

# Assessing Real Option Value in Health Technology Assessment of Drugs

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**Discussion leader:** Meng Li<sup>1</sup>

**Discussants:** David Veenstra<sup>2</sup>, Stacey Kowal<sup>3</sup>, Woojung Lee<sup>2</sup>

<sup>1</sup> Department of Health Services Research, University of Texas MD Anderson Cancer Center, Houston, TX, USA

<sup>2</sup> The CHOICE Institute, School of Pharmacy, University of Washington, Seattle, WA, USA

<sup>3</sup> Evidence for Access, Genentech, Inc, South San Francisco, CA, USA

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*We would also like to thank our fellow collaborators, Lou Garrison and Will Wong*

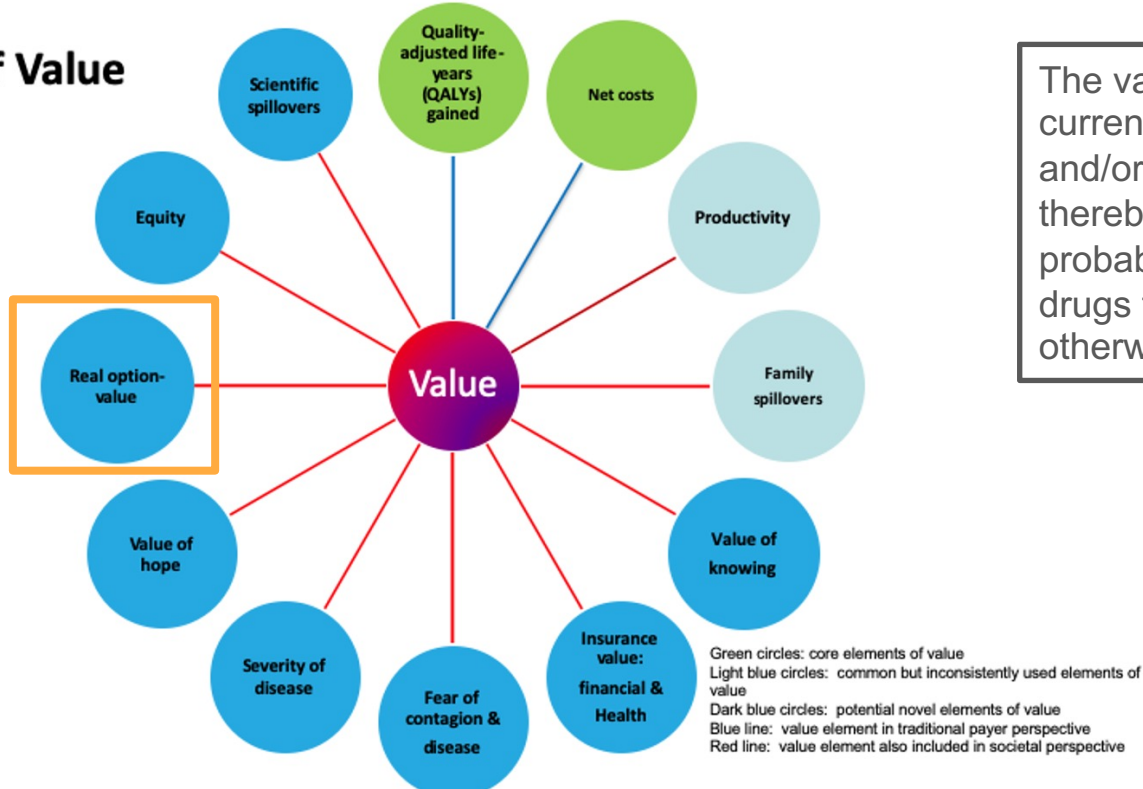
# What to discuss

- Theoretical foundation of ROV and literature *[10 minutes, Meng Li]*
- Types of ROV and mechanisms of ROV generation *[10 minutes, Dave Veenstra]*
- Steps and approaches of estimating ROV *[10 minutes, Woojung Lee]*
- Real-time demonstration of quantification steps *[10 minutes, Stacey Kowal]*
- Final remarks and polling questions *[10 minutes, Meng Li]*

What is ROV?

# What is real option value (ROV)?

## Elements of Value



The value generated when current drugs improve survival and/or disease progression, thereby increasing the probability of receiving future drugs for which would not be otherwise eligible.

