Value for Whom?

Incorporating Patient Perspectives into Value Assessment for Novel Cell and Gene Therapies

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Speakers

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The Landscape

The rapidly expanding cell and gene therapy (C&GT) landscape continues to introduce truly innovative and unprecedented treatments for patients with high unmet needs.

- C&GTs rely on the transfer of genetic or cellular material into a patient to produce therapeutic effects
- In the last three years, new therapies such as Luxturna, Kymriah, Yescarta, and Zolgensma have offered significant clinical benefit to those living with retinal dystrophy, lymphoma, spinal muscular atrophy, and more
- Hundreds of additional C&GTs are in the US drug pipeline
- FDA expects to see 10-20 new C&GTs per year by 2025.
- The “one-time” therapeutic delivery with a lasting therapeutic benefit is a tremendous paradigm shift that requires changes to the ecosystem that supports the delivery of such products.

Julia Gaebler, PhD
Health Advances

Traditional Method of Value Assessment

There are various mechanisms to assess the value of a new medical treatment or intervention, but the most frequently used method to date is Cost-Effectiveness Analysis, CEA

Traditional Cost-Effectiveness Analysis Framework

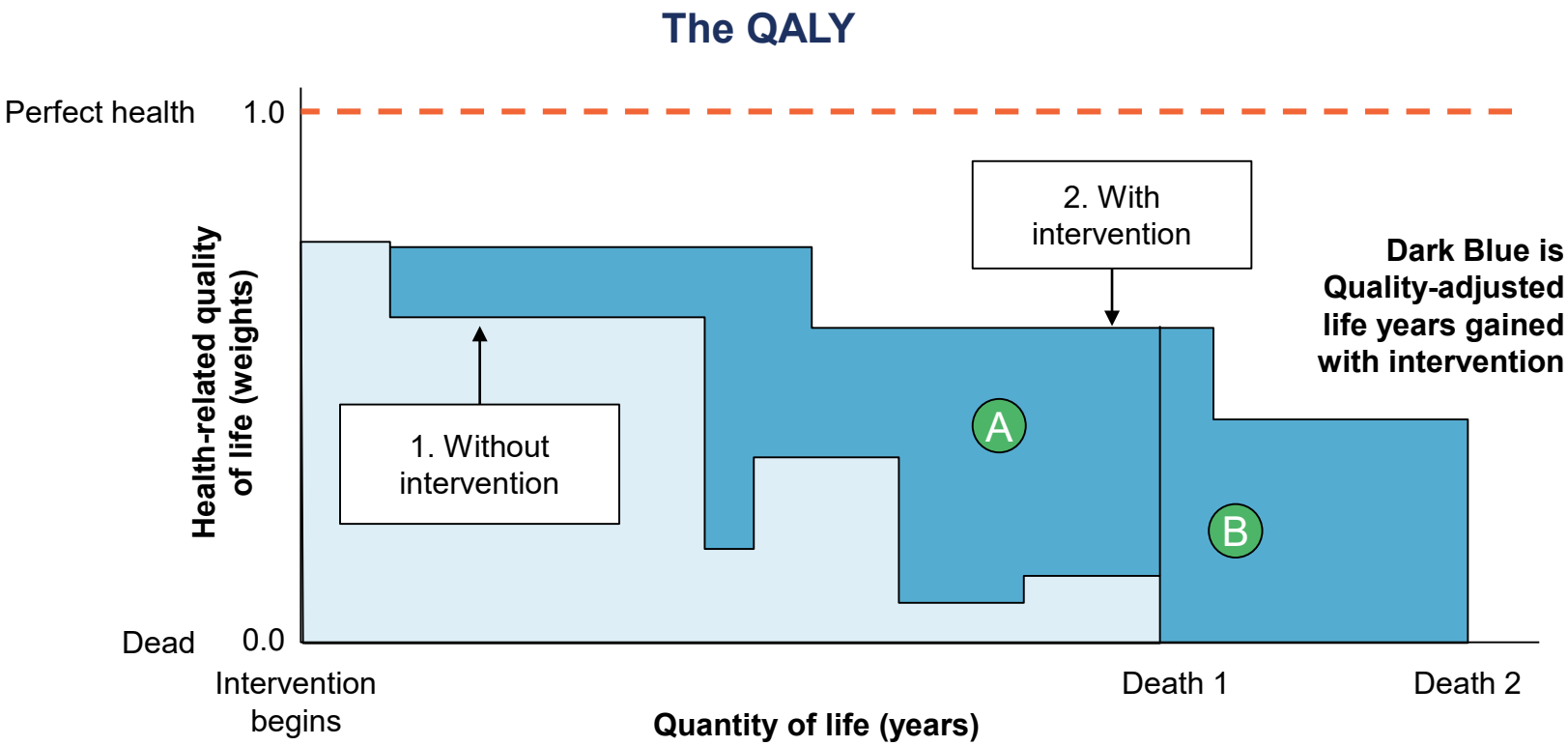
$$Incremental\ cost - effectiveness\ ratio = \frac{Cost_{New} - Cost_{Standard\ of\ Care}}{Effectiveness_{New} - Effectiveness_{Standard\ of\ Care}}$$

