NOVEMBER/DECEMBER 2025 VOL. 11, NO. 6

VALUE & OUTCOMES SPOTLIGHT

An HEOR news magazine

ARTIFICIAL INTELLIGENCE Is Leveling Up HEOR, BUT STILL NEEDS A Humanity Check

ISPOR

VALUE & OUTCOMES SPOTLIGHT

NOVEMBER/DECEMBER 2025
VOL. 11, NO. 6

VALUE & OUTCOMES SPOTLIGHT

An HEOR News Magazine

The mission of *Value & Outcomes Spotlight* is to foster dialogue within the global health economics and outcomes research (HEOR) community by reviewing the impact of HEOR methodologies on health policy and healthcare delivery to ultimately improve decision making for health globally.

ISPOR
Improving healthcare decisions

TABLE OF CONTENTS

ISPOR HEADQUARTERS

505 Lawrence Square Blvd, S
Lawrenceville, NJ 08648
Tel: 609-586-4981
info@ispor.org
www.ispor.org

VALUE & OUTCOMES SPOTLIGHT
EDITORIAL OFFICE:
Value & Outcomes Spotlight
Online: ISSN 2375-8678
Published bimonthly by:
ISPOR
505 Lawrence Square Blvd, S
Lawrenceville, NJ 08648 USA

Direct photocopy permission and reprint requests to Director, Publications.

Cover photo courtesy of AdobeStock/KazeRiver

FROM THE EDITOR

The Intelligent Frontier: Navigating AI's Transformative Role in HEOR

The development of artificial intelligence (AI) has progressed from an emerging concept to a vital instrument used in numerous industries, with significant impact observed within health economics and outcomes research (HEOR). Over the past 2 decades, AI has not merely streamlined HEOR workflows but has fundamentally reshaped how researchers approach data, evidence, and decision making. However, this profound promise comes hand-in-hand with significant ethical considerations and the urgent need for robust regulatory frameworks.

Initially, AI's role in HEOR primarily involved machine learning for predictive and economic modeling. Today, the landscape is far more sophisticated, integrating generative AI, or large-language models, which can engage in text-based conversations, answer complex questions, and even draft research papers. Complementing this, agentic AI operates autonomously, gathering and analyzing data, setting goals, and learning from its experiences. These advancements are not theoretical; they are actively driving efficiency and insight.

The utility of AI truly shines in evidence synthesis, a cornerstone of HEOR. Generative AI is proving invaluable for synthesizing complex literature, providing comprehensive overviews of research topics, and identifying crucial gaps in existing knowledge. AI excels at processing enormous quantities of diverse health data—from electronic health records and genomic information to real-world evidence. This allows researchers to quickly identify subtle patterns, correlations, and predictors that are often imperceptible to humans. In outcomes research, this translates to more accurate risk stratification, better prediction of treatment response, and deeper insights into disease progression and patient journeys. AI can personalize interventions by tailoring treatment plans based on individual characteristics, optimize clinical trial design for greater efficiency, and even accelerate drug discovery by identifying potential candidates. By automating data analysis and generating hypotheses, AI significantly reduces research time and costs, leading to faster evidence generation and, ultimately, improved patient care.

> AI can personalize interventions by tailoring treatment plans based on individual characteristics, optimize clinical trial design for greater efficiency, and even accelerate drug discovery by identifying potential candidates.

In particular, AI is revolutionizing next-generation sequencing (NGS) by dramatically enhancing the speed and accuracy of genomic data analysis. AI algorithms excel at processing the vast amounts of data generated by NGS, identifying subtle genetic variations, and interpreting complex genomic landscapes far more efficiently than traditional methods. This integration is profoundly impacting health outcomes by enabling faster, more precise disease diagnostics, particularly for rare diseases and cancer. It facilitates truly personalized medicine, guiding tailored treatments based on an individual's unique genetic profile. Furthermore, AI-driven NGS accelerates drug discovery, identifies novel therapeutic targets, and improves our understanding of disease susceptibility and progression, ultimately leading to more effective interventions and improved patient care.

Despite its immense potential and impressive capabilities, AI in health outcomes research faces significant challenges. Primary concerns are data quality and inherent biases. If AI models are trained on data that reflect historical inequities or underrepresent certain populations, they can perpetuate or even amplify existing health disparities.

The "black box" problem, where complex AI models lack transparency, makes it difficult to understand why a particular outcome is predicted, hindering trust and clinical adoption. Data privacy and security are paramount, given the highly sensitive nature of health information, requiring robust safeguards. Implementing AI solutions is also costly, demanding substantial investment in infrastructure, specialized expertise, and ongoing maintenance. Ethical considerations regarding accountability, informed consent, and potential unintended consequences also necessitate careful thought and robust regulatory frameworks.

Several of these vulnerabilities highlight the essential role of including a "human-in-the-loop" element. As emphasized by Harlen Hays of Cardinal Health in our feature article, ongoing human engagement is necessary to verify accuracy, establish boundaries for autonomous agentic AI, and enforce privacy and security protocols when managing patient data. Additionally, the independence of agentic AI presents challenges in distinguishing authentic patterns from potential "hallucinations" by the system.

> The prevailing view that regulation consistently lags innovation underscores the necessity for proactive collaboration between AI leaders and policy makers regarding the technology's use in healthcare and HEOR.

To address these multifaceted challenges, organizations like the World Health Organization (WHO) and ISPOR have begun publishing ethical frameworks for AI in healthcare and HEOR. These guidelines aim to provide direction for responsible AI deployment. However, the consensus from experts is that enforceable, global regulatory frameworks will ultimately be required to govern AI's development and use. The prevailing view that regulation consistently lags innovation underscores the necessity for proactive collaboration between AI leaders and policy makers.

AI is undoubtedly a transformative force in HEOR, revolutionizing everything from NGS to evidence synthesis. Its capacity to enhance efficiency and uncover insights is unparalleled. Nevertheless, its responsible implementation depends on thoroughly resolving ethical issues and establishing comprehensive legal and regulatory frameworks. Navigating the future of AI in health outcomes research requires a balanced approach, harnessing its power while rigorously addressing its limitations and ethical implications to ensure equitable and effective advancements. The future of HEOR with AI is one of augmentation, where human expertise remains paramount.

As always, I welcome input from our readers. Please feel free to email me at zeba.m.khan@hotmail.com.

Zeba M. Khan, RPh, PhD
Editor-in-Chief,
Value & Outcomes Spotlight

FROM THE CEO

Reflections on the Past, Present, and Future of AI in HEOR and Healthcare Decision Making

Rob Abbott, CEO & Executive Director, ISPOR

In 1955, when John McCarthy had the idea to organize a summer workshop at Dartmouth College to develop ideas about "thinking machines", I wonder if he could have imagined what the future might hold. McCarthy—alongside his workshop co-organizers, Claude Shannon, Nathaniel Rochester, and Marvin Minsky—is today considered to be one of the founding fathers of artificial intelligence (AI).

The history of AI in healthcare can be traced from those formative discussions at Dartmouth College in the 1950s through to the sophisticated machine learning and large language model applications that are rapidly changing the way we think about and undertake diagnostics in medical imaging, power robotic surgeries, accelerate drug discovery, and streamline hospital and clinic administration. Key milestones in this journey over the past 70 years include:

- The development of MYCIN in the early 1970s. MYCIN was an expert system to diagnose bacterial infections and recommend appropriate antibiotics based on a set of 600 "if-then" rules.
- The application of neural networks and pattern recognition to medical images in the late 1980s and 1990s, and the first commercial computer-aided detection system for mammography receiving approval from the US Food and Drug Administration (FDA) in 1998.
- The onset of IBM Watson in 2011. IBM's question-answering system, Watson, gained wide prominence by winning the TV show *Jeopardy!* This helped advance public awareness of AI capabilities and demonstrated Watson's ability to handle complex natural language queries. Soon after, Watson's capabilities were applied to healthcare for processing unstructured clinical data and identifying new research insights.
- In 2017, CardioAI received FDA approval for analyzing cardiac MRI images—a significant milestone for clinical integration.

In light of the above, it seems fitting that *Value and Outcomes Spotlight* should undertake a deep dive into the shape of current thought on AI in health economics and outcomes research (HEOR) and healthcare decision making more broadly. We know, for instance, that natural language processing has advanced significantly in recent years to the point where it is possible to extract information from physician notes and bring the idea of virtual health assistants—Pharmbot—to life. We also know that large language models like ChatGPT have the potential to transform personalized medicine, drug discovery, and clinical decision support through their ability to analyze vast, diverse datasets.

As the papers gathered here make clear, AI has become a dominant theme in HEOR and healthcare. Three examples underscore just how pervasive AI's influence is in this regard. In **next-generation sequencing**, AI is used to analyze large data sets, which helps accelerate sequencing, reduce errors, identify genetic variations, and enable personalized medicine. AI-powered tools can also improve disease diagnosis, predict treatment responses, and identify potential drug targets by integrating genomic data with other health information. In **evidence synthesis**, AI automates various stages of the process, such as literature searching, article screening, and data extraction, which increases efficiency and speed. AI tools such as machine learning and natural language processing can identify relevant studies, extract data, and help with tasks such as trial design and synthesizing information for summaries. Importantly, the role of AI in this context is one of enhancing efficiency; human oversight is still needed—indeed it is critical—for validation and to avoid errors. In **medical imaging**, AI can enhance the analysis of medical images such as X-rays, MRIs, and CT scans by identifying patterns that human radiologists might miss. These insights help to diagnose diseases earlier and more accurately.

> Large language models like ChatGPT have the potential to transform personalized medicine, drug discovery, and clinical decision support through their ability to analyze vast, diverse datasets.

As the use of AI in HEOR and healthcare decision making increases, it is inevitable that we must address ethical and legal considerations. While this is a domain that is changing quickly, it is fair to say that the ethical frameworks for AI in HEOR are generally expansions of the 4 core principles of biomedical ethics: beneficence (doing good), non-maleficence (doing no harm), autonomy (respecting individuals' decisions), and justice (fairness and equity). On the legal side of the equation, the emerging frameworks reflect a desire to adapt existing law to AI-specific applications, and equally, to develop new AI-specific guidelines and regulations. In the United States, the Health Insurance Portability and Accountability Act sets standards for protecting patient health information. Compliance requires data encryption, access controls, audit trails, and Business Associate Agreements with third-party vendors. In the European Union

(EU), the General Data Protection Regulation mandates lawful, transparent data processing for specific purposes and grants individuals rights such as access, correction, deletion, and the right not to be subject to decisions based solely on automated processing. FDA has started elaborating guidance for AI and machine learning as Software as a Medical Device, focusing on safety, effectiveness, and a total product lifecycle approach. The EU AI Act is a key regulation for establishing a uniform legal framework governing the development and use of AI systems within the EU, often following a risk-based approach.

> Human oversight is vital to justify causal assumptions, interpret HTA-specific requirements, ensure structural validity, or meet transparency and auditability requirements.

I am proud to report that ISPOR has developed guidance and recommendations emphasizing transparency, accountability, and best practices for using AI in HEOR.

Alongside the excitement and rapidly growing profile of AI—and with it, a good deal of hype—it is important to emphasize that the best outcomes will be achieved through a combination of both artificial and human intelligence. For instance, AI is not going to fully automate systematic reviews and evidence synthesis. It can, and likely will, accelerate evidence synthesis, but full automation is not acceptable to regulators or health technology assessment (HTA) bodies. Tools like DistillerAI help with screening and data extraction but require human oversight. In the same vein, AI is not going to replace traditional economic models. Health economists still own the core model logic, and while AI can simulate scenarios, detect model inconsistencies, speed up parameter searches, and generate model code (Markov, partitioned survival, microsimulations), human oversight is vital to justify causal assumptions, interpret HTA-specific requirements, ensure structural validity, or meet transparency and auditability requirements.

This is an exciting time to be in HEOR; the accelerated use of AI represents a new frontier that we need to step onto. As your CEO, I pledge that ISPOR will do so courageously and responsibly.

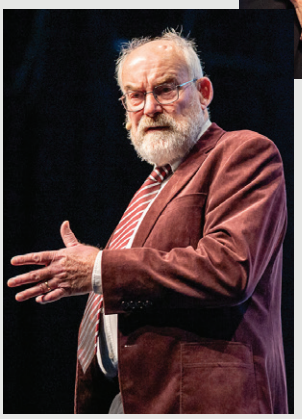
Collaboration, Connection, and Community: ISPOR Europe 2025

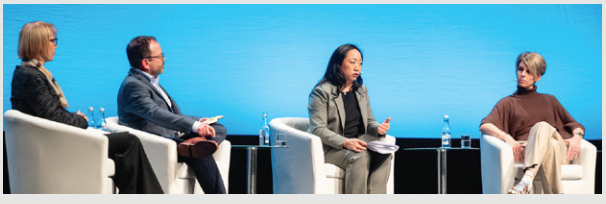
Nearly 6000 professionals from around the world (about half of whom were first-time attendees) converged November 9-12 at the Scottish Event Campus in Glasgow, Scotland for the annual ISPOR Europe 2025 conference.

The event drew a mix of global stakeholders from 89 different countries. Under the theme "Powering Value and Access Through Patient-Centered Collaboration," the conference brought together researchers, policy makers, industry leaders, and patient representatives to shape the future of HEOR.

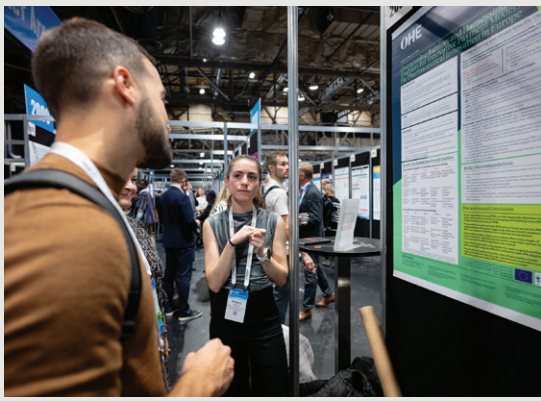
These photos capture the energy, connection, and collaboration that are hallmarks of ISPOR conferences.

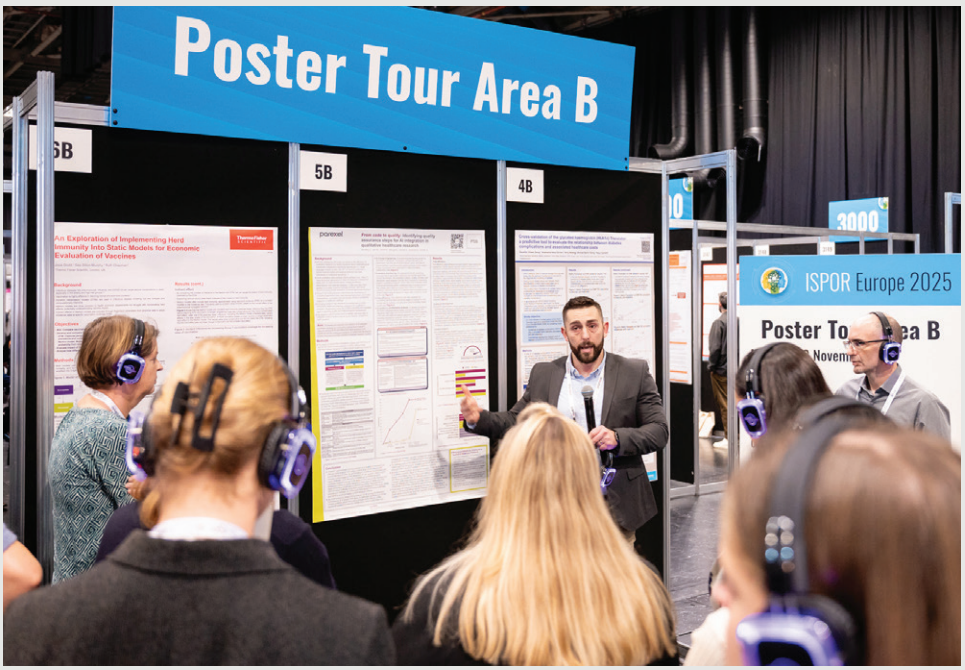
For more news and photos from the conference, visit ISPOR's HEOR News Desk.





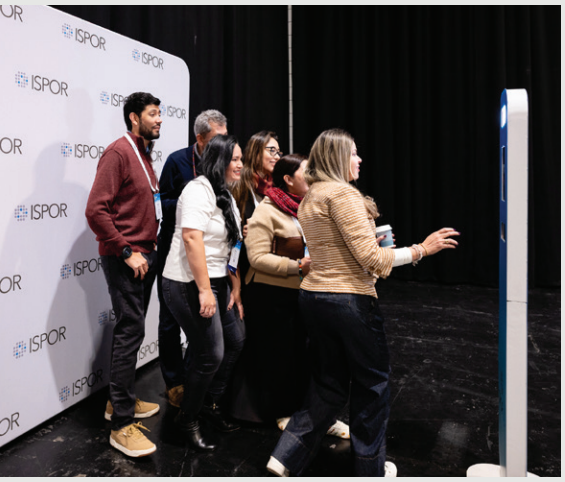
Photos by Christian Dusek





Collaboration


ISPOR


ISPOR


Pharmacoevidence


ISPOR


ThermoFisher
SCIENTIFIC
ppd


STRATEGY • SUBMISSION
NICE |
#ISPOREurope
ISPOR Europe 2025
The Leading European Conference for Health Economics and Outcomes Research
ISPOR


ISPOR


ISPOR
ISPOR


ISPOR
HEOR Awards
Celebration
2025


BRASS
GUMBO

Community


Wellness Hub
Join the Path to Wellness Challenge!


Recognizing Our Valued Corporate Partners
ANALYSIS GROUP
cencora
OVO Hydro Drop Off + Pick Up
Halls 1-4
Meeting Academy
Loch Suite - Level 1
Mark Your Calendars!
ISPOR 2026
May 17-20
Philadelphia, PA, USA
ISPOR
Badge


IQVIA
IQVIA


ISPOR
Poster Area
Poster Help Desk
1000
1000
2000

HEOR NEWS

1 Shaping the Future of Global Health Technology Assessment (NICE)

The new Health Economics Methods Advisory has published its first draft report for public comment. The report examines whether factors other than health benefits and costs to the system should be considered when deciding if treatments should be recommended. The final report is due January 2026.
Read more

2 Institute for Clinical and Economic Review Publishes Evidence Report on Treatments for Obesity (ICER)

ICER has published its revised Evidence Report assessing the comparative clinical effectiveness and value of semaglutide (injectable Wegovy, and a yet to be approved oral formulation) and tirzepatide (Zepbound) for the treatment of obesity and additional obesity-related outcomes such as cardiovascular-related risk. The organization has calculated a health benefit price benchmark to be between $9100 and $12,500 for injectable semaglutide, $8300 and $11,400 for oral semaglutide, and $11,500 and $15,800 for tirzepatide.
Read more

3 NICE's Backing of the Prostate Cancer Drug Abiraterone Could Help Thousands and Save the NHS Millions (NICE)

The final draft guidance for the drug marks a significant shift from the 2021 guidance, which at the time could not recommend abiraterone because it did not represent significant value for money to the National Health Service. Pushing the change in view is the availability of lower-cost generic versions of the drug.
Read more

4 European Projects Insight Report (HIMSS)

The report captures the strategic direction, systemic challenges, and transformative potential of 12 European Union-funded digital health initiatives: CYLCOMED, EDiHTA, ENTRUST, FLUTE, Gravitate-Health, IDERHA, MedSecurance, NEMECYS, ONCOVALUE, SHAIPED, TRUMPET, and XiA. The goal of these projects is to develop solutions that improve interoperability, strengthen cybersecurity, embed ethical artificial intelligence, advance health technology assessment, support value-based care, and promote patient empowerment.
Read more

5 Advancing AI in Bowel Cancer Screening (CORDIS)

In an effort to enhance the early detection of bowel cancer, Ireland's BowelScreen program is taking part in the European Union-funded Microb-AI-ome project that investigates how the artificial intelligence (AI)-driven analysis of gut microbiome data could improve future colorectal cancer screening. Patients at 3 research hospitals will be providing stool samples for microbiome analysis.
Read more

6 Cost-Effectiveness of Linkage Case Management for Hospitalized People With HIV (JAMA Network Open)

While Daraja, a linkage case management intervention to improve HIV care engagement, was found to cost more than enhanced standard care, researchers found it was associated with improvements in disability-adjusted life-years. They concluded that the social worker-administered solution had a high probability of being regarded as cost-effective according to various cost-effectiveness threshold estimates.
Read more

7 WHO Calls for a New Era of Strategic Urban Health Action With Global Guide to Unlock Healthy, Prosperous, and Resilient Societies (WHO)

A new guide for decision makers, "Taking a strategic approach to urban health," responds to the growing demand for integrated solutions that address health challenges and promote health more broadly in urban settings. It is the first comprehensive framework of its kind to help governments plan urban health strategically, integrating evidence into policy and practice.
Read more

8 RWE Is Growing Up, and Here's Why That Matters (Clinical Leader)

An interview with ISPOR's Chief Science Officer, Laura Pizzi, MPH, PharmD, offers a pragmatic, global-minded view of real-world evidence—one that's both hopeful and candid about where the field of health economics and outcomes research still needs work.
Read more

9 Epidemiological Characteristics of Heatstroke in China, 2010-2023: A Longitudinal Study Based on a National Heatstroke Surveillance System (The Lancet Regional Health Western Pacific)

With epidemiological studies of heatstroke limited in number and scope, researchers conducted an observational study of reported cases in China to better understand the epidemiological characteristics of heatstroke and advance evidence-based prevention and control strategies. The results, which highlight differences by population, region, and time of year, should inform formulation of evidence-based strategies for enhanced heatstroke preparedness and response.
Read more

10 EMA Confirms Suspension of Sickle Cell Disease Medicine Oxbryta (EMA)

Officials say the marketing authorization of the drug remains suspended after European Medicines Agency human medicines committee reviewed emerging safety data and found the benefits of Oxbryta (voxelotor) no longer outweigh its risks.
Read more

ISPOR Conferences and Events

ISPOR Europe 2025 | 9-12 November

Scottish Event Campus | Glasgow, Scotland, UK

Thank you to the sponsors of the ISPOR Europe 2025 Conference!

Registration Sponsor

Elevio Group

Educational Symposia Sponsors

ANALYSIS GROUP

cencora

GSK

OPEN HEALTH

ThermoFisher SCIENTIFIC

And a Special Thanks to Our Corporate Partners:

ISPOR CORPORATE PARTNER 2025

Analysis Group, Cardinal Health, Cencora, Datavant, Genesis Research Group, OPEN Health, Premier Applied Sciences, Thermo Fisher Scientific, Truveta

ISPOR Conferences and Events

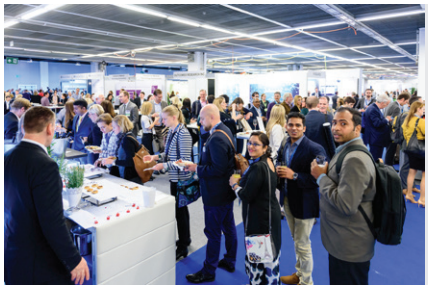
ISPOR 2026 | May 17-20
Philadelphia Convention Center | Philadelphia, PA, USA

Healthcare stakeholders will convene at ISPOR 2026, the leading global conference for HEOR, for discussion and dissemination of the latest trends in healthcare. Contribute your research, ideas, and knowledge to advance the science of HEOR—submit your abstract and help shape the conversation!

Submit Your Abstract!

Research Abstract Submission Closes	**January 9, 2026**

Learn more about ISPOR 2026 and submitting abstracts: www.ispor.org/ISPOR2026



Get in front of your target audience for 2026.
Contact sales@ispor.org for opportunities!

ISPOR Education

ISPOR Short Courses

The ISPOR Short Course Program is designed to enhance knowledge and techniques in core HEOR topics as well as emerging trends in the field. Taught by expert faculty, short courses are offered across 7 topical tracks and range in skill levels from introductory to experienced.

Visit the website for upcoming 2026 short courses: www.ispor.org/shortcourses

ISPOR Education Center

The ISPOR Education Center provides instant access to HEOR education with on-demand programs delivered through a personalized, powerful, and flexible learning platform. Working at your own time and pace, drive your professional development by growing your knowledge and skills with topical, relevant, and innovative course curricula.

Recently released courses include:

- Planning Digital Health Apps With Evidence in Mind

- Poster Presentations That Stand Out: From Design to Delivery

- Mastering the Art of Presentations: Engaging Audiences With Impact

- Unlocking the Power of Real-World Evidence

*Take a test run of the ISPOR Education Center with our new "What Is HEOR?" **free** microcourse!*

- What Is HEOR?

View more featured courses, topics covered, and the growing list of courses available at www.ispor.org/EducationCenter.

ISPOR Education

HEOR Learning Lab™

The HEOR Learning Lab™ provides high-value, unlimited, on-demand, educational video content selected from the Society's conferences, summits, and other seminal events, to facilitate learning and innovative approaches in the field.

