PRecision oncology Evidence Development in Cancer Treatment (PREDiCT):
Life-cycle economic evaluation of entrectinib

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# Acknowledgments and disclosures

I am from Vancouver, British Columbia and have the privilege to reside, work and play on the traditional, ancestral and unceded territories the Coast Salish peoples, including Sḵwx̱wú7mesh Úxwumixw (Squamish), Sel̓íl̓witulh (Tsleil-Waututh), Xʷməθkʷəy̓əm (Musqueam), and Stó:lō Nations.
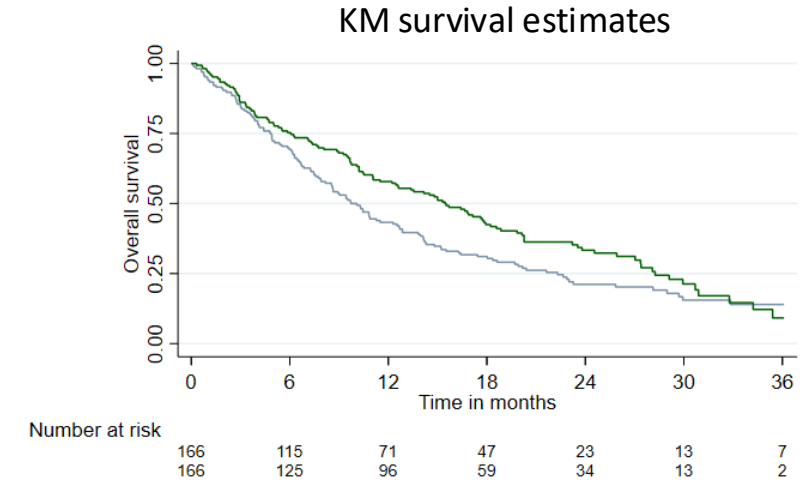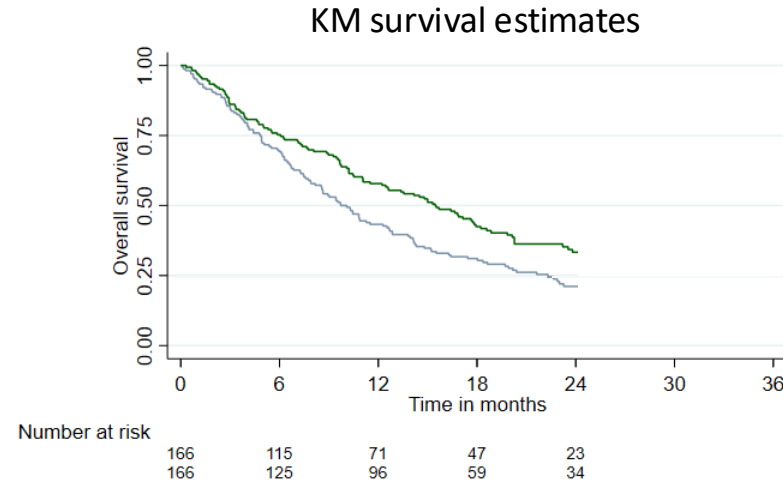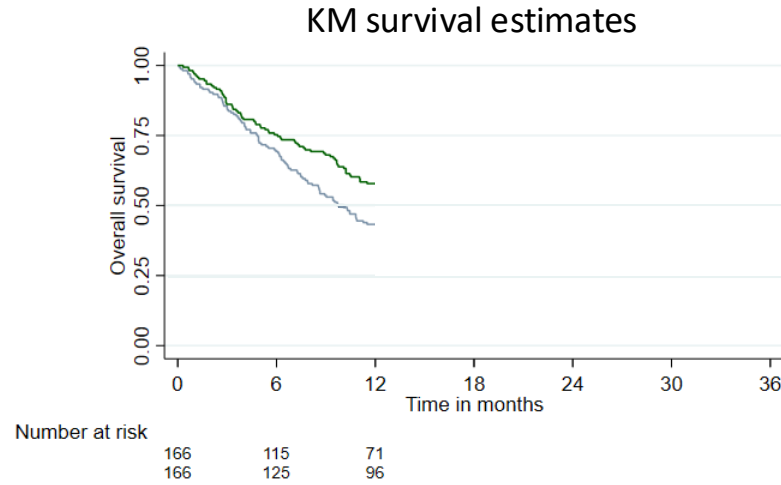
I have no disclosures to report.

