



Association Between Information Sources of Manufacturer-Proposed Utility Values and the NICE Technology Appraisal Committee's Acceptance

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Conclusions

- Manufacturers make efforts to apply the EuroQOL 5-dimension (EQ-5D) in their main clinical trials with the aim of utilizing the resultant scores for the NICE technology appraisals. However, to obtain technology appraisal committee's acceptance in this regard, it is not sufficient merely to meet the NICE method guide.
- Manufacturers must consider in advance the possible differences between their clinical trial settings and real-world settings in United Kingdom, as well as the prospective quality of the EQ-5D data available from their trials, and then refine plans for EQ-5D measurement in order to obtain convincing evidence.

Introduction

- According to the National Institute for Health and Clinical Excellence's (NICE's) guide concerning the technology appraisal (TA) (NICE method guide), NICE encourages the use of the EuroQOL 5-dimension (EQ-5D), which has been evaluated in relevant clinical trials, to estimate the utility values [1].
- EQ-5D is said to lack sensitivity to changes in health; therefore, it seems logical that manufacturers would prefer to use more specialized scales other than EQ-5D in the clinical trials to underline health-related quality-of-life (HRQOL)-improving effect [2, 3].
- To our knowledge, no previous study has investigated whether the technology appraisal committee (TAC) accepted manufacturer-proposed utility values (MPUVs) based on various information sources.

Objective

- To investigate whether the TAC's acceptability of MPUVs is dependent on the information sources and to explore characteristics of manufacturer's evidence submission affecting the acceptability.

Methods

< Data Sources and Eligibility Criteria >

- Data were drawn from publicly available from the NICE's website.
- Any single technology appraisal (STA) for a cancer medicine completed between January 2011 and December 2020 was included.
- Appraisals were excluded if they were: 1) terminated before completion, 2) appraisals of medical devices, 3) appraisals that reviewed previous appraisals, or 4) appraisals that had been replaced by subsequent reviews.

< Data Extraction >

Sources	Extracted items [classification]
Manufacturers' Evidence Submission	Clinical trials utilized in the economic model (main trials; MTs)
	HRQOL measures applied in MTs. [EQ-5D / EORTC QLQ / FACT / others]
	Information sources of MPUVs for pre- and post-progression states. [EQ-5D / mapping other measures to EQ-5D / literature or TA guidance]
	Median follow-up period in MTs
TA guidance	Interval of EQ-5D measurements in MTs [≤ 2 weeks / ≤ 1 month / ≤ 2 months / > 2 months]
	TAC's judgement on MPUVs [Acceptable / Unacceptable]
	Reason for TAC's non-acceptance of MPUVs [inappropriate value for the UK / inappropriate data adjustment / unreliable data source]

Abbreviation: EORTC QLQ: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EQ-5D: EuroQol 5 Dimensions; FACT: Functional Assessment of Cancer Therapy; HRQOL: health-related quality-of-life; MPUV: manufacture-proposed utility value; MT: main trial; TAC: technology appraisal committee.

< Statistical Analysis >

- Information sources for MPUVs were classified into two categories (EQ-5D in main trials / others) and following hypotheses were tested.

Method	Hypothesis
Fischer's exact test	There were differences in the TAC's acceptance of MPUVs.
	There were differences in the reason for TAC's non-acceptance of MPUVs

Abbreviation: MPUV: manufacture-proposed utility value; TAC: technology appraisal committee.

- TAC's judgement for MPUVs were classified into two categories (acceptable / unacceptable), and following hypotheses were tested.

Method	Hypothesis
Mann-Whitney U test	There were differences in median follow-up period in MTs.
Fischer's exact test	There were differences in the Interval of EQ-5D measurement in MTs.

Abbreviation: EQ-5D: EuroQol 5 Dimensions; MT: main trial.

References

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Disclosures

This research received no specific grant from any funding agency, commercial, or not-for-profit sectors. ST is an employee of Daiichi Sankyo Co., Ltd. MN does not have any conflict of interest related to this study.

Results

- The number of appraisals for which the EQ-5D was the information source of MPUVs increased consistently over the period of 2011 to 2020.
- The TAC's acceptance of MPUVs was not dependent on the manufacturers' information sources, or whether they met the NICE method guide.
- The primary reasons for non-acceptance by the TAC differed between the manufacturers' evidence submissions that featured EQ-5D-sourced utility values and those that sourced utility values through other means.
- Long-term survival follow-up at the time of manufacturer's submission and frequent EQ-5D measurements in main trials resulted in lowering the risk of non-acceptance by the TAC.