The following are examples of popular sessions available for viewing:

- **Global Impact of JCA: Evaluating the Implications of the New EU HTA Regulation**
- **Navigating the Evolving Landscape of US Healthcare Policy Reforms: Implications for Drug Pricing and Access, Health Equity, and Healthcare Research**
- **Evolution of Evidence—Innovating for the Future of HTA**

Explore the HEOR Learning Lab at www.ispor.org/LearningLabWelcome

Section Editor: **Paula Lorgelly, PhD**, Auckland, New Zealand

The Advancing Patient-Centered Outcomes Down Under Conference

Jessica Roydhouse, PhD, University of Tasmania, Hobart, Australia; and **Brendan Mulhern, PhD**, University of Technology Sydney, Australia on behalf of the Organizing Committee

Attracting 101 delegates, including 16 students, the inaugural *Advancing Patient-Centered Research Down Under Conference* was jointly hosted by the International Society for Quality of Life Research Australia and New Zealand Special Interest Group (ISOQOL ANZSIG) and ISPOR's Australian and New Zealand Chapters.

Held at the University of Technology Sydney Aerial Function Centre (1-2 December), the conference facilitated regional networking and collaboration among academic and industry researchers, early- and mid-career researchers, and higher degree research students. Building on the experience of the conveners of the ISOQOL ANZSIG virtual conference held in 2020 during the COVID-19 pandemic, the conveners of this 2025 jointly hosted in-person conference were delighted by the interest and participation of the conference attendees.

The conference was opened by Michael West from the Metropolitan Local Aboriginal Land Council, who gave the Welcome to Country, a ceremony which honored the land upon which we gathered. We were pleased to have 2 international keynote speakers: Mark Sculpher, PhD, MSc from the University of York and Melanie Calvert, PhD from the University of Birmingham, both in the United Kingdom. Professor Sculpher talked about making economic evaluation patient centered. Professor Calvert discussed patient-reported outcomes in early phase trials and inclusive data collection. The 2-day conference featured 6 themed presentation sessions, 3 panel sessions, a Poster Walk, and several networking opportunities, including Dine Arounds on Day 1. Dine-Arounds are an ISOQOL annual conference tradition. For those who take part, attendees are grouped according to cuisine preferences and they have dinner together. It is an opportunity to meet and network with new people who you may not otherwise have met.

The conference Co-Chairs were the outgoing ISPOR Australia Chapter President, Brendan Mulhern, and the outgoing ISOQOL ANZSIG Chair, Jessica Roydhouse. Key to the success of the conference was the hard work of the Organizing Committee, including Rachel Campbell (University of Sydney); Ingrid Cox (Menzies Institute for Medical Research); Melanie Hawkins (La Trobe University); Alicia Norman (Macquarie University); Imogen Ramsey (Flinders University); and Elizabeth Walkley (Austin Health) and Vanessa Nolasco, who provided invaluable administrative support. The Steering Committee (Paula Lorgelly [University of Auckland; ISPOR New Zealand Chapter President]; Sandra Nolte [Monash University; ISOQOL President]; Richard Norman [Curtin University]; and Alicia Norman and Claudia Rutherford [University of Sydney]) provided guidance.

We are grateful for the generous sponsorship of Gilead (Gold Sponsor) and FACIT (Silver Sponsor), which enabled us to recognize and reward research excellence through 5 awards: Best Presentation, Best Symposium/Panel, People's Choice, Best Poster, and Best Student/Early Career Presentation. The breadth and depth of work presented at this conference was exciting and shows the high standard of patient-centered health economics and outcomes research in Australia, New Zealand, and beyond. Research abstracts from the conference will be published as conference proceedings in a supplement of *Quality of Life Research* in 2026.

Chinese Diabetes Outcome Model: Using Data to Transform Care and Save Patient Lives

Juliana NM Lui, PhD, MSc and **Juliana CN Chan, MBChB, MD, FRCP**, The Chinese University of Hong Kong, Shatin, Hong Kong

The Chinese Diabetes Outcome Model (CDOM) is the first Asian diabetes patient-level simulation model, an innovation from more than 3 decades of focused research aimed at resolving the unique health challenges faced by the Chinese population with type 2 diabetes. Conventional diabetes models were developed in Western populations which cannot accurately reflect the risk profiles and complications of Asian patients with diabetes, characterized by young age at diagnosis, low body mass index, high visceral fat and propensity for kidney disease and cancer.

The CDOM used high-quality data with minimal missing information of the Hong Kong Diabetes Register for accurate modeling. The Hong Kong Diabetes Register was created in 1995 by the Chinese University of Hong Kong as a data-driven care model implemented through the Prince of Wales Hospital's Diabetes and Endocrine Centre. This ongoing comprehensive register includes demographics, clinical data, patient-reported outcomes (eg, quality of life, depression, distress, anxiety) and experiences (eg, self-care practices), prescriptions, outcomes and hospitalization costs.

The development cohort of CDOM included 21,453 patients with type 2 diabetes enrolled between 2002 and 2019 with quality-of-life data, followed up for a median of 8 years. For external

validation, we utilized territory-wide electronic medical records of patients with type 2 diabetes who attended public clinics in Hong Kong from 2002 to 2019 (n=176,120). The latter represented a larger, diverse patient population to increase the model's generalizability despite their higher missing data rates. This approach combines the reliability of the Hong Kong Diabetes Register and the broad applicability of Hong Kong territory-wide data.

The CDOM includes risk equations on 10 major cardiovascular-renal-cancer events, severe hypoglycemia, and premature mortality associated with type 2 diabetes. Compared to existing models, CDOM offers more outcome risk equations, longer follow-up, and time-varying covariates. The CDOM is the first model with separate risk equations for ischemic and hemorrhagic strokes, which have different prognostic and therapeutic implications.

By integrating the temporal cost and quality of life regressions utilizing local Hong Kong Diabetes Register data, CDOM will be the definitive model for health economic evaluation of cost-effectiveness of strategies, including drug therapies, diagnostics, devices, digital technologies, as well as program interventions tailored to Chinese populations. As a patient-level simulation model, CDOM enables flexible subgroup analysis that facilitates the identification of high-risk subpopulations in pursuit of personalized medicine with value, accessibility, and precision.

In this global epidemic of diabetes, nearly 500 million people are affected and 50% of them are living in Asia. Given the similar phenotypes for risk factors and outcomes in Asian populations, the external validation of CDOM in other Asian cohorts will serve as a model for design, implementation, and evaluation of prevention and control strategies to combat the rising tide of chronic diseases in Asia.

Strengthening the National HTA Framework for Greece

The "Strengthening the National Health Technology Assessment (HTA) Framework for Greece" initiative is a joint effort supported by the World Health Organization (WHO/Europe) and the European Commission (via DG REFORM and Structural Reform/ Technical Support mechanisms) aimed at reinforcing Greece's capacity to evaluate health technologies in line with European norms.

This program responds to the European Union's (EU) HTA Regulation 2021/2282, which sets out harmonized rules for clinical assessment of health technologies across Member States. Greece's existing HTA system—launched in 2018 with an HTA Committee responsible for assessing new pharmaceuticals and guiding pricing and reimbursement decisions—has achieved early successes but retains gaps in methodology, process, transparency, and capacity.

Under this program, Greece is revising its national HTA guidance, aligning methods and procedures with EU best practices and the new HTA regulation, and developing processes to reduce delays and enhance transparency and consistency. It also involves stakeholder consultations (government bodies, patient groups, academia, industry) to refine the framework.

Beyond pharmaceuticals, the program anticipates expanding HTA to medical devices and diagnostics and contemplates establishing an independent HTA body detached from direct ministerial influence. The ultimate objective is to embed evidence-based decision making into Greece's health system, improve access to safe and cost-effective innovations, and support the sustainability of public health expenditures.

In sum, this initiative marks a significant step toward a more resilient, transparent, and patient-centered health system in Greece, ensuring that innovative technologies deliver maximum value to both citizens and the healthcare system.

POLICY BRIEF

Policy Briefs offer concise insights into emerging developments in the global health policy space that shape access, innovation, and affordability. Each Policy Brief will spotlight timely issues with relevance for the health economics and outcomes research (HEOR) community and beyond. The goal is to provide readers with a rapid overview of how policy shifts are influencing global markets and stakeholders. The Briefs present an overview of the issue and its implications for the HEOR field, followed by concise summaries that reflect key stakeholder perspectives.

US Drug Prices and the Medicare Drug Price Negotiation Program

Ana Amaris, MD, MPH, Director, Health Policy Initiatives, ISPOR, Lawrenceville, NJ, USA

Overview: This inaugural column focuses on the evolving role of international reference pricing (IRP) and related mechanisms in the US Medicare Drug Price Negotiation Program. The column will also cover the ripple effects these reforms are having across the European Union. These policy shifts mark a pivotal moment in how governments, payers, and industry define "value" and balance cost containment with access and innovation.

US STAKEHOLDER PERSPECTIVES

Pharmaceutical Industry
As of October 2025, Pfizer, AstraZeneca, Amgen, AbbVie, Novo Nordisk, Lilly, Bristol-Myers Squibb, Sanofi, and EMD Serono have made announcements to lower select US drug prices, with some firms citing plans to remove third-party supply chain entities or reference to Most Favored Nation (MFN) international benchmarks. The announcement of several direct-to-consumer programs is viewed as pharma's response to MFN through sales channels that bypass the intermediaries (ie, payers and pharmacy benefit managers [PBMs]). PhRMA warns that international reference pricing-linked mechanisms could deter early US launches and delay or redirect research and development towards less-regulated markets. Lilly's CEO warned that importing foreign price controls would import the low productivity of Europe's biopharma sector without solving for high out-of-pocket costs of the US insurance market.

Payers and PBMs
CVS introduced a new pricing model called CostVantage that replaces traditional PBM-based systems with formulas reflecting actual drug acquisition cost, a fixed markup, and a standard dispensing fee. Express Scripts (Evernorth) issued a public statement defending the role of PBMs in drug affordability. They argued that removing PBMs is "oversimplified and shortsighted," and emphasized that PBMs help keep 93% of prescriptions under $20 out-of-pocket. Mark Cuban of CostPlusDrugs publicly endorsed Trump's MFN executive order.

Regulatory
The US Food and Drug Administration (FDA) announced that affordability will be incorporated as a consideration in the agency's new Commissioner's National Priority Voucher (CNPV) Pilot Program, which seeks to shorten review times from approximately 10-12 months to 1-2 months for selected products. FDA named the first 9 products eligible for priority review vouchers from Regeneron, Sanofi, Merck KGaA, Revolution Medicines, and Disc Medicine.

Academia and Research
Experts cautioned that MFN creates a prisoner's dilemma for pharmaceutical companies. If one company refuses to launch its drug in MFN-referenced countries to protect its higher US price, it risks losing international revenue while competitors who do launch abroad anchor the US benchmark price downward. If all companies launch abroad, they collectively suffer price compression in the United States, but if one defects, it gains short-term market share while triggering long-term losses for everyone.

Providers
Providers broadly support efforts to improve affordability but continue to raise concerns about transitional risks under the new Medicare Drug Price Negotiation framework. For hospitals and specialty practices operating under "buy-and-bill" models, sharper reimbursement controls could threaten financial stability and limit access to costly biologics or infusions without additional safeguards. Clinicians are calling for clear guidance on billing codes and transitional financing to maintain service continuity during implementation.

Patient Groups
Patient groups share the affordability goals of the Inflation Reduction Act but warn that negotiated price reductions must translate into lower out-of-pocket costs at the pharmacy

counter. Advocacy networks note that vulnerable populations, particularly Medicaid beneficiaries, dual-eligibles, and individuals with chronic or rare diseases, remain at risk of delayed access when drug manufacturers recalibrate launch strategies to manage international price referencing. Many groups also point to gaps in direct-to-patient platforms, which may not reach patients dependent on traditional provider networks.

EUROPEAN PERSPECTIVES

Brussels
European leaders voiced concerns over the US MFN policy, warning that it could lead to delayed drug launches and higher prices across Europe. Industry leader Alexander Natz (EUCOPE) and public health expert Helmut Brand noted that orphan drug companies may avoid launching in Europe to prevent setting low price benchmarks that could be referenced by US regulators.

United Kingdom
The United Kingdom is facing stalled pharmaceutical investment from Merck and AstraZeneca, which have paused or canceled major projects due to market uncertainty. In response, the government is considering raising the National Health Service's drug prices by up to 25% and revising the Voluntary Scheme for Branded Medicines to attract investment and align with international pricing standards. Finance Minister Rachel Reeves emphasized that the United Kingdom must remain competitive in pricing while securing more inward investment from global drug manufacturers.

France
French Prime Minister François Bayrou has requested the Economic Committee for Health Products (CEPS) to release a report in Q3 2025, outlining its drug pricing policy recommendations. Bayrou cited "changing geopolitical context" and "investment dynamics" for the European pharma sector. France is advancing reforms through its 2026 Social Security Finance Bill and CEPS pricing framework. These include price premiums for domestically manufactured drugs and lower discount ceilings for generics and biosimilars, aimed at improving financial viability and protecting local industry. The CEPS has also shown increased openness to price increase requests, signaling a more flexible stance amid global pricing pressures.

Central and Eastern Europe
Experts warn that MFN could disproportionately affect smaller Eastern European markets. Companies may delay or skip launches in these countries to avoid setting low price benchmarks that the Centers for Medicare and Medicaid Services could reference. The list prices of nonreferenced markets feed into the list prices of MFN-referenced markets, effectively pulling them into the MFN framework and thus risking delays or "no launch" strategies.

SUGGESTED READING:

- Application of International Reference Pricing Rules to Forecast Pharmaceutical Launch Prices in 5 European Countries
- Cost-Effectiveness of the 15 Drugs Selected for Initial Price Applicability Year 2027 by Centers for Medicare and Medicaid Services Drug Price Negotiation Program
- Integrating Price Benchmarks and Comparative Clinical Effectiveness to Inform the Medicare Drug Price Negotiation Program
- Referencing Drug Prices of Other Countries May Not Sustainably Lower Prices in the United States: Lessons From Europe
- Informing the United States Medicare Drug Price Negotiation for Apixaban and Rivaroxaban: Methodological Considerations for Value Assessments Many Years After Launch
- Estimated Savings From Using Added Therapeutic Benefit and Therapeutic Reference Pricing in United States Medicare Drug Price Negotiations
- Medicare Drug Price Negotiation in the United States: Implications and Unanswered Questions

US Drug Policy Reforms and Global Policy Reactions

Ana Amaris, MD, MPH, Director, Health Policy Initiatives, ISPOR, Lawrenceville, NJ, USA

Overview: This column focuses on the evolving landscape of US pharmaceutical policy following the government's recent agreements with some drug manufacturers and the results from the second round of Medicare Drug Price Negotiation (MDPN) under the Inflation Reduction Act (IRA). Occurring amid the 43 day-long government shutdown that began on October 1, 2025, these developments introduce new layers of complexity to an already dynamic policy environment.

The column also examines emerging international reactions and global stakeholder perspectives on the potential implications of these US policy shifts for access, regulation, and market stability.

US STAKEHOLDER PERSPECTIVES

Academia and Research

An article described the deal between US President Donald Trump and Pfizer, part of the administration's ongoing "Most Favored Nation" (MFN) effort to align US drug prices with those in other high-income countries, as largely symbolic. The direct-to-consumer "TrumpRx" platform, expected to launch in 2026, is seen as unlikely to make drugs more affordable, since insured patients already benefit from negotiated prices and uninsured individuals would still face high out-of-pocket costs. Experts caution that linking US prices to international benchmarks could prompt higher prices or restricted market access abroad, reinforcing calls for domestic value-based pricing reforms.

Private Sector/Innovators

Cost Plus Drugs, the online pharmacy founded by Mark Cuban, will participate in the TrumpRx drug-price transparency platform, sharing real-time access to its pricing database so users can compare costs across direct-to-consumer websites. The partnership aligns with the administration's goal of expanding access to upfront pricing and bypassing traditional intermediaries. Cuban, who has long criticized pharmacy benefit managers (PBMs) for inflating US drug costs, said participation will boost Cost Plus's visibility and potentially lower prices as volumes grow. His comments at the HLTH 2025 conference reflected cautious optimism, noting that while TrumpRx could improve transparency, PBMs have yet to feel major disruption.

Industry

On November 6, 2025, the White House announced new agreements with Novo Nordisk and Lilly that will sharply reduce the prices of several leading GLP-1 medicines. Under the deal, Ozempic pricing will drop from $1000 to $350 per month and Wegovy from $1,350 to $350, while Zepbound and Orforglipron will be priced at $346 per month through the new TrumpRx platform, to be launched in 2026. The agreements also reduce Medicare prices for these treatments to $245 per month with a $50 patient copay and extend $35 monthly pricing for insulin products such as Novo Nordisk's NovoLog and Tresiba. In exchange, the companies will guarantee MFN pricing for future products, repatriate additional foreign earnings, and grant state Medicaid programs access to MFN prices. The administration frames these measures as a "historic reduction" in drug costs aimed at expanding affordability and reshaping US pricing norms.

Payers and PBMs

The Centers for Medicare and Medicaid Services (CMS) announced in late November the second round of price negotiations under the IRA, securing 38%–85% reductions for 15 high-expenditure medicines, with new prices taking effect in 2027. CMS estimates these cuts will reduce Medicare's net spending on the selected products by 44% compared to 2024, generating approximately $12 billion in savings and lowering beneficiary out-of-pocket spending by $685 million. Recent analyses suggest that, although the reductions seem substantial, many manufacturers already provide significant rebates in Part D, meaning the differences from net prices are more limited based on the estimated prices reported in *Value in Health*. CMS will select 15 additional drugs for negotiation in 2026 and up to 20 annually thereafter, signaling a continued expansion of Medicare price setting.

Cigna's Evernorth division announced a rebate-free, pass-through model for Express Scripts, shifting away from traditional PBM rebates toward greater transparency and upfront discounts. The model, which will roll out across all plans by 2028, aims to lower brand-name drug costs by about 30%, expand real-time price comparisons for patients, and introduce a cost-plus reimbursement system for pharmacies beginning in 2026.

Regulatory

The FDA has accepted Sanofi's Tzield for expedited review under the Commissioner's National Priority Voucher pilot program, a new pathway aimed at accelerating access to therapies that address high unmet medical needs. If approved, Tzield would be the first disease-modifying treatment to delay the progression of stage III type 1 diabetes in both adults and children. The FDA's evolving fast-track mechanisms, including the Commissioner's National Priority Voucher program and accelerated approval programs, are intended to balance innovation with access, even amid operational constraints linked to the 43-day government shutdown.

INTERNATIONAL PERSPECTIVES

The United States and the United Kingdom announced an agreement in principle on pharmaceutical pricing as part of the new US–UK Economic Prosperity Deal, aimed at addressing perceived imbalances in bilateral pharmaceutical trade. Under the arrangement, the United Kingdom will increase the net prices paid by the National Health Service (NHS) for new innovative medicines by 25% and limit the use of broad portfolio-wide rebates under schemes such as the Voluntary Scheme for Branded Medicines Pricing, Access, and Growth, with repayment rates expected to fall to 15% in 2026 and remain at or below that level thereafter. In return, the United States will exempt UK-origin pharmaceuticals, ingredients, and medical technologies from Section 232 tariffs, refrain from initiating Section 301 investigations into UK pricing practices during the current administration, and support access to emerging pharmaceutical innovations for UK patients. US officials describe the agreement as part of a broader effort to foster more "fair" international contributions to pharmaceutical innovation and to ensure that American consumers no longer shoulder a disproportionate share of global drug costs, while also reinforcing US–UK cooperation in life-sciences investment and manufacturing.

In Asia, Japan's pharmaceutical market is emerging as one of the first to feel the effects of US MFN drug pricing policies, given their inclusion among the 8 countries named as pricing comparators. Industry leaders warn that unless Japan reforms its current pricing approach, which already reduces drug prices annually, the country could face declining investment and limited access to new medicines. A recent survey of multinational pharmaceutical companies operating in Japan found that MFN is influencing both global pricing and research and development strategies, with several firms delaying launches or adjusting development plans.

These results highlight Japan's vulnerability to ripple effects from US pricing reforms and underscore the need for renewed dialogue between the Japanese government and industry on sustaining innovation and access.

In Europe, the United Kingdom is reportedly preparing to raise the cost-effectiveness threshold used by the National Institute for Health and Care Excellence by around 25%, from the current £20,000–£30,000 per quality-adjusted life year, in response to pressures related to US drug-pricing reforms and threatened tariffs on pharmaceuticals. This move is seen as part of efforts to strengthen the United Kingdom's life-sciences sector, maintain the country's attractiveness as a launch market, and address industry concerns that the longstanding threshold has become misaligned with inflation and innovation. The proposal has drawn commentaries from health economists who caution that raising the threshold could increase cost pressures on the NHS and affect population-health trade-offs.

METHODS EXPLAINED

In this installment of Methods Explained, we delve into distributional cost-effectiveness analysis (DCEA). Our insights are drawn from a conversation with 2 leading experts: Richard Cookson, PhD, Professor at the Centre for Health Economics, University of York, and Visiting Professor at the National University of Singapore, who pioneered DCEA's development and adoption; Stacey Kowal, PhD, Senior Director and Head of Public Policy Evidence at Genentech and Past Chair of the ISPOR Special Interest Group on Health Equity Research, who developed the building blocks for DCEA in the United States.

Distributional Cost-Effectiveness Analysis

Section Editor: **Koen Degeling, PhD**

What is DCEA and how is it used?
DCEA is an essential extension to standard cost-effectiveness analysis (CEA). Standard CEA focuses on achieving the maximum health gain for a population, but population-based gains may inadvertently increase health inequalities between different social groups. DCEA addresses this limitation by explicitly quantifying equity in the distribution of health outcomes alongside efficiency in terms of overall health outcomes.

When comparing options, DCEA provides quantitative insights into which social groups benefit the most and which benefit the least. Where traditional CEA quantifies total costs and benefits, DCEA additionally measures the distribution of these costs and benefits across social groups. By understanding these consequences, policy makers can take preventive or corrective actions.

DCEA was originally developed to inform policy decisions in public health, such as assessing the impact of implementing a cancer screening program. It also has become increasingly relevant for health technology assessment. Although decision makers have traditionally taken equity issues into account in health technology assessment implicitly, DCEA helps to solidify this by explicitly calculating health inequality impacts using standardized methods that allow comparisons between different decisions.

How DCEA works: the conceptual framework
The starting point for a DCEA is a robust, payer-appropriate cost-effectiveness model, which must be adapted to estimate cost-effectiveness outcomes for clearly defined social groups. This requires explicitly modeling inequalities at all steps along the *staircase to health inequality impact*,[1] each of which can shift the ultimate impact in a different direction. These inequalities can include social differences in the eligible population, intervention uptake, long-term health effect, and health opportunity cost.

Quantifying the distributional impact using standardized methods requires 2 critical building blocks: information on baseline health inequality and health inequality aversion.

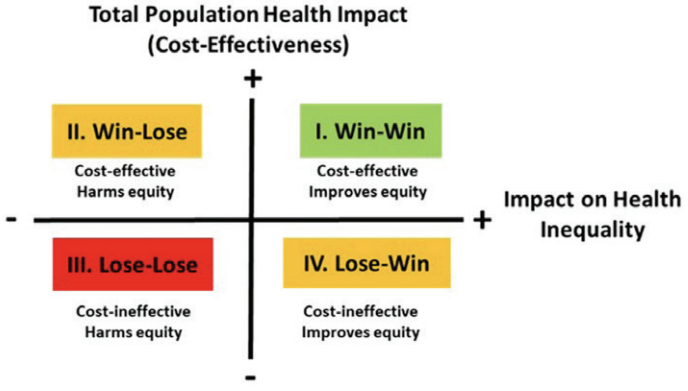
1. **Baseline health inequality**: This is information on the current health differences between social groups in the country of interest. These data are often readily available from national statistics bureaus (eg, differences in life expectancy and health-related quality of life by area deprivation or ethnicity).
2. **Health inequality aversion**: This refers to the degree to which decision makers and members of the public are willing to forgo total health gains to achieve a more equal distribution of health outcomes. This metric is formalized to quantify the value of decreasing (or increasing) health gaps between social groups.

Crucially, distributional analysis requires a broad general-population perspective rather than a narrow clinical perspective. The aim is to reduce social inequality in health within the general population, not just within one specific group of patients.

DCEA can be performed using standard spreadsheet software, but is often performed using R. The *York health equity impact calculator*[2] was developed using R Shiny as an interactive online tool to perform DCEA.

After estimating the breakdown of impacts by social group, the results can be summarized visually in an Equity-Efficiency Impact Plane (**Figure**). This plane looks like an incremental cost-effectiveness plane but combines costs and effectiveness into

Figure. Equity-efficiency impact plane combining both the traditional cost-effectiveness outcomes (vertical axis) with the impact on health inequality (horizontal axis)



Source: Griffiths et al, 2025.[1]

a single cost-effectiveness measure on the vertical axis (eg, net health benefit). The impact on health inequality is shown on the horizontal axis. This visual tool allows for easy interpretation:

- **Win-Win (northeast quadrant)**: The intervention is cost-effective *and* has a positive effect on health inequality.
- **Win-Lose (northwest quadrant)**: The intervention is cost-effective *but* has a negative effect on health inequality.
- **Lose-Win (southeast quadrant)**: The intervention is not cost-effective *but* has a positive effect on health inequality.
- **Lose-Lose (southwest quadrant)**: The intervention is not cost-effective *and* has a negative effect on health inequality.

Are there alternative methods?

