MAY/JUNE 2026 VOL. 12, NO. 3

VALUE & OUTCOMES SPOTLIGHT

An HEOR news magazine

WALKING THE DRUG PRICING TIGHTROPE

BALANCING AFFORDABILITY VS. INNOVATION

ISPOR

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MAY/JUNE 2026
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An HEOR News Magazine

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FROM THE EDITOR

Beyond Price Tags: Using HEOR to Balance Affordability and Innovation

Prescription drug pricing has become a lightning rod for public frustration, but underneath the politics of prescription drug pricing lies a harder question: What is the right price for health? Health economics and outcomes research (HEOR) does not resolve that moral dilemma, but by discussing drug prices in relation to clinical effectiveness, economic impact, and real-world outcomes, HEOR moves the debate from rhetoric toward measurable value.

Recent drug pricing reforms in the United States have crystallized the tension. The Inflation Reduction Act's (IRA's) Medicare provisions aim squarely at affordability, capping annual out-of-pocket spending for beneficiaries (around $2100) and imposing negotiated price limits on high-cost Part D drugs for conditions like diabetes and cardiovascular disease. These steps are designed to expand coverage and reduce financial toxicity for seniors who have long faced difficult trade-offs at the pharmacy counter.

Yet the same reforms have sparked deep concern about the future of innovation. A white paper published by the USC Schaeffer Center for Health Policy & Economics found that a 10% reduction in expected US revenues would be associated with a 2.5%–15% decline in pharmaceutical innovation, measured by clinical trial starts or new drug approvals. The Congressional Budget Office and others similarly project that lower long-run revenues will reduce the expected profitability of drug candidates and modestly decrease annual approvals over time.

> The elasticity of innovation with respect to revenue is real but not infinite; a modest reduction in approvals may be a tolerable price for broader access to existing therapies, particularly when many launches bring marginal clinical improvement at premium prices.

Industry and trade organizations interpret these figures as a warning sign. Trade groups argue that shortening the period of market-based pricing and penalizing price increases above inflation will deter postapproval research, especially for new indications and secondary populations, and push companies to reorient portfolios toward products less exposed to early government price setting. They contend that policies such as Most Favored Nation (MFN) pricing and mandated Medicare "negotiation" will strip billions from manufacturing and research and development (R&D) in the United States, disproportionately harm small and emerging firms, and erode American leadership in this field as China's share of global clinical trials climbs.

Reform advocates counter that high prices already delay or deny access for millions, and that expanding affordability through negotiation and caps is itself a public health intervention. In their view, the elasticity of innovation with respect to revenue is real but not infinite; a modest reduction in approvals may be a tolerable price for broader access to existing therapies, particularly when many launches bring marginal clinical improvement at premium prices.

This is precisely where HEOR is essential: not to choose a side, but to quantify trade-offs between affordability today and innovation for tomorrow.

The global picture is no less complex. International reference pricing (IRP)—where countries benchmark their drug prices against a basket of comparable peer countries—was intended as a straightforward cost-containment tool. In practice, it has created powerful spillovers. Manufacturers often delay or avoid launching in lower-price markets

to prevent a single discounted list price from cascading into wealthier reference countries. Lower-income nations can paradoxically end up facing higher effective prices relative to their purchasing power, and uniform international price bands limit the flexibility needed for genuine tiered pricing.

Tying US drug prices to foreign benchmarks through MFN and IRP may sound like painless savings, but it threatens the engine of biomedical innovation. Because the United States is the global pharmaceutical industry's main revenue engine, deep drug price cuts under MFN rules would sharply limit reinvestment in research. Economic modeling suggests such policies could halve global biopharmaceutical R&D spending and result in hundreds fewer innovative medicines reaching patients worldwide over the coming decade.

By reducing pharmaceutical company revenues, these policies become blunt tools that devalue fragile biotechs, discourage launching in countries with strict price controls, and push investment away from Medicare and high-risk science toward safer, commercial markets with fewer restrictions on government price controls. Patients will not feel the impact overnight, but they will feel the cumulative effects of fewer clinical trials, narrower pipelines, and fewer therapies a decade from now.

Smarter reforms would target affordability and transparency without weaponizing foreign prices or sacrificing the breakthroughs that patients, and our entire health system, depend on.

Value-based pricing (VBP) offers a more principled alternative. In VBP, prices are set to reflect the health and economic outcomes a treatment delivers, not simply the number of units sold. HEOR underpins this model, providing cost-effectiveness and budget impact analyses, real-world evidence of long-term effectiveness, and comparative effectiveness research to identify which options truly improve outcomes. Health technology assessment bodies, such as the National Institute for Health and Care Excellence in the United Kingdom or the Institute for Clinical and Economic Review in the United States, then use these data to translate clinical benefit into pricing and coverage recommendations.

> This is precisely where HEOR is essential: not to choose a side, but to quantify trade-offs between affordability today and innovation for tomorrow.

VBP is not just a revenue tactic; it is a discipline that protects and propels innovation. By anchoring prices in the real economic and experiential gains a product delivers, it prevents transformative technologies from being underpriced and deprived of reinvestment. Those stronger margins are not windfalls; they are the fuel for future R&D, especially for high-risk, high-reward projects. Equally important, prioritizing value during development forces teams to design around what customers will truly pay for, aligning pipelines with meaningful impact rather than cosmetic features or me-too offerings.

In practice, VBP is most advanced for high-cost cell and gene therapies, where multi-million-dollar one-time treatments have made outcomes-based contracts almost unavoidable. Payers increasingly link payment to real-world performance, paying in full only if patients avoid hospitalizations, achieve remission, or meet other agreed outcomes. But the roadblocks are substantial: fragmented data systems, lack of interoperability, mistrust between payers and manufacturers, and heavy administrative burdens all limit widespread adoption. Many healthcare systems still run on fee-for-service logic, creating friction with value-based approaches.

Amid these competing forces, the role of HEOR is not simply technical—it is normative. HEOR techniques help drug developers target resources, design smarter studies, and de-risk decisions across the pipeline.

- Predictive modeling and risk stratification refine target populations and trial design.
- Cost-effectiveness and budget impact models, plus scenario (ie, an enhanced regulatory or testing pathway that grants a drug candidate additional benefits), sensitivity, and value-of-information analyses, help prioritize projects and quantify uncertainty.

- Discrete choice experiments and willingness-to-pay studies reveal which product attributes matter most to patients and payers, guiding feature selection and differentiation.
- Comparative cost-effectiveness analysis helps keep prices grounded in incremental value rather than marketing narratives.
- Real-world evidence reveals how drugs actually perform beyond clinical trials, especially in diverse and vulnerable populations.
- Value-based contracting and managed entry agreements align financial risk with therapeutic performance, while health technology assessment (HTA) processes formalize deliberation about budget impact, ethical goals, and fair access.
- Early HTA and payer feasibility assessments ensure innovations align with reimbursement realities, improving launch success and sustaining efficient, value-focused R&D.

The central question is no longer whether drug prices should change—they will—but how. If reforms rely on blunt instruments like rigid price caps or poorly designed reference pricing, they risk trading visible short-term savings for invisible long-term harms. If policy makers instead capitalize on HEOR and value-based frameworks, they can design pricing policies that make trade-offs explicit, protect access for today's patients, and preserve incentives to tackle tomorrow's unmet needs.

Evidence cannot tell us what we value most, but it can ensure we pay for what truly works and stop paying so much for what does not. This will ensure a better balance between affordability and innovation.

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

The Price Is Right–Or Is It?

Rob Abbott, Chief Executive Officer, ISPOR

One of the most consequential topics in health economics and outcomes research (HEOR), and healthcare more broadly, is drug and medical device pricing. Choices about pricing have a direct impact on access to medicines, and equally, future investment in research and development (R&D). Against this backdrop, value-based drug pricing is attracting considerable attention, but what does it look like in practice?

This issue of *Value and Outcomes Spotlight (VOS)* addresses these topics and questions directly. In so doing, it reflects ISPOR's commitment to threading the metaphorical needle in bringing rigorous, unbiased scientific evidence to these topics *as well as* a considered view of the more nuanced environment of policy discourse. Both inputs are critical to improving decisions that affect literally billions of people worldwide.

To suggest that drug pricing reforms such as the Medicare negotiations under the Inflation Reduction Act (IRA) in the United States and reference pricing models globally have altered the biopharma landscape is to perfect the art of understatement. This can be clearly seen in effects on access to medicines and R&D investment, respectively.

> Drug pricing illustrates John Muir's adage that when you pull on a single thread in nature you find it connected to the rest of the world. Reforms, even if well-intentioned, often have unintended consequences.

By imposing a cap on out-of-pocket costs and enabling direct price negotiations for high-expenditure drugs, Medicare price reforms have reduced financial barriers for elderly and low-income populations in the United States. This is a good thing. At the same time, in markets with strict external reference pricing (such as Canada and several European countries), manufacturers have delayed the launch of new drugs and/or prioritized launch strategies in high-price, unregulated regions to protect global revenue. This is understandable from the perspective of the companies concerned, but it is not good for patients who need access to potentially life-saving medicines. It should also be noted that imposing price ceilings without due consideration of supply chain and manufacturing costs could inadvertently lead to product withdrawals or reduced supply, disproportionately impacting vulnerable patient populations.

With respect to effects on R&D investment, price controls that penalize small-molecule drugs (the IRA's shorter negotiation timelines relative to biologics is a good example) can result in portfolio shifts as companies pivot investment decisions to large-molecule biologics, gene therapies and complex indications. Faced with smaller profit margins, pharmaceutical and biotechnology firms are striving to reduce R&D costs without sacrificing success rates. This has fueled the rapid adoption of artificial intelligence (AI) in drug discovery and a greater focus on acquiring third-party, clinical-stage companies.

One of the lessons to be drawn from the above is that drug pricing illustrates John Muir's adage that when you pull on a single thread in nature you find it connected to the rest of the world. Reforms, even if well-intentioned, often have unintended consequences. This is especially true with international reference pricing (IRP).

