AMERICAN SOCIETY FOR BIOETHICS + HUMANITIES

25TH ANNUAL CONFERENCE

Engaging the Past to Energize the Future:
Creating Space for Inclusive Public Discourse

Value or Villain? Balancing gene therapy patient access and financial challenges

Hadley Stevens Smith, PhD, MPSA – Harvard Medical School & Harvard Pilgrim Health Care Institute

Meghan Halley, PhD, MPH – Stanford University School of Medicine

Mark Trusheim, MSc – Tufts University Medical Center

Ryan Fischer – Foundation for Angelman Syndrome Therapeutics

CELEBRATING 25 YEARS
AMERICAN SOCIETY FOR
BIOETHICS + HUMANITIES

Disclosures

- I have no financial interest or other relationships that could be considered a conflict of interest related to the content of this presentation.

- The opinions I express are my own and not those of my employer.

The Value Ethics Working Group


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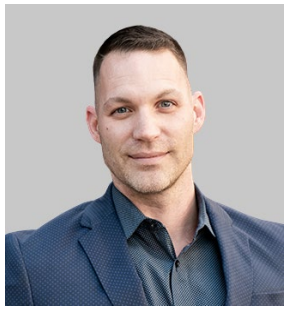
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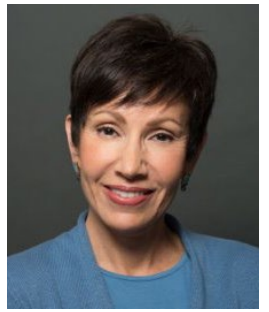
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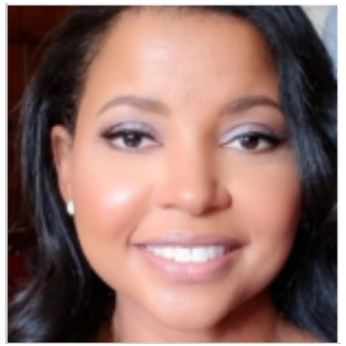
Erika Cox

With support from the Center for ELSI Resources and Analysis

Agenda for panel presentation: Perspectives on gene therapy value in the US context

- Thought experiment (Hadley)
- Perspectives of:
  - Multiple stakeholders (Meghan)
  - Payers and developers (Mark)
  - Patient advocacy organizations (Ryan)
- Conclusion: Value or Villain?

Thought experiment

- Your role: Chief Medical Officer of American Health & Longitudinal Perseverance (AHeLP), a leading health insurance company
  - Oversee medical policy, equity considerations, payment innovations

Thought experiment

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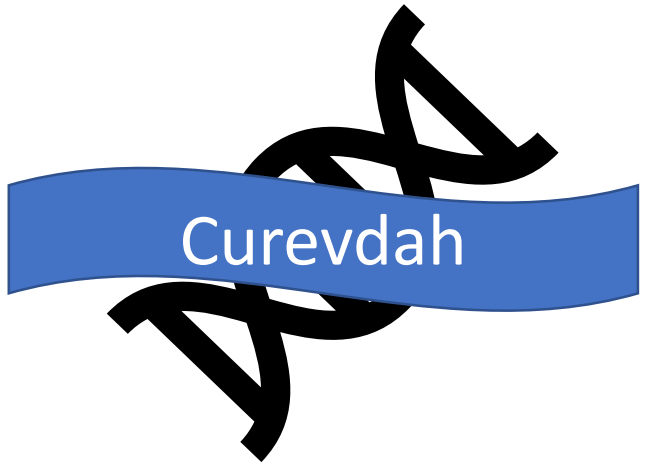


Factors to weigh in decisions about coverage of a novel, high price therapeutic or cure

Budget impact

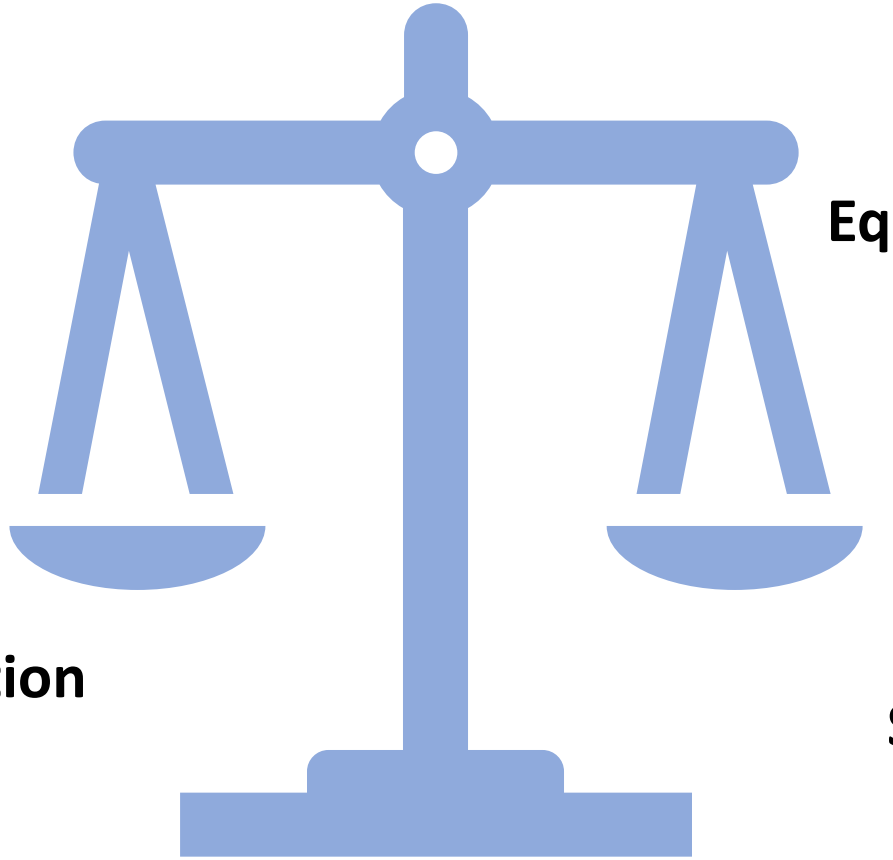
Equity & distribution of benefit

Plan reputation

Stewardship responsibilities

Customer satisfaction

Strength of evidence



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In your role as CMO of AHeLP, what else would you consider?

ⓘ Start presenting to display the poll results on this slide.

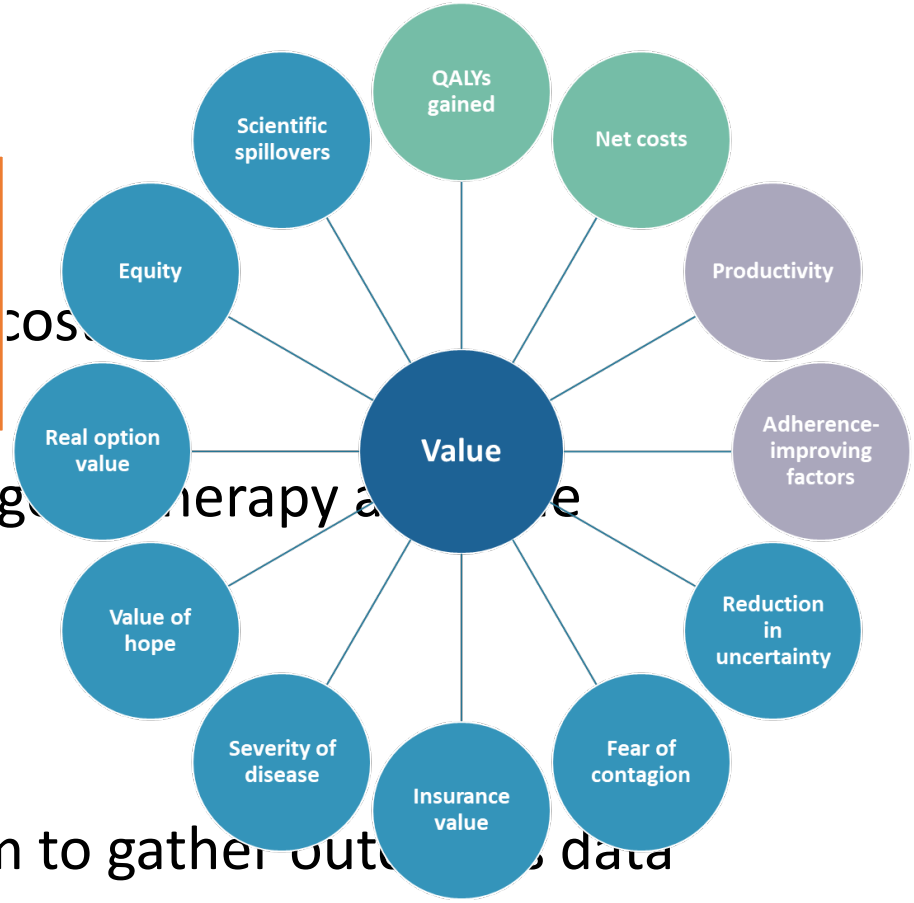
Coverage decision making considerations

- Budget impact – affordability of the intervention
- Cost offsets – impact on downstream health care costs
- Risk pool – rare nature of genetic conditions with gene therapy available
- Incentives – how to share risk with manufacturer
- Evidence development – coverage as a mechanism to gather outcomes data

Coverage decision making considerations

- Budget impact – affordability of the intervention
- Cost offsets – impact cos
- Risk pool – rare nature of genetic conditions with g herapy a e
- Incentives – how to share risk with manufacturer
- Evidence development – coverage as a mechanism to gather outc data

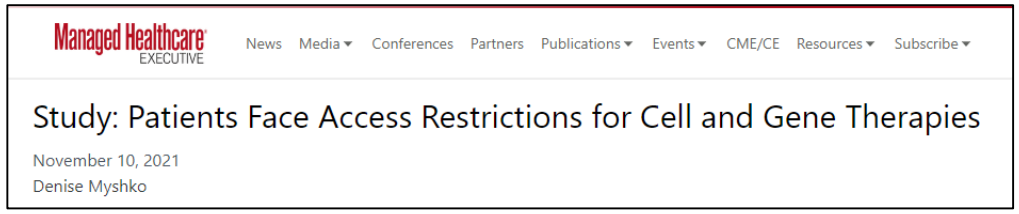
Other elements of value?



Health plan decision makers are facing real questions about coverage of gene therapy

Restrict coverage

Coverage is often more restrictive than FDA labels



Innovate

Develop outcomes-based contracts

Involve patient groups

- Smith, HS et al. Conversations With the Editors: Stewardship in Genomic Medicine—Insights From Health Care Payers at the Forefront of Clinical Innovation and Partnerships. *Clinical Therapeutics*. 2023.
- Allen, J et al. Medicaid coverage practices for approved gene and cell therapies: existing barriers and proposed policy solutions. *Mol Ther Methods Clin Dev.* 2023;29:513-521.
- Tunis S, et al. Variation in market access decisions for cell and gene therapies across the United States, Canada, and Europe. *Health Policy.* 2021.

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In your role as CMO of AHeLP, which consideration do you prioritize?