The term DCEA is often used as an umbrella term to refer to different methods that incorporate equity considerations. A full DCEA requires redesigning the cost-effectiveness model to estimate outcomes across different social groups. If there is not enough capacity or time to adapt the model, an aggregate or simple DCEA may be performed, which takes aggregate results from a standard CEA and performs some simple distributional calculations on top. This can still allow for inequalities as elements along the *staircase to inequality impact* to be considered. However, it does not fully capture all elements, may be less accurate than a full DCEA, and will not provide insight into how accounting for social inequalities may alter the standard cost-effectiveness results themselves.

A similar method is extended cost-effectiveness analysis, which is essentially the same but adds further information on the distribution of impacts on household finances as well as impacts on health. This can be especially important in countries without universal health coverage, where out-of-pocket costs can generate substantial financial hardship. There are other ways to incorporate equity considerations into decision making, but DCEA is the only one that is an extension of CEA to explicitly quantify outcomes across groups.

To what extent is it currently being used?

There has been a steep increase in the number of DCEA applications over the past 5 years, in both public health and healthcare.

The National Institute for Health and Clinical Excellence (NICE) in England and Wales encourages use of DCEA as supplementary analysis both in the development of clinical and public health guidelines and in evaluation of new technologies.[3] In the context of technology evaluation, NICE recommends that evidence of *substantial* health inequality impact be considered alongside an intervention's cost effectiveness.[4] In this context, DCEA can be used as supplementary analysis to measure health inequality impact and assess its magnitude, but use of equity weights to value health inequality impact is discouraged.

Beyond the United Kingdom, China has included DCEA in its guidelines for pharmacoeconomic evaluation,[5] and other countries in the Asia-Pacific region and Latin America are also thinking about including DCEA in decision-making processes.

What is next for DCEA?

To further increase the adaptation and impact of DCEA, development of the methods may focus on 4 key areas:

1. **Demystification and training**: Focusing on simple outcomes and summary graphs will be crucial to helping decision makers understand and use DCEA results.
2. **Building experience**: Building broader experience in applying and reviewing DCEA studies is vital. Performing the first DCEA is a steep learning curve, but subsequent analyses benefit greatly from the experience and gathered data on health gaps.
3. **Standardization**: Building experience will facilitate a certain level of standardization, ideally through establishing a reference case. This would support comparisons across different studies and disease areas.
4. **Data availability**: Greater availability of more granular baseline (income) data linked to health outcomes will be helpful in further increasing the relevance and impact of DCEA.

Key References for Further Reading

A great starting point for a deeper read into health equity considerations in health economics and outcomes research is the primer from the ISPOR Special Interest Group on Health Equity Research, which also provides several insightful case studies.[1] For those interested in the comprehensive technical details of DCEA, the textbook by Cookson and colleagues is the go-to resource.[6]

References

1. Griffiths MJS, Cookson R, Avanceña ALV, et al. Primer on health equity research in health economics and outcomes research: an ISPOR Special Interest Group Report. *Value Health*. 2025;28(1):16-24. doi: 10.1016/j.jval.2024.09.012.

2. Love-Koh J, Schneider P, Cookson R. York health equity impact calculator. 2022. University of York. Accessed October 23, 2025. https://shiny.york.ac.uk/dceasimple

3. National Institute of Health and Care Excellence. Developing NICE guidelines: the manual: NICE process and methods: 7.8 Using economic evidence to formulate guideline recommendations. Published October 31, 2014. Updated October 23, 2025. Accessed October 23, 2025. https://www.nice.org.uk/process/pmg20/chapter/incorporating-economic-evaluation#using-economic-evidence-to-formulate-guideline-recommendations.

4. National Institute of Health and Care Excellence. Technology evaluation methods support document: health inequalities. 2025. Accessed October 23, 2025. https://www.nice.org.uk/consultations/2817/6/distributional-cost-effectiveness-analysis-methods

5. Liu G, Hu S, Wu J, et al. China guidelines for pharmacoeconomic evaluations. Beijing: China Market, 2020.

6. Cookson R, Griffin S, Norheim O F, Culyer AJ, eds. Distributional Cost-*Effectiveness Analysis: Quantifying Health Equity Impacts and Trade-Offs*. Oxford University Press. 2020.

FROM THE REGIONS

Korea, South Africa, and Central America and the Caribbean Chapters Recognized for Their Leadership and Innovation in 2025

The ISPOR Chapter Awards recognize outstanding Regional Chapters that advance ISPOR's mission through impactful activities in research, education, and member engagement. The chapters were evaluated on their achievements over the past year, including contributions to ISPOR publications, events, and collaborations with local stakeholders, and 3 Regional Chapters were commended for their performance in 2025.

Large-Sized Chapter Category – ISPOR 2025 Outstanding Regional Chapter

Hye-Young Kwon, PhD
President, ISPOR Korea Chapter
Associate Professor, Mokwon University

ISPOR: How has your chapter embraced innovation in HEOR, and what role do you see it playing in the future of the field?
Hye-Young Kwon: Our chapter has actively embraced innovation by fostering collaboration among academia, policy makers, and industry, with a particular focus on data-driven approaches such as real-world data/real-world evidence (RWD/RWE) and health technology assessment (HTA) processes. We've also ensured that our members remain connected to the latest global health economics and outcomes research (HEOR) trends by engaging in international conferences and knowledge exchanges.

In the future, we want to serve as a platform for sharing innovative ideas and bridging the gaps between academia, HTA authorities in Korea, and industry stakeholders. We will continue enhancing the knowledge of HTA stakeholders, contribute to the recognition of HEOR studies, and influence future HTA policies. By collaborating with other chapters, we also aim to strengthen the role of our chapter in advancing HEOR and HTA research and policy development in both Korea and Asia.

How does receiving the ISPOR Outstanding Chapter Award influence the legacy and future trajectory of your chapter?
Receiving the ISPOR Outstanding Chapter Award is a great honor that recognizes our dedication to excellence and collaboration. This achievement inspires us to expand our impact, reinforce partnerships, and strengthen our position as a leader in HEOR advancement at both regional and global levels. It adds to our legacy while motivating us to continue raising the visibility and influence of our chapter.

In your opinion, what are the key challenges currently faced by the HEOR field, and how can chapters contribute to addressing those challenges?
The HEOR field currently faces the following challenges:

- Balancing cost-effectiveness with equitable access, particularly for high-cost medicines and innovative therapies
- Bridging the gap between evidence generation and timely policy implementation
- Addressing affordability and access issues during coverage gap periods
- Maintaining methodological rigor while leveraging new data sources such as RWD/RWE

Our chapter contributes to overcoming these challenges by fostering collaboration, creating opportunities for dialogue between researchers and decision makers, and connecting scientific evidence to real-world health policy decisions.

Through these efforts, we help ensure that evidence-based insights translate into better healthcare access, affordability, and outcomes.

What are your goals as a chapter awardee, and how do you plan to inspire and motivate others to contribute to the field of HEOR?
As an awardee, my goal is to build a more inclusive and engaged HEOR community and spotlight the societal impact of our work.

By showcasing the tangible policy impact of HEOR and recognizing the valuable contributions of our members, I hope to inspire others to actively participate. Through collaboration and a strong community focus, we can empower members to see the broader impact of their work and contribute to meaningful improvements in healthcare.

Medium-Sized Chapter Category – ISPOR 2025 Outstanding Regional Chapter

Mark Brand, MBA
President, ISPOR South Africa Chapter
Health Technology Strategy/Market Access Specialist and Owner,
Brandtech Health Technology Consulting

ISPOR: How has your chapter embraced innovation in HEOR, and what role do you see it playing in the future of the field?
Mark Brand: ISPOR South Africa has steadily promoted the use and implementation of HEOR and associated economic methods for priority-setting since its creation in 2008. As the HEOR landscape in South Africa remains largely without formal guidelines or regulations, there is significant room for innovation and for promoting approaches that address healthcare needs within the HEOR space. This includes adopting new methods and pragmatic approaches to reimbursement challenges and decision-making processes.

However, the lack of guidelines and regulations also means that the reimbursement environment remains uncertain, with limited development in the use of real-world evidence and in establishing standards for digital health technologies. Where data are available from healthcare providers and administrators in South Africa, ISPOR SA has implemented a data grant initiative that links student researchers with these organizations to encourage and support real-world evidence generation.

There is also considerable work to be done in establishing multistakeholder national processes for health technology assessments (HTAs) and for generating evidence to inform such processes. South Africa's National Health Insurance, which aims to achieve universal health coverage, emphasizes HTA but has so far provided limited guidance on processes and acceptable technical inputs. ISPOR SA and its membership are well-positioned to assist in reviewing existing processes and guidelines, ensuring they are implementable and aligned with global best practices, and supporting skills development to address capacity gaps.

How does receiving the ISPOR Outstanding Chapter Award influence the legacy and future trajectory of your chapter?
ISPOR South Africa's relevance depends on its ability to provide education, training, and development in HEOR, as well as our capacity to influence policy processes so that HEOR becomes a central part of decision making for health programs and for making interventions available to patients.

Receiving this award will strengthen ISPOR SA's credibility with both current and potential members—who span a diverse range of stakeholders in healthcare decision making—and with policy makers across government, research, academia, and private payer organizations.

In your opinion, what are the key challenges currently faced by the HEOR field, and how can chapters contribute to addressing those challenges?
Key challenges in South Africa include the limited availability of local data and the absence of established guidelines and standards. Methods adopted from other jurisdictions are often not supported by the necessary primary research to inform local methodologies and processes. These difficulties are compounded by the constrained allocation of monetary and other resources toward HEOR projects. Chapters can contribute by facilitating capacity-building initiatives, supporting local research, and promoting the adoption of contextually relevant guidelines.

What are your personal goals as a chapter awardee, and how do you plan to inspire and motivate others to contribute to the field of HEOR?
In preparation for the establishment of the Ministerial Advisory Committee on HTA, ISPOR SA is working to develop a single "submission template" for HTAs in South Africa. Historically, the system has been fragmented, with multiple duplicative processes, as every health maintenance organization and insurer runs its own assessment program using different criteria to determine the value of new technologies. We are optimistic that a clear standard for HEOR and its application in decision making will streamline development, investment, and capacity-building opportunities in both the public and private sectors.

Additionally, ISPOR SA continues to serve as a bridge between academia and the practical application of HEOR to reimbursement decision making, with potential for greater emphasis on HEOR alongside National Health Insurance initiatives. We are excited that the leadership and members of ISPOR SA are recognized as contributors to these developments.

Small-Sized Chapter Category - ISPOR 2025 Outstanding Regional Chapter

Fernando Bonilla, MD, MBA, MSc
President, ISPOR Central America and the Caribbean Chapter
Health Economics & Digital Health Consultant, Health Transformers 360

ISPOR: How has your chapter embraced innovation in HEOR, and what role do you see it playing in the future of the field?
Fernando Bonilla: Innovation is not always about doing new things—it's also about doing things differently. From the outset, our chapter embraced innovation by fostering a dynamic, engaged community across multiple countries through remote working tools and active use of social networks. We prioritized value creation by listening to our members and codeveloping our agenda. Inspired by global trends, we promoted early patient involvement in health technology assessment (HTA) and formalized collaborations with patient organizations. We also maintained consistent engagement through our monthly "HEOR Wednesdays," a dedicated virtual space held on the last Wednesday of each month—designed by and for the community to exchange experiences and knowledge in a safe environment. Finally, we strengthened collaboration with other ISPOR chapters (ie, Mexico, Argentina, Colombia, and Chile), recognizing that regional synergy is key to advancing HEOR in complex and fragmented systems.

How does receiving the ISPOR Outstanding Chapter Award influence the legacy and future trajectory of your chapter?
Receiving this award is a great honor and a powerful recognition of our team's hard work. It reinforces that ISPOR values contributions from all regions—regardless of size—which is very inspiring. Beyond the educational grant, the award enhances the chapter's visibility at a global level, opening the door to new collaborations and synergies with other ISPOR chapters.

> [This award] reinforces that ISPOR values contributions from all regions–regardless of size–which is very inspiring.

More importantly, it energizes our members by reinforcing that they are not isolated in their region, but rather part of a global HEOR community. Motivation is essential for sustaining momentum in volunteer-driven initiatives, and this recognition not only helps us to stay focused on our goals but also inspires us to aim higher and set more ambitious objectives for the future.

In your opinion, what are the key challenges currently faced by the HEOR field, and how can chapters contribute to addressing those challenges?
While the challenges in HEOR vary by region and health system maturity, they exist everywhere. In Central America and the Caribbean, 2 key issues stand out. First, the development of HTA processes is still at an early stage, with limited institutional frameworks to support systematic evaluation. Second, even when HTA is conducted, the integration of its results into final health decision making remains weak or nonbinding. Chapters can serve as enablers of progress by promoting the development of HEOR in a way that is anchored in local realities. They can also foster multisectoral dialogue to find common ground among stakeholders, such as the need for long-term sustainability and patient-centered care, and translate evidence into policy through education, collaboration, and advocacy.

What are your personal goals as a chapter awardee, and how do you plan to inspire and motivate others to contribute to the field of HEOR?
One of my personal goals is to live up to the trust placed in me by the HEOR community as chapter president and to prioritize actions that generate real impact for patients. Helping another human being has always been a powerful source of motivation, and few fields offer such a clear path to that goal as healthcare. Today, health systems face major sustainability challenges, and this has sparked renewed interest, particularly among younger generations who increasingly choose healthcare over tech-related careers. The challenge is not to create motivation but to channel it effectively. By raising awareness of HEOR and its potential to improve health system performance and sustainability, we can engage and empower new contributors who are eager to make a meaningful difference.

In Memoriam

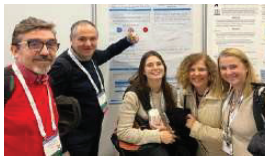
José Manuel Rodríguez Barrios, PhD

First President of ISPOR Spain Chapter

José Manuel Rodríguez Barrios, PhD, 59, a pioneering advocate for health economics and outcomes research (HEOR) in Spain and the first president of the ISPOR Spain Chapter, passed away on September 27 after several months of illness. He is survived by his wife, Teresa, and daughter, Maya.

Rodríguez Barrios was one of the driving forces behind the establishment of the Spain Chapter in 2010 and was known for his efforts to promote the field of HEOR at a time when those concepts were not widely recognized by policy makers and industry stakeholders in that country.

Rodríguez Barrios spent nearly 4 decades with global pharmaceutical companies, most recently as Early Products and Health Economics Senior Manager for Novartis, and taught graduate-level HEOR courses at the Universitat Pompeu Fabra for more than 20 years. Rodríguez Barrios is remembered for his generosity with career advice for colleagues, helping many to take their first steps in the pharmaceutical and healthcare technology fields.



SIEMPRE CON NOSOTROS

Artificial Intelligence Is Leveling Up HEOR, but Still Needs a Humanity Check

The evolution of artificial intelligence (AI) has rapidly accelerated in just the past few years, amplifying the potential impact of health economics and outcomes research (HEOR) on patients and public health. The technology is enabling HEOR professionals to do more complex analyses, drawing on vast amounts of data, faster than ever. But concerns remain about the accuracy and ethical use of AI for healthcare research and patient care, and HEOR experts say it's essential for humans to retain oversight over AI-driven clinical decisions.

By Beth Fand Incollingo

Two decades ago, AI's role in HEOR involved using machine learning to support predictive modeling of health outcomes and costs,[1-3] but in the past few years, the emergence of new AI tools has dramatically compounded those capabilities.

Today, HEOR professionals can aggregate and synthesize vast amounts of content using generative AI,[4] or large-language models, which can "converse" with them via written exchanges, answer their questions, and even draft research papers and dossiers.[5] The field has also started to adopt agentic AI,[6] which works autonomously to gather and analyze data, set goals, make decisions, and even learn from those experiences.

AI's promise in healthcare is immeasurable, from its current capacity to match patients with treatments and improve the diagnostic potential of medical imaging to a future vision of digital twins that will support individual health. The technology's impact was recognized in 2024, when 3 scientists won the Nobel Prize in chemistry for AI-driven innovations that have changed our understanding of proteins, creating new avenues for drug discovery.[7]

While the latest iterations of AI are clearly benefiting HEOR professionals, they're also raising concerns, such as how the technology can be responsibly used in research given that even the most extensive AI databases may be missing key information needed for clinical decision making, as well as the known risk that AI-generated responses may be biased or inaccurate.[5] Although HEOR experts acknowledge that AI offers advantages too important to overlook, they caution that humans must remain involved in all the work AI touches to ensure that goals are achieved.

"We have to stop thinking of AI as a replacement and start thinking of it as an augmentation to our workflows," said Harlen Hays, MPH, who oversees 3 research teams at Cardinal Health, a company that supplies products and insights to healthcare stakeholders. "It is a tool, and that tool is only as good as your skill at using it. It does open up the ability to spend more of your time in HEOR focused on strategy and a lot less on day-to-day tactical tasks."

Integrating AI into HEOR

The generative and agentic functions used in HEOR are applications built on foundational AI models—large systems trained on enormous sets of data using self-supervised learning, which have the versatility to support a range of applications and the adaptability to perform tasks like text summarization and information extraction that are particularly useful for HEOR.[5]

In HEOR, "generative AI is increasingly used to synthesize complex literature, provide overviews of research topics, identify gaps, and support tasks like content organization and improving readability," said Alina Helsloot, director of generative AI for scientific, technical, and medical journals at Elsevier, a global leader in advanced information and decision support for science and healthcare.

Axel Mühlbacher, PhD, a professor and researcher focused on health economics and healthcare management at Hochschule Neubrandenburg, in Germany, uses the technology to structure data he's collected from patient interviews and to conduct literature searches, with the goal of highlighting population subsets and their healthcare decisions. With AI, he no longer needs research assistants to create final reports, and he can more efficiently develop fictional patient personas that represent specific populations.

"AI can summarize information with a speed we've never known before, and despite the critique that some of it might not be perfect, it's hard to find somebody who could do a better job in the same amount of time, or even in 10 times the amount of time," Mühlbacher said.

The HEOR teams that Hays oversees at Cardinal focus on real-world evidence, deploying large-language models from various vendors to seek answers to complex medical questions. Cardinal's AI Center of Excellence tailors that technology by putting "wrappers" around the models for particular use cases, which adds context and specialization and enables the system to learn faster.[8]

> "We have to stop thinking of AI as a replacement and start thinking of it as an augmentation to our workflows."
>
> – Harlen Hays, MPH

Hays's scientists use generative AI to review literature about patient populations, and his data engineering group uses it to scour structured and unstructured health records from community oncology settings (including doctors' notes in patient charts) to find individuals who might benefit from certain treatments. Meanwhile, his data enablement team has assigned agentic AI to search aggregated, de-identified patient data for patterns that might be worth studying.

Despite AI's impressive abilities, Hays cautioned, "you need the human-in-the-loop component to truly understand if results are accurate. We've had times in literature synthesis where the AIs fail and give us an erroneous therapy for a condition."

Due to the autonomy of agentic AI, Hays added, researchers are needed to set boundaries and, when patient information is searched, to build in privacy and security measures. It's also up to HEOR experts to discern whether patterns identified by agentic AI for potential study are reliable, he said. "Is it trying to find an answer to make me happy?"

Finally, Hays said, when agentic AI assists in drug discovery, humans are needed at the back end to formulate strategies for

regulatory submissions, marketing plans, and reimbursement arguments.

"Over the next 5 to 10 years, AI will replace the redundant tasks that people in HEOR don't want to do anyway," he predicted. "Instead, humans will spend a lot more time putting context around findings."

A Shift in Attention

AI is creating another kind of transformation within HEOR as it is integrated into medical devices and advanced systems for hospital management.

This has some HEOR professionals shifting their focus, leveraging the expanding pool of real-world patient data to keep pace with an increasing demand for data about the medical and economic value of AI-powered devices and organizational strategies.

One trend driving this shift involves the pairing of AI-driven software like Google DeepVariant with platforms for next-generation sequencing, such as Illumina NextSeq systems, in efforts by scientists to identify genetic mutations that drive disease.[9,10]

The focus is a bit different at GE HealthCare, where cloud AI and AI machine learning are being deployed to support the work of care teams, enhance outcomes for patients, and boost efficiency for health systems, said Parminder Bhatia, the company's chief AI officer.

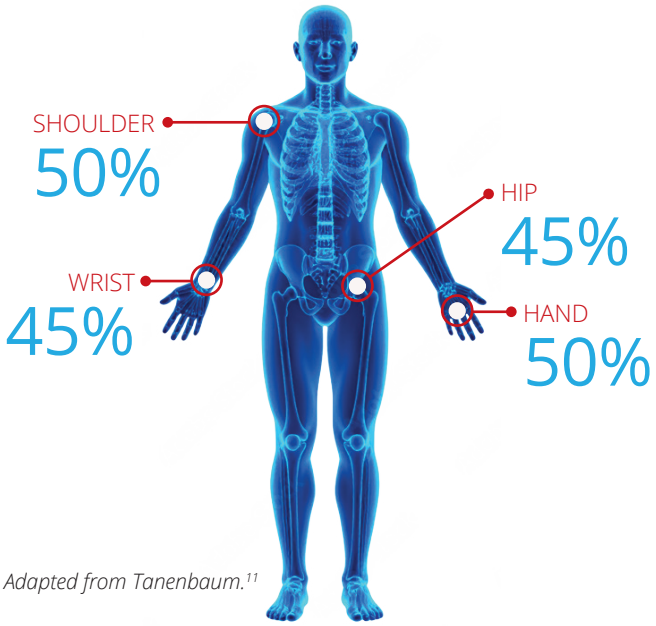
> "AI can summarize information with a speed we've never known before, and despite the critique that some of it might not be perfect, it's hard to find somebody who could do a better job in the same amount of time."
>
> – Axel Mühlbacher, PhD

As of December 2025, GE HealthCare had received 115 AI-enabled medical device authorizations from the US Food and Drug Administration (FDA) to integrate AI into medical devices and processes.

Latest AI-capable and cloud technologies include:

- AIR Recon DL, a deep learning application that enables magnetic resonance imaging machines to produce sharper images in up to half the time,[11] increasing convenience for patients and efficiency for hospitals (**Figure**).
- Intelligent RT (iRT), which streamlines the multivendor, multistep process of managing radiation therapy workflows into a unified view, with early adopters seeing the time reduced from 7 days to 7 minutes to go from simulation to treatment planning with integration of iRT and RayStation by RaySearch Laboratories.[12]
- CareIntellect for Perinatal, a cloud-first application that aggregates data from multiple sources to support clinical decision making, speeding time to treatment, and improving maternal and fetal outcomes.[13] "Every year, 700 women across the world die during labor and delivery, and 80% of that is preventable,"[14] Bhatia said. "By streamlining monitoring, nurse efficiency in handing off patients, and documentation when every second counts, we're moving from reactive to proactive."

Figure: Percent reduction in exam times associated with use of AIR Recon DL



Adapted from Tanenbaum.[11]

To improve healthcare operations, GE HealthCare offers Command Center, which streamlines patient movement through and out of the hospital. Within a year of adopting the AI-enabled software, The Queen's Healthcare Systems in Hawaii had reduced its length of patient stay by more than a day, translating into $20 million in estimated savings and the ability to accept up to 100 new transfer cases per month, a 22% increase, Bhatia said.[15]

A human-in-the-loop component is built into these solutions, too, he said.

"One example is our ultrasound devices that integrate Caption Health AI technologies," he said. "When taking a cardiac scan, these devices give sonographers a navigation system so they can get an image of good diagnostic quality, whether they have

1 year of experience or 15. But at the end of that process, a human makes decisions about the patient's care."[16]

New Potential, New Ethical Concerns

Despite its boundless promise, AI has vulnerabilities that present some ethical dilemmas—including its tendency to return "hallucinations," or false findings. For instance, media outlets reported earlier this year that Elsa, the FDA's generative AI tool for expediting the drug-approval process, was hallucinating studies that didn't exist and misinterpreting research.[17]

In its research and health tools, Elsevier works to minimize hallucinations by ensuring that information picked up in AI searches is clearly linked to exact passages in original articles, book chapters, or other sources, Helsloot said. To accomplish this, the company employs human feedback, assigns large-language models to evaluate their AI "peers" that conduct searches, and stress-tests its systems to ferret out weaknesses.[18]

Meanwhile, Scopus AI—which enables users to search Elsevier's immense database of published content—includes a tool that helps identify hallucinations by classifying its outputs based on its confidence level for each response's relevance and completeness, while also leveraging thorough and constant manual human expert evaluation.[18]

AI works on probabilities, and mistakes happen when it assumes that one piece of information should follow another, Mühlbacher said.

"There is research showing that these hallucinations are embedded within the logic of AI," he said. "And yet, it's impossible to be in competition with somebody who is using the superpower of AI and not use it yourself."

Hallucinations can hurt researchers by impugning their credibility and can harm patients by misrepresenting the likelihood of a positive or negative outcome, Hays said.

"What is the cost in healthcare if AI hallucinates that a patient was not eligible for a clinical trial when, in fact, they were?" he asked. "That's where we get into the human-in-the-loop aspect, but if people have to review every chart again, did we actually help by using AI, or did we actually just create more work?"

Another concern about AI is the vast amount of energy it uses.[19]

"AI doesn't sleep, it doesn't take breaks, and it doesn't take holidays," Hays said. "At some point, are we going to create enough climate change or pollution that our work starts to negatively affect human health?"

To provide guidance about how to navigate these issues, the World Health Organization and ISPOR have published ethical frameworks around AI in healthcare and HEOR.[20-22] But Hays suspects that enforceable, global regulatory frameworks will be needed to rein in AI's energy consumption—and it won't happen without industry buy-in.