IRP attempts to lower local drug costs and increase access to medicines by benchmarking prices against other nations. However, it often decreases access because of 3 key dynamics:

- Pharmaceutical companies delay launching new drugs in smaller or lower-income countries—sometimes by 1 to 3 years—to prevent those lower prices from being referenced by wealthier nations with larger pharmaceutical budgets.
- Global health equity relies on *differential pricing* (charging what a local market can afford) but IRP undermines this because manufacturers are disincentivized from offering discounts to low-income nations, knowing that it will trigger a downward cascade of prices in higher-income reference markets.
- IRP often causes price convergence, a phenomenon in which prices in lower-income countries tend to anchor to the high list prices of larger economies, making treatments structurally unaffordable for many local populations.

As the papers collected here persuasively demonstrate, HEOR has much to offer in the search for drug prices that offer real value for patients and their families. These benefits are fourfold:

1. Helping to define cost-effectiveness.

- HEOR evaluates how much a drug improves a patient's life (using quality-adjusted life years or QALYs) and compares it to the cost of alternative treatments. This allows policy makers to establish a price that aligns with the health gains achieved.

2. Informing reimbursement and coverage decisions

- Public and private payers use HEOR evidence to negotiate fair price discounts. The evidentiary packages we curate provide

a standardized yardstick for determining whether a treatment warrants coverage and at what price tier.

- HEOR can establish "fair value thresholds" that prevent plans from shifting costs onto patients who have no alternative, medically appropriate treatments.

3. Integrating real-world evidence (RWE) into pricing decisions

- Traditional clinical trials occur under highly controlled conditions. HEOR teams use RWE—data drawn from electronic health records, claims, and patient registries—to show that a drug's price matches its safety and effectiveness in everyday, diverse patient populations.
- Payers use outcomes-based contracts, often rooted in RWE, where the price of a drug is tied directly to its real-world success for individual patients.

4. Improving transparency and trust

- HEOR methodologies provide a transparent structure for understanding the relationship between R&D, manufacturing costs, and the therapeutic benefit of a drug. This addresses one of the most pernicious issues in economics: information asymmetry. This occurs in healthcare when, for example, clinicians and drug manufacturers have superior knowledge about medical necessity and treatment efficacy compared to patients and health insurers. HEOR bridges this information gap by conducting rigorous cost-effectiveness analyses and evaluating real-world patient outcomes to provide objective, standardized data to patients, clinicians, and other stakeholders.

At ISPOR 2026 in Philadelphia I said that healthcare "is the economy." My point is that with healthcare accounting for 18% of gross domestic product in the United States, decisions about healthcare have a catalytic effect on decisions that touch virtually every economic aspect of daily life. Getting the price signals "right," therefore, matters a great deal. This is especially true of drugs and medical devices.

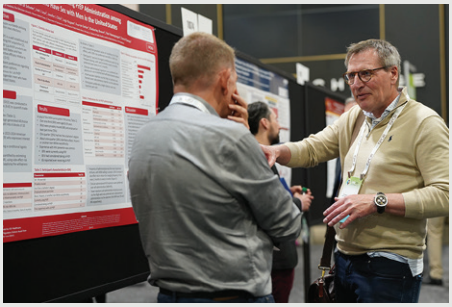
I celebrate the insights contained in this issue of *VOS*, and I know the work is not done. We need to find a way of making novel medicines accessible and affordable to more people while sustaining a vibrant innovation ecosystem for biopharma and others. As ISPOR CEO, I want you to know that I am personally committed to making this happen.

ISPOR 2026: Personal Connections and Professional Inspiration in Philadelphia

The ISPOR Annual Conference returned this year to Philadelphia—the same city where the organization's first-ever conference took place 3 decades earlier. The Association for Pharmacoeconomics & Outcomes Research (the name change came 2 years later) welcomed 382 attendees to its 1st Annual International Meeting in May 1996. This year, there were nearly 4500 attendees.

As technology has evolved in the last 30 years, so has the field of health economics and outcomes research (HEOR) and even the way information is shared at conferences. But some things remain constant: HEOR is still at the forefront of policy, access, and value. And, as seen in these photos, ISPOR conferences are still where HEOR stakeholders come for personal connections and professional inspiration.

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

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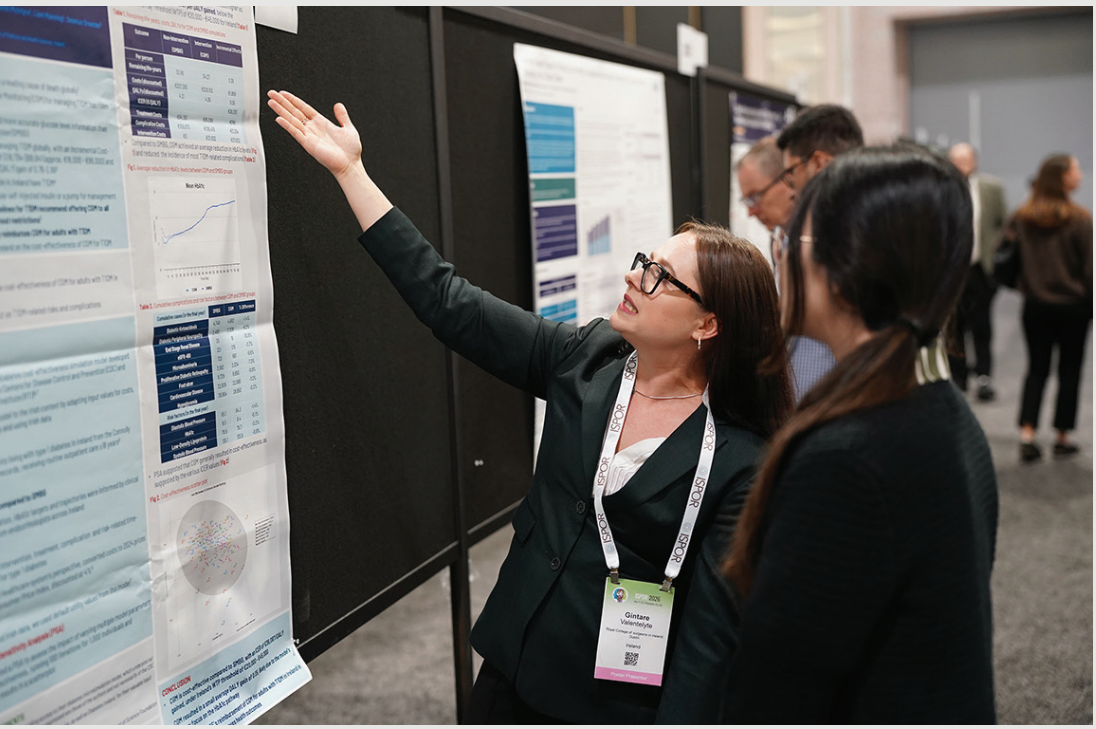


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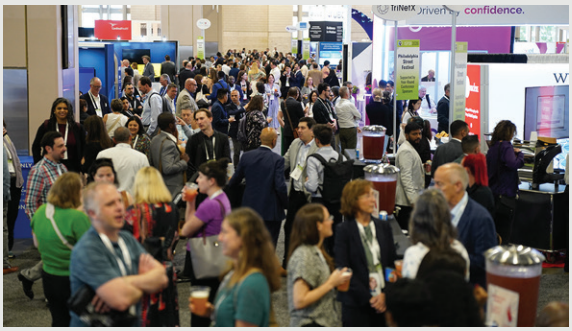
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HEOR NEWS

1 US Democrats Propose Alternate Drug Pricing Policy Ahead of Midterm Elections (Senate Committee on Finance)

The United States Senate Finance Committee minority staff has released a request for information outlining 3 policy options aimed at lowering prescription drug prices, reducing patient out-of-pocket costs, and supporting biopharmaceutical innovation. Comments must be submitted in writing by August 17. Read more.

2 CT-Derived Biomarker Predicts Gastric Cancer Survival Outcomes in Brazilian Study (Clinical Nutrition ESPEN)

Researchers in São Paulo, Brazil, identified a new marker called VMD that could improve staging of gastric adenocarcinoma as a complement to conventional tumor-based screening. They found that higher VMD values were associated with poorer overall survival and disease-free survival. Read more.

3 Modeling Study Makes Economic Case for Structured Exercise in GLP-1 Therapy (Health & Fitness Association)

Economic modeling research from the Health & Fitness Association found that, over 10 years, structured exercise combined with GLP-1 therapy will lead to a greater return on investment and a net monetary benefit in 5 countries compared with GLP-1 therapy alone. Read more.

4 World Health Organization Releases Principles for Managed Entry Agreements (WHO)

The World Health Organization Novel Medicines Platform has published principles for managed entry agreements (MEAs) in Europe to help manage uncertainty about the financial impact and performance of new medicines. The framework includes 8 core MEA principles, an uncertainty scale, a flow chart, and a checklist. Read more.

5 Report Finds Drug Shortages in US Declined in 2025 but Are Lasting Longer (US Pharmacopeia)

Drug shortages decreased by 23% in 2025, but the duration of shortages is on the rise, according to the latest Annual Drug Shortages Report from the United States Pharmacopeia. The average duration of a drug shortage is more than 5 years, up from 4.2 years in 2024 and roughly 2 years in 2019. More than 64% of the drugs currently in short supply have been unavailable for more than 3 years. Read more.

6 Real-World Data Suggest COVID-19 History Increases Tuberculosis Risk (Journal of General and Family Medicine)

A history of COVID-19 is associated with a fourfold increase in the risk of needing treatment for active tuberculosis (TB), according to an analysis of real-world data from Japan's National Insurance Database. That risk is about 15 times higher in people with a history of TB, a subgroup that could warrant further clinical and policy consideration. Read more.

7 UK and US Announce Liaison Program to Promote Regulatory Collaboration (MHRA)

The United Kingdom Medicines and Healthcare products Regulatory Agency and the US Food and Drug Administration have announced a new liaison program to help strengthen the regulatory partnership between the 2 countries. Read more.

