Orchard therapeutics

Evidence generation and principles for articulating value in order to achieve patient access for gene therapies

Francis Pang

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Needing to blend innovation with tradition

"We are proud of our heritage of fine watchmaking, and the craft skills which have been handed down from generation to generation since 1875. Over the years we have demonstrated our mastery of the art of haute horology and yet Audemars Piguet has also always been a **beacon of innovation and creativity that dares to break new grounds**. While the watches that we make are expressions of our **respect for the traditions of hand crafted timepieces** and while we celebrate the fact that we are the one of the few major Swiss brands still in the hands of the descendants of the original founding families, we are also a modern, progressive company famous for our innovations in technology, the daring use of new materials and bold designs."

ATMPs have distinct characteristics

Attribute	Implications for value assessment
Single administration	Cost is front-loaded into a single clinic visit
Long-term benefits	Difficult to quantify the long-term health profile of a patient successfully treated with a transformative therapy
Evidence collection	Benefit of the therapy lasts longer than any practical evidence collection period – cannot objectively prove claimed benefit
Irreversible treatment decision	Cannot stop treatment for a non-responder as therapy has already been applied
Potentially curative nature	Curative treatments may offer benefits beyond conventional treatment by allowing patients to live free of a disease

Valuation

Traditional HTA frameworks may not be flexible enough to accommodate ATMP specificities or allow the ability to capture the full product value.

Funding

Healthcare systems are struggling to pay for innovation. Some ATMPs are raising the question of affordability due to the potential high budget impact.

Funding pathways are evolving for advanced therapies and must include consideration of inpatient procedures

Country	Same process as standard drugs ?	ATMP funding routes	Assessment framework
		• TC Assessment & CEPS negotiation for retail drugs and T2A exclusion drugs • Funding via DRG codes for non T2A exclusion drugs (no access as DRG will not cover costs for ATMPs • Cohort and nominative ATU for drugs for high unmet need diseases prior to MA	HAS HAUTE AUTORITÉ DE SANTÉ
		• AMNOG process & GKV-SV price negotiations for all drugs, except hospital only (orphan benefits) • Possible temp NUB funding negotiated by individual hospitals • ATMPs may also be classified as procedures bypassing AMNOG	IQWiG
		• National clinical assessment & price negotiation, followed by regional and local P&R decisions • Compassionate use program with national funding	AIFA
		• National clinical assessment and price negotiation, followed by regional and local P&R decisions • Compassionate use for hospital drugs which may be funded	Instituto de Salud Carlos III
		• NICE may decide to conduct a TA or HST TA • CRG commissioning policy/ service specification may be developed in some cases • IRF use also possible (however >20 requests per year triggers a CRG policy)	NHS National Institute for Health and Clinical Excellence
		• Funding pathway is the inpatient DRG with Commercial payer and Medicaid DRG reimbursement rates required for appropriate reimbursement of new ATMPS (both drug and associated services) • Carve outs (Commercial) and NTAP (Medicaid) are potential options for additional funding • ICER review of recent ATMPS to propose value-based prices as a guide for some commercial payers	ICER INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

ATMP: Advanced Therapeutic Medicinal Products

It is recognised that the economic analyses of ATMPs have to be slightly different

Table 1. Checklist for assessing gene therapies.

Item
Clinical effectiveness
Surrogate endpoint used
Rare disease
Serious condition
Single-arm trial
Pediatric population
Reporting of adverse consequences and risks
Size of clinical trial
Length of clinical trial
Extrapolation to long-term outcomes
Elements of value
Severe disease
Value to caregivers
Insurance value
Scientific spillovers
Lack of alternatives
Substantial improvement in life expectancy
Other considerations
Discounting
Different discount rates explored
Uncertainty
Alternative payment models explored

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Analytic Considerations in Applying a General Reference Case to Gene Therapy

Michael F. Drummond, PhD,[1,*] Peter J. Neumann, ScD,[2] Sean D. Sullivan, PhD, Omar Dabbous, MD, MPH,[6] Mondher Toumi, PhD[7]

[1]Centre for Health Economics, University of York, York, UK; [2]Center for the Evaluation of Value and Institute, School of Pharmacy, University of Washington, Seattle, WA, USA; [4]Fakultät Betriebswirts Nürnberg, Germany; [5]Center for Medical Technology Policy, Baltimore, MD, USA; [6]AveXis Inc, Bann University, Marseille, France.

ABSTRACT

The concept of a reference case, first proposed by the US Panel on Cost- specify the required methodological features of economic evaluations o there is a difference of opinion on whether a specific methodological re provide a more detailed analysis of the characteristics of gene therapy modifications to the methods suggested in general reference cases for reference case is not required, but propose a tailored checklist that can which aspects of economic evaluation should be considered further, g

