PORTAL
Program on Regulation, Therapeutics, And Law

DoPE BWH

Maryland Prescription Drug Affordability Board

Cost Reviews & Upper Payment Limits

May 22, 2023

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

HARVARD MEDICAL SCHOOL

Brigham and Women's Hospital
Founding Member, Mass General Brigham

PORTAL Disclosures

- We do not receive any funding from pharmaceutical companies.

- PORTAL receives grant funding the following sources:
  - Arnold Ventures, the Elevance Health Public Policy Institute, the Kaiser Permanente Institute for Health Policy, the Massachusetts Health Policy Commission, the Commonwealth Fund, the National Academy for State Health Policy.

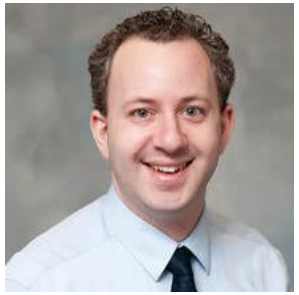
The PORTAL Team

Adam Raymakers, PhD
Postdoctoral Fellow

Leah Rand, DPhil
Research Specialist

Hussain Lalani, MD, MPH
Clinical Research Fellow

Catherine Hwang, MD, MSPH
Clinical Research Fellow



Benjamin Rome, MD, MPH
Instructor in Medicine

Aaron Kesselheim, MD, JD, MPH
Professor of Medicine
Director

Jerry Avorn, MD
Professor of Medicine

Matt Martin, MA
Project Coordinator

Presentation Outline

1. Conducting Cost Reviews
   - Comparative Effectiveness
   - Cost Effectiveness
   - Budget Impact
2. Considerations for Upper Payment Limits (UPLs)
   - Examples of UPLs from the US and other countries
   - Implementation Considerations

Maryland PDAB – Process Overview

Section 2.

Conducting Cost Reviews

Overview – Three Key Topics

1. **Comparative effectiveness:** How much additional benefit a drug provide patients compared to therapeutic alternatives?
2. **Cost-effectiveness:** How much will the additional benefit costs?
3. **Budget impact:** What will be the effect of purchasing a drug on payer budgets?

Comparative Effectiveness

Clinical Benefit Compared to 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

Measuring Clinical Effectiveness

- **Gold Standard:** Increased **longevity and/or quality of life**
  - Examples of improved quality of life: Reducing pain, improved mobility, improved cognitive function
  - Quality of life typically measured using disease-specific metrics or symptom scales
- In some cases, **surrogates measures** may be used instead (e.g. Accelerated Approval pathway drugs)
  - Examples: Hemoglobin A1c, LDL, progression free survival
  - Need to consider strength of 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

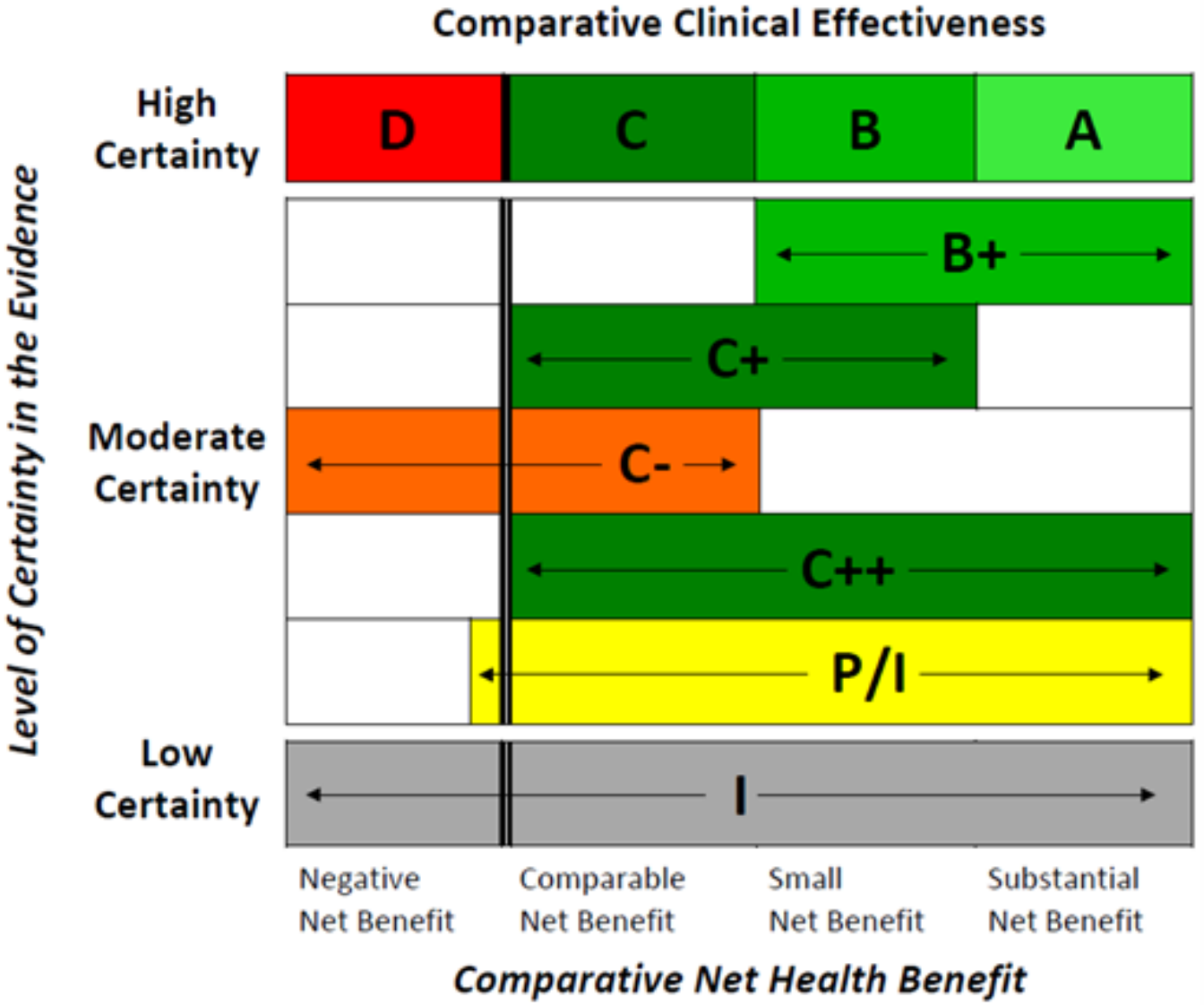
- Inferior
- None
- Minor Benefit
- Moderate Benefit
- Major Benefit

