Informal carer disutility: how many caregivers are captured in cost-utility analyses of treatments for rare diseases submitted for NICE highly specialised technology appraisals?

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BACKGROUND

- The latest National Institute for Health and Care Excellence (NICE) health technology assessment (HTA) methods permit the inclusion of caregiver disutility data, where appropriate, in technology appraisals.[1]
- In the context of severe and chronically disabling/ life threatening rare diseases that would be candidates for NICE appraisal in the UK via the highly specialised technology (HST) route, the impact on the health-related quality of life (HRQoL) of a patients' parents, partner, and other family members can be substantial.

OBJECTIVES

- To review how carer disutility and the number of impacted carers have been considered within previous NICE HST appraisals.

METHODS

- NICE HST appraisals published up until June 2022 were reviewed.
- For efficiency of data collection, the consideration of evidence summary on the NICE HST website for each appraisal was used as the primary source of data. Further information retrieval from the NICE evidence review group (ERG; known as external assessment group [EAG] since January 2022) report and company submission was performed where deemed necessary. A published review by Pennington *et al.* 2020 was used to obtain data on HST 1-8, with extra information retrieval from the NICE website where necessary.[2]
- All data extraction was performed by a single reviewer. Information extracted included the number of caregivers incorporated into the economic model (reported here), as well as: disutility value(s) applied, source of data, and the NICE critique of the methods used.
- The indication of each appraisal identified was analysed and categorised by Medical Subject Headings (MeSH) terms using the National Institute of Health (NIH) MeSH browser search facility. Each indication could have more than one MeSH term attributed to it, and only the top tier terms from identified MeSH trees were recorded.

NICE HST appraisals published up until June 2022

Pennington *et al.* 2020 review

NICE consideration of evidence summary

RESULTS

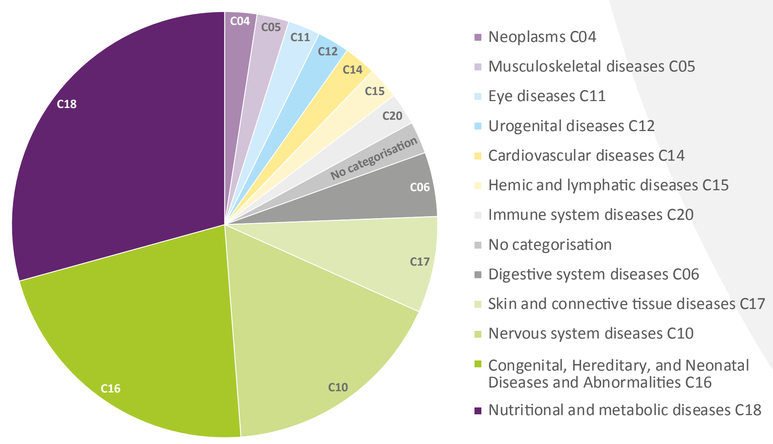
- As of June 2022, 19 HST appraisals had been published on the NICE website. The indications across appraisals were rare genetic disorders, many of which do not fall into a larger disease area (Table 1). Eighteen of the 19 appraisal indications could be categorised into MeSH terms. The most represented MeSH term was nutritional and metabolic diseases (Figure 1).
- Fifteen of the 19 appraisals included consideration of carer disutility to some degree, however the number of carers modelled and how it was incorporated into the model varied greatly. The relationship of the carer to the patient was not defined in most submissions, and only one submission (HST 12) included separate consideration of sibling disutility (Table 2).
- Ten of the appraisals reported the number of carers to whom the disutility was applied. The number of modelled carers ranged from 0.06 to 3 carers (Table 2). Where economic models were revised during the appraisal and/ or alternative values were proffered by the ERG, all values are reported.
- Five appraisals considered a different number of carers for different health states (HST 18, HST 17, HST 12, HST 10, HST 9). Elicitation methods to determine the number of carers in each health state included the use of Delphi Panels and carer surveys.
- Two appraisals considered beyond death carer HRQoL. In HST 7 the family quality adjusted life years (QALY) loss applied was 9% of the QALY lost by the death of a patient, whereas HST 15 acknowledged beyond death carer HRQoL but did not attempt to quantify it (Table 3).

