Approaches to the Collection of Utility Values for Rare Diseases: A Cross-Country Comparison

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OBJECTIVES

To further characterise utility data collection methods in (ultra-) orphan indications by:

- Identifying published utility studies from the EU5 (France, Germany, Italy, Spain, UK) and Canada
- Comparing methodologies reported in submissions to the National Institute for Health and Care Excellence with the Scottish Medicines Consortium and Canadian Agency for Drugs and Technologies in Health.

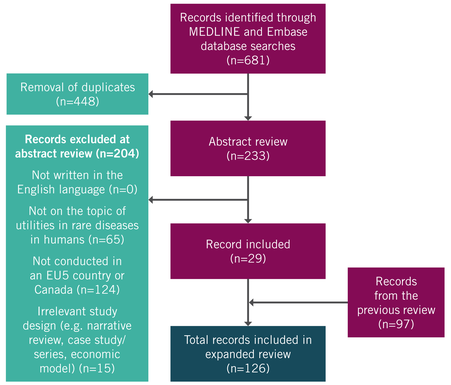
BACKGROUND

- Utility data are essential for the standardised quantification of patients' health-related quality of life (HRQoL).
- Limited numbers of patients able to participate in utility collection studies, due to small and often paediatric patient populations, can render the elicitation of HRQoL in rare diseases particularly challenging.
- Utility data are an important component of health technology assessment (HTA) submissions for orphan drugs.[1–4] However, recommendations about the methodologies for collecting utility data, and how they are used in the context of HTA, vary between different regions and HTA bodies.[5]

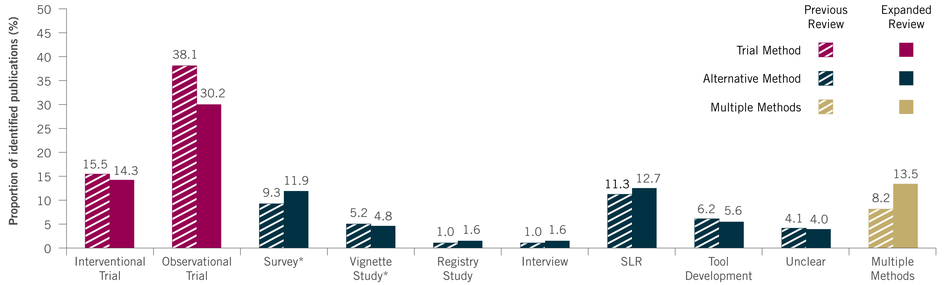
METHODS

- A previous pragmatic literature review (PLR), conducted in May 2019,[6] was expanded to identify utility studies from EU5 countries and Canada (not included in the previous review), published between 1st January 2014–25th June 2020. MEDLINE and Embase were searched simultaneously via the Ovid platform, using search terms for rare diseases and HRQoL.
- Articles were screened by a single reviewer; narrative reviews, case studies, economic models and articles not in the English language were excluded. Included publications were categorised by study type and grouped according to whether a 'trial method', 'alternative method' or 'multiple methods' were used, and specific methods were identified.
- The National Institute for Health and Care Excellence (NICE) website was searched (June 23, 2020) to identify additional highly-specialised technologies (HST) appraisal documents (committee papers, evaluation reports or final evaluation determinations) published since the original search in May 2019. Scottish Medicines Consortium (SMC) and Canadian Agency for Drugs and Technologies in Health (CADTH) websites were then searched for equivalent published appraisal documents corresponding to all available HST submissions.
- Key details, including the study type(s) used to elicit utility values and whether these were used in the economic model, were extracted from available appraisal documents by a single reviewer. Where an alternative methodology other than interventional/observational trials was used, further details on the instrument, methodology and critique published as part of the appraisal, were extracted.

1 Flowchart of the PLR

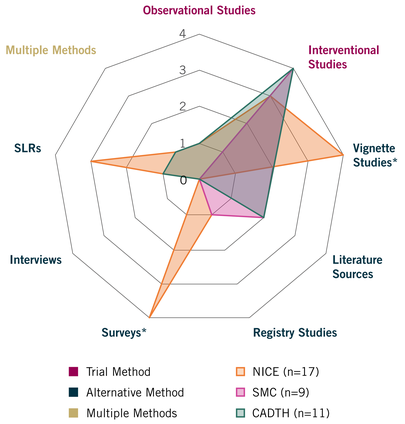


2 Publications identified in the expanded and previous PLR, categorised by utility data collection method (N=126)



*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.