Quality of Evidence

Example – ICER Evidence Rating Matrix

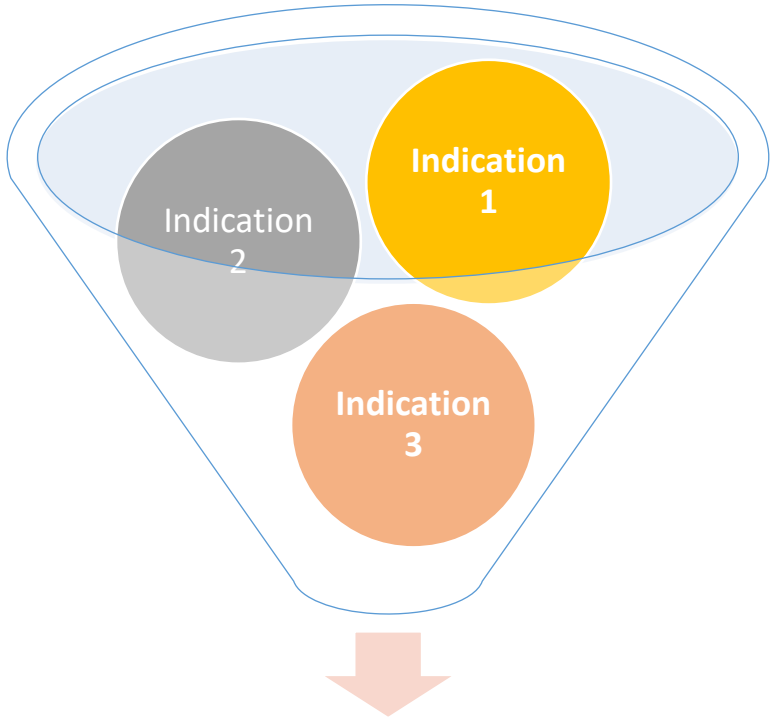
A *= "Superior"*
B *= "Incremental"*
C *= "Comparable"*
D*= "Negative"*

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



ICER. 2020-2023 Value Assessment Framework (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 Clinical Benefit

If drug offers **no or minor** added clinical benefit

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

If drug **offers moderate or major** added clinical benefit

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

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 of economic evaluation 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).

Economic Evaluation: One Input Into HTA

Health technology assessment (HTA) "refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform a policy decision making." (WHO)

Value assessment is used to mean the same thing as HTA. It is a term used by ISPOR and describes approaches "designed to measure and communicate the value of pharmaceuticals and other health care technologies for decision making"[1]

Neumann PJ, Wilke RJ, Garrison Jr. LP. *Value Health* (2018).

