Poster #HTA241

Health Equity and the Health Technology Assessment Process: Are Children and Young People Being Overlooked? A Review of Pediatric National Institute of Health and Care Excellence (NICE) Technology Appraisals

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Technologies targeting children and young people (CYP) constitute a small minority (<5%) of total technologies assessed every year by the National Institute for Health and Care Excellence (NICE). Current health technology assessment (HTA) methods and approaches do not largely account for the unique realities of evidence generation and synthesis in child health and disease experience.

Background

- There are unique methodological, operational, and ethical challenges associated with developing novel technologies for CYP and for generating high-quality evidence for HTA submissions.
- Most drugs for this population are used off label or off license, reflecting the current pediatric treatment landscape.

Challenges related to producing high-quality HTA evidence in CYP

- Trial representativeness
- Difficulties in recruitment
- Age-generalizable evidence

- As a result, HTA bodies recognize that submitted evidence is often compromised (due to disease- and population-specific challenges) and is likely not considered 'robust enough' to adhere to usual HTA standards.
- Although technologies in the CYP population typically receive favorable decisions from HTA agencies, there is limited documentation regarding how the associated challenges are addressed in technology appraisals (TA).
- Recent publications[1] have exclusively focused on issues such as health-related quality of life, as well as limited evidence regarding follow-up data.
- Health equity in healthcare decision-making has recently been identified as a strategic initiative; however, most of the discussion on health equity leaves CYP behind mainly due to unique dimensions of child health and illness.[2]

Objective

- This study aimed to assess the frequency of NICE TAs and highly specialized technologies (HST) for CYP and to explore how these appraisals addressed unique methodological challenges associated with this population.

Methods

- A search was conducted to identify submissions dating from July 2013 (i.e., the publication date of the first full detailed NICE methods guide[3]) to February 2023.
- The NICE website interface was used for the searches to ensure unbiased identification of related submissions.
- HTA appraisals that did not refer to CYP in the title or scope were excluded. In addition, terminated appraisals, appraisals lacking full documentation and those relating to medical device evaluations were omitted from this analysis.
- Full TAs and HSTs with available information on the manufacturer's submission and the NICE committee's discussion were considered for this analysis.
- A standardized, pre-defined template was used for data extraction to collect information on clinical and economic assessments and type of final recommendation (recommended, optimized, recommended for use in the Cancer Drugs Fund, only in research, not recommended) by TA or HST, and corresponding NICE committee critiques.
- The therapeutic areas of the selected TAs and HSTs were categorized according to the therapeutic group described by the European Medicines Agency.

Results

General characteristics

- The search yielded 588 published TAs and HSTs across all age groups. Twenty-two submissions (18 TAs and four HSTs) were identified for the CYP population.
- In total, 17 submissions were included for review across 14 different therapeutic areas.
- The majority of included appraisals were related to rare or very rare diseases (85%); others were epilepsy (n=3) and psoriasis (n=2).
- The literature attrition is shown as a Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) diagram in Figure 1.

Results (cont.)

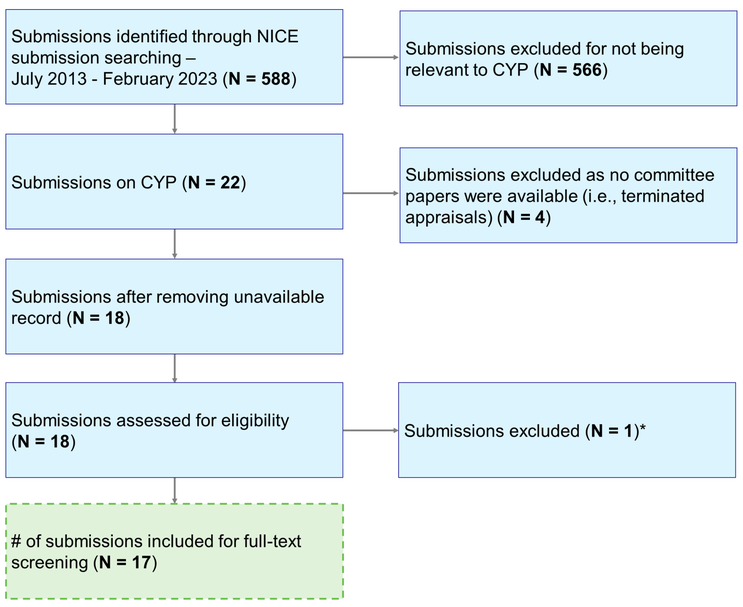
General characteristics (cont.)

- Seven TAs received positive recommendations; nine were recommended with conditions (i.e., until further data collection, with a restricted patient population, or for reasons related to the commercial arrangement). One was rejected for not meeting the end-of-life criteria and due to the uncertainty around the size of the clinical benefit.

