Health Technology Assessment for Gene Therapies: Are Our Methods Fit for Purpose? — A Patient Perspective

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CONSULTANT	NHF

"The safest and most effective drug that no one can afford, is not available or arrives too late is of no benefit to a patient."

Hans-Georg Eichler, Lynn Baird, Richard Barker, et.al.. (2014). From adaptive licensing to adaptive pathways: delivering a flexible life-span approach to bring new drugs to patients. Clin. Pharmacol. Ther. DOI: 10.1002/cpt.59.

Real world evidence (RWE) is transforming the process through which health care payers make coverage and formulary decisions[1]

Standards for prospective RWE analyses … to ensure evidence generated is both rigorous and fully informed by what matters most to patients[1]

Defining and measuring health outcomes with greater direct patient engagement is vital for assessing value of novel technologies[2]

Improved patient involvement can drive the development of innovative medicines that deliver more relevant and impactful patient outcomes[2]

[1]Garrison, L., et al., Using Real-World Data for Coverage and Payment Decisions: The ISPOR Real-World Data Task Force Report. Value Health. 2007 Sep-Oct;10(5):326-35.
[2]Hoos, A et al. Partnering with patients in the development and lifecycle of medicines: a call for action. Ther Innov Regul Sci. 49:929–39.(2015)

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Standardizing Patient Outcomes Measurement

Michael E. Porter, Ph.D., M.B.A., Stefan Larsson, M.D., Ph.D., and Thomas H. Lee, M.D.

The arc of history is increasingly clear: health care is shifting focus from the volume of services delivered to the value created for patients, with "value" defined as the outcomes achieved relative to the costs.[1] But progress has been slow and halting, partly because measurement of outcomes that matter to patients, aside from survival, remains limited. And for many conditions, death is a rare outcome wh
to differen
merely com

viders to embrace accountability for results.

If we're to unlock the potential of value-based health care for driving improvement, outcomes measurement must accelerate. That means committing to measuring a minimum sufficient set of outcomes for every major medical condition — with well-defined methods for their collection and risk adjustment — and then

example, only 139 (7%) are actual outcomes and only 32 (<2%) are patient-reported outcomes (see bar graph).[2] Defaulting to measurement of discrete processes is understandable, given the historical organization of health care delivery around specialty services and fee-for-service payments.

Yet process measurement has had limited effect on value. Such measures receive little attention

Perspective

DECEMBER 23, 2010

What Is Value in Health Care?

Michael E. Porter, Ph.D.

In any field, improving performance and accountability depends on having a shared goal that unites the interests and activities of all stakeholders. In health care, however, stakeholders have myriad, often conflicting goals, including

Value — neither an abstract ideal nor a code word for cost

value is a central challenge. Nor is value measured by the process of care used; process measurement and improvement are important tactics but are no substitutes for measuring outcomes and costs.

Since value is defined as out

- Historically, outcomes measurement has focused on clinical status and left out functional status
  - Survival and "objective" outcomes that are readily captured by laboratory tests
- What matters to patients are outcomes that encompass the whole cycle of care
  - Survival, functional status, quality of life

Porter ME, et al. N Engl J Med 2010, 2016

"One reason ICER and some drug companies disagree on a drug's fair price is the difficulty in capturing the drug's social benefits, such as a patient's increased work productivity, or family members who don't have to be full-time caregivers anymore."[1]

"In assessing the value of treatments for hemophilia, payers should be aware of important benefits and contextual considerations that are not typically captured in cost-effectiveness analyses."[2]

[1]Xconomy Boston 4/23/19 Can We Afford to Be Cured? A Conversation With ICER's Steve Pearson
[2]ICER report reviewing clinical effectiveness and value of emicizumab for patients with hemophilia A and inhibitors to factor VIII – April 2018

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Robust Patient-Centered Evidence Essential

Aims →	Timely collection and reporting of relevant outcomes	Increases predictability and consistency of payer and Health Technology Assessment decisions	Longitudinal data collection on outcomes meaningful to the quality of life and functioning of patients
Uses →	Market Authorization Product Registration	Advocacy Insurance Coverage Ministry of Health	Shared Decision Making Clinical Applications Benchmarking Progress Promoting Health Equity

Reporting outcomes patients deem relevant

- Pain - chronic/acute, interference, occurrence
- Independence - limitations, impact on activities of daily living
- Education - attainment, attendance
- Employment - duration, underemployment, attendance
- Family life - marriage, children
- Mobility - assistance required, impairment
- Current health status (EQ-5D-5L and VAS)

VAS, EuroQol visual analog scale

Skinner MW et al. *Pilot and Feasibility Studies* 2018;4:58.

