PORTAL
Program on Regulation, Therapeutics, And Law

DoPE BWH

Washington Prescription Drug Affordability Board

Assessing "Excess Costs" During Affordability Reviews

Adam Raymakers, PhD and Matt Martin, MA

Program On Regulation, Therapeutics, And Law (PORTAL)
Division of Pharmacoepidemiology and Pharmacoeconomics
Brigham and Women's Hospital | Harvard Medical School

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Outline

1. **PDAB Process Overview**
2. **Tools to Assess Excess Costs**
   a. Excess Costs Relative to Therapeutic Alternatives
   b. Excess Costs to the Health Care System
3. **Q&A**

Section 1.

PDAB Process Overview

Washington PDAB – Process Overview

"By June 30, 2023, and annually thereafter…the board must identify prescription drugs" that meet certain statutory criteria.

RCW 70.405.030

"The board may choose to conduct an affordability review of up to 24 prescription drugs per year identified pursuant to RCW 70.405.030."

RCW 70.405.40

"For prescription drugs chosen for an affordability review, the board must determine whether the prescription drug has led or will lead to excess costs to patients."

RCW 70.405.40

"Each year, the board may set an upper payment limit for up to 12 prescription drugs" that were found to have led or will lead to excess costs.

RCW 70.405.50

Washington PDAB – Process Overview

Identify eligible drugs

"By June 30, 2023, and annually thereafter…the board must identify prescription drugs" that meet certain statutory criteria.

RCW 70.405.030

Select drugs for affordability review

"The board may choose to conduct an affordability review of up to 24 prescription drugs per year identified pursuant to RCW 70.405.030."

RCW 70.405.40

Conduct affordability review

"For prescription drugs chosen for an affordability review, **the board must determine whether the prescription drug has led or will lead to excess costs to patients**."

RCW 70.405.40

Establish upper payment limit

"Each year, the board may set an upper payment limit for up to 12 prescription drugs" that were found to have led or will lead to excess costs.

RCW 70.405.50

Defining "Excess Costs"

By statute, the Board is tasked with assessing **whether a drug has led or will lead to "excess costs to patients"** in the state.

"…**exceed the therapeutic benefit** relative to other alternative treatments"

"…are **not sustainable to public and private health care systems** over a 10-year time frame."

RCW 70.405.010

Leveraging Health Technology Assessments

Health technology assessment (HTA) is the "systematic evaluation of properties, effects, and/or impacts of health technology."

- Includes an evaluation of the **social, economic, organizational, and ethical issues** for a particular treatment to inform policy decisions.

Value assessment is a similar term to HTA, used to describe approaches "to measure and communicate the value of pharmaceuticals and other health care technologies for decision making."

Common Producers/Sponsors of HTA
National HTA Agencies (non-US) e.g., IQWiG in Germany, CDA in Canada
Independent Review Organizations e.g., ICER in US
Academics e.g., in peer-reviewed journals
Manufacturers, Payers, Other Stakeholders

Components of HTA may be valuable resources to help the Board assess whether a drug generates "excess costs."

WHO. 2024.; Neumann PJ, Wilke RJ, Garrison Jr. LP. *Value Health* 2018.

Defining "Excess Costs"

By statute, the Board is tasked with assessing **whether a drug has led or will lead to "excess costs to patients"** in the state.

"…**exceed the therapeutic benefit** relative to other alternative treatments"

Comparative Effectiveness

Efficiency Frontiers

Economic Evaluation (e.g., Cost-Effectiveness Analysis)

"…are **not sustainable to public and private health care systems** over a 10-year time frame."

Budget Impact Analysis

RCW 70.405.010

Section 2a.

Tools to Assess Excess Costs

Relative to Therapeutic Alternatives

Comparative Effectiveness

What is a drug's added therapeutic benefit relative to its therapeutic alternatives?

Factors to Consider

- Clinical effectiveness
- Side effects, interactions, contraindications
- Impact on health resource utilization (i.e., hospitalizations, other medications, caregiver burden)
- Ease of use (setting of administration, dosing frequency, duration of therapy)

Data Sources

- Premarket and post-market clinical trials
- Comparative effectiveness trials or meta-analyses
- Observational studies (real-world evidence)
- FDA approval documents
- Existing health technology assessments
- Consultation with experts (clinicians) and patients

Defining Therapeutic Alternatives

"**Therapeutic alternative**" (TA) **does not mean treatments must be identical** in terms of safety, efficacy, or mode of delivery (e.g., injected vs. oral)

- It also **does not mean the products are interchangeable** for individual patients.

