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Uncertainties In Evaluating Patient And Caregiver Health-Related Quality Of Life And Disease Burden In NICE HST Submissions

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BACKGROUND

The Highly Specialised Technology (HST) programme run by the National Institute for Health and Care Excellence (NICE) is used to appraise interventions for diseases meeting criteria related to their rarity and severity. The approach used within this process is based on NICE's manual for health technology evaluations. However, an amended appraisal framework is used for interventions reviewed under the HST programme.[1]

Rare diseases evaluated within the HST programme frequently have a profound impact on the quality of life of patients and their caregivers and are often associated with large disease burden. There are, however, challenges associated with the collection of appropriate data on the quality of life for patients, their families and/or caregivers. These include the limited sensitivity of generic health-related quality of life (HRQoL) instruments in rare diseases, lack of validated disease-specific alternatives, small populations often including paediatric patients, limited knowledge of the natural history of the condition and disease heterogeneity.[2]

The aim of this study was to review previous NICE HST appraisals and determine the most commonly used methods to overcome uncertainties relating to HRQoL and disease burden for patients and caregivers when modelling rare diseases. The opinions of the evidence review groups (ERG) and NICE committees were also considered.

METHODS

The company submissions for all HST appraisals that were either completed or ongoing where at least one committee meeting has taken place up to March 2022 were reviewed.

Data were collected on the disease area, qualitative and quantitative methods used to capture patient and caregiver HRQoL and disease burden (including in the economic modelling), results of the base case and scenario analyses, and key areas of uncertainty. In addition, the ERG and committee meeting reports were reviewed to determine their position on the appropriateness of the methods used to capture HRQoL and burden of disease throughout the company submissions, with a particular emphasis on the economic modelling. The main elements/uncertainties influencing the committee decisions were also considered.

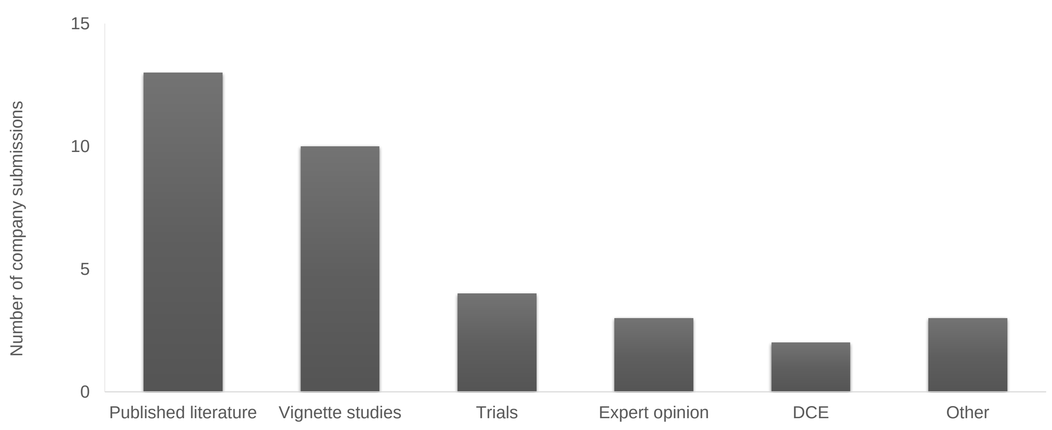
RESULTS

The study included 24 HST appraisals (17 completed and seven ongoing).

Sources of utility values

The majority of the company submissions used multiple sources for the utility data in the economic model. Published literature either on the target condition or on proxy conditions was the most frequently utilised source (13 HSTs). Vignette studies were the second most common approach (10 HSTs). Other sources, such as clinical trials or registry data, were used less frequently (Figure 1).

Figure 1: Major sources of utility data in company submissions



DCE – discrete choice experiment; Other includes registry and natural history studies

Departures from EQ-5D

In the NICE reference case, EQ-5D reported by patients and/or carers is the preferred measure of health effects to be used in cost-effectiveness analyses.[1] However, in HST submissions it was common for companies to use alternative sources of utility values to inform the cost-effectiveness modelling. The most common departures from the use of EQ-5D from patients and/or carers were the use of vignette studies, non-disease specific HRQoL tools and alternative approaches to measuring paediatric HRQoL. Alternatives methods, such as newly developed disease-specific measures and discrete choice experiments, were also used.