A "core outcome set" to measure, demonstrate and differentiate the effectiveness and value of gene therapy

	Domain	Outcome
coreHEM Core Outcomes	Physiological/Clinical	• Frequency of bleeds • Factor activity level • Duration of expression
	Pain/Discomfort	• Chronic pain
	Resource Use	• Utilization of healthcare system (direct costs)
	Emotional Functioning	• Mental health
Additional Outcomes	• Duration/frequency/type of physical activity/sport/play • Physical health/general health perception	
Adverse Events	• Short-Term, Long-Term, Mortality	

coreHEM

Green Park Collaborative
A partnership for innovation and effectiveness

National Hemophilia Foundation
for all bleeding disorders

McMaster University

coreHEM mental health

National Hemophilia Foundation
for all bleeding disorders

Visit Poster Code PCR45 - Development of a Patient-reported Outcome Measure (PROM) to Fully Report a Proposed Core Outcome Set

Iorio A, Skinner MW, Clearfield E, et al. ; for the coreHEM panel. Core outcome set for gene therapy in haemophilia: Results of the coreHEM multistakeholder project. Haemophilia. 2018;00:1–6. https://doi.org/10.1111/hae.13504

Is the World Ready for Gene Therapy?

HAEMOPHILIA Volume 28, Supplement 2, March 2022

Contents

SUPPLEMENT ARTICLES

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Is the World Ready for Gene Therapy?

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Haemophilia WILEY

SUPPLEMENT ARTICLE

Health technology assessment for gene therapies in haemophilia

Jamie O'Hara[1,2] | Peter J. Neumann[3] | on behalf of the International Haemophilia Access Strategy Council[1]

KEY POINTS OF CONSIDERATION

- It is important for HTA bodies to consider the limitations to conduct randomized controlled trials for gene therapy and to consider intra-patient data as evidence of comparative effectiveness.
- Given the uncertainties around the long-term gene therapy use, clinical trial data should be extrapolated ~10 years, using scenarios that consider different durations of effect.
- The major value drivers in a model, in addition to drug pricing itself, will be based on assumptions about duration of effect and savings/cost offsets from reduced use of replacement therapy.
- Assessment methodologies and modelling configurations need to evolve to fully capture the value of gene therapy, including patient meaningful outcomes, in a validated and quantitative fashion.
- Regardless of payment system archetype, the intersection between NGOs, the clinical community's voice, HTA willingness to collaborate, and alignment with regulatory acceptance of benefit is critical.

O'Hara, J, Neumann, PJ. Health technology assessment for gene therapies in haemophilia. *Haemophilia*. 2022; 28(Suppl. 2): 19– 26. https://doi.org/10.1111/hae.14413

Is the World Ready for Gene Therapy?

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Haemophilia WILEY

SUPPLEMENT ARTICLE

A preliminary application of a haemophilia value framework to emerging therapies in haemophilia

Mark W. Skinner[1,2] | Gerry Dolan[3] | Hermann Eichler[4] | Brian O'Mahony[5,6] |
on behalf of the International Haemophilia Access Strategy Council

KEY POINTS OF CONSIDERATION

- With the emergence of high-cost, paradigm changing treatments across multiple areas of medicine, we, the haemophilia community, need to be equipped to meet the growing demands for more rigorous evidence-based value assessments using the tools expected by assessors.
- The traditional access toolbox needs to evolve to meet the paradigm shift in treatment options. Value can no longer be defined by annualized bleed rates alone. To realize the full impact of new therapies, we need to utilize tools, such as a value framework, to organize evidence, identify data gaps, and assess patient-defined, meaningful outcomes across a multi-faceted dimension.
- The haemophilia value framework is an effective tool for organizing the available evidence and identifying gaps in the evidence. This can be used for assessing the value of emerging therapies in haemophilia utilizing data generated through randomized clinical trials and real world evidence generation.
- This is a call for incorporating the Value Framework into official submissions to authorities, as it captures a broader range of outcomes, including patient meaningful outcomes, in ways that better assess the potential benefits of new therapies.