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)

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

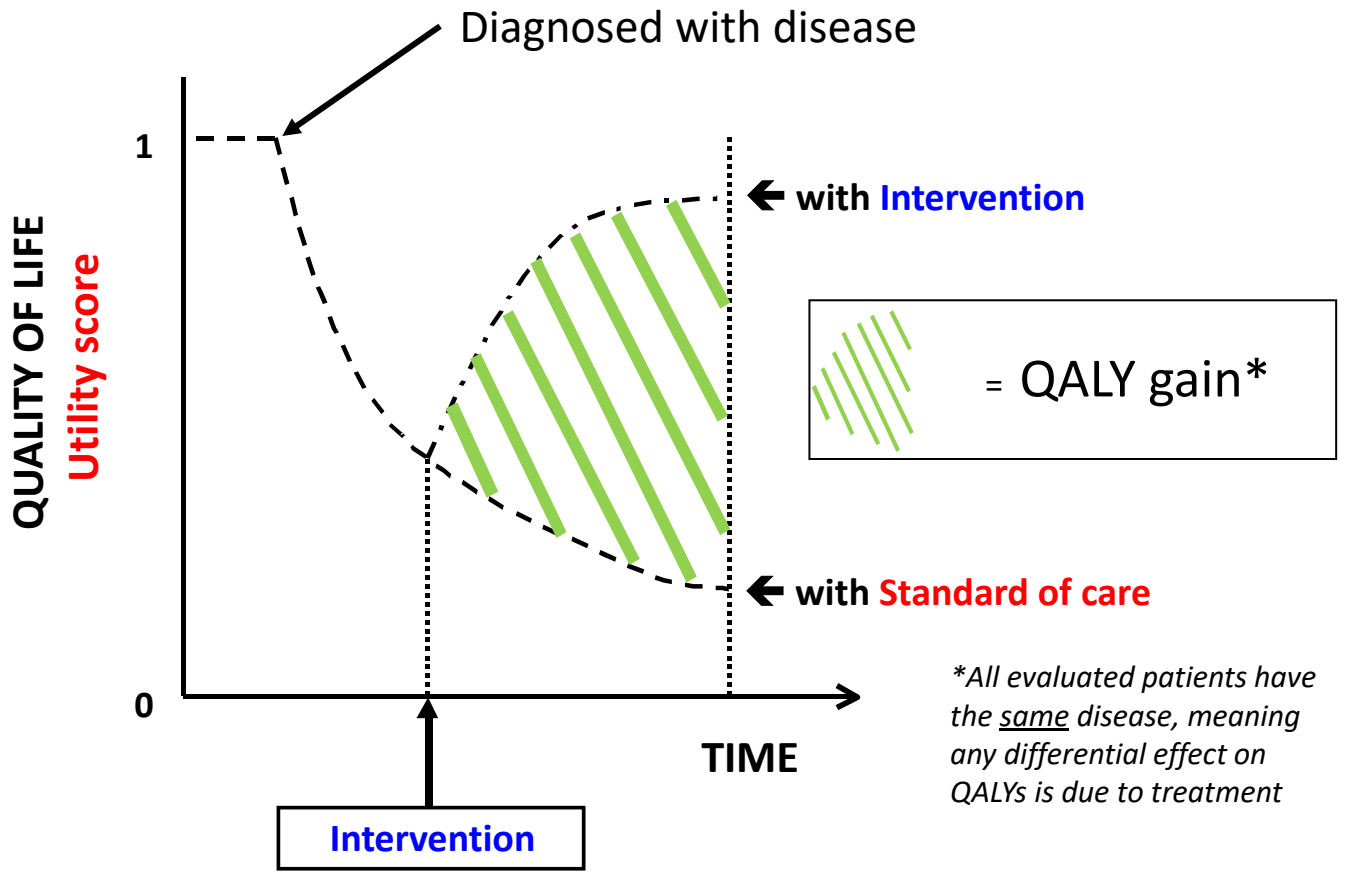
$$\textbf{Incremental Cost-Effectiveness Ratio (ICER)} = \frac{\text{Costs}_{\text{New}} - \text{Costs}_{\text{Current}}}{\text{Benefits}_{\text{New}} - \text{Benefits}_{\text{Current}}}$$

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)



