TELUS Health

Gene Therapy: Challenges in determining value for money to make evidence-informed reimbursement decisions

TELUS Health Annual Conference

April 27, 2021

Cell and gene therapies

Keynote conversation

Joan Weir
Director, Health and Disability Policy, CLHIA

Karen Lee
Director, Health Economics, CADTH

Dr Mike Drummond
Professor, Health Economics, University of York

Cell + Gene Therapy: Private Insurance

Telus Health Annual Conference, April 27, 2021

Overview

- Overview of Cell and Gene Therapy
- Payer Process Considerations
- Potential Funding Models

Overview of Gene Therapy

- **Cell and Gene therapy** is a medical field which focuses on the genetic modification of cells to produce a therapeutic effect or the treatment of disease by repairing or reconstructing defective genetic material.
- **Treatments approved in Canada**:
  - Luxturna (mutation-induced blindness)
  - Kymriah (cancer)
  - Yescarta (cancer)
  - Zolgensma (spinal muscular atrophy)

Conventional Therapy

Uses small molecules, peptides, proteins

Treatment contains a small (most drugs) or large (biologics) molecule that mimics or disrupts processes associated with a condition or disease

Chronic therapy

Many conventional treatments must be taken by pill, injection or infusion on a continual basis. and usually the effect of treatment stops once the medication is stopped

Manage or treat symptoms long-term

Usually relieves the signs and symptoms of disease

Cell and Gene Therapy

Uses DNA, RNA, Cells

Reprograms the body to directly fight disease

One-time Treatment

Effect of treatment may be permanent after a single administration

Potentially Curative

Potential to transform medicine. halting the progress of a disease or alleviating the underlying cause of a disease

https://www.novartis.com/our-focus/cell-and-gene-therapy/new-era-medicine

Practical Considerations of Cell + Gene Therapy

- Place of administration
- Placing the treatment order
- Ex vivo vs in vivo
- Accredited laboratories

Payer Considerations

- Overall affordability of treatments
- One-time treatment vs ongoing
- Not eligible for pooling
- Patients may move between payers, including private-public-private
- Uncertainties around longer-term effects

Funding Models

- Direct payment
- Pay for performance
- Negotiated pricing maximums
- Annuity
- Negotiated discounts


CLHIA
ACCAP
Thank you
Joan Weir, jweir@clhia.ca

Gene Therapies – Considerations for Public Reimbursement

TELUS HEALTH ANNUAL CONFERENCE

APRIL 27, 2021

KAREN LEE, DIRECTOR, HEALTH ECONOMICS

CADTH

Disclosure

Employed by CADTH

Adjunct professor with the School of Epidemiology and Public Health at the University of Ottawa

- CADTH is funded by contributions from the Canadian federal, provincial, and territorial ministries of health, with the exception of Quebec.
- CADTH receives application fees from the pharmaceutical industry for:
  - CADTH Pharmaceutical Reviews, including Common Drug Review, pan-Canadian Oncology Drug Review, and Interim Plasma Protein Product Review
  - CADTH Scientific Advice

CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence about the optimal use of drugs and medical devices.

CADTH

CADTH

- Considers clinical effectiveness and cost effectiveness to assess health technologies
- Also considers patient concerns, implementation considerations, and ethical issues

Clinical evidence for technologies

- Focus on RCTs as high quality evidence
- Considered gold standard
- Strong scientific rigor / internal validity

CADTH

Clinical evidence – some limitations

- Short duration
- Efficacy outcomes (surrogates, intermediate outcomes)
- Specific patient populations
- Not comparative

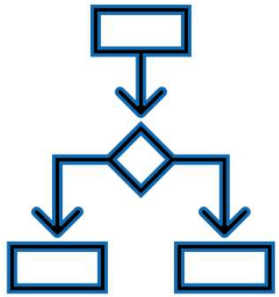
- Not necessarily reflective of actual clinical practice – designed to address specific question
- May have limited applicability to decision making

How we make decisions…

- Is the new technology better than what we are current using/doing?
- How should we use the technology to maximize benefits (and minimize harms)?
- What about the value of the technology to the health system/setting?

