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HTA220

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AI-Assisted Review of NICE Guidance for Highly Specialised Technologies: Economic Modelling of Ultra-Rare Conditions

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Introduction

Reimbursement of treatments for ultra-rare diseases is associated with specific challenges, often due to limited availability of clinical and economic evidence (1). These challenges have led to the development of dedicated reimbursement frameworks, including Highly Specialised Technology (HST) processes (2).

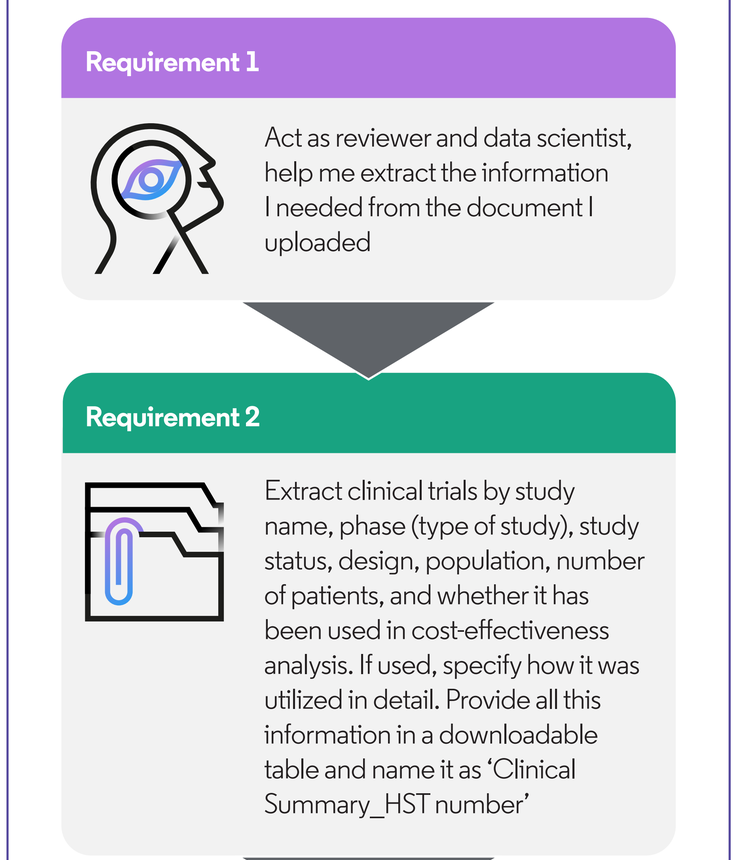
Objectives

To better understand how ultra-rare conditions are modelled for the UK National Institute for Health and Care Excellence (NICE), we analysed all 28 HST assessments published between January 2012 and May 2024.

Methods

We systematically analysed clinical evidence, statistical analyses, economic evaluations, and critiques from the Evidence Review Group (ERG) or External Assessment Group (EAG) for each included appraisal. Due to the length and complexity of the committee papers for each submission, human-supervised artificial intelligence (AI) (ChatGPT-4, OpenAI) was employed to enhance efficiency in data extraction. Manual extraction of three appraisals was conducted by two analysts independently to develop and validate prompts. Figure 1 provides example prompts used for the extraction of clinical effectiveness data. All AI-extracted data were cross-checked by a third analyst before analysis.

Figure 1. Three step prompts used for the extraction of clinical effectiveness data



Results

A total of 28 appraisals (HST1, HST4-5, HST7-31) were included in the assessment, with some submissions marking certain information as confidential. A detailed review of the results can be found in Table 1.

Perspective and time horizon

All models were conducted from the UK NHS and Personal Social Services (PSS) perspective and utilized a lifetime horizon, in accordance with NICE reference case (PMG36)(3).

