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Improving healthcare decisions

ISPOR 2023 Forum:

Generalized Cost Effectiveness Analysis – from Theory to Practice

ISPOR Boston Regional Chapter

May 8, 2023

Our Panel



Noam Kirson
Managing Principal
Analysis Group



Lou Garrison
Professor Emeritus
CHOICE Institute
University of Washington



Patty Synnott
Director
CEA Registry
CEVR

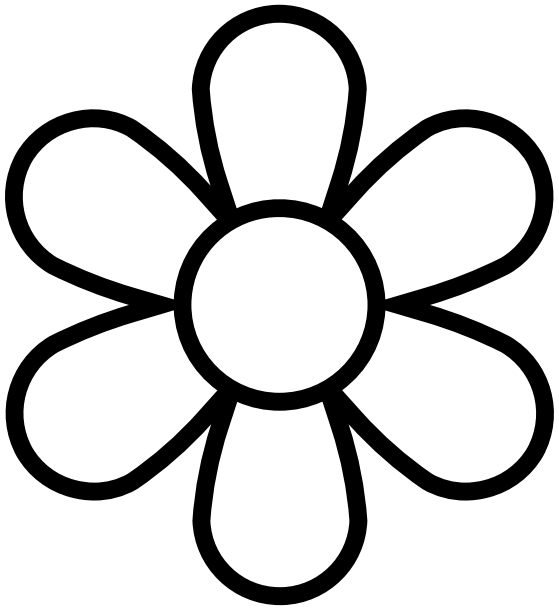


Jon Campbell
Senior Vice President
ICER



Chris Leibman
Senior Vice President
Biogen

ANALYSIS GROUP

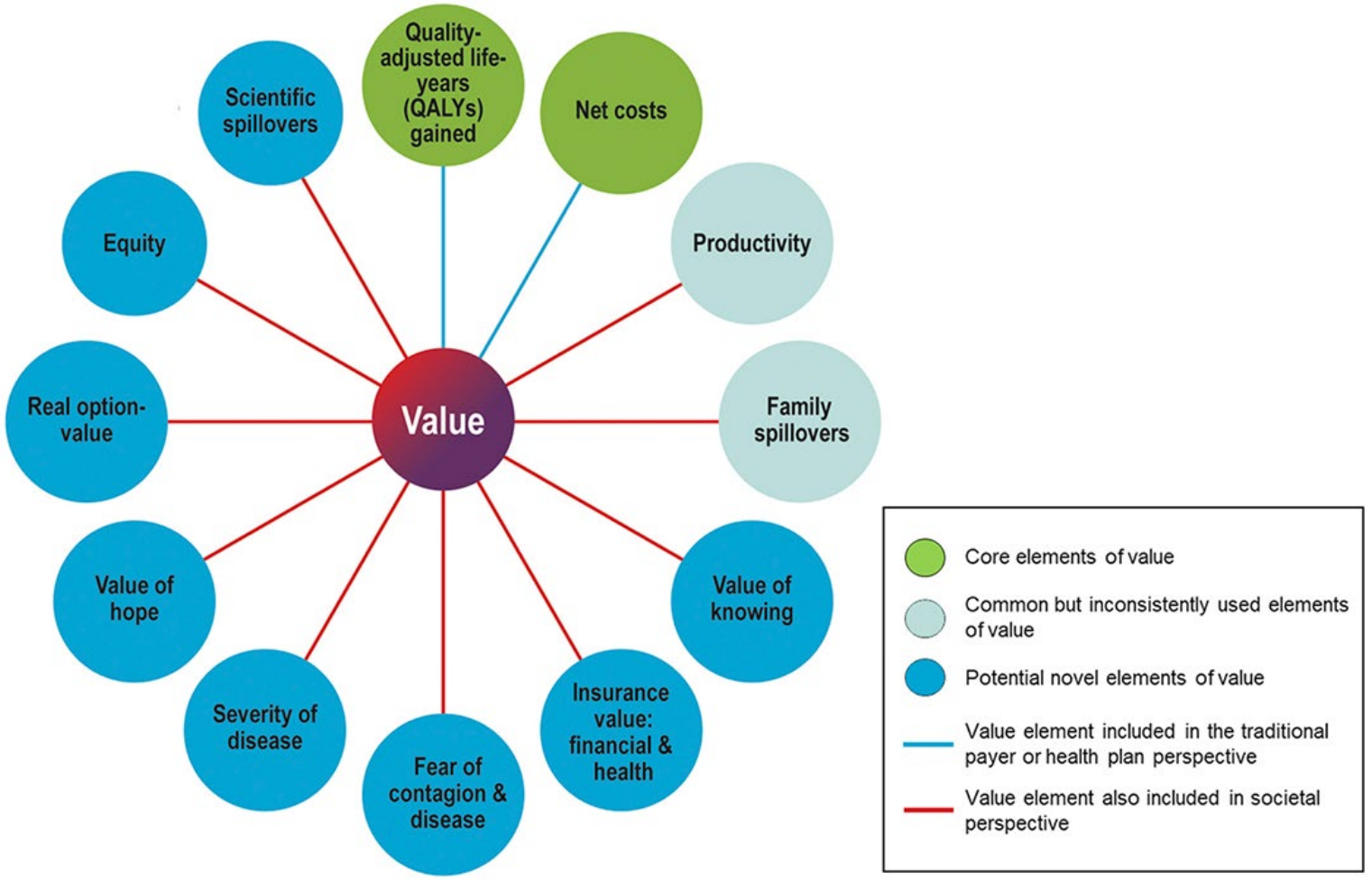


GCEA: What, How, and Where Does it Take Us?

Noam Kirson
Managing Principal

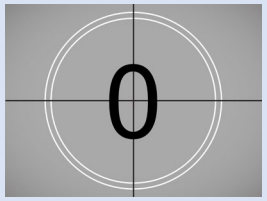
Operationalizing the Value Flower: Practical Questions

- How big are the petals, and how do they vary across therapeutic areas?
- What can be measured: Now? In the future?
- Can we agree on what to include, even for currently included petals? (e.g., genericization, HRU costs)



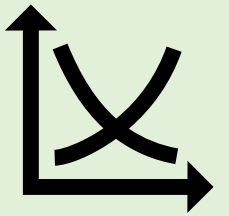
* Adapted from Lakdawalla et al, ViH (2018)

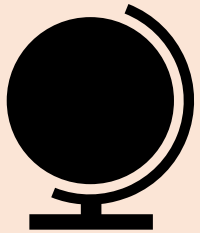
Key Topics for Discussion



Does lack of precision justify omission?
→ zero is a strong assumption

Cost-effectiveness vs. societal value: guidance for pricing?



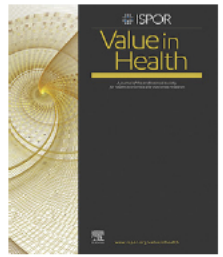


Will elements of GCEA be implemented in HTA or HTA-like frameworks? Is there a US vs. ex-US difference?

The ISPOR Value Flower and Value Frameworks: Update and Future Directions

Lou Garrison, PhD, Professor Emeritus
The CHOICE Institute, School of Pharmacy
University of Washington, Seattle WA, USA
Founder, Global Health Economics LLC (2022) USA

Generalized Cost Effectiveness Analysis – from Theory to Practice
Forum: ISPOR International Meeting, Boston MA
Monday, May 8, 2023



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Brief Report

The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis

Peter J. Neumann, ScD, Louis P. Garrison, PhD, Richard J. Willke, PhD

ABSTRACT

Objectives: Since its publication as part of the 2018 ISPOR Special Task Force (STF) on US Value Assessments, the "ISPOR value flower," with its petals highlighting elements that may be overlooked or underappreciated in conventional drug value assessments, has been discussed and debated. We review the history of the value flower, describe recent developments, and

Value Frameworks and Decision Contexts



Some Recent U.S. Value Frameworks: 2014-18

Plan Level

Inclusion in Health Benefit Package
Assess Cost-Effectiveness
Negotiate Price

ICER, MSKCC, 2nd Panel

Benefit Management Level

Management of Access and Utilization
Update Standard Treatment Guidelines
Incorporate in Clinical Pathways
Manage Utilization in Plan