Model characteristics

- Age distribution of the CYP targeted population varied across the included appraisals; 10 submissions included patients up to age 17 or 18 years, five considered patients younger than 12, and two submissions considered children and young adults (≤25 years).
- The primary efficacy and safety evidence was based on randomized controlled trials (RCT) and single-arm trials. One submission used real-world evidence (RWE) to report efficacy data.
- Ten CYP submissions performed indirect treatment comparisons mainly reflecting the study design of primary trial evidence; six appraisals submitted evidence from network meta-analyses and the remainder conducted matching-adjusted indirect treatment comparisons.
- Various model structures were used across the included appraisals including Markov (n=11), partitioned survival (n=2), decision tree (n=1), and patient-level simulation (n=1). Two submissions did not mention model structure details (not required for a cost-consequence analysis).
- Most submissions (65%) used a lifetime horizon in their economic models (where applicable); in 24%, the time horizon was limited to patients reaching 18 and 11% used defined time horizons, enough to capture relevant costs and treatment effects.

Figure 1. PRISMA diagram



* Medical device evaluation
Abbreviations: CYP, children and young people; NICE, National Institute for Health and Care Excellence

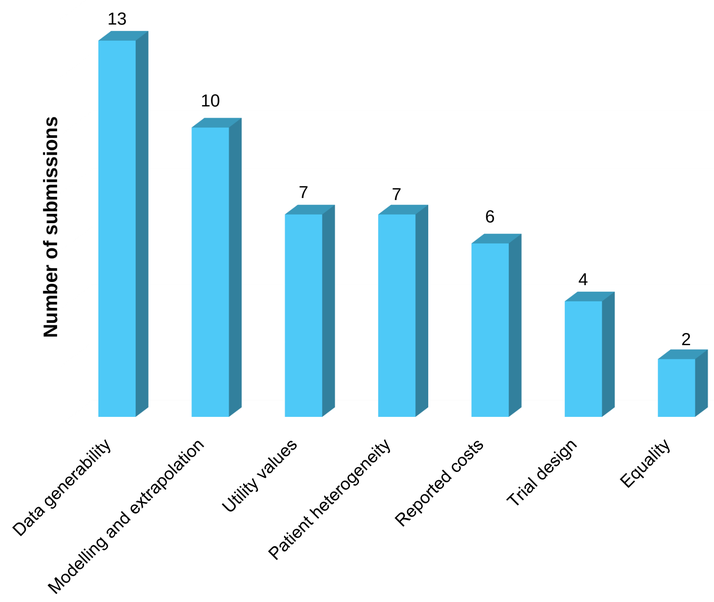
Main critiques

- The main areas of criticism were centered on 1) confidence in data generalizability, 2) modelling and extrapolation, and 3) utility values in economic modelling.
- Most of the discussion focused on lack of transparency in how utility data were handled. Main critiques were around the mapping algorithm to convert to EQ-5D-Y (i.e., child-friendly version of EQ-5D without a United Kingdom (UK) value set available yet), lack of EQ-5D population norms for below 18 years, and indirect utility scoring by clinicians rather than patients. In the absence of CYP-specific utility values, the companies extrapolated values from adult utility value sets.
  - Nine submissions used the same utility value set as adults, whereas six used EQ-5D-Y or Pediatric Quality of Life Inventory™ value set for pediatric patients, and two did not report what value set was used.
- Several submissions pointed out that the data generalizability of studies considered in the submissions did not represent the UK population or population of interest.
  - Therefore, numerous submissions used indirect evidence which was further critiqued by the committees due to lack of transparency in the assumptions used.

Results (cont.)

- Maturity of data and lack of appropriate length of follow-up were the main challenges in testing the modeling transitions.
- Additional concerns were related to the primary study design, patient heterogeneity, equality, and the accuracy of reported costs in the model (Figure 2).

Figure 2. Main critiques in CYP submissions



Discussion

- This review revealed that <5% of NICE submissions targeted CYP populations; this reflects both the low prevalence of diseases in this population as well as the different levels of investment in health technologies compared with adults. The identified critiques aligned with challenges addressed in Moretti et al., 2021[1] (utility values, data generalizability, modeling, and equality issues).
- Committee criticisms within CYP submissions reflected the data complexity for this age population including sample size, difficulties in recruitment, data generalizability and lack of mature data that creates uncertainties in modeling analyses.
- Mapping of age-appropriate health utilities was a frequent critique. However, the committees could not suggest alternative options as there is neither population norms for EQ-5D-Y nor a UK-specific utility value set for young children.
- A lack of clarity exists on the most methodologically sound approach to be used in CYP submissions.

Recommendations

- A mapping algorithm translating EQ-5D-Y values is needed for the UK CYP population as it is considered a benchmark for HTA processes.
- The increasing trend of RWE use in NICE appraisals is not captured in current CYP technology submissions. NICE-grade RWE data collection may fill in some evidentiary gaps from RCTs for these technologies and can address issues such as patient generalizability and validate model assumptions.
- Formal recognition that current HTA processes may not apply in CYP technologies may be needed.

Conclusions

- Significant methodological drawbacks were noted during NICE CYP technology submissions. Overall, however, this did not largely translate into negative recommendations by HTA bodies.
- This result may indirectly underscore unique evidence generation challenges for this patient population.
- Equity issues for CYP remain an under-researched HTA topic.

References

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