

# Use of General Population Utilities in NICE Highly Specialised Technology Appraisals of Treatments with the Potential to Restore Normal Physiology

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## Background

The NICE Highly Specialised Technology (HST) appraisal process evaluates novel treatments for very rare diseases.<sup>1</sup>

Although there is no universally accepted definition of a very rare disease, to be eligible for the HST process, one criterion is that the target patient group must be sufficiently small that treatment is concentrated in very few centres in the English National Health Service (NHS).<sup>1</sup>

Modelling the cost-effectiveness of interventions for very rare diseases over a lifetime horizon can be challenging due to sparsity of clinical data, which is often based on a small, heterogeneous population.

For potentially curative therapies, such as enzyme replacement therapies (ERTs) or gene therapies, modelling the long-term impact of treatment on health-related quality of life (HRQoL) can be a particular challenge, because any assumptions can have a large impact on the total number of quality-adjusted life years (QALYs) gained.

One modelling approach is to assume that patients who fully respond to treatment with potentially curative therapies have HRQoL equivalent to the general population.

However, it is unclear if this assumption is accepted by NICE HST committees and Evidence Review Groups (ERGs).

## Objective

To conduct a review to investigate modelling of long-term HRQoL benefit in NICE HSTs of treatments with the potential to restore normal physiology, with a focus on the use of general population or full health utilities.

Table 1. Review results

HST number	Intervention	Disease	Patient population (adult or paediatric)	Intervention type	General population/full health utilities used	General population utility assumption amended by NICE ERG
HST4	Migalastat	Fabry disease	Adult	Alternative to ERT	No	-
HST5	Eliglustat	Gaucher disease	Adult	Alternative to ERT	No	-
HST6	Asfotase alfa	Hypophosphatasia	Paediatric	ERT	No	-
HST7	Strimvelis	ADA severe combined immunodeficiency	Paediatric	Gene therapy	Yes - general population utilities	Yes – ERG implemented disutility to account for bilateral deafness and intravenous immunoglobulin treatment
HST11	Voretigene neparvovec	Inherited retinal dystrophies	Paediatric	Gene therapy	No	-
HST12	Cerliponase alfa	Ceroid lipofuscinosis type 2	Paediatric	ERT	No	-
HST15	Onasemnogene abeparvovec	Spinal muscular atrophy	Paediatric	Gene therapy	Yes - general population utilities	No
HST18	Atidarsagene autotemcel	Metachromatic leukodystrophy	Paediatric	Gene therapy	Yes - general population utilities	No – ERG noted that use of general population utilities may overestimate treatment benefit but did not make amendments
HST19	Elosulfase alfa	Mucopolysaccharidosis type 4A	Adult and paediatric	ERT	Yes - HRQoL of 1 (full health)	No

ERG, Evidence Review Group; ERT, enzyme replacement therapy; HRQoL, health-related quality of life; HST, highly specialised technology

## Methods

A review of all 19 NICE HSTs was conducted in April 2022, to identify appraisals of enzyme replacement therapies (ERTs), alternatives to ERTs, and gene therapies. These treatments were selected because they have the potential to restore normal physiology and therefore restore patients' HRQoL to that of the general population.

Key information on submitted cost-effectiveness models was extracted for identified HSTs, including patient population, intervention and comparator, use of general population/full health utilities, NICE ERG feedback on utility modelling approach, and NICE appraisal decision.

## Results

### Included HST appraisals

- Out of the 19 NICE HST appraisals, nine were included in the review (Table 1): four assessing gene therapies, three assessing ERTs, and two assessing alternatives to ERTs
  - Of the included HSTs, seven assessed paediatric populations and three assessed adult populations