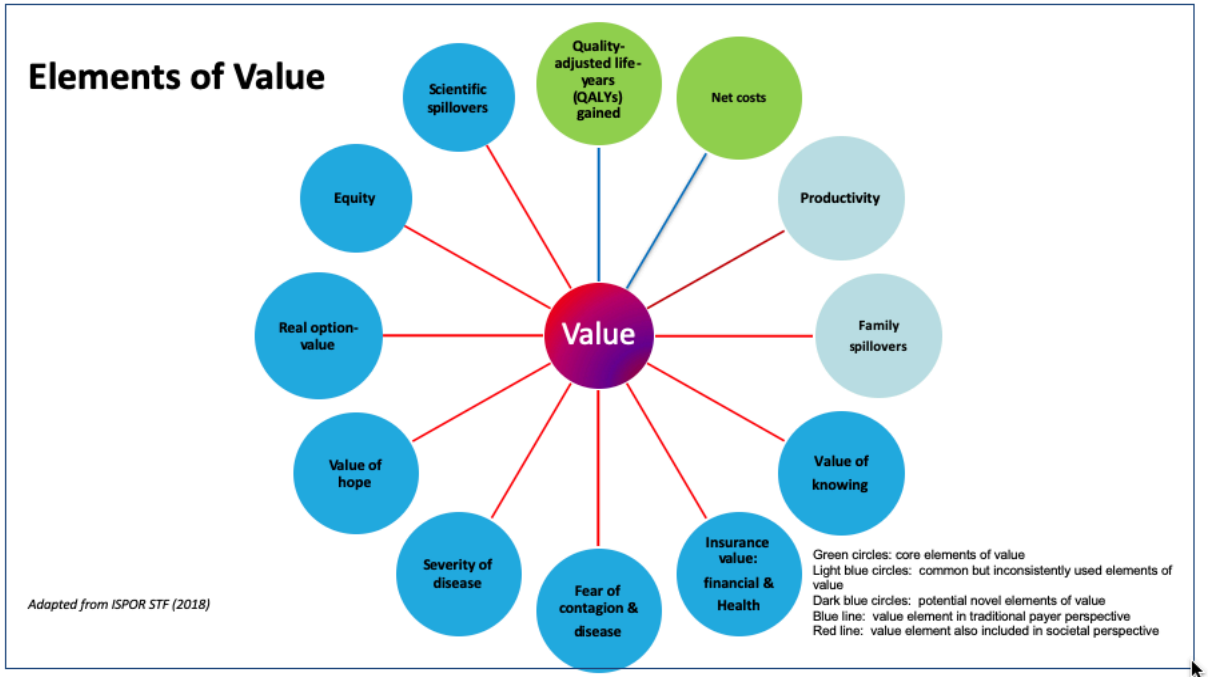
ACC/AHA, NCCN

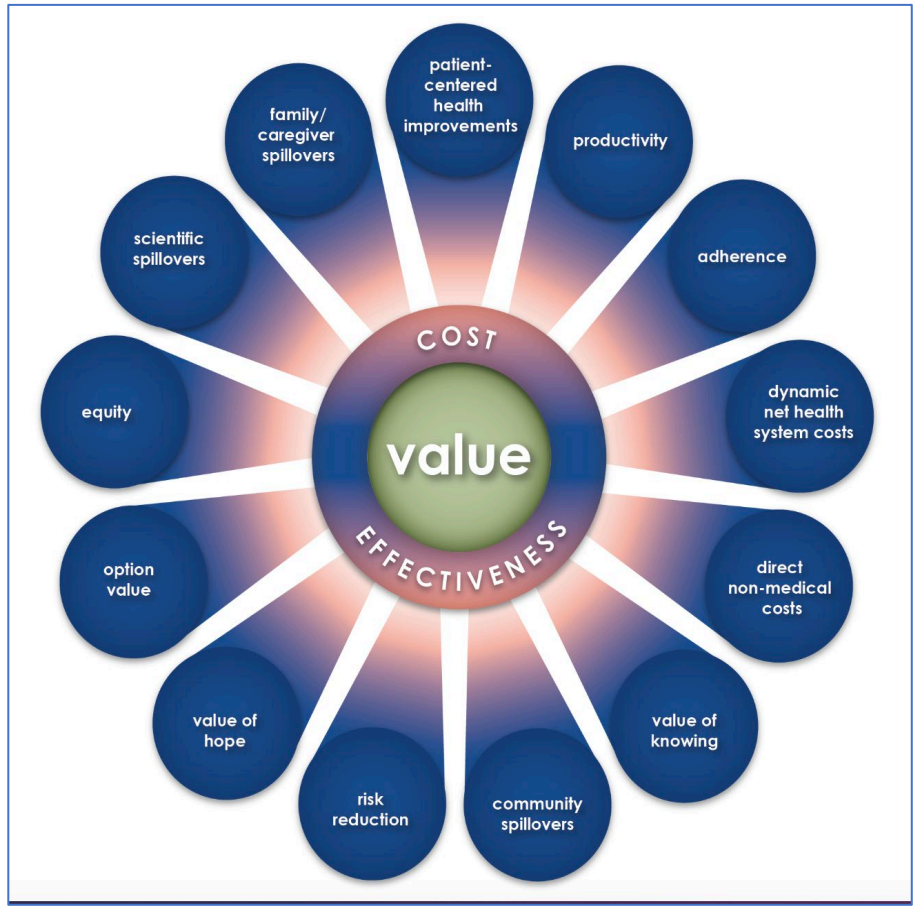
Patient Level

Use in Shared Clinical Decision-Making
Patient & Provider Choose Treatment

ASCO, NCCN, Avalere/FC

ISPOR Value Flower
Augmented CEA



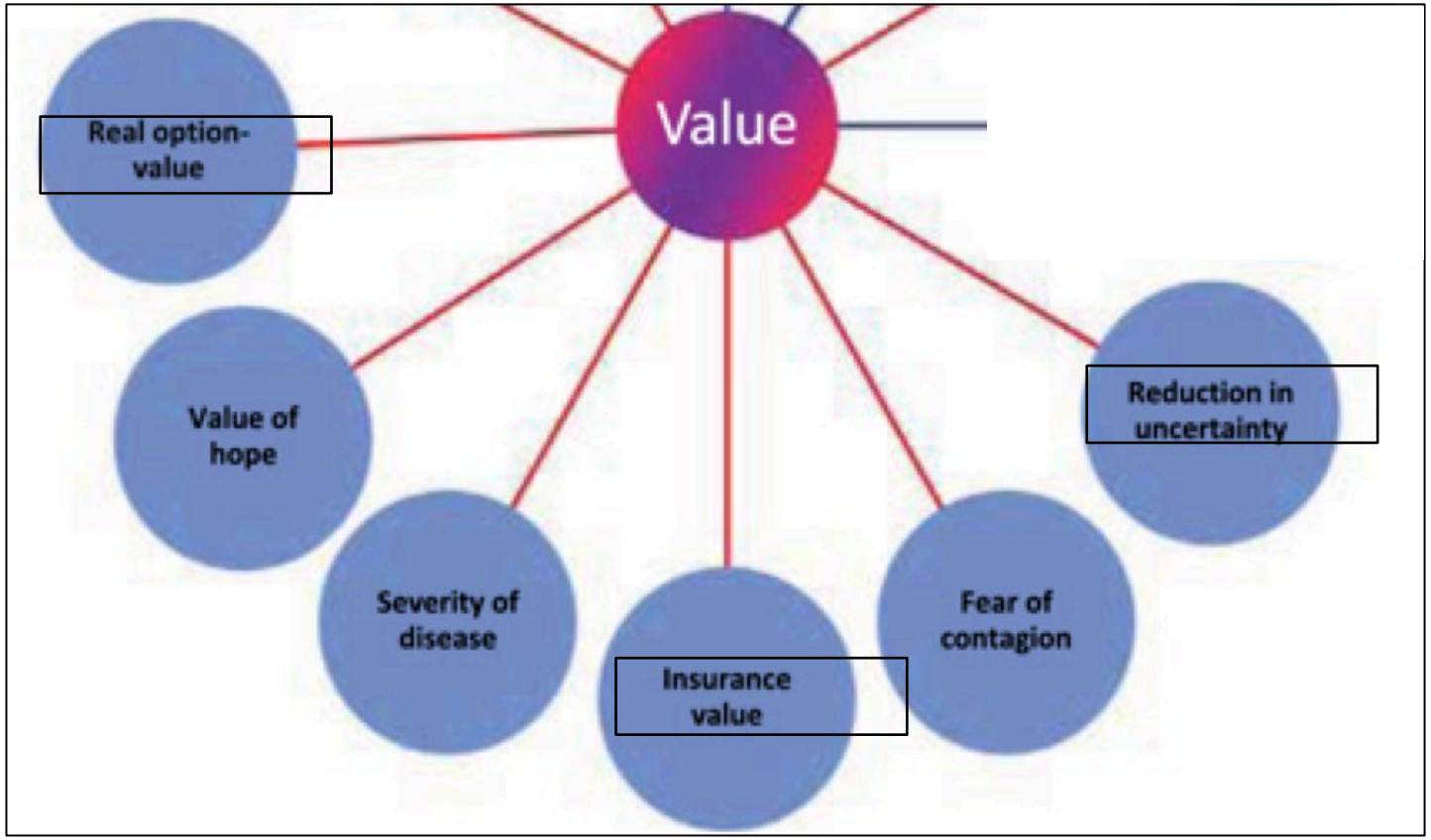


Potential Elements of Value: Elements Related to Uncertainty (1)

- **Reduction in uncertainty due to Dx test (also called "Value of Knowing")**
  - Text-drug combination is more valuable
  - Value in prognosis

