Impact of Treatment Discontinuation on Long-Term Cost-Effectiveness Estimates in Health Economic Models

EE527

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INTRODUCTION

- CEAs underpin reimbursement decisions in HTA; structural model assumptions directly influence cost-effectiveness estimates and coverage outcomes
- A prevalent but often unjustified assumption in health economic models is continuous treatment until death - in practice, patients discontinue due to adverse events, lack of efficacy, comorbidities, or personal preference
- Failure to incorporate discontinuation may systematically overestimate lifetime health benefits and underestimate ICERs, potentially leading to suboptimal reimbursement decisions

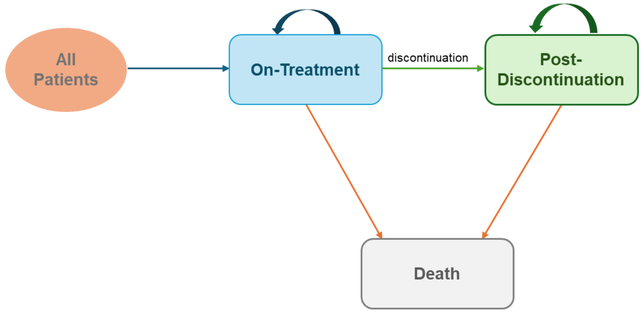
OBJECTIVE

- To develop a health economic model explicitly incorporating treatment discontinuation and evaluate its impact on lifetime cost-effectiveness outcomes relative to the continuous treatment assumption
- To quantify the systematic bias introduced by ignoring discontinuation, measured in terms of QALYs, total costs, and the incremental cost-effectiveness ratio (ICER)
- To examine the sensitivity of cost-effectiveness estimates to key discontinuation parameters - including discontinuation rates and post-discontinuation health outcomes - through one-way and scenario analyses

METHODS

- A cohort-based Markov model was developed with annual cycles and a lifetime horizon of 40 years, conducted from a healthcare payer perspective as described in Table 1
- Three mutually exclusive health states were included: On-Treatment, Post-Discontinuation, and Death (absorbing state) as shown in Figure 1
- Half-cycle correction was applied to all cycles to reduce bias in the estimation of accumulated costs and QALYs

Figure 1: Markov model state-transition diagram showing the three health states and transitions between them



- Two treatment strategies were compared: (1) continuous treatment until death with no discontinuation assumed, and (2) treatment with discontinuation modelled as a constant annual hazard, assuming an exponential process over time
- Patients who discontinued treatment transitioned to the Post-Discontinuation state, which was associated with reduced health-related quality of life (HRQoL) and increased mortality risk compared with the On-Treatment state
- Model parameters were derived from published literature and representative health economic modelling sources. The annual treatment discontinuation probability was set at 15%, while annual mortality risks were assumed to be 3% for patients receiving treatment and 6% following discontinuation
- Health state utility values were 0.80 for the On-Treatment state and 0.65 for the Post-Discontinuation state. Annual healthcare costs were estimated at USD 15,000 for patients receiving treatment and USD 4,000 following discontinuation
- Future costs and QALYs were discounted at an annual rate of 3%
- Scenario analyses were conducted to compare outcomes between the continuous treatment and discontinuation strategies over the full model horizon
- One-way sensitivity analyses were performed to evaluate the impact of key model parameters, including discontinuation rates and post-discontinuation mortality and utility values, on the ICER

Table 1: Model Parameters

Clinical Parameters	Economic Parameters
Discontinuation rate: 15%/yr	On-Tx cost: USD 15,000/yr
On-Tx mortality: 3%/yr	Post-disc cost: USD 4,000/yr
Post-disc mortality: 8%/yr	Discount rate: 3%
On-Tx utility: 0.80	
Post-disc utility: 0.65	

RESULTS

- Continuous treatment yielded 12.31 lifetime QALYs at a total discounted cost of USD 230,722; incorporating discontinuation reduced QALYs to 8.16 and costs to USD 92,490 (Table 2)
- Discontinuation reduced lifetime health benefit by 34% relative to the continuous treatment assumption, driven primarily by patient transition into the post-discontinuation state (Figure 4)

Table 2: Outcomes summary table

Outcome	Continuous Treatment	With Discontinuation	Difference
Lifetime QALYs	12.31	8.16	-4.15
Total Costs (USD)	230,722	92,490	+138,231
ICER (USD/QALY)	—	—	33,321

