Approaches to model patient and carer utilities and disutilities of adverse events in economic models for rare disease treatments in NICE appraisals

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Introduction

Previous studies have shown that patient health state utility v (HSUVs) in economic models used in National Institute for Hea Care Excellence (NICE) appraisals of rare disease treatments (I England are often uncertain [1-3]. Additionally, other work has highlighted methodological challenges in modelling carer hea related quality of life (HRQoL) [1,4,5]. Reporting of adverse eve (AEs) modelling is also frequently poor, with limited justification the approaches used [6,7], and there remains a lack of guidan how AEs should be included in economic evaluations [8].

Objective

To systematically review approaches to modelling patient and HRQoL, and disutilities of AEs in economic models for RDTs in appraisals.

Methods

<u>Appraisal selection:</u>

- We analysed RDT appraisals completed between 2011-2023
- This included all appraisals published in the Technology App guidance available for a treatment listed in the UK Orphan I of the Medicines & Healthcare Regulatory Agency, and all ap published under the Highly Specialised Technology appraisa guidance.
- We excluded terminated appraisals, multiple technology ap appraisals which had been replaced by updated guidance, comparisons, and indications without economic model.

Data extraction and categorisation:

- Published NICE appraisal documents were the primary dat for the analysis.
- We extracted appraisal characteristics, including the therap area, and the type of appraisal process.
- We also extracted characteristics of the final economic mod including the source of patient HSUVs, how carer HRQoL w included, and the approach used to model disutilities and treatment-related AEs for patients receiving the intervention
- For AEs, we distinguished between 'explicit' modelling (cost managing AEs and disutilities were added as model param 'implicit' modelling (costs and disutilities were assumed to implicitly included in HSUVs and healthcare resource costs inclusion, or no information.

<u>Data analysis:</u>

- We presented descriptive statistics of the extracted data.
- We mapped the data on patient and carer HRQoL against N hierarchy of preferred HRQoL methods [9] and analysed to extent the hierarchy works for patient HSUVs and carer HRC economic models for RDTs.

References

1. Looby A, Dymond A, Green W, et al. Uncertainties in evaluating the health-related quality of life and disease burden of people with rare diseases and their caregivers in NICE HST submissions. Orphanet J Rare Dis. 2024;19:391. Nicod E, Meregaglia M, Whittal A, et al. Consideration of quality of life in the health technology assessments of rare disease treatments. Eur J Health Econ. 2022;23:645-69

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3. Meregaglia M, Nicod E, Drummond M. The estimation of health state utility values in rare diseases: do the approaches in submissions for NICE technology appraisals reflect the existing literature? A scoping review. Eur J Health Econ. 2022;24:1151-216 . 4. Pennington BM. Inclusion of Carer Health-Related Quality of Life in National Institute for Health and Care Excellence Appraisals. Value Health. 2020;23:1349-57. 5. Pennington B, Al-Janabi H. Modelling Informal Carers' Health-Related Quality of Life: Challenges for Economic Evaluation. Appl Health Econ Health Policy. 2024;22:9-16. 6. Craig D, McDaid C, Fonseca T, et al. Are adverse effects incorporated in economic models? A survey of current practice. Int J Technol Assess Health Care. 2010;26:323-9.

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the Technology Appraisal guidance (73.9%), ialised Technology appraisal guidance.

nodels (n=111)

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У	Not included	No information			
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	20 (18%)	-			
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elevant study

	55 (49.5%)	С	If evidence shows EQ-5D not appropriate, then use in order of preference	18 (16	.2%)
	12		other generic preference-based measure	1	
	<i>11</i> 11		condition-specific preference- based measure	0	
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	nc,		direct valuation of own health	0	
Τ	7		from the literature		
	1		• EQ-5D • non-EQ-5D	1 1	
			clinical expert input	4	1
	3				3
	2		a mix of sources		
	6		• DCE + literature	2	
	1		 condition-specific preference- based measure + literature 	1	
	1		 vignette study + literature 	1	

el (n=29)

	ay		
27 (93.1%)	С	If evidence shows EQ-5D not appropriate, then use in order of preference	1 (3.4%)
6 0		other generic preference- based measure	0
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Key results (continued)

- conditions.
- appropriate.
- from a mix of sources.
- 93.1% of indications.

Limitations

- subjective.
- elsewhere [5].

Conclusions

- of AEs in economic models for RDTs.





About half of the indications analysed were for RDTs targeting oncological conditions (49.5%) and 50.5% for non-oncological

 \succ In the majority of appraisals, disutilities and costs due to AEs were either explicitly included in the economic model or not at all. > EQ-5D data from a relevant study was used in 34.2% of indications to inform patient HSUVS; it was not available from a relevant study in 49.5%, and in 16.2% evidence showed that EQ-5D was not

> Patient HSUVs were derived from a variety of sources, and often

Carer HRQoL was included quantitatively in 26.1% of indications; among those, EQ-5D data was not available from a relevant study in

 \succ The impact of carer HRQoL was often based on proxy conditions. > Sources informing patient HSUVs and carer HRQoL do not all appear to fit neatly into NICE's hierarchy of preferred HRQoL methods.

• We examined approaches used in the final economic model only, other assumptions were not necessarily captured.

• We defined 'relevant study' as study from which the treatment effect was estimated; using a different definition may change the findings. • We categorised only one appraisal as using proxy patient HSUVs as all HSUVs were based on the proxy condition; this reflects both a subjective decision and the challenge of defining a 'proxy condition'. • We categorized appraisals as pertaining to the category that EQ-5D was not appropriate when the manufacturer or the EAG mentioned this, and this was not dismissed by the committee, which may be

• Analyses determining the extent to which health gains came from improved HRQoL were not possible based on published appraisal documents because of redacted information and inconsistent reporting of factors driving QALY gain.

• We reviewed approaches used to include HRQoL in economic models; methodological issues and alternatives are discussed

> We found heterogeneity in the sources used for patient HSUVs and carer HRQoL, questioning how well the NICE hierarchy reflects HRQoL methods used in appraisals for RDTs.

> Overall, findings reflect challenges in the generation and interpretation of robust evidence for RDTs, emphasise the need for improving methods to include carer HRQoL in economic models, and highlight a lack of consistency of including disutilities and costs

7. Lu Y, Dai Z, Chang F, et al. Whether and How Disutilities of Adverse Events were Used in the Economic Evaluation of Drug Therapy for Cancer Treatment. Pharmacoeconomics. 2023;41:295-306. 8. Ghabri S, Dawoud D, Drummond M. Methods for Including Adverse Events in Economic Evaluations: Suggestions for 9. National Institute for Health and Care Excellence (NICE). NICE health technology evaluations: the manual. Manchester,

Improvement. Value Health. 2024;27:936-42. UK:NICE;2022 [updated 31 October 2024].