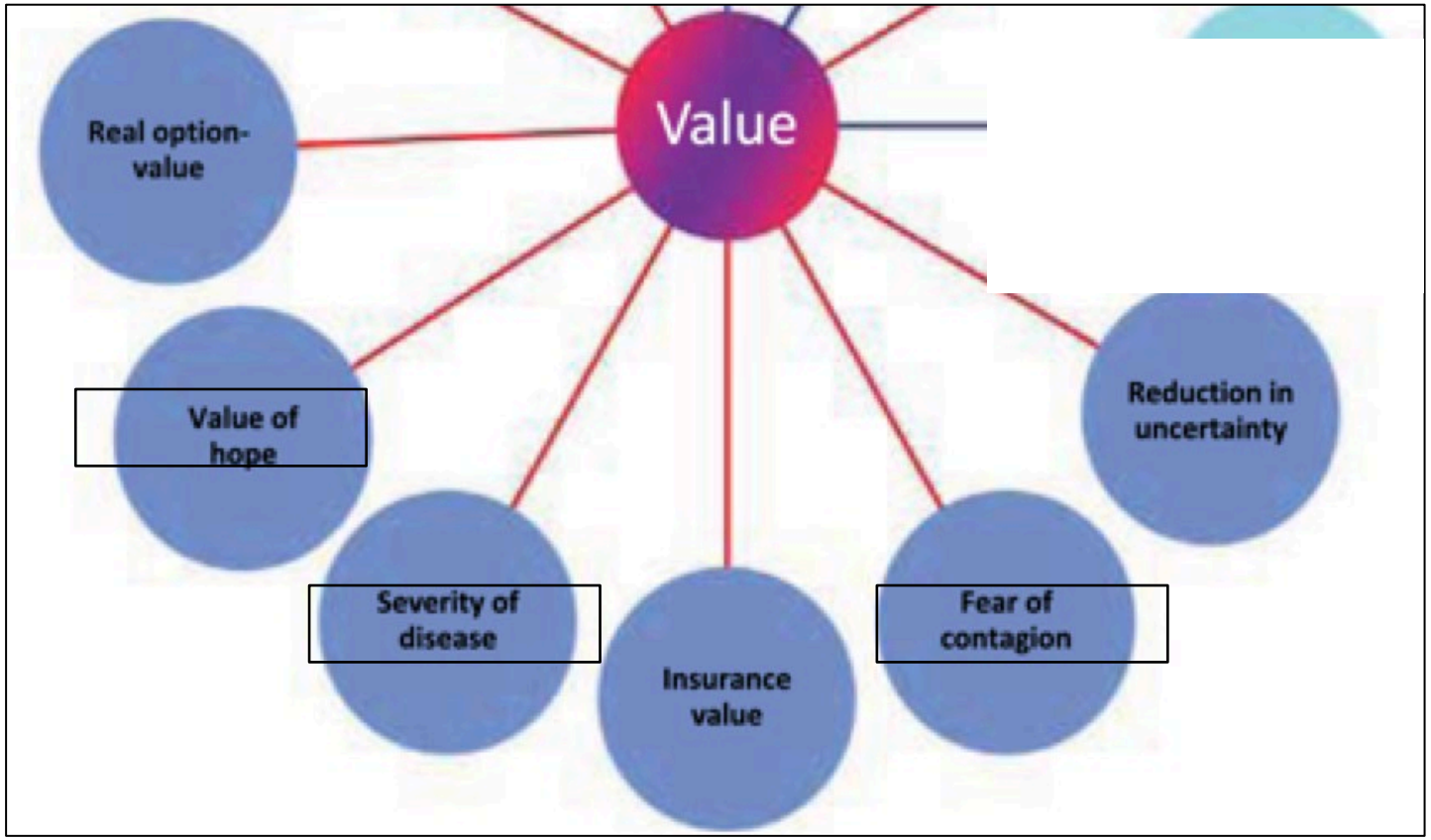
- **Insurance value (in GRACE)**
  - Financial risk protection AND
  - Health risk protection
  - Can adjust for severity and rarity
  - In "Extended Cost-Effectiveness Analysis"

- **Real option value**
  - Investing in a life-extending treatment provides more value in disease area with more promising pipeline



Potential Elements of Value: Elements Related to Uncertainty (2)

- **Value of hope**
  - Many patients are willing to sacrifice some life expectancy for the chance for a cure.
- **Severity of disease**
  - Greater willingness to pay for more severe diseases (beyond the QALY loss)
- **Fear of contagion**
  - A psychic externality due to worry about spread of infectious disease (e.g., Zika virus)



Recent Literature Summary—Elements Related to Uncertainty

PERSPECTIVES ON AUGMENTING COST-EFFECTIVENESS ANALYSES

Augmenting Cost-Effectiveness Analysis for Uncertainty: The Implications for Value Assessment—Rationale and Empirical Support

Louis P. Garrison, Jr., PhD; Bernarda Zamora, PhD; Meng Li, PhD; and Adrian Towse, MS, MPhil

FIGURE 1 Potential Elements of Value

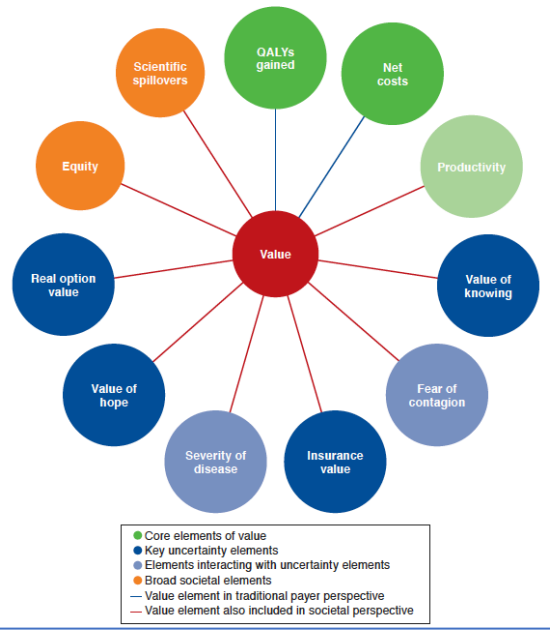


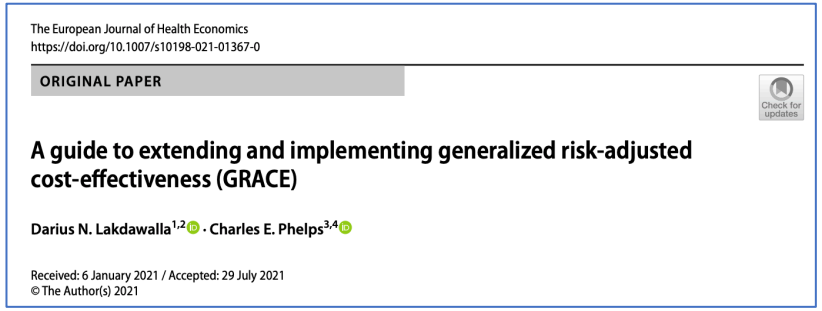
TABLE 1 Empirical Studies Relevant to the Measurement of Novel Uncertainty-Related Elements of Value

Element/Study	Context	Method	Monetary Effect Above Conventional ICER
Insurance value: financial risk protection			
Verguet et al., 2013[14]	Rotavirus-India (I) and Ethiopia (E)	Dynamic CEA modeling	Financial risk protection (FRP) of $16k (I) and $8K (E) per 1 million households. Largest FRP in lowest income quintile.
Verguet et al., 2015[15]	Tuberculosis in India	Universal public finance model (90% coverage)	Per million people in India, insurance value is $9,000, and 80% would accrue to the bottom 2 quintiles.
Insurance value: financial and physical health risk protection			
Shih et al., 2016[16]	Multiple sclerosis in United States	Parameterized utility function	33% of conventional value
Lakdawalla et al., 2017[10]	General U.S. population	Numerical exercise with a parameterized utility function	38%-62%: The physical insurance values greatly exceed the financial insurance value
Real option value			
Sanchez et al., 2012[17]	Small molecule medicine for chronic myeloid leukemia in United States	Projection of mortality trends	9% of conventional survival benefit
Snider et al., 2017[18]	Monoclonal antibody medicine for renal cell carcinoma and lung cancer in United States	Projection of mortality trends	5%-18% of conventional survival benefit
Li et al., 2019[19]	Monoclonal antibody medicine for metastatic melanoma in United States	Projection of mortality trends and new drug approvals and economic modeling	Incremental QALY gained increased by 5%-8% and ICER decreased by 0%-2%
Value of hope			
Lakdawalla et al., 2012[13]	Treatments for metastatic melanoma and metastatic breast cancer in United States	Discrete choice/contingent valuation	WTP $35,000 for a 1 standard deviation increase in survival
Shafrin et al., 2017[23]	Treatments for advanced stage melanoma or lung cancer in United States	Patient and physician surveys	Majority of patients prefer higher variance in survival; physicians do not
Shafrin et al., 2018[24]		Economic estimation	0.04 QALY
Value of knowing			
Neumann et al., 2012[25]	Predictive testing for diseases with no preventive option in United States	Stated-preference study	$109-$263 per test
Goldman et al., 2013[26] (Sood et al., 2013, technical analysis)[27]	Dx testing in personalized medicine: RA patients at risk for CV event on an NSAID in United States	Population economic modeling	Test generates $1,284 per patient

CEA = cost-effectiveness analysis; CV = cardiovascular; Dx = diagnostic; ICER = incremental cost-effectiveness ratio; NSAID = nonsteroidal anti-inflammatory drug; QALY = quality-adjusted life-year; RA = rheumatoid arthritis; WTP = willingness to pay.







". . . cost-effectiveness decision thresholds should be about 5 times higher for severe Alzheimer's disease than for peptic ulcer disease."

In my view: this framework is a pathbreaking advance.

The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model

Lakdawalla-Phelps (2020a;b;c): Formal development of augmented CEA

Incorporates uncertainty and risk aversion:

- Variance in health outcomes
  - ➢ Not just mean effects
- Risk aversion for health outcomes
- Baseline severity of disease
- Likelihood of cures/value of hope

Implies →

- **Cost-effectiveness thresholds should vary, and they should be higher for rare, health-catastrophic diseases**
- Variance in outcomes generally reduces value, except for cures.