Figure 2: Cumulative QALYs over time

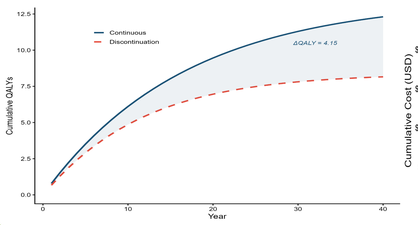
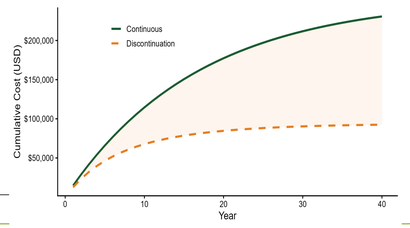


Figure 3: Cumulative discounted costs over time

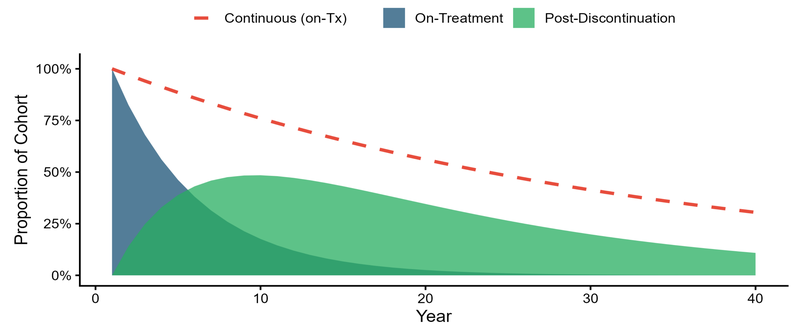


RESULTS

- Continuous treatment produced an incremental gain of 4.15 QALYs at an additional cost of USD 138,231 versus the discontinuation strategy, yielding an ICER of USD 33,321/QALY
- This ICER is substantially higher than estimates derived under the continuous treatment assumption — demonstrating that ignoring discontinuation systematically underestimates the true cost per unit of health benefit

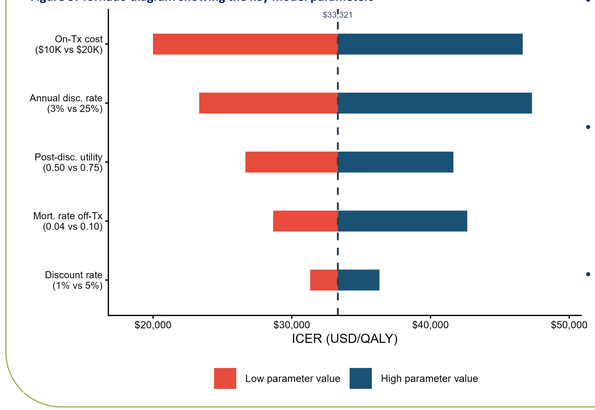
Ignoring discontinuation underestimates ICER by approximately 34%

Figure 4: Health state membership over time under the with-discontinuation strategy



- Annual discontinuation rate was the most influential parameter; higher rates substantially increased the ICER (Figure 5)
- Post-discontinuation utility and mortality were the second key drivers - poorer outcomes in this state amplified the ICER, consistent with base-case assumptions

Figure 5: Tornado diagram showing the key model parameters



- This model represents a hypothetical methodological framework; findings are illustrative and not intended to reflect any specific disease, treatment, or payer context
- A constant annual discontinuation hazard was assumed throughout the model horizon; time-varying hazards, which may better reflect real-world patterns, were not explored
- PSA was not performed; uncertainty characterization is therefore limited to one-way and scenario analyses, which do not capture parameter correlation

CONCLUSION

The model said stay.
The patient already left.

- Treatment discontinuation has a clinically and economically meaningful impact on long-term cost-effectiveness estimates; its omission introduces systematic directional bias - overestimating lifetime QALYs and underestimating ICERs
- Models that ignore discontinuation risk producing estimates that misrepresent the true value of treatment, with potential consequences for coverage and reimbursement decisions in HTA
- Health economic models submitted for HTA should explicitly incorporate discontinuation as a structural assumption, with transparent justification of the hazard function, rate applied, and health state consequences
- Standardized guidance on modelling treatment discontinuation would strengthen the consistency and credibility of economic evidence across HTA submissions

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Disclosure:
PB, AS, KP, SM, and SP, the authors declare that they have no conflict of interest

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