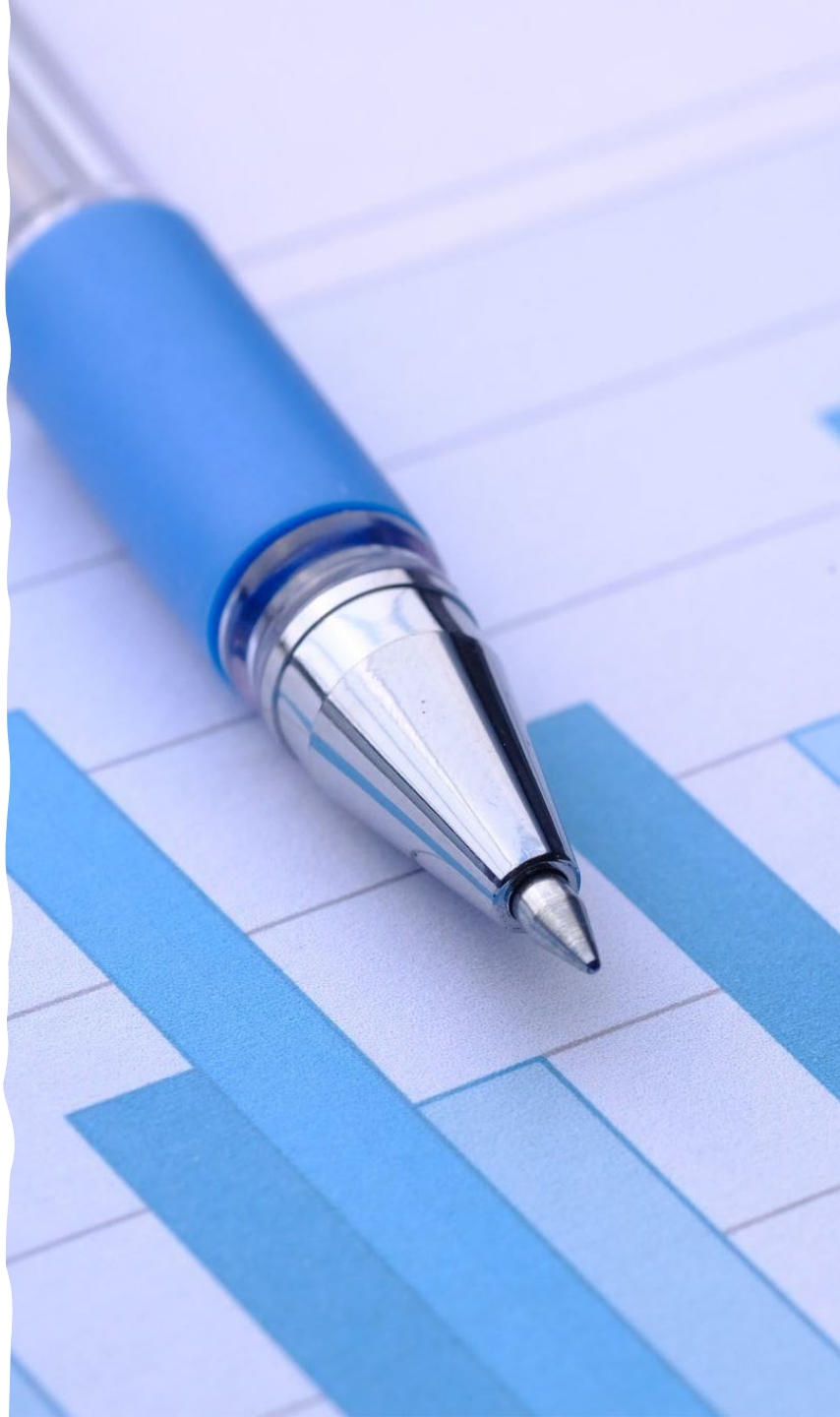
ⓘ Start presenting to display the poll results on this slide.

Verdict: Value or Villain?

Whose Values Define Value?

Meghan Halley, PhD, MPH
Senior Research Scholar
Stanford Center for Biomedical Ethics

October 11, 2023



Disclosures and Notes

Financial Conflicts of Interest	I have no financial conflicts of interest to disclose
Affiliations	President, Board of Directors, Undiagnosed Diseases Network Foundation (UDNF)
	Member, Rare Disease Advisory Panel, Patient-Centered Outcomes Research Institute (PCORI)

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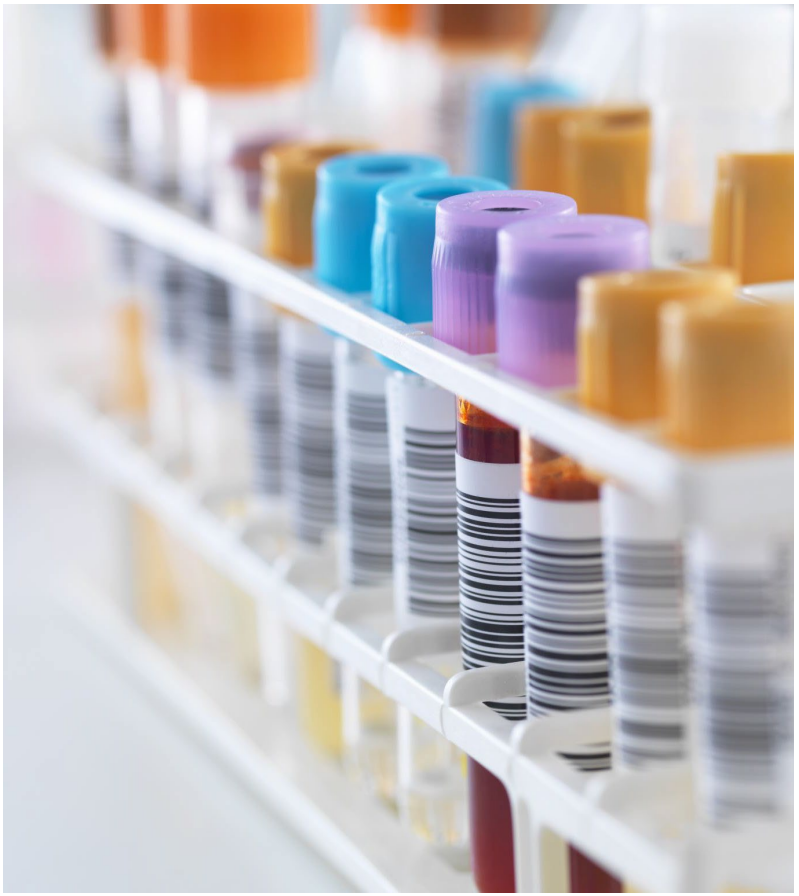
In healthcare, a good or service has value when:

ⓘ Start presenting to display the poll results on this slide.

How do different stakeholders define the value of gene therapies for rare diseases?

- Participants from different sectors (academic, industry, payer, patient)
- Semi-structured, anonymous interviews
- Ranking value elements in order of importance of inclusion in value assessment of gene therapies for rare diseases.



Quality-Adjusted Life Year (QALY)	Life expectancy adjusted for “quality,” e.g., 2 years impacted by side effects of treatment = 1.5 QALY.
Net Cost	Cost of the therapy minus cost savings from other care no longer needed.
Productivity & Family Splllover	Impact on patient and/or family ability to work or otherwise contribute to society.
Adherence improving Factors	Ease of use for patient resulting is higher adherence compared to alternatives.
Insurance Value	Value to healthy individuals of being protected from the physical and financial burden of a particular illness.
Severity of Disease	Gives greater weight to therapies that are targeted to those with a lower health endowment.
Value of Hope	Additional value associated with the possibility of curing disease, even if the likelihood is uncertain.
Real Option Value	When a medical technology that extends the life of patients creates opportunities to benefit from future medical advances.
Equity	Extent to which a new therapy is likely to mitigate or exacerbate current inequities in access to health.
Scientific Spillover	The potential for a new technology to also benefit future generations of patients or lead to development of other therapies.

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Rank the following value elements from 1-10 (10 = most important)

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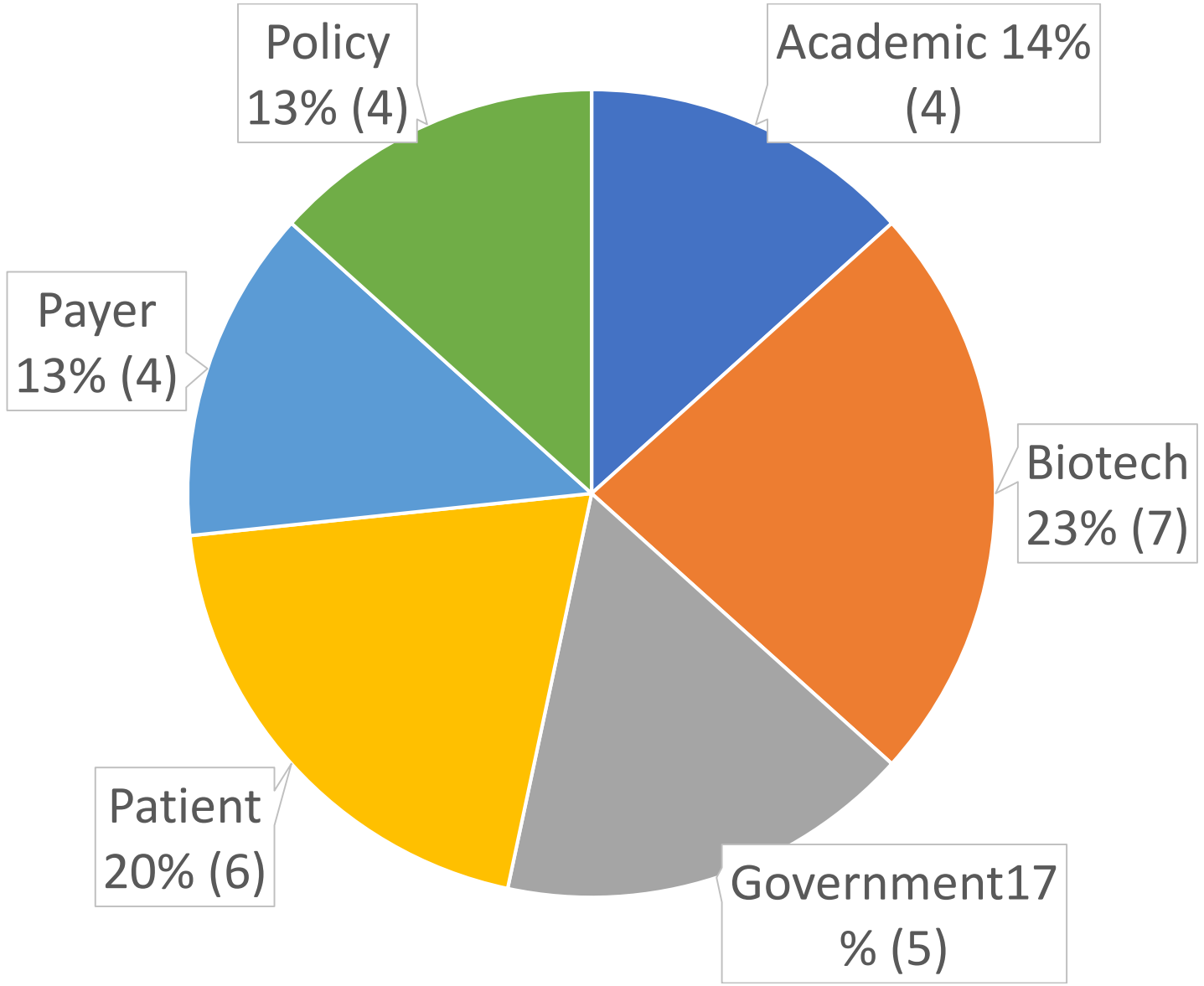
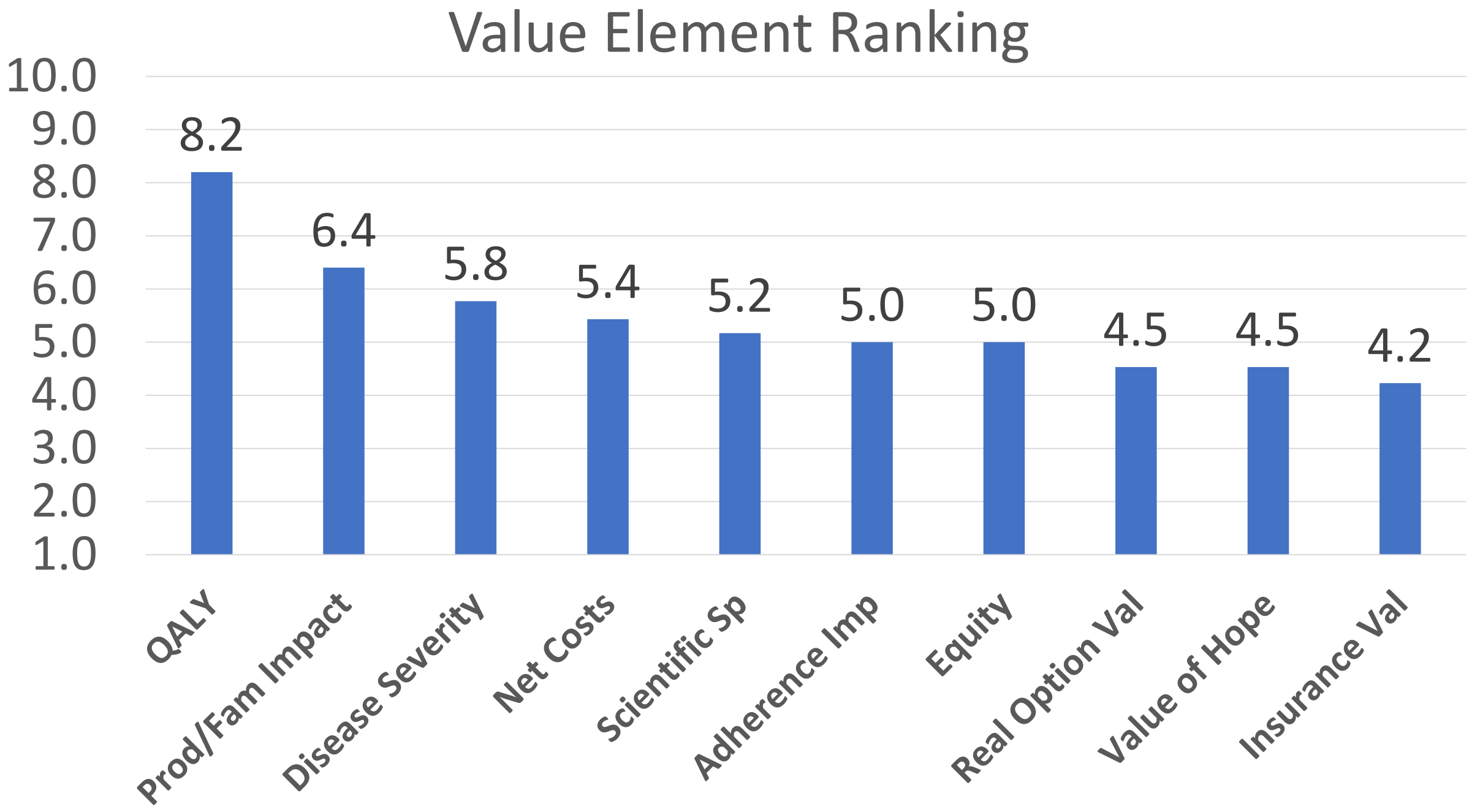
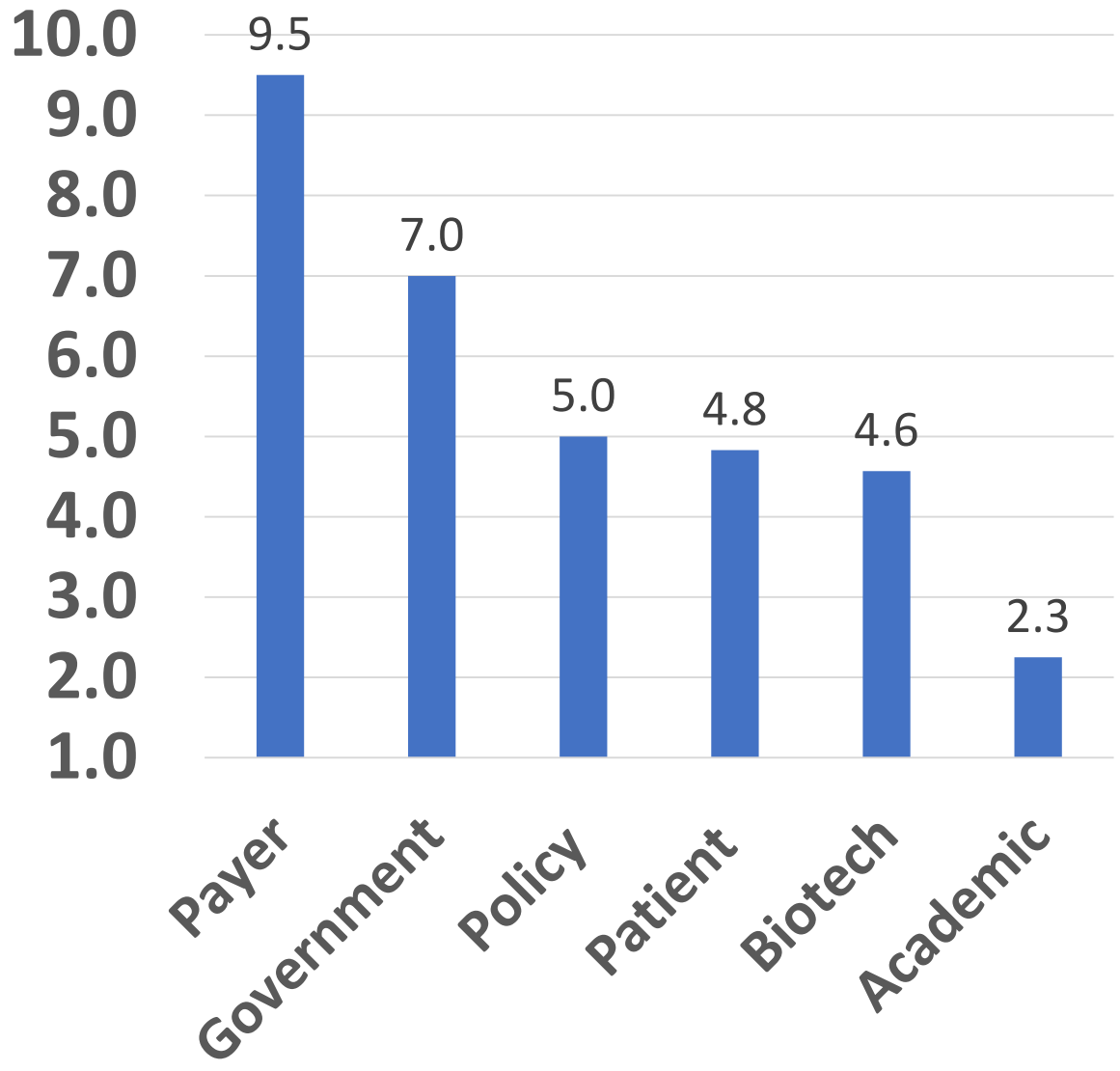
Participant Perspectives (n=30)