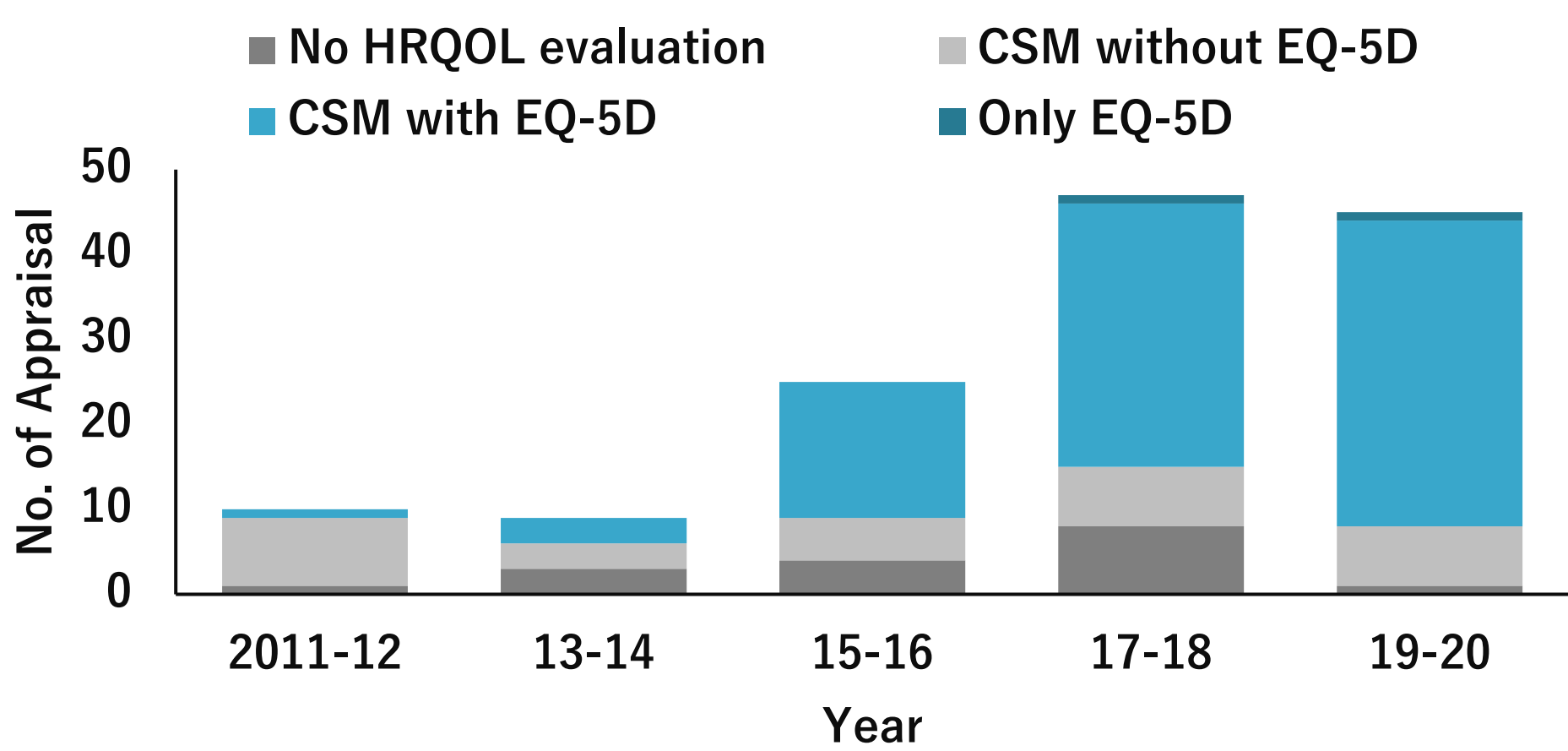


Figure 1. HRQOL Measurements Used in Main Trials

Abbreviation: CSM: Cancer-specific measures; EQ-5D: EuroQol 5 Dimensions; HRQOL: health-related quality-of-life.