Skinner, MW, Dolan, G, Eichler, H, O'Mahony, B. A preliminary application of a haemophilia value framework to emerging therapies in haemophilia. *Haemophilia*. 2022; 28(Suppl. 2): 9– 18. https://doi.org/10.1111/hae.14511

Haemophilia Value Framework Integrated with coreHEM

		coreHEM Outcome					
		1. Frequency of bleeds	2. Factor activity level	3. Duration of expression	4. Chronic pain	5. Utilization of healthcare system	6. Mental Health
Tier 1: Health Status Achieved or Retained	Statistical life expectancy						
	Overall survival						
	Function/activity						
	Bleeding						
	Serious bleeds						
	Pain						
	Musculoskeletal complications						
	HRQOL						
	"Cure"						
Tier 2: Process of Recovery	Time to initial diagnosis						
	Time to onset of treatment						
	Time to recover from a bleeding episode						
	Time missed at education or employment for treatment						
	Development of inhibitors						
	Pathogen transmission						
	Orthopedic intervention						
	Infection						
	Long-term venous access						
Tier 3: Sustainability of Health	Frequency of breakthrough bleeds						
	Joint preservation						
	Lifelong productivity						
	Sustained good health						
	Long-term disutility of insufficient/ inappropriate therapy						
	Age-related comorbidities & complications						

- coreHEM outcomes are related to multiple value framework outcomes
- Mapped data from the value framework literature review showed differentiating clinical data between GT and SOC for each coreHEM outcome
- **Several mapped outcomes (dark gray) lacked accompanying clinical data representing areas that warrant additional research and <u>timely</u> publication**

M. Skinner et al; Haemophilia Gene Therapy Outcomes: Integration of the Haemophilia Value Framework with coreHEM; (2022), Poster Presentations (PO066). Haemophilia, 28: 25-126.
Filled cells = mapped outcome; BLUE = differentiating for GT vs replacement factor; GREEN = differentiating for GT vs replacement factor, supported by primary research; GRAY = no published data available

Beware of Panglossian* Thinking

Haemophilia. 2018;24(Suppl. 6):60–67.

Past, present and future of haemophilia gene therapy: From vectors and transgenes to known and unknown outcomes

G. F. Pierce[1,2] | A. Iorio[3]

Haemophilia. 2020;00:1–3.

Gene therapy to cure haemophilia: Is robust scientific inquiry the missing factor?

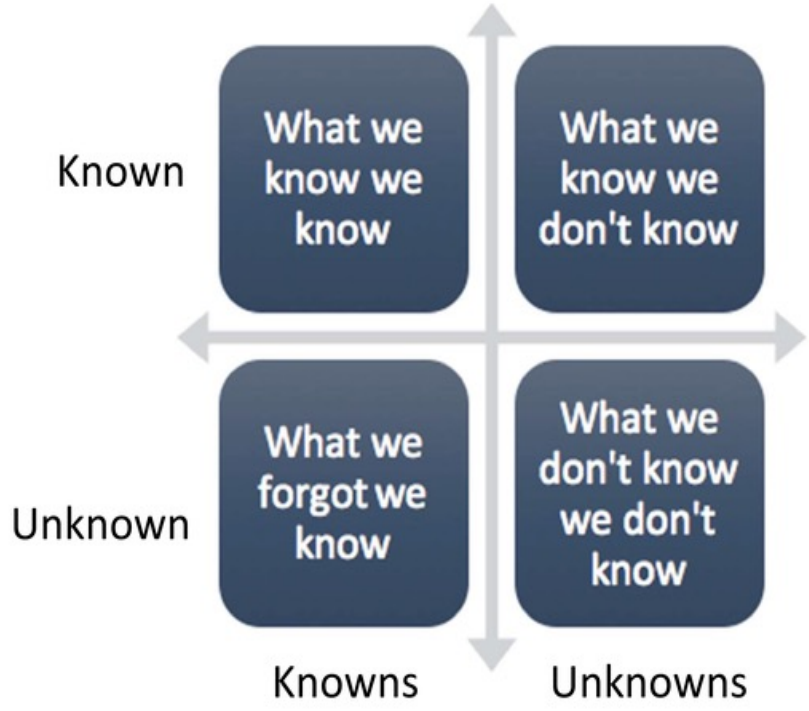
Glenn F. Pierce[1] | Radoslaw Kaczmarek[2] | Declan Noone[3] | Brian O'Mahony[4] | David Page[5] | Mark W. Skinner[6]

Molecular Therapy Vol. 29 No 12 December 2021

Eliminating Panglossian thinking in development of AAV therapeutics

Radoslaw Kaczmarek,[1] Glenn F. Pierce,[2] Declan Noone,[3] Brian O'Mahony,[4] David Page,[5] and Mark W. Skinner[6]

https://doi.org/10.1016/j.ymthe.2021.10.025



*Characterized by or given to extreme optimism, especially in the face of unrelieved hardship or adversity.
Adapted from R Kaczmarek WFH World Congress 2022; May2022

Thank you.
Questions?

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