8 Diabetes Drug Could Help Lower Heart Failure Risk in Genetically Predisposed Patients (Mass General Brigham)

Dapagliflozin, a drug used to treat type 2 diabetes, is particularly effective at reducing the risk of hospitalization for heart failure in people who are genetically predisposed to developing cardiomyopathy, according to research from Mass General Brigham Heart and Vascular Institute and the Broad Institute of MIT and Harvard. Read more.

9 Health Systems Strengthening Gaps Persist for Newborn Care in Africa (Lancet Global Health)

Investments in health systems strengthening in sub-Saharan Africa remain far below what is needed to achieve national care standards for small and sick newborns, according to research from the London School of Hygiene & Tropical Medicine that analyzed neonatal care costs in Malawi, Kenya, Nigeria, and Tanzania. Read more.

10 Shingles Vaccine Associated With Decreased Dementia Risk in Older Adults (Annals of Internal Medicine)

Older adults who received a shingles vaccine after a stay in a skilled nursing facility had a 24% lower risk of being diagnosed with dementia over a 4-year period than those who were not vaccinated, according to a target trial emulation study that included an analysis of health records and Medicare data for more than 500,000 people. Read more.

11 AI Mammogram Scores Flag Elevated Levels 10 Years Before Breast Cancer Diagnosis (Radiology)

Using artificial intelligence (AI)-based computer-aided detection to score sequential mammograms in individuals diagnosed with breast cancer, researchers from Sweden found elevated scores up to 10 years before diagnosis. The findings suggest AI scores could be part of an early alert process for supplemental imaging. Read more.

12 EHR-Based Marker Can Identify Transplant Patients at Risk of Organ Rejection (Texas Children's)

An electronic health record–based marker derived from routine lab values can help clinicians identify transplant patients who are at high risk for organ rejection due to not taking their medications as prescribed, according to a study involving 13 pediatric transplant centers in the United States and Canada. Read more.

ISPOR NEWS

Revolutionizing HEOR and Patient-Facing Digital Health: Targeted Tools for Defining, Conceptualizing, and Reporting the Evidence

Carl Asche, PhD, University of Utah, Salt Lake City, UT, USA; **Zsombor Zrubka, MD, PhD**, Óbuda University, Budapest, Hungary; **Annette Champion, MBA**, Healthcare Research Insights, Inc, Lake Forest, IL, USA; **Rossella Di Bidino PhD**, Fondazione Policlinico Universitario Agostino Gemelli IRCCS and The Graduate School of Health Economics and Management, Rome, Italy; **Nachiket Gudi, MPH**, Independent Researcher, Bangalore, India; **Anita Burrell MA, MBA**, Anita Burrell Consulting LLC, Flemington, NJ, USA; on behalf of the ISPOR Digital Health Special Interest Group.

Background

For many of us, the realm of patient-facing digital health interventions (DHIs) is a bewildering array of different technologies—including virtual reality, digital therapeutics, wearables, remote monitoring, and software as a service—that can be overwhelming to approach. This is also a complex area for health economics and outcomes research (HEOR) professionals seeking evidence to inform and guide healthcare-related decision making, whether in clinical, delivery system, financing, or development decision contexts. Determining how to systematically evaluate these interventions in all their different forms and report the results can be daunting. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement[1] for comparative economic evaluations did not specifically address DHIs in its 2022 update, but several guidelines[2,3] were developed to standardize the methodological and reporting quality of DHIs.

> To support consistent definition and evaluation, the article noted, DHIs need their own structured frameworks rather than those used for evaluating drugs and devices.

While results from individual DHI studies are hardly generalizable, identifying comparable interventions for economic evaluations or pooled analysis presents a further challenge. Systematic reviews of patient-facing digital health interventions often end up with a range of modalities and applications that is too heterogenous to support meaningful recommendations—which can negatively affect the funding and dissemination of these cutting-edge tools.

In the March-April 2024 issue of *Value & Outcomes Spotlight*, the cover story on defining digital health for HEOR[4] underscored the importance of conceptual clarity in this space and highlighted ongoing challenges related to terminology, classification, and comparability across digital health interventions. To support consistent definition and evaluation, the article noted, DHIs need their own structured frameworks rather than those used for evaluating drugs and devices.

In parallel with ongoing methodological advancements, efforts to standardize economic evaluation and reporting for DHIs continue to evolve rapidly. Notably, the increasing use of artificial intelligence (AI) and large language models (LLMs) to enable literature searches and inform the evidence base for economic research highlights the need for tools that meet rigorous standards and provide decision-relevant evidence for HEOR researchers.

Our goals were multifaceted:

1) To develop a patient-facing DHI definition framework for HEOR purposes that
   - Allows the identification of comparable DHIs with similar intended effects and
   - Is specific and detailed enough to enable assessment of the appropriateness of patient-facing DHIs in specific decision contexts

2) To compare the resulting DHI definition framework with other established DHI frameworks and guidelines to determine:
   - The degree of overlap in definition items
   - The additional value of the new framework and
   - How they might be used together

3) Design, test, and refine guidance on prompts that could be used for LLMs to improve the speed and quality of evidence synthesis, thereby bridging human experience and AI-assisted reasoning

4) Develop tailored guidance for reporting the results of economic evaluations of DHIs, addressing their unique complexities through the development of a new CHEERS-DHI extension that incorporates elements of the DHI definition framework

Research Results

The ISPOR Digital Health Special Interest Group (SIG) team conducted a systematic scoping review of patient-facing DHI definitions occurring in systematic reviews of digital health and mapped these against established research frameworks such as PICOTS (population, intervention, comparator, outcomes, timing and setting),[5] Shannon-Weaver Model of Communication[6] (sender, message, encoder, channel/medium, decoder, received and information exchange/transmission pattern), and several others.

Following a Delphi Study of a geographically and professionally diverse group of SIG members, a minimum set was defined, and

the final framework was given the acronym PICOTS-ComTeC, where "Com" stands for communication, "Te" for technology, and "C" for context (**see Table**). It was endorsed by the EQUATOR network and has been cited multiple times since being published in *Value in Health*.[7]

The full framework can be used in many contexts, such as writing study reports; framing clinical, financing, or development decision questions; formulating research questions for evidence syntheses; or applying for regulatory approval or reimbursement. PICOTS-ComTeC enhances decision making by helping users develop specific, detailed definitions for identifying comparable patient-facing DHIs (intended to deliver the same effect as the one being evaluated) and comparators that deliver a similar effect but differ in relevant determinants of value.

PICOTS-ComTeC not only structures the definition of DHIs but also provides a practical bridge to health technology assessment (HTA). By clarifying intervention characteristics, comparators, and contextual factors, the framework supports the development of more transparent and comparable evidence packages. This is particularly relevant in HTA settings, where heterogeneity in digital interventions has historically limited the interpretability and transferability of findings.

We compared PICOTS-ComTeC with 15 established DHI frameworks and guidelines, including 6 national HTA guidelines such as the German DiGA,[8] 3 DHI reporting guidelines (CONSORT-EHEALTH,[2] iCHECK-DH,[3] and mERA)[9] and the World Health Organization classification scheme (CDISAH[10]). While a significant degree of commonality was found, PICOTS-ComTeC contributed items (domains or subcategories) not uniformly present in other frameworks. The DHI frameworks matched between 4 and 9 domains (mean 7.2). Even within CDISAH and DiGA (the frameworks that most closely matched PICOTS-ComTeC), while all 9 domains were present, approximately 20% of the subcategories were missing, and the 2 frameworks were missing different subcategories. With the sole purpose of defining DHIs, PICOTS-Com-TeC provides a convenient, comprehensive framework and a useful common ground for defining DHIs.[11]

To further support researchers in adopting PICOTS-ComTeC, the ISPOR Digital Health SIG is also designing, developing, testing, and refining a prompt that enables LLMs to identify and extract PICOTS-ComTeC items from scientific reports. Consistent use of a standard prompt for this task will improve the speed and quality of AI-assisted evidence synthesis pipelines, bridging human experience and digital efficiency.

Specific guidance is still needed for health economists seeking to publish the results of their economic evaluations of DHIs, given that existing guidelines don't address all the topics in PICOTS-ComTec. CHEERS-DHI, a checklist specific to DHIs, is being developed based on the existing CHEERS[1] health economic reporting standards to help authors, editors, and peer reviewers improve reporting.

Complementing this work, recent discourse, including our forthcoming (fall 2026) letter to the editor in *Value in Health*, has emphasized the need for greater conceptual alignment between evidence-generation frameworks and reporting standards to ensure that DHI evaluations are both rigorous and decision-relevant.

Lessons Learned

A lack of clear terminology in digital health, compounded by its rapid advancement, hinders evidence-based decision making because heterogeneity across the technologies evaluated will limit high-quality synthesis. Furthermore, this could impede the diffusion and adoption of DHIs, which add value to healthcare settings. Despite existing checklists, standardizing evidence

Table. The PICOTS-ComTeC Framework

Domain	Subcategories					
Population (P)	Target Population/ Diagnosis	Demographic Characteristics	Special User Characteristics			
Intervention (I)	Key Function/ Intended Use	Modality	Limits of intervention			
Comparator (C)	Model of Care	Alternative Digital Health Interventions	Usual Care Alternatives			
Outcomes (O)	Health Benefits	Improved Care Structure or Process	Social/ Societal Benefits	Safety	Non-health Related Risks	Efficacy, Convenience, & Economic Benefits
Timing (T)	Timeliness	Frequency & Duration of Intervention				
Setting (S)	Care Setting	Patient Location	Geographic Scope			
Communication (Com)	User	Message	Interaction Pattern	User Experience		
Technology (Te)	Channel/ Medium	Device	Software	System	Data Management	
Context (C)	Regulatory status	Medical / legal liability	Financing			

Zrubka Z, Champion A, Holtorf AP, Di Bidino R, Earla JR, Boltyenkov AT, Tabata-Kelly M, Asche C, Burrell A. The PICOTS-ComTeC Framework for Defining Digital Health Interventions: An ISPOR Special Interest Group Report. Value in Health; 2024. https://doi.org/10.1016/j.jval.2024.01.009.

generation and assessment for DHIs remains difficult because of their personalized nature, complex technologies, and linkages to larger systems.