Keywords: cost-effectiveness analysis, drug pricing, reimbursement, sp

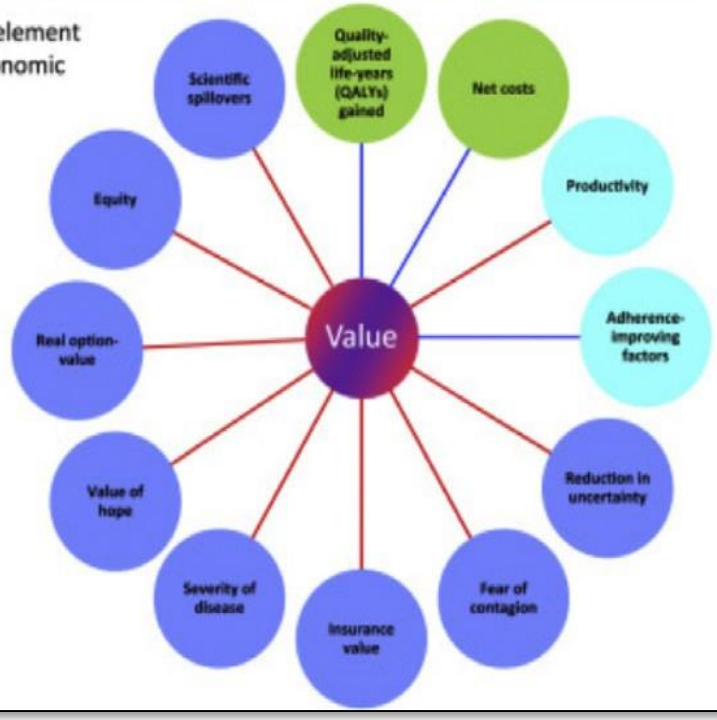
VALUE HEALTH. 2019; ■(■):■–■

Introduction

The concept of a "reference case," first proposed by the US Panel on Cost-Effectiveness in Health and Medicine,[1] has been used to specify the required methodological features of economic evaluations of healthcare interventions in different jurisdictions.[2,3] In the United States, the Institute for Clinical and Economic Review has recently produced a reference case that is based, in part, on the Second US Panel.[4] The rationale for the allow tients to ge muta (2) in tionir to he throu have

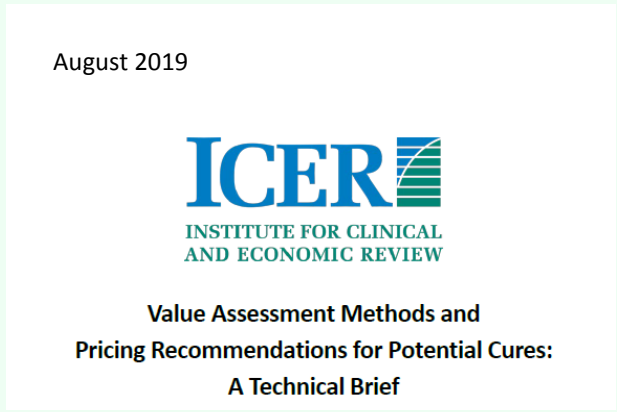
Elements of Value

Challenge: Map each element into an underlying economic framework for value assessment.



Drummond et al. 2019

Both NICE and ICER are reviewing their methods for ATMP assessment


August 2019

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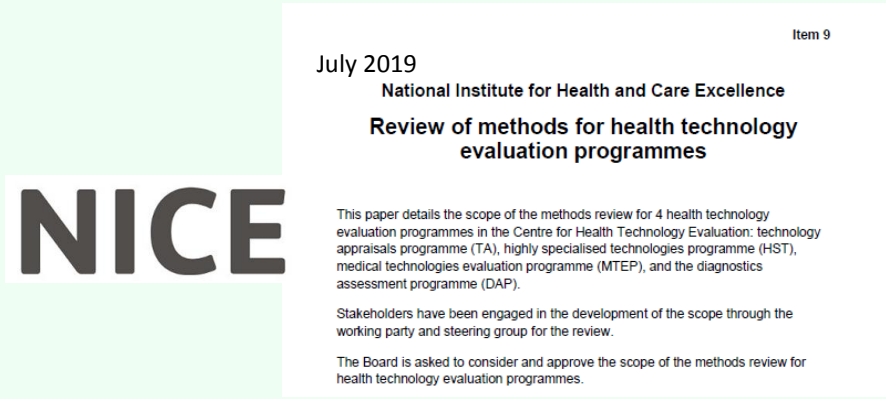
Value Assessment Methods and Pricing Recommendations for Potential Cures: A Technical Brief

- **Uncertainty with unrecoverable costs**
- **Discounting: Time divergence between costs and benefits**
- **Additional elements of value**
- Affordability and sharing of economic surplus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July 2019

National Institute for Health and Care Excellence

Review of methods for health technology evaluation programmes

NICE

This paper details the scope of the methods review for 4 health technology evaluation programmes in the Centre for Health Technology Evaluation: technology appraisals programme (TA), highly specialised technologies programme (HST), medical technologies evaluation programme (MTEP), and the diagnostics assessment programme (DAP).

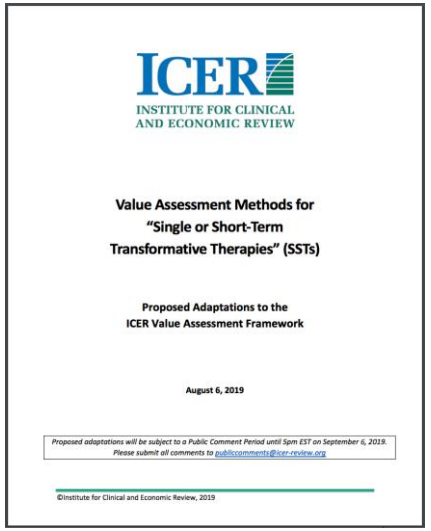
Stakeholders have been engaged in the development of the scope through the working party and steering group for the review.