How the Board defines therapeutic alternatives should be guided by how TAs will be used to inform the affordability review.

- **Narrower definition**: Drugs within the same pharmacologic class
- **Broader definition**: Drugs in different classes or non-pharmaceutical alternatives (e.g., devices, procedures)

Measuring A Drug's Clinical Effectiveness

Many drugs are measured by their effect on **longevity and/or quality of life**

- Examples of improved quality of life: Reducing pain, improved mobility, improved cognitive function
- Quality of life is typically measured using disease-specific metrics or symptom scales

In some cases, **surrogate measures** may be used (e.g., accelerated approval)

- Examples: Hemoglobin A1c, LDL, progression-free survival
- Need to consider the strength of the evidence supporting the surrogate measure in predicting clinical outcomes.

Clinical Benefit Compared to Therapeutic Alternatives

Need to consider both **amount** of benefit **AND** the **level of evidence** in the literature

Net Clinical Benefit

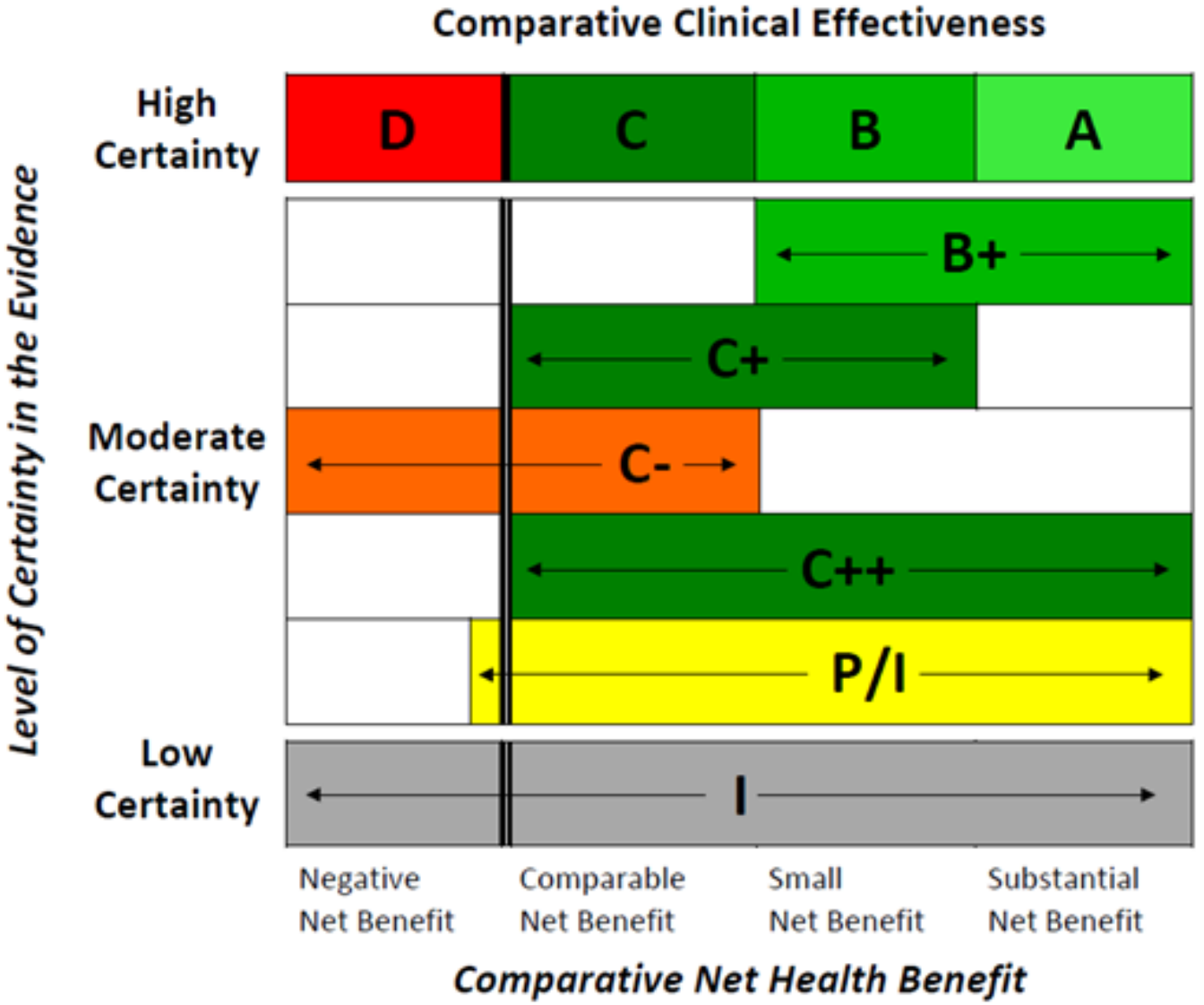
- Inferior
- None
- Minor Benefit
- Moderate Benefit
- Major Benefit