Vignette studies

The majority of the vignette studies were undertaken to inform the utility of the health states in the economic model for the base case (seven HSTs) or scenario analysis (two HSTs). In one case a vignette study was used to inform the disutility associated with treatment infusion. The valuation of the vignette health states was undertaken by either clinical experts (five HSTs) or members of the general population (five HSTs). The major concerns raised by the ERG referred to the wording of the vignette descriptions of health states and when health states were valued by clinicians as opposed to patients and/or carers themselves (as recommended in the reference case). Furthermore, the use of separate vignettes for each treatment arm should be avoided. The committee comments broadly indicated the approach provides highly uncertain values. However, overall the use of vignettes was generally considered acceptable.

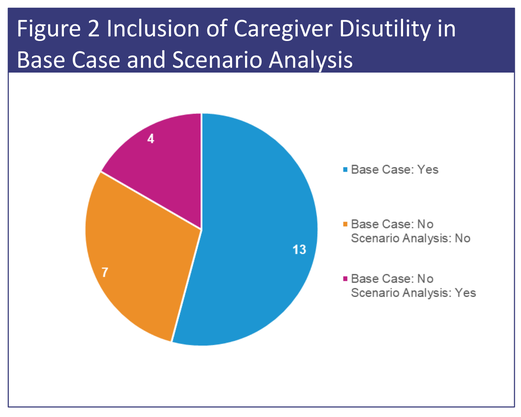
Paediatric HRQoL instruments

NICE does not recommend specific measures of HRQoL in children and young people and recommends that a generic measure shown to have a good psychometric performance in the relevant ages should be used.[1] The PedsQL was used to measure quality of life of paediatric patients in five HSTs submissions. However, it was generally described qualitatively or only used in a scenario analysis. The main reasons for this were that the available mapping algorithm is based on a study in healthy people[3] and the results obtained by using the algorithm provide values not reflective of the disease severity. However, the ERG and the committee were supportive of the use of the mapping algorithm.

Inclusion of caregiver disutility

The inclusion of caregiver disutility, where appropriate, is in line with the NICE reference case.[1] EQ-5D should be used to quantify caregiver disutilities where possible and this should be presented separately from patients' HRQoL. Caregiver disutility was included in either the base case or a scenario analysis in 17 HSTs (Figure 2). The inclusion of caregivers disutility was generally considered appropriate by the ERG and the committee. Nevertheless, a couple of major concerns were raised around the number of caregivers and the duration for which the disutilities were applied.

Figure 2 Inclusion of Caregiver Disutility in Base Case and Scenario Analysis



Disease burden

All submissions qualitatively discussed the disease burden including, for example, the psychological impact on patients and their families, home adaptations for living with a disability, or limited ability to work. Two submissions included wider societal costs in the base case and seven in a scenario analysis. The reasons for not including patient and caregiver burden quantitatively were mostly provided as following the requirements of the NICE reference case and difficulties in quantifying the true impact of the rare disease.

LIMITATIONS

The findings of this study are based on publicly available documents and some of the relevant information was redacted. In addition, the committee views on the methods used for evaluating HRQoL and disease burden may not have been fully captured in the published documents.

CONCLUSIONS

A range of methods, often outside the NICE reference case, were used to obtain the utility values for use in economic models, highlighting the challenges of the standard approach in rare diseases. Some of the methods used were criticised or considered highly uncertain by the ERG and/or the Committee. However, there also appeared to be an understanding of the limitations encountered in modelling patient and caregiver HRQoL and disease burden in rare diseases. Nevertheless, common themes were identified that indicate the need to further develop the methodology that will allow appraisals to more fully reflect the impact of rare diseases on patients and their families, including approaches to be used where EQ-5D is not appropriate, evaluation of paediatric HRQoL, or quantification of the disease burden.

REFERENCES

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DISCLOSURES

This study was sponsored by Sanofi. KM, and HW are Sanofi employees.

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