Scientific Spillovers as an Element of Value and Innovation



International Journal of Technology Assessment in Health Care

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Should We Pay for Scientific Knowledge Spillovers? The Underappreciated Value of "Failed" R&D Efforts

Richard Z. Xie[1*], Adrian Towse[2] and Louis P. Garrison, Jr.[3]

[1]The Innovation and Value Initiative, Alexandria, VA, USA; [2]Office of Health Economics, London, United Kingdom and [3]The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, WA, USA

Commentary

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Key words:
Health economics; Drug development; Health policy; Reimbursement; Social welfare

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Abstract

Recent experience with COVID-19 has reminded us of the importance of scientific progress in enabling pharmaceutical innovation. Developing novel therapies is a highly risky but rewarding process: it not only produces innovative drugs, but also valuable scientific knowledge that benefits the community of innovators. This paper examines whether the existing reward system for pharmaceutical research and development (R&D) leads to socially optimal levels of scientific knowledge generation and sharing, with a particular focus on the value of failures in the pharmaceutical R&D efforts. We first outline a conceptual approach based on the idea that pharmaceutical R&D efforts produce both medicines and scientific knowledge, and illustrate this with some examples of how failures may generate information beneficial to concurrent and subsequent R&D efforts. We then summarize the relatively small literature on failures in pharmaceutical R&D and their impact on R&D decision making. Lastly, we discuss several market-based and nonmarket-based policy approaches that can address potential shortcomings in the current reward system which may lead to suboptimal R&D and knowledge sharing.

- Scientific spillovers are knowledge externalities.
- 'There is more to value than QALY gains, cost-savings, and uncertainty reduction at the individual level.
- Firms in the healthcare ecosystem learn from each other's successes and failures.

Insurance Value =

Health Risk Protection
+
Financial Risk Protection



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Measuring the Value Healthy Individuals Place on Generous Insurance Coverage of Severe Diseases: A Stated Preference Survey of Adults Diagnosed With and Without Lung Cancer

Jason Shafrin, PhD, Suepattra G. May, PhD, MPH, Lauren M. Zhao, BA, Katalin Bognar, PhD, Yong Yuan, PhD, John R. Penrod, PhD, John A. Romley, PhD

"After accounting for the likelihood that healthy individuals are diagnosed with lung cancer in the future, we estimated that 89.8% of the total value of new lung cancer treatments comes from the WTP healthy individuals place on generous insurance coverage."

"Conclusion: Total societal willingness to pay for lung cancer is much higher than conventionally thought, as most healthy individuals are risk-averse and highly value having lung cancer treatments available to them in the future."

Value-Based Pricing and Product Life Cycle

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Themed Section

Value-Based Pricing for Patent-Protected Medicines Over the Product Life Cycle: Pricing Anomalies in the "Age of Cures" and Their Implications for Dynamic Efficiency

Louis P. Garrison Jr, PhD, Boshen Jiao, MPH, PhD, Omar Dabbous, MD

ABSTRACT

Objectives: Conventional cost-effectiveness analysis (CEA) for the value-based pricing of new medicines largely ignores the implications of limited market exclusivity (ie, patent-protection periods plus any exclusivity granted by regulators). This paper explores the implications of this methodological shortcoming, which produces several pricing anomalies with potentially unintended effects on research and development (R&D) incentives.

Methods: We illustrate these implications by comparing 4 stylized examples of increasing complexity, from short-term cures for acute conditions to long-term cures for rare, health-catastrophic conditions.

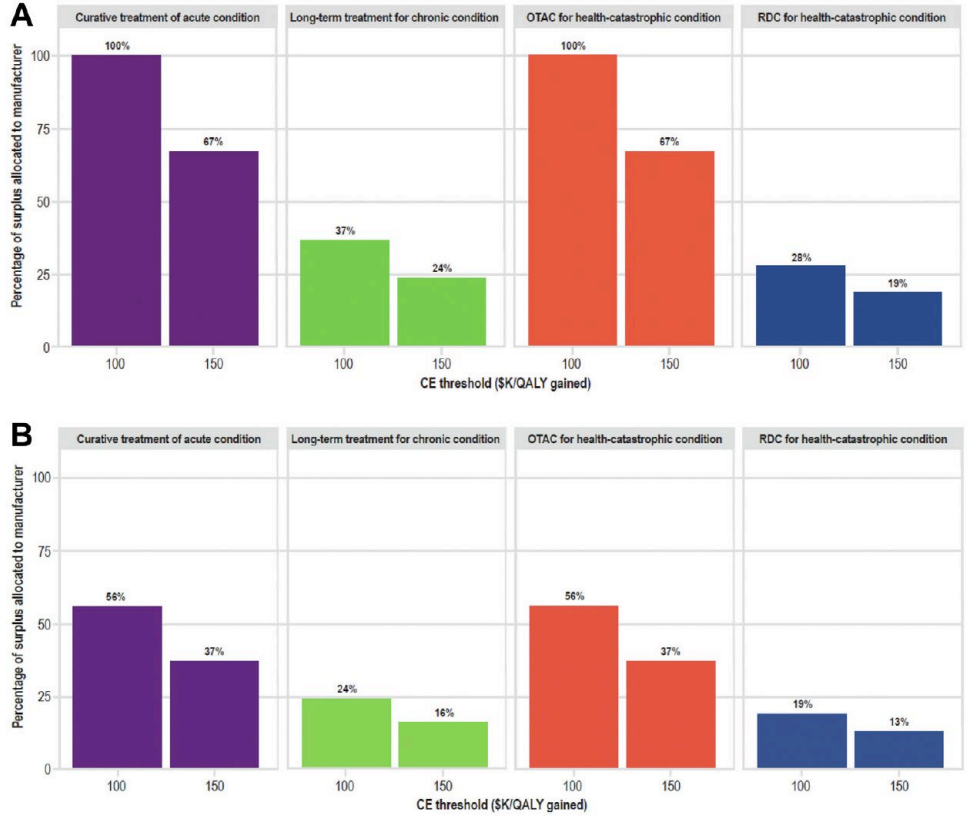
Results: (1) Conventional-CEA will project a different result than an adjusted CEA that considers generic or biosimilar entry; (2) free and flexible pricing of long-term treatments (eg, statins for hypercholesterolemia) or repeated-dose cures (eg, insulin for type 1 diabetes) for chronic conditions will likely result in predictable price increases at the end of the exclusivity period that may be perceived as unjustified or unsupported; and (3) one-time administration "cures" (eg, gene therapy for spinal muscular atrophy) have the potential to allocate a large share of the social surplus to the manufacturer over the product lifetime, which may or may not be dynamically efficient *per se*, but may also inadvertently disadvantage the development of valuable long-term treatments or repeated-dose cures for chronic conditions.

Conclusions: We highlight the need for additional research on long-term solutions to these issues that would aim to promote dynamically efficient global R&D. More work is needed on the following: (1) relationships between social surplus allocation and the amount and composition of global R&D, as we may be as likely to be encouraging excessive R&D in some areas as to be undersupplying it in others; and (2) relating the size of the surplus reward to R&D cost and, thus, the return on investment.

Keywords: consumer surplus, cost-effectiveness analysis, cures, dynamic efficiency, genericization, social surplus, value-based pricing.

VALUE HEALTH. 2022; ■(■):■–■

Figure 1. Percentage of surplus allocated to manufacturers of (1) a curative treatment of acute condition, (2) a long-term treatment for chronic condition, (3) an OTAC, and (4) an RDC for health-catastrophic condition under current launch price, for the first 12 annual cohorts (A) versus 30 annual cohorts (B).



CE indicates cost-effectiveness; K, 1000; OTAC, one-time administration cure; QALY, quality-adjusted life-year; RDC, repeated-dose cure.

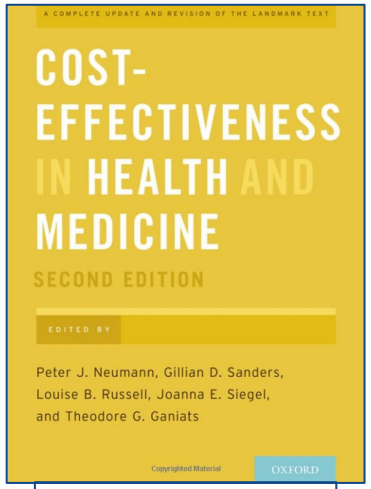
TuftsMedicine

Are Cost-Effectiveness Analyses Deviating from the Conventional?