The convergence of frameworks such as PICOTS-ComTeC with reporting standards like CHEERS-DHI highlights an emerging ecosystem for DHI evaluation. While CHEERS-DHI focuses on how evidence should be reported, PICOTS-ComTeC is a flexible framework that addresses how interventions should be defined and conceptualized at the outset. Together, these efforts respond to a broader need—articulated in recent contributions to *Value in Health*—to reduce ambiguity in generating digital health evidence and to improve the usability of findings for HTA bodies, payers, and clinicians. The PICOTS-ComTeC framework, therefore, represents a foundational step toward more structured, decision-oriented evaluation of DHIs within HTA processes.

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ISPOR NEWS

Thrilling Quiz Bowl Sets Tone for Slate of ISPOR Student Network Events in Philadelphia

Ivy Leong, BSPharm, MSc

The ISPOR Student Network's continuing expansion of its portfolio of engaging and intellectually stimulating events for students was demonstrated during the ISPOR Annual 2026 conference in Philadelphia. This year, the Student Network led several key initiatives, including a forum, a collaboration with the New Professionals Network, student poster tour, and the Quiz Bowl.

Each of these events was thoughtfully designed to enhance participants' knowledge of health economics and outcomes research (HEOR) concepts while fostering collaboration and professional growth. Collectively, they attracted record-high attendance, bringing together a diverse mix of students and industry professionals and generating meaningful interactions and discussions throughout the conference.

High Stakes at the Quiz Bowl

Among these, the Quiz Bowl stood out as a highlight event. This year, it brought together students from 14 institutions with diverse academic backgrounds to test their HEOR expertise through a fast-paced, team-based bracket-style tournament. Johns Hopkins University, participating in the competition for the first time, came in third place. University of Illinois, Chicago (UIC), and University of Rhode Island (URI) battled to a *Jeopardy*-style double tiebreaker in which each team wagered a portion of its points prior to hearing the question. Both teams answered incorrectly, and the championship was ultimately decided by the point wager, with UIC edging out URI to claim first place.

I witnessed firsthand how the Quiz Bowl serves as a platform for learning, networking, and building confidence. The competition featured questions spanning a wide range of topics, including health economics, research methodologies, statistics, and even machine learning. This breadth not only reinforced existing knowledge but also exposed students to new and emerging areas within HEOR. Students demonstrated strong teamwork and quick thinking as they worked under pressure to deliver accurate answers—hitting the buzzer! The excitement and camaraderie generated during the Quiz Bowl extended beyond the competition, strengthening connections among students and encouraging continued engagement in ISPOR activities.

Preparation for the Quiz Bowl was equally impactful. Many student chapters organized practice sessions, reviewed key concepts, and shared HEOR-related resources in advance of the competition. These efforts strengthened foundational knowledge while promoting peer-to-peer learning and mentorship. For newer students, the preparation process provided valuable exposure to the field and its diverse topics. For more experienced students, it offered an opportunity to deepen their understanding, stay current with evolving HEOR trends, and mentor junior peers. Many participants described this year's Quiz Bowl as a uniquely rewarding experience and expressed enthusiasm for future competitions.

From an organizational perspective, the Quiz Bowl also served as a valuable leadership opportunity. Planning and execution required coordination across multiple stakeholders, including student leaders, industry professionals who contributed to the question pool, administrative staff who supported logistics, and our Student Network advisor. As a Student Network leader, I found this experience instrumental for developing leadership, communication, and organizational skills, all of which are essential for future roles in academia, industry, and policy.

Communication and Community

Beyond the Quiz Bowl, the Student Network programming helped foster a strong sense of community. As the first Student Network event of the conference, the Quiz Bowl provided a welcoming starting point for students to engage with the broader HEOR community. This momentum continued with the Student Network forum, "Global Value Frameworks: Aligning HEOR, Access, and Policy Across Borders," where panelists from diverse healthcare systems shared real-world insights and perspectives on global policy development.

In addition, a collaborative session with the New Professionals Network, titled "Communicating Value in the Age of AI—Skills, Tools, and Confidence for HEOR Careers," offered a forward-looking discussion on integrating artificial intelligence with essential communication skills. Unlike many AI-focused sessions, this discussion emphasized not only technical applications but also the importance of maintaining human judgment and ensuring that AI remains a tool to support, rather than replace, professional expertise.

Overall, the Quiz Bowl and accompanying Student Network events exemplified ISPOR's mission to promote education, collaboration, and excellence in HEOR. These initiatives not only challenged participants intellectually but also equipped them with the skills, confidence, and professional connections needed to succeed in their careers.

I hope these events continue to attract strong engagement from students, faculty, and industry professionals, further enhancing opportunities for mentorship, collaboration, and career development. As a Student Network leader, I am proud to contribute to these efforts and look forward to their continued impact on the next generation of HEOR professionals.

ISPOR Events & Education

Use these quick links to learn more about ISPOR and the HEOR issues that matter most to you.

Resources for This Issue's Primary Theme

Drug Pricing: Trend #4 in the 2026-2027 ISPOR Top Ten Trends
Drug Pricing Reform: #1 of 5 Health Policy Trends to Watch This Year
Drug Pricing as Part of US Healthcare System Overview
Drug Pricing Policy: Workshop at ISPOR Healthcare Investment Summit 2026
Access and Drug Pricing: Trending Topic Track at ISPOR 2026
Drug Pricing: ISPOR Presentations Database
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Chronic Diseases
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Patient-Reported Outcome Measures
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POLICY BRIEF

The ISPOR Policy Brief offers concise insights into emerging developments in the global health policy space that shape access, innovation, and affordability. Each monthly installment spotlights timely issues relevant to the health economics and outcomes research (HEOR) community and beyond, providing a rapid overview of how policy shifts are influencing global markets and stakeholders.

Most-Favored-Nation Pricing Expands, Reshaping Global Access and Market Dynamics

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

Overview: This May installment examines the continued expansion of Most-Favored-Nation (MFN) drug pricing arrangements in the United States and their broader implications for pricing, market behavior, and global policy dynamics. As agreements with pharmaceutical manufacturers grow in scale and scope, MFN is increasingly shaping how companies approach pricing, access, and investment decisions.

US UPDATES & PERSPECTIVES

MFN Agreements Expand, Reshaping Pricing Dynamics

Additional agreements between the administration and pharmaceutical manufacturers have been signed in the United States. A recent agreement with Regeneron marks the latest development, with 17 companies—representing a substantial share of the branded drug market—now participating. These agreements include commitments to align prices with those in other high-income countries, expand access through public programs, and invest in domestic manufacturing and research. While the long-term implications remain uncertain, the growing scale of these arrangements suggests that MFN is increasingly influencing pricing strategies and market behavior. Questions also remain regarding the transparency of these agreements and the extent to which they will translate into sustained reductions in overall drug spending.

CMS Proposes Reforms to Accelerate Access and Increase Transparency

CMS has proposed reforms aimed at accelerating patient access to therapies and increasing transparency in drug coverage decisions. The proposed rule would require faster prior authorization timelines, expand the use of electronic authorization processes for prescription drugs, and introduce new reporting requirements for approval rates and decision timelines. Public comments were due by June 15. While still under consideration, the proposal reflects broader efforts to streamline administrative processes and improve the predictability of access to treatments.

INTERNATIONAL UPDATES

Concerns Emerge Over Access to New Medicines in MFN-Referenced Countries

Early signals from Europe suggest that MFN pricing policies may already be influencing market behavior. In Sweden, a recent industry survey indicates that a significant proportion of pharmaceutical companies may delay or avoid launching new medicines in response to evolving global pricing dynamics. Concerns also extend to potential reductions in clinical trial activity and broader investment decisions. While the long-term effects remain uncertain, these findings highlight the potential for MFN-linked policies to affect access to new treatments in countries referenced in international pricing frameworks.

Pricing Pressures Raise Questions About Europe's Competitiveness

Additional signals from industry point to growing concerns about the impact of pricing policies on Europe's competitiveness. Recent commentary from AstraZeneca suggests that cost-containment measures under consideration in Germany could affect the launch of new medicines, reflecting broader uncertainty about the region's attractiveness for pharmaceutical investment. These dynamics may reinforce ongoing shifts in research, development, and manufacturing activity toward other markets, including the United States and China. Similar signals are emerging across the pharmaceuticals industry, with companies like Roche highlighting growing uncertainty around how evolving pricing dynamics may affect future launches and innovation across European markets.

WHAT TO WATCH

As US pricing policies continue to expand and interact with broader reforms, several signals may shape how stakeholders respond across markets:

- **Increasing global interdependence in pricing and access decisions:** As US pricing policies reference international markets, actions taken in one country may have cascading effects on launch strategies, pricing negotiations, and access conditions in others.
- **Growing alignment between pricing policy, access mechanisms, and industrial strategy:** Efforts to control costs are increasingly accompanied by reforms aimed at accelerating access and strengthening domestic investment, suggesting a more integrated approach to managing affordability and innovation.
- **Rising uncertainty around real-world impact and implementation:** While early signals point to potential effects on access, investment, and competitiveness, questions remain regarding how these policies will translate into sustained changes in pricing, availability, and health system outcomes.

As these dynamics evolve, they are likely to shape ongoing policy discussions around pricing, access, and value, including global forums such as ISPOR 2026, where stakeholders are increasingly focused on the role of evidence in navigating complex trade-offs across health systems.

POLICY BRIEF

ISPOR 2026: Navigating the Interconnections Among Policy, Access, and Value

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

Overview: This June installment reflects on a broader theme that emerged at ISPOR 2026. Increasingly, policy decisions are influencing not only pricing and reimbursement, but also evidence generation, innovation incentives, launch strategies, and access pathways across health systems. Recent developments across countries and regions suggest that these issues are interconnected priorities aimed at improving healthcare worldwide and can no longer be considered in isolation.