Hierarchy for acceptability
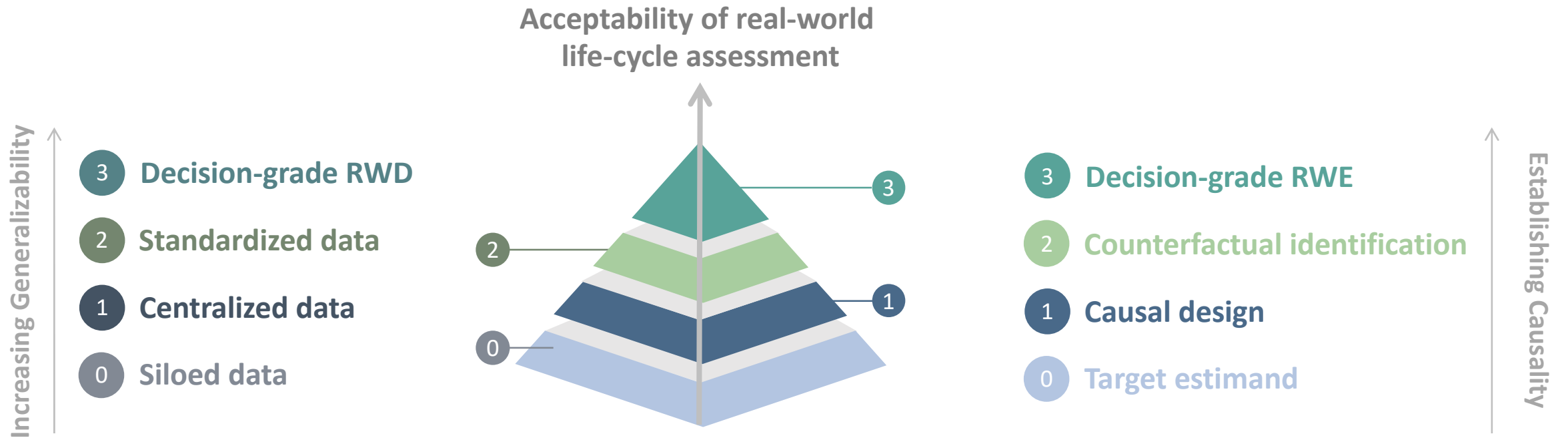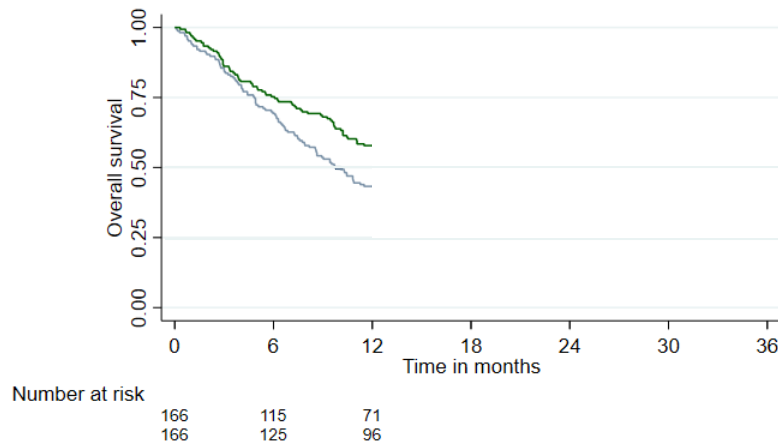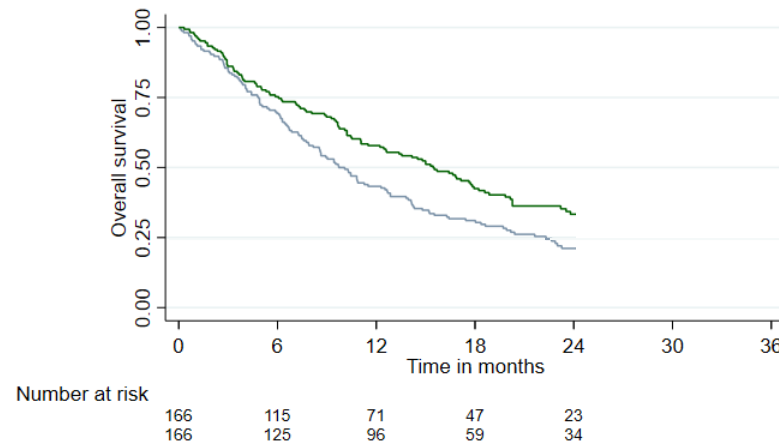
How we understand evolving evidence

How (do) we understand evolving (economic) evidence?

