HTA75

Clinical Benefit vs. Reimbursement Decisions: Examining Misalignments between ESMO-MCBS and HTA Outcomes in Oncology

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BACKGROUND

- Rising cancer treatment costs and high-priced new drugs are putting pressure on health systems and challenging the balance between innovation, affordability, and equity.
- To ensure fair and sustainable access, it is crucial to align how clinical benefit is measured with how treatments are reimbursed.
- The **European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)** standardises the evaluation of clinical benefit by grading therapies based on survival and quality-of-life outcomes.
- ESMO-MCBS scores often diverge from the **reimbursement outcomes** of Health Technology Assessment (HTA) agencies, which additionally consider cost-effectiveness, budget impact, and other contextual factors.
- This study benchmarks **ESMO-MCBS ratings** against **HTA recommendations** from **NICE (UK), SMC (Scotland), and CDA (Canada)** for **oncology drugs**, identifying and analysing **misalignment cases** and the clinical and economic factors that can contribute to these divergences.

STUDY DESIGN & ANALYSIS FRAMEWORK

A four-step **structured methodology** implemented to examine alignment between ESMO-MCBS scores and HTA outcomes.

The process involved data collection, data matching, development of an alignment framework, and data analysis.

HTA & ESMO Data Collection

- HTA reports from NICE, SMC, CDA (2010–2024)
- ESMO-MCBS scorecards for solid tumours

Matching HTA / ESMO data set

- Match drug–indication–trial across HTA and ESMO
- Use highest ESMO-MCBS score when multiple trials

Classification Framework

- Framework design for misalignment case identification: Discordance between HTA outcomes and ESMO-MCBS scores
  - Positive: HTA positive, ESMO low benefit (1–2/C/NEB)
  - Negative: HTA negative, ESMO high benefit (4–5/A)

Data Analysis

- HTA uncertainty collection and tagging: Qualitative review and categorical tagging of identified uncertainties into clinical and economic domains based on predefined criteria.
- Statistical analysis models
  - Chi-square (χ^2) test → association between ESMO-MCBS & HTA outcomes
  - Binary logistic regression → misalignment occurrence likelihood
  - Multinomial regression → misalignment direction (positive vs negative)

RESULTS

Misaligned Drug–Indication Pairs by Agency and ESMO MCBS Grade

Across all agencies, 71 cases were classified as misaligned, of which 77% (n=55) were positive and 23% negative (n=16).

By agency:

- CDA: 21 misaligned cases (13%), 18 (86%) positive and 3 (14%) negative
- NICE: 28 cases (17%), with 20 (71%) positive and 8 (29%) negative
- SMC: 22 cases (15%), with 17 (78%) positive and 5 (22%) negative

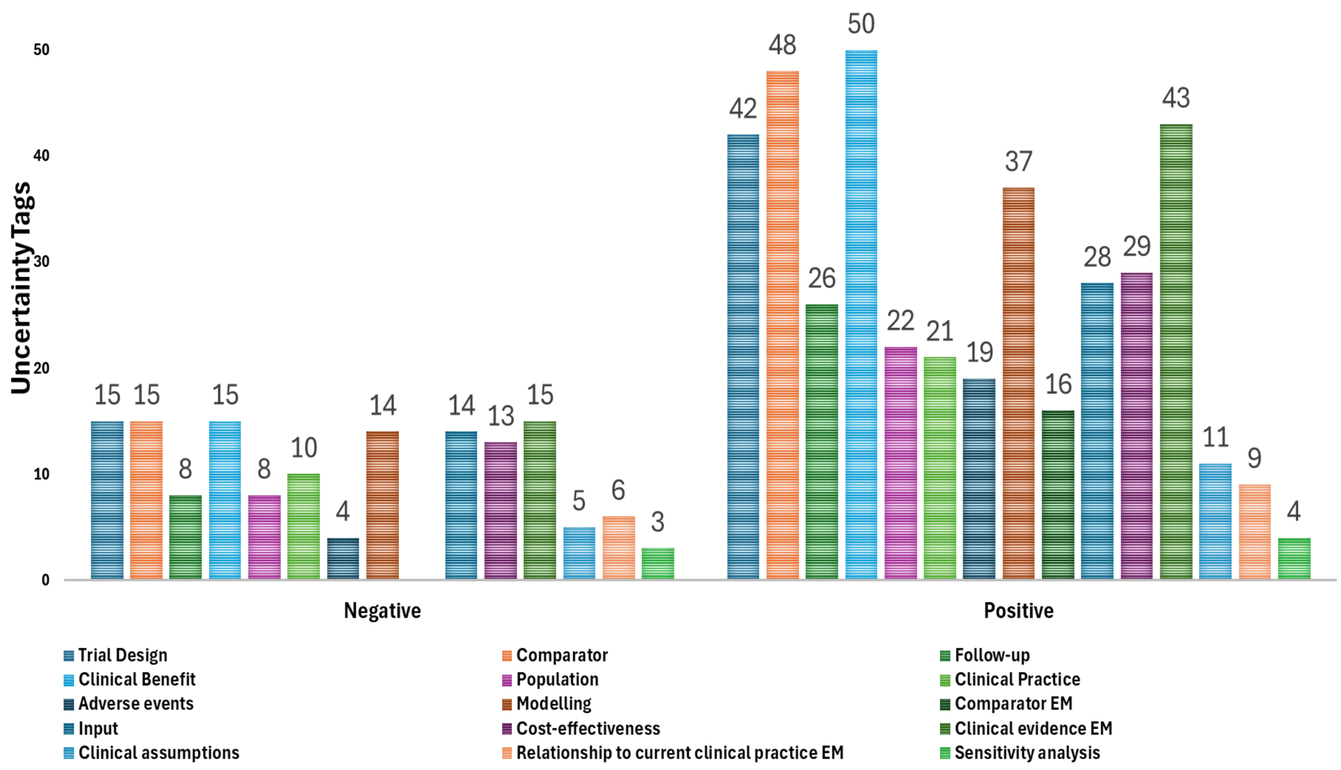
Characterisation of Clinical and Economic Uncertainties