Decision analysis

- Decision analysis provides a framework to piece together various data sources and evaluate effect of parameters on estimated outcomes
  - Allows experimentation not possible in real world
  - Allows extrapolation beyond the time horizon of existing data
  - Brings together data and assumptions explicitly
  - Allows assessment of value for money – what we are gaining in terms of population health
  - What drives the results and areas where additional research could be informative

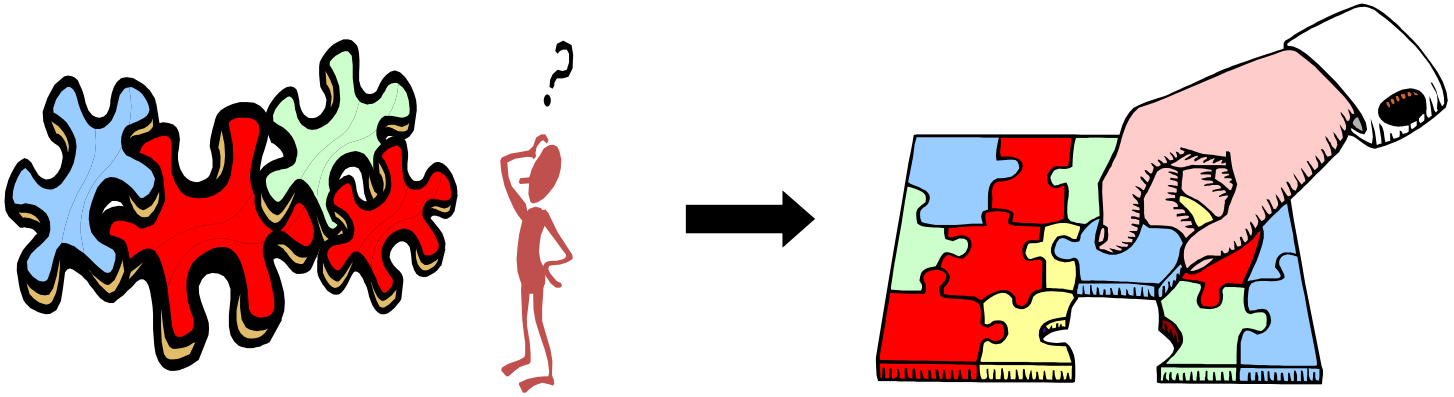


Health economics

- Comparison of technology and relevant comparators (current management) – opportunity cost
- Consideration of total costs and meaningful effects (ratio of costs and effects – single metric) – incremental cost effectiveness ratio (ICER)
- Effects often reported in terms of clinically meaningful effects or quality adjusted life years (QALYs) – allowing comparisons across various conditions, technologies

What does it provide us?

- Consistent framework – ability to understand the impact of making decisions
- Ability to understand impact of uncertainty
- Tool to understand evidence gaps and where to focus future research



What happens for gene therapies?

- Should we consider economics?
- Do potentially curative therapies need different considerations?
- Do treatments warrant a premium over other treatments?

Gene therapies @ CADTH

- Reviewed through the same process for all drug reviews at CADTH, with additional requirements for submission
- Additional considerations for reviews: ethical implications, implementation issues
- Economics remains a consideration
  - Issue of constrained budgets and choice – how to optimize the health of Canadians within a fixed budget
  - How to prioritize and what to forgo
  - A framework to understand what we don't know (uncertainty)
  - A tool for decision making

What are some of the issues?

- High upfront costs - certain
- Clinical benefits realized over longer term – uncertain
- Some aspects we don’t know (need for retreatment) - uncertain

How to manage certain costs and less certain benefits??

How to manage uncertainty?

- Pay for performance
- Installments
- Rebates

Who bears the risk?

Summary

- Economics remains an important consideration for the assessment of gene therapies
- Economic evaluations allows us to better understand the impact of clinical uncertainty and potential ways to manage it
- Additional considerations may also be relevant in the assessment of these technologies

Should Gene Therapy be Valued Differently from Other Therapies?