Value Element Ranking
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
8.2
6.4
5.8
5.4
5.2
5.0
5.0
4.5
4.5
4.2
QALY
Prod/Fam Impact
Disease Severity
Net Costs
Scientific Sp
Adherence Imp
Equity
Real Option Val
Value of Hope
Insurance Val

Net Costs: Of Course Payers Care



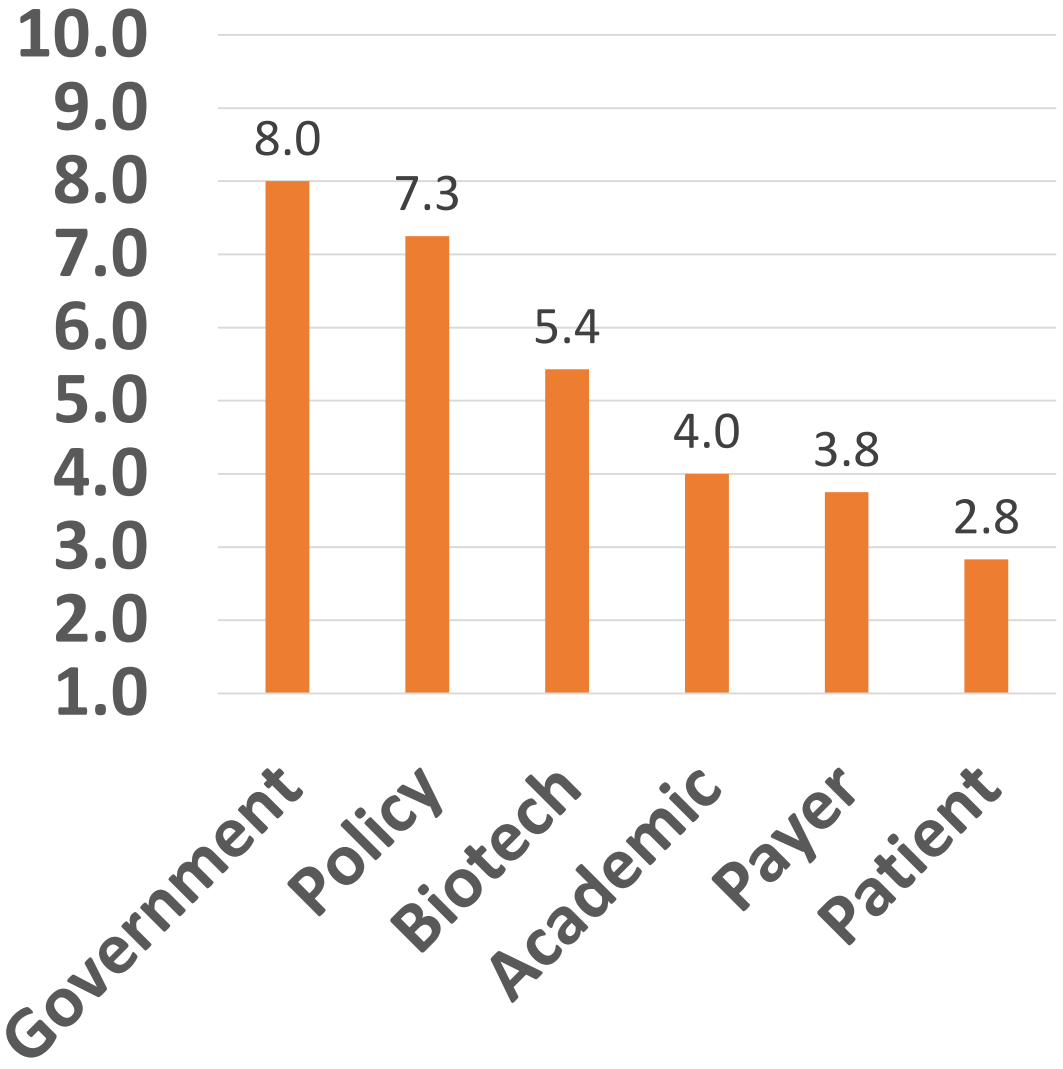
"Medicaid gets their budget assigned about a year in advance. So once you have a set budget you have 1-million-dollar products coming to the market, you really have to have a focus on cost… because we could run out of money technically."

(Payer P29)

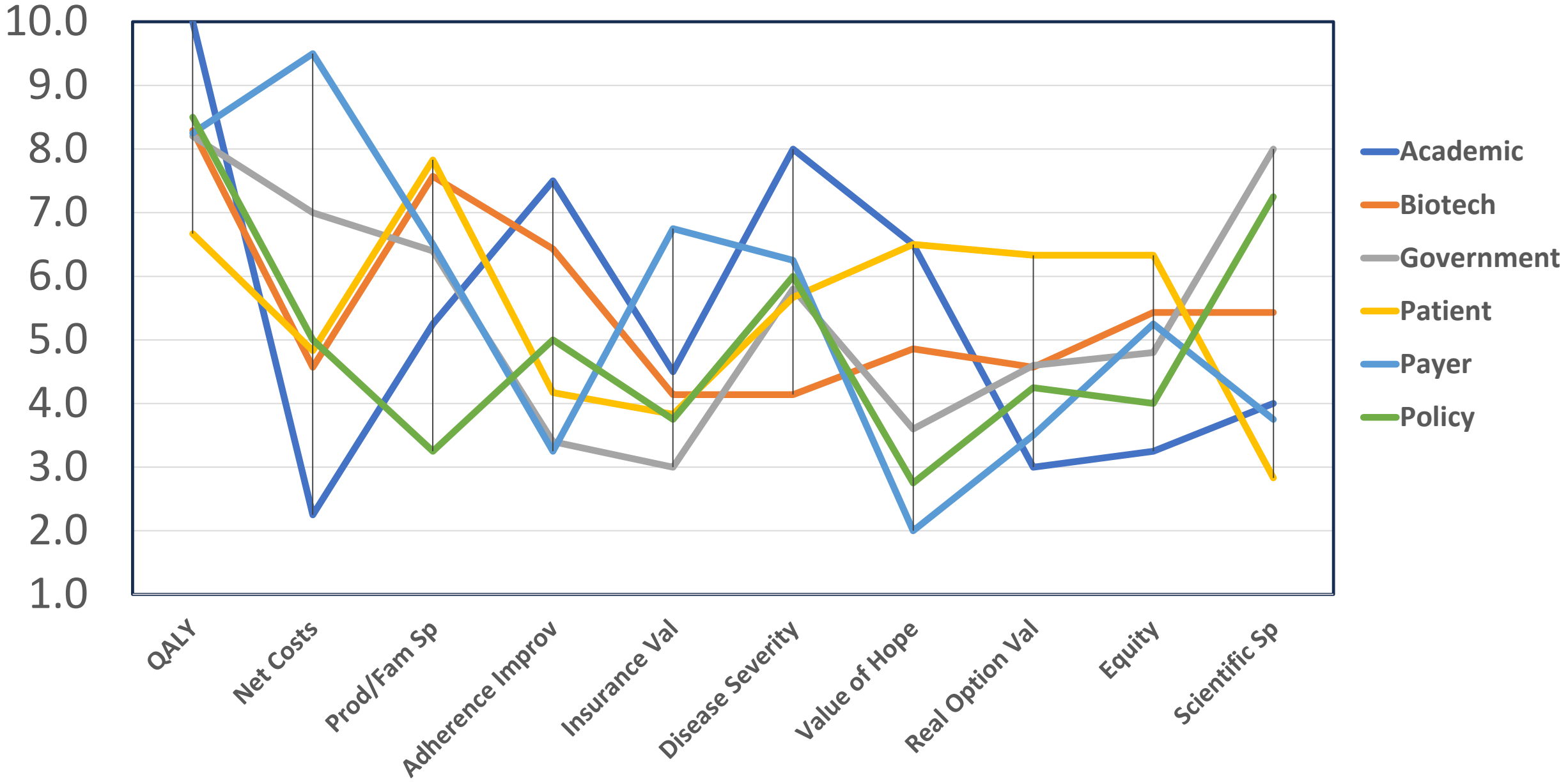
Scientific Spillover: Of Course NIH Cares

"You're opening a scientific door….And there are so many examples of rare disease opening the door for what is often many, many more people."