# ROV in healthcare value assessment



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“Extending life provides patients with an option to enjoy benefits from uncertain future advances in medicine”



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“Intervention offers the potential to increase access to future treatments that may be approved over the course of a patient’s lifetime”

# Theoretical foundation of ROV

Project appraisal and investment decision-making under uncertainty

Option: The right, with no obligation to take certain action at a later time

- Financial options: The right with no obligation to buy or sell at a pre-specified price on or before a given date
- Real options: Delay an investment, modify (abandon, expand, contract, etc.) the investment at a later time, or make subsequent investments
  - Option to delay: Management holds a lease on land or resources and can wait to see if output prices justify constructing a building or plant
  - Growth option: An early investment (e.g., R&D), which is a prerequisite in a chain of interrelated projects that open up future growth opportunities (e.g., new generation product)

# Existing *ex ante* studies on ROV of drugs

Tyrosine kinase inhibitors for chronic myeloid leukemia (Sanchez 2012)

- Extending survival

Nivolumab for renal cell carcinoma and non-small cell lung cancer (Snider 2017)

- Extending survival

Ipilimumab for Metastatic melanoma (Li 2019)

- Extending survival

Alectinib for non-small cell lung cancer (Lee 2022)

- Extending progression-free survival

# ROV not negligible in terms of its size and impact on treatment decisions

5% to 18% of conventional life-years or quality-adjusted life-years gained

Disclosure of ipilimumab's phase II result was associated with a nearly twofold immediate increase in receiving surgical resection of metastatic relative to no treatment among metastatic melanoma patients (Li 2019)

# Polling question 1

Q. Based on the definition of ROV, when is its consideration most relevant?

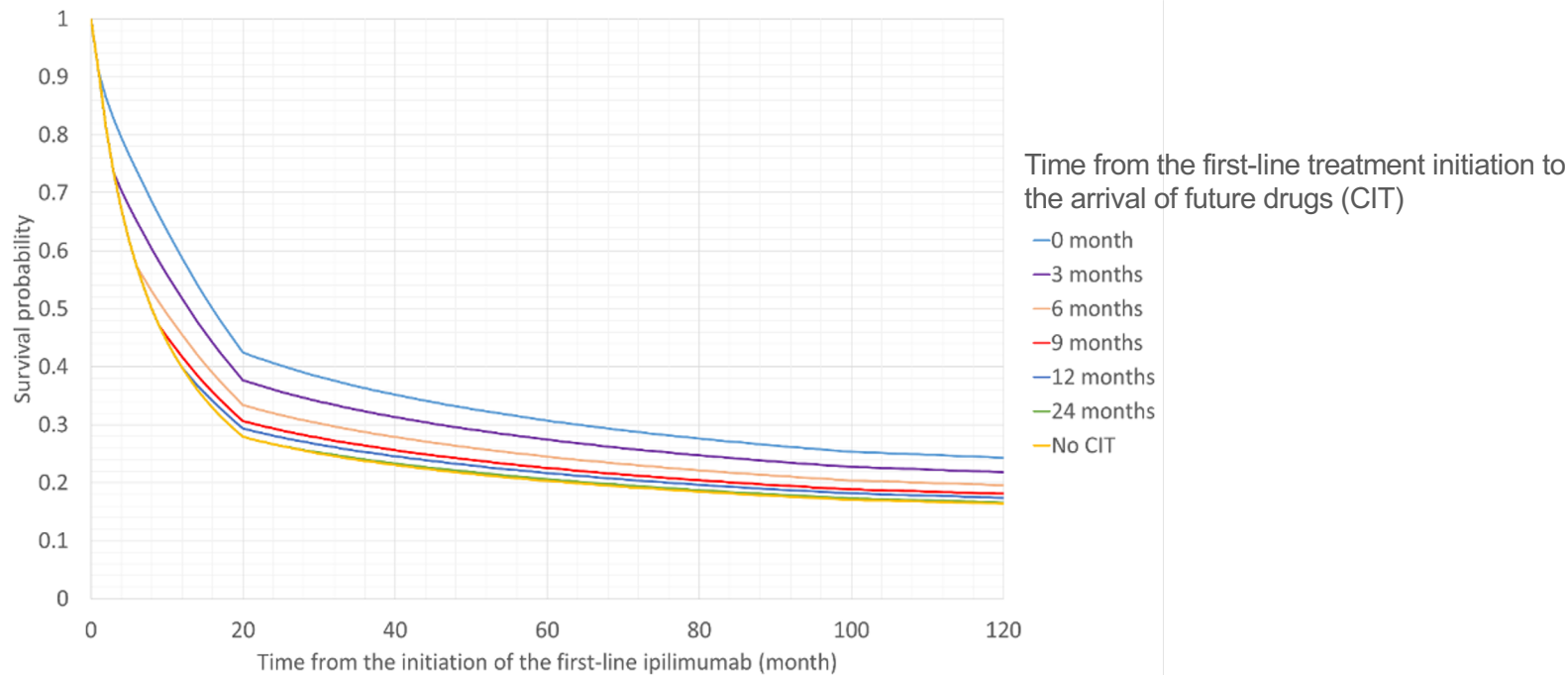
1. When technology identifies a new mechanism of action
2. When technology extends the life of patient
3. When baseline health status is particularly poor