Michael Drummond, DPhil
Professor of Health Economics
Centre for Health Economics
University of York, UK

Outline of Presentation

- What value do gene therapies offer?
- Are there any important characteristics of gene therapies?
- What are the implications for the assessment of gene therapies?

Estimates of QALYS gained from the literature for a selection of cell and gene therapies

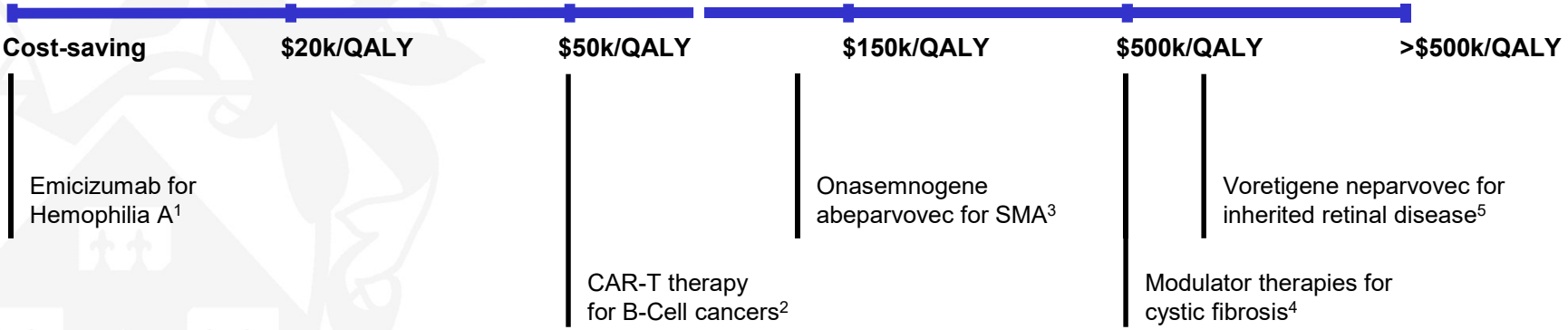
Treatment name	Indication	Incremental QALY gain estimate
Onasemnogene abeparvovec (Zolgensma®)	Spinal muscular atrophy	11.77[1]
GSK2696273 (Strimvelis®)	Adenosine deaminase deficiency	11.7[2]
Experimental gene therapy for hemophilia A	Hemophilia A	8.33[3]
Tisagenlecleucel (Kymriah®)	Refractory B-cell acute lymphoblastic leukemia	8.18[4]
Axicabtagene ciloleucel (Yescarta®)	Refractory B-cell acute lymphoblastic leukemia	3.19[5]
Voretigene neparvovec (Luxturna®)	RPE65-mediated inherited retinal disease	1.3[6]
ChondroCelect®	Knee cartilage lesions	1.28[7]
Talimogene laherparepvec (Imlygic®)	Melanoma	0.16[8]

QALY, quality-adjusted life year.

1. ICER (2019). Value Assessment Methods and Pricing Recommendations for Potential Cures: A Technical Brief. Available at: https://icer-review.org/wp-content/uploads/2019/08/ICER_TechnicalBrief_SSTs_080619.pdf. Last accessed November 2020; 2. NICE (2017). Evaluation consultation document: Strimvelis for treating adenosine deaminase deficiency–severe combined immunodeficiency. Available at: https://www.nice.org.uk/guidance/hst7/documents/evaluation-consultation-document. Last accessed November 2020; 3. Machin N, *et al. Blood Adv*. 2018;2(14):1792–8; 4. Whittington MD, *et al. JAMA Ped*. 2018;172(12):1161–8;
5. Whittington MD, *et al. JAMA Netw Open*. 2019;2(2):e190035; 6. Zimmermann M, *et al. Value Health Reg Issues*. 2019;22(2):161–7; 7. Gerlier L, *et al. Pharmacoeconomics*. 2010;28(12):1129–46 [ABSTRACT]; 8. Almutairi AR, *et al. JAMA Dermatol*. 2019;155(1):22–28.

Are Cell and Gene Therapies Cost-Effective?