Quality of Evidence

Example – ICER Evidence Rating Matrix

A *= "Superior"*
B *= "Incremental"*
C *= "Comparable"*
D*= "Negative"*

B+ *= "Incremental or Better"*
C+ *= "Comparable or Incremental"*
C- *= "Comparable or Inferior"*
C++ *= "Comparable or Better"*
P/I *= "Promising but Inconclusive"*
I *= "Insufficient"*



ICER. 2023 Value Assessment Framework.

Example: ICER Evidence Assessment of Ulcerative Colitis (UC) Biologics

How strong is the evidence that these therapies improve outcomes in patients with ulcerative colitis?

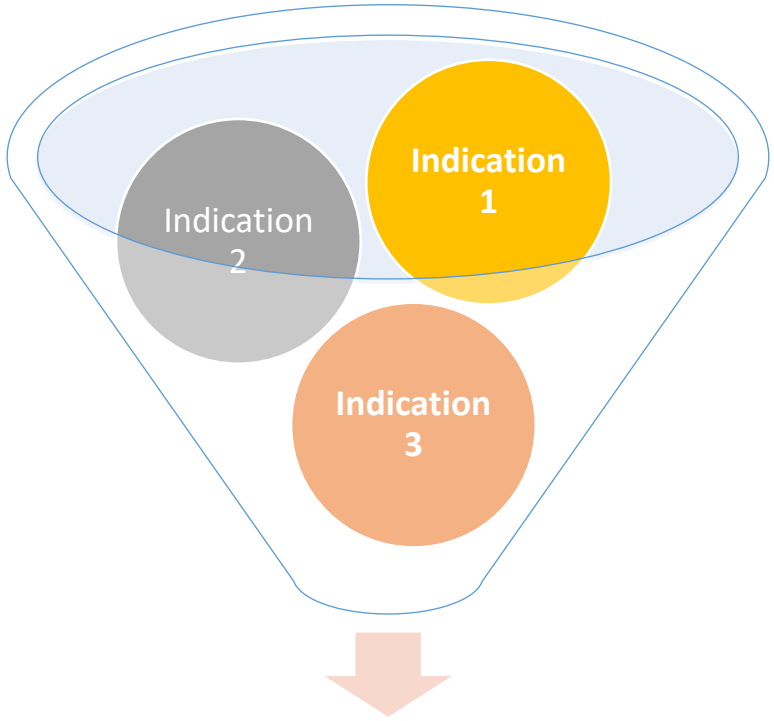
ICER EVIDENCE RATINGS

TIM	Comparator	Rating
Infliximab	Infliximab biosimilars	C
Infliximab	Placebo	A*
Golimumab	Placebo	A*
Tofacitinib	Placebo	B+†
All other TIMs	Placebo	A
Vedolizumab	Adalimumab	B+
Ustekinumab	Adalimumab	C+
Infliximab	Adalimumab	C+*
Tofacitinib	Adalimumab	P/I†
Vedolizumab	Golimumab	C+*
All other TIM Comparisons	–	I

*Biologic-naïve only.
†Biologic-experienced only.

ICER. 2020.