KM survival estimates

Regulatory data

Literature model inputs

Real-world individual-level data

Answer: Life-cycle economic evaluation

Source: Krebs, Weymann, Regier. (2025). Life-cycle economic evaluation to understand evolving value in learning healthcare systems. *Forthcoming*.
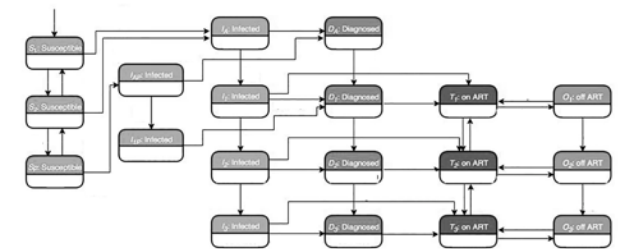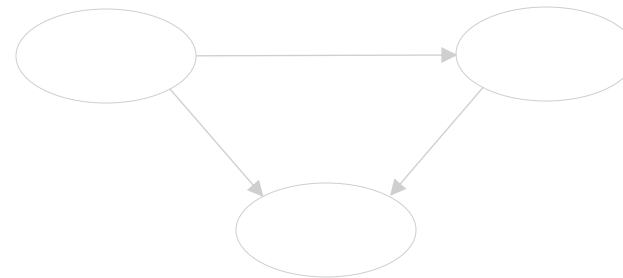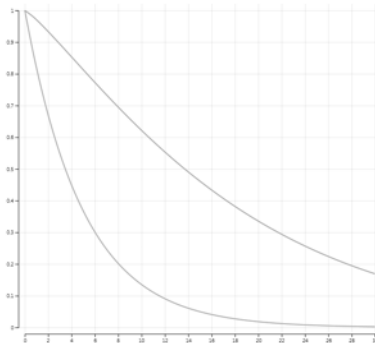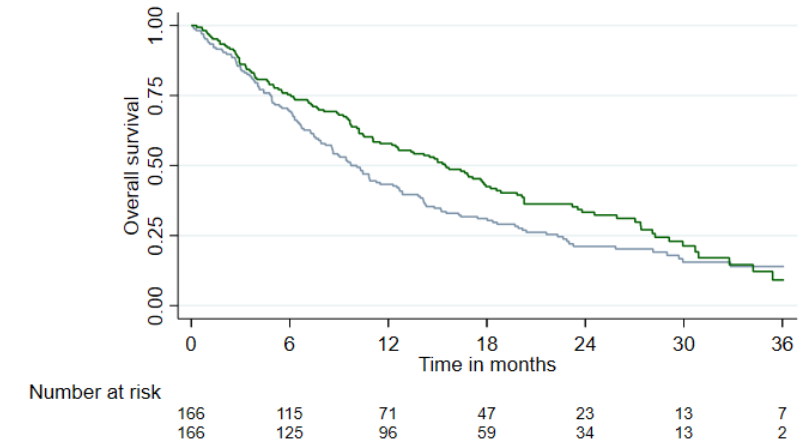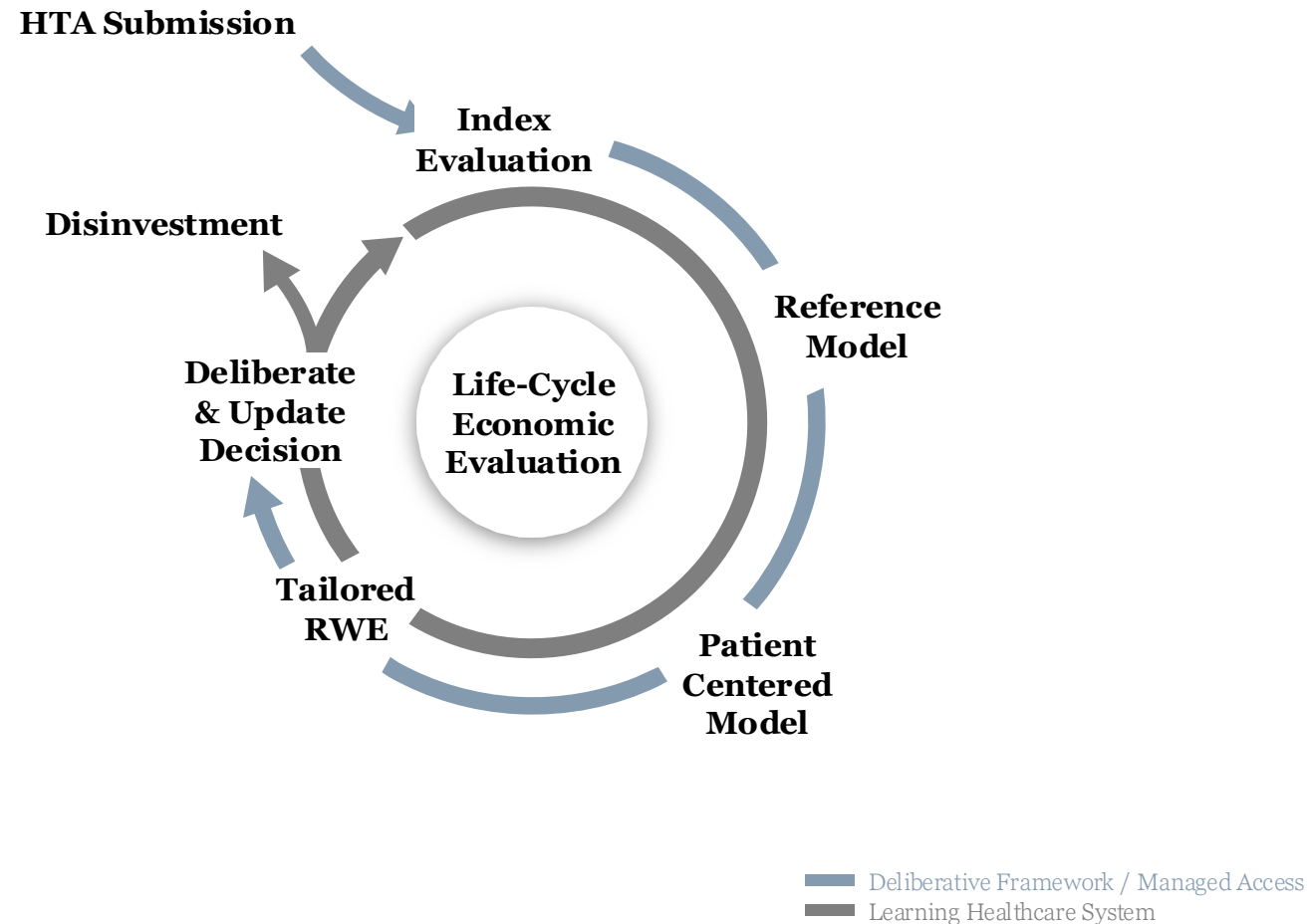
Life-cycle HTA

Cost-effectiveness evidence supporting reimbursement decisions for tumour-agnostic therapies is highly uncertain.

On/off decision making is frequently based on simplistic analysis informed by incomplete or immature data and aggregate inputs.

A life-cycle approach using individual real-world patient data with a patient centered economic model is necessary to inform evolving comparative value.

Understanding evolving evidence of value

Source: Krebs, Weymann, Regier. (2025). Life-cycle economic evaluation to understand evolving value in learning healthcare systems. *Forthcoming*.

What is the cost-effectiveness of entrectinib
compared to BC Cancer standard care
for advanced *NTRK+* solid tumours?

Index economic evaluation

We replicated the initial Canadian HTA report[1] for entrectinib, with and without testing costs.[2]

Inputs were from publicly available information included in HTA reports.