(Government P19)



Mean Rank by Participant Group



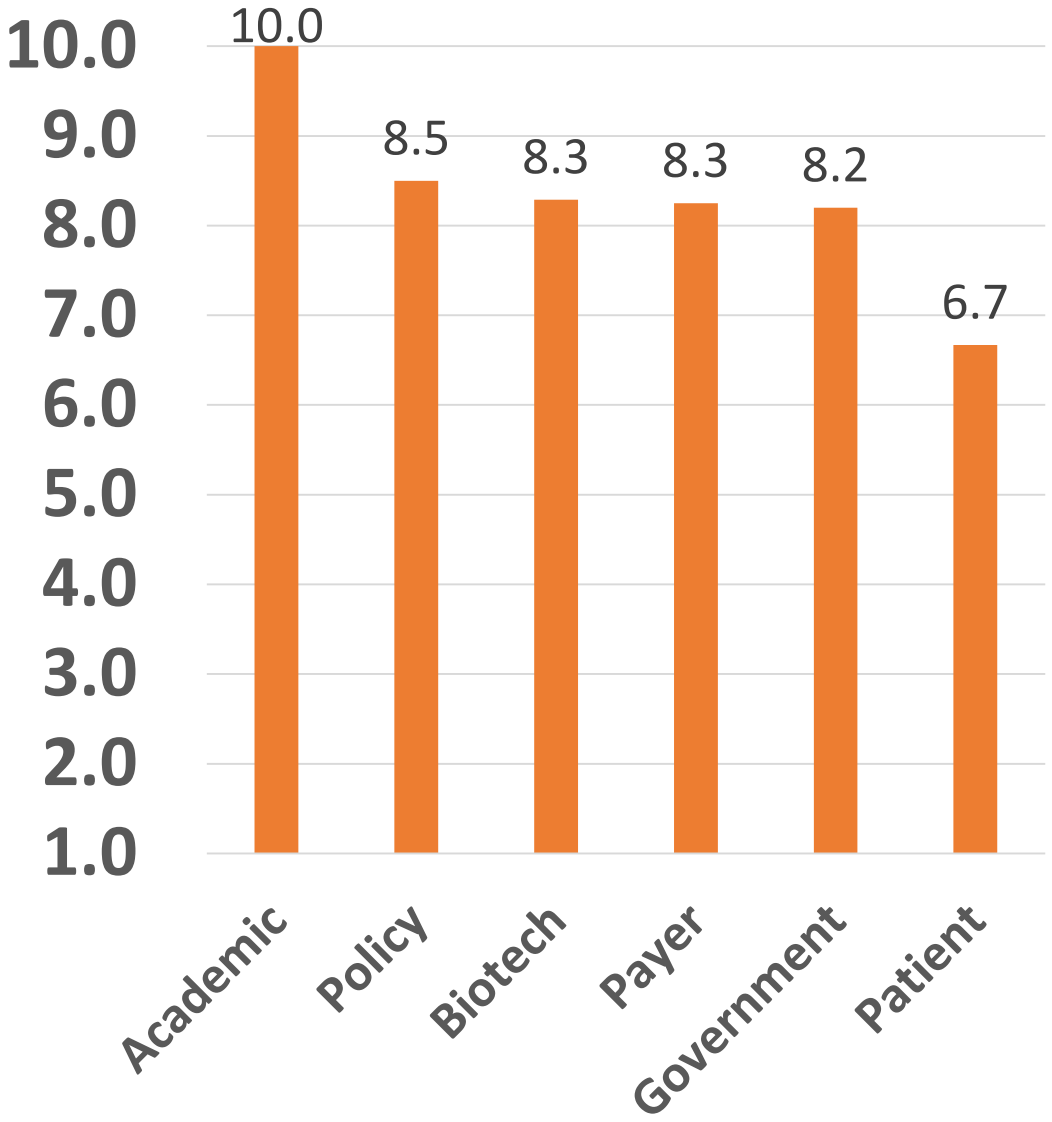
Other Value Elements

- Significance of improvements to population
- Value of Early Intervention
- Taking all the risk at the beginning, when disease is mild vs. taking gradual risk as the disease progresses
- Talking to patient communities and learning from them/including their viewpoints and the real value
- Social Costs
- Private Costs/Accommodations
- Complex logistics
- future cost of care
- Lack of alternatives
- Impact on pts actual life
- Mental Health/outlook
- Lack of or suboptimal treatment options
- Caregiver Burden
- Caregiver Burden
- Opportunity cost of not treating
- Global Value
- Total value capture
- Education/complexity
- Perceived societal value
- Longterm cost analysis (greater cost of futurity/survival--individually and globally)
- Reduction in suffering, patient and family
- Involvement of patient in the process, patient voice, patient driven
- Novel therapy for condition with no therapy
- Psychosocial impacts on family
- Mental Health
- Patient churn, high upfront costs then pts leave
- Growing use of expensive technologies
- Safety & Long-term outcomes data
- individual patient goals, partially based on severity
- actual cost for insurance companies
- prevalence of disease
- limitations
- expansion of productivity to include extended family
- individual interpretations of productivity
- Disease-dependence
- Mortality realization or perception of mortality
- Area of unmet need
- Hospital/ER visits, need for add-on therapy

QALYs: Why so high?

"I know QALYs have somewhat of a bad rep in the U.S., but it really goes a long way….you're saying, with this new met medicine, what will that life look like? Will they be sick and unable to go to school because they are going to be extremely immunocompromised? Then they might start thinking that maybe they don't really need it."

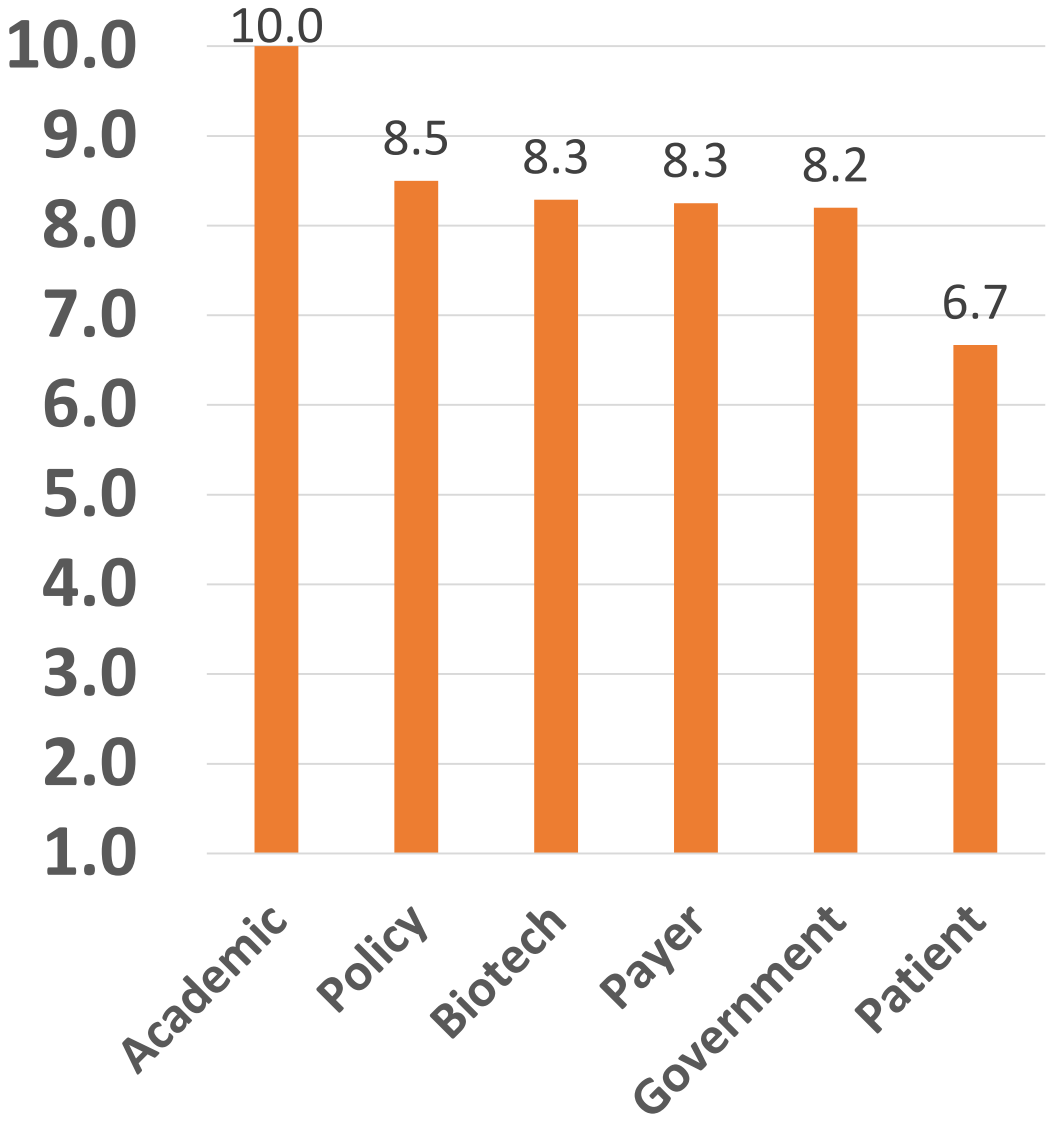
(Biotech P30)



QALYs: Why so high?

"We don't use that in any of our analysis of coverage. One reason is, there was legislation that passed in our State that does not allow that term to be using at all."

