Should HTA methodology and reimbursement frameworks adapt to ensure patient access to cell and gene therapies?

Stephen Palmer

Professor of Health Economics
Centre for Health Economics
University of York, UK

Scientific advisor, PharmEcons Easy Access

2020 HTA conference, Athens

Background

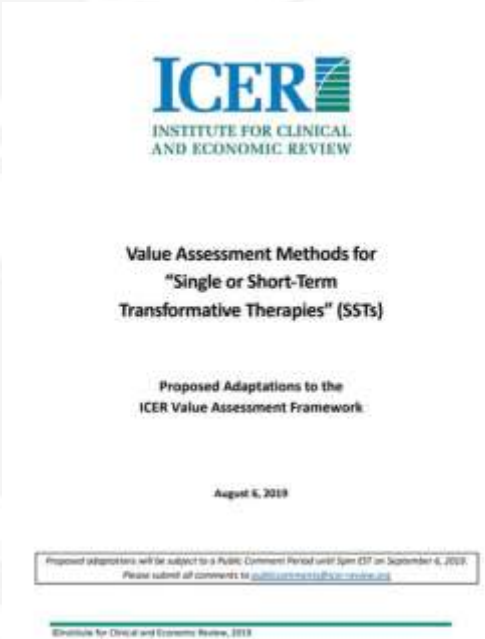
- Unique opportunities for improving patient management but important HTA challenges
- First indications in small populations but significant pipeline activity
  - 30-60 products by 2030; $12.5-$100bn haematological cancer treatment costs*
- Separate HTA process for C&G therapies not yet developed
  - High levels of clinical uncertainty
  - Affordability and budget impact concerns
- Should HTA and reimbursement methods frameworks adapt?
  - Broader value elements?
  - Greater financial risk?
  - Different market dynamics?

* Quinn C et al. Estimating the clinical pipeline of cell and gene therapies and their potential economic impact on the US healthcare system. Value Health. 2019;22(6):621–626.

Key HTA challenges for cell & gene (C&G) therapies

Evidential	Price and affordability	Uncertainty
• Surrogate endpoints • Curative potential • Small trials • Historical data comparisons • Generalizability of evidence	• One-time administration • Large upfront price • Infrastructure costs • “Real challenge is not HTA but budget impact“ (Towse, 2014)	• Uncertain duration of benefit • Strength of surrogate relationship • Role of outcomes based and financial agreements

Are existing HTA/reimbursement processes fit for purpose for C&G therapies?



ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

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 publiccomment@icer-review.org

©Institute for Clinical and Economic Review, 2019

https://icer-review.org/material/valuing-a-cure-technical-brief/

Exploring the assessment and appraisal of regenerative medicines and cell therapy products

Produced by Centre for Health Technology Evaluation, National Institute for Health and Care Excellence (NICE)

Authors Nick Crabb, Programme Director, Scientific Affairs
Andrew Stevens, Technology Appraisals Committee Chair

Acknowledgements:

Cell and Gene Therapy Catapult staff are thanked for their substantial support, including providing initial evidence summaries on the example products, hosting technical meetings, providing members for the Project Advisory Group and providing ad-hoc support throughout the project.

Centre for Reviews and Dissemination/Centre for Health Economics, University of York staff are thanked for leading this study, undertaking extensive analyses and producing a comprehensive report.

Department of Health Regenerative Medicine Expert Group Secretariat is thanked for supporting this project through recruitment of the Project Advisory Group and hosting the meeting of the Project Advisory Group.

Expert Panel members (appendix 2) are thanked for their participation in the Expert Panel meeting and for reviewing the resulting sections of the York report.

Project Advisory Group members (appendix 1) are thanked for contributing to the study design, reviewing drafts of the study protocol, York report and this report and for their ad-hoc support throughout the project.

https://www.nice.org.uk/Media/Default/About/what-we-do/Science%20policy%20and%20research/Regenerative-medicine-study-march-2016.pdf

