Precedents in decision-making for Highly Specialised Technologies appraised by NICE: key takeaways and recommendations

Bappoo Y, Sandhu D, Burton M, Wright W, Freemyer K.
FIECON Ltd.

FIECON

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Objective

To determine the key precedents for decision-making and acceptability of evidence in completed NICE HST appraisals.

Background

- National Institute of Health and Care Excellence (NICE) highly specialised technology (HST) appraisals are recommendations on the use of new and existing highly specialised medicines for the treatment of very rare conditions in the NHS in England.[1]

- It can be challenging to achieve patient access in the UK for HSTs given the limitations in the evidence base for very rare diseases and the rigour of the NICE appraisal process. Therefore, an understanding of the typical evidence packages, common challenges, and typical outcomes of previous NICE HSTs may help manufacturers to achieve a positive recommendation and timely patient access.

Methods

- The NICE website was searched in May 2024 for all completed HST appraisals from 2015-present, appraisals currently 'in development' were excluded.

- All completed HST appraisals were reviewed for multiple criteria including NICE recommendation, pricing arrangements, inclusion of carer disutility, 1.5% discount, quality of life (QoL) source, and quality-adjusted life year (QALY) weighting.

- Following the extraction, the data were analysed to identify key trends and challenges, as well as acceptability of evidence to NICE.

Results

- **Appraisal outcome:** Of 28 completed HSTs, 27 received a positive recommendation (96.4%).[3-30]

- **Pricing agreements:** The most common pricing agreement in HSTs is a simple patient access scheme (PAS) (21/28, 75%). Only 6 HSTs (22.2%) included a managed access agreement (MAA). No HST have entered the innovative medicine fund (IMF) since its inception in 2022.

- **Carer disutilities:** Carer disutilities were submitted in 24/28 (85.7%) HSTs.

  - NICE quantitatively accepted carer disutilities in the cost-effectiveness calculations in 15/24 HSTs (62.5%). In 9/24 (37.5%) appraisals, NICE considered the qualitative impact on carers.

  - Of the appraisals with carer disutility quantitatively accepted, 13/15 (86.7%) were accepted in the base case and 2/15 (13.3%) in scenario analyses.

  - In 6/15 (40%) HSTs that quantitatively captured carer disutilities in the cost-effectiveness calculations, NICE accepted that the disutility would apply to >1 carers. Of these, 3/15 (20%) had an increasing number of carers with increasing disease severity.

Figure 1. Inclusion of carer disutility in all HSTs

- **QALY weighting:** An incremental patient lifetime QALY gain of >10 was shown in 17/28 (60.7%) positive appraisals, resulting in an ICER threshold of between £100,000–£300,000. The remaining 11/28 (39.3%) appraisals did not meet the criteria as incremental patient QALY gains were <10, so the ICER threshold was £100,000 (Figure 2).

- **Discount rate:** NICE HSTs allow for a 1.5% discount rate on costs and QALYs if the technology provides potentially life-long benefits in a very severe condition with very high unmet need. The 1.5% discount rate has been accepted in only 2/28 (7.1%) positive appraisals. Trends in the 1.5% discount rate are shown in Figure 3.

- **Utility instrument:** EQ-5D is the preferred NICE utility measure and was used in 15/27 (55.6%) approved HSTs. Other scales included PedsQL and disease-specific scales.

- **Utility data source:** HSTs explore multiple sources of utility data in base case and scenarios. Vignette studies were used to derive utilities in 13/27 (48.1%) HSTs. Utilities were derived from clinical trial data in 7/27 (25.9%) HSTs and published literature in 8/27 (29.6%) HSTs.