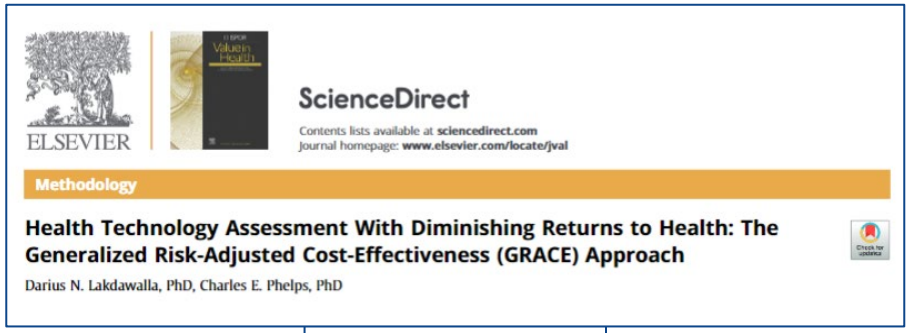
Insights from the CEA Registry

Patty Synnott
Director, CEA Registry

May 8, 2023

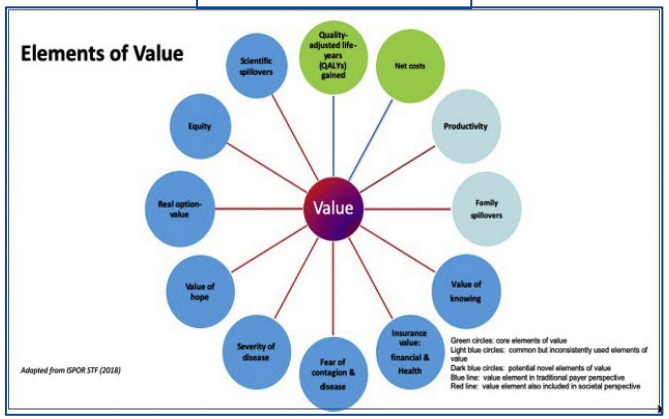


2016



2021

2018



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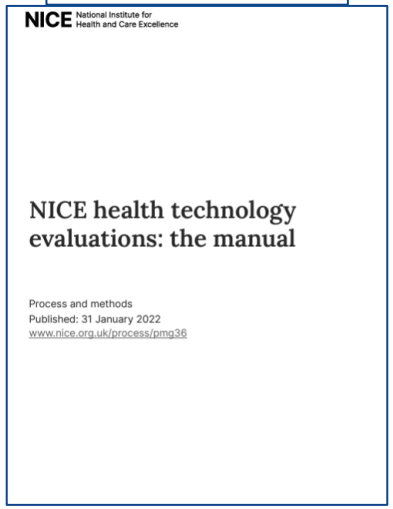




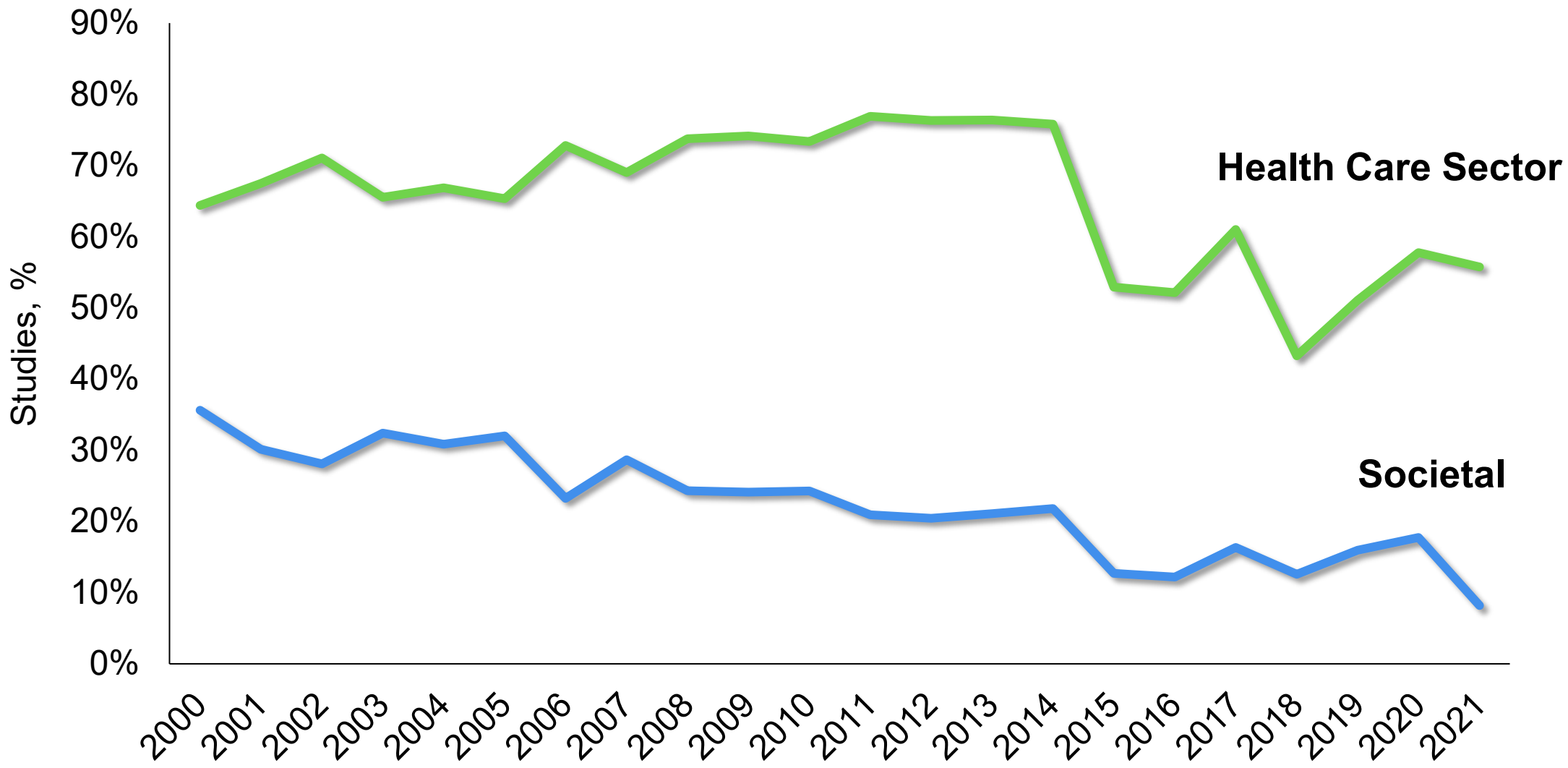
Database of 12,000 cost-effectiveness analyses

1. Societal impacts

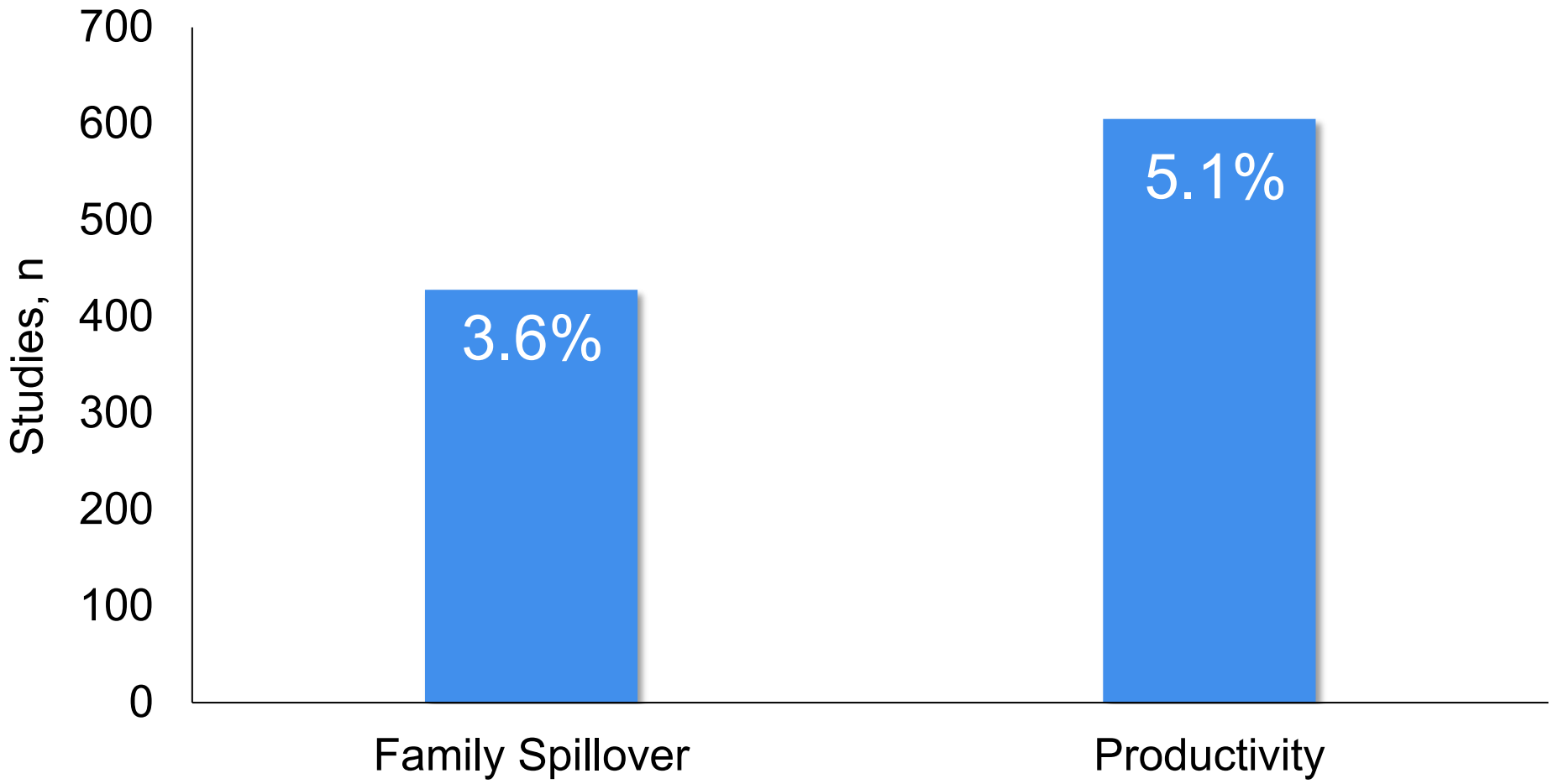
2. Life cycle pricing

Societal Impacts

Perspectives in CEAs over Time



Common Value elements



What about the new kids on the block?