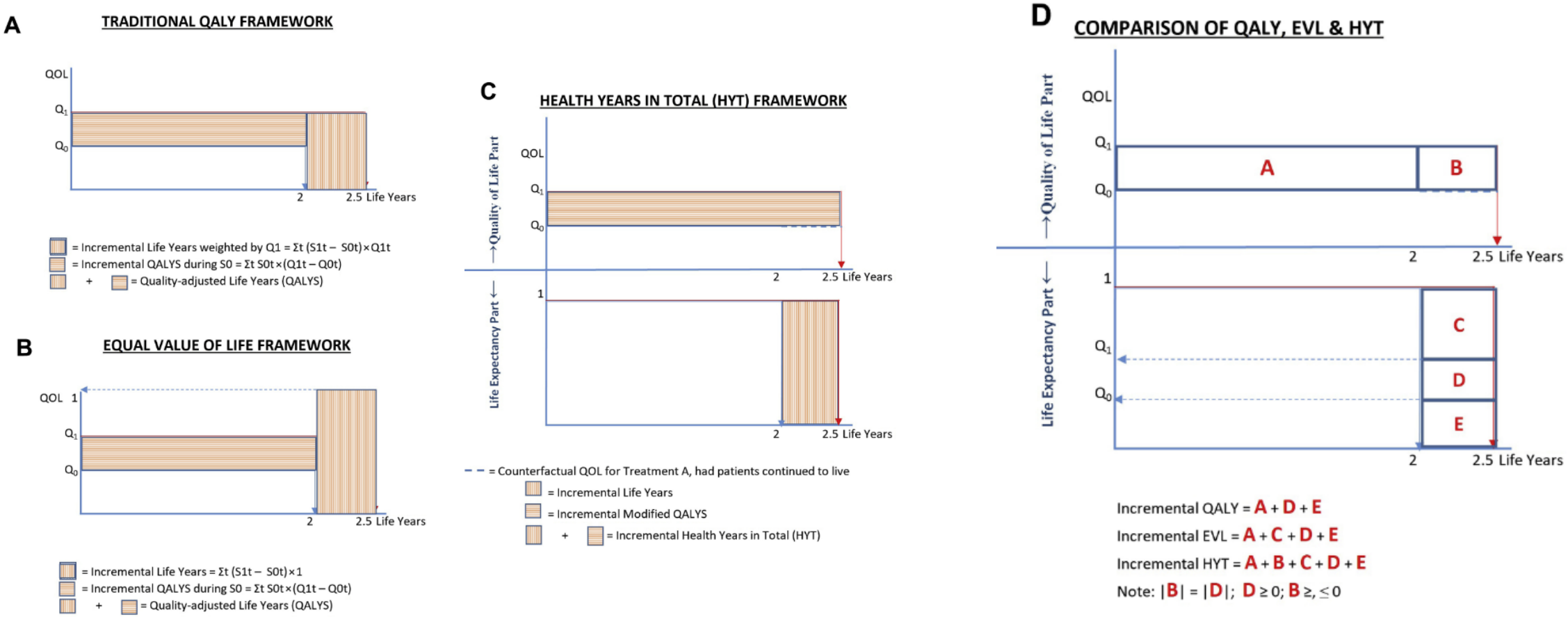
Other Measures of Benefit in CEA

- **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.
  - This measure was developed by the Institute for Clinical and Economic Review (ICER)

- **'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).

Some proposed alternatives to traditional CEA have industry support but have not 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, non health 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, value of hope, insurance value, scientific spillovers.

* Largely supported by industry. By factoring in additional considerations, the ICER typically becomes lower, thereby making new technologies appear more cost-effective. Some benefits may be double counted.