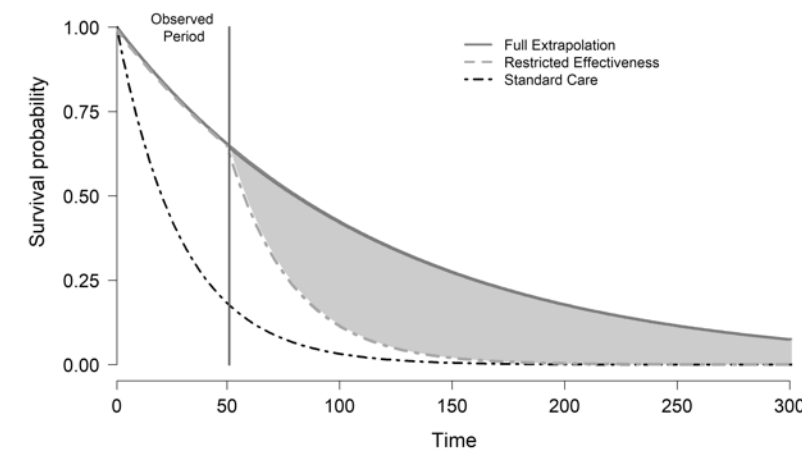Our replication was done in R, and our code is publicly available for enabling jurisdiction-specific adaptation.
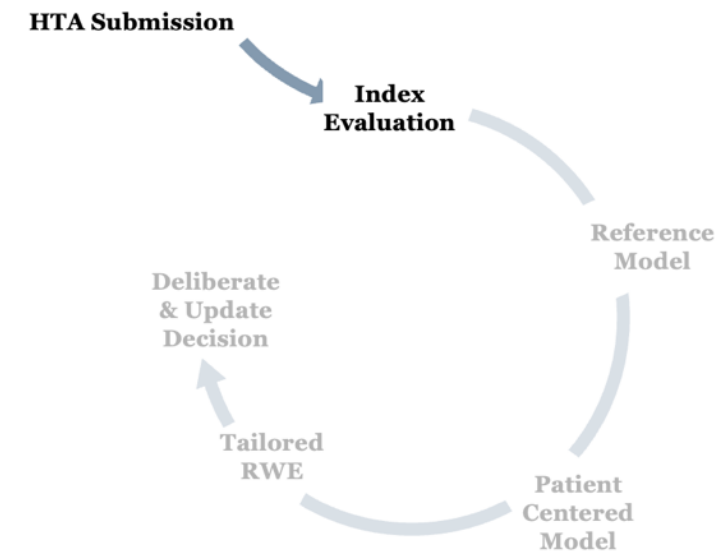
1. CADTH, Entrectinib (Rozlytrek) For the Treatment of Extracranial Solid Tumours with NTRK gene fusion. 2023: CADTH Reimbursement Review.
2. Cupples, Krebs et al. (2025). Adopting life-cycle HTA: A tumor-agnostic precision oncology index economic evaluation from publicly-available reimbursement reviews. *IJTAHC*, In Press.

Reference economic model

A two-step process

First: We validated our individual-level state transition model using HTA inputs against replication outputs to have an index model.

Second: We incorporated regulatory individual-level patient data, and updated comparators to current BC Cancer standard care.