Fear of contagion

Real option value

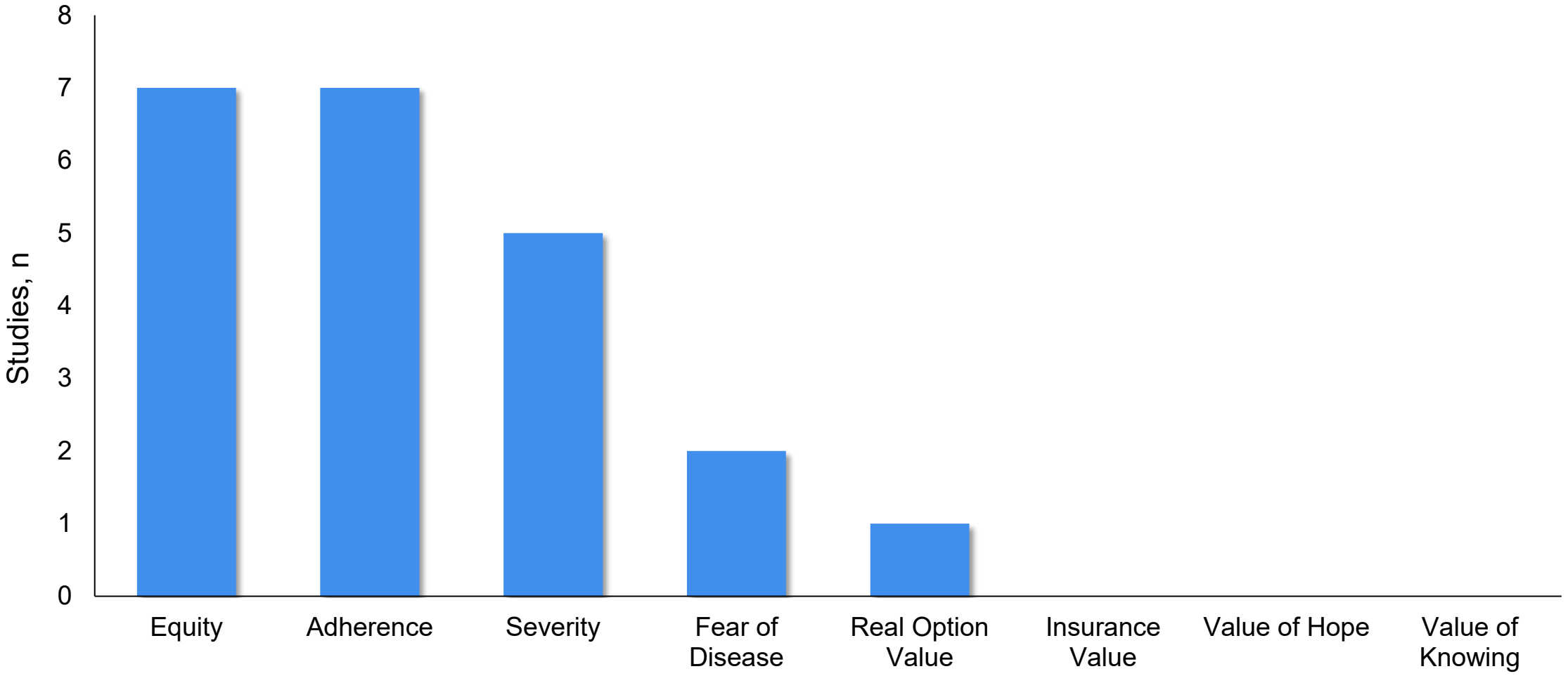
Value of knowing

Value of Hope

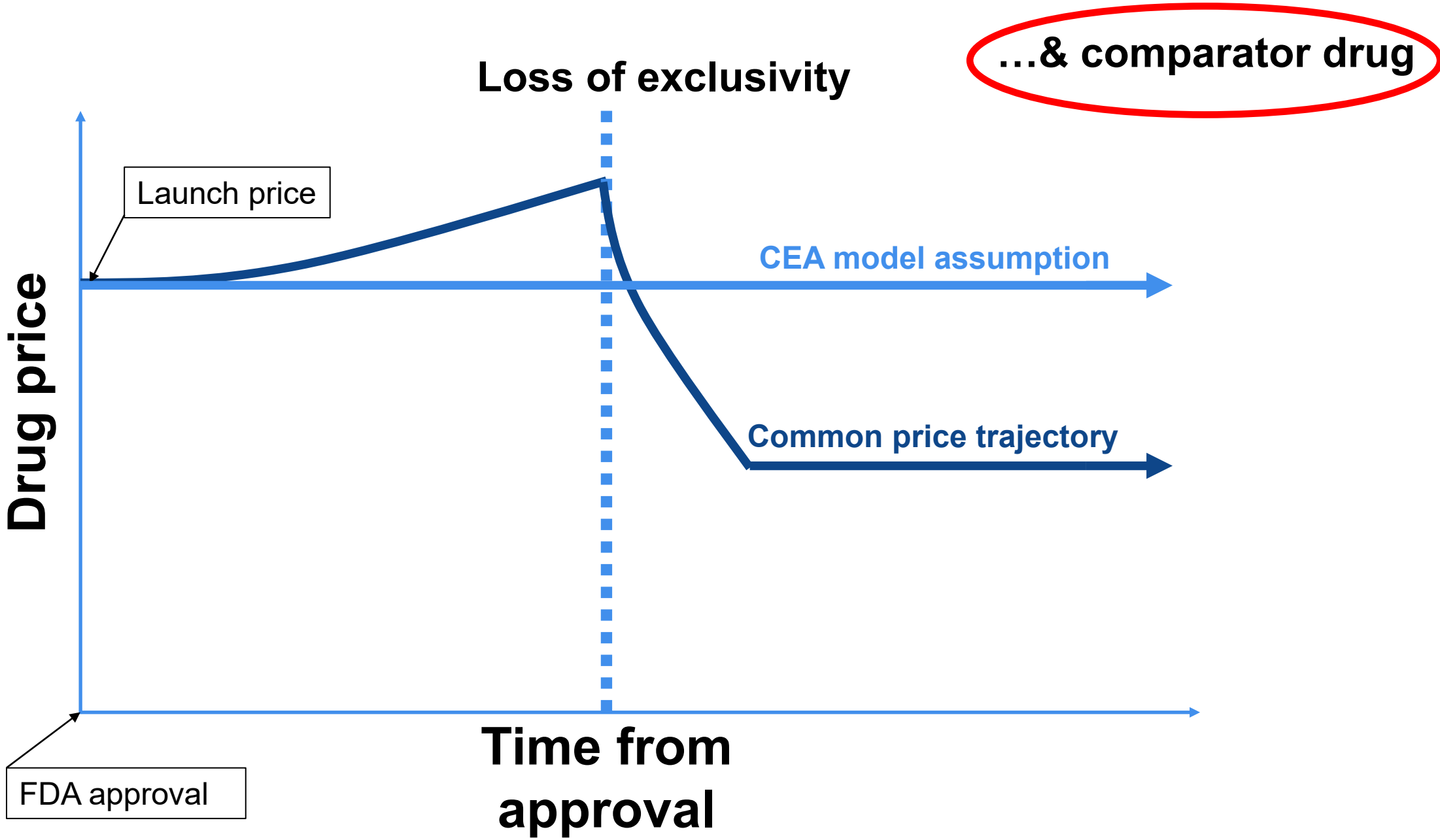
Insurance value



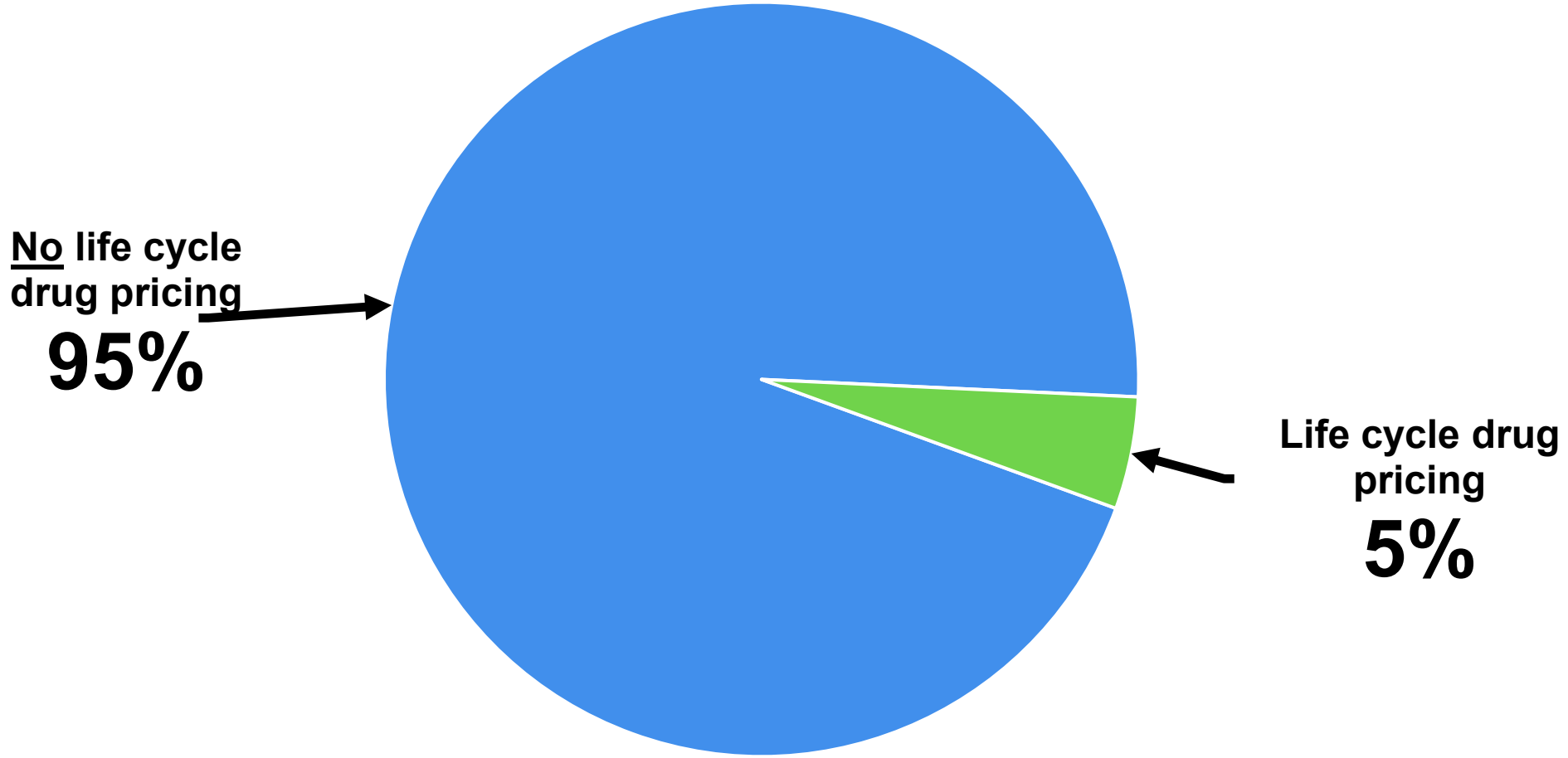
CEAs that Integrate Broader Value Elements



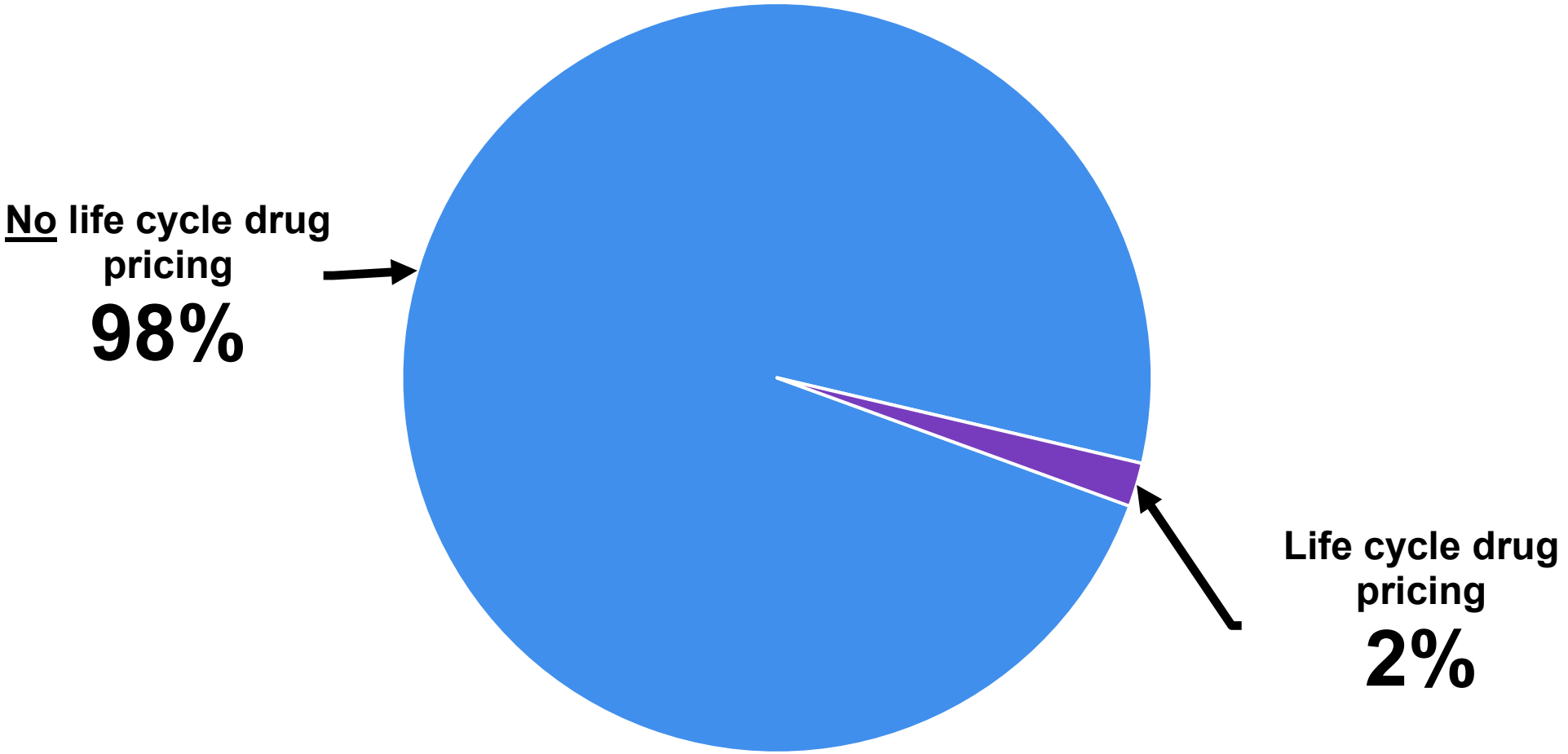
Life Cycle Pricing


…& comparator drug
Loss of exclusivity
Launch price
CEA model assumption
Common price trajectory
Drug price
Time from approval
FDA approval

What % of US-Based CEAs include life cycle drug pricing?