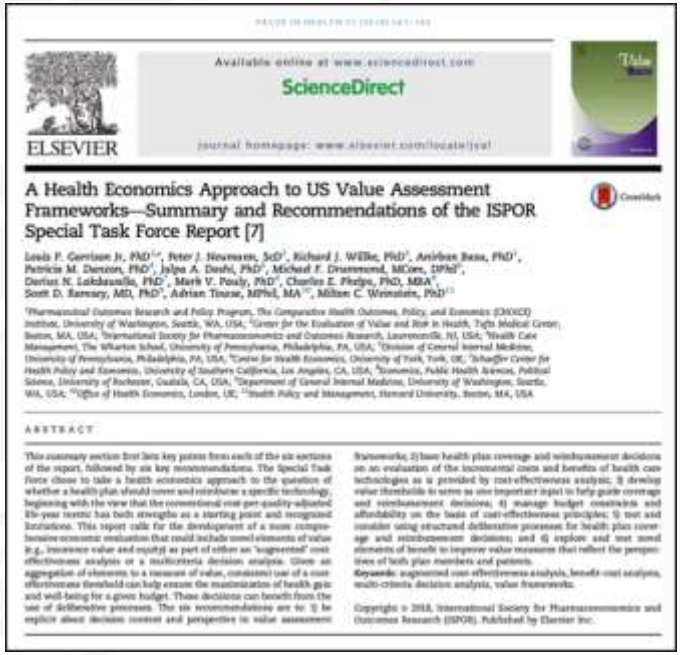
Key Findings

- **NICE**
  - Existing methodology and decision framework applicable
  - Decision uncertainty major factor
  - Concerns over irrecoverable costs
  - Practical payment methodologies important in managing uncertainties
- **ICER**
  - Core elements of ICER's assessments suitable
  - Adaptations may help address distinctive issues:
    - Relationship of evidence to value
    - Transparent/consistency in approach to elements of additional value
    - Broader societal discussion on how to share economic surplus

NICE Reference Case – cost-effectiveness

- ‘Best’ practice recommendations
- Outcomes: Quality-Adjusted Life Years (QALYs)
- Perspective: Health service
- Range of motivating factors
  - The nature of NICE’s decisions
  - Consistency between appraisals
  - Consistency within appraisals
- Reference case ≠ standardization
- Similar reference case approaches now widely applied internationally

ISPOR Task Force Recommendations – Value Frameworks



Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

ELSEVIER

A Health Economics Approach to US Value Assessment Frameworks—Summary and Recommendations of the ISPOR Special Task Force Report [7]

Louis P. Garrison Jr., PhD[1,*], Peter J. Neumann, ScD[2], Richard J. Willke, PhD[3], Anirban Basu, PhD[4], Patricia M. Danzon, PhD[5], Jalpa A. Doshi, PhD[5], Michael F. Drummond, MCom, DPhil[6], Darius N. Lakdawalla, PhD[7], Mark V. Pauly, PhD[5], Charles E. Phelps, PhD, MBA[8], Scott D. Ramsey, MD, PhD[9], Adrian Towse, MPhil, MA[10], Milton C. Weinstein, PhD[11]

[1]Pharmaceutical Outcomes Research and Policy Program, The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, Seattle, WA, USA; [2]Center for the Evaluation of Value and Risk in Health, Tufts Medical Center, Boston, MA, USA; [3]International Society for Pharmacoeconomics and Outcomes Research, Lawrenceville, NJ, USA; [4]Health Care Management, The Wharton School, University of Pennsylvania, Philadelphia, PA, USA; [5]Division of General Internal Medicine, University of Pennsylvania, Philadelphia, PA, USA; [6]Centre for Health Economics, University of York, York, UK; [7]Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, USA; [8]Economics, Public Health Sciences, Political Science, University of Rochester, Coalida, CA, USA; [9]Department of General Internal Medicine, University of Washington, Seattle, WA, USA; [10]Office of Health Economics, London, UK; [11]Health Policy and Management, Harvard University, Boston, MA, USA

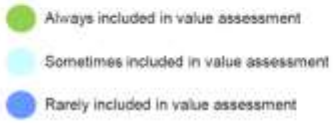
ABSTRACT

This summary section first lists key points from each of the six sections of the report, followed by six key recommendations. The Special Task Force chose to take a health economics approach to the question of whether a health plan should cover and reimburse a specific technology, beginning with the view that the conventional cost per quality-adjusted life-year metric has both strengths as a starting point and recognized limitations. This report calls for the development of a more comprehensive economic evaluation that could include novel elements of value (e.g., insurance value and equity) as part of either an "augmented" cost-effectiveness analysis or a multicriteria decision analysis. Given an aggregation of elements to a measure of value, consistent use of a cost-effectiveness threshold can help ensure the maximization of health gain and well-being for a given budget. These decisions can benefit from the use of deliberative processes. The six recommendations are to: 1) be explicit about decision context and perspective in value assessment frameworks; 2) base health plan coverage and reimbursement decisions on an evaluation of the incremental costs and benefits of health care technologies as is provided by cost-effectiveness analysis; 3) develop value thresholds to serve as one important input to help guide coverage and reimbursement decisions; 4) manage budget constraints and affordability on the basis of cost-effectiveness principles; 5) test and consider using structured deliberative processes for health plan coverage and reimbursement decisions; and 6) explore and test novel elements of benefit to improve value measures that reflect the perspectives of both plan members and patients.

Keywords: augmented cost-effectiveness analysis, benefit-cost analysis, multi-criteria decision analysis, value frameworks.