"The big leaders in this area need to be having these conversations: Open AI, Google, AWS, Microsoft, Claude," Hays said. "At some point, there will have to be regulation, but regulation is always way behind innovation."

Science Fiction or Simply the Future?

With everything AI can do, its potential in healthcare seems boundless.

In the future, Hays imagines that agentic AI will be able to flag new studies as they are added to clinicaltrials.gov and make lists of patients who might be eligible. AI might even achieve truly personalized medicine, he said, by helping to devise individual treatment plans for people with rare conditions.[23]

In health technology assessment, AI may help regulatory panels use a more inclusive approach to drug approval decisions by creating personas that represent the patients who could benefit, Mühlbacher said.

"These decisions would normally be made by panels of about 6 people, usually older and predominantly male," he said. "Can they really assess the benefits and risks for other populations, maybe female, maybe younger? My brain's not big enough, but AI can do it."

> "Despite AI's impressive abilities, you need the human-in-the-loop component to truly understand if results are accurate."
>
> – Harlen Hays, MPH

Similarly, Mühlbacher said, when a patient's eligibility for lifesaving drugs must be debated immediately, tumor boards might eventually be populated by AI personas rather than people.

But perhaps the most fantastical use of AI on the near horizon is the creation of digital twins, or virtual patients, which will incorporate a consenting individual's personality and point of view, physique, lifestyle details, and medical history collected through health records and wearable devices.[24,25] These twins will be able to represent patients at doctor's appointments while their human counterparts stay at home, test potential treatments for an illness to determine which will work best, and even independently make medical decisions, Mühlbacher said.

Hays guesses that digital twins could also become crucial as controls in clinical trials, something Roche is already exploring.[26,27] Deploying them to create synthetic control arms could allow retrospective data to virtually mature within a predictive model, he said; digital twins might also populate standard-of-care control arms in oncology clinical trials, for example, so that all participating humans can receive investigational drugs.

Those are exciting visions, Hays said, but they come with concerns.

"By allowing a patient's data to mature into something different, which may or may not be true to life, we'd be introducing a lot of potential for error," he said. "At what point is a digital twin no longer the patient? While we use digital twins in marketing all the time, the impact is smaller there. In healthcare, the repercussions of a false study are much higher, so we would have to add more vigor."

> "When applied responsibly and with human oversight, we support the use of AI tools by authors. However, AI is not a substitute for human critical thinking."
>
> – Alina Helsloot

Mühlbacher wonders how much personal health information patients should be willing to share to create their digital twins, and what kinds of risks could ensue if those data were misused.

"Will a time come when AI is smarter than humans?" he asked. "What could happen, then, if humans were competing with AI for resources?"

Moving Ahead With AI

As HEOR professionals rely more and more on AI, they'll need to understand how to ask it questions that will elicit their intended results.

In both generative and agentic AI, prompt engineering involves not only asking a question in the most effective way but also directing the technology to take on specific personas while searching for answers.[28] "The result actually changes if the AI considers itself a computer engineer versus a researcher," said Hays, whose company is providing training in the discipline for its employees.

To complicate matters, he said, identical questions and personas may elicit varying answers if different AI systems are used.

As a result, Hays said, HEOR professionals must be transparent in their published studies about the queries and AI versions they used, so that other scientists can seek to reproduce their results.

That's just 1 of many checks and balances that Elsevier requires of authors who use AI in their published research and writing, Helsloot said.

"When applied responsibly and with human oversight, we support the use of AI tools by authors, including AI agents and deep research tools," she said. "However, AI is not a substitute for human critical thinking, and authors are responsible and accountable for the content of the manuscript, including accountability for reviewing and editing content, ensuring privacy, and disclosing the use of AI upon submission."

Learn More About HEOR and AI

In This Issue:

Integrating Artificial Intelligence Into Systematic Literature Reviews: A Review of Health Technology Assessment Guidelines and Recommendations

Harnessing Large Language Models in Health Economics and Outcomes Research: Overcoming the Hallucination Hazard

From Concept to Commercialization: AI's Emerging Role in HEOR

***Value in Health* Journal:**

Themed Section on HEOR and AI (November 2025)

ISPOR Working Group Report on AI Taxonomy in HEOR (November 2025)

ISPOR Working Group Report on Guidelines for Use of LLMs in HEOR (November 2025)

ISPOR Working Group Report on AI for HTA (February 2025)

ISPOR Education:

Streamlining Systematic Literature Reviews With Software and AI

The Application of AI in Clinical Outcome Assessment Research

References:

1. Roebuck C. AI in HEOR: Reflections on early innovations. Rxeconomics. Published March 19, 2025. Accessed November 18, 2025. https://www.rxeconomics.com/insights/ai-in-health-economics.

2. Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Affairs*. 2011;30(1):91-99. doi:10.1377/hlthaff.2009.1087.

3. Doupe P, Faghmous J, Basu S. Machine learning for health services researchers. *Value Health*. 2019;22(7):808-815.

4. Fleurence RL, Wang X, Bian J, et al. A taxonomy of generative artificial intelligence in health economics and outcomes research: An ISPOR Working Group report. *Value Health*. 2025;28(11):1601-1610.

5. Avalere Health. Contextualizing artificial intelligence for HEOR in 2023. Published November 1, 2025. Accessed November 18, 2025. https://advisory.avalerehealth.com/insights/contextualizing-artificial-intelligence-for-heor-in-2023.

6. Lee K, Paek H, Ofoegbu N, et al. A4SL: An agentic artificial intelligence-assisted systematic literature review framework to augment evidence synthesis for health economics and outcomes research and health technology assessment. *Value Health*. 2025;28(11):1655-1664.

7. Chan K, Larson C, Valdes M. Nobel Prize in Chemistry honors 3 scientists who used AI to design proteins – life's building blocks. AP. Published October 9, 2024. Accessed November 18, 2025. https://apnews.com/article/nobel-chemistry-prize-56f4d9e90591dfe7d9d840a8c8c9d553.

8. Cardinal Health. Inside Cardinal Health's AI Center of Excellence. Published March 26, 2025. Accessed November 18, 2025. https://newsroom.cardinalhealth.com/Inside-Cardinal-Healths-AI-Center-of-Excellence.

9. Ultima Genomics. Ultima Genomics partners with Sentieon and Google DeepVariant to deliver high-performance variant calling. Published May 31, 2022. Accessed November 18, 2025. https://www.ultimagenomics.com/blog/ultima-genomics-partners-with-sentieon-and-google-deepvariant-to-deliver-high-performance/

10. Elric G. Google's DeepVariant: AI with precision healthcare. AI For Healthcare. Published May 20, 2025. Accessed November 18, 2025. https://aiforhealthtech.com/googles-deepvariant-ai-with-precision-healthcare/.

11. Tanenbaum L. Shorter exam times and more predictive patient scheduling with AIR Recon DL. GE HealthCare. Published 2021. Accessed December 2, 2025. https://www.gehealthcare.com/-/jssmedia/gehc/us/files/products/molecular-resonance-imaging/air/airrecondltanenbaumsellsheetmijb03495xxglob.pdf.

12. GE HealthCare. GE HealthCare debuts AI-supported solution, designed to improve and shorten the radiation therapy workflow, at ASTRO 2025. Published September 25, 2025. Accessed December 2, 2025. https://www.gehealthcare.com/about/newsroom/press-releases/ge-healthcare-debuts-ai-supported-solution-designed-to-improve-and-shorten-the-radiation-therapy-workflow-at-astro-2025.

13. GE HealthCare. How digital perinatal solutions strengthen care consistency and continuity to improve maternal health outcomes. Published August 18, 2025. Accessed December 2, 2025. https://clinicalview.gehealthcare.com/infographic/how-digital-perinatal-solutions-strengthen-care-consistency-and-continuity-improve.

14. World Health Organization. Maternal mortality. Published April 7, 2025. Accessed November 18, 2025. https://www.who.int/news-room/fact-sheets/detail/maternal-mortality.

15. GE HealthCare. GE HealthCare collaborates with two major medical systems to advance AI technology designed to transform hospital operations and improve patient care. Published October 20, 2025. Accessed November 18, 2025. https://www.gehealthcare.com/about/newsroom/press-releases/ge-healthcare-collaborates-with-two-major-medical-systems-to-advance-ai-technology-designed-to-transform-hospital-operations-and-improve-patient-care.

16. GE HealthCare. GE HealthCare to acquire Caption Health, expanding ultrasound to support new users through FDA-cleared, AI-powered image guidance. Published February 9, 2023. Accessed November 18. 2025. https://www.gehealthcare.com/about/newsroom/press-releases/ge-healthcare-to-acquire-caption-health-expanding-ultrasound-to-support-new-users-through-fda-cleared-ai-powered-image-guidance-

17. Shyrock T. FDA's new AI tool "Elsa" faces accuracy concerns despite commissioner's high hopes. *Med Econ*. Published July 23, 2025. Accessed December 2, 2025. https://www.medicaleconomics.com/view/fda-s-new-ai-tool-elsa-faces-accuracy-concerns-despite-commissioner-s-high-hopes.

18. Evans I. Preventing AI hallucinations in our research and health tools. Elsevier. Published February 24, 2025. Accessed November 18, 2025. https://www.elsevier.com/connect/preventing-ai-hallucinations-in-our-research-and-health-tools.

19. UN Environment Programme. AI has an environmental problem. Here's what the world can do about that. Published November 13, 2025. Accessed November 18, 2025. https://www.unep.org/news-and-stories/story/ai-has-environmental-problem-heres-what-world-can-do-about.

20. World Health Organization. WHO issues first global report on Artificial artificial Intelligence intelligence (AI) in health and six guiding principles for its design and use. Published June 28, 2021. Accessed November 18, 2025. https://www.who.int/news/item/28-06-2021-who-issues-first-global-report-on-ai-in-health-and-six-guiding-principles-for-its-design-and-use.

21. World Health Organization. WHO releases AI ethics and governance guidance for large multi-modal models. Published January 18, 2024. Accessed November 18, 2025. https://www.who.int/news/item/18-01-2024-who-releases-ai-ethics-and-governance-guidance-for-large-multi-modal-models.

22. Fleurence RL, Dawoud D, Bian J, et al. ELEVATE-GenAI: Reporting guidelines for the use of large language models in health economics and outcomes research: An ISPOR Working Group report. *Value Health*. 2025;28(11):1611-1625. doi: 10.1016/j.jval.2025.06.018.

23. Karako K. Artificial intelligence applications in rare and intractable diseases: Advances, challenges, and future directions. *Intractable Rare Dis Res*. 2025;14(2):88-92. doi: 10.5582/irdr.2025.01030.

24. Gabelein K. A patient twin to protect John's heart. Siemens Healthineers. Published August 16, 2022. Accessed November 18, 2025. https://www.siemens-healthineers.com/perspectives/patient-twin-johns-heart.

25. Thangaraj PM, Benson SH, Oikonomou EK, Asselbergs FW, Khera R. Cardiovascular care with digital twin technology in the era of generative artificial intelligence. *European Heart Journal*. 2024;45(45):4808-4821. https://doi.org/10.1093/eurheartj/ehae619.

26. Rodero C, Baptiste TMG, Barrows RK. A systematic review of cardiac in-silico clinical trials. *Prog Biomed Eng*. 2023;5(3):032004. doi: 10.1088/2516-1091/acdc71.

27. Schmich F. Towards digital twins for clinical trials. PRISME Forum. Published May 21, 2024. Accessed November 18, 2025. https://prismeforum.org/wp-content/uploads/2024/05/PRISME-Forum-2024-Fabian-Schmich-Digital-Twins-1.pdf.

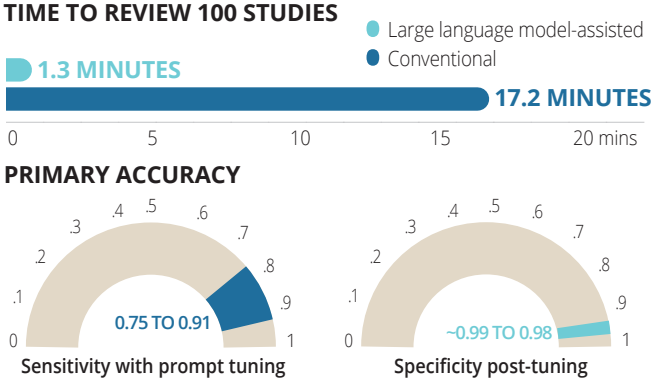
28. Shastri S. The art and discipline of prompt engineering. Communications of the ACM. Published October 27, 2025. Accessed November 18, 2025. https://cacm.acm.org/blogcacm/the-art-and-discipline-of-prompt-engineering/.

***Beth Fand Incollingo** is a freelance writer who reports on scientific, medical, and university issues.*

By the Numbers: Artificial Intelligence in Healthcare

Section Editor: **The ISPOR Student Network**
Contributors: **Dominique Seo**, University of Maryland, Baltimore, Baltimore, MD, USA; **Ahmad Furqan Kazi**, College of Pharmacy, Purdue University, West Lafayette, IN, USA; **Martyna Zielinska**, The Open University, Health Sciences, United Kingdom; **Lamis Alomair**, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia; **Oluwadotun Catherine Balogun**, The University of Texas Health Science Center at Houston, TX, USA

Large Language Models Versus Conventional Screening: Speed and Accuracy at a Glance



Real-World Impact of AI in Healthcare

SUCCESSFUL USE CASE	IMPACT
AI for hospital workflow	**80% of hospitals worldwide** use artificial intelligence to **enhance care efficiency**
AI-enabled diagnostic imaging	**98% diagnostic accuracy** **compared with** standard methods
AI screening for diabetic retinopathy (NHS pilot)	**+14% increase** in detection **accuracy**
FDA regulatory approvals	**692 artificial intelligence** and large language model medical devices **approved in 2025** (91 in 2019)

Cost-Effective Impact of Artificial Intelligence Interventions in Healthcare

Per-Patient Savings

Lung Cancer Screening	Tuberculosis Treatment Monitoring	ICU Sepsis Detection
AI-assisted CT nodule detection	*AI-enabled adherence (AiCure)*	*ML early detection*
Reduced false positives and improved detection	Increased treatment adherence	Reduced ICU length of stay
$68 per patient	**$2226 per patient**	**$14,000 per patient**
Germany	United States	Sweden, United States

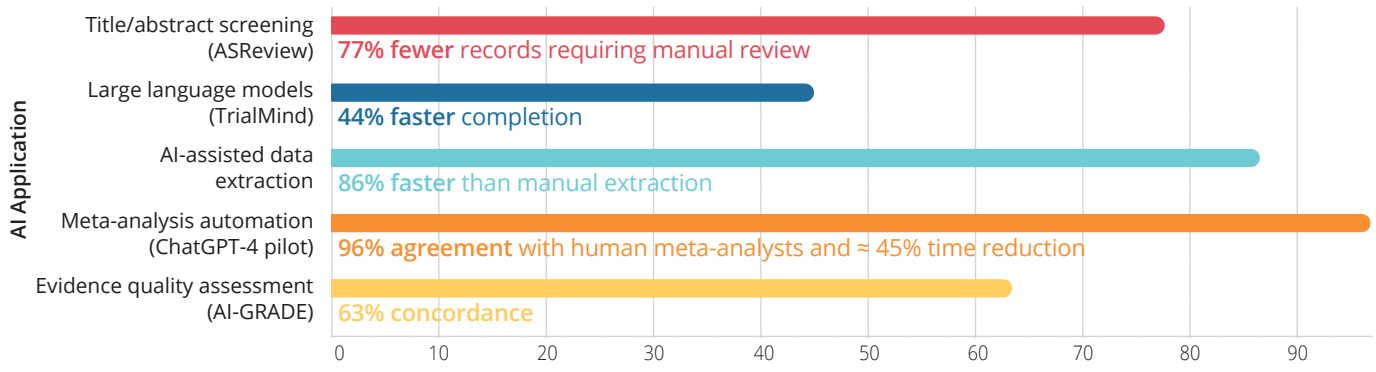
Per-QALY Savings

Atrial Fibrillation Screening	Diabetic Retinopathy	Breast Cancer Screening
Machine learning-based risk prediction	*Deep learning-based screening*	*AI-guided risk prediction*
Early detection of stroke risk	Earlier detection in rural areas	Early-stage detection
£4847–£5544 per QALY	**$1108 per QALY**	**$23,755 per QALY**
United Kingdom	China	United States

AI interventions can save up to $14,000 per patient or reduce cost per QALY by as low as $1,108

AI, artificial intelligence; CT, computed tomography; ER, emergency room; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; M, million; ML, machine learning; PACG, primary angle-closure glaucoma; QALY, quality adjusted life year; ROI, return on investment

AI-Enabled Evidence Synthesis: Accelerating Systematic Reviews and Meta-Analyses



Integrating Artificial Intelligence Into Systematic Literature Reviews: A Review of Health Technology Assessment Guidelines and Recommendations

Yifei Liu, BSc, formerly Roche, Welwyn, United Kingdom; **Seye Abogunrin, MD, MPH, MSc**; **Clarissa Emy Higuchi Zerbini, BSc**, F. Hoffmann-La Roche Ltd, Basel, Switzerland

KEY TAKEAWAYS

While artificial intelligence (AI) has the potential to enhance the efficiency of systematic literature reviews (SLRs), health technology assessment (HTA) agencies currently offer very limited guidance on incorporating AI tools into SLRs for HTA.

Text mining tools for search strategy development, as well as randomized controlled trial classifiers and priority screening tools for study selection, are recommended by IQWiG[a], NICE[b], EUnetHTA[c], and the *Cochrane Handbook*.

AI should assist rather than replace human reviewers at this stage.

Introduction

Systematic literature reviews (SLRs), a critical part of health technology assessments (HTAs), are often used to systematically evaluate the efficacy, safety, and effectiveness of health interventions. However, the SLR process remains highly labor-intensive and time-consuming. It involves a sequence of interdependent steps, starting with the formulation of the research question and development of a review protocol, followed by the design and execution of a comprehensive search strategy, screening of titles and abstracts, full-text assessment, manual data extraction and validation, risk of bias assessment, and finally, evidence synthesis. Among these, tasks such as screening large volumes of records and manually extracting data are particularly resource-heavy and contribute significantly to the overall time burden.

> With rapid development of artificial intelligence, there is great potential to streamline and automate many tasks within the systematic literature review process.

Due to this complexity, completing an SLR typically requires the sustained effort of 5 reviewers and takes, on average, over 67 weeks to complete.[1] Moreover, SLRs often struggle to keep up with the rapid influx of new evidence, requiring frequent updates and repetition of the lengthy process. These challenges can increase the workload and complexity of preparing HTA submissions, potentially contributing to delays in evaluations.

With the rapid development of artificial intelligence (AI), there is great potential to streamline and automate many tasks within the SLR process. For example, AI tools such as Rayyan, DistillerSR, and EPPI Reviewer can facilitate study screening by predicting the relevance of unscreened records, while tools like RobotReviewer and SWIFT-Review can be used to automate data extraction.[2] By incorporating these AI technologies into the current SLR workflow, the overall efficiency can be greatly improved. This could ultimately accelerate the SLR process, and consequently, HTA dossier preparation, potentially supporting timelier HTA submissions.

However, it remains unclear whether HTA agencies endorse or recommend the use of AI tools in SLRs. Therefore, this study aims to review and summarize the current HTA guidelines regarding the use of AI in conducting SLRs.

Methods

We manually searched the websites of 54 HTA agencies, including all 53 members of the International Network of Agencies for Health Technology Assessment[3] and the European Network for Health Technology Assessment (EUnetHTA), for manuals or guidelines on SLRs and reviewed them for relevant AI-related guidance. Additionally, we reviewed guidelines from the *Cochrane Handbook for Systematic Reviews of Interventions*,[4] the *Centre for Reviews and Dissemination's Guidance for Undertaking Reviews in Health Care*,[5] and the *Joanna Briggs Institute Manual for Evidence Synthesis*,[6] given their influence on HTA guideline development. No AI technologies were used in the conduct of this study.

Results

Out of the 54 HTA agencies reviewed, we found guidelines or recommendations from 3 agencies—Institute for Quality and Efficiency in Health Care (IQWiG), National Institute for Health and Care Excellence (NICE), and EUnetHTA—

[a] IQWiG: Institute for Quality and Efficiency in Health Care.
[b] NICE: National Institute for Health and Care Excellence.
[c] EUnetHTA: European Network for Health Technology.

relevant to the use of AI in conducting SLRs. For IQWiG, information was sourced from the *General Methods* document.[7] As for NICE, while the *Health Technology Evaluations Manual*[8] did not include information about the use of AI in SLR, relevant guidance was found in the *Developing NICE Guidelines Manual*.[9] EUnetHTA's guidelines were drawn from the *Methodological Guidelines - Process of Information Retrieval for Systematic Reviews and Health Technology Assessments on Clinical Effectiveness*.[10] Among the 3 SLR handbooks, only the *Cochrane Handbook* included relevant guidance on AI tools. A summary of these guidelines can be found in **Table 1**.

Literature Search

IQWiG, NICE, EUnetHTA, and the *Cochrane Handbook* all recommend the use of text-mining and frequency analysis tools to develop more effective and comprehensive search strategies. These tools can be used to identify important keywords, synonyms, and subject headings from previously identified relevant articles. Specific tools recommended include PubReMiner, Medline Ranker, searchbuildR, Voyant, and EndNote.

Study selection

For study selection, 2 main types of AI tools are recommended: randomized controlled trial (RCT) classifiers and priority screening tools. RCT classifiers are machine learning (ML) tools trained to predict the likelihood of a record being an RCT, while priority screening tools predict the relevance of unscreened records based on a training set or prior decisions by human reviewers and re-rank the records from most to least relevant.

All 4 organizations support the use of validated ML classifiers to enhance the efficiency of study selection, though with caution. NICE, for example, stresses the importance of ensuring that classifiers are used on appropriate data with known performance characteristics. Currently, these ML classifiers are primarily validated for identifying RCTs, and EUnetHTA explicitly advises against their use for nonrandomized studies. Some of the ML-based RCT classifiers recommended include the Cochrane RCT Classifier, RobotSearch, EPPI-Reviewer, RobotReviewer, and DistillerSR.

Table 1. Summary of HTA guidelines on the use of AI in SLRs.

	Search strategy	Study selection			Data extraction	RoB assessment
	Text mining tools	RCT classifier	Priority screening	Other tools	ML tools	ML tools
IQWiG General Methods (Version 7) 2023	**Yes**	**Yes**	**Maybe** "Machine learning approaches (eg, prioritization) can be tested and used to support study selection."			
NICE Developing NICE Guidelines: The Manual 2024	**Yes** eg, PubReMiner, Medline Ranker	**Yes** eg, Cochrane RCT Classifier	**Yes, with caution** Stopping rules used need to be documented and agreed with the quality assurance team.			
EUnetHTA Methodological Guidelines 2019	**Yes**	**Yes** eg, RobotSearch, Cochrane RCT Classifier	**Maybe** "Current automation approaches aim to prioritize screening results in order to sort relevant references at the start of the screening process."			
Cochrane Handbook for Systematic Reviews of Interventions 2023	**Yes** eg, PubReMiner, Voyant, EndNote	**Yes** eg, Cochrane RCT Classifier, EPPI Reviewer, RobotReviewer, DistillerSR	**Yes, with caution** No validated stopping rules, should not eliminate records automatically without manual review.	Large language models (eg, ChatGPT) may soon become useful	Inadequate evidence, but can be used to check manual data extraction	Reliability uncertain

AI, artificial intelligence; EUnetHTA, European Network for Health Technology; HTA, health technology assessment; IQWiG, Institute for Quality and Efficiency in Health Care; ML, machine learning; NICE, National Institute for Health and Care Excellence; RCT, randomized controlled trial; RoB, risk of bias; SLR, systematic literature review.

Similarly, all 4 organizations recognize priority screening as a valuable tool. However, both NICE and Cochrane point out that when using priority screening, there is currently no validated stopping rule—a predefined criterion that indicates when it is safe to stop manually screening additional records once the likelihood of finding more relevant studies becomes low. As a result, NICE recommends that the specific priority screening method used be documented and agreed upon in advance with the quality assurance team, while the *Cochrane Handbook* advises against automatically excluding records without manual review.

Additionally, the *Cochrane Handbook* highlights emerging tools based on large language models (LLMs), such as ChatGPT, which may soon enable automatic study selection without the need for training. However, as of now, there are insufficient evaluations of the performance of these LLMs.

Data extraction and risk of bias assessment

The *Cochrane Handbook* recognizes the availability of ML tools designed to automate data extraction and risk of bias assessment. However, these tools are currently limited in their ability to extract many of the necessary elements for SLRs, and there is insufficient

evidence regarding their performance and reliability. Consequently, no specific tools have been recommended for these purposes. Despite this, Cochrane suggests that these automated or semi-automated approaches can still be utilized as supplementary checks for the manually extracted data.

Conclusions

The findings of this study show that most HTA agencies have not yet provided specific guidelines regarding the use of AI in SLRs, with only a few, including IQWiG, NICE, and EUnetHTA, offering relevant recommendations. Even among those that recognize the potential of AI to improve the efficiency of SLRs, there is a clear sense of caution. None of the agencies advocate for widespread adoption of AI tools, and the guidance emphasizes the importance of using well-validated tools. This cautious approach is likely driven by concerns about the reliability, accuracy, and transparency of AI-based methods.