Net Comparative Benefit May Vary by Indication



Factors to Consider

- Net comparative benefit for each indication
- Prevalence of each indication
- How drug is used for each indication
- Off-label indications

Assessing Comparative Cost Depends on Net Benefit

Drug offers **no or minor** added benefit

Can **reference** drug's price to therapeutic alternatives, assuming they are priced affordably

Drug offers **moderate or major** added benefit

Need to quantify **how much more we are willing to pay** for a drug's incremental benefit, compared to alternatives

Efficiency Frontiers

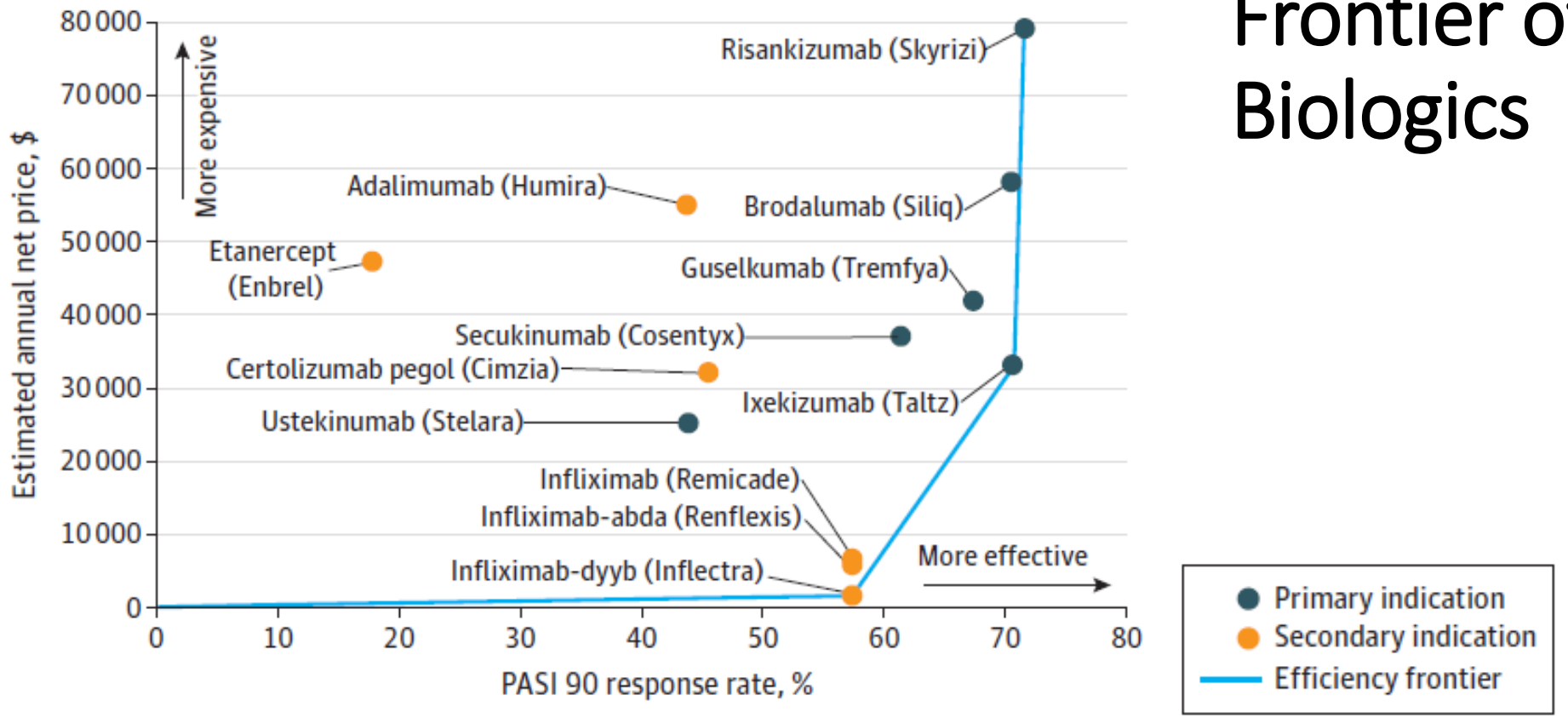
- Efficiency frontiers compare the price and effectiveness of drug with its therapeutic alternatives
- Most useful if there are several (>2) treatment alternatives
- Can still model long-term costs (including savings) and health benefits of each drug

Benefit: Can use disease-specific measurements of health benefits; no need to standardize across disease types

Limitation: Assumes that comparator treatments are priced affordably

Example: Efficiency Frontier of Psoriasis Biologics

Figure 1. Efficiency Frontier for Psoriasis Biologics in the US



Egilman et al. *JAMA Dermatology.* 2024.