# **Types of ROV and mechanisms of ROV generation**

ROV is created (positive) when patients have an increased probability of receiving or benefiting from a future innovation

# Type 1: Patients live longer

- Most commonly considered Type



## **Type 2: Patients have higher functional status**

- There also could be ROV when current treatment offers no clear survival benefit over alternatives, but slows irreversible disease progression and the deterioration of functional status.
- In these cases, without treatment, a patient's function (Hr-QoL) may decline irreversibly such that they will no longer benefit from future innovations.
- For example, extending progression-free survival (PFS) could affect the eligibility of receiving future drugs
- Supportive care could help keep one's performance status high enough to receive future drugs

## **Type 3: Patients benefit more (or less) from future treatment**

- The third type of ROV can occur when current treatment modifies the efficacy (or safety) of future innovations due to mechanisms of action.
- For example, antibiotic resistance could prevent patients from using new antibiotics from the same class in the future.
- In this particular case, ROV is 'negative'

## Polling question 2

Q) What type of ROV is generated in the following example?

A current drug for Alzheimer's Disease significantly slows progression.  
There are multiple drugs in late-stage development that halt progression.

1. Type 1: patients live longer
2. Type 2: patients have higher functional status
3. Type 3: patients benefit more (or less) from future treatment

How do we implement  
ROV?

# 7 Steps for implementing ROV in CEA

## **STEP 1.** Determine if ROV is likely negligible

- When technological progress is slow, potential future innovations are unlikely to offer substantial gains in health, and current treatment does not expand eligibility for future innovations

## **STEP 2.** Define study population, intervention, comparator, and treatment pathways

- How potential future innovations enter the treatment pathways (e.g., as an additional line of treatment, switching from the current treatment)

