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Current Scenario of 'Scenario Analysis' in Health Economic Models in Oncology: A Review of NICE Appraisals

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INTRODUCTION

- A health economic model is a critical piece of evidence considered by health technology assessment (HTA) agencies globally to inform reimbursement decisions. However, within the health economic model, multiple sources of uncertainty inevitably exist.
- Uncertainty analysis in the model is relevant to study because of insufficiency of data and the assumptions made to structure the model.
- Probabilistic and deterministic sensitivity analysis, and scenario analysis are commonly undertaken to check parameter and methodological uncertainties within the model.
- In scenario analysis, assumptions made around the model are altered and the impact is studied on the change in Incremental Cost Effectiveness Ratio (ICER).
- However, there is limited guidance on scenario analysis and mostly, it is modeller's choice on selection of scenarios to vary within the model.

OBJECTIVE

To conduct a review of National Institute for Health and Care Excellence (NICE) Technology Appraisals (TAs) within oncology to understand variation in scenario analyses within the models, and to identify scenarios that are commonly missed or ignored during uncertainty checks alongside their impact on ICERs.

METHODOLOGY

- A targeted literature review was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines with predefined protocol for inclusion and exclusion of studies.
- NICE TAs database was searched to identify relevant literature for the study.
- NICE was preferred to conduct this targeted literature review because of its diligence with respect to the guidelines on economic assessment of new and existing health technologies. Besides, the submissions to NICE for TAs are freely accessible and are expected to follow the guidelines rather rigorously.
- The duration considered for this targeted literature review is of one year from 1st May 2021 to 30th April 2021.
- Two reviewers were involved to conduct the targeted literature review and any disagreement about the inclusion or exclusion of studies was resolved via discussion between them.
- A data extraction form was developed in MS-Excel to comprehensively identify and compile the data on scenarios presented in the included studies.
- From each identified study, data under following categories were extracted:
  A. Scenario Analysis related to Costs parameters and assumptions (including dose intensity, wastage, costs etc.)
  B. Scenario Analysis related to Utility parameters and assumptions
  C. Scenario Analysis related to Treatment Effect assumptions
  D. Scenario Analysis related to Subsequent Therapy assumptions
  E. Scenario Analysis on Other measures (including, time horizon, discount rates, etc.)
  F. Additional Scenario Analysis conducted by Evidence Review Group (ERG)
- Impact on ICER due to usage of different scenarios were studied using indexation approach.

RESULTS

A. Common Scenarios considered in NICE TA models

I. Twenty-eight models were included in the review and several scenarios were assessed within the models.
II. A huge variation was seen across the models relating to the scenarios conducted around the parameters and the assumptions.
III. Most common scenarios assessed were related to treatment effect assumptions: survival distribution choice (n=18), treatment duration (n = 13), treatment waning (n=6) and related to assumptions around health state utility values (n=16).
IV. Many key scenarios were not included within the models. This led the ERG to perform additional scenarios to check the consistency and robustness of the models (e.g., considering complete survival scenarios, different time horizons and appropriate treatment waning rate).
V. A tabular representation of number of studies that conducted the scenarios is given in Table 1.

Figure 1: Distribution of studies with respect to scenarios considered:

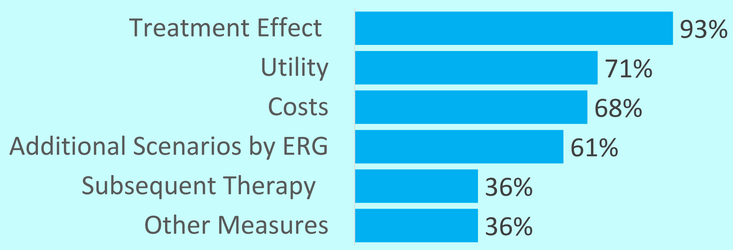


Figure 2: A matrix representation of distribution of studies with respect to scenarios considered

Scenarios Related to	Costs	Utility	Treatment effects	Subsequent therapy	Other measures	ERG's additional scenarios
Costs	**19**	**17**	**18**	**7**	**7**	**11**
Utility		**20**	**19**	**8**	**8**	**12**
Treatment effects			**27**	**10**	**9**	**16**
Subsequent therapy				**10**	**6**	**5**
Other measures					**10**	**6**
ERG's additional scenarios						**17**