QALYs as a Means of Measuring Health Quality

- Measure of disease or disability burden and treatment efficacy in mitigating it;
- 1 QALY = 1 year in ’perfect health’,
- 0 QALY = Death
- 0< x > 1 = Disabled or sick life

The Quality Adjusted Life Year (QALY)

The QALY is commonly used in cost-effectiveness analysis as a measure of the improvement a health technology may have on a patient's quality of life over time.



Think of this as quality-adjusted life expectancy, or averaged-out quality-adjusted survival

A = QALYs gained due to quality of life improvements

B= QALYs gained due to survival improvements (life extension)

Source: Gold et al.

Where do we see CEA?

The paper examines where we see CEA used by HTAs, both governmentally sanctioned and NGOs

- Nationally recognized health technology assessment (HTA) bodies outside of the United States to determine which treatments should be financed by national health systems.
  - NICE
  - CADTH
- Institute for Clinical and Economic Review (ICER)

Shortcomings of CEA when evaluating Cell and Gene Therapies

- Difficult to choose an **appropriate duration** of effect for clinical benefits.
- **Patient heterogeneity** and subgroup analyses are often not considered
- CEA relies on **Quality-Adjusted Life Year (QALY)** gains as a generic measure of health or disease burden, but the QALY cannot capture societal preferences around resource allocation and is widely seen as discriminatory towards patients with disabilities.
- **Estimating QALYs gained is difficult** for the rare diseases that many C&GTs treat
- Commonly cited cost-effectiveness **thresholds may be too low** for the rare diseases
- **Additional elements of value** afforded by C&GTs, such as increased productivity and reduction of caregiver burden, are often omitted
- Further elements of value important to patients are generally not quantified.
- The **discount rate** used for value assessment may be overly punitive when applied to C&GTs with durable clinical effects.

Annie Kennedy
EveryLife Foundation for Rare Diseases

The Need for Patient Centricity

CEA has historically been intended only for a payer audience, while data on the perspectives of other stakeholders, including patients, are often not fully incorporated.

The outcomes of CEA can lead to very real consequences for patients in the form of restricted and delayed access to novel therapies. It is therefore essential that value assessors incorporate patient experience data more fully into their analyses.