> While artificial intelligence tools hold significant promise for addressing inefficiencies in the systematic literature review process, it is crucial that these efficiency gains do not come at the expense of quality.

While AI tools hold significant promise for addressing inefficiencies in the SLR process, particularly in automating tasks such as screening large volumes of records, it is crucial that these efficiency gains do not come at the expense of quality. Currently, many of the available AI tools are still limited in scope and have not been thoroughly evaluated, making them unsuitable for independent use at this stage.

Nevertheless, AI tools can serve as valuable assistants in the current SLR workflow rather than replacing human reviewers entirely. For instance, priority screening algorithms could be leveraged to identify the most relevant records earlier in the screening process. Moreover, AI-driven data extraction can act as a check against manually extracted data, helping to identify potential errors or omissions. In some cases, AI tools could potentially replace 1 human reviewer, reducing the labor intensity. However, this approach might be more controversial as it challenges the current best practice of involving 2 independent human reviewers.[4]

There is a clear need for further evaluations to assess the performance and reliability of AI tools in SLRs. Comprehensive studies are required to evaluate their accuracy across different datasets and study types. As more evidence becomes available, HTA agencies will be better equipped to update their guidelines and offer more definitive recommendations on the use of AI in SLRs. Until then, a cautious and balanced approach—using AI tools to assist but not replace human input—remains essential to ensure both efficiency and quality in SLRs for HTA.

Implications to Key Stakeholders

Researchers and review authors: AI tools can enhance the efficiency of SLRs, but researchers should use them as supportive tools rather than replacements for human reviewers. It is essential to select AI tools based on their validated performance characteristics.

HTA agencies: Many HTA agencies have yet to provide specific guidelines for the use of AI in SLRs and the extent of documentation required for any AI tools that are used. Updating their guidelines to reflect the current state of AI technologies would offer clearer direction on how to effectively and safely integrate AI into the HTA process.

References

1. Borah R, Brown AW, Capers PL, Kaiser KA. Analysis of the time and workers needed to conduct systematic reviews of medical interventions using data from the PROSPERO registry. *BMJ Open*. 2017;7(2):e012545. doi:10.1136/bmjopen-2016-012545

2. Blaizot A, Veettil SK, Saidoung P, et al. Using artificial intelligence methods for systematic review in health sciences: a systematic review. *Research Synthesis Methods*. 2022;13(3):353-362. doi:10.1002/jrsm.1553

3. INAHTA Members List. INAHTA. Accessed September 10, 2024. https://www.inahta.org/members/members_list/.

4. Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions Version 6.4*. Cochrane. Updated August 22, 2024. Accessed July 15, 2024. www.training.cochrane.org/handbook.

5. Centre for Reviews and Dissemination. *CRD's Guidance for Undertaking Reviews in Health Care*. York Associates International. Published January 2009. Accessed July 15, 2024. https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf.

6. Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z. *JBI Manual for Evidence Synthesis*. JBI. Published March 2024. Accessed July 15, 2024. https://synthesismanual.jbi.global.

7. IQWiG. *General Methods - Version 7.0*. Published September 19, 2023. Accessed July 17, 2024. https://www.iqwig.de/methoden/general-methods_version-7-0.pdf.

8. NICE. *NICE Health Technology Evaluations: The Manual*. NICE. Published January 31, 2022. Accessed July 17, 2024. https://www.nice.org.uk/process/pmg36.

9. NICE. *Developing NICE Guidelines: The Manual*. NICE. Published October 31, 2013. Updated May 29, 2024. Accessed July 17, 2024. https://www.nice.org.uk/process/pmg20.

10. EUnetHTA JA3WP6B2-2 Authoring Team. *Process of Information Retrieval for Systematic Reviews and Health Technology Assessments on Clinical Effectiveness (Version 2.0)*. Accessed July 17, 2024. https://www.eunethta.eu/wp-content/uploads/2020/01/EUnetHTA_Guideline_Information_Retrieval_v2-0.pdf.

Harnessing Large Language Models in Health Economics and Outcomes Research: Overcoming the Hallucination Hazard

Manuel Cossio, MMed, MEng, Cytel Inc, Geneva, Switzerland, Universitat de Barcelona, Barcelona, Spain; **Benjamin D. Bray MBChB, MD**, Lane Clark & Peacock, London, United Kingdom

KEY TAKEAWAYS

Large language models (LLMs) can automate health economics and outcomes research (HEOR) tasks like literature review and evidence synthesis but risk generating inaccurate information ("hallucinations").

Hallucinations occur because LLMs predict text based on patterns rather than understanding content, influenced by factors like model architecture, task complexity, and prompt quality.

Continuous monitoring, error tracking, and quality control processes are essential to ensure the reliability and accuracy of LLM-generated outputs in HEOR applications.

Introduction

There is a lot of interest in the potential for generative artificial intelligence (AI) to enable new capabilities or automate aspects of health economics and outcomes research (HEOR). Many tasks in HEOR, such as literature review, evidence synthesis, programming, adapting health economic models, and writing reports, are often manual and time-consuming. Generative AI can be a helpful partner, making some of the previous HEOR activities more manageable and efficient.

Large language models (LLMs) are designed to predict and generate plausible language, making them powerful tools for various applications. They work by predicting how likely a token, or a piece of text such as a word or part of a word, is to appear in a longer sequence of tokens. The term "large" in LLMs refers to the vast number of parameters they possess. For instance, Meta's latest LLM, LLaMA 3.1, has 405 billion parameters—nearly 6 million times more than one of the first convolutional neural networks (CNNs) used for digit recognition, which had only 60,000 parameters.[1] This immense scale allows LLMs to handle and generate high volumes of written data with remarkable versatility.

As with any new technology, the path to large-scale adoption is not straightforward. One of the critical challenges in using LLMs in HEOR is the risk of generating inaccurate or misleading information, often referred to as "hallucinations." Hallucinations are instances where the model generates information that is not based on the input data or real-world facts. These hallucinations can be very plausible and hard to detect, potentially making LLMs risky or unreliable for specific tasks.

We believe, however, that hallucinations are a tractable problem, at least for many potential applications in HEOR. This guide aims to navigate these hazards, providing practical advice on hallucination mitigation tactics to allow LLMs to be used in a risk-proportionate way for HEOR activities.

The Mechanics of LLMs

LLMs are neural networks that utilize part of a specialized architecture known as transformers. Transformers are designed to process sequential data by leveraging self-attention mechanisms, which allow them to effectively capture and utilize context within the data.

Transformers offer 2 significant advantages over their predecessors, such as long short-term memory (LSTM) networks. First, transformers excel at managing longer text sequences. LSTM networks often struggled with lengthy sequences, frequently forgetting the initial words as the sequence grew longer. In contrast, transformers can handle extensive text without losing track of the context, making them far more effective for processing large volumes of text.[2]

> One of the critical challenges in using LLMs in HEOR is the risk of generating inaccurate or misleading information, often referred to as "hallucinations."

Second, transformers introduce the concept of attention, a game-changing feature in natural language processing. Attention mechanisms allow transformers to focus on the most critical parts of the input text, much like how humans read by paying varying levels of attention to different words. This ability to develop attention helps transformers understand and process the context and relationships between words more accurately.[2]

These 2 traits—handling long sequences and developing attention—make LLMs powerful for text handling, enabling them to generate coherent, contextually relevant, and insightful text across a wide range of applications.

Why LLMs Hallucinate

Hallucinations occur because LLMs, despite their advanced capabilities, do not truly understand the content or the semantic meaning of the content they process. Instead, they predict the next token in a sequence based on patterns learned from vast amounts of text data. This prediction process can sometimes lead to the generation of information that appears coherent but lacks factual basis.

> To effectively assess and mitigate the risk of hallucinations in LLMs, thorough testing and analysis are crucial.

The transformer architecture that underpins LLMs contributes to their ability to generate fluent and contextually relevant text. However, it also means that the models can sometimes overfit to patterns in the training data, leading to the creation of spurious correlations and details. This is where the attention mechanism, while powerful, can also inadvertently emphasize irrelevant or incorrect aspects of the input text.

Key Factors Influencing Hallucinations

Several key factors can influence the propensity of LLMs to generate hallucinations.

First, model-specific factors play a crucial role. The specific architecture and training data of an LLM can significantly impact its likelihood of hallucinating. Some models, depending on their design and the quality of data they were trained on, may be more prone to generating incorrect information than others.

Second, task complexity is a major contributor. More complex or nuanced tasks can increase the chances of hallucinations. LLMs often struggle with processing intricate information or understanding subtle nuances, which can lead to errors in their outputs.

Last, the quality of prompts provided to LLMs is critical. The specificity and clarity of the prompts can greatly affect the accuracy of the model's responses. Poorly constructed prompts can mislead the model, resulting in inaccurate or irrelevant outputs.

The Importance of Testing and Analysis

To effectively assess and mitigate the risk of hallucinations in LLMs, thorough testing and analysis are crucial. This process involves several key steps:

1. Sample Testing: Conducting tests on a representative sample of tasks or prompts helps identify patterns of hallucinations. For example, when using an LLM to extract data from research papers in evidence synthesis, sample testing can reveal how accurately the model identifies and summarizes key findings.

2. Error and Hallucination Tracking: Recording the types and frequency of errors and hallucinations encountered during testing is essential. This tracking helps in understanding how often the model generates incorrect information. For instance, if an LLM frequently misinterprets statistical data from clinical studies, this pattern needs to be documented.

3. Error Analysis: Analyzing the specific types of errors and hallucinations provides insights into their underlying causes. By examining instances where the LLM incorrectly extracts data from a paper, researchers can identify whether the errors stem from complex language, ambiguous phrasing, or other factors.

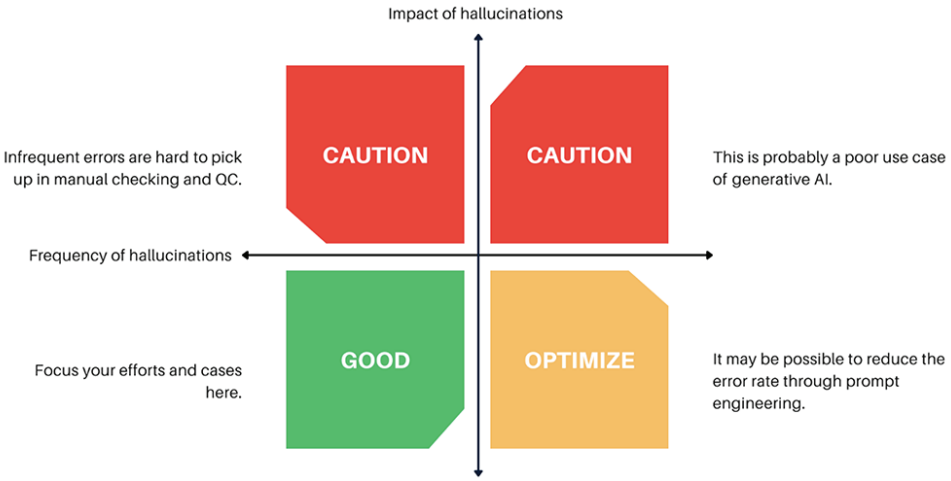
4. Impact Assessment: Evaluating the severity and potential consequences of hallucinations is vital to determine their impact on the overall quality of the generated evidence. For example, consider a systematic literature review conducted using an LLM that incorrectly extracts data. If these flawed data are then used to inform health policy decisions, it could lead to ineffective or even harmful policies being implemented (**Figure**).

Strategies for Minimizing Hallucinations

To minimize hallucinations in LLMs, several strategies can be employed. A *structured framework* for assessing hallucination risk can help to guide decisions about LLM implementation and risk management (**Figure**). *Human oversight* is crucial; experts should carefully review and verify the evidence generated by LLMs, especially in high-stakes applications. Ensuring the *quality and accuracy of the data* used to train and input into LLMs is also essential for preventing hallucinations. *Crafting clear, concise, and informative prompts* through prompt engineering can help guide LLMs toward accurate and relevant responses. *Retrieval augmented generation* (RAG) is a technique that provides the LLM with additional factual information beyond its training data and can increase the accuracy of the LLM outputs.

Additionally, *selecting models* that have been shown to have a lower propensity for hallucinations in similar applications

Figure. Case Scenarios of Hallucination Impact and Frequency in LLMs.



AI, artificial intelligence; LLMs, large language models; QC, quality control.

can reduce the risk of errors. Continuous monitoring, involving regular testing and evaluation of the LLM's performance, is necessary to identify and address any emerging issues related to hallucinations. *Quality control processes* and quality management systems should be adapted to make sure that they provide appropriate checking and assurance of LLM-generated content. By implementing these strategies, the reliability and accuracy of LLM-generated outputs can be significantly improved.

Choosing the Right Model: The Last Strategy

The last strategy to minimize hallucination is to select models that excel in specific benchmarks. These benchmarks, typically detailed on the model developers' websites, evaluate various aspects of a model's performance. Key benchmarks to consider include massive multitask language understanding (MMLU), which assesses the model's ability to handle a wide range of tasks accurately; discrete reasoning over paragraphs (DROP), which evaluates the model's reasoning capabilities over paragraphs; GPQA-Diamond (general purpose question answering), which measures the accuracy of the model in answering questions correctly on the first attempt; and LongBench, which evaluates the model's ability to handle tasks requiring long-context understanding. By selecting models that perform well in these benchmarks, researchers can reduce the risk of hallucinations and ensure the reliability of the model for tasks such as data extraction in HEOR. There are other benchmarks as well, and regular testing and monitoring of the model's performance are crucial to maintain its accuracy and reliability over time.

Looking Forward

As the field of HEOR continues to evolve, the integration of LLMs offers unprecedented opportunities for innovation and efficiency. However, the potential for hallucinations underscores the need for careful implementation and oversight. By understanding the mechanisms behind LLMs, recognizing the factors that contribute to hallucinations, and employing robust testing and analysis, researchers can harness the power of these models while minimizing risks. Through strategic prompt engineering, continuous monitoring, and human oversight, the reliability and accuracy of LLM-generated outputs can be significantly enhanced. As we navigate this exciting frontier, a balanced approach that combines technological advancement with rigorous validation will be key to unlocking the full potential of LLMs in HEOR.

References:

1. LeCun Y, Boser B, Denker JS, et al. Handwritten digit recognition with a back-propagation network. In: Touretzky DS, ed. *Advances in Neural Information Processing Systems*. Vol 2. Morgan Kaufmann; 1989:396-404.

2. Vaswani A, Shazeer N, Parmar N, et al. Attention is all you need. In: Guyon I, Luxburg UV, Bengio S, et al, eds. *Advances in Neural Information Processing Systems*. Vol 30. Curran Associates Inc; 2017:5998-6008.

From Shopping for Utilities to Investing in Societal Impact: Realizing the Promise of a Broader Value Definition in Economic Evaluation

Ahmed Seddik, PhD, MSc, BDS, University of Groningen, Groningen, the Netherlands

KEY TAKEAWAYS

The health economics and outcomes research (HEOR) community has long advocated for expanding the definition of value in healthcare. Incorporating impact measurement into HEOR practice can support efforts to realize this.

This article critiques the use of willingness-to-pay (WTP) thresholds in economic evaluations, arguing that they limit the adoption of more comprehensive evaluation frameworks.

The article introduces the impact maximization paradigm, which, unlike WTP thresholds, aligns industry and payer incentives to deliver long-term value for both patients and society.

Recent efforts to standardize measuring the societal impact of medicines have been mounting, yet the application of the societal perspective in routine health economic evaluations remains limited. This article explores potential foundational barriers in HEOR that limit the uptake of proposed forward-looking frameworks and ways to accelerate this. Drawing from my doctoral research at the University of Groningen,[1] this article builds on a growing body of evidence that calls for the integration of societal impact into health economic evaluations.

"Each of us puts his person and all his power in common under the supreme direction of the general will; and, in our corporate capacity, we receive each member as an indivisible part of the whole." Jean-Jacques Rousseau, The Social Contract (1762).[2]

In recent decades, societal priorities (or the general will, as Rousseau puts it) have been slowly shifting. Issues like climate change, sustainability, and equity are driving demand for long-term planning across industries, including healthcare. Rousseau's philosophy reminds us that societal progress requires collective action and decision making aligned with the broader good. In healthcare, this means expanding health technology assessment (HTA) frameworks to reflect societal benefits like workforce productivity, economic, and fiscal impacts—elements that traditional models often overlook. Advances in data availability, statistical tools, and computational power have made it possible to evaluate such complex, long-term impacts. Yet, current decision-making frameworks often remain unaligned with society's broader expectations. This often creates a dissonance between payer priorities and societal needs.

As an example, consider the rise of gene therapies, which promise transformative outcomes for rare diseases but come with high upfront costs. A narrow payer perspective may focus on immediate expenses, whereas a societal perspective considers the long-term benefits of reduced lifetime healthcare needs and improved quality of life with its broader implications socioeconomically. Such clear disconnect between the payer and societal perspectives highlights an urgency for reframing decision-making frameworks in a way that better aligns with societal goals.

Another quite contrasting example can be drawn from the debate around vaccine funding during a pandemic. Traditional frameworks evaluate vaccines based on direct health benefits and costs saved in treating infections. However, adopting a societal perspective reveals additional value: vaccines reduce workforce absenteeism, stabilize economies, and even foster public trust in health systems. These long-term societal benefits often remain underexplored in short-term models, which reinforces the need for a broader approach.

> Current health technology assessment practices are falling short of adopting the societal perspective: Very few guidelines recommend the inclusion of broader value elements.

As shown in **Figure 1**, broadening the perspective of analysis entails considering further elements of value. To that end, research and discussions around this topic have been mounting in recent years, resulting in a growing interest from HTA bodies to recognize the importance of considering societal and novel value elements in economic evaluations. However, it has also been shown that current HTA practices are falling short of adopting the societal perspective: Where many national HTA bodies mention broader value elements in their guidelines, very few of those guidelines effectively recommend the inclusion

Figure 1. Current perspectives in pricing and reimbursement decision making are limited to measuring outcomes, those that can be mapped to the payer and healthcare system perspectives. Reflecting the societal preferences in decision making requires broader frameworks that enable the measurement of impacts.

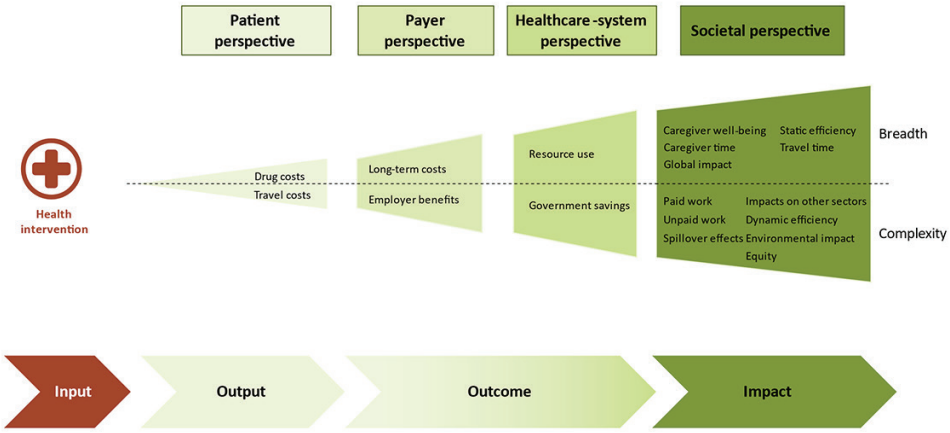
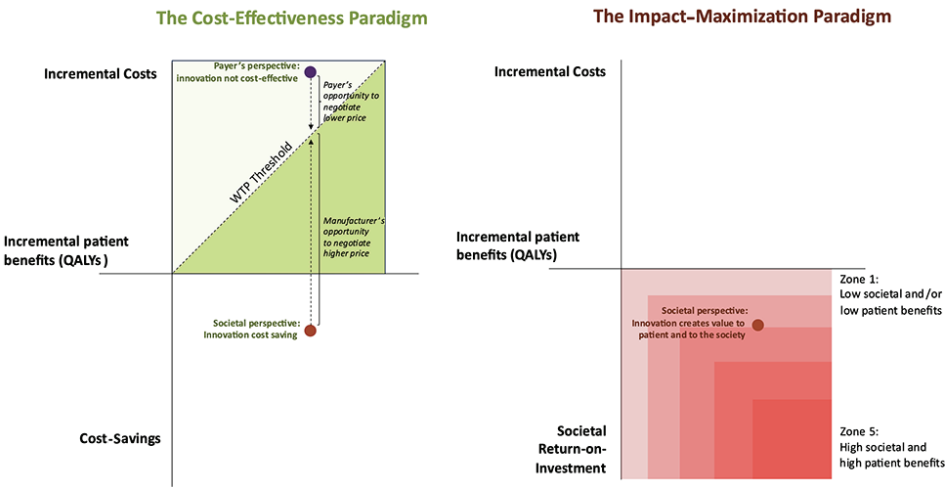


Figure 2. Within a conventional cost-effectiveness paradigm (left side), the societal perspective allows manufacturers to negotiate higher prices. In a rethought impact-maximization paradigm (right side), the societal perspective enables payers to assess and prioritize innovations based on their patient benefit and societal return on investment.



QALYs, quality-adjusted life-years; WTP, willingness to pay

of these elements as the reference case of model analyses. Furthermore, except for the Netherlands' HTA body (ZIN) recommending the application of iPCQ questionnaire to capture paid and unpaid work benefits, no other HTA guideline document worldwide currently recommends an explicit approach to measuring broader societal benefits of healthcare innovations.[3-6]

Studies attribute this hesitancy of HTA bodies to adopt and recommend evaluation frameworks that incorporate elements of societal value to various factors, including the narrow remits of payers' decision making, the feasibility of conducting such analyses, and the lack of local expertise to build broader models.

It is argued here that one important foundational barrier in health economics needs to be further explored and tackled for broadening the definition of value to come to true effect: While weighing patient outcomes against total costs (ie, cost-effectiveness) has proven useful in many instances, it is perhaps time to re-evaluate the maxim that underpins this premise.

The Impact-Maximization Paradigm

Revisiting cost-effectiveness through an impact-maximization view requires rethinking traditional evaluation methods. Cost-effectiveness analyses (CEAs) aim to maximize utility by measuring and weighing incremental costs against incremental patient utility, typically measured in quality-adjusted life years (QALYs). This consumer economics–inspired framework places payers in the role of "shoppers for utilities" in the healthcare marketplace, focusing on maximizing efficiency within limited budgets.

However, healthcare interventions, unlike consumer goods, are meant to generate broader societal benefits beyond the individual, patient-level utility. Analyses adopting the societal perspective consistently reveal higher cost savings and greater long-term impacts. A useful analogy from the world of physics can offer some clarity. In this analogy, traditional (narrow-scope) health economics can be likened to classical physics—effective at explaining the middle ground but inadequate when addressing extremes. Just as classical physics struggles to explain the vastness of the cosmos (astrophysics) or the peculiarities of subatomic particles (quantum physics), so too does classical health economics with the examples given earlier. It struggles with the extra-large—vaccines and public health interventions—and the extra-small, like gene therapies for rare diseases. These outliers require a paradigm shift to frameworks that can address complexity, scale, and long-term societal impacts comprehensively, all under one umbrella and within a standardized set of tools.

Figure 2 illustrates this paradigm shift with a reimagined cost-effectiveness plane. In traditional CEAs, interventions are judged based on their position in the northeastern quadrant, balancing incremental costs with incremental QALYs, where an innovation's price is determined by willingness-to-pay (WTP) thresholds. This method for price determination is useful to payers, provided that narrower perspectives are adopted. On the other hand, models adopting societal perspectives while aiming to determine drug prices by the WTP thresholds present manufacturers with leverage to negotiate higher prices

for their innovations. To the detriment of evolving societal preferences, this paradigm where the societal perspective has proven advantageous to manufacturers risks leaving payers reluctant to engage in discussions around broadening the definition of value in healthcare.

Therefore, an adoption of the societal perspective in health economic evaluations would only make sense if it were combined with a paradigm shift for evaluation, where manufacturers are expected to produce innovations that benefit both patients and society. In this way, a cost-effectiveness analysis of an innovative therapy adopting the societal perspective should aim for the southeastern quadrant, where the intervention seeks to demonstrate an improvement in incremental QALYs alongside maximized long-term societal impacts.

> Healthcare interventions, unlike consumer goods, are meant to generate broader societal benefits beyond the individual, patient-level utility.

This visualization reframes the role of payers as strategic investors in societal health. Payers are empowered to demand evidence demonstrating both patient and societal returns on investment. The goal becomes clear: innovative therapies must deliver value for patients while advancing societal objectives, with optimal results falling as far into the southeastern quadrant of a cost-effectiveness plane as possible. According to this paradigm, the price of innovative therapies is determined based on the opportunity cost, not on an exposing and disempowering WTP threshold.

Therefore, it is strongly argued that this shift would have significant implications:

- Empowering Payers: When the societal perspective is coupled with impact maximization as a paradigm for decision making, HTA bodies and payers can gain tools to assess societal return on investment, allowing them to align healthcare investments with long-term societal priorities. This shift reframes payers not as mere "buyers" but as strategic "investors" in societal health.
- Incentivizing Innovation: In this view, manufacturers are encouraged to design therapies that meet multidimensional value expectations. With patient-centricity still in focus, innovation for societal impact comes closer to the foreground. Growing societal priorities for topics such as pandemic preparedness, antimicrobial resistance, rare diseases, and others become more clearly reflected in manufacturers' innovation agendas.
- Redefining Metrics: In line with current trends for long-termism as a lens for decision making, success becomes no longer limited to efficiency thresholds and evolves to include a broader capacity to drive societal welfare.