POLICY DEVELOPMENTS SHAPING THE LANDSCAPE

US Pricing Reforms and Global Implications

Recent developments in the United States highlight how pharmaceutical policy conversations are extending beyond affordability alone. The continued expansion of Most-Favored-Nation (MFN) agreements has linked drug pricing discussions with broader considerations related to domestic investment, manufacturing, and competitiveness. At the same time, the implementation of the Medicare Drug Price Negotiation Program under the Inflation Reduction Act (IRA) has shifted attention toward operational questions, including evidence requirements, negotiation processes, and long-term evaluation. These trends illustrate how pharmaceutical policy is evolving beyond pricing alone, intersecting with broader questions related to investment, competitiveness, and implementation.

Growing Attention to Competitiveness and Innovation

Across Europe, stakeholders are deeply focused on the relationships connecting affordability, competitiveness, and innovation. Concerns regarding launch sequencing and market attractiveness have prompted broader conversations about how pricing and reimbursement policies may influence investment decisions and research activity, which ultimately impacts patient access. These exchanges are taking place within a rapidly evolving global innovation landscape, including the growing role of China in pharmaceutical R&D and drug development. Policy makers around the world are therefore increasingly considering how affordability, access, innovation, and sustainability interact within broader health and economic systems.

Increasing Expectations for Evidence

Expectations regarding the evidence used to inform healthcare decision making are also evolving. Spain's recently approved Royal Decree on Health Technology Assessment (HTA) establishes a more structured national framework while aligning with the implementation of the European Union HTA Regulation and Joint Clinical Assessments (JCAs), reflecting broader efforts to strengthen coordination and transparency in evidence assessment. More broadly, the introduction of JCAs across Europe represents an important shift toward shared clinical evidence assessments while preserving national decision making on economic, organizational, and contextual considerations.

At the same time, discussions at ISPOR 2026 highlighted growing interest in topics such as real-world evidence, AI-enabled analytics, transparency, and model validation. These developments reflect growing recognition that increasingly complex health policy decisions require robust approaches to evidence generation and assessment.

Balancing Affordability, Access, and Value

Questions regarding how value should be incorporated into healthcare decision making also are proliferating across policy dialogues. At ISPOR 2026, these themes were reflected in a plenary session on innovation under pressure, which explored how evolving pricing and trade policies may influence evidence generation, launch strategies, development decisions, and long-term incentives for innovation in drug development.

Similar questions were examined during an issue panel on value-based pricing in Medicare drug price negotiations, which explored whether negotiated prices align with conventional approaches to value assessment and discussed the practical, methodological, and policy considerations associated with integrating value into pricing decisions. Topics such as transparency, evidence requirements, feasibility, innovation, and patient access were prominently featured.

These conversations reflect growing interest in how healthcare systems define, assess, and incorporate value while pursuing broader goals related to affordability, access, innovation, and sustainability.

LOOKING AHEAD

The themes highlighted throughout ISPOR 2026 underscored the growing interconnectedness of policy, access, value, innovation, and evidence generation. As policy discussions continue to evolve globally, several themes may be particularly important to monitor:

- **The evolving relationship between pricing policy and industrial policy:** As governments pursue affordability objectives, policy conversations are increasingly expanding beyond healthcare spending to include competitiveness, domestic manufacturing, supply chain resilience, and investment incentives.
- **Evolving approaches to value assessment and evidence generation:** Ongoing implementation of the EU HTA Regulation, national HTA reforms, and growing interest in real-world evidence and AI-enabled analytics may influence how value is assessed and how evidence is incorporated into healthcare decision making.
- **The global geography of innovation:** Continued growth in pharmaceutical R&D activity and investment outside traditional markets is prompting renewed dialogue about how policy environments influence innovation, research, and future product development.

FROM THE REGIONS

United Arab Emirates and India Chapters Recognized for Their Leadership and Innovation in 2026

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 2 regional chapters were commended for their performance in 2026.

ISPOR 2026 Outstanding Regional Chapter Large-Sized Chapter Category

Nadia Al Mazrouei, PhD, MSc
ISPOR UAE Chapter President
Expert Advisory Board Panel, World Health Organization
Associate Professor at University of Sharjah

ISPOR: How is the HEOR landscape evolving in your country or region, and what role has your chapter played in supporting this development?

Nadia Al Mazrouei: The health economics and outcomes research (HEOR) landscape in the United Arab Emirates has reached a new level of maturity, transitioning into a sophisticated ecosystem where high-quality evidence is no longer a "luxury" but a mandatory prerequisite for market access. A landmark moment in this evolution is the recent release of the Department of Health – Abu Dhabi (DOH) Health Technology Assessment (HTA)Guidelines, which now provide a formal framework for the evaluation of health technologies.

> Our focus remains on the science of quality—establishing how regional data must be evaluated for robustness, reliability, and clinical relevance.

The ISPOR UAE Chapter has mirrored this growth, evolving from a professional society into a strategic catalyst for policy shaping. We have established ourselves as a trusted partner for a diverse spectrum of stakeholders, including government, industry, academia, healthcare providers, and payers. We have cultivated a "neutral ground"—a safe, scientific space—where aspiring candidates can master HEOR science and where veteran experts collaborate under 1 umbrella to identify data gaps. By facilitating this synergy, we generate the evidence-based blueprints necessary to inform national health policies, ensuring that localized data remains the primary driver for regional decision-making.

How is your chapter incorporating emerging approaches such as real-world evidence, digital health, or artificial intelligence into its activities and discussions?

For our chapter, innovation is a collaborative imperative. To ensure we remain at the cutting edge of technological integration, we have moved beyond theory into practical application:

- **Artificial intelligence:** At the ISPOR UAE Conference 2026, we hosted a high-impact masterclass on "AI-Enabled HTA Innovation for the MENA [Middle East and North Africa] Region." In partnership with Access Forum and RAFED—the region's premier group procurement entity leading AI integration for supply chain optimization—this session provided more than 30 key stakeholders with a roadmap for using AI to streamline value-based decisions.
- **Real-world evidence (RWE)**: We have actively partnered with PureHealth and IROS (Insights Research Organization & Solutions) to trigger critical conversations on the practical application of RWE. Our focus remains on the science of quality—establishing how regional data must be evaluated for robustness, reliability, and clinical relevance.

What are your chapter's priorities for the next few years, and how do you envision contributing to ISPOR's global mission of advancing HEOR excellence?

Our vision is expanding from local excellence to regional synergy. As we look toward the future, our mission is anchored by several strategic pillars:

- **Ensuring inclusive expertise**: We are actively diversifying the perspectives within our Board and Scientific Committees. This ongoing integration of experts from every sector of the UAE healthcare landscape ensures that our strategic dialogues and initiatives are perpetually grounded in both scientific excellence and operational reality.
- **Building regional networks**: We are spearheading the creation of cross-border networks to foster regional collaborations. While the UAE leads the way, the true impact of HEOR is maximized when we align standards across the Gulf Cooperation Council and MENA regions to address shared healthcare challenges.

- **Continuous discussion platforms**: We are committed to expanding our footprint through a perpetual calendar of activity. Rather than being a "once-a-year" organization, we are building an ongoing ecosystem of conferences and workshops to keep the HEOR community synchronized with global advancements in real time.
- **Policy leadership and evidence generation**: We will continue to refine our policy-shaping efforts and targeted evidence generation to ensure the United Arab Emirates remains a global case study for how a professional chapter can influence national healthcare sustainability.

By fostering these regional collaborations and maintaining a highly inclusive scientific leadership, we contribute to ISPOR's global mission by proving that a dedicated chapter can be the primary engine for HEOR excellence and policy evolution in emerging markets.

ISPOR 2026 Outstanding Regional Chapter Medium-Sized Chapter Category

Y. Padmanabha Reddy, MPharm, PhD
India-Andhra Pradesh Chapter President
Professor and Principal, Raghavendra
Institute of Pharmaceutical Education and Research (RIPER)
Anantapur, Andhra Pradesh, India

ISPOR: How is the HEOR landscape evolving in your country or region, and what role has your chapter played in supporting this development?

Y. Padmanabha Reddy: The HEOR landscape in India—particularly in Andhra Pradesh—is undergoing rapid transformation driven by expanding health insurance coverage, digital health adoption, and increasing demand for evidence-based decision making within both public and private sectors. Policy makers, hospital networks, and payers are progressively seeking real-world evidence, insights into cost-effectiveness, and value-based frameworks to guide reimbursement policies, formulary decisions, and the adoption of new technologies.

Our ISPOR India—Andhra Pradesh Chapter has played a catalytic role in this evolution by building HEOR capacity across academia, clinical institutions, and emerging health tech ecosystems. We have conducted workshops on pharmacoeconomics, outcomes research, and health technology assessment; mentored students and early career researchers; and facilitated collaborations among academia, clinicians, and industry. Through these initiatives, we have strengthened regional awareness of HEOR methodologies and supported the integration of evidence-based approaches into local healthcare planning and policy discussions.

How is your chapter incorporating emerging approaches such as real-world evidence, digital health, or artificial intelligence into its activities and discussions?

Our chapter has strategically positioned itself at the intersection of HEOR, digital health, and data science, recognizing that modern evidence generation depends on high-quality, real-world data and advanced analytics. We operationalize this through:

- RWE-focused capacity building on study design, data quality, and electronic medical record-based analytics
- digital health and AI seminars covering predictive modeling, mobile patient-reported outcome measurement, and AI-enabled decision support and
- collaborative research across maternal-infant health, infectious diseases, and chronic disease outcomes

We also convene interdisciplinary innovation forums to examine how AI and digital technologies can strengthen HEOR, HTA, and value-based care.