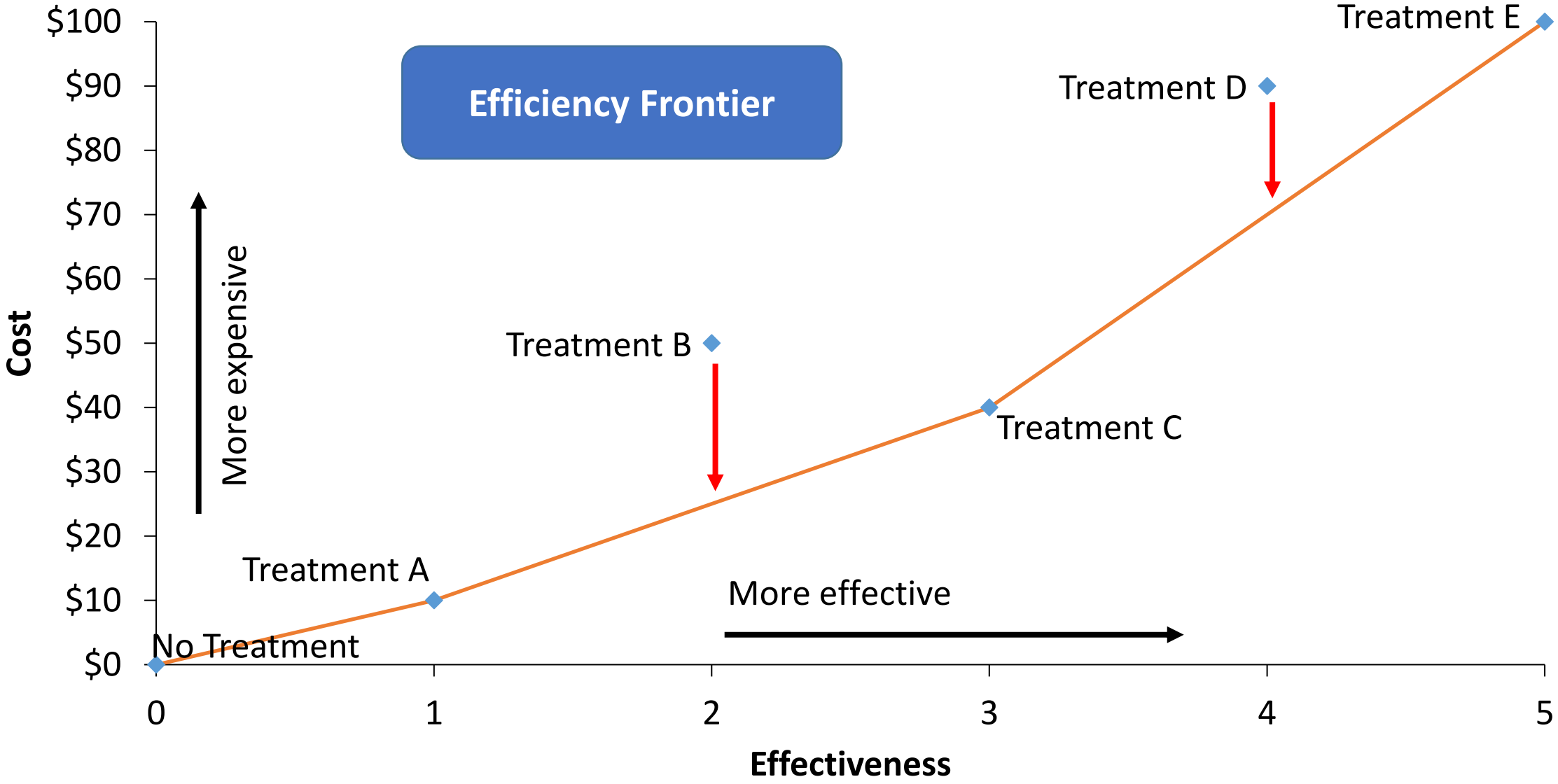
Asaria M, Griffin S, Cookson R. *Medical Decision Making* (2016); Verguet S, Kim JJ, Jamison DT. *Pharmacoeconomics* (2016); Neumann PJ, Garrison LP, Wilke RJ. *Value in Health* (2022).

Efficiency Frontiers

- Compares price and effectiveness of drug with 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


Efficiency Frontier
Cost
$100
$90
$80
$70
$60
$50
$40
$30
$20
$10
$0
More expensive
Treatment E
Treatment D
Treatment B
Treatment C
Treatment A
No Treatment
More effective
0
1
2
3
4
5
Effectiveness

Cost-Effective Drugs May Still Be Unaffordable due to high budgetary impact

- **Budget impact analysis** is an analytical method that incorporates actual cost to the health system, considering issues around price/cost, volume, market uptake, displaced alternatives, etc.

- Example: 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

Najafzedeh M, Andersson K, Shrank WH, et al. *Ann Intern Med* (2015).

Section 3.

Considerations for Upper Payment Limits (UPLs)

U.S. and International Examples

Maryland PDAB UPL Authority

Establish an upper payment limit

Health-Gen §21-2C-13

For drugs determined to pose an affordability challenge, the Board shall develop a "plan of action" for setting UPLs

Criteria considered include:

- Cost of administering the drug
- Cost of delivering the drug to consumers
- Other administrative costs

UPLs **cannot be established for drugs on the shortage list**, and should be reevaluated in the event of changes in drug availability

For now, UPLs will apply to drugs purchased or paid for by:

- State or local government (or an organization acting on the government's behalf)
- Health benefit plans on behalf of state or local government
- Maryland State Medical Assistance Program

UPL Authority at the State Level

In addition to Maryland, two state PDABs currently have statutory authority to establish UPLs for eligible drugs:

- **Colorado** can set UPLs for drugs determined to be "unaffordable for CO consumers" following an affordability review.
  - The CO PDAB has also implemented regulations operationalizing its UPL process.
- **Washington** can set UPLs for drugs found during affordability review to "lead to excess costs."

To date, no state PDAB has formally established a UPL on a drug.

Colorado's UPL Process – Statutory Requirements

If the CO PDAB finds a drug to be "unaffordable to Colorado consumers," the Board can choose to establish a UPL for that drug via a methodology that must include the following considerations:

- **Cost of administering or dispensing the drug**
- **Cost of distributing the drug to CO consumers**
- **Status on the FDA drug shortage list**
- **Impact to older adults and persons with disabilities***
- **Other relevant costs**

*The CO PDAB is prohibited from considering research or methods involving cost-per-QALYs or similar measures in setting UPLs

See C.R.S. 10-16-1407(2)-(4) (2021).