- Patients have indicated that the elements of value captured and quantified in these assessments, and the resulting implications, do not reflect their true preferences.
    - Reliance on averages
    - Omission of societal perspective
    - Omission of elements like value of hope
    - Caregiver Impact

Research societies such as The International Society for Pharmaceutical Outcomes Research **(ISPOR**) have highlighted the need for **increased inclusion of patient perspectives in value assessments.**

Context from an adjacent ecosystem

Patient Focused Drug Development – Data collection informing regulatory decision making related to:

- ✓ ***Impact of disease & treatment of symptoms***
- ✓ **Patients perspectives about potential and current treatments**
- ✓ **Views on unmet medical needs & available medical interventions**
- ✓ **Enhanced understanding of the natural history of the disease of condition**

Patient Experience Data

Patient Experience Data (PFDD Tools) include:

- ***PROs***
- **Registry Data**
- **Burden of Disease Data**
- **Natural history data**
- **Benefit-Risk/ Patient Preference studies**
- **Testimony for patients, caregivers, & clinical experts**

If submitting patient experience data as part of an application for marketing approval, the following table should be populated and included in the Reviewer's Guide (section 1.2). Patient experience data (e.g., clinical outcome assessments) collected as part of a clinical trial should be submitted as part of the relevant clinical trial data. Other patient experience data that is separate from clinical trials should be submitted to section 5.3.5.4.

	The patient experience data that was submitted as part of the application, include:	Section(s) and if applicable, file names where data are located and discussed in the application
	□ Clinical outcome assessment (COA) data, such as	
	□ Patient reported outcome (PRO)	
	□ Observer reported outcome (ObsRO)	
	□ Clinician reported outcome (ClinRO)	
	□ Performance outcome (PerfO)	
	□ Qualitative studies (e.g., individual patient/caregiver interviews, focus group interviews, expert interviews, Delphi Panel, etc.)	
	□ Patient-focused drug development or other stakeholder meeting summary reports	
	□ Observational surveys studies designed to capture patient experience data	
	□ Natural history studies	
	□ Patient preference studies (e.g., submitted studies or scientific publications)	
	□ Other: (Please specify)	

Evolution of Patient Input in Medical Research and Development

There has been a growing awareness for the need to engage patients and accurately gather patient perspective data. The science of patient input has transformed the clinical trial and regulatory landscape

- PFDD
- PCORI
- Enhanced collection and use of real-world data

It is essential that the science of patient input evolve into the value assessment space

Cell & Gene Therapies

- Many C&GTs are expected to utilize single or short-term administration, with durable benefits potentially extending over the lifetime.

- While payers require information to inform short-term coverage determinations, value assessment frameworks and methods must also incorporate longer-term considerations
  - For example:
    - how patients weigh long-term benefits against short-term costs
    - unique elements of therapeutic value to patients (ie - tolerability, side effects, ability to maintain relationships with family, ability to work, availability of treatment, etc)

Real-World Implications

Where are we seeing CEA used and why does it matter?

- Payer determinations
- ICER assessments
- Policy proposals such as International Price Index of Most Favored Nations
- QALY’s implications on patients

How can we do better?

- It is critical to ensure that the methods used when assessing value of healthcare interventions **reflect the value to the patient receiving the treatment** and not just the payer.
- Value assessments should be anchored in evidence and values deemed meaningful to patients and caregivers
- Optimally, value assessments could become an additional resource to aid in patient-provider healthcare decision making

Jenn McNary
Rare Disease Advocate

Patient Impact

- Value assessments that miss the mark on capturing actual value to patients have the detrimental impact of limiting patient access to needed therapies
- 95% of rare diseases still do not have an FDA approved therapy – new innovation is necessary
- These policies have the impact of stifling this and ultimately harming patients

Looking to the Future

- With treatments and cures in sight, patients and families should be able to plan for the future instead of worrying about an obscure economic model limiting their access to medications

Jennifer Bright, MPA

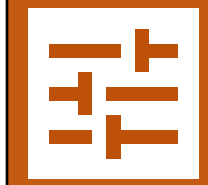
Innovation and Value Initiative

IVI's approach is multi-criteria-focused

MISSION: Advance the science and improve the practice of value assessment in healthcare to make it more meaningful to those who receive, provide and pay for care.