In parallel, our chapter is developing applied analytical tools, including digital medication adherence monitoring algorithms for eclampsia, AI-based drug safety prediction models to support proactive pharmacovigilance, and predictive frameworks for antimicrobial resistance to inform stewardship programs. By embedding these innovations into training and mentoring, we are preparing future HEOR professionals to work effectively within data-intensive, technology-enabled healthcare systems.

> We have strengthened regional awareness of health economics and outcomes research methodologies and supported the integration of evidence-based approaches into local healthcare planning and policy discussions.

What are your chapter's priorities for the next few years, and how do you envision contributing to ISPOR's global mission of advancing HEOR excellence?

By expanding HEOR capacity, promoting methodological excellence, and fostering evidence-based decision making, our chapter will contribute meaningfully to ISPOR's global mission of advancing HEOR science and improving healthcare value worldwide. With our expanding portfolio of AI-enabled HEOR tools, we aim to establish our chapter as a central hub for innovation, interdisciplinary collaboration, and methodological leadership within India's evolving healthcare ecosystem.

Over the next 3 years, our chapter aims to scale its impact through 3 strategic priorities that align with ISPOR's global mission and the evolving needs of the Indian healthcare ecosystem:

- **Strengthening HEOR capacity and workforce development**. We plan to expand structured training programs, certification-oriented workshops, and mentorship for students, clinicians, and researchers. Our goal is to build a strong regional talent pipeline aligned with global HEOR standards.
- **Advancing real-world evidence and digital health research**. We will promote high-quality RWE studies, support digital health evaluation frameworks, and encourage interdisciplinary collaborations that apply AI and analytics to real-world datasets. Our ongoing development of medication adherence tools for eclampsia, drug safety prediction algorithms, and AMR predictive models will serve as flagship initiatives demonstrating how HEOR, AI, and digital health can converge to address critical public health challenges.
- **Enhancing policy engagement and value-based healthcare adoption**. We aim to support state-level health programs, insurance schemes, and hospital networks by providing HEOR insights that inform reimbursement, technology adoption, and patient-centered care. Our chapter will serve as a bridge between evidence and policy, especially in areas such as maternal health, infectious disease control, and antimicrobial stewardship.

FROM THE REGIONS

Updated, Policy-Responsive HEOR Guidelines for India Announced at ISPOR 2026

A defining moment for India's healthcare innovation and evidence-informed policy ecosystem occurred at the 2026 ISPOR Annual Meeting in Philadelphia with the launch of the updated Health Economics and Outcomes Research (HEOR) Guidelines for India – 2026, formally announced by ISPOR CEO Rob Abbott.

India's healthcare system stands at a defining crossroads, where scientific ambition, fiscal prudence, and equitable access must converge with unprecedented precision. As healthcare financing expands, disease burdens evolve, and policy decisions increasingly demand measurable value, the need for a robust, context-sensitive HEOR framework has never been more urgent.

Within this transformative national moment, the 2026 HEOR Guidelines for India are not merely an update to the 2016 Pharmacoeconomics & Outcomes Research Guidelines. The new guidelines represent a strategic recalibration of how India evaluates health technologies, allocates resources, and institutionalizes evidence-informed decision making.

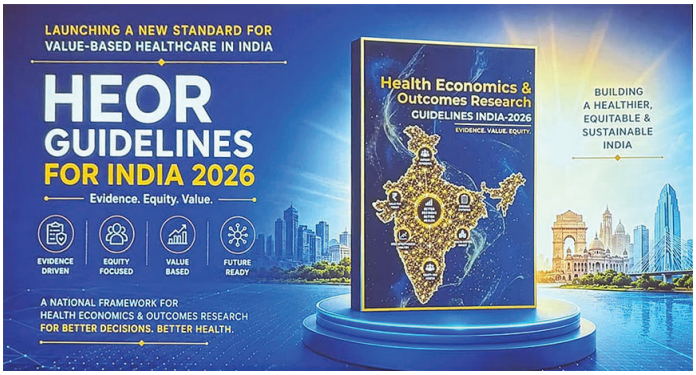
Keeping Pace With Policy Shifts
The 2016 guidelines were foundational. They established India's first structured framework for pharmacoeconomic evaluation and introduced methodological discipline into an emerging field. However, over the past decade, India's healthcare architecture has evolved dramatically.

Today's policy environment demands more than isolated cost-effectiveness analyses. It requires integrated frameworks capable of evaluating pharmaceuticals, diagnostics, devices, digital interventions, and service delivery models across increasingly complex healthcare realities.

The 2026 revision was therefore driven by a singular imperative: to modernize India's HEOR standards in line with contemporary health system needs while preserving contextual relevance.

These updated guidelines address critical methodological gaps, including:

- expanded scope from pharmacoeconomics to full-spectrum HEOR
- greater emphasis on policy translation and implementation relevance
- standardized methodological rigor aligned with global best practices
- enhanced applicability for resource-constrained and heterogeneous systems



- stronger integration of outcomes research, affordability, and value-based healthcare principles

In essence, this revision reflects India's transition from adopting economic evaluation to architecting it as a national policy instrument.

Closing Gaps for Informed Decisions
India's healthcare ecosystem is uniquely complex, marked by epidemiological diversity, variable healthcare access, state-level heterogeneity, and competing resource priorities.

Historically, decision makers often faced 3 major challenges:

- **Fragmented methodological standards:** Different institutions and stakeholders used inconsistent approaches, limiting comparability and policy utility.
- **Limited contextual adaptation**: Global HEOR frameworks often lacked applicability to India's socioeconomic realities, local cost structures, and implementation pathways.
- **Translation gap between evidence and policy**: Research frequently remained academic rather than actionable.

The 2026 guidelines directly address these challenges by creating a nationally harmonized framework that is scientifically rigorous, operationally practical, and policy-responsive. They reflect India's progression from fragmented economic evaluation toward a mature, globally aligned HEOR ecosystem.

Leadership and Teamwork
This initiative exemplifies the power of collaborative scientific institution building.

The Kalam Institute of Health Technology (KIHT) served not merely as a coordinating body, but as the principal architect of the initiative, leveraging its position as a World Health Organization Collaborating Center for Health Innovation and a national health technology policy institute to convene an extraordinary coalition of domestic and international expertise.

This achievement was led by KIHT, under the strategic leadership of Jitendra Kumar Sharma, Executive Director, and the

operational stewardship of Kavita Kachroo, Scientist F and Chief Operating Officer, and a dedicated team of scientists.

Through structured consultations with ISPOR global leadership, methodological advisors from leading academic institutions, health technology assessment (HTA) experts, and ISPOR India regional chapters, the guideline development process was both nationally grounded and globally benchmarked.

This collaboration achieved something particularly rare: a framework that is internationally credible without being contextually detached.

ISPOR's engagement strengthened methodological alignment with global standards, while India's regional chapters ensured practical feasibility across diverse implementation landscapes. KIHT's leadership unified these perspectives into a coherent national blueprint.

Guidelines' Impact Beyond India

For low- and middle-income countries (LMICs), one of the greatest barriers to HEOR adoption is the absence of frameworks that reconcile scientific sophistication with system realities. India's 2026 guidelines may serve as an important reference model for countries seeking to institutionalize value-based healthcare without relying on frameworks designed exclusively for high-income settings.

By embedding methodological rigor within pragmatic policy architecture, India offers a replicable paradigm: global standards, locally operationalized.

For India itself, these guidelines are poised to:

- strengthen HTA-informed policy decisions
- improve prioritization of health investments
- advance transparency in economic evaluation
- support sustainable healthcare financing
- build national HEOR capacity across academia, government, and industry

India is now positioned to advance from being primarily a consumer of global HEOR standards to also contributing to the evolution of those standards.

From Publication to Implementation

Formal publication of the 2026 HEOR guidelines is in progress. But publication is only the beginning. The true success of the 2026 HEOR guidelines will be defined by adoption, institutionalization, and capacity building. KIHT envisions this being facilitated by implementation science, training ecosystems, stakeholder integration, and methodological stewardship.

Key next steps include:

- national dissemination across policy makers, researchers, and industry
- capacity-building initiatives through ISPOR chapters and academic networks
- integration into HTA and evidence-generation pathways
- ongoing refinement based on emerging technologies and policy demands

This is not a static document—it is a living strategic framework designed to evolve alongside India's healthcare transformation.

A National Milestone With Global Resonance

The 2026 HEOR guidelines signal more than methodological advancement; they reflect India's growing confidence in shaping its own evidence architecture. At its core, this work underscores a powerful principle: Healthcare value must be measured not only by innovation, but by informed, equitable, and sustainable impact.

India has taken a decisive step toward institutionalizing that principle—creating a framework capable of informing national priorities today while inspiring broader global health systems tomorrow.

Pursuing Affordability WHILE Supporting Innovation: Walking THE Drug-Pricing Tightrope

Prescription drug prices and national priorities vary widely across the globe, leaving patients with uneven access to potentially life-changing treatments.

How can health economics and outcomes research (HEOR) help healthcare stakeholders negotiate lower costs for countries and households without compromising pharmaceutical innovation?

By Beth Fand Incollingo

The power of pharmaceutical innovation is nothing short of awe-inspiring, and it goes without saying that patients across the globe want access to the latest treatments, preventive measures, or cures for disease.

But the intricate push and pull of healthcare economics—often driven by health policy—generates divergent prices for the same drugs depending on where in the world a patient lives, and that means access to these treatments is far from balanced.

In addition to having different standards of value that dictate which drugs confer enough benefit to fund—and at what price—national healthcare systems are constrained by budgets that force difficult choices about adding expensive new technologies to their formularies. Across the European Union's 27 member states, for example, the annual percentage of approved new drugs to actually reach patients has dropped as the wait time for government reimbursement has grown.[1]

While large, affluent countries like Germany and France tend to reimburse for a broad variety of new drugs, markets in middle-income countries are more likely to support reimbursement for just half of the new products receiving regulatory approval, with the most expensive drugs remaining out of reach, said Jens Grueger, PhD, a Senior Advisor to Curta and Boston Consulting Group, health economics and drug pricing policy consulting firms.

