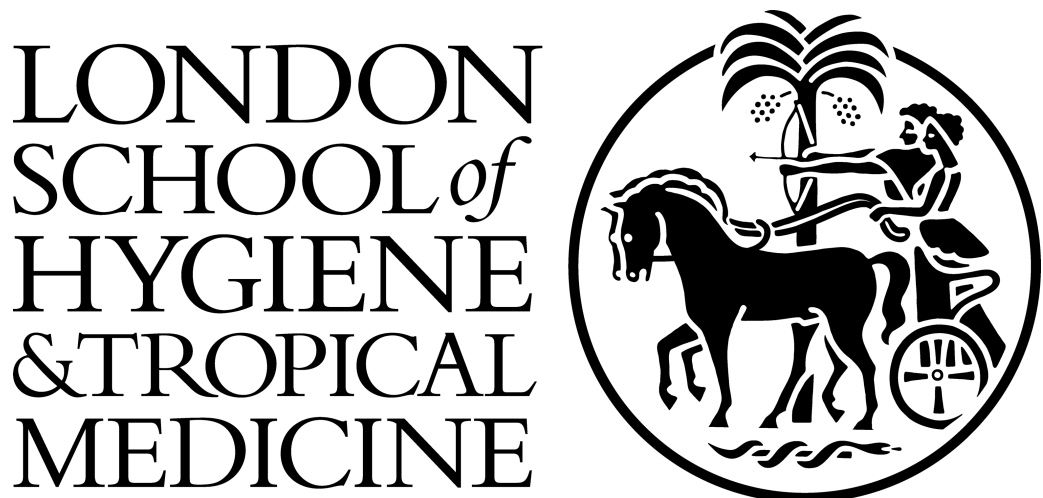


Approaches to model patient and carer utilities and disutilities of adverse events in economic models for rare disease treatments in NICE appraisals

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Introduction

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

Objective

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

Methods

Appraisal selection:

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- We excluded terminated appraisals, multiple technology appraisals, appraisals which had been replaced by updated guidance, cost comparisons, and indications without economic model.

Data extraction and categorisation:

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

Data analysis:

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

Key results

- Inclusion of 101 appraisals (80 active substances, 111 indications).
- The majority of indications were for RDTs appraised under the Technology Appraisal guidance (73.9%), with only 26.1% for RDTs appraised under the Highly Specialised Technology appraisal guidance.

Table 1: Approaches used to include disutilities and costs of AEs in economic models (n=111)

		Health-related quality of life (disutilities)			
		Explicitly	Implicitly	Not included	No information
Costs	Explicitly	53 (47.7%)	17 (15.3%)	10 (9%)	-
	Implicitly	2	2	2	-
	Not included	1	2	20 (18%)	-
	No information	-	-	-	2

Figure 1: Sources of patient health state utility values (n=111)