Economic Evaluation

Economic evaluation is the process of systematic **identification**, **measurement,** and **valuation** of the inputs and outcomes of two or more alternative activities.

The purpose is to **identify the best course of action** (i.e., delivering the treatment that exhibits the best value), based on all available evidence.

Importantly, economic evaluation should also consider and quantify the **uncertainty** in this evidence and the eventual decision.

Drummond MF, Sculpher MJ, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes* (2005).

Approaches to Economic Evaluation

Cost-benefit analysis
benefits are measured in monetary terms

Cost-consequence analysis
presenting all costs and benefits in a disaggregated format

Cost-minimization analysis
assume the two therapies under investigation are the same, only focus on costs

Cost-effectiveness analysis
benefits are measured in natural units (i.e., life years gained, infections avoided, etc.)

Cost-utility analysis
benefits measured in terms of quality-adjusted life-years (QALYs) or other measure

Measuring Cost-Effectiveness

- Evaluate **costs** and **health benefits** of 2 or more alternative treatments (e.g., drug A vs drug B)
- **Costs** include treatment costs plus downstream costs / savings
  - Includes **health care costs** (e.g. hospitalizations averted)
  - Can also include **societal costs** or savings (e.g. productivity), although difficult to measure so introduces uncertainty
- The incremental cost-effectiveness ratio (ICER) can be applied to an explicit threshold or as a means of negotiating price

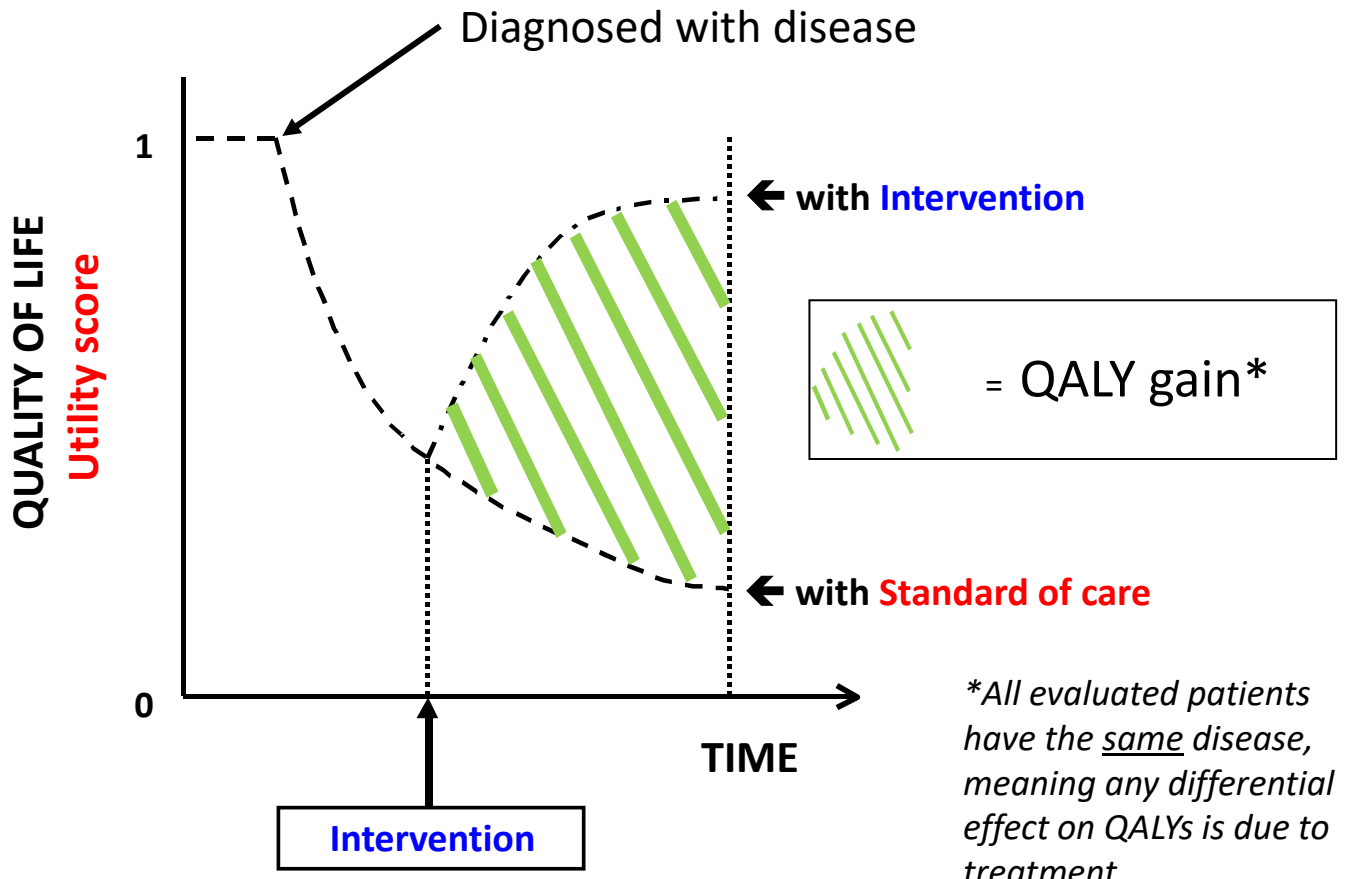
$$\textbf{Incremental Cost-Effectiveness Ratio (ICER)} = \frac{\text{Costs}_{\text{New}} - \text{Costs}_{\text{Current}}}{\text{Benefits}_{\text{New}} - \text{Benefits}_{\text{Current}}}$$