3 Methods used to generate utility data used in economic evaluations in submissions to HTA bodies



Graph shows the number of submissions that utilised each utility data collection methodology in economic evaluations, for each of the three HTA bodies e.g. four SMC submissions (pink) used interventional studies in the economic evaluation, two used vignette studies, two used literature sources and one used registry studies. *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.

4 Utility data collection methods used to inform economic evaluations of the same treatment in submissions to different HTA bodies

Treatment* / HTA Body	NICE HST	SMC	CADTH
Eculizumab	Interventional Study		
Elosulfase Alfa	Survey†	Interventional Study	
Egliustat	Registry Study	Interventional Study	
Burosumab	Vignette Study†		Interventional Study
Inotersen	SLR	Literature Source	
Human a1-proteinase inhibitor	Observational Study	Registry Study	SLR
Patisiran	Interventional Study		

*Only including the seven treatments that were covered (within the same indication) across all three HTA bodies. Trial methods used are indicated in purple; Alternative methods used are indicated in blue. †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.

RESULTS

Published Rare Disease Utility Studies

- In total, 126 articles were included in the expanded review (including 29 newly identified articles in addition to 97 articles from the previous review; **Figure 1**). 30.2% (38/126) and 14.3% (18/126) collected utilities using observational or interventional studies, respectively **(Figure 2)**. Alternative study designs included surveys (11.9% [15/126]), systematic literature reviews (12.7% [16/126]), and vignette studies (4.8% [6/126]). Multiple methods were used in 13.5% (17/126) studies. As compared with the previous review conducted in May 2019, there was a slight increase in the use of alternative (4.0% increase) or multiple (5.3% increase) methods as compared to trial methods (9.2% decrease).

Utility Data in NICE HST, CADTH and SMC Appraisals

- One new NICE HST appraisal (HST11) had been published since the original review, conducted in May 2019.
- Nine SMC and 11 CADTH appraisals corresponding to 17 completed/ ongoing HST appraisals were identified, with seven appraisals being identified on all three websites.
- In line with previous findings, submissions often reported utility data from interventional studies (15/17 [88.2%] HST, 5/9 [55.6%] SMC and 8/11 [72.7%] CADTH); however, the proportion of appraisals using these data for economic evaluations varied (3/15 [20.0%] HST, 4/5 [80.0%] SMC and 4/8 [50.0%] CADTH). Methodologies used to supplement utility data for economic evaluations are shown in **Figure 3**.
- Surveys were used in economic evaluations as part of NICE HST (4/17 [23.5%]) but not SMC (0/9 [0.0%]) or CADTH (0/11 [0.0%]) submissions. On the other hand, vignette studies were used in economic evaluations across all three HTA bodies (4/17 [23.5%] HST, 2/9 [22.2%] SMC and 2/11 [18.2%] CADTH). As in the previous review,[6] survey respondents included the general public and carers, whilst clinical experts and patients/carers were involved in development of vignettes. HTA body critiques raised concerns over low respondent numbers, use of survey/vignette data over trial data and valuation of vignettes by clinicians rather than patients.

Utility Data Collection Methodologies Across Common NICE, SMC and CADTH Appraisals

- A comparison of the submissions of the seven treatments appraised by all three HTA bodies further highlights the variation in methods used to inform economic evaluations, with only two therapies utilising the same method (i.e. interventional studies) for all three appraisals **(Figure 4)**.
- Interestingly, submissions to SMC and CADTH utilised the same utility data collection methods more often (5/7 [71.4%]). Conversely, the majority of NICE HST submissions (4/7 [57.1%]) used a different methodology to the equivalent SMC and CADTH submissions.

CONCLUSIONS

Submissions for very rare diseases across NICE, CADTH and SMC rely to different degrees on alternative utility data collection methods for informing economic evaluations, corresponding with the variety of published utility study types. Further to this, the methods of utility data collection used to inform economic evaluations for the same treatment, can vary across the different HTA bodies.

This variation suggests that best practice guidance on the appropriate application of alternative utility collection methods in rare diseases is needed.

Abbreviations: CADTH: Canadian Agency for Drugs and Technologies in Health; EU5: France, Germany, Italy, Spain, UK; HTA: health technology assessment; NICE: National Institute for Health and Care Excellence; PLR: pragmatic literature review; SLR: systematic literature review; SMC: Scottish Medicines Consortium.

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