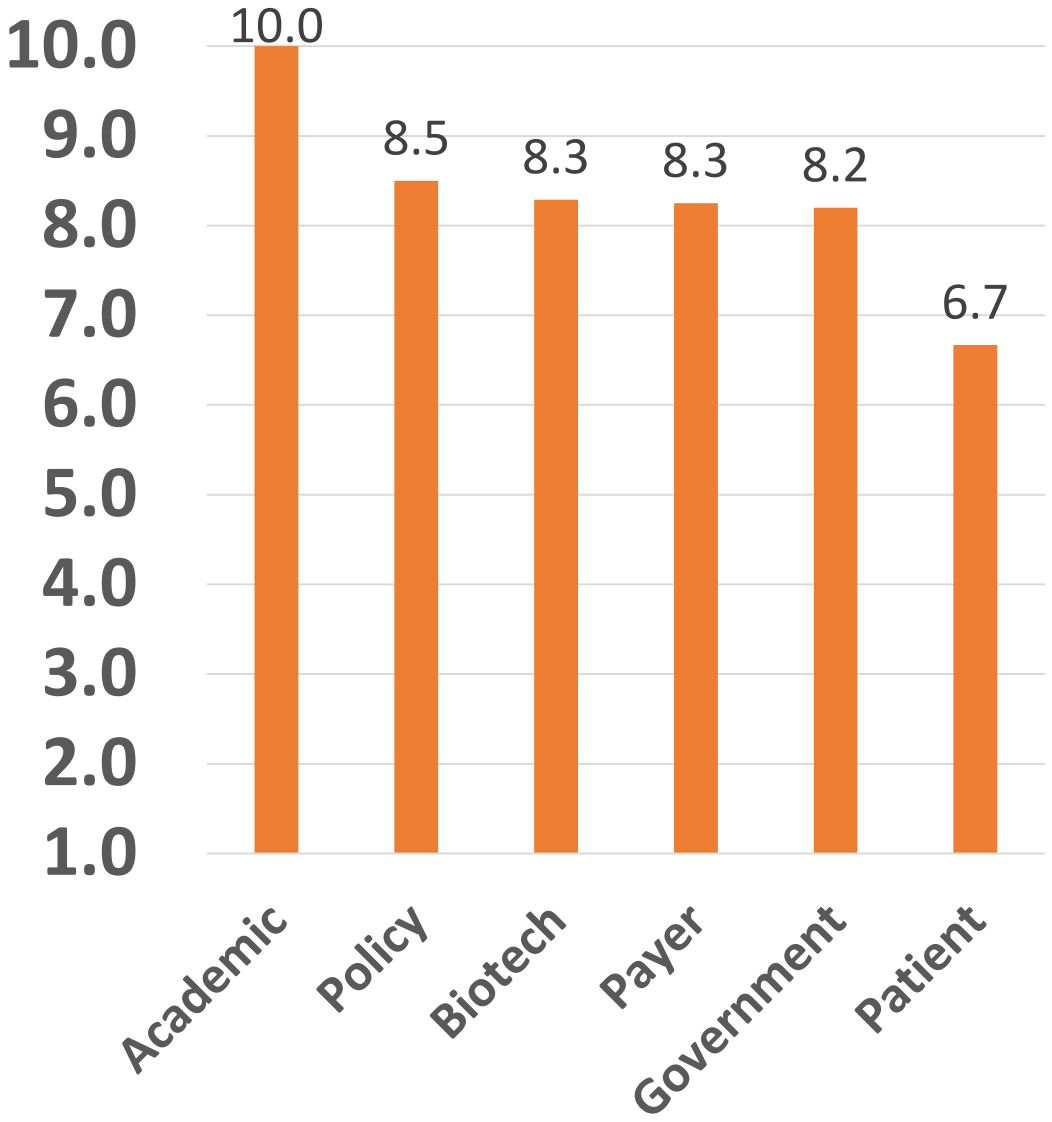
("Payer P29)



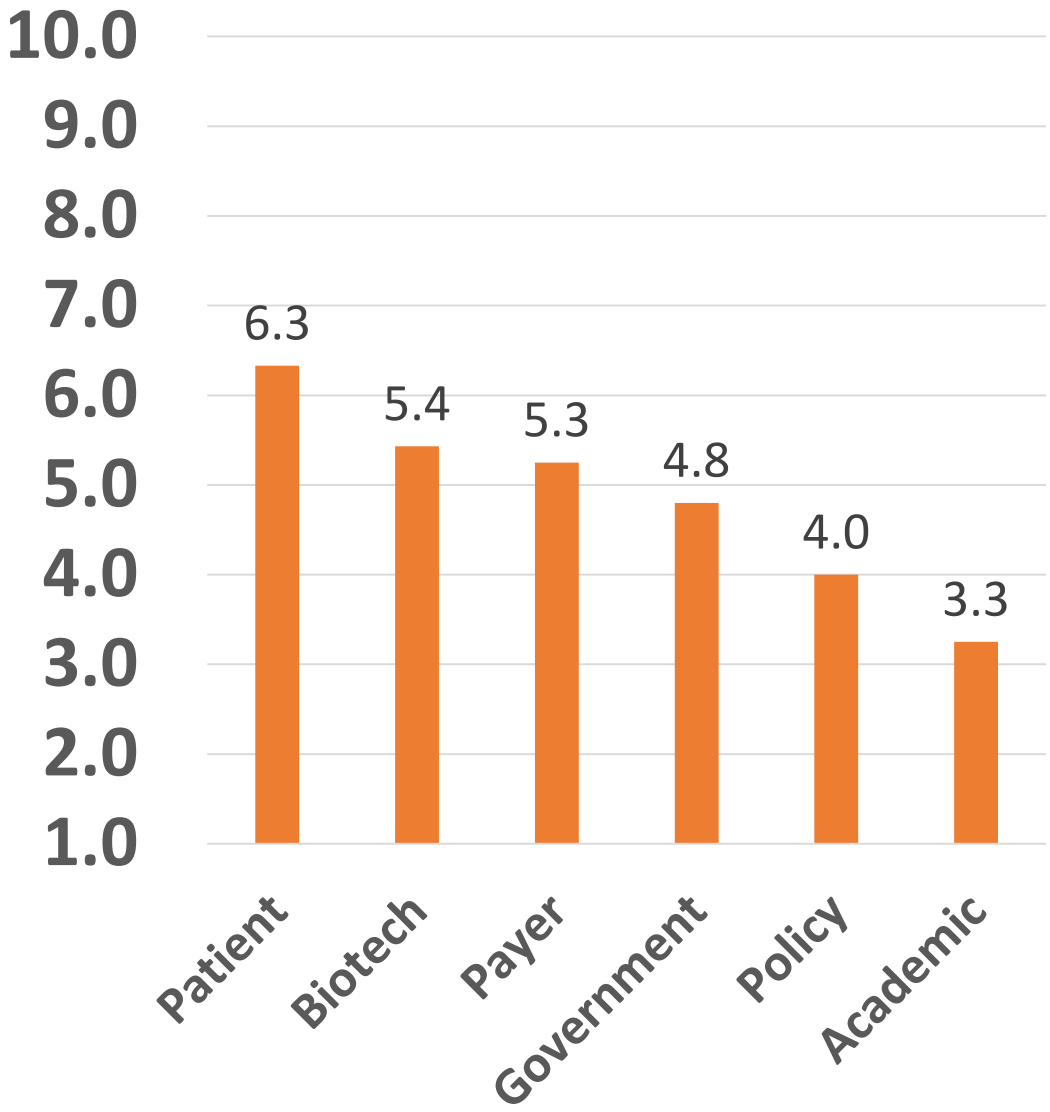
QALYs: Why so high?

"Because like QALY is so, is not really, I mean, there is also a lot of, like the new QALY calculations that are kind of trying to incorporate. You know little more information in detail, you know. But it's…yeah. It's hard. The tighter the more defined you get, the more gaps you end up creating. So it's tough."

(Government P16)

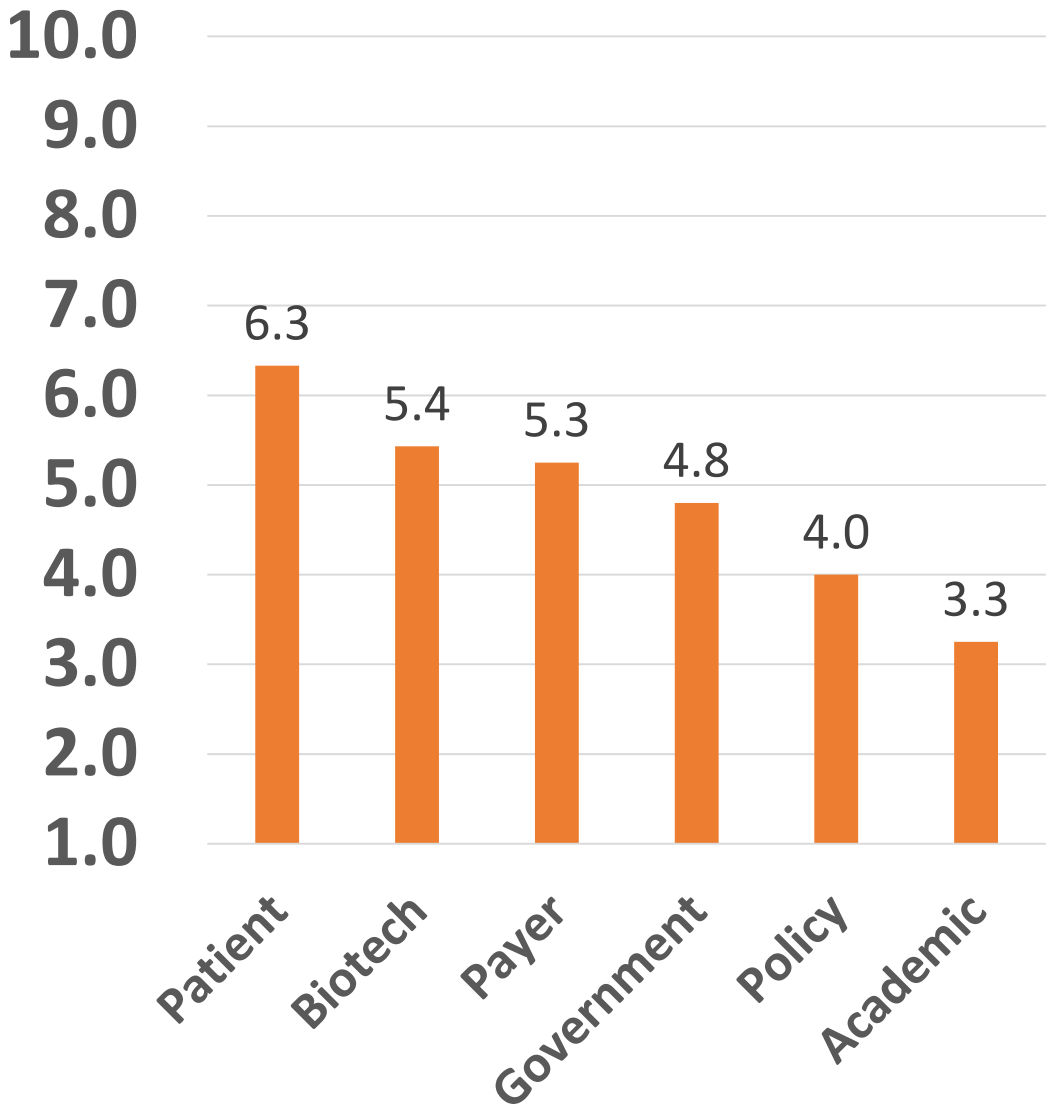


Equity: Why so low?



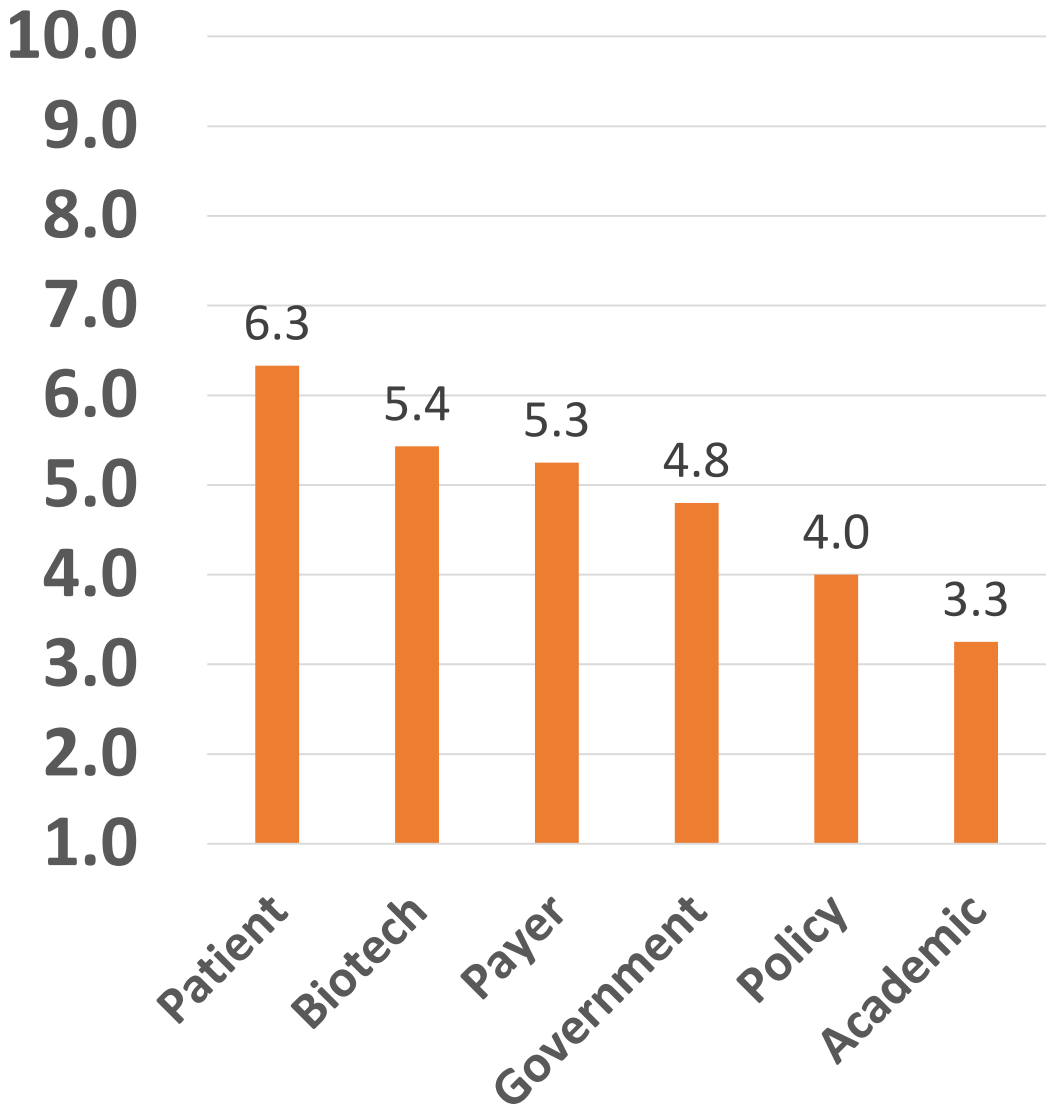
"I think, eventually, when all the other things are met, we're gonna get to equity. I think it's a long time before we get there. I think having the equity conversation now is early when we don't even have the conversation about those that have access that can't get their drugs."
(Patient P01)

Equity: Why so low?