Table 1: Disease areas of previous HST appraisals

HST number	Indication
20	**Symptomatic and inoperable plexiform neurofibromas associated with type 1 neurofibromatosis**
19	**Mucopolysaccharidosis type 4A**
18	**Metachromatic leukodystrophy**
17	**Progressive familial intrahepatic cholestasis**
16	**Acute hepatic porphyria**
15	**Spinal muscular atrophy**
14	**Lipodystrophy**
13	**Familial chylomicronaemia syndrome**
12	**Neuronal ceroid lipofuscinosis type 2**
11	**Inherited retinal dystrophies caused by RPE65 gene mutations**
9 & 10	**Hereditary transthyretin amyloidosis**
8	**X-linked hypophosphataemia**
7	**Adenosine deaminase deficiency-severe combined immunodeficiency**
6	Paediatric-onset hypophosphatasia
5	Type 1 Gaucher disease
4	Fabry disease
2	**Duchenne Muscular Dystrophy with a nonsense mutation in the dystrophic gene**
1	Atypical haemolytic uraemic syndrome

Abbreviations: HST, highly specialised technology; RPE65, retinoid isomerohydrolase gene.
Appraisals in bold included consideration of carer HRQoL.

Figure 1: Summary of MeSH term representation amongst previous HST appraisal indications



Each indication could have more than one MeSH term attributed to it. Only the top tier term from MeSH trees were are recorded. One disease indication returned 0 MeSH term results. Categorisation was performed using the NIH MeSH browser search facility.

Table 2: Number of carers considered in previous HST appraisal cost-effectiveness analyses

HST number	Number of carers
20	Company: 1.4 EAG: 1
19	NR
18	Company: 0-2; 0 carers to HS 0-4 and 2 carers HS5-6 EAG: 0-2.0; no carers to HS0; 0.5 carers to HS1, one carer to HS2-3, and two carers to HS4-6
17	Company: 0-1.7; 1.78 carers applied in all but one health state where no carers were applied
16	NR
15	Company: 1[a]
14	Company: 2 EAG: 1.67
13	NR
12	Company: 0.06-0.8322 dependent on disease health state HS1: 0.06 HS2: 0.67 HS3: 0.75 HS4: 0.86 HS5: 0.78 HS6: 0.79 HS7: 0.9375 HS8: 0.8322 HS9: 0.8322 Also considered 0.94 siblings
11	Company: 1 EAG: 1.78
10	Company revised: 1-2; 1 carer to HS1-3b and 2 carers to HS4
9	Company: 2 Revised to 1-2; 1 carer to HSs in stages 1 and 2, and 2 carers to HSs in stage 3
8	Company: 1
7	NR
3	Company: 1 Company revised: 3 EAG: 2

Abbreviations: EAG, external assessment group; HS, health state; HST, highly specialised technology; NR, not reported
[a] assumed based on calculations relating to the model

Table 3: HST appraisals that considered beyond death carer HRQoL

HST number	Methodology	Evidenced by
HST15	Acknowledged but not quantified	NA
HST7	In a scenario analysis, applied a family/ network QALY loss equal to 9% of the QALY lost by the death of a patient Number of carers in this scenario was not reported	Adopted from an approach used in Christensen et al. (2014),[4] an economic evaluation of a universal meningitis vaccination in England

Abbreviations HST, highly specialised technology; NA, not applicable; QALY, quality adjusted life years.

DISCUSSION AND CONCLUSIONS

- There is a strong precedence for including carer disutility in NICE HST appraisals, regardless of disease indication, which indicates it is an important consideration in cost-effectiveness evaluations performed for decision making purposes in the UK. However, the number of carers that disutilities are applied to in the model, and how they are applied, is inconsistent, a conclusion supported by a recent review of published cost utility analyses by Scope *et al.* (2022), which found a range of 1-4 family members considered per patient, with unclear justifications.[3]
- Further exploration is required into how best to incorporate the impact on the HRQoL of a patients' family and carers into cost-effectiveness analyses of new healthcare interventions. Furthermore, best practice guidance should be developed on the appropriate number of carers to include in cost-effectiveness analyses undergoing NICE appraisal, as well as other related considerations, such as the relationship of the carer to the patient. Currently the number of carers included in models undergoing appraisals appears arbitrary, with justification rarely reported, and would benefit from further qualitative and quantitative research to provide more robust estimates for different scenarios.
- This research represents a top-level analysis of the precedence for including carer disutility in economic analyses in HST appraisals. Supplementary research could be performed to further analyse the documents submitted and produced during each appraisal, and could be broadened to explore approaches to incorporating carer disutilities in NICE single technology appraisals covering a wider range of disease types.

REFERENCES

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