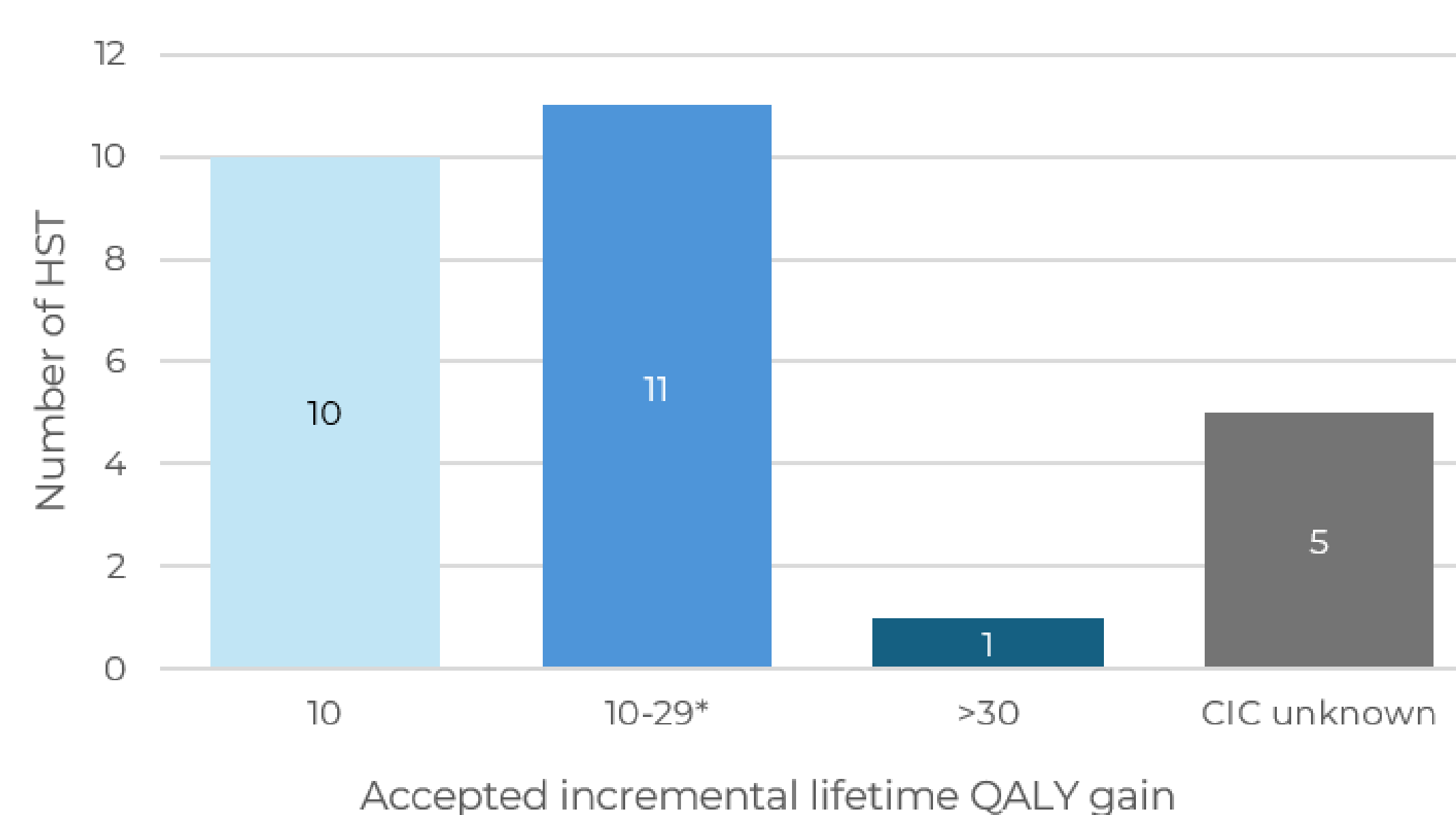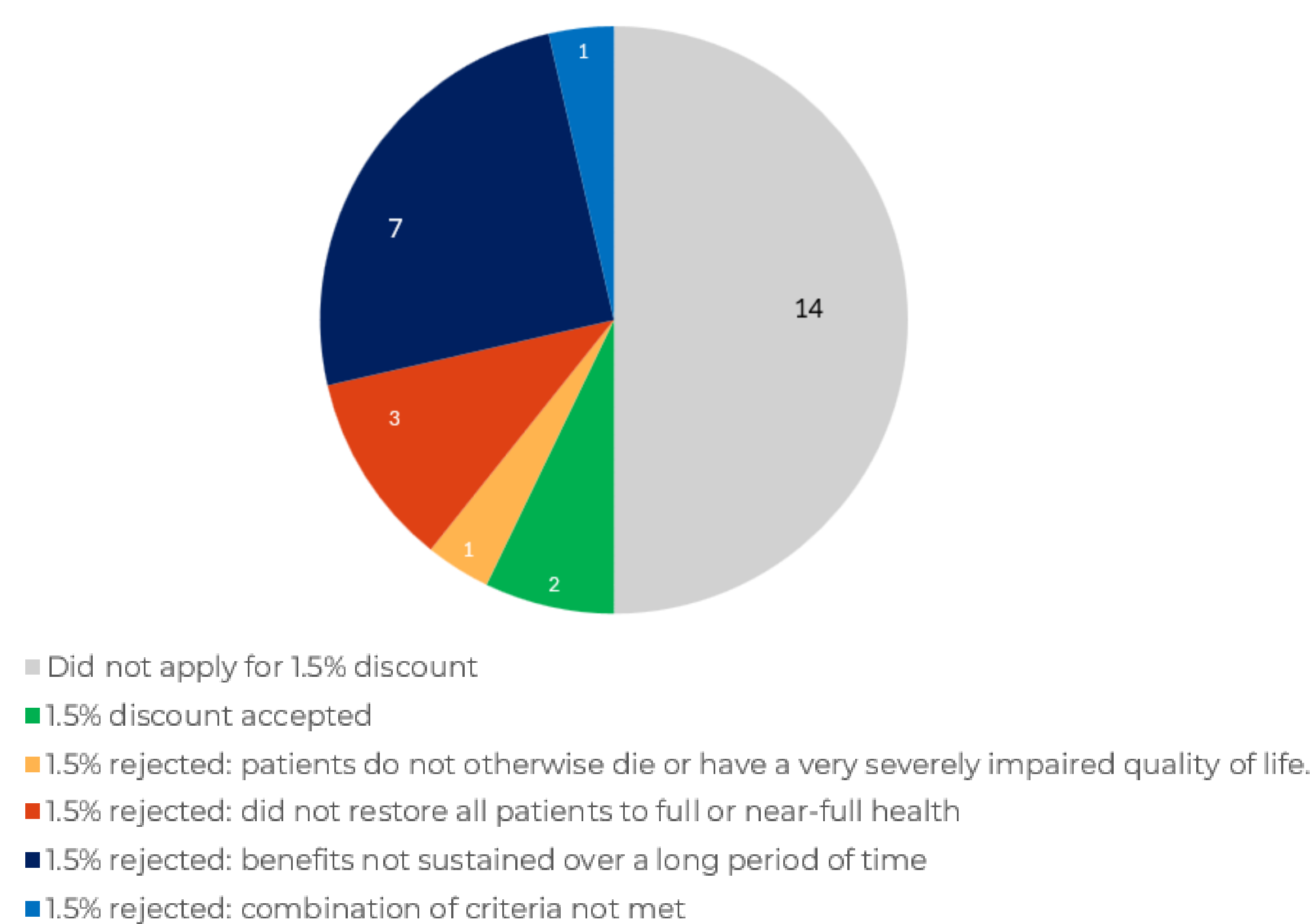**Figure 2.** QALY Weighting in Accepted HST Appraisals