Colorado's UPL Process – Methodology

The CO PDAB has promulgated rules for its UPL process; under the reules, factors the Board can consider in establishing an UPL include:

Drug Cost and Price Metrics

- WAC
- Average Sales Price
- NADAC
- Out-of-Pocket Cost
- Carrier Paid Amount
- Retail Discount Amount
- Public Health Care Fee Schedule
- Manufacturer Net-Cost and Net-Sales
- Medicare MFP
- Other Voluntarily Provided Cost Information

Shortage Status

- Shortage Status at Time of UPL Adoption
- History of Resolved or Discontinued Shortage(s)
- If on Shortage List:
  - Drug Availability
  - Duration of & Reason for Shortage
  - Therapeutic Classification
  - Other Relevant Factors

Impact to Older Adults (65+) & Persons with Disabilities

- Utilization Among Given Population
- Cost Among Given Population
- Insurance Coverage of Drug Among Given Population
- For Drugs Addressing a Disability:
  - Therapeutic Classification
  - Purpose
  - Treatable Conditions or Diseases
- Relevant Quantitative or Qualitative Analyses

Stakeholder Input

- Public Input Provided During Rulemaking
- Input from Stakeholders with Relevant Lived Experience
- Input from Stakeholders with Relevant Expertise on the Drug's Impact on a Given Population

See 3 CCR 702-9 (2023).

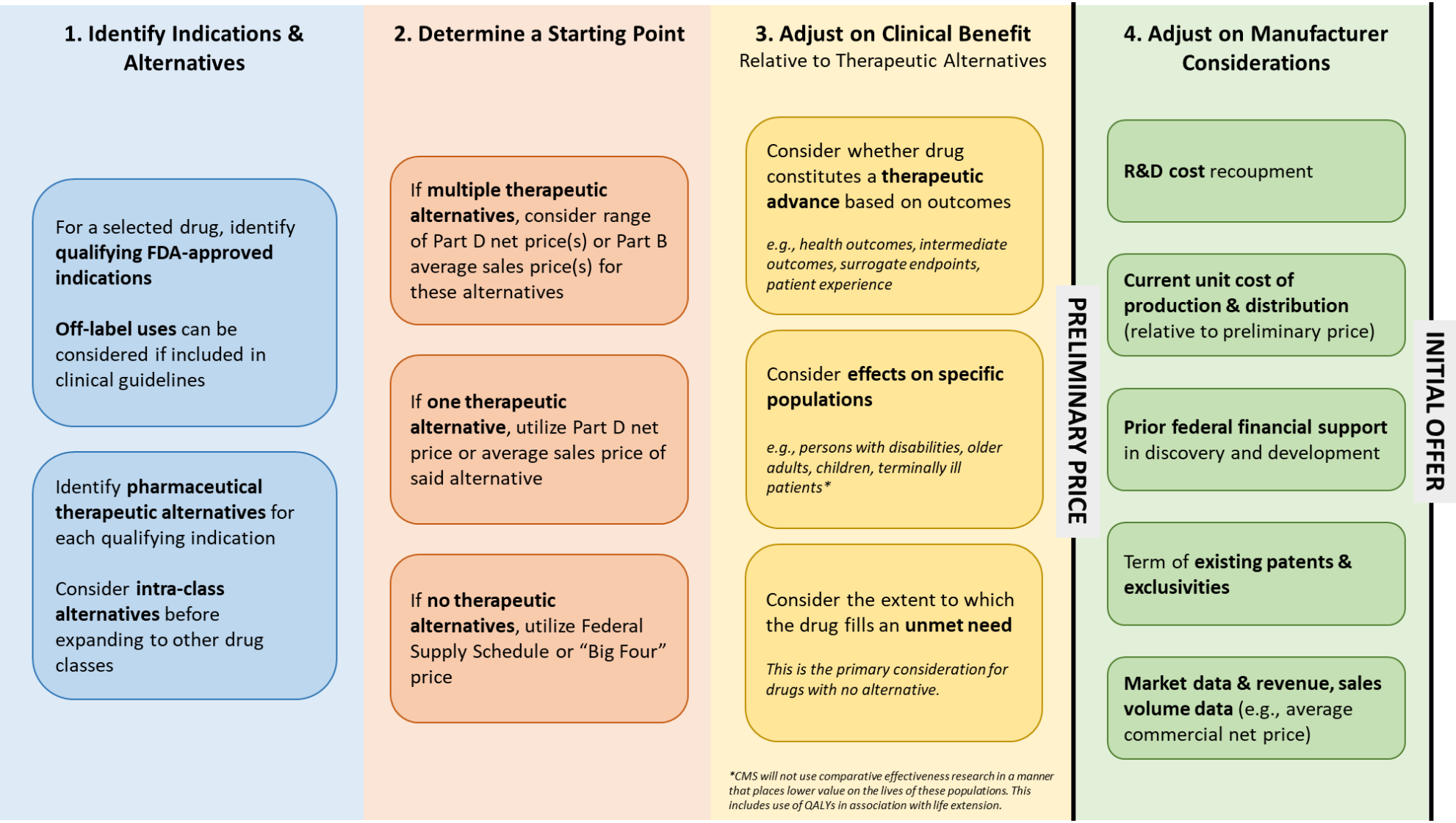
Under the Inflation Reduction Act, Medicare will begin negotiating maximum fair prices