"There are things that could get tossed by the wayside because of an equity issue, and then everyone loses. If you can get to the the treatment first and then worry about equity."
(Government P26)

Equity: Why so low?



"Companies will say things like, 'you should go with intra-fecal delivery instead of an intra-cisterna magna, because it's a real equity [issue] if you do ICM you're going to need a neurosurgeon to deliver it.' Whereas we're thinking - we want the best damn drug that we can get."
(Patient P18)

TuftsMedicine
Tufts Medical Center

CGTs: Value or Villian?

October 12, 2023
ASBH

NEWDIGS

Mark Trusheim, MS

Strategic Director | NEWDIGS Initiative

Institute for Clinical Research and Health Policy Studies, Tufts Medical Center

NEWDIGS

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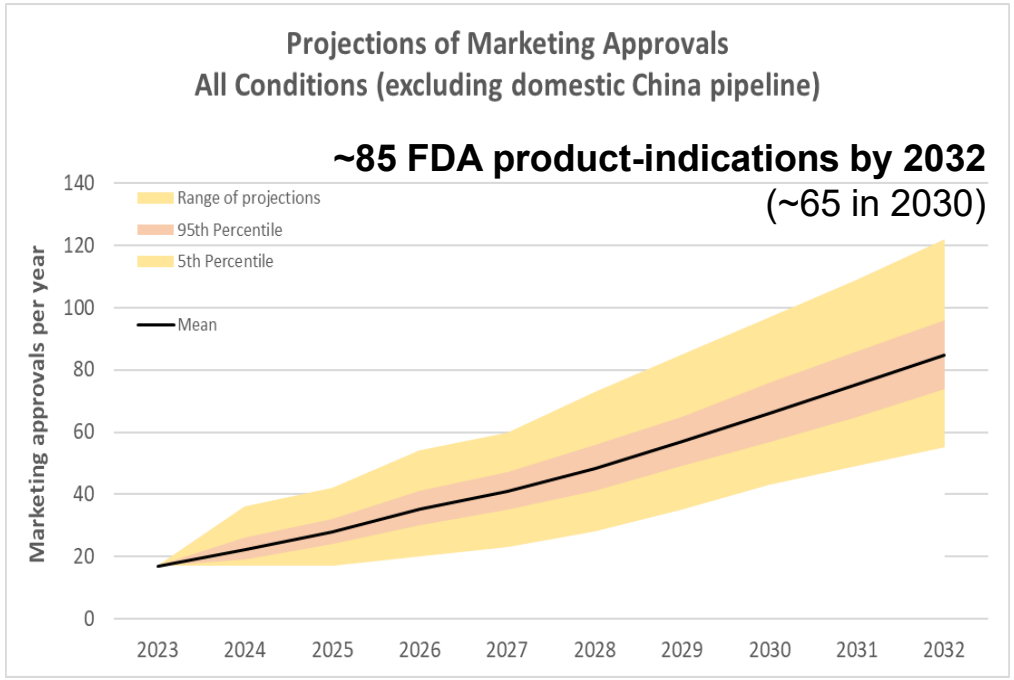
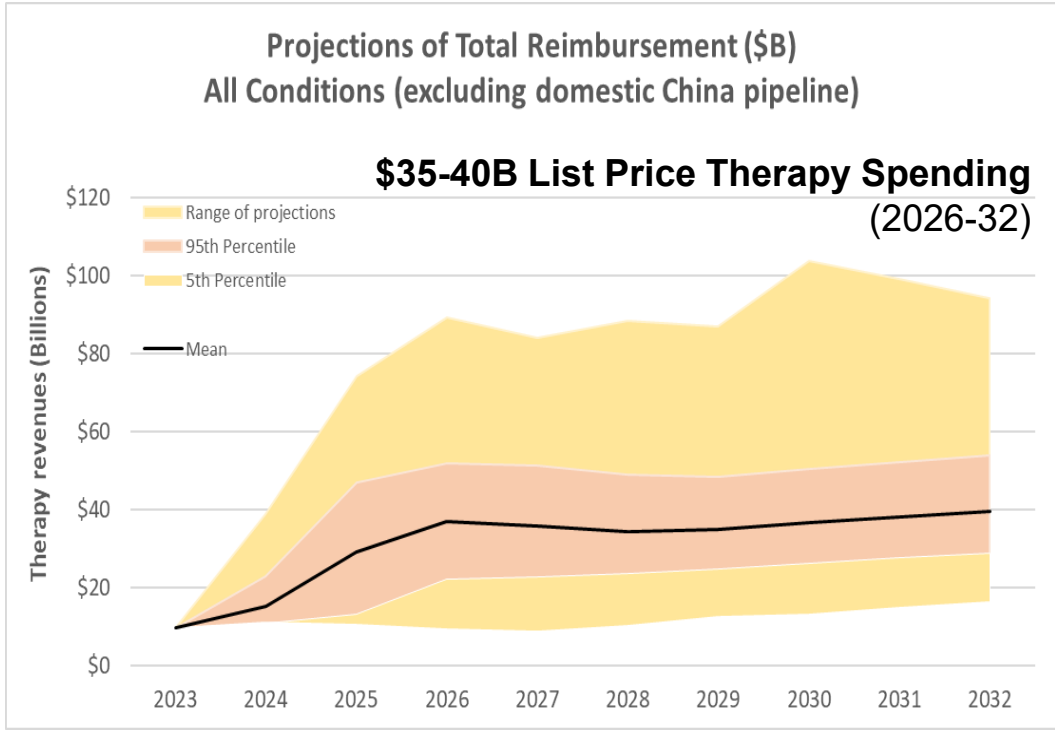
How should high-cost conditions such as neo-natal, oncology, and gene therapies be approached?

ⓘ Start presenting to display the poll results on this slide.

CGT Financial Impact Limited in Total, Even Before Cost Offsets

ICER finds CAR-Ts, hemophilia, and beta thalassemia add minimal healthcare total cost over time,
And for those gene therapies without cost offsets, that their prices can be justified





NEWDIGS

The Developer's View: Comparative Value
We pay for many other rare and high-cost events

Cell and Gene Therapy List Prices

(Net is lower)

$400-800K Luxturna: for a form of blindness

$2.1M Zolgensma: for fatal infant SMA (Spinal Muscular Atrophy)

$3.5M Hemgenix for hemophilia

ICER has found these prices mostly cost-effective

VOYA FINANCIAL

Top 10 largest Stop Loss claims (includes medical and prescription)	2022 allowed charges
1. Injury and poisoning	$5,770,286
2. Diseases of the blood and blood-forming organs	$5,280,957
3. Congenital anomalies	$4,488,221
4. Diseases of the blood and blood-forming organs	$4,195,624
5. Injury and poisoning	$4,137,342
6. Diseases of the blood and blood-forming organs	$4,119,624
7. Diseases of the circulatory system	$4,116,541
8. Diseases of the musculoskeletal system and connective tissue	$4,099,288
9. Neoplasms	$3,908,400
10. Certain conditions originating in the perinatal period	$3,840,786

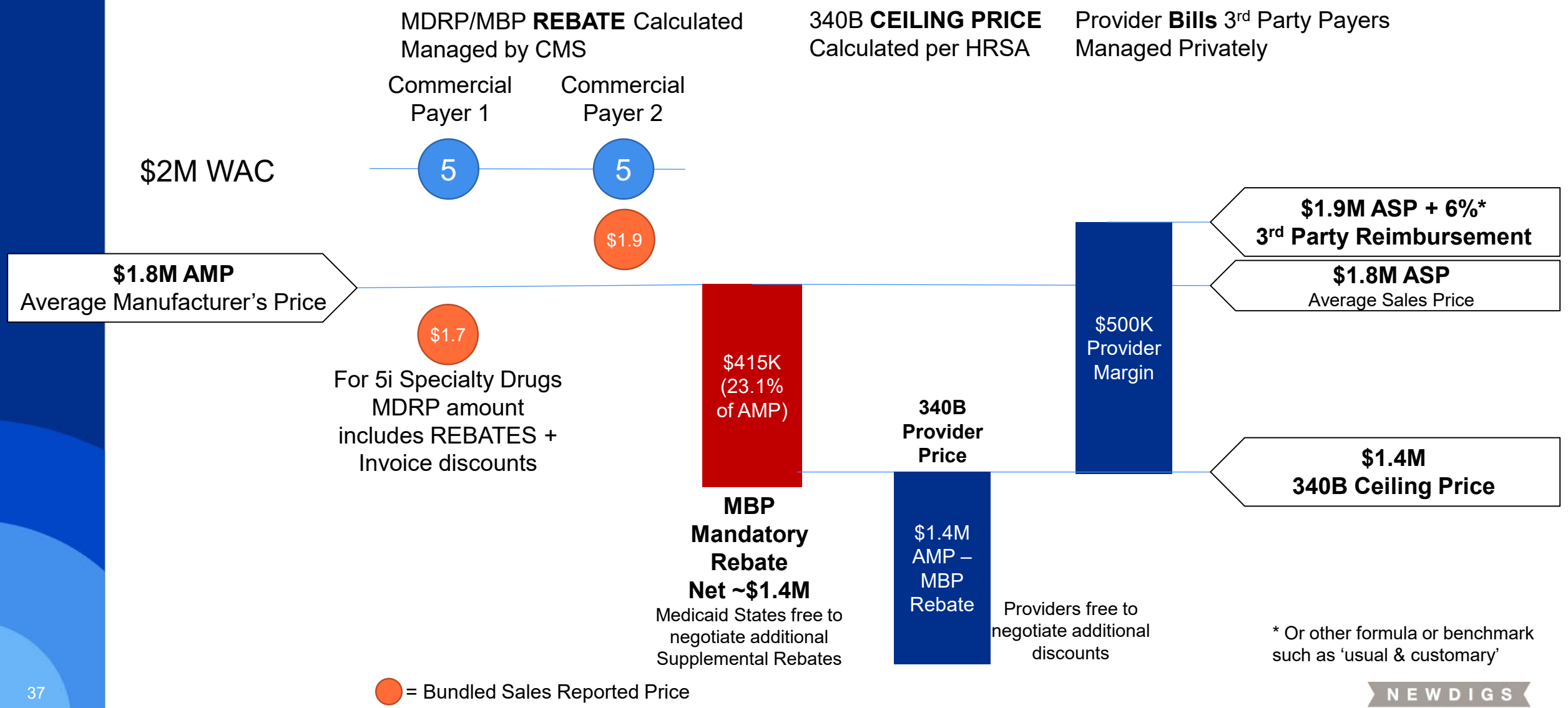
All statistics and trends are based on our book of business. The average Stop Loss claim allowed charge amount in 2022: $475,401.