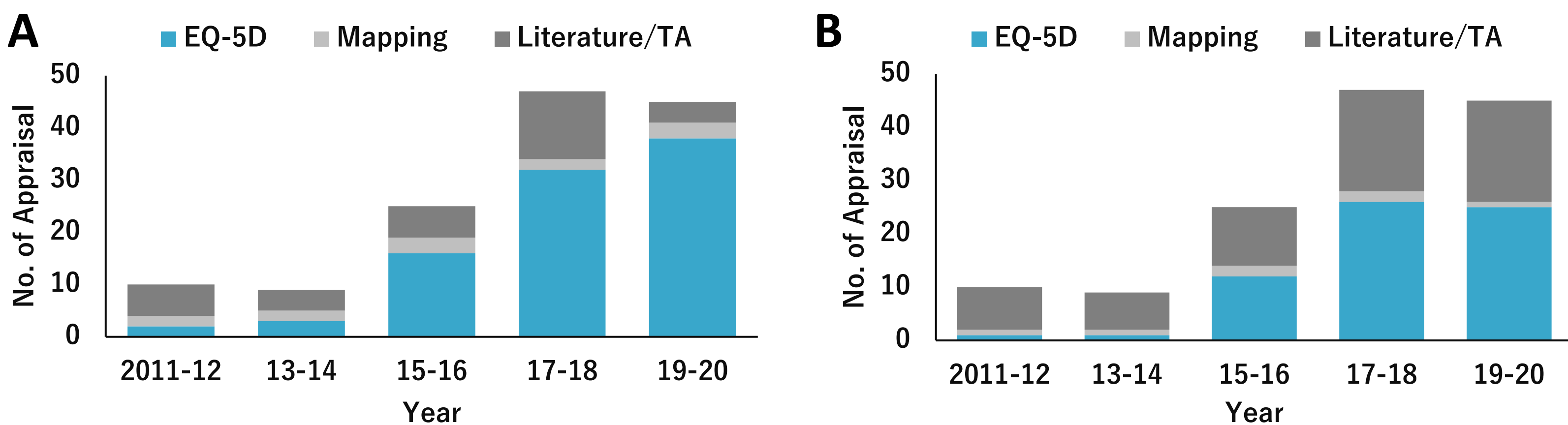


Figure 2. Information Sources of MPUVs

Note. (A) Utility values for the pre-progression state, (B) utility values for the post-progression state.

Abbreviation: EQ-5D: EuroQol 5 Dimensions; TA: technology appraisal; MPUV: manufacture-proposed utility value.

Information sources for MPUVs		TAC's judgement, n (%)		P value
		Acceptable	Not-acceptable	
Pre-progression state	EQ-5D in MTs (n=87)	58 (67)	29 (33)	0.458
	Others (n=49)	29 (59)	20 (41)	
Post-progression state	EQ-5D in MTs (n=87)	35 (56)	27 (44)	1.000
	Others (n=49)	42 (57)	32 (43)	

Table 1. The TAC's Judgments on MPUVs.

Abbreviation: EQ-5D: EuroQol 5 Dimensions; MPUV: manufacture-proposed utility value; MT: main trial; TAC: technology appraisal committee.

Reasons for non-acceptance by the TAC		Sources for MPUVs, n (%)		P value
		EQ-5D in MTs	Others	
Pre-progression state	Inappropriate value for the UK pop.	15 (52)	7 (35)	< 0.001
	Inappropriate data adjustment	13 (45)	3 (15)	
	Unreliable data source	1 (3)	10 (50)	
Post-progression state	Inappropriate value for the UK pop.	11 (41)	14 (44)	0.014
	Inappropriate data adjustment	14 (52)	7 (22)	
	Unreliable data source	2 (7)	11 (34)	

Table 2. Reasons for the TAC's Non-acceptance of MPUVs

Abbreviation: EQ-5D: EuroQol 5 Dimensions; MPUV: manufacture-proposed utility value; MT: main trial; TAC: technology appraisal committee.

TAC's judgment		Interval, n (%)				P value
		≤ 2 wks	≤ 1 mo	≤ 2 mos	> 2 mos	
Pre-progression state	Acceptable	6 (10)	37 (64)	10 (17)	5 (9)	0.002
	Unacceptable	0 (0)	11 (38)	11 (38)	7 (24)	
Post-progression state	Acceptable	3 (9)	19 (54)	12 (34)	1 (3)	0.007
	Unacceptable	0 (0)	17 (63)	3 (11)	7 (26)	

Table 3. Interval of EQ-5D Measurement in Main Trials

Abbreviation: EQ-5D: EuroQol 5 Dimensions; mo: month; MPUV: manufacture-proposed utility value; TAC: technology appraisal committee; wk: week.