- **Guiding principles:**
  - > **Collaborate with patients** to define value factors that should be represented in value assessment
  - > **Demonstrate transparency** in all processes and outputs
  - > **Build and test** new methods and models

The IVI Toolbox

Tool	Importance
Patient-defined priorities (preferences) 	• Identifies **outcomes important to patients** for evaluation of effectiveness • Prioritizes **real-world data use** in analysis • Insight into **unmet needs and factors affecting adherence**
Novel Elements of Value  (Insurance value; value of hope; Caregiver burden; fear of contagion)	• Supports **flexible, localized decision making** that can adapt to different viewpoints • Facilitates **transparent view** of how contextual aspects of care and choice impact optimal sequence of treatment.
Multi-Criteria Decision Analysis (MCDA) 	• Provides a **comparator analytical tool** to traditional CEA • Allows analysis based on attributes of importance to **patients and payers**

Example: Perspectives of Patients with RA

2017 study with adult RA patients to assess key factors defining value to their treatment and experience

- *Findings:* Value must incorporate patient preference attributes to be relevant
  - Assessing functional status and daily quality of life factors high priority
  - Frequency, site, and mode of administration key considerations in addition to OOP cost
- *Action:*
  - IVI included attributes in OSVP-RA model allowing for adjustment e.g., mode of administration

Technical Report: https://www.thevalueinitiative.org/voice-patient-ra/
OSVP RA Model: https://www.thevalueinitiative.org/ivi-ra-value-model/

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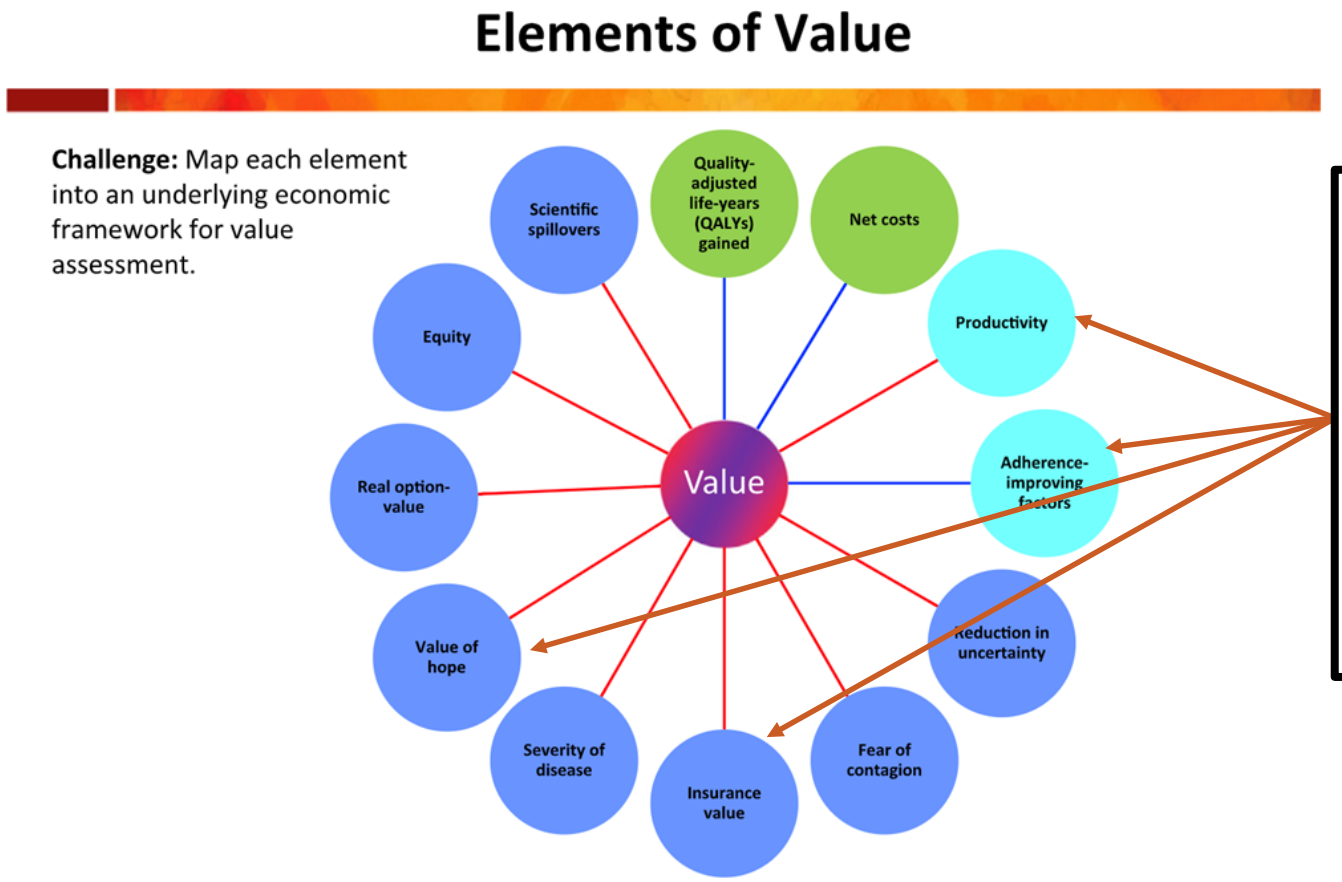
Our Targets for Improving Value Methods