- Maximum fair price (MFP) applies to selected top-selling drugs in Medicare that are eligible for negotiation
- The MFP cannot exceed a ceiling price, which is the lower of:
  - Average net price for Medicare plans (price after rebates and discounts)

  -OR-

  - A percentage of the drug's non-federal average manufacturer price (non-FAMP)
    - 75% non-FAMP for drugs approved < 12 years ago and vaccines
    - 65% non-FAMP for drugs approved 12-16 years ago
    - 40% non-FAMP for drugs approved > 16 years ago

CMS. Medicare Drug Price Negotiation Program, Initial Guidance, Section 60.3.1-60.3.4 (2023).



MFP Initial Offer

Proposed Methodology

In arriving at its initial offer, CMS will draw from:

- Clinical guidelines
- Part D compendia
- Literature reviews
- Expert input and analyses
- Manufacturer-submitted data
- Public-submitted data
- Other materials as appropriate

CMS. Medicare Drug Price Negotiation Program, Initial Guidance, Section 60.3.1-60.3.4 (2023).

Sample Adjustments Based on Manufacturer Factors

In its initial guidance, CMS has indicated various scenarios in which the preliminary price of a selected drug may be shifted in determining an initial offer:

Factors that may shift preliminary price **upward**	Factors that may shift preliminary price **downward**
• Manufacturer has **not yet recouped** R&D costs for the selected drug • Unit cost of production and distribution of the selected drug is **near the preliminary price**	• Manufacturer **has recouped** R&D costs for the selected drug • Unit cost of production and distribution of the selected drug is **less than the preliminary price** • Discovery and development of the selected drug **was funded through public sources** • Selected drug has patents & exclusivities that will **last for several years** • Average commercial net price of the selected drug is **lower than the preliminary price**

CMS. Medicare Drug Price Negotiation Program, Initial Guidance, Section 60.3.4 (2023).

Other Countries routinely negotiate payment limits for new drugs

- In other countries, the **negotiated price is based on the value of the drug**, usually how much additional benefit it provides.

- Negotiated national price serves as UPL: maximum reimbursement price for national insurance programs
  - Hospitals, pharmacy purchasers, wholesalers and other purchasers of prescription drugs may negotiate prices below the national UPL

- Requires methods to:
  - **Identify comparators or therapeutic alternatives** in relevant market
  - **Measure the amount of additional benefit** for that health system
  - **Link additional benefit to reasonable price** based on national budgets or guidance

UPL Examples – Other Countries

Germany	**Efficiency frontier**	National max. reimbursement price; insurers may negotiate lower prices
UK and Australia	**Cost-utility analysis**	National max. reimbursement price; purchasers may negotiate lower prices
Canada	**International reference pricing** (compare CA prices to other countries)	Set national max. price for "excessively" priced drugs

Section 3.

Implementing Upper Payment Limits (UPLs)

