Quantifying the impact of inconsistencies in economic modelling assumptions: A case study in metastatic colorectal cancer

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Introduction

Health economic models are essential tools for evaluating the value of new and existing medical interventions, and are often used to support reimbursement and policy decisions. Over time, methodological standards have evolved, with organisations such as the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) (1) and ISPOR (2) publishing detailed guidance, such as Technical Support Documents and Good Practice Reports, to promote consistency and transparency in modelling practices. These documents typically focus on high-impact methods such as survival modelling, extrapolation techniques, and utility estimation.

However, certain structural and methodological assumptions and technical modelling choices (such as time-preference discounting methods, the application of population characteristics, and assumed probability distributions for costs) are often considered lower priority and receive limited attention in formal guidance. Despite their perceived minor role, these assumptions can introduce variability across evaluations, in turn reducing comparability between analyses, and potentially influencing cost-effectiveness outcomes (particularly when decisions are based on formal willingness-to-pay thresholds).

Objectives

The objectives of this research were to:

- Reconstruct a published cost-effectiveness model from a NICE case study using transparent inputs and pseudo patient-level data
- Systematically test alternative modelling approaches to explore the impact of structural assumptions often overlooked in formal guidance
- Quantify the effect on key outcomes such as the incremental cost-effectiveness ratio (ICER) and assess whether these methodological discrepancies could influence decision-making

Methods

A case study was identified by searching the NICE website. TA405, which assessed an intervention in previously treated metastatic colorectal cancer was selected based on the transparency of reporting, which allowed the model to be reconstructed (3). A three-state partitioned survival model was recreated using pseudo patient-level data, generated by digitising published Kaplan–Meier curves. Inputs were consistent with those reported in TA405, where possible.

The following six alternative modelling approaches were tested using the reconstructed model:

1	Continuous (i.e. per cycle) versus annual time-preference discounting
2	Dynamic (due to differences in mortality rates by sex) versus constant general population sex distribution for the calculation of mortality and utilities
3	Adverse event (AE) costs applied per cycle versus as a one-off in the first model cycle only
4	Half-cycle correction applied only in the first and last cycles versus each cycle
5	Costs varied using a normal distribution (due to central limit theorem) versus gamma distribution in sensitivity analysis
6	Varying parameters using ±10% of the mean versus a probability distribution using an assumed standard error for a one-way sensitivity analysis (OWSA)

Results

Scenarios impacting base case results

Table 1 presents the results of the different structural scenarios. The approach taken for discounting outcomes had the largest impact on incremental quality-adjusted life years (QALYs) (1.5% increase when discounting annually versus continuous discounting).

The general population sex distribution approach had a minimal impact on results (it should be noted that due to the high mortality rates of this patient population, survival was not adjusted by the general population rate). As such, only the general population QALYs were affected by this scenario. This may have a larger impact in other disease areas with lower mortality rates.

Of the scenarios tested, the AE approach had the largest impact on the ICER, although the difference between the cost per cycle and one-off cost approach was just 2%.

Applying half-cycle correction in the first and last cycles had a large impact on the total costs in each arm (18.9 and 34.4% decrease for intervention and comparator, respectively); however, the incremental cost impact was small (1% decrease).

Scenarios impacting sensitivity analyses

Varying the cost inputs using a gamma distribution compared with a normal distribution had little impact on the overall uncertainty (<£5 difference between the spread in uncertainty). The difference in distributions also had little impact on uncertainty within probabilistic sensitivity analysis (PSA) (see Figure 1).

There was little change between the top 10 parameters with regard to which had the largest impact in ICER across OWSA approaches. However, the spread in uncertainty was greater using the ±10% approach for utilities, and less for the cost inputs (see Figure 2).

Table 1: Results of the alternative modelling approaches

Topic	Scenario	INT costs, £	INT QALYs	COMP costs, £	COMP QALYs	Incremental costs, £	Incremental QALYs	ICER
1. Discounting	Continuous†	18,876	0.576	10,116	0.423	8,760	0.153	57,426
	Annual	19,125	0.584	10,260	0.429	8,866	0.155	57,065
	Absolute difference, %	**1.3%**	**1.5%**	**1.4%**	**1.3%**	**1.2%**	**1.9%**	**0.6%**
2. General population sex distribution	Constant over time horizon†	18,876	0.576	10,116	0.423	8,760	0.153	57,426
	Dynamic	18,876	0.576	10,116	0.423	8,760	0.153	57,427
	Absolute difference, %	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
3. AEs	One-off cost†	18,876	0.576	10,116	0.423473643	8,760	0.153	57,426
	Cost per cycle	18,426	0.576	9,843	0.423473643	8,584	0.153	56,275
	Absolute difference, %	**2.4%**	**0.0%**	**2.7%**	**0.0%**	**2.0%**	**0.0%**	**2.0%**
4. Half-cycle correction	Each cycle†	18,876	0.576	10,116	0.423	8,760	0.153	57,426
	First and last cycles	15,313	0.577	6,638	0.424	8,675	0.153	56,763
	Absolute difference, %	**18.9%**	**0.2%**	**34.4%**	**0.2%**	**1.0%**	**0.2%**	**1.2%**