IVI Invests in Research and Models that:

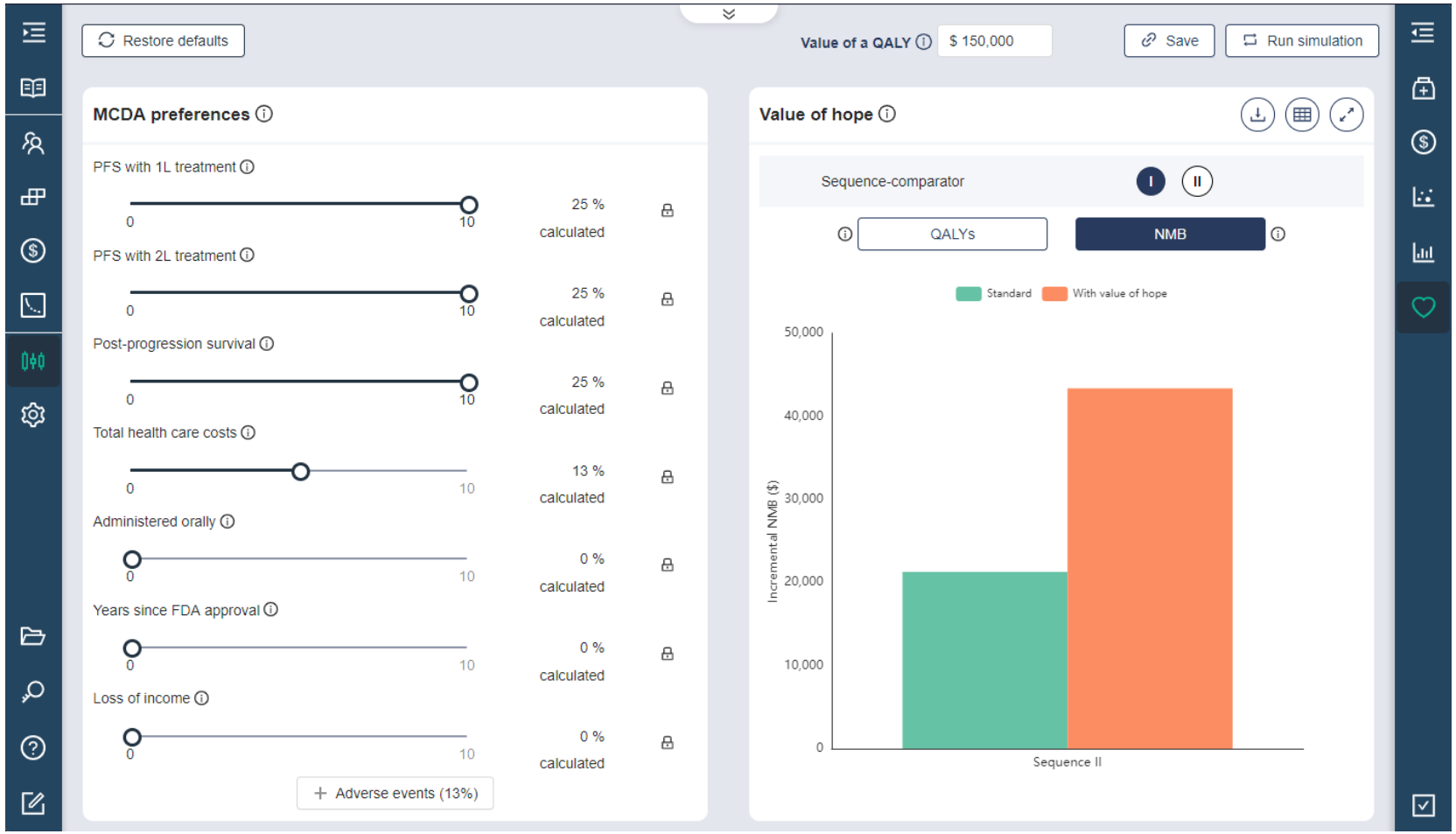
- Incorporate novel elements of value
- Account for uncertainty
- Use multiple approaches to value assessment (e.g., CEA and MCDA)
- Define patient factors that influence choice and adherence