HTA Submission

Index Evaluation

Reference Model

Deliberate & Update Decision

Tailored RWE

Patient Centered Model

On Systemic Therapy c,i

Off Systemic Therapy c,i

Progression c

Death

Model entry
c = tumour type
i = line number (1st, 2nd, 3rd)
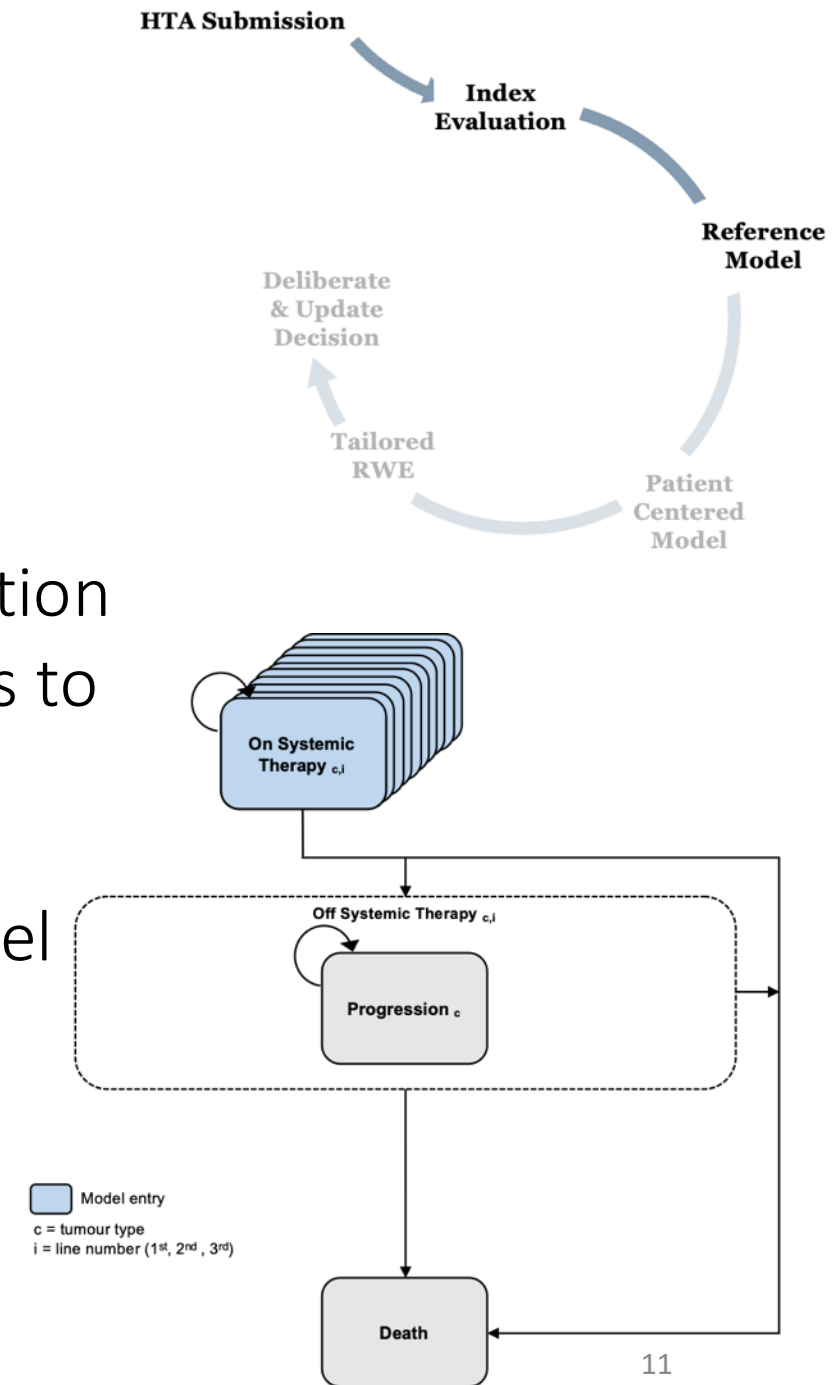
Patient centered model
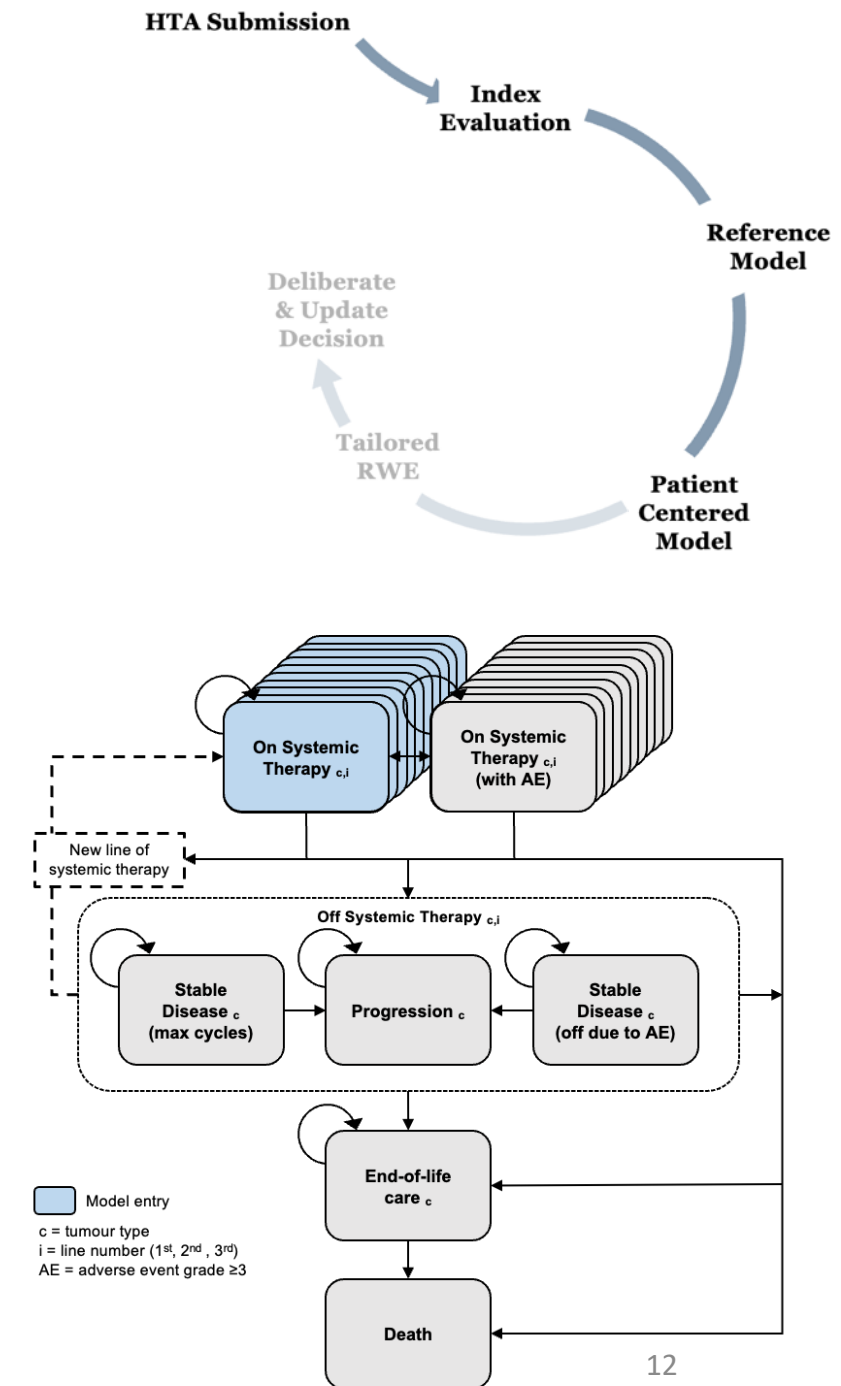
Expanded health states to reflect patient value and real-world clinical trajectories.[1]
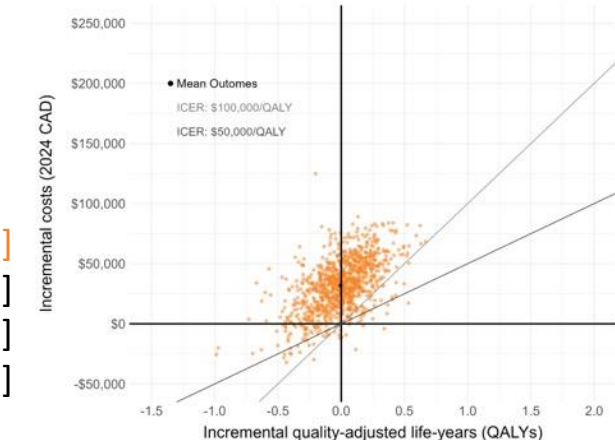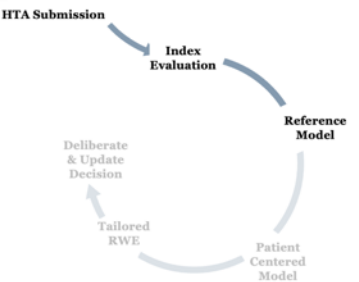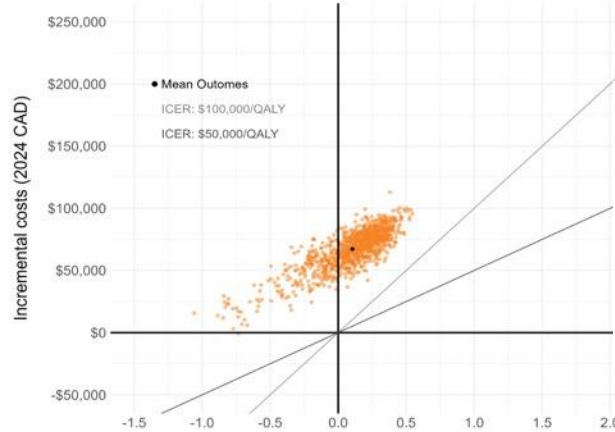
Flexibility for line placement.