Sanders GD, Neumann PJ, Basu A. *JAMA*. 2016.

Quality-Adjusted Life Years (QALYs)

QALY = duration × health-related quality of life (HRQoL)

- Intended as an **incremental/comparative** measure of benefit (e.g., to determine the incremental effect of a drug within a disease)
- Can be utilized for both **life-extending *and* non-life-extending** interventions
- Concerns persist over QALYs' **value of life extension at low HRQoL** as discriminatory toward certain populations (e.g., older adults, people with disabilities, terminally ill)



*All evaluated patients have the same disease, meaning any differential effect on QALYs is due to treatment

Other Measures of Benefit in CEA

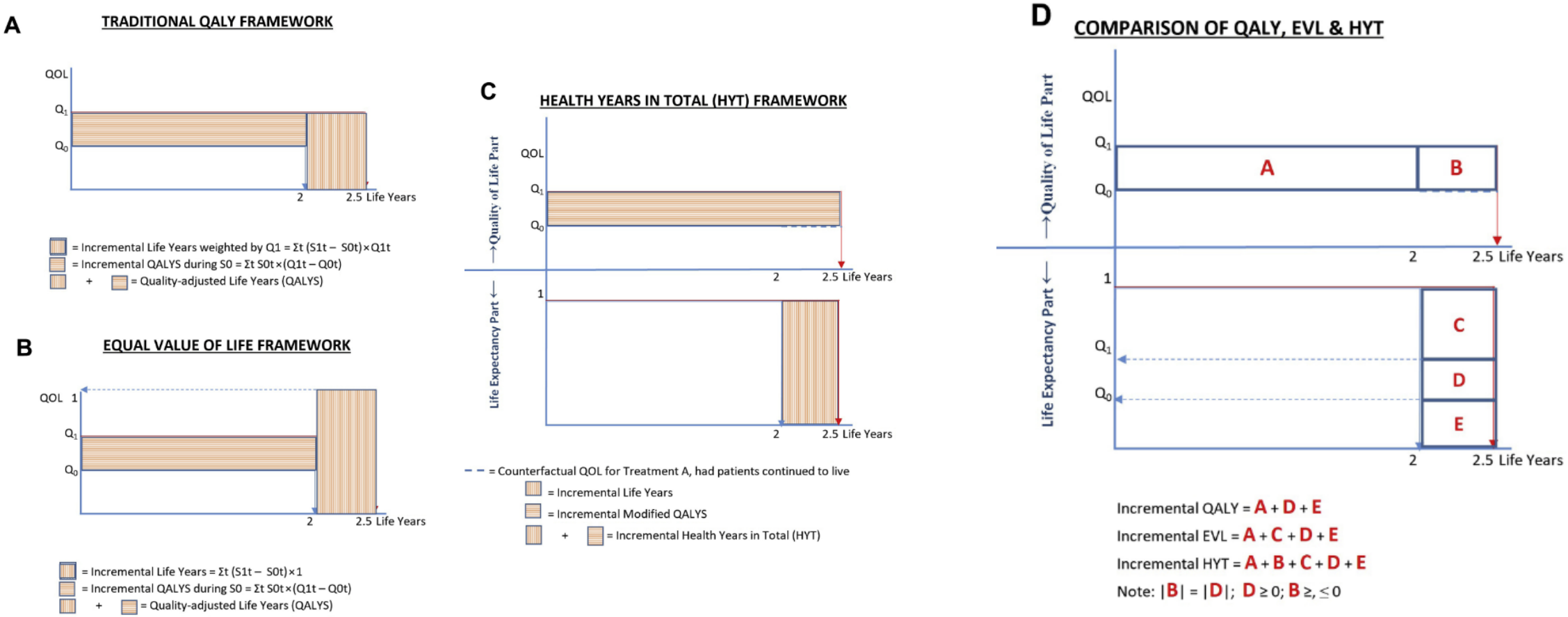
- **Life years gained (LYG)** - estimating gains in survival between the two treatment arms (no weighting applied).
  - Most cost-effectiveness analyses report both QALY and LYG outcomes