Fig. 1 – Elements of value. Note. Green circles: core elements of value; light blue circles: common but inconsistently used elements of value; dark blue circles: potential novel elements of value; blue line: value element included in traditional payer or health plan perspective; and red line: value element also included in societal perspective.

Source: Darius N. Lakdawalla, Jalpa A. Doshi, Louis P. Garrison, Charles E. Phelps, Anirban Basu, Patricia M. Danzon, Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report [3], Value in Health, Volume 21, Issue 2, 2018, Pages 131-139. Accessed at https://doi.org/10.1016/j.jval.2017.12.007.

Example: Novel “Value of Hope” Element for NSCLC

- Captures the **added value** that a patient may get from a therapy that has the low-probability chance of a really large benefit.
- Estimates the number of QALYs a patient would need to gain on the more certain treatment to be indifferent between the two options, to estimate the additional net monetary benefit (value) of that hopeful treatment.



Why Can MCDA Help on C&GT?

- Patient-focused – can account for attributes important to unique patient subgroups
- Creates (more) order from multiple inputs

- Can account for uncertainty in data inputs
- Addresses standardization and validity of methods

Thokala P, Devlin, N, Marsh K, et al. Multiple criteria decision analysis for health care decision making—an introduction: report 1 of the ISPOR MCDA Emerging Good Practices Task Force. Value Health. 2016;19(1):1-13. https://www.ispor.org/heor-resources/good-practices-for-outcomes-research/article/multiple-criteria-decision-analysis-for-health-care-decision-making---an-introduction

Marsh K, IJzerman M, Thokala P, et al. Multiple criteria decision analysis for health care decision making—emerging good practices: report 2 of the ISPOR MCDA Emerging Good Practices Task Force. Value Health. 2016;19(2):125-137. https://www.ispor.org/heor-resources/good-practices-for-outcomes-research/article/multiple-criteria-decision-analysis-for-health-care-decision-making---emerging-good-practices