Clinical domains:

- Most frequent issues involved magnitude of clinical benefit, including non-significant endpoints, modest effects, uncertain effect sizes, and heterogeneous results.
- Additional concerns related to placebo or non-standard comparators and trial design limitations.

Economic domains:

- Common uncertainties stemmed from clinical evidence in models & structural modelling assumptions, such as parameter uncertainty & outcome extrapolation.



Regression Analysis of Factors Associated with HTA–ESMO Misalignment

- **Overall misalignment** more likely when there was no complete trial match between ESMO & HTA evaluations or when placebo-controlled designs were used.
- **Positive misalignments**, greater alignment observed in assessments based on OS or PFS outcomes.
- **Negative misalignments**, no variables were statistically significant, whereas positive misalignments reflected the overall results, with a higher number of cases.

Misalignment Type	Variable	OR	P>|z|	[95% Conf. Interval]
Overall Misalignments	Complete trial match	2,129	0,048	1,006 - 4,504
	Placebo-controlled trial (Y/N)	2,178	0,008	1,222 - 3,882
	DFS evaluated outcome	0,418	0,007	0,222 - 0,788
Misalignment Type	**Variable**	**RRR**	**P>|z|**	**[95% Conf. Interval]**
Positive Misalignment	Complete trial match	2,656	0,026	1,125- 6,273
	Placebo-controlled trial (Y/N)	3,007	0,002	1,490 - 6,071
	OS evaluated outcome	0,414	0,024	0,193 - 0,889
	PFS evaluated outcome	0,321	0,002	0,158 - 0,652

Determinants of Positive and Negative Misalignment by Uncertainty Domain

- Clinical uncertainties related to trial design & clinical practice, strongly associated with relatively greater probability of negative misalignment ($p < 0.05$).
- Adverse-event & clinical-benefit uncertainties, linked to a lower probability of negative misalignment ($p < 0.05$ and $p < 0.10$, respectively).
- Economic uncertainties not significant predictors of misalignment direction, yet uncertainties in clinical evidence used in economic models showed a weak association ($p = 0.084$).

Misalignment Type	Variable	OR	P>|z|	[95% Conf. Interval]
Clinical Uncertainty	Trial Design	2,986	0,041	1,045 - 8,533
	Clinical Practice Generalisability	3,346	0,005	1,439 - 7,778
	Adverse Events	0,381	0,039	0,152 - 0,953

CONCLUSIONS

- These findings reveal **systematic divergences between clinical benefit frameworks and reimbursement decisions**, particularly in cases where therapies with high clinical benefit are not recommended for reimbursement.
- Addressing these misalignments requires **greater collaboration among stakeholders to harmonize evaluation criteria**, improve transparency of decision-making processes, and refine methodologies.
- Ultimately **promoting patient-centred value assessment** and equitable access to beneficial oncology treatments.