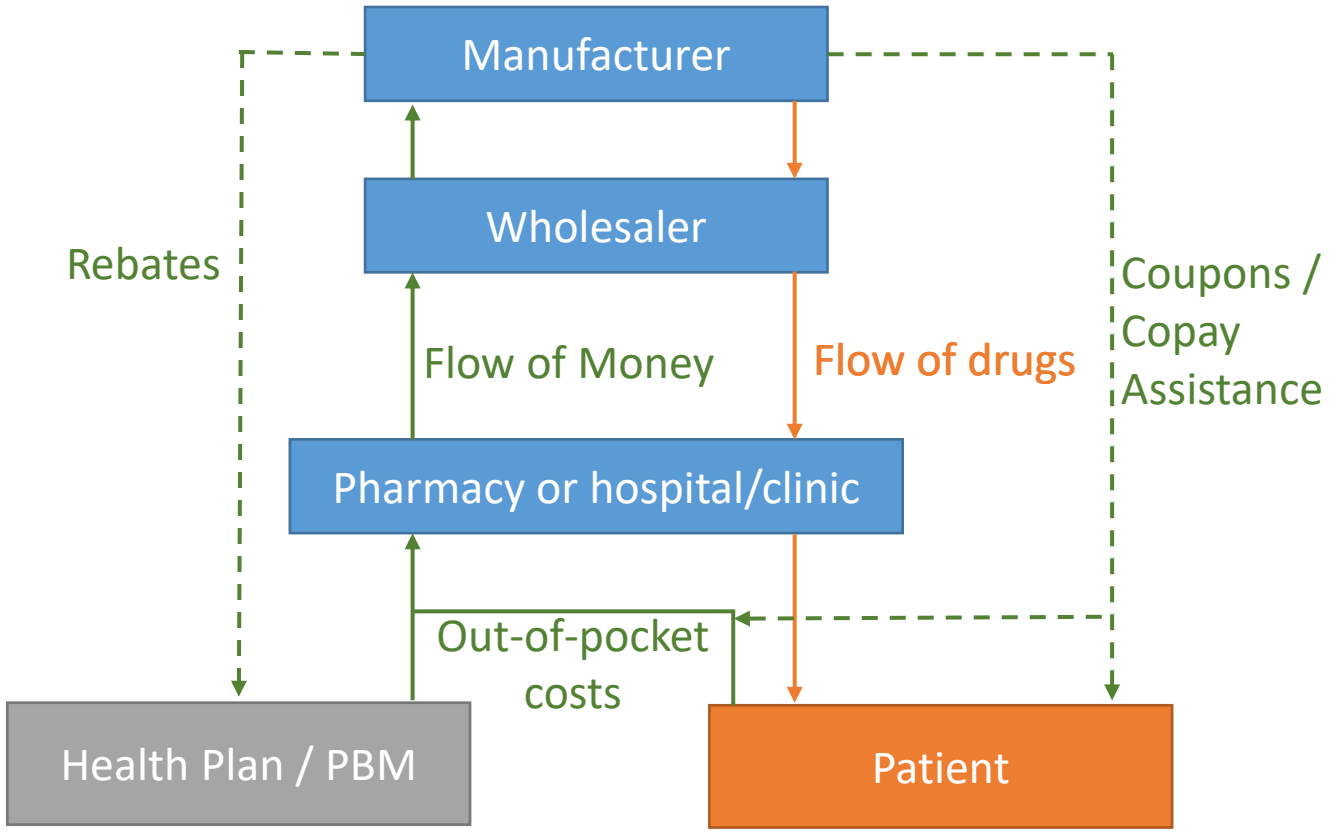
The Pharmaceutical Supply Chain

1. Drug manufacturers set the **list price** (wholesale acquisition cost = WAC)

2. Health plans or pharmacy benefit managers (PBMs) set the formulary and **out-of-pocket costs**

3. Health plans / PBMs negotiate **rebates** in exchange for preferred formulary position (↓ out-of-pocket costs)
   - **Net price** = list price - rebates

4. Drug manufacturers offer **coupons** to offset out-of-pocket costs charged by insurance.



Colorado PDAB - UPL Implementation

CO PDAB regulations permit UPL implementation at the **reimbursement level** (consumer purchases) ***and*** **supply chain purchases** (e.g., pharmacies, wholesalers).

- For insured patients, the payment to the pharmacy, including the portion paid by the patient and that paid by the insurer on their behalf, cannot exceed the UPL (plus "reasonable fees" charged by pharmacies for dispensing the drug).

Stakeholder perspectives have varied on how UPLs should be implemented in the supply chain.

See 3 CCR 702-9 Part 4.2 (2023).

CMS – Medicare MFP Implementation

CMS intends to implement MFPs at the reimbursement level using existing supply chain mechanisms, including:

- Part D processor identification (RxBIN) and control numbers (RxPCN) to allow pharmacies to identify MFP-eligible Part D payers at point-of-sale.
- Chargeback and rebate mechanisms between pharmacies, wholesalers, and manufacturers to enable MFP access.
- Reporting mechanisms to flag instances in which the MFP was insufficiently made available.

MFP access must be assured by each supply chain member, though **ultimate responsibility falls to manufacturer**

CMS. Medicare Drug Price Negotiation Program, Initial Guidance, Section 90.2 (2023).

Other Considerations for Implementing UPLs

Medicaid "Best Price" Policy - Statutory requirements that manufacturers offer state Medicaid programs the best price available to other purchasers for use in rebate determinations; may be affected by state-enacted UPLs

Example: if enacting a UPL results lowers the price of a selected drug in the state below the current Medicaid "best price," manufacturers could owe additional rebates to all state Medicaid programs.

Opportunities for Cost-Shifting - Implementing UPLs may result in cost-shifting in the supply chain toward fees

Example: After Medicaid programs changed reimbursement formulas from average wholesale price (AWP) to average acquisition cost (AAC), many states also increased dispensing fees that offset decreases in ingredient costs.

KFF. Pricing and Payment for Medicaid Prescription Drugs (2020); Baghdadi R. *Health Affairs* (2017).

Questions?