Evidence from ICER reviews in the US



ICER, Institute for Clinical and Economic Review; QALY, Quality-adjusted life year.

1. ICER (2018). Emicizumab for Hemophilia A: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/08/ICER_Hemophilia_A_Draft_Report_012618.pdf. Last accessed November 2020; 2. ICER (2018). Chimeric Antigen Receptor T-Cell Therapy for BCell Cancers: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf. Last accessed November 2020; 3. ICER (2019). Spinraza® and Zolgensma® for Spinal Muscular Atrophy: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2018/07/ICER_SMA_Final_Evidence_Report_052419.pdf. Last accessed November 2020; 4. ICER (2020. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2019/09/ICER_CF_Draft_Report_022020.pdf. Last accessed November 2020; 5. ICER (2018). Voretigene Neparvovec for Biallelic RPE65- Mediated Retinal Disease: Effectiveness and Value. Available at: https://icer-review.org/wp-content/uploads/2017/06/MWCEPAC_VORETIGENE_EVIDENCE_REPORT_01122018-1.pdf. Last accessed November 2020.

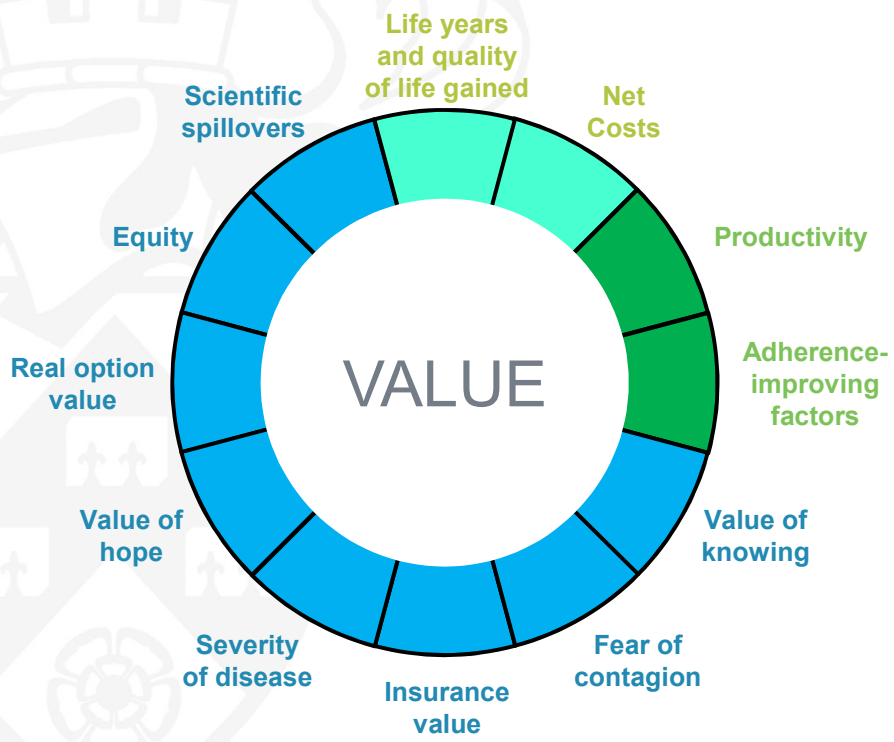
Is there a case for paying more for gene therapies?

J Manag Care Spec Pharm. 2019 Jul;25(7):793-799. doi: 10.18553/jmcp.2019.18378.
Epub 2019 Feb 20.

Value-Based Pricing for Emerging Gene Therapies: The Economic Case for a Higher Cost-Effectiveness Threshold

Louis P Garrison [1], Tristen Jackson [2], Douglas Paul [2], Mike Kenston [3]
Affiliations + expand
PMID: 30784347 DOI: 10.18553/jmcp.2019.18378

Potential Elements of Value to Consider[1]



- Core elements of value
- Common but inconsistently used elements of value
- Potential novel elements of value

- Figure adapted from Lakdawalla DN, *et al. Value Health* 2018;21:131–139.