The Board is asked to consider and approve the scope of the methods review for health technology evaluation programmes.

- **Exploring uncertainty**
- **Discounting**
- **Modifiers considered in decision-making**
- Types of evidence, sources & synthesis
- Health-related quality of life
- Technology-specific issues
- Cost minimisation analysis questions
- Equality considerations in guidance development
- Costs used in HTA
- Position of technologies in care pathway
- General approach to decision-making

Proposed adaptations to HTA methods: ICER – cure proportion methodology

For short-term transformative therapies, ICER have proposed measuring the proportion of patients likely to be cured by an intervention, rather than traditional curve-fitting, as it is less susceptible to distortion as a result of population heterogeneity.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Value Assessment Methods for "Single or Short-Term Transformative Therapies" (SSTs)

Proposed Adaptations to the ICER Value Assessment Framework

August 6, 2019

Proposed adaptations will be subject to a Public Comment Period until 5pm EST on September 6, 2019. Please submit all comments to publiccomments@icer-review.org

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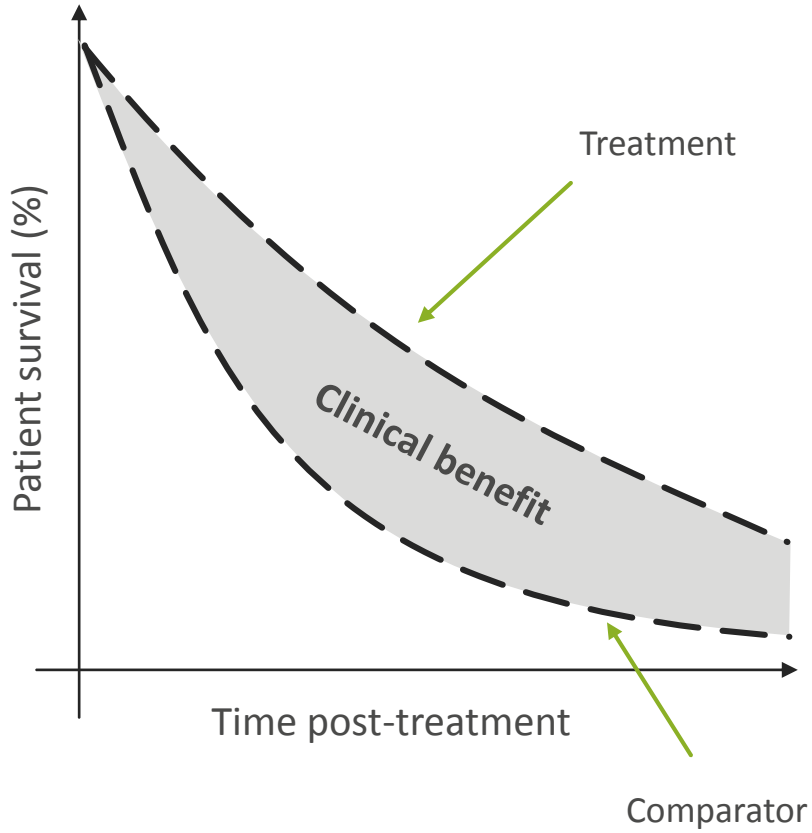
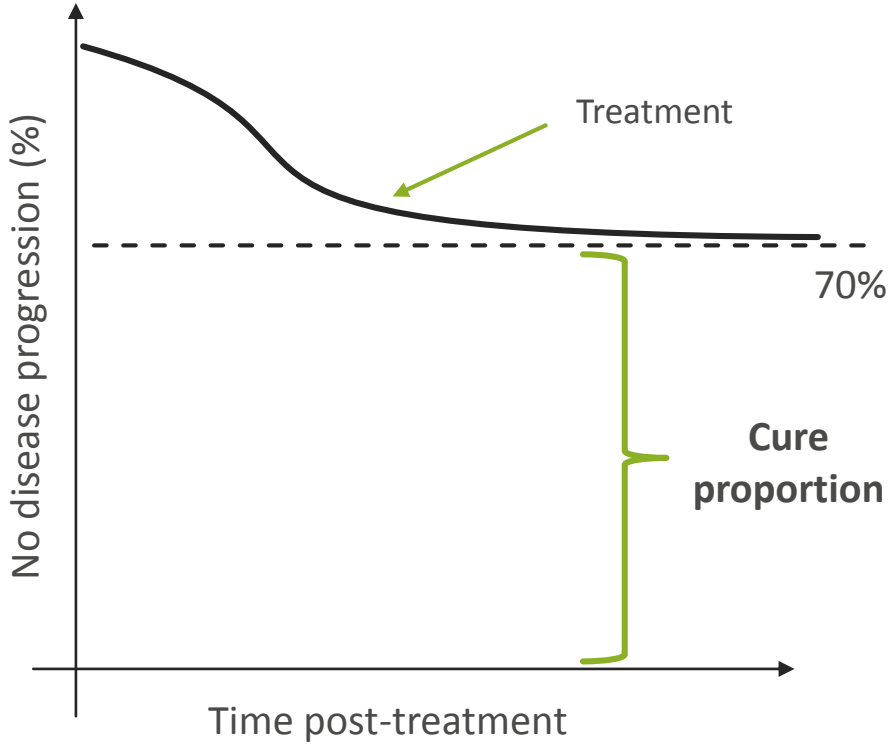
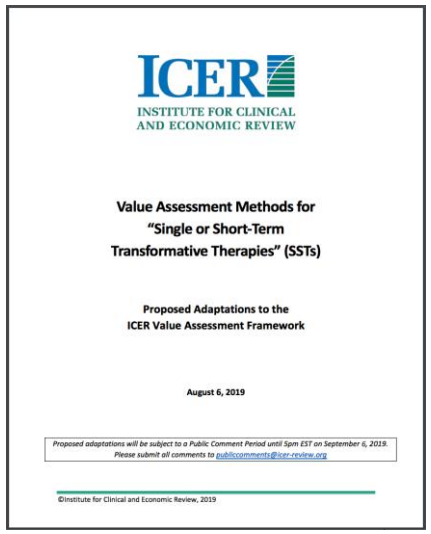




