Approaches to the Collection of Utility Values for Rare Diseases

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OBJECTIVES

- To characterise the methods used to collect utility data in rare diseases, by analysing published literature and National Institute for Health and Care Excellence highly specialised technology appraisals.

BACKGROUND

- Utility data enable the standardised quantification of patients' health-related quality of life (HRQoL).
- Evaluating HRQoL in rare diseases is challenging, as small and often paediatric patient populations can mean limited numbers of eligible patients that are able to participate in utility collection studies.
- Utility data and collection methods are a crucial and well-scrutinised component of health technology assessment (HTA) submissions, such as National Institute for Health and Care Excellence (NICE) highly specialised technology (HST) appraisals, which consider treatments for very rare conditions.[1–4]

METHODS

- A pragmatic literature review was performed to identify rare disease utility studies from EU5 countries (France, Germany, Italy, Spain, UK) published between 1 January 2014 and 26 May 2019. MEDLINE and Embase were searched simultaneously via the Ovid platform, using rare disease and HRQoL search terms. Abstracts were screened by a single reviewer to include English language articles; narrative reviews, case studies and economic models were excluded. Included articles were classified according to study type(s).
- The NICE website was searched (22 May 2019) to identify all available HST appraisals. Key details, such as study type(s) used to elicit utility estimates and the utility data used in the economic model, were extracted from available project documents by one reviewer and checked by a second reviewer. Further details on survey and vignette study methodologies, the two most commonly used methods outside of interventional/observational trials, were extracted for appraisals published in 2017 onwards. The information extracted included critique published as part of the appraisal.

RESULTS

Published rare disease utility studies

- 97/378 published articles identified through Ovid were included **(Figure 1)**, of which 8.2% (8/97) used multiple methods to collect utility data. 38.1% (37/97) and 15.5% (15/97) collected utilities using observational and interventional trials, respectively. Systematic literature reviews (SLRs; 11.3% [11/97]), surveys (9.3% [9/97]), tool development studies (6.2% [6/97])) and vignette studies (5.2% [5/97]) were also common **(Figure 2)**.

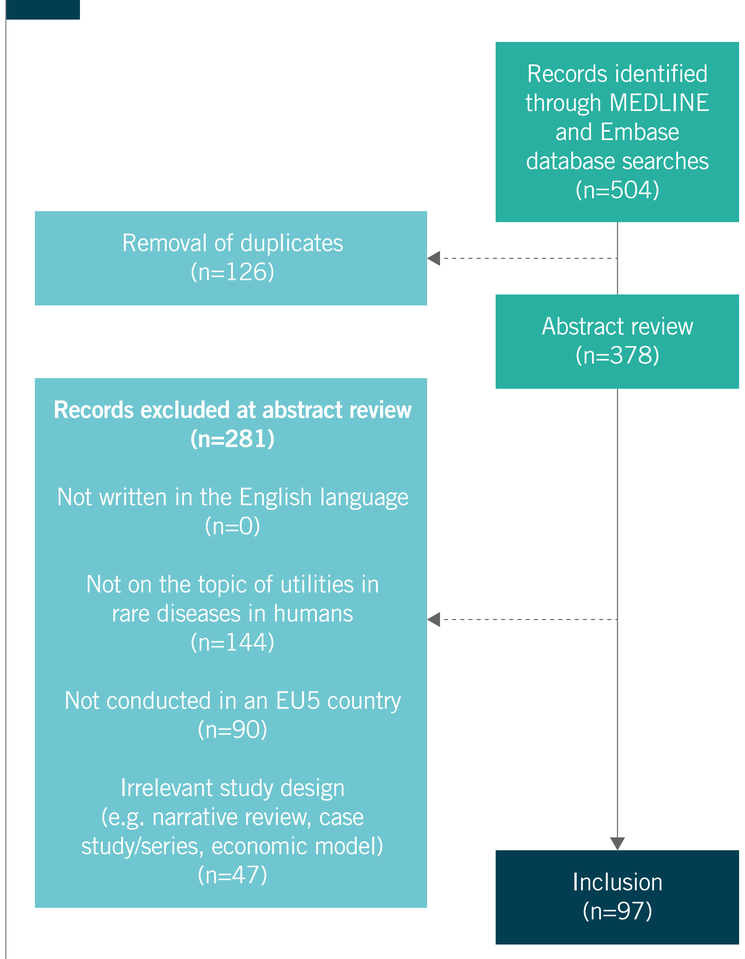
Utility data in NICE HST appraisals

- The majority of HST appraisals (87.5% [14/16]) included utility data collected in interventional studies. Of these, 78.6% (11/14) also included alternative methods such as surveys (35.7% [5/14]), vignette studies (21.4% [3/14]), SLRs (14.3% [2/14]) and/or a registry study, observational study or interview (7.1% [1/14] each). The two HSTs that did not collect utility data using an interventional study both used data from a survey and an SLR **(Figure 3)**.
- Data collected outside of interventional trials were preferentially chosen to inform the economic model, with only 21.4% (3/14) using interventional trial-derived utility data (HST1, HST10, ID927). The challenge of obtaining comprehensive data sets from paediatric rare disease patients in the relevant interventional study was typically stated as a main reason for this choice.