The Big Picture on MCDA

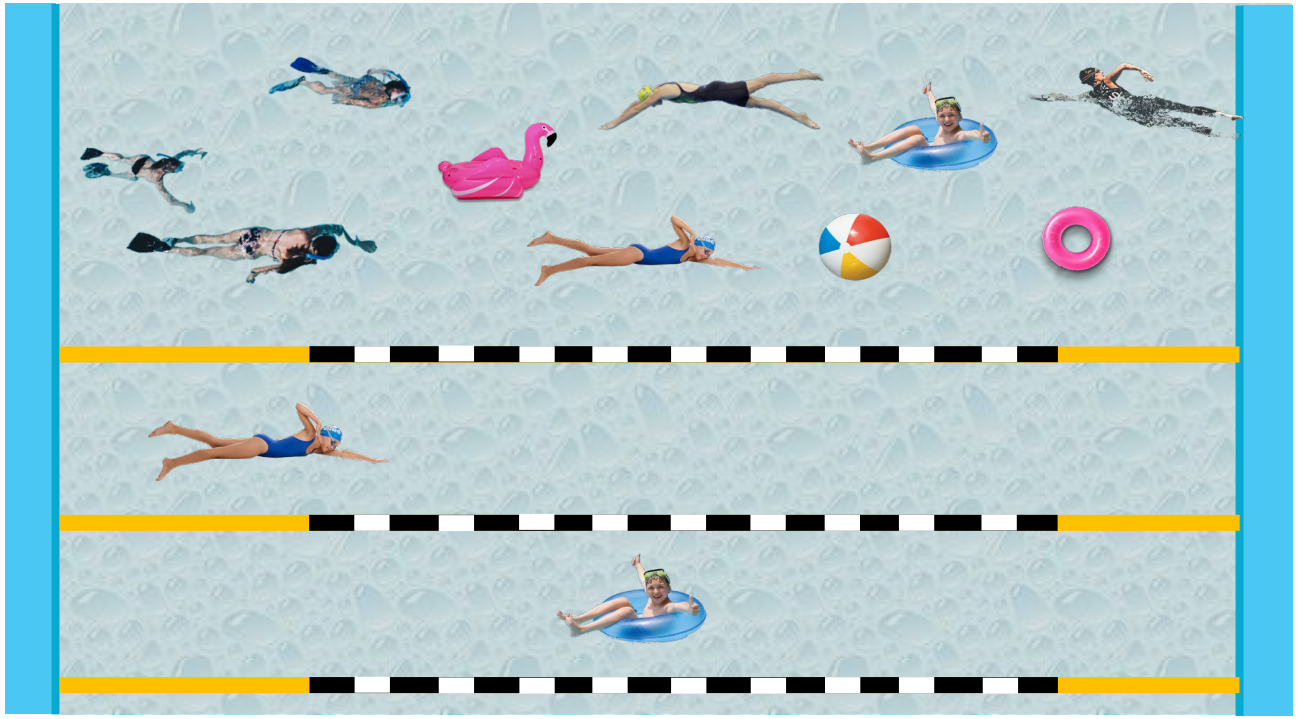
Value assessment today

- Several sources of patient data, but very little structure/order
- Lack of agreement on what's important
- **No clear lanes of understanding**

Value assessment in future

- MCDA offers the opportunity to provide structure, transparency, and order
- Incorporates patient-centered information in value assessment

Patients



- Payers
- Regulators
- Value assessors

Patients

- Payers
- Regulators
- Value assessors

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Leaning In: Methods Must Be "Future Ready"

- Current IVI research to identify patient perspectives to drive MCDA studies and improved measurement
  - RAND partnership on Goal-Attainment Scaling (RA)
  - Defining Patient Preferences
  - Quantifying Patient Perspectives
    - Modified Health Utilities (CEA)
    - MCDA

- Ongoing challenge: Improving **data inputs** on factors that matter to patients

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Be a Part of our Value Assessment Laboratory – Join IVI Today

For a more in- depth analysis, please see entire paper here.

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