Proposed adaptations to HTA methods:
ICER – sensitivity analysis and outcome-based payment recommendations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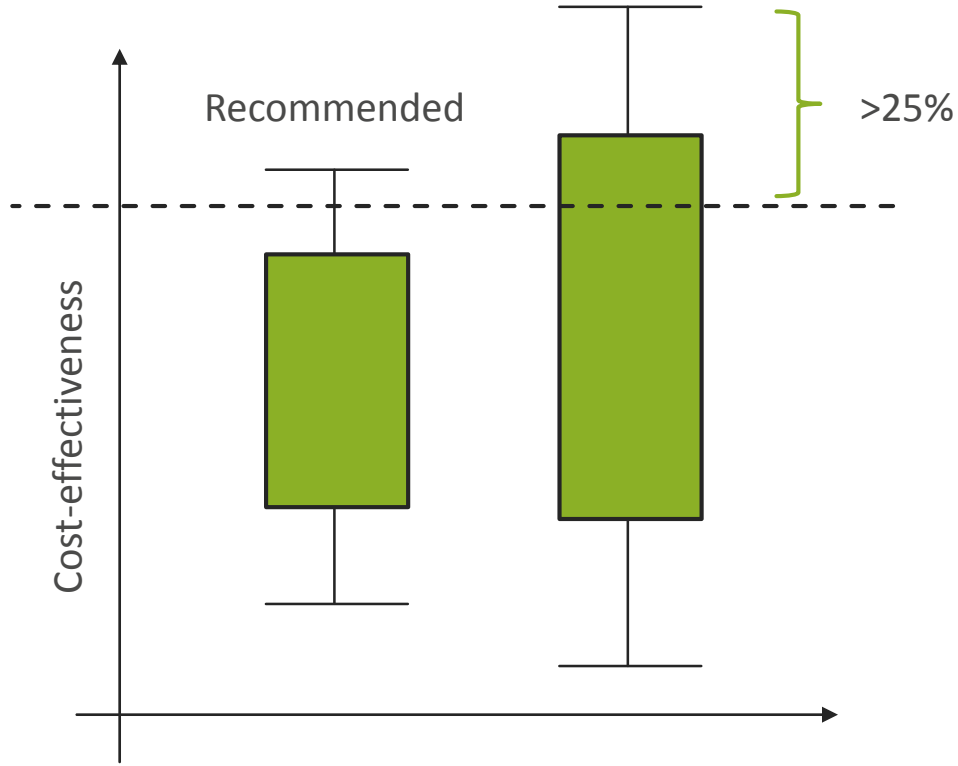
Where >25% of scenarios lead to an ICER greater than the accepted threshold, ICER proposes recommending payors adopt outcomes-based reimbursement

Cost / Benefit analysis → **Sensitivity analysis** →

ICER value (cost/QALY)

Range of potential ICER values

$200k/QALY threshold
(note: this is above the typical $150k threshold)



Other frameworks have been proposed for value assessment but have limited applicability for evaluations of ATMPs