Vignette and survey based collection of utility data in NICE HST appraisals

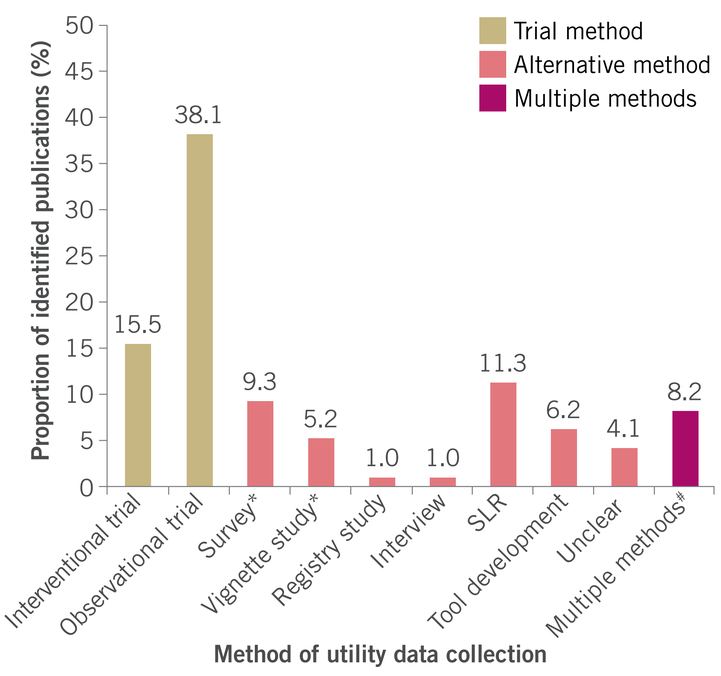
- As shown in **Figure 4**, there was variation in the extent and nature of external involvement in the surveys and vignette studies. NICE often raised concerns over the use of survey or vignette-based data over trial-based data in HST economic models.

1 Flowchart of the PLR



EU5: France, Germany, Italy, Spain, UK; PLR: pragmatic literature review.

2 Publications identified in the PLR, categorised by utility data collection method (n=97)



*Surveys were defined as stating the use of a survey, online method or remote completion of a questionnaire; vignette studies were defined as mentioning the use or development of vignettes and/or including descriptions of hypothetical patients or case studies. #Multiple methods included the following combinations: an interview and a tool development study (n=2); an interventional trial and a registry study (n=1); an interventional trial, observational study, survey and vignette study (n=1); an interview, SLR and tool development study (n=1); an observational study and an economic evaluation (n=1); survey and a vignette study (n=1); a vignette study and an interview (n=1). PLR: pragmatic literature review; SLR: systematic literature review.

3 HST appraisal recommendations, categorised by utility data collection method (n=16)

*Indicates that the utility data collected using this alternative method were used in the economic model. **Indicates that interventional trial-derived utility data were used in the economic model. Surveys were defined as stating the use of a survey, online method or remote completion of a questionnaire; vignette studies were defined as mentioning the use or development of vignettes. HST: highly specialised technology; ID: in development; SLR: systematic literature review.

4 Analysis of survey and vignette methods used in HST appraisals published in 2017 onwards (n=12)

	SURVEYS	VIGNETTE STUDIES
METHODS	4 HST appraisals included data from surveys (HST6, ID737, ID800, ID861)	3 HST appraisals included data from vignette studies (HST6, HST8, ID943)
EXTERNAL INVOLVEMENT	Survey respondents included the general public (ID861, discrete choice experiment [DCE]), patients (ID737) and carers (HST6, ID737, ID800)	Clinical experts valued the vignettes in all 3 HSTs, and were involved in the development of the vignettes in 2/3 HST appraisals (HST6, HST8)
ECONOMIC MODELLING	ID861 and ID800 used these data in the economic model, despite the availability of trial data in ID800	3/3 HST appraisals with vignette data used these data in the economic model (HST6, HST8, ID943)
NICE CRITIQUE	Concerns were raised over low numbers of respondents in ID800 and use of DCE to collect disutilities in ID861, due to the use of survey data over trial data in economic modelling	Use of vignette data over clinical study data was mentioned as a concern in HST6 and ID943, with valuation by clinical experts rather than patients flagged as a limitation in HST8

Surveys were defined as stating the use of a survey, online method or remote completion of a questionnaire; vignette studies were defined as mentioning the use or development of vignettes. DCE: discrete choice experiment; HST: highly specialised technology; ID: in development; NICE: National Institute for Health and Care Excellence.

CONCLUSIONS

- The variety of utility study types identified in both the published literature and HST appraisals point towards the challenges in collecting utility data within clinical trials.
- Technical concerns raised during NICE HST appraisals suggest that best-practice guidance on alternative utility collection methods, such as vignettes and surveys, may improve the robustness of these studies.
- Future research could further evaluate how methodologies found in the published literature compare to those covered in HST appraisals, and whether they are subject to the same limitations that were identified by NICE.

References

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