This approach enables healthcare decision makers to step beyond transactional buyer-seller dynamics founded on principles of consumer economics, to embrace investment partnerships that deliver long-term societal benefits.

An Opportunity for Pharma: Bridging Stakeholder and Shareholder Interests Through Social Impact

Beyond HTA, societal impact is gaining traction in corporate environmental, social, and governance (ESG) frameworks. These frameworks, although distinct from HTA, share common goals with HTA practices. Pharmaceutical companies traditionally separate communication pathways for stakeholders (eg, patients, payers, physicians, and patient advocacy groups) and shareholders (eg, investors). This division can often lead to fragmented strategies that fail to capitalize on shared corporate objectives.

To that end, company-wide messaging can aim to utilize and promote the results from social impact studies to address shareholders and stakeholders simultaneously. Monetized social impact is a means that can allow the analyst to conduct cost-benefit analyses assessing a payer's or investor's return on investment. In this view, both the shareholder and the stakeholder are parties that are effectively investing in society's healthcare, each at a different stage and in different context, with the shared objective of maximizing their return on investments. Whether driven by frameworks that prioritize societal preferences (HTA) or ones that call for conscious investment (ESG), stakeholders and shareholders, when operating within a social impact–oriented decision-making paradigm, both seek to maximize the social welfare function.

Conclusion

This article advocates for a transformative shift in health economics along 3 critical pathways:

1. Reframing HEOR: The discipline must expand its definition to include long-term impacts, evolving into the science of Health Economics, Outcomes, and Impact Research (HEOIR).

2. Adopting the Societal Perspective: Economic evaluations should make the societal perspective their reference case, and HTA bodies should strive to give manufacturers clear guidance on ways to measure the societal elements of value, ensuring decisions reflect broader benefits beyond immediate outcomes.

3. Impact-Maximization Decision Making: Hand in hand with the previous points, and as demonstrated in Figure 2, decision-making frameworks should prioritize societal impact, repositioning healthcare spending as a strategic investment rather than a cost.

By embracing these changes, healthcare decision makers, industry leaders, and policymakers can align healthcare investments across various decision-making contexts with societal progress, building a sustainable, inclusive, and impactful ecosystem for all stakeholders.

References

1. Seddik A. *The Social Impact of Medical Innovations*. University of Groningen; 2024. doi:10.33612/diss.1121096942

2. Rousseau JJ. *The Social Contract*. Cranston M, trans. London, UK: Penguin Classics; 1968. Originally published 1762.

3. Gerves-Pinquie C, Nanoux H, Borget I, et al. Adopting a societal perspective in health-economic evaluation: a review of 9 HTA

methodological guidelines on how to integrate societal costs [abstract HTA24]. *Value Health*. 2024;27(6,S1):S248. doi:10.1016/j.jval.2024.03.1375

4. Breslau RM, Cohen JT, Diaz J, Malcolm B, Neumann PJ. A review of HTA guidelines on societal and novel value elements. *Int J Technol Assess Health Care*. 2023;39(1):e31. doi:10.1017/S026646232300017X

5. Ministerie van Volksgezondheid W en S. Guideline for economic evaluations in healthcare (2024 version). National Health Care Institute. Published January 16, 2024. Accessed May 16, 2025. https://english.zorginstituutnederland.nl/documents/2024/01/16/guideline-for-economic-evaluations-in-healthcare

6. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Roijen LH van. The iMTA productivity cost questionnaire. *Value Health*. 2015;18(6):753-758. doi:10.1016/j.jval.2015.05.009

Unlocking Real-World Evidence for Market Access of Medical Devices and Diagnostics in Europe

Bjoern Schwander, PhD, AHEAD GmbH, Bietigheim-Bissingen, Germany; **Axel Mühlbacher,, PhD**, Hochschule Neubrandenburg, Neubrandenburg, Germany; **Stephen Duffield, PhD, MD**, NICE, Manchester, United Kingdom; **Sandrine Bourguignon, PhD**, RWEality, Paris, France; **James Lavin**, Intuitive Sàrl, Aubonne, Switzerland

KEY TAKEAWAYS

Real-world evidence (RWE) is increasingly recognized as a valuable source of information to support market access for medical devices and diagnostics in Europe, as acknowledged by regulatory agencies, the medical device industry, payers, and decision makers.

While clinical trials remain the gold standard, RWE can play a crucial role in bridging evidence gaps, informing regulatory decisions, supporting reimbursement, and optimize market uptake.

Different European countries have varying approaches to incorporating RWE into decision-making processes, highlighting the need for harmonized frameworks and data standards.

Introduction

The growing demand for innovative medical devices and diagnostics (MD&D) presents both opportunities and challenges for market access in Europe. While clinical trials remain the gold standard for demonstrating safety and efficacy, the need for robust real-world evidence (RWE) is increasingly recognized.

Across Europe, RWE has become an essential component in assessing the value, safety, and effectiveness of MD&D. The following examples from Germany, the United Kingdom, and France illustrate how health authorities leverage diverse RWE sources to support regulatory decisions, reimbursement, and ongoing evaluation in routine clinical practice:

Germany: A digital therapeutic (DTx) developed for type 2 diabetes management aims to enhance standard care through features like real-time glucose monitoring, personalized feedback, and lifestyle coaching.[1] Although clinical trials demonstrated significant improvements in glycemic control, such as reduced HbA1c levels, payers and health technology assessment (HTA) bodies raised concerns regarding its long-term effectiveness, cost-effectiveness, and real-world patient adherence. To address these critical questions, the manufacturer implemented a comprehensive real-world evidence strategy, integrating data from multiple sources, including electronic health records that provided longitudinal patient data, wearable device data for continuous glucose monitoring, and patient-reported outcomes that captured behavioral changes and quality-of-life improvements. This systematic approach not only strengthened the evidence base but also facilitated ongoing evaluation of the therapeutic's impact on patient adherence and healthcare utilization.

United Kingdom: A new medical device used for diagnosing complex cardiovascular conditions is entering the early value assessment (EVA) stage with the National Institute for Health and Care Excellence (NICE).[2] Given its innovative design, limited trial data are available, so NICE recommends the collection of RWE through pragmatic studies and registry data to support the decision process. The manufacturer collaborates with National Health Service (NHS) providers to gather observational data on device performance, durability, and patient outcomes in routine clinical practice over several years. These real-world data help fill evidence gaps on long-term safety, effectiveness, and health economic impact, facilitating ongoing assessments as the device transitions from early access to wider NHS adoption. By systematically integrating these data sources, NICE aims to ensure that reimbursement and clinical use decisions are evidence-based and reflective of real-world performance.

> Across Europe, real-world evidence has become an essential component in assessing the value, safety, and effectiveness of medical devices and diagnostics.

France: The French National Health Data System (SNDS) has been extensively used to support the postmarket surveillance and long-term assessment of implantable cardiac devices, such as pacemakers and implantable defibrillators.[3] These studies leverage SNDS data to analyze device longevity, complication rates, re-interventions, and overall safety in real-world clinical practice. For example, analysis of SNDS data has demonstrated sustained safety profiles and durability of these devices over several years, providing critical evidence that informs regulatory and reimbursement decisions. This comprehensive use of real-world data ensures continuous monitoring

of device performance, helping to maintain safety standards and guiding the clinical management of patients with these implants. Such examples illustrate the value of RWE in France for the life-cycle management of high-risk medical devices, supporting their safe and effective use in routine healthcare settings.

> Real-world evidence can complement clinical trial evidence by defining unmet medical needs and refining risk assessment.

This article explores the evolving role of RWE in supporting market access for MD&Ds in Europe, drawing on insights from a recent webinar hosted by the ISPOR Medical Devices and Diagnostics Special Interest Group. As presented in **Figure 1**, RWE plays a significant role throughout the entire product life-cycle of MD&Ds, informing decisions and improving outcomes at each stage. The article places special emphasis on the use of RWE for market access purposes, recognizing its potential to bridge evidence gaps and foster better decision making.

Germany: Navigating the Strict Regulatory Landscape

Germany's healthcare system, which is strictly regulated by the laws in the Social Code Book 5 (Sozialgesetzbuch V, SGBV), emphasizes evidence-based decision making, particularly relying on clinical trials for demonstrating causality.[4]

Furthermore, it was emphasized that RWE can complement clinical trial evidence, required by SGBV:

- Defining Unmet Medical Needs: Leveraging existing registries and data sources can help identify unmet medical needs and validate the clinical relevance of new technologies. While registries provide structured data on diagnosed conditions and treatment patterns, RWE encompasses a wider array of data sources, such as electronic health records, claims databases, and patient-reported outcomes. This integration of diverse data types helps identify unmet medical needs and validate the clinical relevance of new technologies.
- Refining Risk Assessment: RWE can provide insights into the real-world safety and performance of medical devices, complementing data from controlled environments. This can lead to more accurate risk classifications and better-informed decisions regarding product development and approval.

Despite these opportunities, the challenges related to data availability, access, and the validation of causality in RWE studies remain critical considerations in Germany. While randomized controlled trials (RCTs) are the gold standard for demonstrating efficacy, RWE serves as a crucial complement by providing insights into long-term outcomes and real-world treatment effectiveness—factors that RCTs may not fully capture.

In line with these efforts, the German Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Healthcare (IQWiG) to develop a methodology for real-world data collection in a rapid report. This initiative aims to advance the use of RWE by addressing key methodological challenges in nonrandomized comparative studies. IQWiG will evaluate best practices for identifying statistical confounders, estimating sample sizes, handling treatment switches and missing data, and applying propensity score analyses in small patient populations.

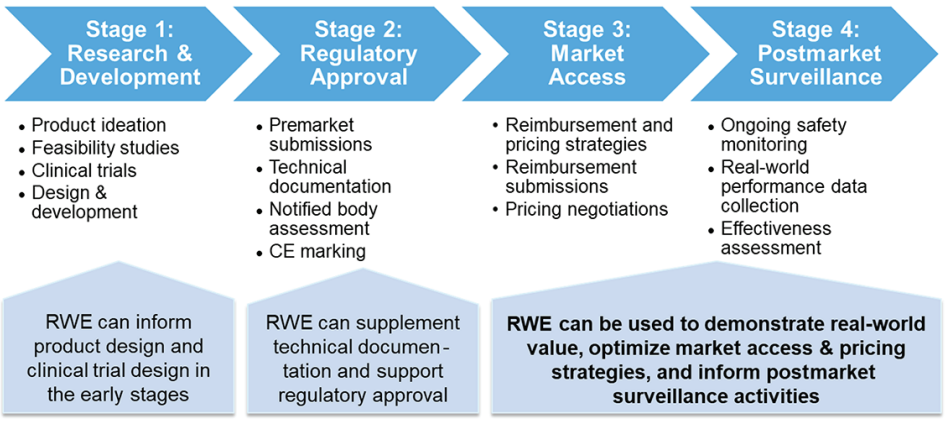
Additionally, input from pharmaceutical companies and stakeholders is being encouraged to refine the methodological framework for RWE collection.

The United Kingdom: Embracing RWE for Innovation and Efficiency

The UK healthcare system, with its centralized NHS and the influential role of NICE, presents a unique context for understanding RWE's role in market access. Although some terminology may sound drug-centric, the NICE framework for RWE explicitly applies to all health technologies, including MD&D. Stephen Duffield, PhD, MD, Associate Director for Real-World Evidence Methods at NICE, emphasized the increasing use of RWE in NICE appraisals, particularly for health technologies, including medical devices and digital health solutions, and in areas of unmet need. He highlighted the value of RWE in:

- Complementing Clinical Trial Data: RWE can support the comprehensive evaluation of long-term safety, performance, and use in diverse patient populations, which are critical parameters for MD&D.
- Supporting Late-Stage Assessment: RWE can support late-stage assessment by monitoring real-world performance and identifying rare adverse events.
- Informing Early Value Assessments: NICE's EVA program utilizes RWE to support the adoption of promising technologies while generating evidence.[5]

Figure 1. MD&D Product Life-cycle and RWE Integration



MD&D, medical devices and diagnostics; RWE, real-world evidence.

Finally, the challenges associated with the United Kingdom's diverse healthcare system, particularly in the devolved nations of England, Scotland, Wales, and Northern Ireland, were acknowledged. While there are national health policies and guidelines, healthcare delivery, budgeting, and adoption decisions occur at a regional level, which may vary across these nations and even regions. Additionally, the need for robust data standards and methodologies to ensure the reliability and validity of RWE was emphasized.

France: Navigating a Multifaceted System for MD&D

France, with its multifaceted healthcare system and a strong focus on clinical trials, presents a distinct landscape for utilizing RWE. Sandrine Bourguignon, CEO of RWEality, highlighted the importance of understanding the various pathways and committees involved in evaluating and reimbursing medical devices. While clinical trials remain the gold standard, RWE plays an important role in:

- Postmarket surveillance and safety monitoring: RWE is frequently used to monitor the real-world performance and safety of medical devices. Additionally, real-world data is a requirement for innovative biological and in vitro devices under the new RIHN 2.0 framework, which was implemented as of November 2024.[6]
- Epidemiology and target population identification: RWE supports the identification of specific patient populations, their characteristics, and their needs.
- Organizational impact assessments: France is exploring the use of RWE to assess the organizational impacts of new technologies, considering cost savings and improvements in patient pathways.

Finally, the importance of proactive data collection, robust methodologies, and the availability of comprehensive data sources, such as the French National Health Insurance database, to support RWE studies was emphasized.

Overview of Country-Specific Key Information

Table 1 provides a comparison of RWE approaches for market access in Germany, the United Kingdom, and France. This table provides a concise overview of the key differences and similarities in the approaches to RWE across the 3 countries, highlighting both convergence and divergence in policy and practice. It should help readers understand the nuanced landscape of RWE in Europe and identify key areas for improvement and harmonization.

Table 1. Comparison of RWE Approaches for Market Access in Germany, the United Kingdom, and France

Feature	Germany	United Kingdom	France
Data Sources	• Registries (registry database of medical registers in Germany[7]) • Claims data (eg, GePaRD database[8]) • Real-world patient database (eg, Honic® database combines data from different RWE sources[9])	• Registries and clinical audit data (NHS list of registries & audit data[10]) • NHS Electronic Health Records (eg, GPDPR program[11]) • Real-world patient database (eg, OPCRD® GP data from > 24 million patients[12]	• National Health Data System (SNDS)[13] combines data from all relevant health databases in France: – Observational studies & registries – Claims data – Hospital data – Cause of death data – Disability data
HTA Processes	G-BA (Federal Joint Committee): Emphasizes clinical trial evidence but increasingly considers RWE for specific use cases.	NICE (National Institute for Health and Care Excellence): Embraces RWE in its appraisals, particularly for health tech and in areas of unmet need.	HAS (French National Authority): Clinical trials remain the gold standard, but RWE is used for epidemiology, target population unmet need, organizational impact assessments, and postmarket surveillance.
Regulatory Requirements	BfArM (Federal Institute for Drugs and Medical Devices): Requires robust evidence, often clinical trials, but open to RWE for specific aspects of product approval and surveillance.	MHRA (Medicines and Healthcare Products Regulatory Agency): Similar to BfArM, with emphasis on clinical trials, but acknowledges RWE for post-market surveillance and real-world performance evaluation.	ANSM (French National Agency for Medicines and Health Products Safety): Clinical trials are the primary focus, with RWE used as complementary evidence for specific aspects of approval and surveillance.
Challenges	• Data accessibility and sharing (due to diverse data holders) • Validation of causality (due to the emphasis on RCT as the gold standard)	• Harmonizing data standards across regions (most data managed by the NHS but with regional differences) • Integration of RWE into the HTA process	• Faster access to data for research studies • Better acceptance of more RWE data in HTA process
Opportunities	• Demonstrating organizational impacts to add value in the HTA process • Demonstrating cost-effectiveness	• Adoption of the EVA program • Demonstrating cost-effectiveness	• Demonstrating organizational impacts to add value of product in HTA process • Demonstrating cost-effectiveness

EVA, early value assessment; GPDPR, General Practice Data for Planning and Research; HTA, health technology assessment; NHS, National Health Service; RCT, randomized clinical trial; RWE, real-world evidence.

Industry Perspective: Navigating a Complex Landscape

James Lavin, senior manager at Intuitive Surgical, provided a valuable industry perspective on utilizing RWE in a complex European market access landscape. He highlighted the importance of a structured approach to developing robust RWE, focusing on these key pillars:

- Clearly Defined Research Question: The research question should be specific, relevant to the target market, and aligned with the evidence needs of HTA bodies and other stakeholders. [*Example: In France, RWE based on the SNDS database has been used to evaluate the long-term safety and performance of implantable cardiac devices such as pacemakers and defibrillators, supporting regulatory and reimbursement decisions.*[3]]

- Fit-for-Purpose Data: The choice of data sources should be carefully considered, ensuring that the data are of high quality, representative of the target population, and relevant to the research question. [*Example: In Germany, a recent DTx for type 2 diabetes, which uses real-world data such as electronic health records and wearable device data, has been evaluated to support ongoing assessment and market access decisions.*[1]]

- Methodological Rigor: Statistical methods used to analyze RWE should be robust and statistically sound to address potential biases and ensure generalizability of findings. [*Example: The United Kingdom's EVA program employs rigorous methodologies, including the collection of observational and registry data, to support late-stage evaluations of health technologies, such as diagnostics and devices.*[5]]

- Transparency: Transparency throughout the research process is crucial, including clear documentation of methods, data sources, and analysis techniques. Sharing these details with HTA bodies and other stakeholders fosters trust in the research and its findings.

The importance of early engagement with HTA bodies, seeking their guidance on research questions, methods, and the types of evidence they are looking for, was emphasized. Collaboration with methodologists and other experts is also essential to validate research designs and ensure methodological rigor.

In practice, these principles are exemplified across Europe: in France through the use of SNDS data for implantable cardiac devices,[3] in Germany through postmarket surveillance of wound dressings and diagnostics,[1] and in the United Kingdom through the collection of RWE within the framework of the EVA program,[5] which supports the evaluation of medical devices and diagnostics. These examples demonstrate how MD&D can be integrated into the RWE framework to support market access and life-cycle management.

These aspects are visualized in **Figure 2**. Each pillar is crucial for building trust in RWE and ensuring its value in supporting market access decisions.

Conclusion

The webinar highlighted the growing importance of RWE in navigating the complex landscape of MD&D market access in Europe. While each country faces unique challenges related to data availability, HTA processes, and regulatory requirements, there is a clear consensus that RWE can play a valuable role in bridging evidence gaps, informing decision making, and enhancing patient outcomes.

Manufacturers have an important role to play in developing robust RWE strategies, ensuring that their research is aligned with the needs of HTA bodies and other stakeholders. Proactive data collection, rigorous methodologies, and transparent communication are essential for building trust in RWE and maximizing its value in supporting market access.

> Proactive data collection, rigorous methodologies, and transparent communication are essential for building trust in real-world evidence.

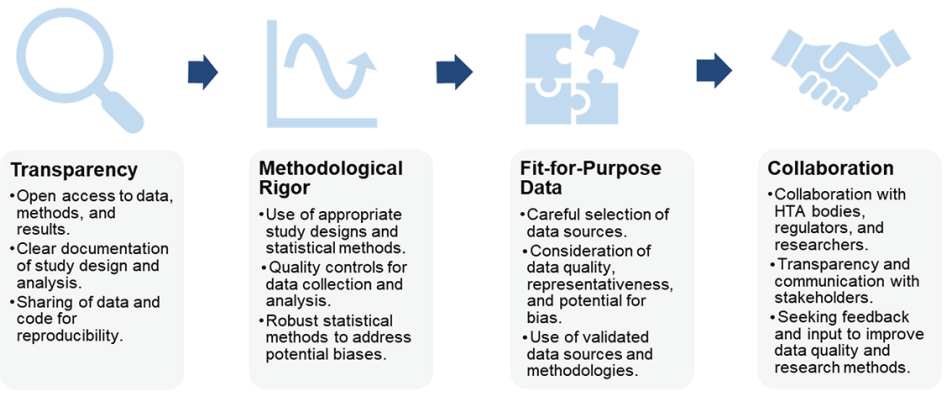
Collaboration is key. HTA bodies need to develop clear guidelines and processes for evaluating and incorporating RWE into their assessments. Policymakers must work collaboratively to establish data standards and facilitate data sharing, making RWE more readily accessible and reliable. By fostering a culture of collaboration and transparency, stakeholders can unlock the full potential of RWE to drive innovation, improve patient outcomes, and enhance the European market access landscape for medical devices and diagnostics.

Implications

- Manufacturers: Manufacturers must proactively develop robust RWE strategies to support market access, including data collection, analysis, and communication.

- HTA bodies: HTA bodies need to develop clear guidelines and processes

Figure 2. Pillars of Robust RWE Development



RWE, real-world evidence.

for evaluating and incorporating RWE into their assessments.

- Policymakers: Policymakers should work collaboratively to establish data standards and facilitate data sharing, making RWE more readily accessible and reliable.

Lessons Learned:
The webinar highlighted several key lessons learned for maximizing the value of RWE in MD&D market access:

- Proactive data collection: Data collection should be strategically planned early in the innovation process, ensuring the integration of real-world data elements into clinical trials, regulatory submissions, and postmarket surveillance to support continuous evidence generation throughout the product life-cycle.

- Fit-for-purpose data: Carefully select real-world data sources relevant to the research question, considering data quality, representativeness, and potential for bias.

- Rigorous methodology: Ensure that RWE studies are designed and conducted with methodological rigor, using appropriate statistical analysis to draw valid conclusions.

- Transparency and collaboration: Ensure transparency throughout the research process by systematically sharing methods and data with stakeholders, while fostering collaboration with HTA bodies, regulators, and academic researchers to enhance data quality, optimize processes, and support continuous evidence generation across the product life-cycle.

- Focus on value: Demonstrate the value of RWE to key stakeholders, emphasizing its ability to address evidence gaps, inform decision making, and ultimately improve patient outcomes.

References

1. Kannenberg S, Voggel J, Thieme N, et al. Unlocking potential: personalized lifestyle therapy for type 2 diabetes through a predictive algorithm-driven digital therapeutic. *J Diabetes Sci Technol*. 2024:19322968241266821.

2. National Institute for Health and Care Excellence. Transcatheter heart valves for transcatheter aortic valve implantation to treat aortic stenosis: late stage assessment. Published August 21, 2025. Accessed September 23, 2025. https://www.nice.org.uk/guidance/indevelopment/gid-hte10027.

3. de Pouvourville G, Armoiry X, Lavorel A, et al. Real-world data and evidence in health technology assessment: when are they complementary, substitutes, or the only sources of data compared to clinical trials? *Therapie*. 2023;78(1):81-94.

4. Bundesministerium für Gesundheit. Sozialgesetzbuch (SGB) - Fünftes Buch (V) - Gesetzliche Krankenversicherung. Published December 20, 1988. Accessed March 3, 2025. https://www.gesetze-im-internet.de/sgb_5/.

5. National Institute for Health and Care Excellence. Early value assessment (EVA) for medtech. Accessed March 3, 2025. https://www.nice.org.uk/about/what-we-do/eva-for-medtech.

6. Haute Autorité de Santé (HAS). RIHN (Réseau d'Innovation en Santé Numérique) 2.0 Framework. Published December 6, 2024. Accessed on March 3, 2025. https://www.has-sante.fr/jcms/p_3566839/fr/deposer-une-demande-d-inscription-au-referentiel-des-actes-innovants-hors-nomenclature-rihn-2-0.

7. Institut für Qualität und Patientensicherheit (BQS) GmbH. Register database of medical registers in Germany. Accessed March 3, 2025. https://registersuche.bqs.de/search_ext.php.

8. Leibniz-Institut für Präventionsforschung und Epidemiologie (BIPS). Die pharmakoepidemiologische Forschungsdatenbank (GePaRD). Accessed March 3, 2025. https://www.bips-institut.de/forschung/forschungsinfrastrukturen/gepard.html.

9. Health Data Technologies. The German Real-World Data Platform - honic. Accessed March 3, 2025. https://honic.eu/de.

10. National Health Service (NHS) - England. List of national clinical databases, registries and audits. Published March 16, 2024. Accessed March 3, 2025. https://www.england.nhs.uk/publication/list-of-national-clinical-databases-registries-and-audits/.

11. National Health Service (NHS) - England. General Practice Data for Planning and Research (GPDPR). Accessed March 3, 2025. https://digital.nhs.uk/services/general-practice-data-for-planning-and-research.

12. Optimum Patient Care. Optimum Patient Care Research Database (opcrd). Updated January 23, 2025. Accessed March 3, 2025. https://opcrd.optimumpatientcare.org/.

13. Caisse Nationale de l'Assurance Maladie des Travailleurs Salariés (CNAMTS). Système National des Données de Santé (SNDS). Accessed March 3, 2025. https://www.snds.gouv.fr/SNDS/Qu-est-ce-que-le-SNDS.