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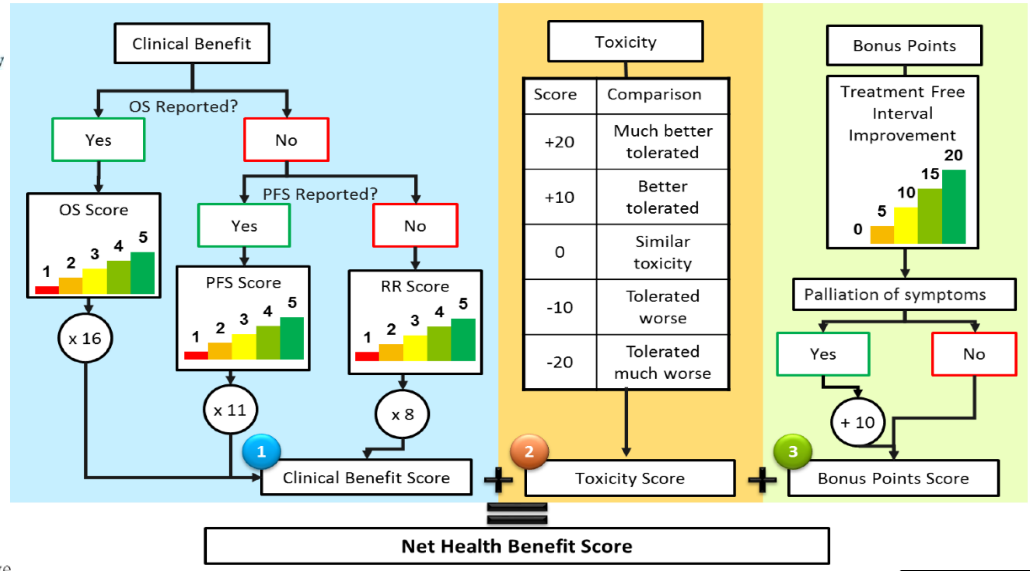
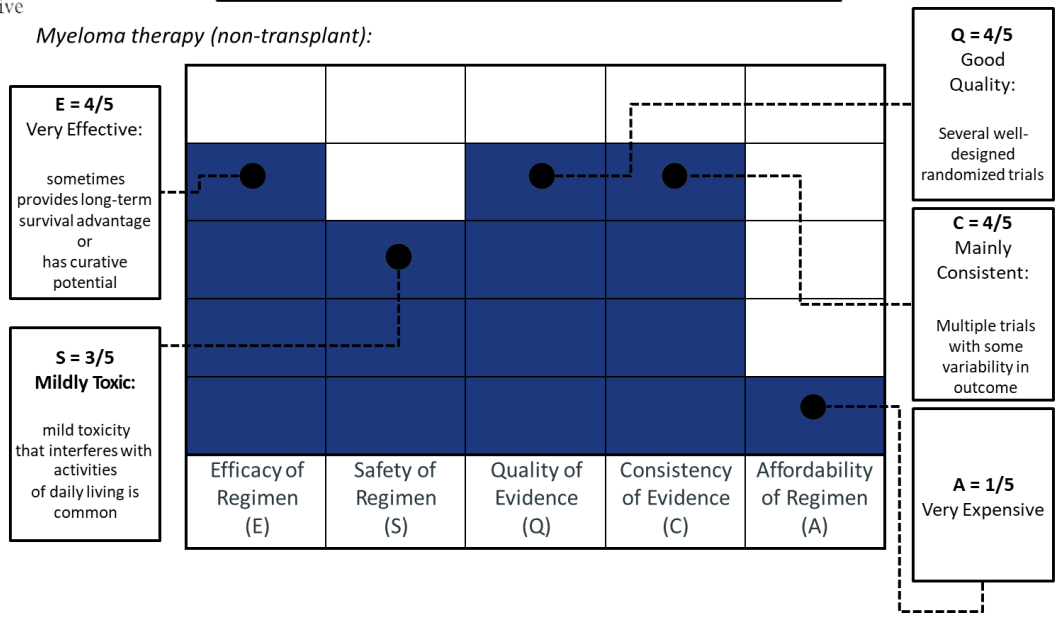
ASCO American Society of Clinical Oncology

Points are earned through comparison of certain outcome metrics to the standard of care or a placebo