What % of CEAs include life cycle drug pricing for the comparator?



Why so few CEAs?



- Methods and data gaps
- Concerns about “double-counting”
- Relevance to decision problem
- CEA is not the only framework for evaluating value
- Buy-in?

Thoughts on Generalized Cost-Effectiveness Analysis

Jon Campbell
SVP for Health Economics

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

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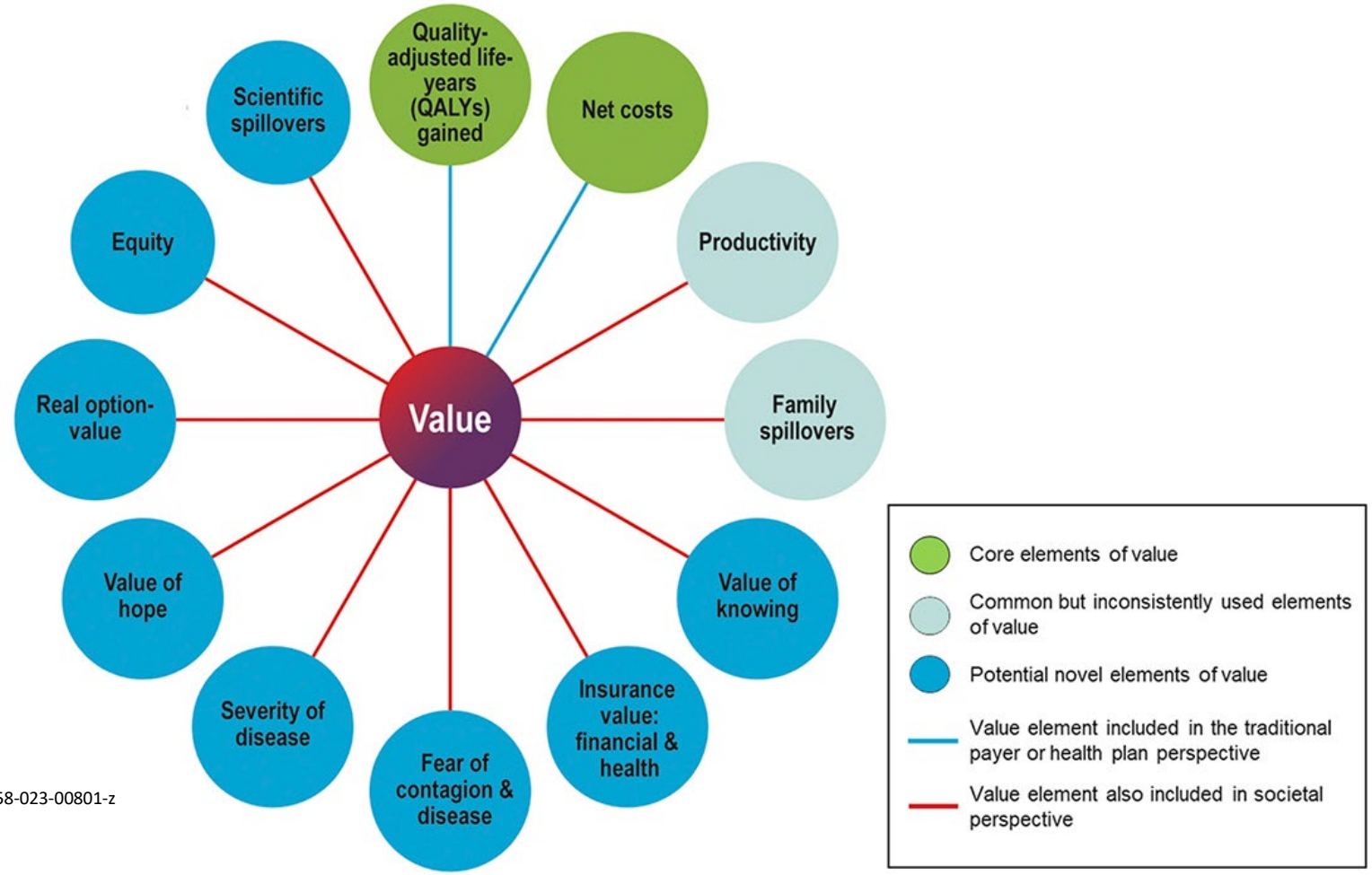
Operationalizing the Value Flower: Practical Challenges