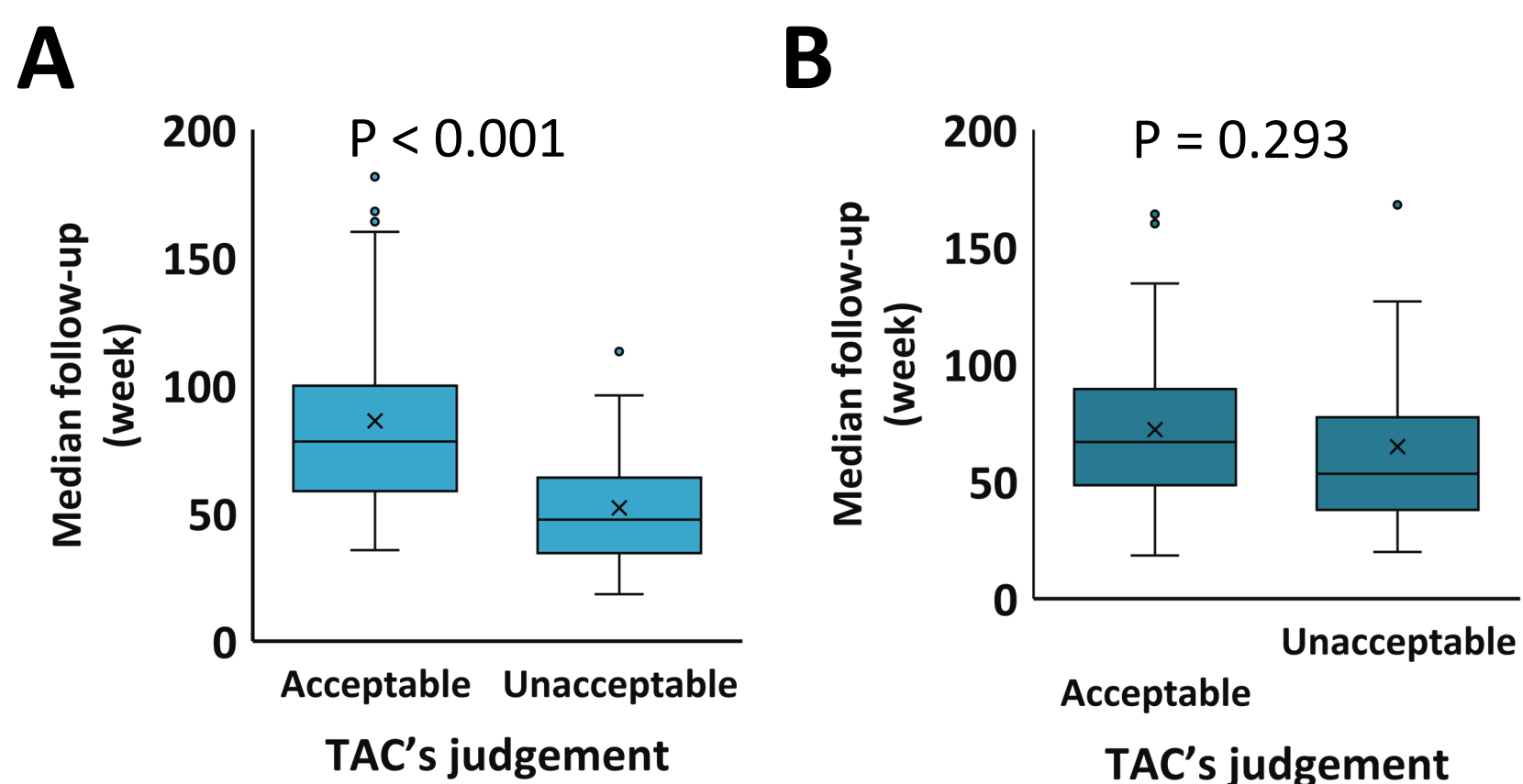


Figure 3. Median Follow-up Period of Main Trials at the Time of Evidence Submissions

Note. Utility values for the pre-progression state (A) and for the post-progression state (B). The upper and lower whiskers are the upper or lower quartiles plus 1.5 times the interquartile distance. The horizontal lines that split the boxes in two represents median value. The white circles denote outliers.