient-centered care that can improve the child's quality of life, there is a lack of pediatric-specific PRO instruments in trials for new treatments. Data on burden are being included and discussed as part of the assessment, but quantitative data on patient and caregiver perspectives are often sparse within submissions to HTA agencies such as NICE. The impact on final assessment outcomes appears variable. Future studies should carefully evaluate ways in which pediatric patient/caregiver data can be collected to support clinical and economic value.

Scan here for poster references

Poster presented at ISPOR EU, 17–20 November 2024, Barcelona, Spain