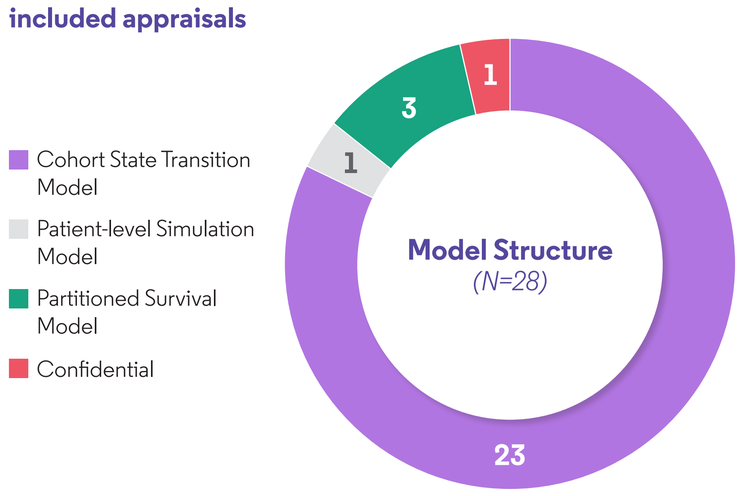
Discount rate

11 out of 28 submissions adopted a 1.5% per annum discount rate for both costs and health effects in their base case, following NICE's guidance. NICE recommends a discount rate of 1.5% when treatments are expected to restore patients who would otherwise die or suffer from severe impairments to full or near-full health, with sustained benefits over a long period (typically at least 30 years). However, many of these submissions were challenged by the ERG/EAG, citing uncertainty over whether the technology would truly restore patients to full or near-full health.

Model structure

Of the 27 submissions that made their model structure information publicly available, 23 (85%) used a cohort state transition model, 1 (4%) chose a patient-level simulation model, and 3 (11%) utilized a partitioned survival model. The number of health states in the models varied significantly, ranging from a simple three-state model to more complex models with four main health states, each incorporating 12 tunnel states based on age, and one additional death state. Due to the limited data and evidence in submissions for ultra-rare conditions, a less complex model structure with fewer health states was recommended by the EAG/ERG in multiple appraisals.

Figure 2. Summary of the model structures used in the included appraisals



Comparators

Given the absence of effective treatments before the introduction of the technology, best supportive care (BSC) or off-label treatments were selected as the comparator in most (17 out of 28) submissions.

Model inputs

31% of the clinical data used in the model comes from Phase I/II trials, 51% of the clinical trials have fewer than 35 patients, 22% supported by real-world data such as registry and external data. Given the large proportion of single-arm clinical trials used in the submissions, comparator arm efficacy data were typically sourced from natural history studies or expert elicitation. The most widely used methods for eliciting expert opinions were structured expert elicitation with the Sheffield Elicitation Framework (SHELF), or Delphi panel.

Table 1. Summary of model specification

Model specification		
Model settings	Time horizon	**100%** lifetime, with varies years from the start of the model
	Perspective	**100%** NHS and Personal Social Services [PSS] for the base case, in line with NICE reference case (PMG36) (3)
	Discounting	**11/28 (39%)** used 1.5% for both costs and health outcomes for the base case **2/28 (7%)** used 3.5% for costs; 1.5% for health outcomes for the base case **15/28 (54%)** used 3.5% for both costs and health outcomes for the base case
	Cycle length	2-52 weeks
	Comparators	**17/28 (61%)** chose best supportive care (BSC) as the comparator
	Outcomes	**27/28 (96%)** reported QALYs **1/28 (4%)** reported DALYs
Modelling approach	Model structure	**23/28 (82%)** Cohort State Transition Model **1/28 (4%)** Patient-level Simulation Model **3/28 (11%)** Partitioned Survival Model **1/28 (4%)** Confidential
	Health states	**16/28 (57%)** of the model has 5-7 health states

Note: Some percentages do not sum to 100% due to rounding.

Abbreviations: BSC: Best Supportive Care; DALYs: Disability-Adjusted Life Years; NICE: National Institute for Health and Care Excellence; PSS: Personal Social Services; QALYs: Quality-Adjusted Life Years.

Learnings from using AI in review

The use of AI significantly enhanced the efficiency of reviewing lengthy appraisals spanning hundreds of pages. However, there were instances where AI produce inaccurate outputs, particularly when the requested information is complex or ambiguous. Breaking down prompts into smaller, simpler segments can mitigate this issue, and it is highly recommended that all AI-generated summaries or extracted data be validated by an independent reviewer. In addition to ChatGPT, which was employed in this review, emerging AI tools specifically designed for systematic reviews, such as Pitts AI (4) and Laser AI (5), could also offer valuable insights for future quick non-HTA reviews.

Conclusion

Analysis of HST submissions suggests modelling in ultra-rare diseases remains challenging due to limited data and small patient populations. To address these challenges, the use of simpler modelling approaches can be beneficial. Natural history and registry studies offer valuable insights into disease progression and patient outcomes, helping to refine economic evaluation models. Additionally, expert elicitation is essential, as it incorporates the knowledge of clinicians and specialists with experience in these rare diseases, leading to more informed decision-making.

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Presented at ISPOR Europe 2024, Barcelona, Spain | November 17-20 2024

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Acknowledgments and Disclosures:
QX, SH, SW, RM, SCD and SN are all employees of Clarivate. The study has been funded by Clarivate.