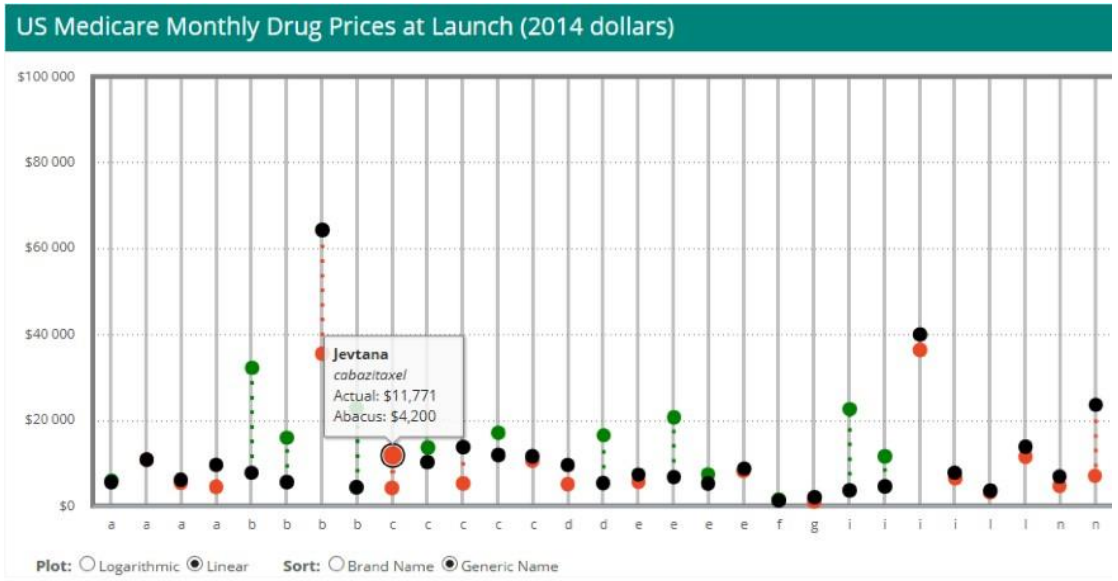


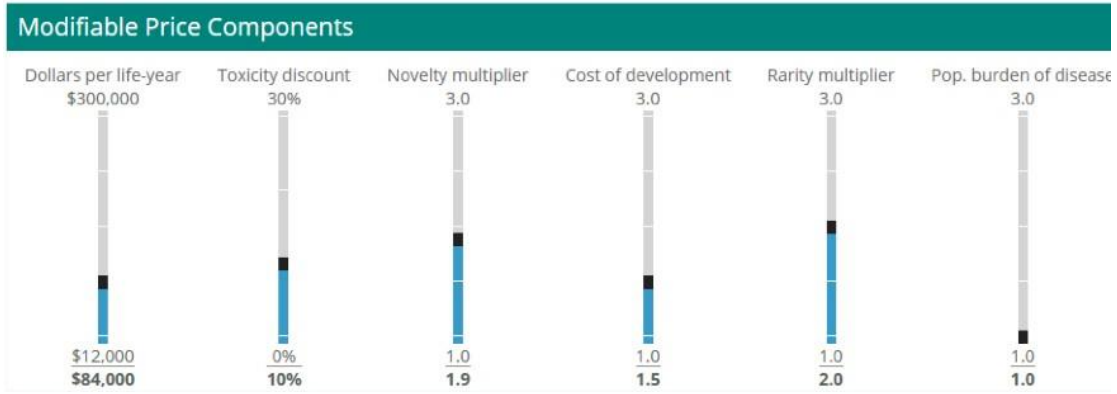
NCCN National Comprehensive Cancer Network®

Myeloma therapy (non-transplant):

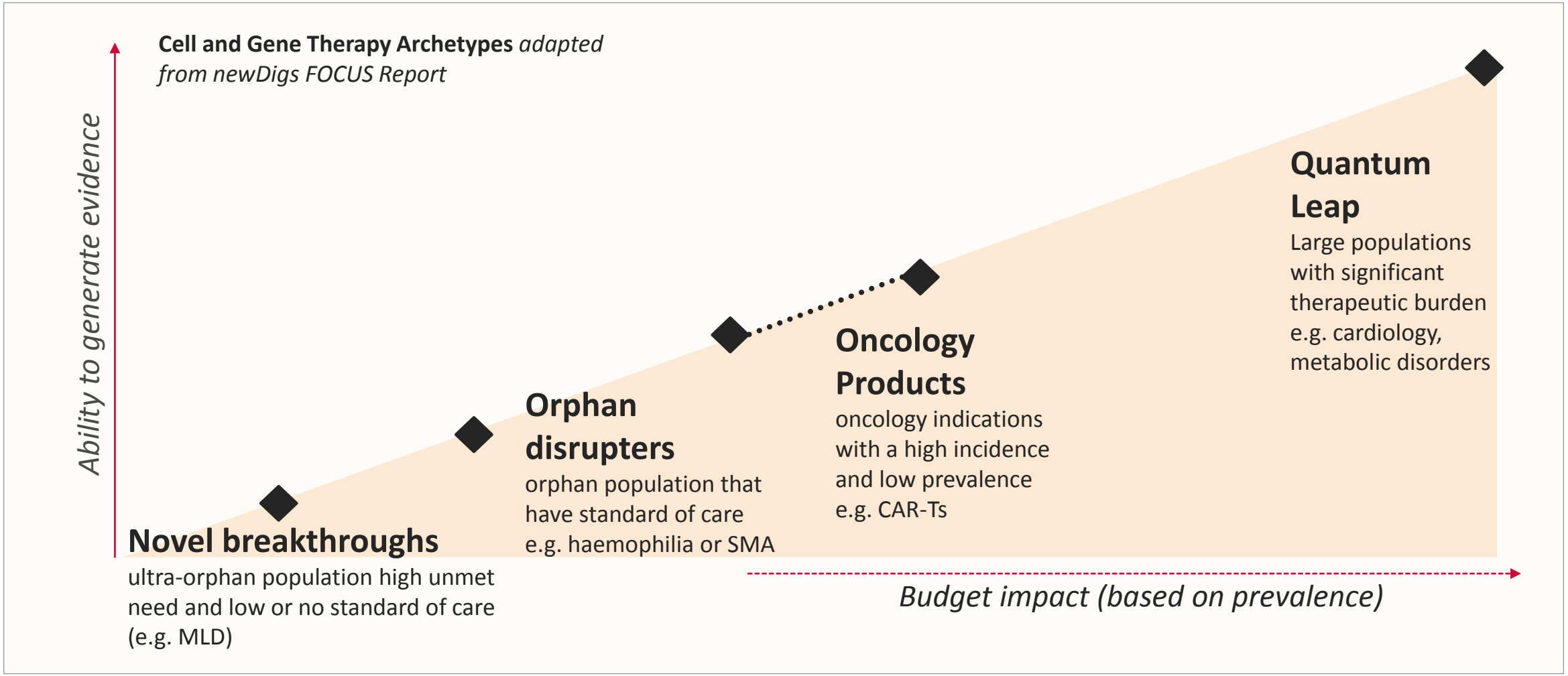


Memorial Sloan Kettering Cancer Center





Different archetypes of ATMPs have differing levels of evidence available for value assessment



https://newdigs.mit.edu/sites/default/files/NEWDIGS%20FoCUS%20Frameworks%2020180823.pdf