## **STEP 3.** Estimate incremental quality-adjusted life-years (QALYs) gained in a conventional CEA model without ROV

# 7 Steps for implementing ROV in CEA (cont'd)

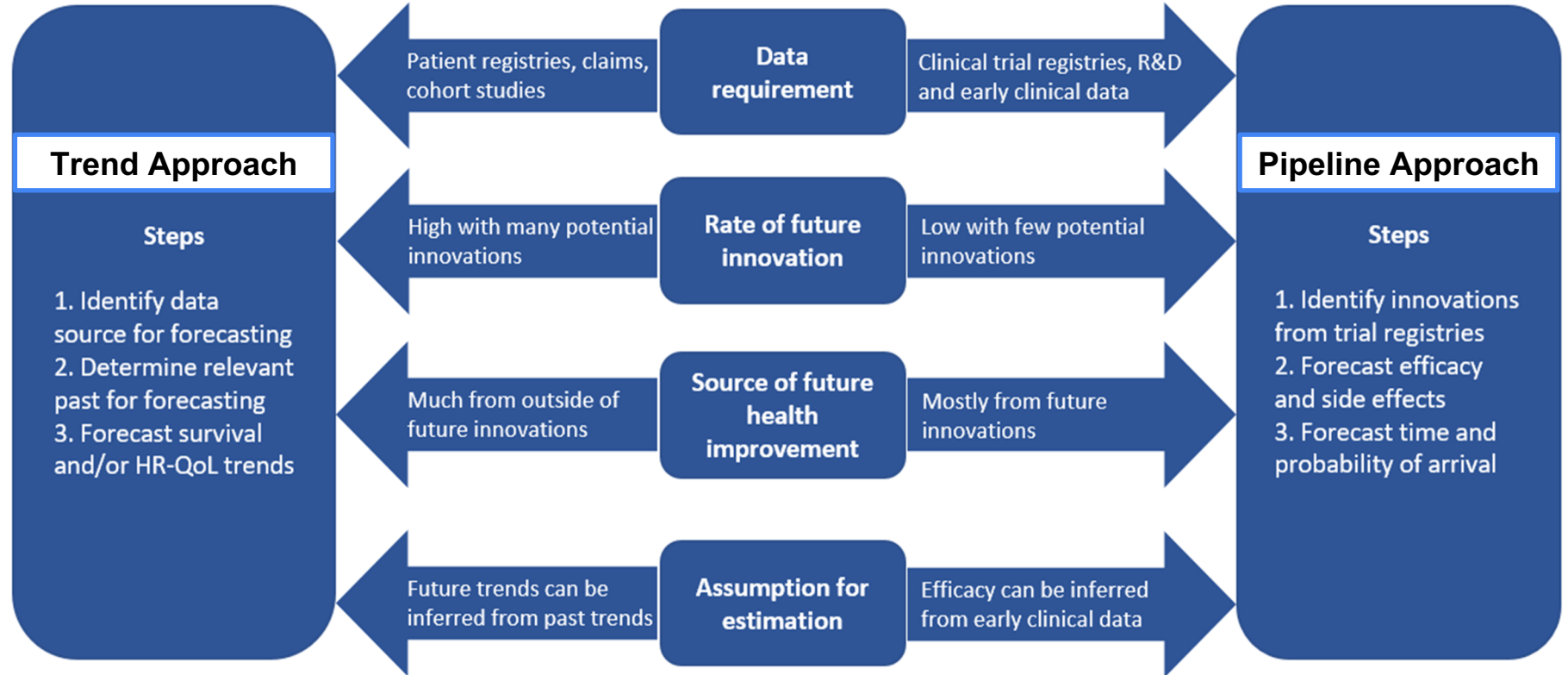
## STEP 4. Forecast future health

- Two general approaches
  - Trend approach: forecasting the trends in survival and/or HR-QoL for the target population using retrospective observational data
  - Pipeline approach: identifying future drugs from trial registries and forecasting their treatment effectiveness, likelihood of arrival, timing of arrival, and the uptake level.

## STEP 5. Incorporate forecasted parameters for future health in the model to estimate incremental QALYs with ROV

- Health state transition probabilities and utilities can be modified to reflect better survival and HR-QoL in the future. New health states may be created to represent adoption of new innovations.

# Two approaches for forecasting future health



# 7 Steps for implementing ROV in CEA (cont'd)

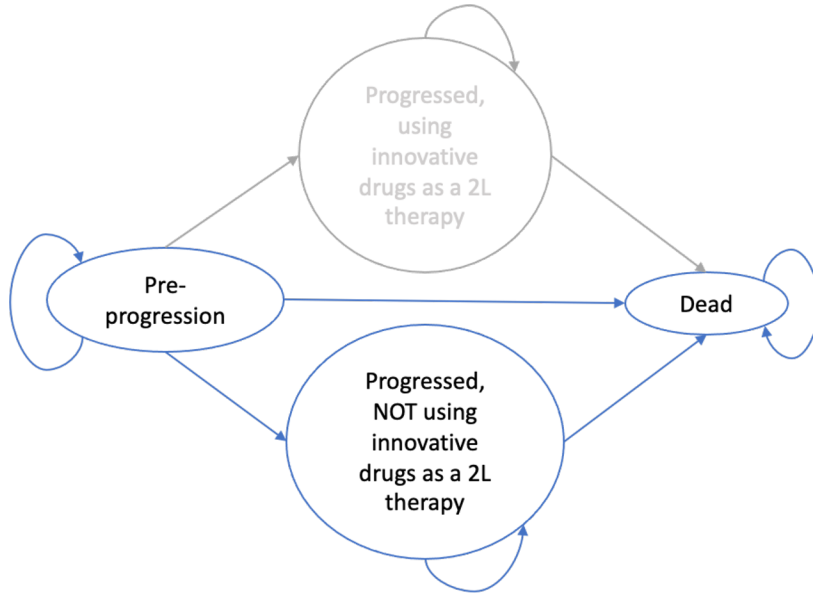
## STEP 6. Calculate and report base-case ROV

- ROV should be expressed in an incremental value (treatment vs. comparator) and should be presented alongside the conventional value as an additional element of value.