1. Drummond M, *et al. Value Health.* 2019;22(6):661–668.

The economic case for a higher cost-effectiveness threshold for innovative therapies[1]

Several organizations assessing the value of health technologies have a higher cost-effectiveness threshold for treatments for ultra-rare or health-catastrophic conditions[1]

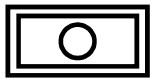
Some of the broader concepts of value are particularly relevant, such as:[1]

Severity of disease

Insurance value

Real option value

Value of hope



Equity

1. Garrison LP, *et al. J Manag Care Spec Pharm*. 2019;25(7):793-799.

Modifiers* used by the Scottish Medicines Consortium (SMC)[1]

Evidence of a substantial increase in life expectancy (>3 months)

Evidence of a substantial improvement in quality of life

Evidence that a sub-group may derive specific or extra benefit

Absence of other therapeutic options of proven benefit

Possible bridging to another proven therapy

Emergence of a licensed medicine as the only therapeutic option for a specific indication

*Modifiers represent situations where a higher cost per quality-adjusted life year threshold may be accepted.
SMC, Scottish Medicines Consortium.

1. SMC (2012). SMC modifiers used in appraising new medicines. Available at: https://www.scottishmedicines.org.uk/media/3565/modifiers.pdf. Last accessed: November 2020.

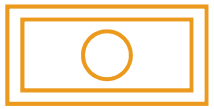
Experience from the National Institute for Health and Care Excellence (NICE) in England

No special treatment of gene therapy *per se*

Some gene therapies for rare conditions may qualify for the "Highly Specialised Technologies' (HST) programme[1]

eg the condition is chronic and severely disabling

the patient group is small and treatment is delivered exclusively in the context of a highly specialized service



The HST programme provides for a higher cost-effectiveness threshold of £100,000 per QALY, with the possibility of rising to £300,000 per QALY if 30 QALYs are gained over the patient's lifetime[1]

HST, Highly Specialised Technologies; QALY, quality-adjusted life year.

1. NICE (2017). NICE and NHS England consultation on changes to the arrangements for evaluating and funding drugs and other health technologies assessed through NICE's technology appraisal and highly specialised technologies programmes. Available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/board-paper-TA-HST-consultation-mar-17-HST-only.pdf. Last accessed: November 2020

Important characteristics of gene therapy affecting their assessment

- Rare conditions
- Single-arm trials
- Pediatric populations
- More uncertainty about long-term effects
- Large caregiver impacts
- Role of discounting
- Scientific spillovers

1. Drummond M, *et al. Value Health*. 2019;22(6):661–668.

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Contents lists available at sciencedirect.com
Journal homepage: www.elsevier.com/locate/jval

Analytic Considerations in Applying a General Economic Evaluation Reference Case to Gene Therapy

Michael F. Drummond, PhD,[1,*] Peter J. Neumann, ScD,[2] Sean D. Sullivan, PhD,[3] Frank-Ulrich Fricke, PhD,[4] Sean Tunis, MD, MSc,[5] 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 Risk in Health, Tufts Medical Center, Boston, MA, USA; [3]CHOICE Institute, School of Pharmacy, University of Washington, Seattle, WA, USA; [4]Fakultät Betriebswirtschaft, Technische Hochschule Nürnberg Georg Simon Ohm, Nürnberg, Germany; [5]Center for Medical Technology Policy, Baltimore, MD, USA; [6]AveXis Inc, Bannockburn, IL, USA; [7]Public Health Department, Aix-Marseille University, Marseille, France.

ABSTRACT

The concept of a reference case, first proposed by the US Panel on Cost-Effectiveness in Health and Medicine, has been used to

Checklist for assessing gene therapies[1]

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	☐	☐	

1. Drummond M, *et al. Value Health*. 2019;22(6):661–668.

Conclusions

Cost/QALY analyses provide a starting point for discussions of value

A completely new approach for assessing gene therapies is not required, but a tailored checklist for analysts and decision makers can be helpful

Payers need to consider carefully how they cover and reimburse gene therapies for rare diseases, based on their objectives and budget

QALY, quality-adjusted life year.

Questions


Thank you
TELUS Health