How we think about Value at Orchard

When We Think about Value It All Starts with the Child
and What Our Therapies, If Approved, Could Do for That Child and Beyond

Impact on Society

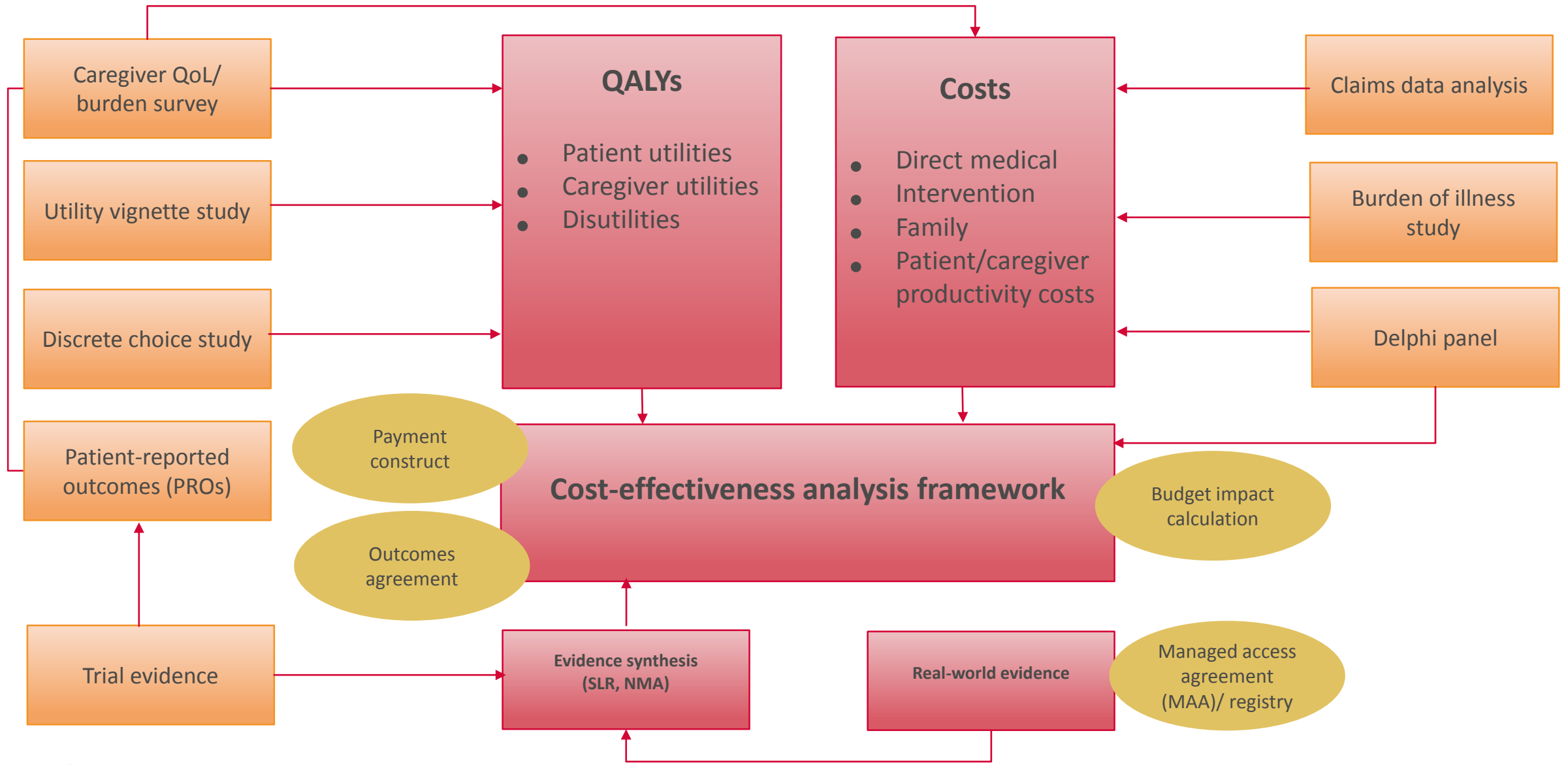
	From	To
The Child	Severely limited lifespan	Life free from symptoms & suffering
The Family	Immense financial & emotional toll	Lives of everyone in the family transformed
The Community	School, civic organization and employer resources engaged	Community resources re-deployed
The Health System	Chronic / costly interventions & palliative care	Deliver potentially curative therapy & save significant resources

A world where deadly diseases could potentially be stopped in their tracks

Evidence heatmaps are used for identifying priorities for value demonstration

Color	Evidence Rating
	Strong Evidence
	Moderate Evidence – Published, but with limitations
	Weak Evidence – Published but not relevant disease specific/Incomplete/aggregate/high level
	No Evidence
	Internal Evidence Available (not published)
	Evidence Not Applicable