"What does it mean for patients if their needs are not met by reimbursement coverage? If a prescribed drug can be obtained in a country but isn't covered, patients will have to pay full price," said Grueger, who is based in Germany and is a Past President of ISPOR and an Affiliate Professor of Health Economics and Drug Pricing at the University of Washington. "If the drug is an expensive cancer therapy, that means these patients probably can't access it."

The trickiest dance in global drug pricing may be lowering costs for health systems and households without either decimating the revenues that support pharmaceutical innovation or further reducing patient access to drugs. It will be up to HEOR professionals to help policy makers and other healthcare stakeholders devise and refine strategies for increased affordability while offering drug developers opportunities for their treatments to enter markets, reach patients at significant volumes and speeds, and remain available long-term.

The most meaningful solutions will come from global, multidisciplinary cooperation, something HEOR experts are uniquely positioned to drive, said Caroline Solon, Vice President of Market Access Strategy for Lumanity, a global consulting firm that helps pharmaceutical and biotechnology companies price and launch treatments.

"The struggle with drug costs has been going on for a very long time, and it's only going to get worse, given the rise in advances such as personalized medicines and gene therapies, which have very high upfront costs," said Solon, who is based in London. "Everyone needs to be ready to come to the table with a common goal of identifying practical, tangible solutions and making concessions to optimize patient care. If not now, when?"

International Reference Pricing: A Key Strategy

For decades, international reference pricing (IRP), which includes strategies such as most-favored-nation (MFN) pricing, has been a key factor in determining how much countries pay for drugs.

Under IRP, pharmaceutical companies negotiate with selected high-income countries to establish mutually acceptable prices. Then, those prices are used as comparators to help determine what peer nations—and, later in the game, low- and middle-income countries—will pay for the same medications.

Although list prices for drugs are shared publicly, some negotiated prices are not. If pressured to increase transparency, companies may choose to delay or halt drug launches instead, so their negotiated lower prices can't be used as comparators. This results in even longer waits and fewer options for patients, especially in low- and middle-income countries (LMICs).

> "If a prescribed drug can be obtained in a country but isn't covered, patients will have to pay full price. If the drug is an expensive cancer therapy, that means patients probably can't access it."
>
> – Jens Grueger, PhD

"This pricing approach has not been shown to improve affordability across countries and may instead exacerbate disparities, particularly in LMICs," said Mouna Jameleddine, PharmD, MSc, Director of Health Technology Assessment (HTA) for Tunisia's National Authority for Assessment and Accreditation in Healthcare and Past President of the ISPOR HTA Roundtable for Middle East and Africa. "This highlights the need for a structured and transparent approach to differential pricing. Aligning prices with countries' ability to pay, often proxied by gross domestic product per capita, could improve affordability and access in LMICs. In the absence of such a framework, current pricing dynamics may generate unintended cross-country effects that complicate access."

A new twist in the existing dynamic arose in May 2025, when the United States announced it would begin demanding MFN pricing for certain drugs.[2] The initiative has grown to include 3 policy strategies that lower the prices of specific drug types covered by Medicare or Medicaid to MFN levels through manufacturer rebates. The government has also struck agreements with 17 pharmaceutical companies to lower their

prices for certain key drugs, in many cases through direct-to-consumer sales on the website TrumpRx.[3]

President Donald Trump says the new policy direction is fair, as Americans have been paying list prices 3 to 4 times higher than the amounts shouldered by their peers in other high-income countries, essentially subsidizing discounts for those nations.[4] But some HEOR experts believe the initiatives will reduce pharmaceutical innovation, limit marketing of the treatments in both LMICs and high-income nations, or both.

Solon also highlighted a potential issue with America's onshore manufacturing requirements for drug developers involved in its MFN programs,[5] saying those measures will increase pharmaceutical production costs which, typically, leads to higher prices.

"If you ask anyone in our field what keeps them up at night, it's how the United States will perform as a pricing manager in these situations," Grueger said.

Changes in the United States Spark Changes Across the World

In Western Europe, drug comparator prices have historically been established in higher-priced markets such as Germany, with lower prices struck in France; other relatively affluent countries have typically paid amounts between those numbers. But now that the United States is participating, the sheer size of its market will mean that reference pricing must begin there, and that presents some problems, Grueger said.

President Donald Trump says the new policy direction is fair, as Americans have been paying list prices 3 to 4 times higher than the amounts shouldered by their peers in other high-income countries.

Brand-name drug prices have often been highest in the United States because the market is large, regulatory approvals are relatively swift, and there's an expectation that the newest and best technologies will be made available, he said. But if prices for new drugs are established in America first, developers may find it challenging to set reasonable and comparable prices for the same products in other countries, and to sell them in sufficient volumes to make the effort worthwhile. Conversely, setting initial reference prices in Europe might lower US prices beyond what pharmaceutical companies are willing to bear.

Key healthcare systems are already reacting to that uncertainty. According to one global data analysis, in the 10 months following the Trump administration's executive order demanding MFN status, the number of new products launched in Europe declined by 35%.[6] Comments from industry executives suggest that companies are delaying launches until they have more clarity on what MFN-driven pricing in Europe will look like.[7]

"It's not that we had fewer products approved by the European Commission, or that 35% fewer products will ever reach the markets," Grueger said. "It just indicates that companies are much more inflexible now with their prices, because they're concerned about the implications these prices might have for the United States."

The analysis also found an increase in the number of products withdrawn from European markets during the same 10-month period and blamed it, in part, on Trump's call for MFN status in America.

The changing reference pricing dynamics may limit new indications for existing drugs, too. Added indications may launch at prices so low that companies will question whether to roll them out in smaller nations.

These changing IRP dynamics may limit new indications for existing drugs, too. If swept up in America's MFN programs, added indications may launch at prices so low that companies will question whether to roll them out in smaller nations, Grueger said.

The European Commission, however, is fighting for continued commercialization in its member countries. In a recent pharmaceutical directive expected to be finalized by the end of this year, it threatened to remove market protection from new indications if companies take longer than 3 years to respond to a member nation's access request.[8]

Developers may also buck the system by altering their drugs slightly for each market so the prices of the products can't be compared, suggested Michael E. Chernew, PhD, the Leonard D. Schaeffer Professor of Health Care Policy at Harvard Medical School.

"They might offer a different formulation, dosage, or package size in one country compared with another," he said, "depending on how the regulations address that."

The Role of Value-Based Pricing

But where do the prices used in IRP mechanisms come from?

Most high-income countries use value-based pricing to negotiate with pharmaceutical companies, meaning that they decide what they're willing to pay based on their assessments of the health outcomes associated with a drug.

The United Kingdom employs the quality-adjusted life year (QALY) as the key measurement in its HTA process, considering a drug cost-effective if its price per QALY gained falls below a certain threshold. Germany focuses instead on comparative effectiveness, probing how much benefit a new drug is expected to bring compared with treatments already on the market.

"The key to sustainable pricing policy that enables patient access today, but also incentivizes future research and development, is recognizing and rewarding innovation in very high unmet-need areas rather than 'me-too' products," Solon said. "Of the approaches used today, I think the German HTA process is a good example of assessing and rewarding incremental value."

While comparative effectiveness analyses sometimes lead to higher prices in Germany for the most groundbreaking drugs compared with other EU member states, the United Kingdom's approach results in a more controlled range of prices that, overall, sit at the low end of the spectrum represented by its peer countries, Grueger said.

Yet, lower IRP pricing in high-income countries can pull comparator prices down, threatening innovation. To encourage Britain to take on more responsibility for supporting innovation, the United States recently signed a trade agreement with the country encouraging it to raise its price threshold.[9]

Under the agreement, the United Kingdom agreed to raise its cost-effectiveness threshold from £20,000 to £30,000 per QALY to £25,000 to £35,000 per QALY, ultimately paying a premium of up to 25% more for similarly valued new medicines starting in April 2026. In return, the country will be allowed to import medicines into the United States tariff-free for 3 years.

> "The key to sustainable pricing policy that enables patient access today, but also incentivizes future research and development, is recognizing and rewarding innovation in very high unmet-need areas rather than 'me-too' products."
>
> – Caroline Solon

Value-based pricing can also mean that countries approve expensive drugs with the caveat that their health systems will pay manufacturers in full only if the treatments bring promised health outcomes.

"Conceptually, this is very appealing, but from an operational perspective, the agreements often are not feasible to complete," Solon said. "To make them a better option, public health systems require enhanced digital, data, and staffing infrastructures so they can more readily track patient health outcomes long-term."

Although there have been examples in Europe where the administrative burden of an outcomes-based agreement ultimately became a barrier to commercialization, Solon said, there have also been examples demonstrating more success with outcomes-based and managed-entry agreements.[10-12]

Jameleddine pointed out that many LMICs have not fully developed value-based pricing or HTA systems but could benefit from starting small and combining those processes with other pricing policies and direct manufacturer negotiations.

"Value-based pricing, within the framework of HTA, can be used as a tool for structuring our discussions around evidence-based data on effectiveness, clinical benefit, and economic impact," she said. "Even a partial application can contribute to a transparent and multidisciplinary evaluation of what matters most to patients."

Should the United States Adopt Value-Based Pricing?

Although IRP is typically based on value judgements, the United States has long rejected the idea of a value-based nationwide drug-pricing approach.

In Chernew's opinion, that stance is reasonable, as long as the government generally treats value decisions as price caps rather than floors and supports National Institutes of Health-funded research into the clinical effectiveness of drugs.

"We should work to avoid paying for drugs whose clinical benefit doesn't justify the cost, but I don't think we necessarily need to have a full-blown value process for every new drug," he said. "I think we might have too much administrative burden in running that."

Grueger, however, believes that value-based principles would lower drug prices in America by tying costs to clinical benefit,[13] and Solon thinks the country's healthcare system requires more comprehensive reform.

"Without fundamental health system reform, the individual and very specific policies being attempted now are probably not going to have a huge upside for patients," she said. "Drug prices are the easy targets, but that's often not what's driving healthcare costs in the United States."