- **Equal value life year gained (evLYG)** – applies the same weighting (0.851) to estimated gains in survival between the two arms, reflecting average health. Developed by the Institute for Clinical and Economic Review (ICER).

- **Health years in total (HYT)** –attempts to disaggregate life years gained and HRQoL impacts using an additive model, relying on the estimation of counterfactual HRQoL during the additional time period. Developed by Basu et al.

- **'Natural' units –** Disease-specific outcome measurements
  - May be measured directly in clinical trials
  - E.g., biomarker, surgeries avoided, hospitalizations avoided

Other Measures of Benefit in CEA



Basu A, Carlson J, Veenstra D. *Value in Health.* 2020.

Proposed Alternatives to CEA

Some alternatives to traditional CEA have gained industry support but have not been adequately tested.

- **Distributional cost-effectiveness analysis -** attempts to incorporate equity considerations into cost-effectiveness analysis.
- **Extended cost-effectiveness analysis* -** incorporates issues beyond traditional CEA, such as financial risk, nonhealth benefits and can include distributional/equity impacts.
- **'Generalized' cost-effectiveness analysis* -** incorporates 'novel elements of value' that are missed by standard approaches to CEA. For example, the value of hope, insurance value, and scientific spillovers.

***When these frameworks factor in additional considerations, the ICER typically becomes lower, thereby making new technologies appear more cost-effective. Some benefits may be double-counted.**

Asaria M, Griffin S, Cookson R. *Medical Decision Making.* 2016.; Verguet S, Kim JJ, Jamison DT. *Pharmacoeconomics*. 2016.; Neumann PJ, Garrison LP, Wilke RJ. *Value in Health*. 2022.

Section 2b.

Tools to Assess Excess Costs to the Health Care System

Cost-Effective Drugs May Still Be Unsustainable to the Health Care System

- **Example 1: Hepatitis C Antivirals**
  - Despite high price tag ($80k/treatment course), they were deemed highly cost-effective
  - But given the large number of patients in need of treatment, Medicaid programs faced budget shortfalls, leading states to severely restrict access
- **Example 2: Beremegene Geperpavec (B-VEC)**
  - No alternative treatments for patients with dystrophic epidermolysis bullosa. B-VEC, a topical gene therapy, offered a promising treatment
  - The reported cost of treatment was $300K, per year. While it is likely cost-effective, there would be a substantial overall impact to health payers.

Najafzedeh M et al. *Ann Intern Med*. 2015.; Raymakers AJN et al. *JAMA Dermatology*. 2024.

Budget Impact Analysis (BIA)

Budget impact analysis is an analytical method that incorporates the actual cost to the health system, considering issues around price/cost, volume, market uptake, displaced alternatives, etc. This approach can be very useful for decision-makers concerned with the **feasibility of adopting a new drug** or with **overall spending**.

Key Aspects:

- BIA **does not assess health outcomes**.
- BIA typically uses a **much shorter time horizon** because of the changing landscape of treatment (i.e., 3 to 5 years).
- BIA is typically **performed before a new drug enters the market**.

The Board may need to modify traditional BIA methods to assess current spending on on-market drugs. Thus, BIA could instead help elucidate a threshold beyond which spending on a drug may be unsustainable.