Incorporated updated health-related quality of life utility values:

- Estimated using a Bayesian hierarchal model
- Used baseline weights from entrectinib trials
- Adjusted literature-based values

HTA Submission → Index Evaluation → Reference Model → Patient Centered Model → Tailored RWE → Deliberate & Update Decision

New line of systemic therapy

On Systemic Therapy c,i

On Systemic Therapy c,i (with AE)

Off Systemic Therapy c,i

Stable Disease c (max cycles)

Progression c

Stable Disease c (off due to AE)

End-of-life care c

Death

Model entry
c = tumour type
i = line number (1st, 2nd, 3rd)
AE = adverse event grade ≥3

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1. Roberts et al. (2012) "Conceptualizing a Model: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force–2." Med Dec Making.

Evolving economic evidence

All Panels Tumour-agnostic cost-effectiveness plane
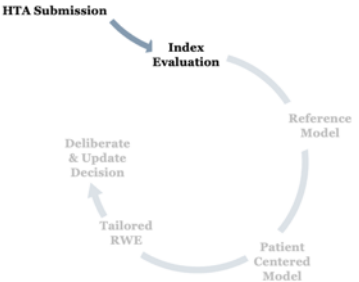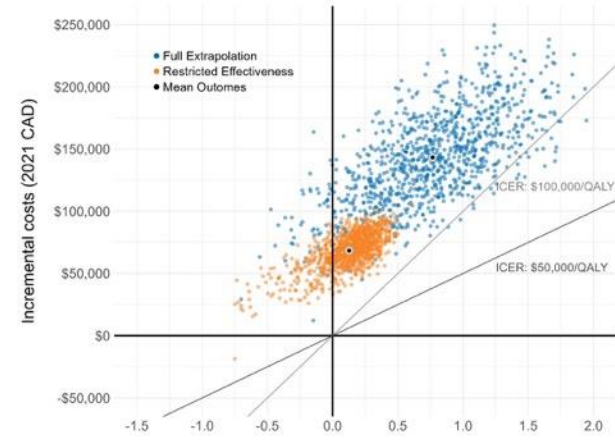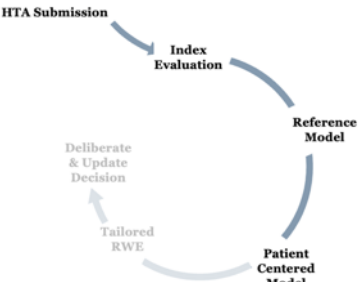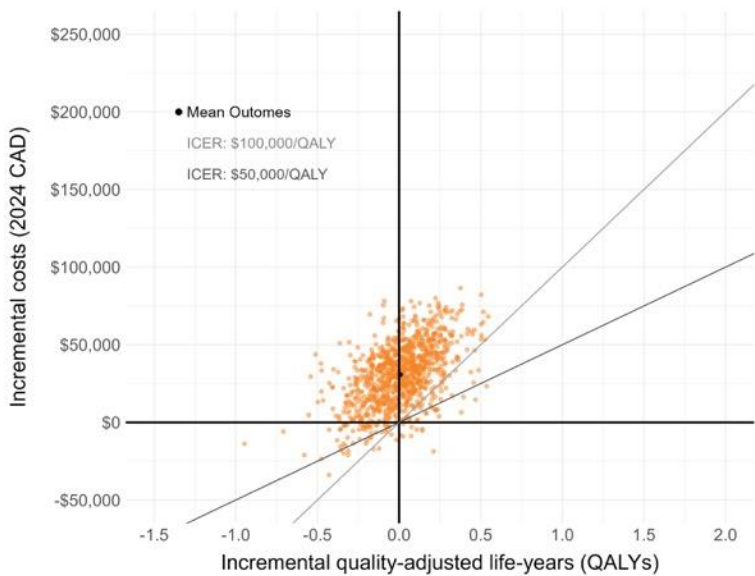
|	ΔC	ΔE	INMB @ 100K/QALY (95% CI)	[%CE / %D]
HTA submission:[1]	$133,338	0.88	-$45,338	
HTA revisions:[1]	$101,377	0.07	-$94,377	
Index evaluation:	$143,308	0.77	-$104,986 (-$161,810, -$55,640)	[2.5% / 5.0%]
Index evaluation:	$68,451	0.13	-$55,803 (-$89,102, -$29,736)	[0.0% / 20.5%]
Index model:	$67,247	0.10	-$56,800 (-$90,722, -$33,686)	[0.0% / 25.0%]
Reference model:	$31,396	-0.01	-$32,231 (-$70,215, $7,626)	[5.2% / 40.5%]
Patient centered:	$30,810	0.01	-$29,997 (-$65,944, $9,629)	[5.5% / 41.1%]

1.   CADTH, Entrectinib (Rozlytrek) For the Treatment of Extracranial Solid Tumours with NTRK gene fusion. 2023: CADTH Reimbursement Review.   %CE: % cost-effective; %D: % dominated.