- 1. Frameworks that **focus on coverage/reimbursement** should **consider cost per QALY, as a starting point**
- 2. **Consider elements not normally included in CEAs** (e.g., severity of illness, equity, risk protection) but **more research needed.**
- 3. Test and consider **using structured deliberative** processes

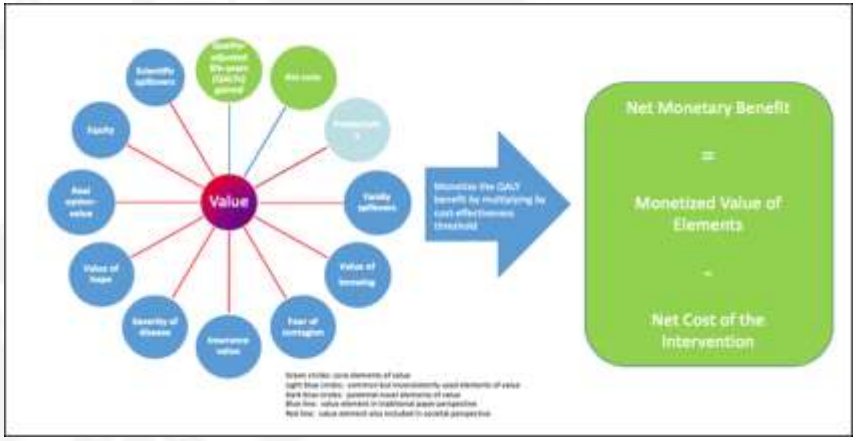
Additional elements of value for C&G therapies?



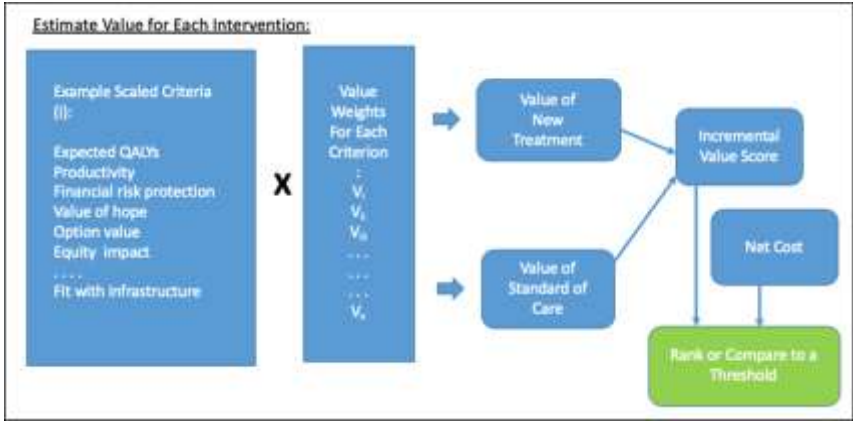
Source: Lakdawalla et al. Value in Health (2018) 131-139