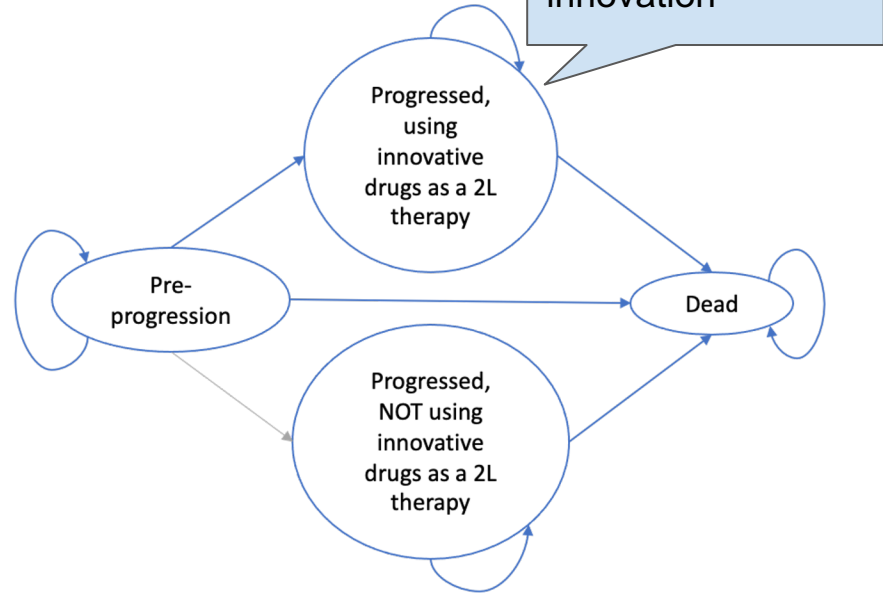
## STEP 7. Assess and report uncertainty of ROV

- One-way, two-way and probabilistic sensitivity analyses can be done for parameters specific to ROV (e.g., future trends in health, potential efficacy, probability and timing of arrival of future innovations)
- Uncertainty pertaining to model structure can be assessed by comparing the trend and the pipeline approaches

# CEA Structural Changes for ROV



Before time T (before the arrival of the next innovative drugs)



After time T

# CEA Inputs for ROV

- Most model inputs will remain unchanged from conventional CEA
- Who will receive the next innovation?
  - Probability of FDA approval
  - Time of arrival
  - Anticipated level of uptake
- What are the outcomes for patients who receive the next innovation?
  - Hazard ratio for next innovation (vs current comparator)
  - (Option) Test alternate survival extrapolations

# ROV Calculator - Inputs

Review and Amend Key Inputs ?

Restore Defaults

Key ROV Inputs

Value

Efficacy of new innovations

0.78

Probability of approval

78%

Time to arrival (months)

24

Level of uptake

75%

Description

Hazard ratio of post-progression survival of future drugs vs. standard of care

The likelihood of FDA approval for future drugs

Timing of FDA approval for future drugs from the initiation of the treatment

The probability of receiving future drugs among the eligible patient population

Additional Model Inputs

Value

PFS (constant)

1.8

OS (constant)

2.2

Utility - progression free

0.81

Utility - progressive disease

0.72

Time horizon (mos.)

500

Description

$\lambda$  value for PFS, assuming an exponential distribution

$\lambda$  value for OS, assuming an exponential distribution

Health state utility value for 'progression free' disease

Health state utility for progressive disease

Time horizon for the model, in months

# ROV Calculator - Results

## ROV Deterministic Results

|                       | W/out accounting<br>for future drugs | With accounting<br>for future drugs | Health gains from<br>future drugs (ROV) | Clinical ROV (as %<br>of conventional) |
|-----------------------|--------------------------------------|-------------------------------------|-----------------------------------------|----------------------------------------|
| Discounted life years | 7.12                                 | 7.50                                | 0.30                                    | 4.2%                                   |
| Discounted QALYs      | 5.59                                 | 5.87                                | 0.22                                    | 3.9%                                   |

*Updated  
patient  
outcomes with  
ROV*

*ROV expressed  
as % change  
from  
conventional  
CEA*

# **ROV Calculator Demonstration**

# Future Issues

- Methods for forecasting (e.g., validating methods and dealing with uncertainty)
- Behavioral change in anticipation of future innovations
- Generalizability of ROV across countries
- Costs of future innovations (value-based pricing)
- Implications on pricing, coverage decisions, and budget

## Polling question 3

Q) When and how should ROV be used in policy making?

1. Clinical/patient value only
2. Value assessment
3. Never

# Implications of ROV

- Clinical shared decision making
  - A change in the expectations about future treatments may affect treatment utilization
- Value-based pricing and coverage decisions
  - Adding an option premium to the value-based price for life-extending treatments

**Thanks!**