Our Stop Loss insurance covers employers with a total of 1.9 million employees. The data included reflects policies effective January 2, 2021 with coverage through January 1, 2022 and claims completed through April 30, 2023.

Sun Life

Medical condition	Highest member cost in 2022	Cost contributing factors
Newborn/infant care	$6.5 million	Hospital stays, comorbidities, high-cost drugs
Blood disorder	$4.6 million	Hospital stays, comorbidities, high-cost drugs
Orthopedic/Musculoskeletal	$4.5 million	High-cost drugs
Cardiovascular disease	$4.3 million	Hospital stays, comorbidities, high-cost drugs, complicated surgeries
Cancer	$4 million	Hospital stays, comorbidities, high-cost drugs

Federal Programs Create A Rebate and Discount Cascade: MBP rebate to 340B ceiling price to ASP+6% Provider margins



NEWDIGS

Durable Therapy Financial Challenges Drive New Payment Models

Three financial challenges exacerbated

Payment timing
One-time high cost

Performance risk:
Effectiveness & durability

Actuarial risk:
Likelihood of encountering a case

Five Precision Financing solutions designed

Short-term milestone-based contracts

Multi-year performance-based annuities

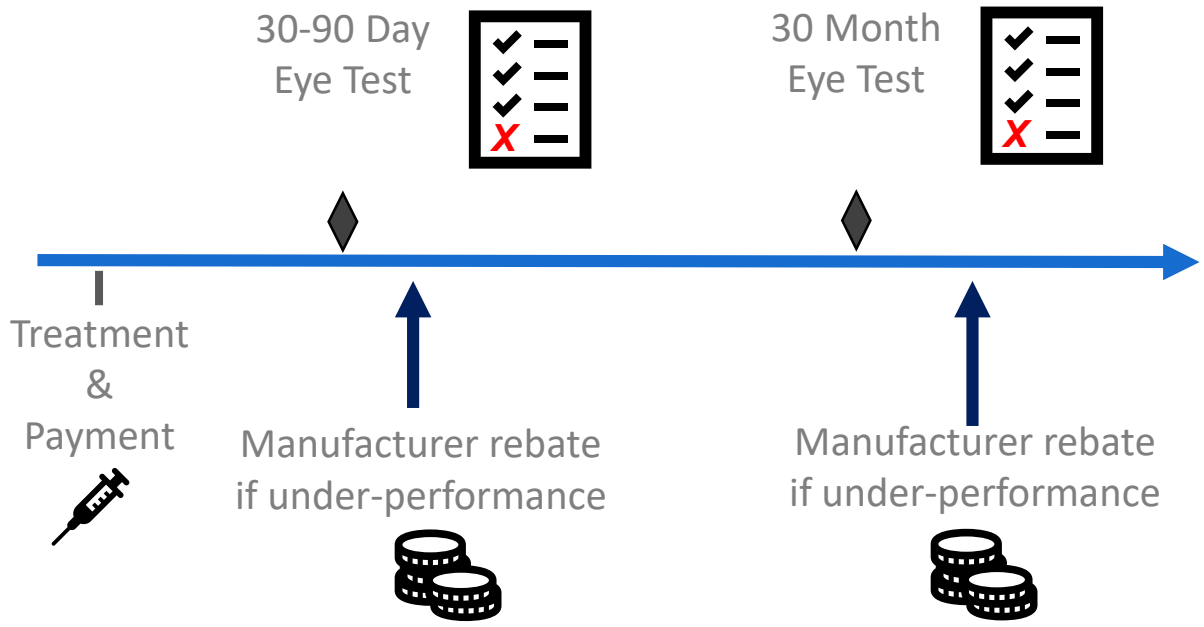
Warranty Model

Orphan Reinsurer and Benefit Manager (ORBM) and Risk Pools

Subscription Model

Example Milestone-based Contracts

- 3 January 2018: Massachusetts insurer Harvard Pilgrim Healthcare announces outcomes-based agreement for Luxturna vision gene therapy (Spark, now Roche)
- 2 May 2017: Hypercholesterolemia PCSK9 Repatha (evolocumab, Amgen) cardiovascular events trigger rebate
- 20 October 2021: ALK+ metastatic Non-Small Cell Lung Cancer therapy Alunbrig (brigatinib, tyrosine kinase inhibitor:Takeda) 3 month discontinuation rebate
- Harvard Pilgrim has 15 or more outcomes-arrangements in place (23 March 2019, Modern Healthcare)



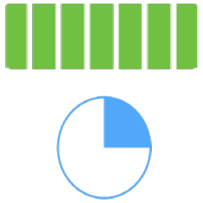
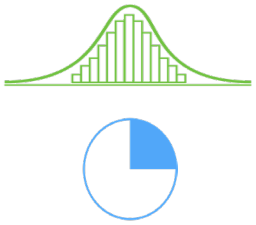
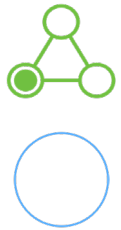
European Area Examples

Therapy	CED	Outcomes MEA
Spinraza for SMA	Belgium, England, Netherlands. (Austria 1 region?)	Bulgaria, Ireland, Italy, Latvia, Lithuania, Poland
Kymriah for Cancer	Austria?, Belgium, England, France	Italy, Spain,

From: Facey, Karen M., et al. "Implementing outcomes-based managed entry agreements for rare disease treatments: nusinersen and tisagenlecleucel." Pharmacoeconomics 39.9 (2021): 1021-1044.

Not Perfect, Precision Financing Designs Leading Move to Value-Based Care

All launched orphan gene therapies employ one, except Elevidys for DMD
CAR-T therapies in oncology evolving to standard rebates as clinical performance risk resolves.

		Payment Timing	Performance Risk	Actuarial Risk	Examples
Short-term milestone contracts					Luxturna, Kymriah (Not reported, up to 100%)
Warranty Model					Hemgenix, Roctavian (up to 100%)
Multi-year performance annuities					Zynteglo (EU) (up to 80%)
Risk Pools					Stop Loss
Subscription Model					Embarc

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Did the cost of CGTs in total and in comparison to other conditions, seem:

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The Patient Voice in Access and Coverage Decision-Making

Ryan Fischer
Chief Operating Officer
Foundation for Angelman Syndrome Therapeutics

cureangelman.org

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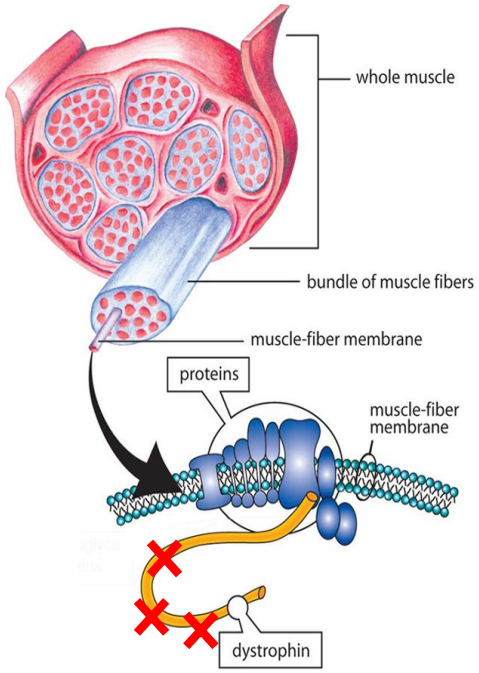
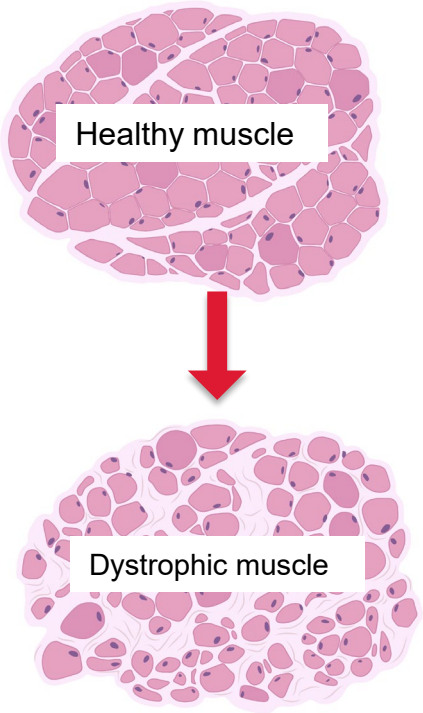
At which stage of drug development do you think patient advocacy groups have the most influence through their direct input and engagement?

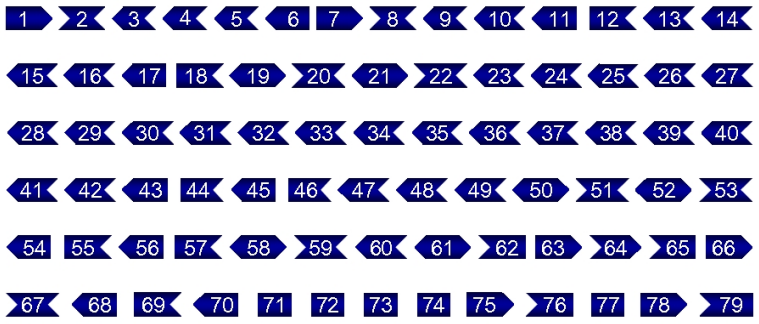
ⓘ Start presenting to display the poll results on this slide.

About Duchenne Muscular Dystrophy

- X-linked, pediatric neuromuscular disease
- Incidence: 1:4600 boys (30% spontaneous)
- Diagnosis: 3-5 years of age
- Predictable course, muscle degeneration
- Progressive loss of function
- Loss of ambulation mid teens, death by age 30
- Impacts all systems not just skeletal muscle







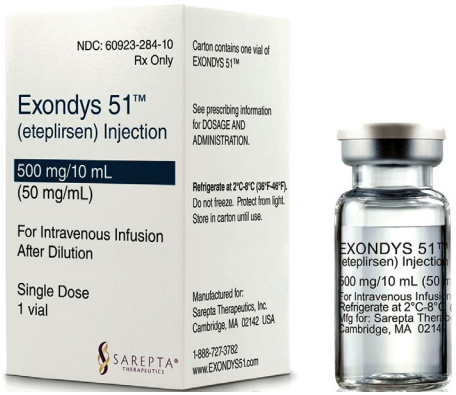
- One of the largest genes & protein in genome
- 2.4 Million base pairs/79 Exons

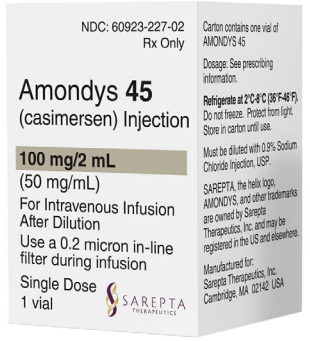
  - 60-70% Deletions
  - 10% Duplications
  - 10-15% point mutations and other small changes

FDA Approved Therapies (2016-2021)