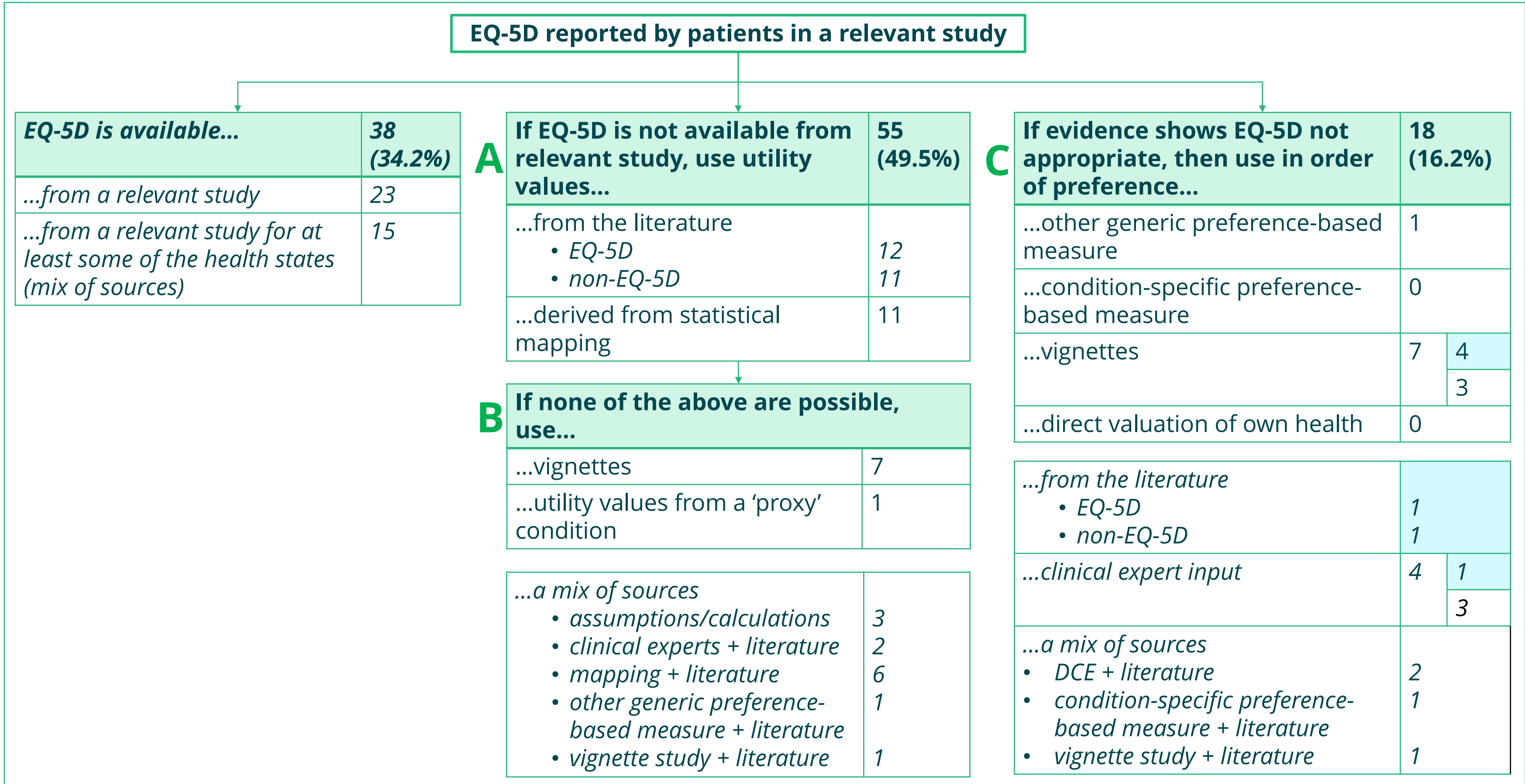
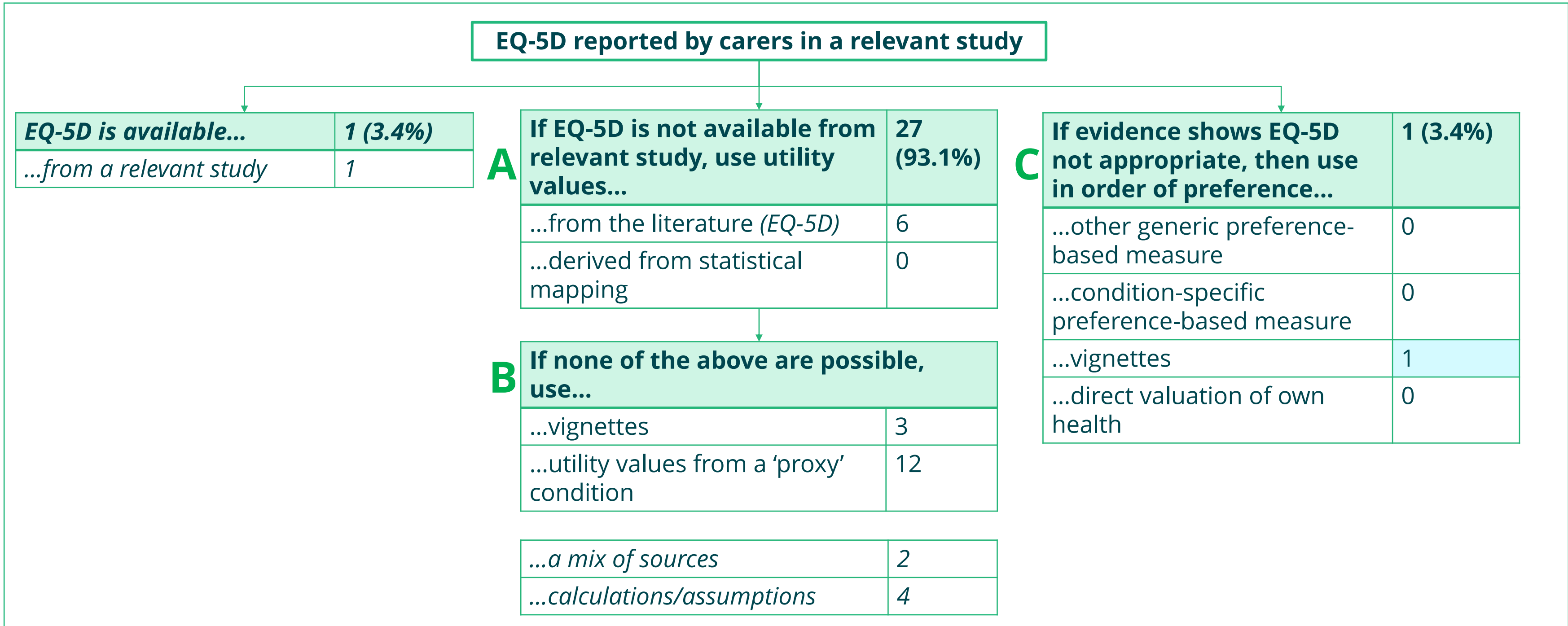


Figure 2: Sources of carer HRQoL quantitatively included in the economic model (n=29)



EQ-5D is available as part of the submission but was not used in the model

Category added by authors

Key results (continued)

- About half of the indications analysed were for RDTs targeting oncological conditions (49.5%) and 50.5% for non-oncological conditions.
- 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 appropriate.
- Patient HSUVs were derived from a variety of sources, and often from a mix of sources.
- Carer HRQoL was included quantitatively in 26.1% of indications; among those, EQ-5D data was not available from a relevant study in 93.1% of indications.
- 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.

Limitations

- 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 subjective.
- 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 elsewhere [5].

Conclusions

- 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 of AEs in economic models for RDTs.

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