Key Parameters of Budget Impact Analysis

- Cost of 'new' drug per year
- Cost of standard of care per year
- Other cost offsets
- Additional costs (i.e., tests, resources/infrastructure required, etc)

- Prevalence of disease
- Incidence of disease
- Size of eligible population
- Percentage of eligible population insured
- Uptake amongst the population (and changes)

Example: Budget Impact of Pembrolizumab for Advanced Endometrial Cancer

HTA agencies will often receive a BIA from the manufacturer for a selected drug and will either **accept that analysis as is** or **conduct their own re-analysis**.

Key values in the estimation of budget impact are presented, which represent epidemiologic data, diagnosis, and treatment considerations, as well as data for market uptake for the new drug.

These values can also be varied to determine a **range of possible budget impacts**.

Table 13: Summary of Key Model Parameters

Parameter	Sponsor's estimate (reported as year 1 / year 2 / year 3 if appropriate)
Target population	
Number of patients with uterine cancers	7,040 / 7,930 / 8,933[40]
Proportion of endometrial cancer	90%[36,37]
Proportion of advanced or metastatic disease	8%[34,39]
Referral rate to medical oncologists or gynecologic oncologists	84%[33]
First-line treatment rate by medical oncologists and gynecologic oncologists	87%[33]
Second-line treatment rate	63%[33]
Diagnosed earlier and progressed to advanced disease (includes recurrent disease)	67%[33]
dMMR or MSI-H testing rate (from baseline to peak)	70% to 90%[33]
Proportion of patients with dMMR or MSI-H EC	15.7%[33]
Market uptake (3 years)	
Uptake (reference scenario)	
Pembrolizumab	0% / 0% / 0%
Paclitaxel	19% / 19% / 19%
Doxorubicin	56% / 56% / 56%
Docetaxel	7% / 7% / 7%
Ifosfamide	0% / 0% / 0%
Gemcitabine	10% / 10% / 10%
Clinical trials	8% / 8% / 8%
Uptake (new drug scenario)	
Pembrolizumab	[redacted]
Paclitaxel	[redacted]
Doxorubicin	[redacted]
Docetaxel	[redacted]
Ifosfamide	[redacted]
Gemcitabine	[redacted]
Clinical trials	[redacted]
Cost of 1L treatment (per patient)[a]	
Cost of treatment over cycle	
Pembrolizumab q.3.w.	$8,800.00

CADTH/CDA. 2023.

Example: Budget Impact of Pembrolizumab for Advanced Endometrial Cancer

Table 16: Detailed Breakdown of the CADTH Reanalyses of the Budget Impact Analysis

Stepped analysis	Scenario	Year 0 (current situation) ($)	Year 1 ($)	Year 2 ($)	Year 3 ($)	3-year total ($)
Submitted base case	Reference	$256,008	$465,976	$667,734	$879,705	$2,013,415
	New drug	$256,008	$1,591,141	$6,150,773	$9,139,055	$16,880,969
	Budget impact	$0	$1,125,165	$5,483,039	$8,259,350	$14,867,554
CADTH base case	Reference	$521,610	$792,914	$851,265	$898,732	$2,542,910
	New drug	$521,610	$2,365,259	$8,709,767	$12,868,038	$23,943,064
	Budget impact	$0	$1,572,345	$7,858,502	$11,969,306	$21,400,154
CADTH scenario analysis: 25% advanced or metastatic rate	Reference	$1,630,032	$2,477,855	$2,660,202	$2,808,536	$7,946,593

In this example, the total budget impact was estimated to be **$21 million over a three-year period**.

This is the additional spending over and above what might would have been otherwise spent for these patients.

It is also noteworthy that there was a **major difference between CADTH estimates and submitted estimates** (roughly $7 million).

Also, note that **scenario analyses** were also conducted to determine the sensitivity of the estimate to key analysis parameters.

CADTH/CDA. 2023.

Additional Considerations

When using external HTA reports and economic assessments, it is important to consider the inputs and limitations of each model, including their **applicability to the Washington state health care system**.

There are **affordability review factors beyond those incorporated in traditional cost-effectiveness or budget impact analysis** that the Board may consider.

- Discussing the context these other factors may provide is important to allow a comprehensive review of each drug.

Questions?