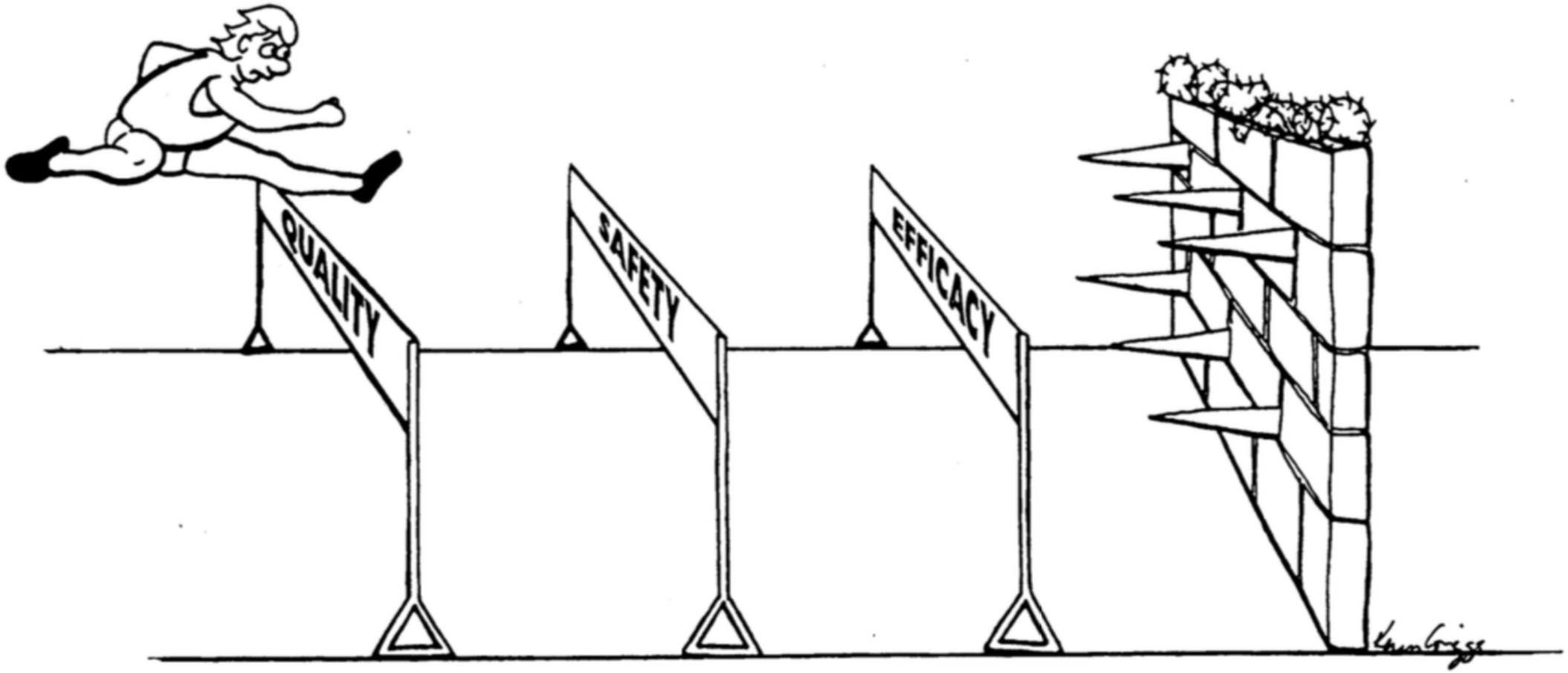
Corticosteroid, Full Approval – SOC

ASO, Accelerated Approvals – 30% of population mutation amenable





THERE WAS GENERAL AGREEMENT THAT THE *FOURTH HURDLE* WAS THE ONE TO LOOK OUT FOR



Approved ASO Therapies
Payer Determination Hurdles

- Plans differ on age-specific restrictions.
- Prior authorizations with different requirements and length of paperwork
- Plans differing on required assessments and testing for authorization and renewal
- Plans differ on renewal times (3 months, 6 months, 1 year)
- Plans differing on ambulatory vs non-ambulatory coverage
- Employer carve-outs
- Plans classifying therapies as *experimental/investigational* due to AA status

Top 25 Commercial Plans – ASO coverage

Not Medically Necessary

- BCBS of IL
- HealthNet
- BS of California
- BCBS of AL
- Molina

Experimental Investigational

- Highmark
- BCBS of MI
- BCBS of NJ
- BCBS of TX
- Florida Blue
- BCBS of MN
- BCBS of NC

Must Remain Ambulatory

- United HealthCare
- Anthem
- Aetna
- Cigna
- Kaiser
- Humana
- Florida Blu
- Emblem

- Age
- Meters walked
- Steroids prior
- Reapproval

Covered per label

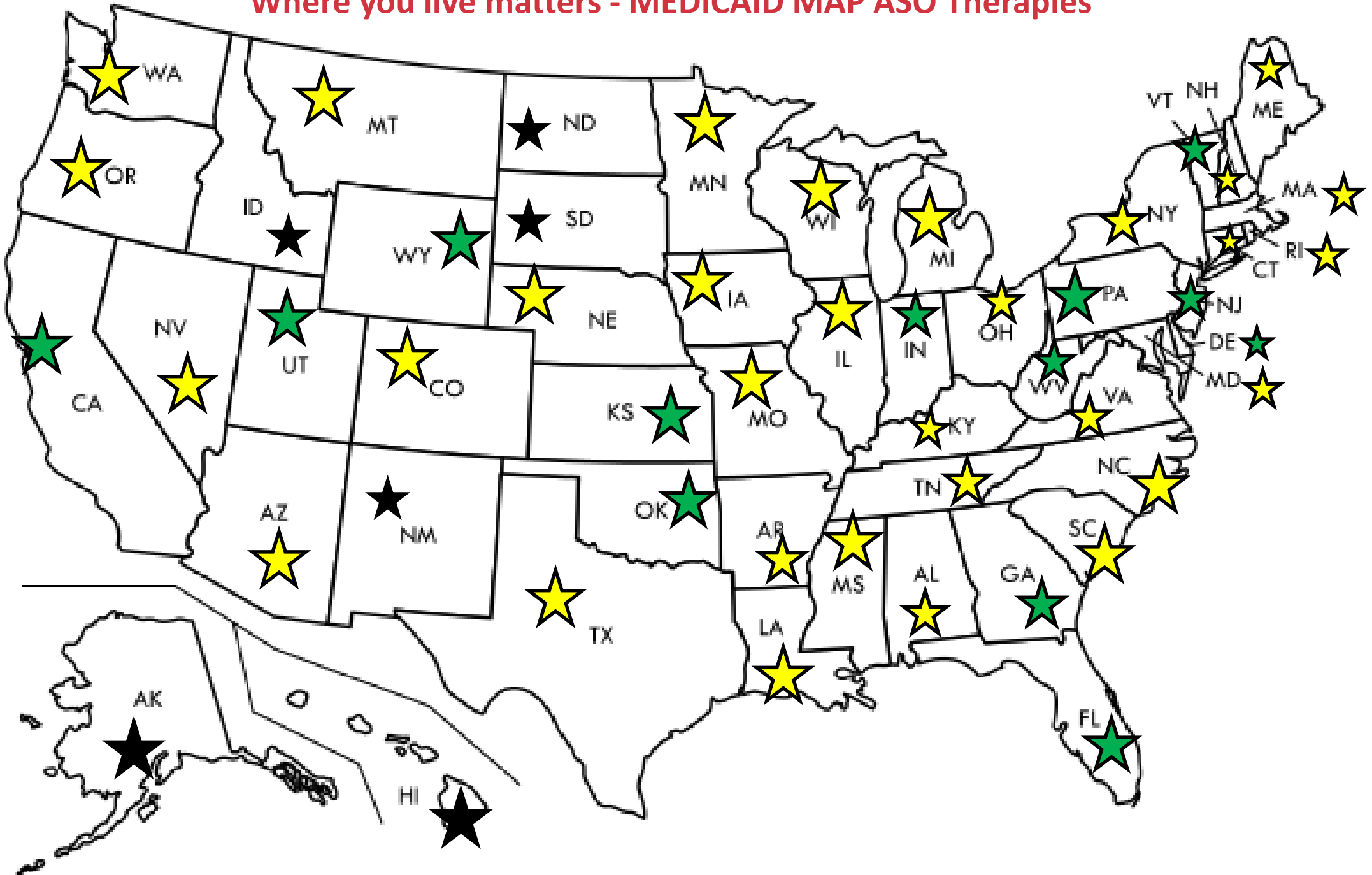
- CareFirst
- BCBS of TN
- FEP

Where you live matters - MEDICAID MAP ASO Therapies

Ambulation Criteria

Favorable/ per label

Unable to locate

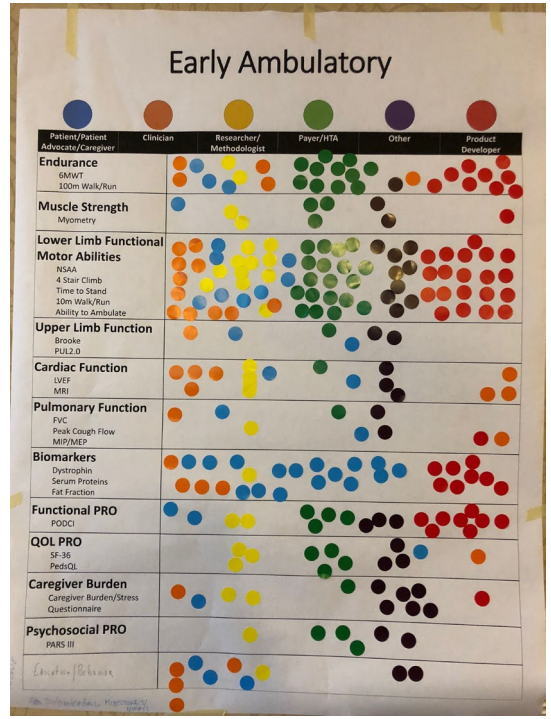


1st **Gene Therapy** Approval in Duchenne – Elevidys (June 2023)

- Narrow Label – 4-6-year-olds (up to 6th birthday), mutation exclusions based on trials.
- Some plans that have traditionally issued restrictive policies for ASO's have come out with good coverage policies for GT **to the label**—*Ex: Anthem, UHC.*
- Some stipulate no ASO following treatment
- Waiting for some policies still to come out
- Confirmatory evidence from a larger study (Q1 2024) may impact future access

Stakeholder Disagreement on the Value of Certain Outcomes

Domain	Outcome Measure	Caregiver/ Patient	Payer	Clinician	Company	Researcher
Endurance Test	6-minute walk test	0	10	5	9	2
Biomarkers	Dystrophin	16	0	4	8	1
Muscle strength	Myometry	1	3	0	1	2
Lower Limb Function	Stair climb	8	16	11	20	11
Upper Limb Function	Brooke scale	2	1	1	0	0
Cardiac	MRI	2	1	4	0	3
Pulmonary	FVC	2	1	1	1	1
PRO	PODCI	2	4	0	8	2



2017 Stakeholder Meeting on Outcomes

- Lower Limb (Stair climb) received a majority vote overall (agreement)
- **Parents view biomarkers as most important** - Payers do not
- Parent and payer disagreement on Endurance (6MWT)

The Patient Voice in Access and Coverage

- How can patients **best advocate for themselves** in the access environment?
- How can patient advocacy groups be **most effective**?
- What are the **lessons learned** for future rare disease communities?
  - **Angelman syndrome** currently has an active pipeline of potential therapeutics
  - ASO trials entering phases 2 and 3
  - Early-stage gene therapy studies moving forward (pre-clinical)

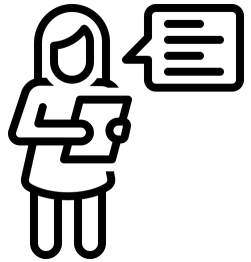
Actions to ensure patient participation in access and coverage decision-making

Partnership with:

Artia SOLUTIONS

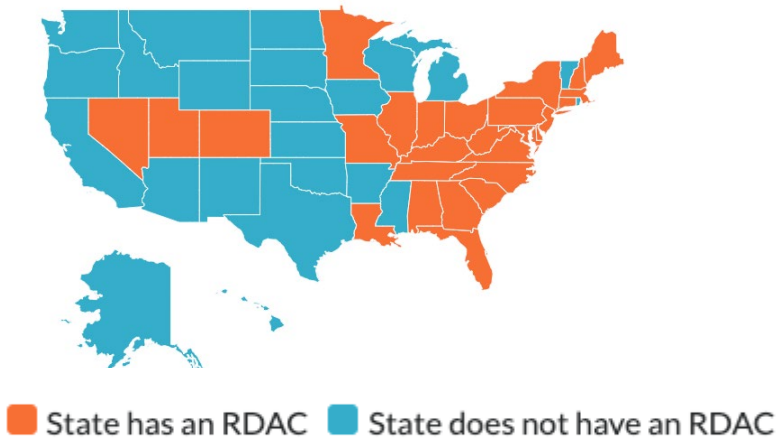
- State proclamations for AS
- Engaging Medicaid Directions and Private Payers directly
- Engaging Rare Disease Advisory Councils (RDACS)

Educate and train state family advoc

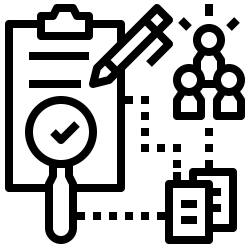


- Understand the process (commercial and Medicaid)
- How to appeal and advocate for yourself
- DUR meeting participation at state level

RDACs:



Fill in the data gaps



- Registries and RWD
- Quantifying patient and caregiver preferences (value of treatments)
- Health Economic Studies (BOI)
- Partnering with companies pre-competitively