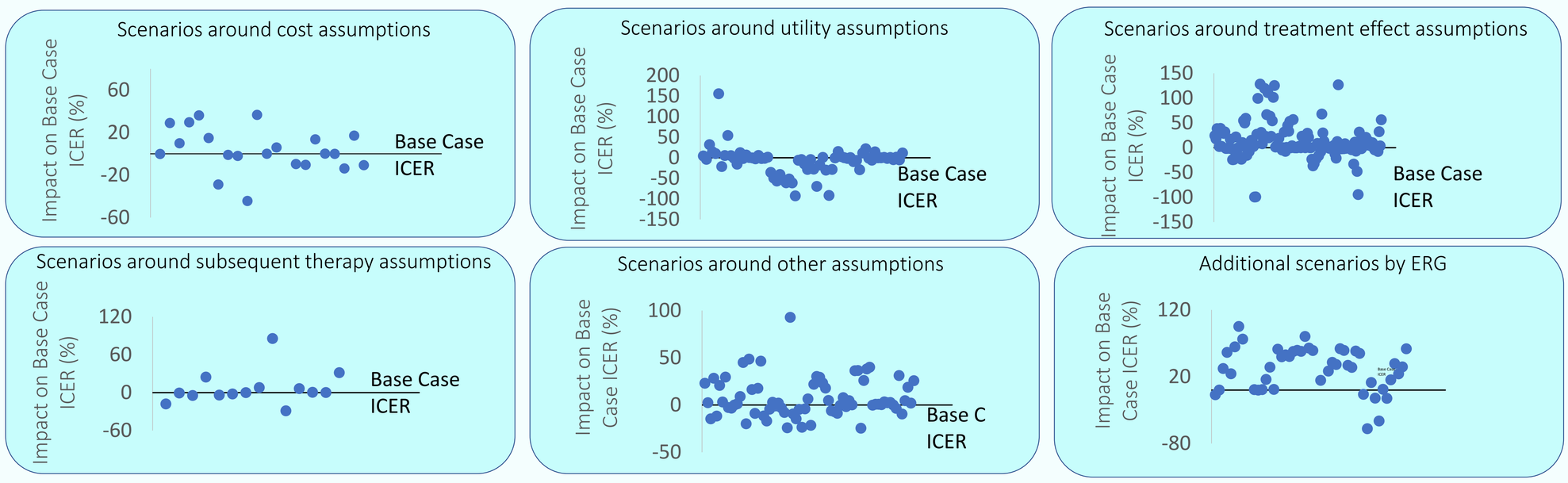
Inferences that can be drawn from the left matrix (Figure 2):

- No study reported conducting all the scenarios considered.
- There was only one study, TA705, Atezolizumab monotherapy for untreated PD-L1 positive metastatic non-small-cell lung cancer, that considered all scenarios (expect one).
- Most scenarios considered were Scenario Analysis on Cost component and assumptions (including dose intensity, wastage, costs etc.), Scenario Analysis on Utility component and assumptions and, Scenario Analysis on Treatment Effect assumptions.

B. Impact on ICER as per different scenarios considered in NICE TA models

- Overall, we identified a considerable variation in ICER when different scenarios were explored within the models.
- The impact on increase in ICER went as high as £21 million/QALY (when scenarios related to utility were explored and QALY difference converges to 0).
- We summarized change in ICER in different scenarios using indexation technique and presented panel scatter plots (Figure 3).

Figure 3: Impact on ICER with different scenarios



DISCUSSION

- Our review demonstrated that the scenarios considered across models were not consistent.
- While mostly the scenario analysis is conducted around treatment effect, cost components and utility component by the manufacturer company, the scenarios regarding the time to event endpoints (survival curve choices) and adverse events are neglected.
- This negligence leads the ERGs to conduct additional scenarios to check robustness of the models.
- Multiple guidance such as ISPOR task force, NICE and CADTH methodological guidance exist in relation to conduct uncertainty analysis, specifically through OWSA and PSA, but limited guidance exists on list of scenarios to be considered
- Due to non-existence of 'go to' document on scenario analysis, it becomes mostly the modeller's choice on selection of scenarios to vary within the model.

CONCLUSION

- There are huge inconsistencies observed around the list of scenarios considered in the models submitted to NICE.
- This may lead to a failure in capturing all key scenarios in the uncertainty checks of the model and may lead to suboptimal healthcare policy decisions.
- Further research is needed to develop the standardized list on 'must-have' and 'good-to-have' scenarios for scenario analysis checks in the health economic models.

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