Figure 3. Acceptability of the 1.5% discount rate on costs and QALYs

- Did not apply for 1.5% discount
- 1.5% discount accepted
- 1.5% rejected: patients do not otherwise die or have a very severely impaired quality of life.
- 1.5% rejected: did not restore all patients to full or near-full health
- 1.5% rejected: benefits not sustained over a long period of time
- 1.5% rejected: combination of criteria not met

Conclusion

The results indicate that:

- The IMF has seen limited uptake since its inception in 2022. A simple PAS discount is the predominant type of price agreement.

- Carer disutilities are generally considered acceptable to NICE and it may be possible to justify a model base case that applies the disutility to >1 carer or an increasing number of carers with increasing disease severity.

- A 1.5% discount rate on costs and QALYs is very challenging to achieve, with the most common reason for rejection being failure to show curative effect. This is unsurprising given the difficulty to derive sufficient long-term evidence to show long-term curative effect. NICE HST methods are due to be updated in March 2025 and will provide further detail on criteria for the 1.5% discount.

- Vignette studies are acceptable to derive utility values, although NICE's clear preference is for trial-based utility data. Manufactures should consider exploring Vignette studies and other utility evidence generation methodologies well in advance of their expected NICE appraisal to ensure their economic models fully capture the nuances of the disease and benefits of treatment.

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