Alternative approaches to aggregation

Augmented cost-effectiveness analysis



Multi-criteria decision analysis



Role for structured deliberative processes

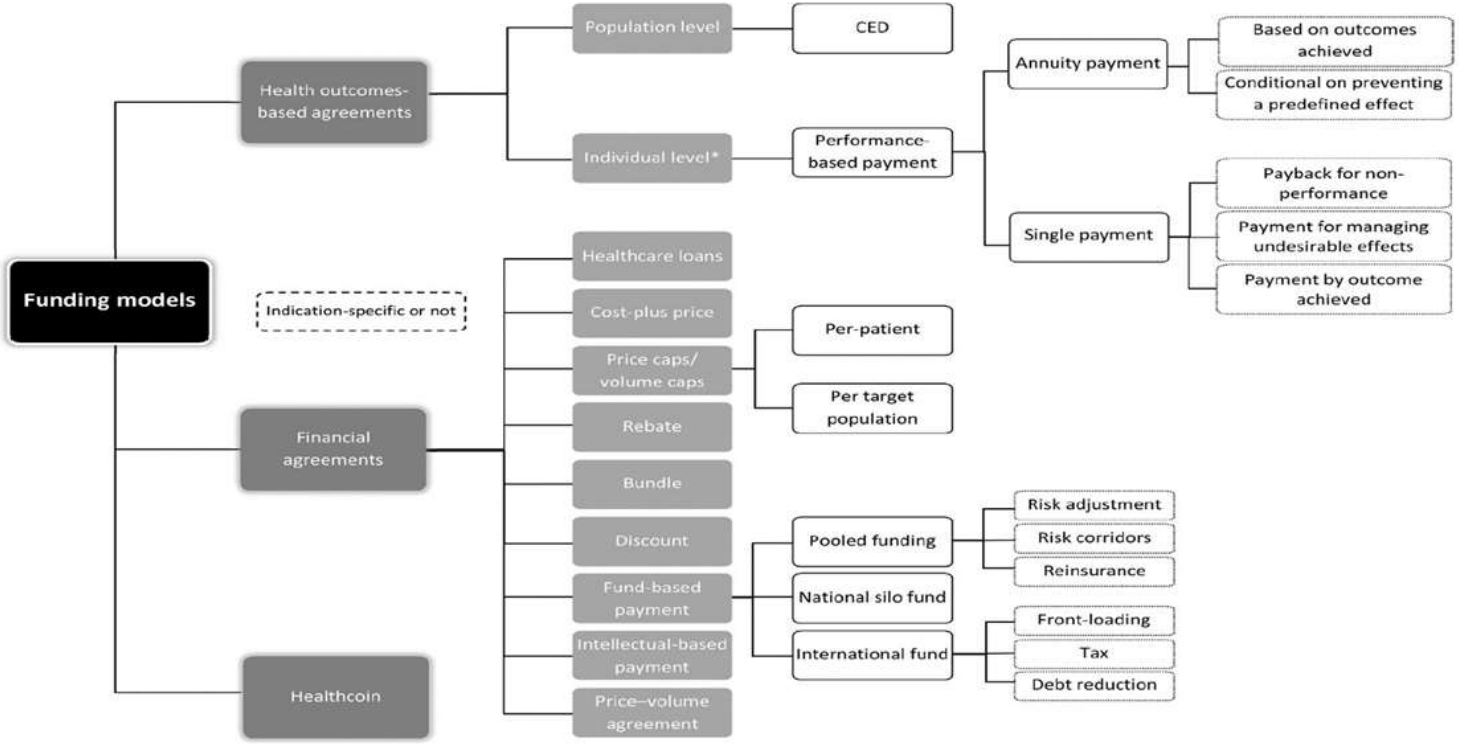
- No existing method of aggregation is perfect
  - Pragmatic approaches needed
  - Severity weights already reality
  - Equity adjusted approaches developing
- Advantages of structured deliberation
  - Transparency and accountability
  - Consistency
- Cost per QALY widely used starting point (US and Europe)
  - ‘Aid to’ rather than ‘substitute for’ informed decision making
  - Form of qualitative MCDA
- Augmented CEA – quantitative MCDA with decision rules

Proposed checklist for cell and gene therapies

Item	Yes	No	Notes
Clinical effectiveness			
Surrogate endpoint used	☐	☐	Validation given?
Rare disease	☐	☐	Prevalence _____
Serious condition	☐	☐	
Single-arm trial	☐	☐	Matched historical cohort used?
Pediatric population	☐	☐	Age range _____
Reporting of adverse consequences and risks	☐	☐	
Size of clinical trial	____ number of patients		
Length of clinical trial	____ duration in months		
Extrapolation to long-term outcomes	____ duration in months		
	Yes	No	Quantification
Elements of value			
Severe disease	☐	☐	
Value to caregivers	☐	☐	
Insurance value	☐	☐	
Scientific spillovers	☐	☐	
Lack of alternatives	☐	☐	
Substantial improvement in life expectancy	☐	☐	
	Yes	No	Notes
Other considerations			
Discounting			
Different discount rates explored	☐	☐	
Uncertainty			
Alternative payment models explored	☐	☐	

Drummond et al. Value in Health. 2019; 22(6): 661–668

Managing risk and uncertainty – *Choosing between policy options?*



*per patient per course, or overall per year

CED: Coverage with Evidence Development

Managing uncertainty and risk sharing

- Risk sharing assessments typically separated from HTA
  - Need greater awareness and consistency in the application of methods to address risks
- One-off treatment increases financial risk to payer
  - Irreversibility vs repeat treatment
  - Financial arrangements or risk sharing can eliminate additional risks
  - Outcomes-related payment and amortization particularly relevant
- Performance based payment linked to real-world monitoring should be encouraged
  - Informed by explicit analyses

Budget impact and affordability

- Broader challenges to conventional HTA methods approaches
  - Affordability and 'fair-price' concerns
  - Prevalent population and first-mover advantage
  - Limited potential for brand-to-brand competition
  - Lack of generic entry
- Development of approaches which explicitly consider different dynamics
  - QALY cap (no allowance for cost-offsets)
  - Mock patent cliff (allowance for cost-offsets for specific period)
  - Shared savings (% of cost offsets)
- Rate of return approaches for orphan products?*

* Berdud et al (2018). OHE Paper 18/05

Conclusions

- Importance of initial starting point
  - Need for general reference case before ‘adapting’
  - Cost per QALY imperfect but a ‘tool not a rule’
  - Structured deliberation process critical
- Unique features of C&G therapies?
  - Further research required on distinctive value elements
  - Can be accommodated in existing frameworks
  - Zero sum game?
- Higher financial risks
  - Role for formally linking HTA assessments to pricing/managed entry schemes
- Consider different market dynamics and implications for conventional HTA approaches