- Mo Petals, Mo Problems
  - Risk of double counting correlated concepts
- Value requires Threshold
- Zero may not be a strong assumption
  - "their potential exclusion does not imply the absence of such effects, but rather that they are similar to the expected effects of displaced care."

Laura Vallejo-Torres. Applied Health Economics and Health Policy https://doi.org/10.1007/s40258-023-00801-z



* Adapted from Lakdawalla et al, ViH (2018)

Are conventional analyses far from observed market price signals?

Are Drugs Priced in Accordance With Value? A Comparison of Value-Based and Net Prices Using Institute for Clinical and Economic Review Reports

Lisa M. Bloudek, PharmD, MS, Victor Nguyen, PharmD, MS, MBA, Jens Grueger, PhD, Sean D. Sullivan, PhD

ABSTRACT

Objectives: The Institute for Clinical and Economic Review (ICER) is an independent organization that reviews drugs and devices with a focus on emerging agents. As part of their evaluation, ICER estimates value-based prices (VBP) at $50 000 to $150 000 per quality-adjusted life-year (QALY) gained thresholds. We compared actual estimated net prices to ICER-estimated VBPs.

Methods: We reviewed ICER final evidence reports from November 2007 to October 2020. List prices were combined with average discounts obtained from SSR Health to estimate net prices. If a drug had been evaluated more than once for the same indication, only the more recent VBP was included.

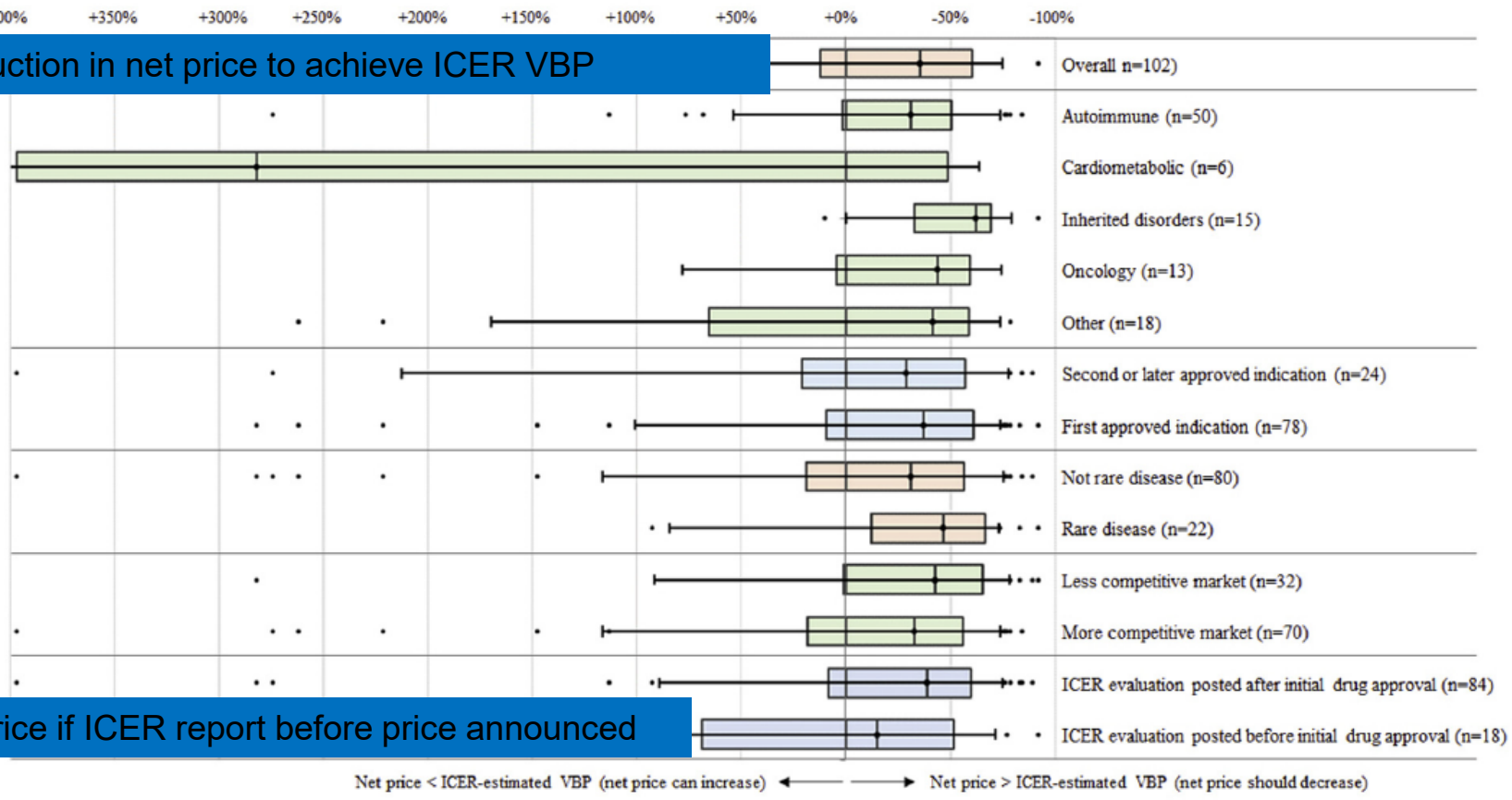
VALUE HEALTH. 2021; 24(6):789–794

Are conventional analyses far from observed market price signals?

Median: 36% reduction in net price to achieve ICER VBP

16% reduction in net price if ICER report before price announced

Figure 1. Change in net price required to reach ICER-estimated VBP at the $150 000 per QALY threshold.



ICER indicates Institute for Clinical and Economic Review; QALY, quality-adjusted life-year; VBP, value-based price.

VALUE HEALTH. 2021; 24(6):789–794

ICER Value Assessment Framework Update Proposals (Opportunity for Public Feedback this Summer)

- Societal Perspective in all assessments
  - Including patient and carer time impacts
- Dynamic Price Scenario
- Severity and Equity Considerations for Voter Deliberation

Generalized Cost Effectiveness Analysis From Theory to Practice

Chris Leibman, Biogen
SVP, Value, Access, Public Policy and Government Affairs

Generalized Cost Effectiveness Analysis

Cause of and solution to, all of life's problems

Chris Leibman, Biogen

SVP, Value, Access, Public Policy and Government Affairs

GCEA: How and Where to Apply

- What problem are we seeking to solve
- Standardization ‘One size fits all’ vs. Customization
- Where to begin and when to end

NPLB Generalized Cost-Effectiveness Analysis | **November 9, 2021**

I find it helps to put the bottom line at the top, then get into all the supportive arguments. So if this doesn't make sense, keep going and I promise it will.
– Peter Kolchinsky

Bottom line for Biotech CEOs

DON'T LET ANYONE DO CEA ON YOUR DRUG BEFORE YOU'VE PUBLISHED A GCEA ON YOUR DRUG.

Ideally, that means:

- **Commission a GCEA about 9 months before starting a registration study.**
  - Use crude inputs for values you believe your drug will offer.
  - Do sensitivity analysis to identify variables that make the most difference and that are worth measuring carefully.
    - E.g. does drug reduce burden on caregivers? If yes, then measure that as best you can.
- **In parallel with registration study, measure all variables you care to include in GCEA.**
- **Upon completing registration study, update GCEA.**
  - In sensitivity analysis, demonstrate that ignoring many of your values (e.g. that drug goes generic) would underestimate value of the drug.
  - This is a vaccination against what ICER, NICE, Australia, Canada, and others might claim using CEA.
- **Publish GCEA before approval.** Don't need to input intended price. Just need to show magnitude of value below which price would still be cost-effective.
- **When finally launch drug and price, public will be surprised to see that your market price is below the upper limit on what GCEA showed as cost-effective.**

Source: https://nopatientleftbehind.com 'How GCEA can Rebut Questions of Value' Used with permission.

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Discussion and Q & A

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