From Concept to Commercialization: AI's Emerging Role in HEOR

Grace E. Fox, PhD, OPEN Health, New York, NY, USA; **Shea O'Connell, PhD**; **Craig Bennison, MSc**, OPEN Health, London, England, UK; **Siddharth Kakked, MBBS, MPH**; **Kelly McCarrier, PhD**, OPEN Health, New York, NY, USA; **Elisabeth Fenwick, PhD**, OPEN Health, London, England, UK

KEY TAKEAWAYS

Artificial intelligence readiness in health economics and outcomes research is highest for structured, protocol-based activities such as literature reviews, model updates, and real-world data analytics, but remains limited for judgment-driven processes like Delphi consensus and adverse event interpretation.

Overcoming barriers such as regulatory uncertainty and limited workforce readiness will be essential to achieving responsible and scalable artificial intelligence adoption in health economics and outcomes research.

Although still nascent in health economics and outcomes research (HEOR), artificial intelligence (AI) has the potential to reshape the field. Already, AI applications such as machine learning and statistical learning, along with automation tools like rules-based algorithms, are transforming how data are synthesized, interpreted, and communicated.[1-3] There has been some uptake in HEOR, but it is uneven, constrained by technical immaturity, limited validation, and uncertainty as to regulatory expectations.[4,5] Compounding these issues, many HEOR stakeholders lack the expertise to critically evaluate AI-generated evidence.

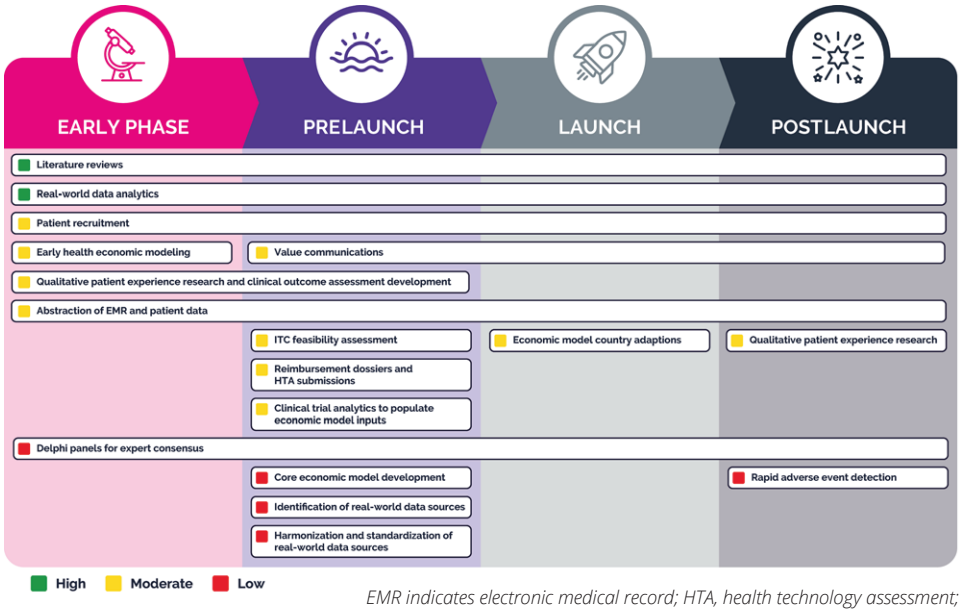
Stakeholders across HEOR would benefit from clarity on where AI-based technologies are approaching routine use and where their use remains experimental. In addition, understanding how AI applications can be integrated into the product life cycle can help organizations prioritize investment, plan operations, and ensure alignment with emerging standards.

With input from subject matter experts across our organization, we assessed the state of AI deployment across HEOR domains (eg, evidence synthesis, economic modeling, real-world data [RWD], market access, patient-centered outcomes). In describing how AI and automation have been deployed in HEOR activities, we drew upon peer-reviewed and gray literature, internal case studies, and relevant regulatory and health technology assessment (HTA) guidance.

The subject matter experts classified AI use by activity (eg, literature review) within their specific HEOR domain according to life cycle phase of use (ie, early phase, prelaunch, launch, and postlaunch). Each use of AI was rated in terms of its (1) technical maturity (validation and scalability); (2) regulatory and HTA acceptance (extent of recognition or endorsement by authorities); (3) operational feasibility (ease of integration into existing HEOR workflows); and (4) evidence of impact (measurable gains in efficiency, quality, or decision making). We rated the readiness of AI to support specific activities, using a 3-point scale: high (widely validated, feasible for immediate adoption); moderate (emerging use, requires further validation); and low (early stage or conceptual).

Here we present a summary of our findings divided by phase (see **Figure**).

Figure. Expert-led mapping



EMR indicates electronic medical record; HTA, health technology assessment; ITC, indirect treatment comparison.

Early Phase
For structured, repeatable early phase activities such as literature reviews[4,6-11] and RWD analytics using free-text data,[12-14] AI applications have demonstrated a high state of readiness. In literature reviews specifically, AI can support the process from protocol development through reporting, with scope and extent of use varying by review type.[4,6-11]

AI is also being considered for use in qualitative patient experience research and clinical outcome assessment development[15,16] to support transcript coding of qualitative patient experience data, including concept elicitation, cognitive interviews, and patient journey studies, but shows only moderate readiness.

> Understanding how AI applications can be integrated into the product life cycle can help organizations prioritize investment, plan operations, and ensure alignment with emerging standards.

Another early phase activity where AI shows moderate readiness is the conceptualization and generation of simple economic models to support pricing and positioning.[4,17] AI also shows moderate readiness for extracting structured data from clinician notes, case reports, lab reports, and other unstructured clinical text for the abstraction of electronic medical record and patient data.[18,19]

AI may aid in patient recruitment for noninterventional trials,[18,20] as it can access multiple healthcare data sources to scan digitized patient records, chatbots, and web platforms to assess individuals' eligibility to participate in large, real-world studies.[18,20]

AI cannot yet be employed reliably to summarize and analyze panelist input between Delphi rounds[21,22] or to participate alongside human experts in drafting consensus statements. Currently, these applications of AI have low readiness, with human oversight and consensus validation needed.[21,22]

Prelaunch
In the prelaunch phase, AI can support literature reviews with high readiness.[4,6-11] It also shows high readiness for RWD analytics, where generative models can be used for extracting free text, generating structured queries, and drafting statistical coding.[12-14]

AI-assisted development of reimbursement dossiers and HTA submissions represents a major efficiency frontier, with moderate readiness.[4,23-26] AI can be leveraged to develop, curate, update, and adapt reimbursement dossiers and HTA submission materials from a central source, dynamically tailoring them to the requirements of different markets and agencies.[4,23-26] Similarly, AI-driven value communication tools can be used to develop, curate, update, and adapt relevant content and transform static single-market deliverables into dynamic, multimarket tools tailored in real time to stakeholder needs.[4,23-26] This application currently demonstrates a moderate level of readiness.

Potential is evident in the use of AI-augmented transcript coding of qualitative patient experience data and AI-assisted clinical outcomes assessment development.[15,16] These capabilities are moderate in readiness. Using AI for feasibility assessments for indirect treatment comparisons, clinical trial analytics to populate economic model inputs,[27,28] and the abstraction of electronic medical record and patient data[18,19] has promise but also shows only moderate readiness at this time.

In the prelaunch phase, AI has yet to demonstrate much utility in the identification, harmonization, and standardization of RWD sources,[12] in the support of Delphi panels for expert consensus, or in core economic model development,[21,22] although the potential is there in all these areas.

Launch
At launch, AI can continue to support repetitive, data-heavy tasks, such as literature reviews.[4,6-11] In addition, AI models can continue to support development, curation, updating, and adapting value communication materials as they do in the prelaunch phase.[4,23-26] The automated adaptation of economic models[29,30] to local markets also shows moderate readiness. As noted above, AI is not yet developed to a point where it can support Delphi panels for expert consensus.[21,22]

Postlaunch
In the postlaunch phase, AI and automation are key to managing the continuous flow of RWD and post-marketing evidence. Because many analytic workflows are standardized, generative coding models[12-14] show high readiness to execute statistical analyses from text inputs and to interpret and explain study results.[12,20,21] AI for literature reviews[4,6-11] continues to show high readiness in the postlaunch phase.[4,6-11] While there is some evidence that AI can be used for patient recruitment[18,20] in real-world, postmarketing studies to cast a wide net across multiple healthcare data sources, the use case shows just moderate readiness.[18,20] Similarly, AI-assisted qualitative patient research,[15,16] abstraction of electronic medical record and patient data,[18,19] and value communications[4,23-26] continue to evolve in parallel, maintaining moderate readiness.[6-10,18,19]

> Our read is that AI readiness mirrors the methodological structure of HEOR activities, thriving in systematic, protocol-based processes such as evidence synthesis and analytics but lagging where expert deliberation, uncertainty, and qualitative interpretation predominate.

Applications in adverse event detection[31] are developing, but their utility is currently limited to academic proofs-of-concept and methodologies that require additional validation to ensure that adverse events are not missed. Likewise, AI applications show low readiness for

supporting with Delphi panels for expert consensus.[21]

Ready or Not (Yet)

The readiness of AI to support HEOR activities is highest in domains that are structured and rules based, such as literature reviews, model updates, and routine, repeatable RWD analytics. In contrast, the readiness of AI remains low in areas where contextual judgment and consensus building, such as Delphi processes or adverse event interpretation, are required. Our read is that AI readiness mirrors the methodological structure of HEOR activities, thriving in systematic, protocol-based processes such as evidence synthesis and analytics but lagging where expert deliberation, uncertainty, and qualitative interpretation predominate.

Although several barriers hinder widespread AI adoption in HEOR—among them data privacy, intellectual property considerations, evolving regulatory and HTA guidance, and limited workforce readiness—there remain clear opportunities for advancement. Many HEOR professionals have yet to fully understand how these tools can be effectively leveraged, highlighting the need for broader education and upskilling, particularly around generative AI. Embedding AI and automation into standard HEOR workflows and leveraging hybrid human-AI models to balance efficiency benefits with methodological rigor offer pathways toward responsible adoption.

Looking ahead, the development of formal guidance from regulatory authorities and HTA agencies, along with cross-industry collaborations that promote testing, integration, and shared learning, could further accelerate adoption and standardization. It is also important to recognize that pharmaceutical research is inherently conservative, as it must be to protect patient safety. This means that adoption of AI in safety-facing or adjacent roles must be approached with particular caution, ensuring that systems are validated and reliable from the outset rather than following a typical technology sector "release and refine" model.

Our analysis highlights clear areas of maturity, which include literature reviews, RWD analytics, and model updates, while identifying the key barriers of regulatory acceptance and data governance concerns. With our research, we aim to help stakeholders prioritize investment and implement strategies that align with emerging regulatory and HTA expectations.

Acknowledgments

The authors thank Christina DuVernay of OPEN Health for editorial support in developing this article.

References

1. Macia G, Ray J. Artificial intelligence in HEOR. *Value & Outcomes Spotlight*. 2024;10(2):33-35. https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/defining-digital-health---getting-clarity-for-heor/artificial-intelligence-in-heor

2. Fleurence RL, Wang X, Bian J, et al. A taxonomy of generative artificial intelligence in health economics and outcomes research: an ISPOR Working Group report. *Value Health*. 2025;28(11):1601-1610. doi:10.1016/j.jval.2025.04.2167

3. ISPOR—The Professional Society for Health Economics and Outcomes Research. *ISPOR 2024-2025 Top 10 HEOR Trends Report*. 2025. https://www.ispor.org/heor-resources/top-10-heor-trends

4. Fleurence RL, Bian J, Wang X, et al. Generative artificial intelligence for health technology assessment: opportunities, challenges, and policy considerations: an ISPOR Working Group report. *Value Health*. 2025;28(2):175-183. doi:10.1016/j.jval.2024.10.3846

5. Tachkov K, Zemplenyi A, Kamusheva M, et al. Barriers to use artificial intelligence methodologies in health technology assessment in Central and East European countries. *Front Public Health*. 2022;10:921226. doi:10.3389/fpubh.2022.921226

6. National Institute for Health and Care Excellence (NICE). Use of AI in evidence generation: NICE position statement, version 1. Published August 15, 2024. Accessed October 10, 2025. https://www.nice.org.uk/position-statements/use-of-ai-in-evidence-generation-nice-position-statement

7. Canada's Drug Agency. Canada's Drug Agency position statement on the use of artificial intelligence in the generation and reporting of evidence. Published April 2025. Accessed October 10, 2025. https://www.cda-amc.ca/sites/default/files/MG%20Methods/Position_Statement_AI_Renumbered.pdf

8. Institute for Quality and Efficiency in Health Care (IQWiG). General Methods Version 7.0. 2023. Accessed October 10, 2025. https://www.iqwig.de/en/about-us/methods/methods-paper/

9. Fox GE, Ames JT, Santpurkar N, Avissar J, Arcà E. Smarter SLRs or risky shortcuts? Perspectives from global HTA stakeholders. OPEN Health Group; 2025. https://www.openhealthgroup.com/wp-content/uploads/AI-Perceptions-Study.pdf

10. Cochrane. Cochrane's focus is on responsible use of AI in systematic reviews. Accessed October 10, 2025. https://training.cochrane.org/sites/training.cochrane.org/files/public/uploads/Ella%20Flemyng_part%203.pdf

11. Thomas J, Flemyng E, Noel-Storr A, et al. *Responsible AI in Evidence Synthesis (RAISE): Guidance and Recommendations*. 2025. https://osf.io/fwaud/files/cn7x4

12. Adams MCB, Perkins ML, Hudson C, et al. Breaking digital health barriers through a large language model-based tool for automated observational medical outcomes partnership mapping: development and validation study. *J Med Internet Res*. 2025;27:e69004. doi:10.2196/69004

13. Huang J, Yang DM, Rong R, et al. A critical assessment of using ChatGPT for extracting structured data from clinical notes. *NPJ Digit Med*. 2024;7(1):106. doi:10.1038/s41746-024-01079-8

14. Pan Y, Wang C, Hu B, et al. A BERT-based generation model to transform medical texts to SQL queries for electronic medical records: model development and validation. *JMIR Med Inform*. 2021;9(12):e32698. doi:10.2196/32698

15. Food and Drug Administration (FDA). *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products: Guidance for Industry and Other Interested Parties - Draft Guidance*. January 2025. https://www.fda.gov/media/184830/download

16. Morgan DL. Exploring the use of artificial intelligence for qualitative data analysis: the case of ChatGPT. *Int J Qual Methods*. 2023;22:16094069231211248. doi:10.1177/16094069231211248

17. Reason T, Rawlinson W, Langham J, Gimblett A, Malcolm B, Klijn S. Artificial intelligence to automate health economic modelling: a case study to evaluate the potential application of large language models. *Pharmacoecon Open*. 2024;8(2):191-203. doi:10.1007/s41669-024-00477-8

18. Astorino T. AI-powered non-interventional research delivers what DCTs promised. *Appl Clin Trials*. Published August 8, 2025. Accessed October 10, 2025. https://www.appliedclinicaltrialsonline.com/view/ai-powered-non-interventional-research-dcts

19. Schneider ME. TRIALSCOPE: using AI to scale real-world data. *Regul Focus*. September

22, 2025. Accessed October 10, 2025. https://www.raps.org/news-and-articles/news-articles/2025/9/trialscope-using-ai-to-scale-real-world-data

20. Lu X, Yang C, Liang L, Hu G, Zhong Z, Jiang Z. Artificial intelligence for optimizing recruitment and retention in clinical trials: a scoping review. *J Am Med Inform Assoc*. 2024;31(11):2749-2759. doi:10.1093/jamia/ocae243

21. Speed C, Metwally AA. The human-AI hybrid Delphi model: a structured framework for context-rich, expert consensus in complex domains. *arxiv*. Published August 12, 2025. Accessed October 10, 2025. doi:10.48550/arXiv.2508.09349 https://arxiv.org/abs/2508.09349

22. Calleo Y, Pilla F. Real-time AI Delphi: a novel method for decision-making and foresight contexts. *Futures*. 2025;174:103703. doi:10.1016/j.futures.2025.103703

23. Walters J, Guerra I, Rtveladze K, et al. SA62 Evaluating generative artificial intelligence (GenAI) in health technology assessment (HTA) content generation: a proof-of-concept using Canadian Agency for Drugs and Technologies in Health (CADTH) reimbursement dossier forms. *Value Health*. 2024;27(12):S626. doi:10.1016/j.jval.2024.10.3143

24. Jost J, Walzer S, Vollmer L. HTA113 Comparative analysis of traditional vs AI-assisted health technology assessment dossier writing. *Value Health*. 2024;27(12):S375. doi:10.1016/j.jval.2024.10.1938

25. Dietrich ES. Artificial intelligence in key pricing, reimbursement, and market access (PRMA) processes: better, faster, cheaper—can you really pick two? *J Med Econ*. 2025;28(1):586-595. doi:10.1080/13696998.2025.2488154

26. Reason T, Klijn S, Rawlinson W, et al. Using generative artificial intelligence in health economics and outcomes research: a primer on techniques and breakthroughs. *Pharmacoecon Open*. 2025;9(4):501-517. doi:10.1007/s41669-025-00580-4

27. Wu Y, Klijn S, Teitsson S, Malcolm B, Jones C, Rawlinson W. Innovations in automated survival curve selection and reporting of survival analyses through generative AI. Presented at: ISPOR EU; November 17-20, 2024; Barcelona, Spain. https://www.ispor.org/docs/default-source/euro2024/cjonessurvivalanalysiss155p24143577-pdf.pdf

28. Chhatwal J, Samur S, Yildirim IF, Bayraktar E, Ermis T, Ayer T. Fully replicating published Markov health economic models using generative AI. 2024. Accessed October 10, 2025. https://www.valueanalyticslabs.com/wp-content/uploads/2024/12/Fully-Replicating-Published-Markov-Health-Economic-Models-Using-Generative-AI.pdf

29. Rawlinson W, Teitsson S, Reason T, Malcolm B, Gimblett A, Klijn S. Automating economic modeling: the potential of generative AI for updating Excel-based cost-effectiveness models. Presented at: ISPOR; May 5-8, 2024; Atlanta, GA, USA. https://www.ispor.org/docs/default-source/intl2024/ai-adaptations-excel-ispor-us-2024138676-pdf.pdf?sfvrsn=f85aa30_0

30. Rawlinson W, Teitsson S, Reason T, Malcolm B, Gimblett A, Klijn S. Assessing the generalizability of automating adaptation of Excel-based cost-effectiveness models using generative AI. *Value Health*. 2024;27(12) S2. https://www.ispor.org/heor-resources/presentations-database/presentation/euro2024-4014/144576

31. Algarvio RC, Conceicao J, Rodrigues PP, Ribeiro I, Ferreira-da-Silva R. Artificial intelligence in pharmacovigilance: a narrative review and practical experience with an expert-defined Bayesian network tool. *Int J Clin Pharm*. 2025;47(4):932-944. doi:10.1007/s11096-025-01975-3

Access to Multi-Indication Medicines in Underserved Autoimmune Diseases: Are There Better Approaches to Supporting Sustainable Access?

Amanda Whittal, PhD; **Jacob Epstein, MEng**; **Yulia Lazareva, MSc**, Dolon Ltd, London, UK; **Jens Grueger, PhD**, CHOICE Institute, University of Washington, Seattle, Washington, USA; **Amanda Cole, PhD**, Office of Health Economics, London, UK; **Claudio Jommi, MSc**, Università del Piemonte Orientale, Novara, Italy; **Pedro Pita Barros, PhD**, Nova School of Business and Economics, Carcavelos, Portugal; **Lieve Wollaert, MSc**; **Julien Patris, MSc**, argenx, Ghent, Belgium

KEY TAKEAWAYS

There is a growing opportunity for multi-indication treatments for autoimmune diseases, yet such medicines can face significant hurdles that may impact their availability.

Current approaches to managing multi-indication medicines vary across European markets and can hinder patient access, underscoring the opportunity for pragmatic and effective solutions.

Multiyear multi-indication agreements constitute a promising solution with potential benefits for all stakeholders if implemented pragmatically. Further work will explore the practical implementation of such agreements in different countries and situations.

Introduction

The promise of multi-indication medicines in autoimmune diseases

Autoimmune diseases are a diverse group of conditions in which the immune system attacks the body's own tissues.[1,2] There are approximately 80 to 150 recognized autoimmune conditions, ranging from ultra-rare to more prevalent, affecting an estimated 5% to 10% of the global population.[3,4] Many autoimmune diseases are underserved, in that they are rare[5] and/or have limited therapeutic options.[6] Although such diseases affect relatively small patient populations, their prevalence has been rising steadily.[7]

There is a high unmet need for new treatment options for these conditions, as current approaches are only available for some autoimmune diseases, and many offer only symptomatic relief or rely on broad immunosuppression.[8] Despite this need, innovation has progressed slowly; 50% of all new active substances for autoimmune conditions identified by the European Medicines Agency (EMA) received approval before 2014, and around 16% have been on the market for more than 20 years.[9]

Recent scientific progress has deepened our understanding of disease pathophysiology, revealing clustering of phenotypically different conditions with similar pathways. For example, the neonatal Fc receptor plays a role in the pathophysiology of several autoimmune diseases, such as generalized myasthenia gravis (MG), Grave's disease, and chronic inflammatory demyelinating polyneuropathy (CIDP).[10] Such insights have presented an opportunity for the development of targeted treatments that can deliver therapeutic benefit across a broader range of patients using a single therapeutic agent. However, even with a known mechanism of action and/or safety profile, significant scientific and financial investments are required to prove a therapeutic agent will be safe and effective in a new indication.[11-13] Despite the clinical uncertainties and large investment required to bring multi-indication products to patients, there is a growing focus on multi-indication treatments for autoimmune diseases; targeted immunotherapies launched over the past 25 years have had an average of 4 indications per product, with 1 product (adalimumab) being approved for over 10 indications.[11]

> There is a need to explore the challenges for multi-indication medicines in Europe, determine current policies and best practices, and identify actionable solutions to support value-based pricing and sustainable patient access to these medicines.

Despite their promise, multi-indication medicines face significant development challenges from research and development (R&D) and regulatory approval to health technology assessment (HTA), pricing and reimbursement (P&R), and ultimately, patient access and uptake. These challenges are not new. As different cancer types share biological pathways, many oncology drugs target multiple indications (75% as of 2020[14]), yet these treatments have seen mixed success.[12] One key issue for multi-indication medicines is that the extent of unmet need and added benefit can vary substantially across diseases.[14,15] In a value-based healthcare context, this suggests that prices for such therapies should also vary depending on their use. Forms of indication-based pricing

(IBP) have been implemented in some oncology settings, often through a single list price combined with variable per indication discounts that were applied directly or via performance-based agreements.[16]

Although multi-indication medicines continue to encounter challenges in oncology, 2 disease-specific factors facilitate their adoption, distinguishing this field from immunology. First, patients generally present with a single cancer type, allowing clear attribution of treatment use to a specific indication. Second, outcome measures used for performance-based agreements (eg, survival, progression) are consistent across cancers and correlated with data already captured in claims systems.[17]

This contrasts with underserved autoimmune diseases, where conditions with disparate phenotypes (eg, systemic lupus erythematosus, Sjögren's syndrome[18,19]) often overlap or coexist in the same patient, complicating the attribution of use to a specific indication.[20] Outcome measures also vary substantially across autoimmune diseases, limiting the ability to compare value across indications and complicating development of performance-based agreements.[21] Moreover, and despite the noted challenges and substantial investment required to prove the safety and efficacy for a new use,[13] indication expansion often triggers price erosion of earlier indications in the case of a single price, and the rarity of many underserved autoimmune diseases limits the potential for offsetting this decline through increased volume.[14] Evidence from Italy shows that the average additional discount applied with each new indication (on top of discounts for prior indications) is 13%.[22] These disease-specific factors are likely to make the challenges already faced by multi-indication medicines in oncology even more pronounced in immunology.

These challenges can hinder development and access of valuable medicines. Without effective solutions, patient access may be limited or delayed due to pricing challenges, payers risk issuing payments that do not reflect a treatment's value, and manufacturers may lack incentives to develop medicines in additional indications. There is therefore a need to explore the challenges for multi-indication medicines in Europe, determine current policies and best practices, and identify actionable solutions to support value-based pricing and sustainable patient access to multi-indication medicines.

Methodology

Literature review, stakeholder engagement, and framework analysis

A multipronged approach was used in this research. A targeted literature review and case study identification were first conducted to assess European policies, regulations, and best practices for multi-indication medicines. Interviews were then held with former payers and experts from the United Kingdom, France, Italy, and Spain, with the aim of validating conclusions and discussing country-specific challenges and opportunities.

At ISPOR Europe 2024, a panel was held to disseminate the research findings. A survey was conducted with the audience, which consisted of ~800 stakeholders from industry, academia, and public organizations. The survey enabled participants to provide their perspectives on the key barriers and potential solutions for multi-indication medicines.