† Denotes the setting selected to vary other scenarios. Min Mid Max

Figure 1: OWSA tornado plot using a probability distribution and assumed standard error

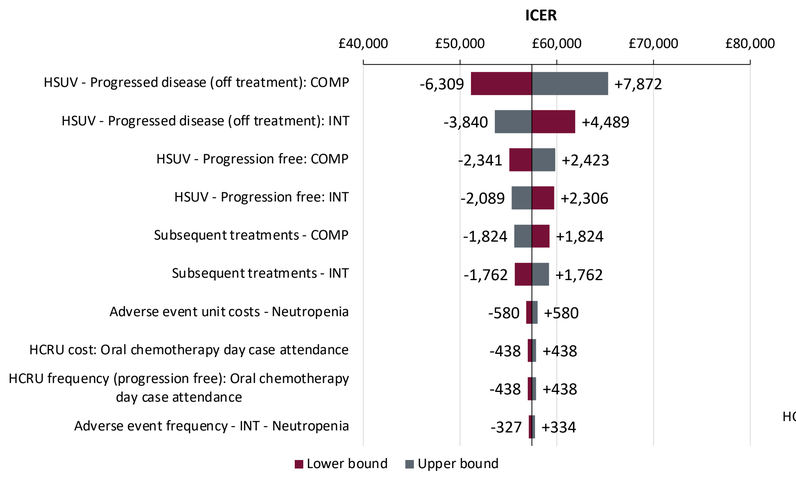
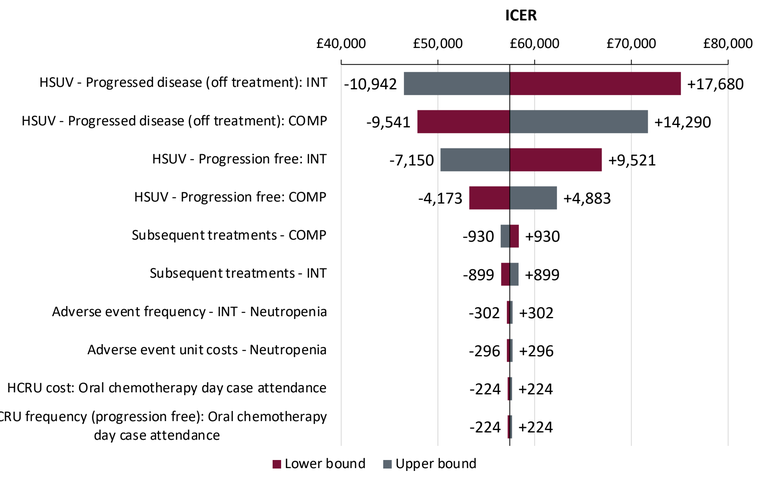


Figure 2: OWSA tornado plot using ±10% of the mean



Conclusion

Although varying common methodological assumptions appeared to have a small impact on cost-effectiveness results, such changes could collectively be important for decision-making, particularly when willingness-to-pay thresholds are applied. The approach to handling uncertainty could also impact the overall assessment of cost effectiveness.

It is also important to consider that the impact of these assumptions may be more substantial in other disease areas, or in models with more complex structures, especially where outcomes are highly sensitive to small changes in model inputs.

Clear methods guidance on structural and methodological modelling assumptions would be beneficial to improve consistency and comparability between economic evaluations.

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2. NICE Decision Support Unit. Technical support documents. Available from: https://sheffield.ac.uk/nice-dsu/tsds. Accessed: September 2025.
3. National Institute for Health and Care Excellence. 2016. [TA405] Trifluridine–tipiracil for previously treated metastatic colorectal cancer. Available from: https://www.nice.org.uk/guidance/ta405. Accessed: September 2025.

Abbreviations

AE, adverse event
COMP, comparator
DSU, Decision Support Unit
HCRU, healthcare resource use
HSUV, health state utility value
ICER, incremental cost-effectiveness ratio
INT, intervention
NICE, National Institute for Health and Care Excellence
OWSA, one-way sensitivity analysis
PSA, probabilistic sensitivity analysis
QALY, quality-adjusted life year