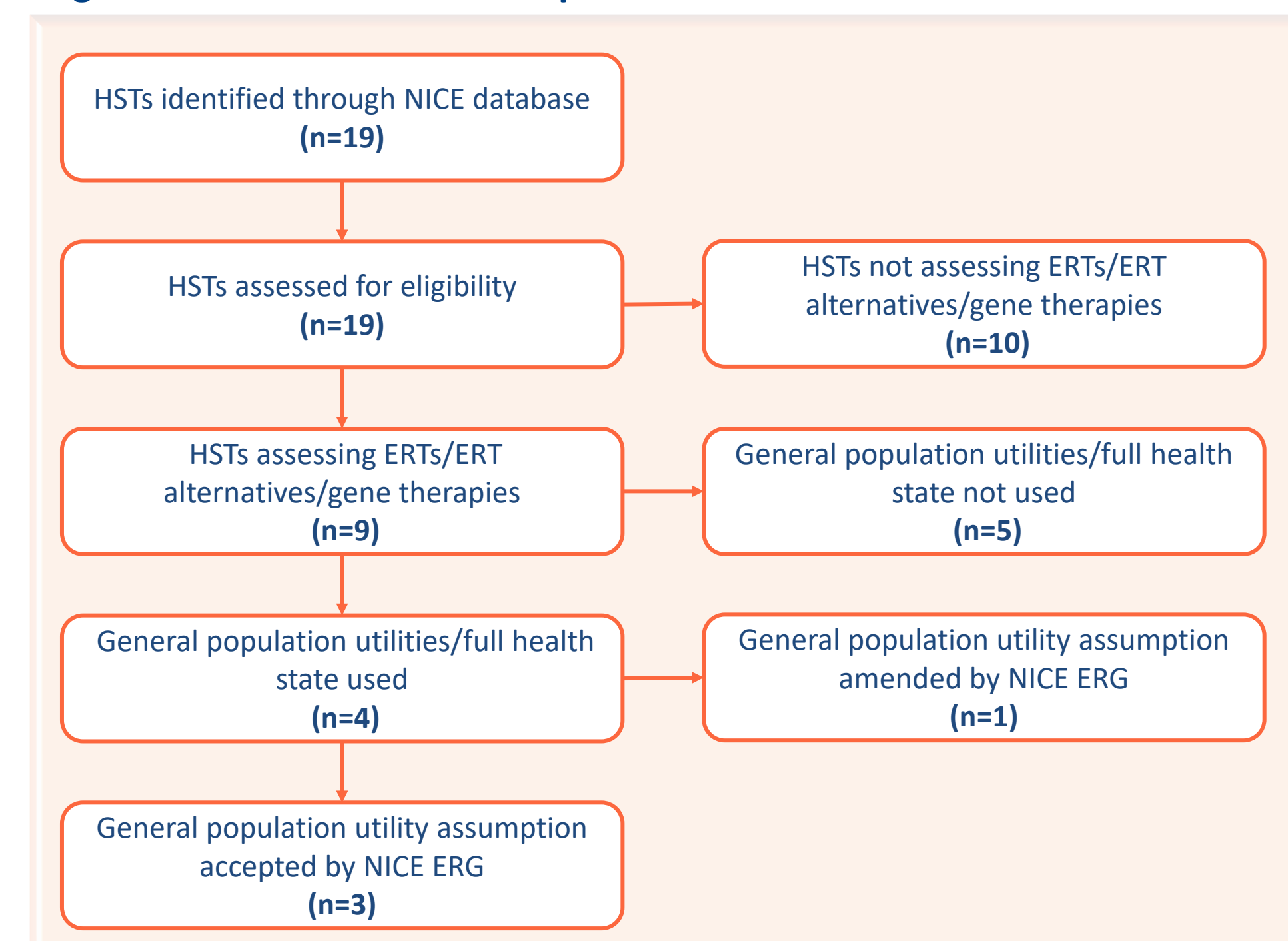
### Use of general population utilities

- In all included HSTs, the submitted economic model used a Markov state-transition structure
- In four HSTs, cost-effectiveness models included a "healed" or "cured" state representing HRQoL equivalent to the general population or full health
  - Three assessed gene therapies (HST7<sup>2</sup>, HST15<sup>3</sup>, and HST18<sup>4</sup>) and one assessed an ERT (HST19<sup>5</sup>)
  - In all four models, the duration of general population/full health HRQoL was assumed to be potentially lifelong

### NICE critique and recommendations

- In all nine HSTs included in the review, the treatment under assessment was approved by NICE
- In three out of the four HSTs which used general population or full health utilities, modelling of HRQoL was not amended by the NICE ERG (HST15, HST18, and HST19)
- In HST7, the NICE ERG and committee agreed that the use of general population utilities was implausible, due to a substantial proportion of successfully treated patients having lifelong impairments
  - To amend this assumption, the ERG applied utility decrements to account for the presence of bilateral deafness and continued requirement for intravenous immunoglobulin in some patients
- Additionally, in HST18, the ERG commented that general population utilities may overestimate the benefit of treatment, but did not amend the model due to the absence of alternative data

Figure 1. Overview of review process



ERG, Evidence Review Group; ERT, Evidence Review Group; HST, highly specialised technology; NICE, National Institute for Health and Care Excellence

## Conclusions

- This review assessed approaches to modelling long-term HRQoL benefit for gene therapies, ERTs, and alternatives to ERTs assessed through the NICE HST appraisal pathway
- Four HSTs included a "cured" or "healed" health state, with HRQoL equivalent to the general population or full health
- Three of these HSTs assessed gene therapies, one assessed an ERT
- NICE accepted the use of general population utilities in three out of four submissions (HST15, HST18 and HST19) and amended one submission (HST7) where lifelong health impairments were still expected despite successful treatment
- All four HSTs which used general population utilities assessed treatment in a paediatric population, indicating that achieving general population HRQoL may be more likely if treatment is initiated early in life, before the accumulation of long-term disease effects
- Additionally, in two of four cases, patients started treatment in the "healed" health state, indicating that treatment was preventive rather than curative
- To conclude: in NICE HST appraisals of treatments which have the potential to restore normal physiology, there is a precedent for use of utilities equivalent to the general population. The acceptance of this assumption by NICE in more than one case demonstrates that this approach can be acceptable to healthcare payers under appropriate circumstances

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