Demonstrating value holistically requires a structured and disciplined approach

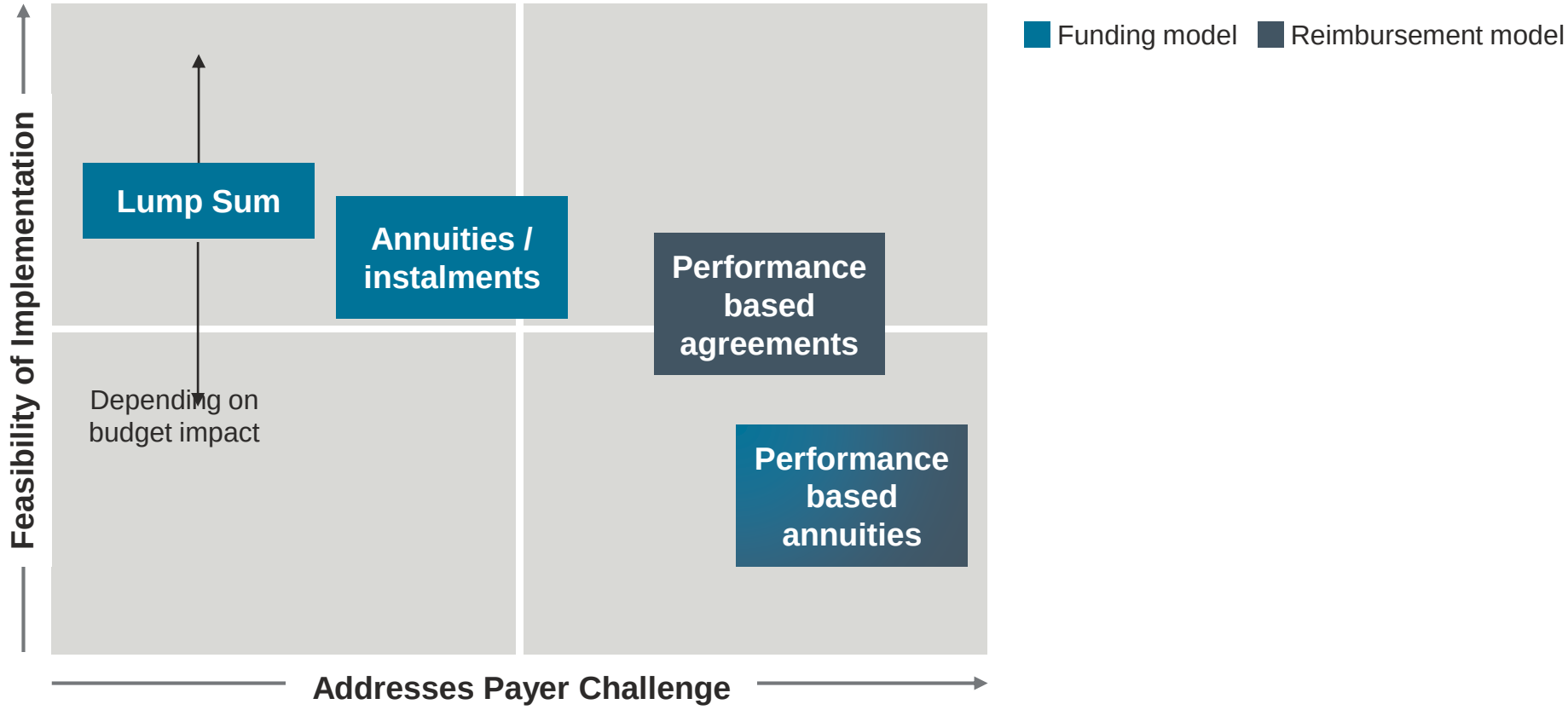


Example of capturing caregiver burden and QoL

Survey Section	*Section Objectives*
A. Background	▪ Identify **caregiver relationship** to patient and **patient age** ▪ Identify **treatments** that patient currently receives or received in the past
B. QoL	▪ Administer **validated parent-reported QoL tool** as part of survey
C. Symptoms	▪ Measure **overall quality of life** as it relates directly to the individual's disease state ▪ Understand **impact of symptoms** on individual's health and disease burden ▪ Identify potential secondary **burdens** to the patient as a result of their disease
D. Treatment Burden	▪ Capture **impact of treatments** on patient's and caregiver's quality of life ▪ Understand burden of **long-term supportive care** and potential complications with **existing care**
E. Time Investment	▪ Measure **time commitment** needed for healthcare visits ▪ Identify distinct time/disease management burden over multiple time periods (e.g., before treatment, current state)
F. Social, Emotional, and Psychological Burden	▪ Measure impact of the disease burden on **social engagement** and **interactions** ▪ Capture impact of disease on **mindset** and **feelings** of the patient and caregiver ▪ Identify **any potential stress** on family and friend relationships
G. Financial and Professional Impact	▪ Measure **financial burden** of disease for caregiver including **impact on work** and stress on **finances** ▪ Identify **any support** utilized by caregiver to alleviate financial burdens
H. Demographics	▪ Capture basic respondent **demographic** information (marital status, education, income, etc.)

It is also important to think about affordability

Orchard will provide an array of options that work across a diverse set of payers



In Summary

Considerations for value assessment and demonstration of ATMPs

1. Value assessment processes should evolve to recognise the specific attributes associated with ATMPs (and rare diseases)

2. Important to focus value demonstration across the entire spectrum of stakeholders and levels in society

3. Different expectations for evidence generation should exist for different archetypes of ATMPs

4. Access for ATMPs is not only based on value assessment. In-patient funding, payment terms (and cross-border implications) are important considerations

Thank You