The literature review and empirical evidence were then compared against a formal theoretical pricing framework developed by Barros et al.[15] The framework analyzes pricing mechanisms and the conditions under which they efficiently align manufacturer incentives with maximizing total therapeutic benefit for patients.[15]

Results and Discussion

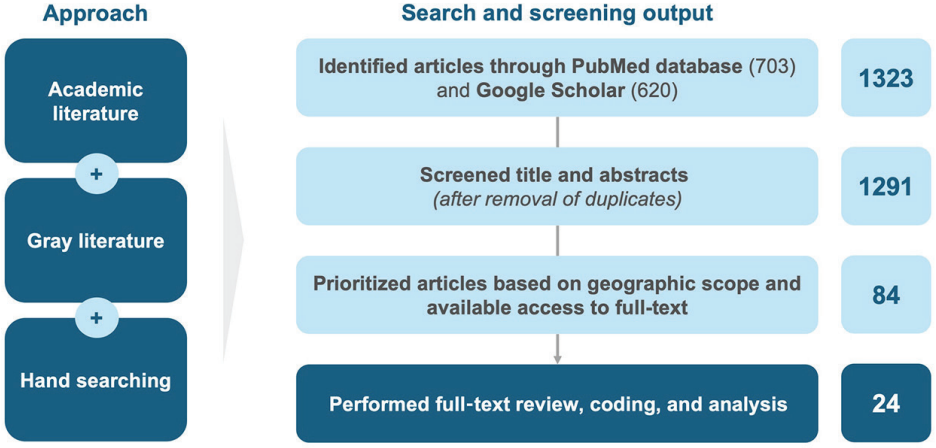
As highlighted in **Figure 1**, the literature review identified 1323 articles from academic and gray literature. Following title and abstract screening, 84 articles were included for full-text screening, of which 24 were prioritized for full-text review, coding, and analysis, based on content relevance, geographic scope, and full-text availability. Findings revealed a lack of detailed evidence on the broader value of multi-indication products, while the challenges affecting such medicines were widely recognized. The review, together with the expert interviews, provided insight into current and proposed approaches to addressing P&R challenges for multi-indication products in Europe, which are outlined below.

Current P&R approaches for multi-indication medicines

Current approaches to managing multi-indication medicines vary across European markets, as shown in **Table 1**. While certain countries (eg, the United Kingdom, Switzerland) support differential discounting, where discounts to the list price are negotiated for each indication resulting in different net prices, the focus among major markets has generally been on blended (weighted-average) pricing.[22-26]

While some healthcare payers may view existing systems as fit for purpose,[23,27]

Figure 1. Summary of literature review methodology.



these indirect forms of IBP do not truly capture incremental value at the indication level.[22,23,28] Rather than enabling both upward and downward price adjustments, these approaches are often associated with substantial price erosion upon indication and volume expansion, irrespective of the value of the new indication.[12,23,28] Moreover, price negotiations are often lengthy in practice.[22] This can result in launch sequencing, reduced R&D incentives to develop and launch new valuable indications, and suboptimal patient access to multi-indication medicines.[12,23,24,28]

An optimal theoretical solution for multi-indication medicines is "pure" IBP, as identified in the literature, discussed by ISPOR panelists and highlighted by Barros et al.[12,15,28] IBP involves assigning distinct prices to each indication based on its clinical benefit, ensuring full alignment of price with value.[24] In practice, this typically involves maintaining a single public list price while confidential net prices are negotiated separately for each indication.[29] However, it has been highlighted that pure IBP may not be a feasible solution in practice, at least in the short-term. This is due to implementation barriers such as insufficient data infrastructure to track utilization by indication and lack of financial systems to support payment and financial reconciliation.[12,23,24]

Moreover, where IBP has been applied previously, there have been significant delays to access (eg, in Italy, negotiations lasted for 603 days for follow-on indications vs 583 days for initial indications).[22]

Proposed approaches for multi-indication medicines

Given the constraints of pure and indirect forms of IBP, the ISPOR panel and Barros et al stressed the opportunity to have pragmatic, short-term, alternative solutions for multi-indication medicine access and the need for these to be developed through multistakeholder collaboration.[15,30]

Through the ISPOR audience survey, participants ranked the following potential solutions as the most effective and feasible (see **Table 2**).[30]

Table 1. Approaches to multi-indication medicine P&R by European market.

Country	Current approach for multi-indication medicines
	Single-blended, weighted-average price set per product (based on value and volume), with possibility of confidential risk sharing/contracts per indication
	Single-blended, weighted-average price set per product across all indications (based on value and volume)
	Single list price is set per product (based on value and volume), with adjustment of net prices for each indication
	Single-weighted list price set per product at the central level (based on volume); generally revised down upon approval of new indications
	All indications must be cost-effective at a single list price. Differential net prices possible via patient access schemes / managed access agreements (discounts can be based on value assessment, consumption, population, or performance, and can be applied either prospectively or retrospectively)

P&R, pricing and reimbursement.

Table 2. ISPOR panel audience results.

Response option	% that selected
A blended pricing approach with explicit weights reflecting value for different indications	28.24%
Innovative agreements, such as multiyear multi-indication agreements (MYMI)	27.78%
Optimization of data infrastructure to support real-world evidence collection and tracking	17.13%
"Pure" IBP in exceptional cases	14.81%
Implementation models with tailored minimum data requirements around usage and value by indication	12.04%

IBP, indication-based pricing.

Of the 2 most-selected options, blended pricing approaches have been thoroughly discussed in the literature. While innovative agreements like multiyear multi-indication (MYMI) have been briefly highlighted in the literature as having high potential, with previous use in European countries (eg, Belgium, the Netherlands),[14,31] further investigation is required to understand if they can offer additional benefits over existing approaches.

A MYMI agreement is a holistic agreement between manufacturers and payers across multiple indications and years, creating a comprehensive framework for value assessment and P&R for a product's current and future indications.[14,31] Instead of full upfront assessments and price negotiations for each new indication, MYMI involves a predefined arrangement with several different elements to enable access to all indications through streamlined value assessment processes, resulting in immediate or accelerated reimbursement of new indications where clinical value meets predefined criteria (see **Figure 2a**).[14] In 2017, the first MYMI agreements were established in Belgium, in which all reimbursed PD-(L)1s would have new indications automatically reimbursed within 1 month of EMA approval. These agreements resulted in patient access being accelerated by over 550 days.[31]

MYMI agreements have been linked to several benefits for a range of

stakeholders, including accelerating and broadening patient access to new indications, reducing submission and assessment workload, and improving budget/price predictablity.[14,24,31] To ensure value is maintained, periodic re-evaluations and price adjustments can occur.[14] Implementation of such agreements does not require tracking of utilization by indication, which would require sophisticated data infrastructure and is, as indicated before, difficult for often overlapping autoimmune conditions.

> Multiyear multi-indication agreements are most useful when a medicine has already demonstrated major benefit for its initial indication with many additional indications launching over an extended period.

The theoretical foundation described by Barros et al aligns closely with elements of MYMI. The authors discuss an approach they term the 2-part tariff, which combines unit prices per indication with a lump-sum payment (see **Figure 2b**).[15] The lump-sum payment is adjusted independently of how unit prices are set to ensure that total payments are proportional to the overall benefit delivered, which the authors suggest could achieve the same outcomes as IBP.[15] The 2-part tariff approach establishes rules for reimbursement of subsequent indications upfront, and it is focused on maximizing clinical benefit across all indications,[15] which aligns with the MYMI approach and goal of encouraging launch across the full set of a product's indications. Additionally, the 2-part tariff allows the lump-sum component to adjust flexibly both upward and downward as new indications are introduced.[15] This flexibility supports long-term sustainability and underscores the shared principles and benefits of MYMI agreements and 2-part tariffs.

While MYMI agreements have benefits, they are not without limitations. Such agreements come with risk, as they are negotiated based on limited evidence for future indications, with uncertainty around the eventual label, added benefit, timelines, and treatment alternatives. Payers and manufacturers may therefore be reluctant to commit to such agreements. MYMI agreements are most useful when a medicine has already demonstrated major benefit for its initial indication with many additional indications launching over an extended period. The uncertainty associated with MYMI can be mitigated by setting minimum benefit thresholds for new indications, and ensuring mutual trust, transparency, and collaboration between payers and manufacturers.

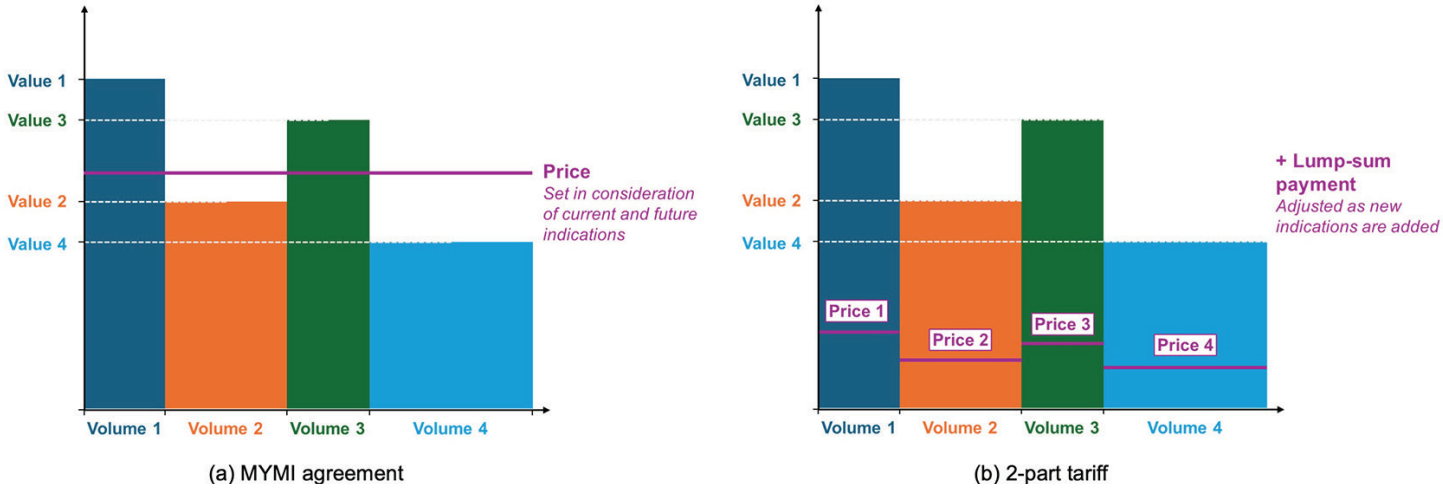
There is still a need to better understand the benefits of MYMI agreements, and if and how they can be practically applied in different countries. Bringing together the empirical evidence gathered so far and Barros et al's framework reveals key elements that could inform the design of an effective MYMI implementation blueprint to determine their potential for improving development and patient access to valuable multi-indication medicines in practice.

Conclusions and Implications

Scientific advances have identified shared biological pathways between distinct autoimmune diseases and have opened the possibility for innovative medicines that can treat multiple conditions in these underserved conditions. At the same time, multi-indication medicines continue to face access challenges, particularly in the field of immunology, due to the complex and often overlapping nature of these conditions. To ensure patients with underserved autoimmune diseases can fully benefit from multi-indication medicines, it is important that they are managed in a sustainable manner for all stakeholders. There is thus a need for novel approaches to support development, approval, and access of multi-indication medicines as practical and effective short-term alternatives to IBP.

One approach that stands out as a potentially promising solution is the MYMI agreement, which may benefit all stakeholders through broad

Figure 2. Simplified illustration of **a)** MYMI agreements compared to **b)** Barros et al's 2-part tariffs.



MYMI, multiyear multi-indication.

and accelerated launches, reduced administrative burden, and improved financial predictability.

A next step to explore this potential further would be to determine if and how MYMI agreements could be practically implemented in different country contexts. This requires stakeholder collaboration to create understanding between different perspectives and find consensus on the best ways forward.

References

1. Arango M-T, Shoenfeld Y, Cervera R, Anaya J-M. Infection and autoimmune diseases. In: Anaya J-M, Shoenfeld Y, Rojas-Villarraga A, Levy RA, Cervera R (eds). *Autoimmunity: From Bench to Bedside* [Internet]. Bogota, Colombia: El Rosario University Press; 2013.

2. Understanding autoimmune diseases. NIH News in Health. Published June 2022. Accessed August 27, 2025. https://newsinhealth.nih.gov/2022/06/understanding-autoimmune-diseases.

3. Conrad N, Misra S, Verbakel JY, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. *Lancet*. 2023;401:1878-1890.

4. Bieber K, Hundt JE, Yu X, et al. Autoimmune pre-disease. *Autoimmun Rev*. 2023;22:103236.

5. Multifaceted autoimmunity: new challenges and new approaches. *eBioMedicine*. 2023;88:104474.

6. Autoimmune diseases. National Institute of Allergy and Infectious Diseases. Updated March 20, 2025. Accessed September 4, 2025. https://www.niaid.nih.gov/diseases-conditions/autoimmune-diseases.

7. Dresser L, Wlodarski R, Rezania K, et al. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. *J Clin Med*. 2021;10:2235.

8. Song Y, Li J, Wu Y. Evolving understanding of autoimmune mechanisms and new therapeutic strategies of autoimmune disorders. *Signal Transduct Target Ther*. 2024;9:263.

9. Download medicine data. European Medicines Agency. Accessed July 24, 2025. https://www.ema.europa.eu/en/medicines/download-medicine-data.

10. Gjølberg TT, Mester S, Calamera G, et al. Targeting the neonatal Fc receptor in autoimmune diseases: pipeline and progress. *BioDrugs*. 2025;39:373-409.

11. Gores M, Scott K. Success multiplied: launch excellence for multi-Indication assets. IQVIA. Published 2023. Accessed October 30, 2025.https://www.iqvia.com/-/media/iqvia/pdfs/library/white-papers/iqvia-launch-excellence-for-multi-indication-assets-02-23-forweb.pdf.

12. Michaeli DT, Mills M, Kanavos P. Value and price of multi-indication cancer drugs in the USA, Germany, France, England, Canada, Australia, and Scotland. *Appl Health Econ Health Policy*. 2022;20:757-768.

13. Position paper on drug repurposing. European Federation of Pharmaceutical Industries and Associations. Published March 2024. Accessed October 2, 2025. https://www.efpia.eu/media/2mlhtlac/position-paper-on-drug-repurposing.pdf.

14. Lawlor R, Wilsdon T, Darquennes E, et al. Accelerating patient access to oncology medicines with multiple indications in Europe. *J Mark Access Health Policy*. 2021;9:1964791.

15. Barros PP, Righetti G, Sa L. Pricing mechanisms for multi-indication drugs. Published August 12, 2025. Accessed September 23, 2025. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=5374679.

16. Griffiths A, Economides S, Favier G, Healy J, Dewan S. The pricing and market access landscape for multi-indication products: challenges and opportunities in Europe. KPMG. Published 2023. Accessed August 27, 2025. https://assets.kpmg.com/content/dam/kpmgsites/uk/pdf/2023/10/the-pricing-and-market-access-landscape-for-multi-indication-products.pdf.

17. Delgado A, Guddati AK. Clinical endpoints in oncology - a primer. *Am J Cancer Res*. 2021;11:1121-1131.

18. Gianordoli APE, Laguardia RVRB, Santos MCFS, et al. Prevalence of Sjögren's syndrome according to 2016 ACR-EULAR classification criteria in patients with systemic lupus erythematosus. *Adv Rheumatol*. 2023;63:11.

19. Cherney K. What to know about lupus and Sjögren disease. Healthline. Published November 22, 2023. Accessed October 30, 2025. https://www.healthline.com/health/lupus/lupus-and-sjogrens.

20. Marques J, Lobato M, Leiria Pinto P, et al. Asthma and COPD "overlap": a treatable trait or common several treatable-traits? *Eur Ann Allergy Clin Immunol*. 2020;52:148-159.

21. Purna Singh A, Shahapur PR, Vadakedath S, et al. Research question, objectives, and endpoints in clinical and oncological research: a comprehensive review. *Cureus*. 2022;14:e29575.

22. Rossini EE, Galeone C, Lucchetti C, et al. From indication-based pricing to blended approach: evidence on the price and reimbursement negotiation in Italy. *Pharmacoecon Open*. 2024;8:251-261.

23. Mills M, Kanavos P. Healthcare payer perspectives on the assessment and pricing of oncology multi-indication products: evidence from nine OECD countries. *Pharmacoecon Open*. 2023;7:553-565.

24. Preckler V, Espín J. The role of indication-based pricing in future pricing and reimbursement policies: a systematic review. *Value Health*. 2022;25:666-675.

25. Jung SM, Kim W-U. Targeted immunotherapy for autoimmune disease. *Immune Netw*. 2022;22.

26. Campillo-Artero C, Puig-Junoy J, Segú-Tolsa JL, et al. Price models for multi-indication drugs: a systematic review. *Appl Health Econ Health Policy*. 2020;18:47-56.

27. Cole A, Neri M, Cookson G. Payment models for multi-indication therapies. OHE. Published November 1, 2021. Accessed October 30, 2025. https://www.ohe.org/publications/payment-models-multi-indication-therapies/.

28. Mills M, Michaeli D, Miracolo A, et al. Launch sequencing of pharmaceuticals with multiple therapeutic indications: evidence from seven countries. *BMC Health Services Research*. 2023;23:150.

29. Pani LC, De Luca A, Mennini FS, et al. Pricing for multi indication medicines: a discussion with Italian experts. *Pharmadvances*. 2022;4:163-170.

30. Pricing and reimbursement of multiple indication medicines: Can a balance be found between different stakeholder perspectives to optimise value and access for patients, while ensuring sustainable and affordable innovation? Reported at: ISPOR Europe; November 17-20, 2024; Barcelona, Spain.

31. Armstrong H, Petrova A, Wilsdon T, et al. Multi-year multi-indication agreements for supporting patient access to oncology medicines with multiple indications: an experimental approach or here to stay? *J Mark Access Health Policy*. 2025;13:2.

Value & Outcomes Spotlight has partnered with PharmaBoardroom to share content that is relevant to the global HEOR community. This interview was originally published on the PharmaBoardroom website in September 2025. For more information and other stories like this, visit PharmaBoardroom.

Q&A

The Next Inflection Point: How Artificial Intelligence Could Shave Years Off Drug Development

Interview With Melanie Ivarsson, PhD, Scientific Advisory Board Member, PhaseV

"AI is another inflection point for the industry, but its impact will depend entirely on how it is implemented and adopted."

– Melanie Ivarsson

As chief development officer of Moderna, Melanie Ivarsson, PhD, spearheaded the rapid development of a COVID-19 vaccine that helped the world emerge from the pandemic. Now back in the United Kingdom and drawing on more than 25 years of clinical development leadership across Lilly, Pfizer, Takeda, and Moderna, Ivarsson recently joined the scientific advisory board of PhaseV, an artificial intelligence (AI)-driven solutions provider for the clinical research industry. In this interview, she gives her insider take on the true potential of AI to reshape the drug development process.

PharmaBoardroom: What has changed in how medicines are developed since you started in the pharma industry around the turn of the millennium, and what challenges persist?

Melanie Ivarsson: When I started out, the process for monitoring drug products, ensuring quality, and collecting data was incredibly manual. Everything was done on paper, using 3-part NCR forms. We would assess how the data was being collected, monitor it with sticky notes, strip out bits of paper, and send them off. Then, the data would be manually entered into a database.

The first major change occurred 20 years ago, when electronic data capture was introduced. This innovation promised to significantly speed up the process by allowing direct data entry into databases, although this revolution has not materialized.

The next major shift, which is happening now, is artificial intelligence (AI). Today, we have real-time access to trial data, which allows us to design trials more efficiently and make adjustments in real time as needed, improving both data quality and the patient experience.

However, while these technological advances are impressive, the challenge is in incorporating them into our processes in a way that truly enhances outcomes. The industry tends to be risk-averse, focusing on maintaining the highest possible quality, which is obviously vital. But this cautious approach can stifle innovation.

AI should be viewed as a team member. It shouldn't be feared or double-checked at every step; instead, it should be integrated into the process. This is where we're likely to see significant progress.

PB: Where do you see the greatest levels of optimism and fear towards AI within pharma?

MI: Right now, we are seeing a very enthusiastic approach from senior executives. They understand the impact that AI will have on every part of drug development, from research and compound discovery to development and commercialization. It's a heavily regulated environment, though, so regulators need to help companies navigate AI's integration, and we're starting to see progressive signals from bodies like the US Food and Drug Administration and the UK Medicines and Healthcare products Regulatory Agency.

> AI will impact every stage of the development pathway. In drug discovery, we should see far better "shots on goal," with compounds that are more on target and less likely to fail later.

However, the real challenge lies in implementation. While senior leadership is on board, there's often hesitancy further down in organizations, especially if adopting new technology could slow things down. Speed tends to be highly rewarded, and if employees are unsure whether AI will assure quality or risk delays, they become concerned.

That's why it's so important for leaders to communicate effectively within their organizations. Leaders need to stay closely connected with their teams and make sure the message is understood and embraced. You can't simply throw new technology at people and expect it to work without proper guidance and support.

PB: How would you attempt to ease the anxiety around AI use for those who fear it may be coming to replace them?

MI: As I mentioned, we need to treat AI like a team member. Companies like PhaseV are taking vast amounts of data—far more than any individual could ever process—and turning it into actionable insights. This enables smarter, faster decisions and allows people to do their jobs better.

Almost everyone working in clinical development feels there's more to do each day than there are hours available. AI helps address that. It is not about replacing people; it is about empowering them. For example, PhaseV's dashboards give teams the data they need in real time to make the right decisions and move faster.

When we were developing the COVID vaccine at Moderna, we tried to build some of that functionality manually, with updates twice a day; morning and evening. The first thing I would do each morning was turn on my computer to check the dashboard and see what actions we needed to take. Today, platforms like PhaseV automate that process and deliver continuous real-time analysis, meaning less time pulling data together and more time thinking, collaborating, and making the right decisions as a team.

PB: Many of the major roadblocks to improving the clinical trial process are quite prosaic: staff turnover, infrastructure gaps, patient mistrust, and lack of information. Given this, are we at risk of over-promising what AI can truly deliver?

MI: There is always a risk of over-promising with new technologies. The move from paper case report forms to electronic data capture 20 years ago was supposed to revolutionize everything, but it fell short because we didn't fully embrace the opportunity or adapt our processes.

AI is another inflection point for the industry, but its impact will depend entirely on how it is implemented and adopted. Additionally, AI will not solve every problem. Issues like patient pathways, staff shortages, and infrastructure will require other types of solutions.

That said, AI can have a huge impact if it is integrated effectively. We're already seeing major investments in the hospital and healthcare sectors. What's crucial is collaboration across stakeholders: industry, regulators, hospitals, investigator sites. The real success will come from working together, sharing data, and improving processes in a way that benefits patients.

PB: What lessons could pharma learn from Operation Warp Speed—a period of unprecedented collaboration at a supercharged pace—as it attempts to embed AI into the drug development process? When might we start seeing a genuine impact?

MI: That period was really extraordinary: the best collaboration I have ever seen between industry and regulators, all working together for the common good. That spirit is something we should try to emulate with AI.

Looking ahead, I think AI will impact every stage of the development pathway. In drug discovery, we should see far better "shots on goal," with compounds that are more on target and less likely to fail later.

> My expectation is that AI should shave years, not months, from drug development timelines in well-identified areas, through optimized trial design, smarter site selection, and better real-time trial execution.

Data will be critical. Federated and curated datasets will allow us to train models effectively, for example, learning from everything that has been done in a particular disease to design the optimal trials of the future. There are still gritty operational processes—contracting, study setup, physically getting drugs to sites—that AI may not solve immediately, but even here we see progress. AI tools in the legal sector suggest contracting timelines could

shrink from months to days, provided people are comfortable adopting them.

My expectation is that AI should shave years, not months, from drug development timelines in well-identified areas, through optimized trial design, smarter site selection, and better real-time trial execution. What we can do with the data once it is collected will also be transformative, providing insights for rapid improvement. And with regulators beginning to commit to using AI in data assessment, approval timelines should also shorten. Taken together, I see this as the next major inflection point for the industry.

> Where I see enormous potential is in rare diseases. AI could speed up trials significantly, for example, by analyzing natural history or control data in ways that currently take months of manual chart review.

PB: Are there any therapeutic areas where you are particularly optimistic about AI's ability to move the dial?

MI: I think AI will apply across all areas but will have a particularly strong impact in those where we already have large amounts of data. For example, around 40% of clinical trials are in oncology, and there have been huge recent advances in Alzheimer's research, metabolic diseases such as obesity, and in vaccines and infectious disease. These are also priority areas for governments because of their societal costs. Alzheimer's disease, cancer, and metabolic and cardiovascular disease are clear targets for AI-driven impact.

But where I see enormous potential is in rare diseases. AI could speed up trials significantly, for example, by analyzing natural history or control data in ways that currently take months of manual chart review. With the right applications, this work could be done much faster, which would be incredibly impactful for rare disease communities.

PB: Having had a long career in big pharma, and now working adjacent to that world as a scientific advisor, how have you found the transition? What kind of impact are you hoping to have in this less hands-on role over the next few years?

MI: Over the past 6 months, I've taken the time to step back and look at the industry from a completely different perspective. When you are in a day-to-day leadership role, so much of your energy is taken up by managing people, timelines, and operational details. Now, I'm enjoying the chance to look at the industry from different angles.

What excites me most is identifying where the next big investments will be and how people need to work together. Collaboration—around new technologies, partnerships, and implementation—is going to be the key to progress.

Stepping back has given me the privilege of a bird's-eye view. I've had some amazing conversations with inspiring people that I wouldn't have had otherwise, and I'm very grateful for that.

ISPOR

Improving healthcare decisions

ISPOR-The professional society for health economics and outcomes research
505 Lawrence Square Blvd, South
Lawrenceville, NJ 08648 USA
www.ispor.org