Patient centered model results

Panel A Tumour-agnostic cost-effectiveness plane
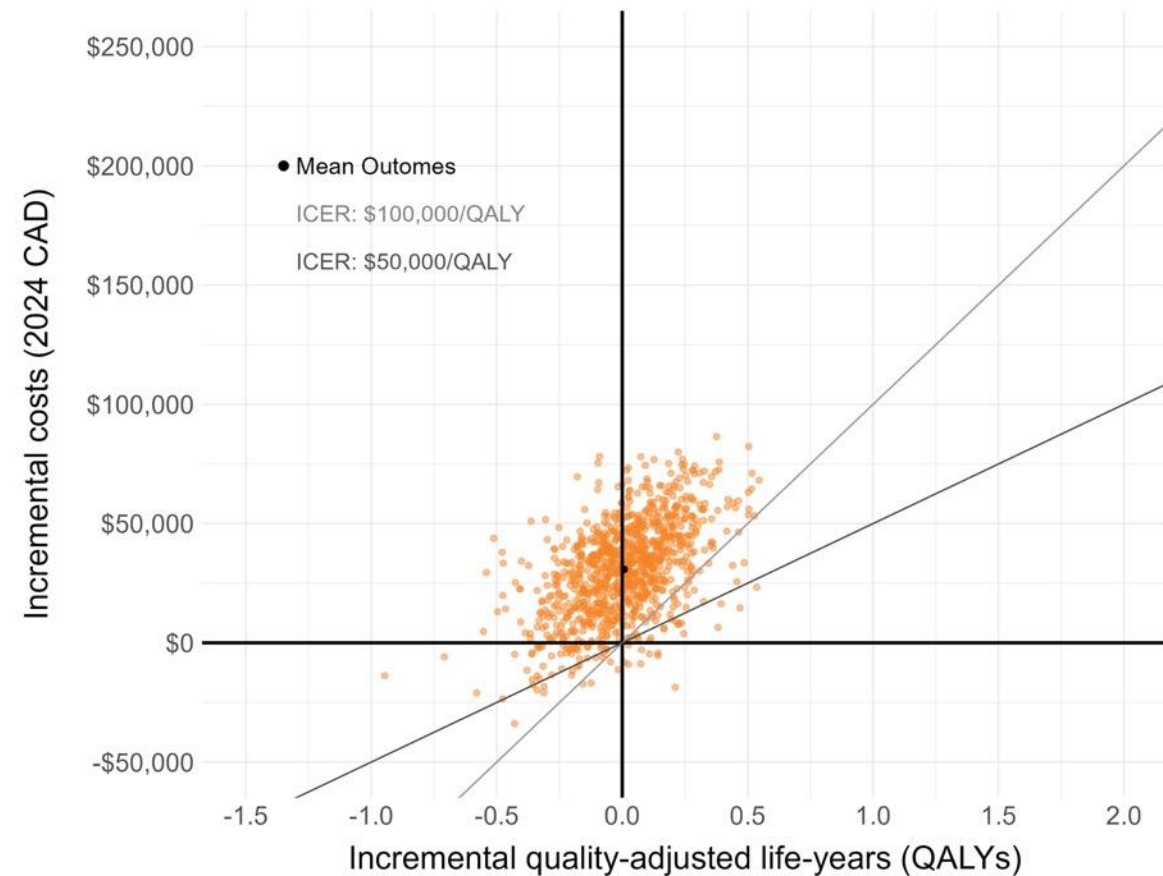
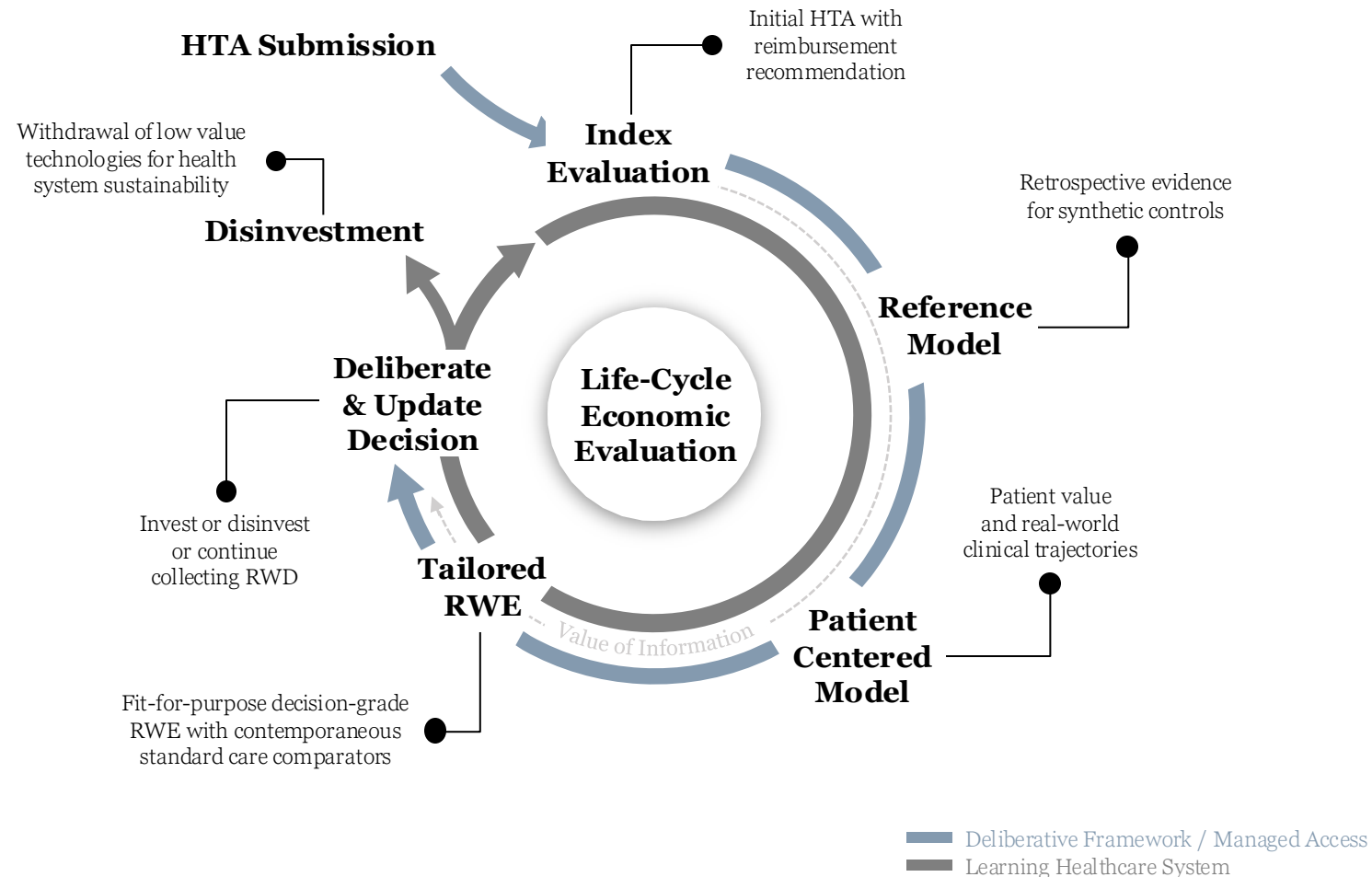**Panel B** Tumour-specific cost-effectiveness plane
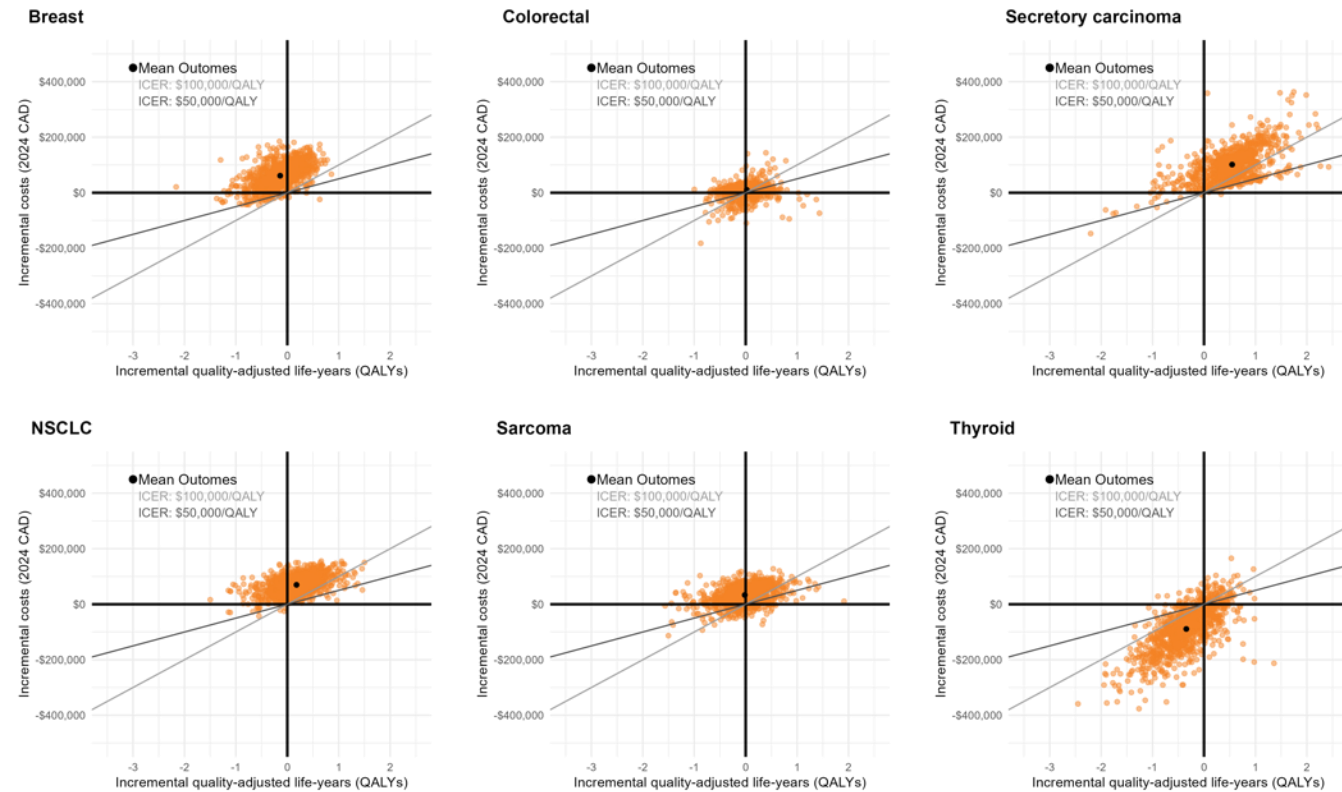
Takeaways

Our life-cycle economic evaluation approach suggests entrectinib is unlikely to be cost-effective at current WTP thresholds in a tumour-agnostic indication.

Entrectinib may provide tumour-specific value for *NTRK+* patients.

Understanding the assumptions behind evolving economic evidence is critical for LC-HTA.

Life-cycle economic evaluation is learning healthcare

Source: Krebs, Weymann, Regier. (2025). Life-cycle economic evaluation to understand evolving value in learning healthcare systems. *Forthcoming.*

Regulatory Science Lab

Hope, accelerated

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ISPOR POLL #1: Multiple choice question

At what stage should RWE be used?

a. First regulatory submission for market authorization.
b. HTA submission for reimbursement recommendation.
c. Post-market surveillance.
d. None of the above.
e. All of the above.

ISPOR POLL #2: Ranking exercise

What needs the most development for trustworthy RWE?

1. Fit-for-purpose study designs (e.g., causal inference).
2. Implementation of life-cycle assessment framework.
3. Transportability of evidence.
4. Open science principles (e.g., code sharing, synthetic data).

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