Pursuing Additional Solutions

To ease the tension between pharmaceutical affordability and innovation, healthcare stakeholders will need to work with HEOR professionals to explore additional solutions.

In privatized health systems, strategies that can save money for patients include rebates and out-of-pocket caps. In the United States, these concepts are at the heart of recent legislation encouraging pharmacy benefit managers to maximize affordability for their customers, and of the Inflation Reduction Act (IRA) of 2022, which is intended to lower patient and government costs for prescription drugs.[14,15]

Under the IRA, an annual out-of-pocket spending cap (starting at $2000 per person and adjusted annually for inflation) on drugs covered under Medicare Part D is expected to improve treatment adherence, Solon said.[16] She's less certain that IRA negotiations establishing "maximum fair prices" for certain Medicare-covered drugs will make a difference.

"A lot of the negotiated drugs were already highly rebated," she said, "so this may not have a substantial impact on patient access or affordability."

Next, Chernew suggests that America boost competition by expediting the introduction of biosimilars and bundling similar drugs within single billing and reimbursement codes. He also favors streamlining drug development; hitting companies with market penalties if they don't complete trials after receiving accelerated drug approvals; and restructuring the federal 340B drug discount program so that savings go directly to underserved patients, rather than to the safety-net hospitals and clinics that treat them.

> "Value-based pricing, within the framework of health technology assessment, can be used as a tool for structuring our discussions around evidence-based data on effectiveness, clinical benefit, and economic impact."
>
> – Mouna Jameleddine, PharmD, MSc

Globally, Jameleddine anticipates that money increasingly will be saved through cross-market collaborations, such as the regional or inter-country pooled procurement mechanisms allowing countries to access essential medicines at prices that would be difficult to achieve through fragmented procurement. Examples include the Beneluxa Initiative on Pharmaceutical Policy, the Pan American Health Organization Strategic Fund, and the Gulf Cooperation Council Health Council.

"Even at the national level, unified procurement mechanisms can ensure that we are negotiating better prices for bigger volumes," she said. For example, South Africa provides antiretrovirals and other medications through a centralized tendering, or pharmaceutical bidding, system, which spurred a 40% average drop in drug prices between 2003 and 2016.[17]

In LMICs, private investors are becoming a new type of stakeholder in the introduction of new medicines, Solon said. Through vaccine, social impact, or development impact bonds, these investors can make a profit—and a difference—by ensuring quick access to medicines while allowing governments time to budget for those expenses.[18]

In addition to supporting the timely introduction of generic medicines and biosimilars in LMICs, Jameleddine advocates for strengthening local manufacturing capacities, particularly for biosimilars. Expanding domestic production can ensure supply security, enhance competition, improve market dynamics, and potentially create greater fiscal space for the adoption of other innovative therapies.

For their part, manufacturers can support affordability by offering national installment plans or volume-based agreements, under which they must provide rebates if their treatments cost a country more than a predetermined, value-based amount.

In the big picture, Solon said, good patient care will depend on stakeholders moving away from a one-size-fits-all approach to drug pricing and using context and nuance to meet countries where they are. HEOR professionals can support that goal, she said, by clearly communicating why data translate into value, conducting relevant and execution-ready studies, and evolving their methodologies to match the pace of innovation.

Ultimately, she said, that work should focus on getting as many life-changing drugs to patients as possible, no matter where they live.

"Healthcare is very much a right," Solon said. "It shouldn't be a privilege, and it shouldn't be reserved only for wealthier countries."

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By the Numbers: Drug Pricing Policy

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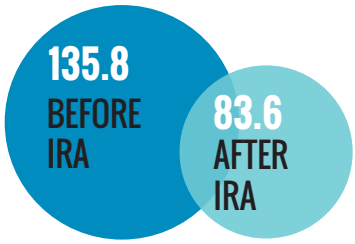
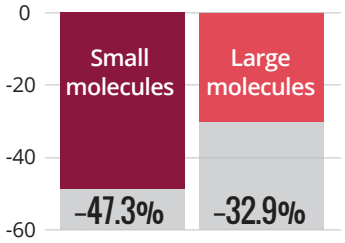
Early Post-Inflation Reduction Act Signals in Postapproval Clinical Development

What changed after pricing reform?



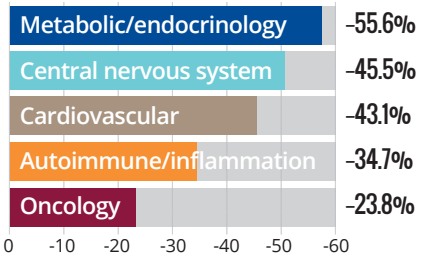
38.4% decrease in industry-funded trials per month

Which drugs were most affected?



Small molecules faced a larger decline in postapproval trial initiation

Where did trial activity decline?



Declines observed across major therapeutic areas

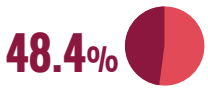
IRA indicates Inflation Reduction Act. **Source**: Zheng H, Patterson JA, Campbell JD. The Inflation Reduction Act and drug development: potential early signals of impact on post-approval clinical trials. *Ther Innov Regul Sci*. 2025;59(4):781-789. doi:10.1007/s43441-025-00774-2

International Reference Pricing: Balancing Drug Affordability and Global Access

100 drugs	High-priced drugs analyzed
76 countries	Countries included (44 of the 76 countries used ERP)
399 days with ERP vs 70 days without ERP	Median time to launch after regulatory approval (likelihood of launch ≤250 days was 73% lower with ERP)
$1285.65/unit with ERP vs $1249.86/unit without ERP	Mean launch price (ERP was not associated with a statistically significant reduction in launch price)

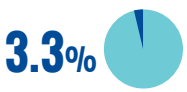
ERP indicates external reference pricing. **Source**: Voehler D, Koethe BC, Synnott PG, Ollendorf DA. The impact of external reference pricing on pharmaceutical costs and market dynamics. *Health Policy Open*. 2023;4:100093. doi:10.1016/j.hpopen.2023.100093

Value-Based Pricing in Practice: Linking Drug Payment to Real-World Outcomes



Of 62 medications analyzed in an Italian study, 30 (48.4%) had outcome-based managed-entry agreements (MEAs)

€74.5 million in manufacturer paybacks over 3 years for outcome-based MEAs (out of €327.5 million in paybacks for all MEAs)



3.3% was the median proportion of payback to expenditure for outcomes-based MEAs (similar to median of 3.8% for all MEAs)

Source: Trotta F, Cangini A, Di Filippo A, Guerrizio MA, Tafuri G. Financial outcomes of managed entry agreements for pharmaceuticals in Italy. *JAMA Health Forum*. 2023;4(12):e234611. doi:10.1001/jamahealthforum.2023.4611.

Mind the Gap: Understanding the Global Imbalance in Spending on New Innovative Medicines

Richard Kane, MIPP*, Pharmaceutical Researchers and Manufacturers of America, Washington, DC, USA; **Sarah McKeown, MSPH***, University of Oxford, Oxford, England, UK

KEY TAKEAWAYS

The United States has a disproportionately high share of global spending on new medicines relative to its economic size.

Worse patient access, not just low government-set prices, drives lower spending on new medicines as a share of gross domestic product in Europe and other high-income countries.

Spending gaps could shrink in high-income countries—and patient access could improve—if they commit to reforms like the United Kingdom committed to in its recent trade agreement with the United States.

The Cost of Investing in Global Innovation Is Not Shared Evenly

The development of new medicines should be celebrated as a triumph of science, but it is equally also a product of sustained global investment. Developing a novel therapy is risky,[1] can take more than a decade,[1,2] and can cost billions of dollars that are recovered only if a medicine successfully reaches patients.[3] While the benefits of medical innovation can help patients worldwide, countries don't evenly share in the cost of funding innovation.

Although biopharmaceutical research and development (R&D) is conducted in clinical trials and laboratories around the world, it is the expected sales of medicines that enable these endeavors to occur. Today's spending on medicines pays for the investment in R&D needed to create them, while also setting expectations for the value of future innovations. Over the past decade, concerns have grown in the United States that it bears a disproportionate share of the costs of investing in biopharmaceutical R&D because it spends much more on new medicines relative to the size of its economy compared to other high-income countries.[4,5] This analysis aims to estimate differences in spending on new medicines between the United States and other high-income countries as a share of their gross domestic product (GDP) and examines the extent to which each of these countries are not paying their fair share for biopharmaceutical innovation.

Measuring the Spending Gap

This analysis measures the gap in spending on new medicines between the United States and other high-income countries in the Organization for Economic Co-operation and Development (OECD). New medicines include new active substances first launched globally during the prior 10 years (2014-2023) and approved for use in the United States, Europe, or Japan. New medicines (up to 10 years old) are a logical focus for this analysis since sales during the first decade of a medicine's product life cycle heavily influence early investment in R&D. The analysis measures spending "net" after accounting for the various pricing and cost-containment policies (eg, rebates, discounts, revenue clawbacks) that high-income countries impose and any rebates or discounts paid to private payers or pharmacy benefit managers, as occurs heavily in the United States. Net spending on new medicines best approximates what public and private payers spend on medicines, as well as the net revenues that biopharmaceutical manufacturers receive.**

> Today's spending on medicines pays for the investment in R&D needed to create them, while also setting expectations for the value of future innovations.

The analysis examines the extent to which each high-income country is not paying its fair share for biopharmaceutical innovation by comparing its share of economic resources with its share of spending on new medicines among high-income countries. If each high-income country contributes the same share of its GDP to new medicines, then each high-income country's contribution to the cost of biopharmaceutical innovation will match its share of economic resources. To calculate combined spending on new medicines and GDP across high-income countries, the analysis converts both net spending on new medicines and GDP for each country into purchasing power parity (PPP) dollars. Using PPP conversion factors, as opposed to more volatile currency exchange rates, enables more meaningful cross-country comparisons that best account for differences in each country's overall price levels.[6]

Results

The results show that the United States contributes 0.78% of its GDP to new

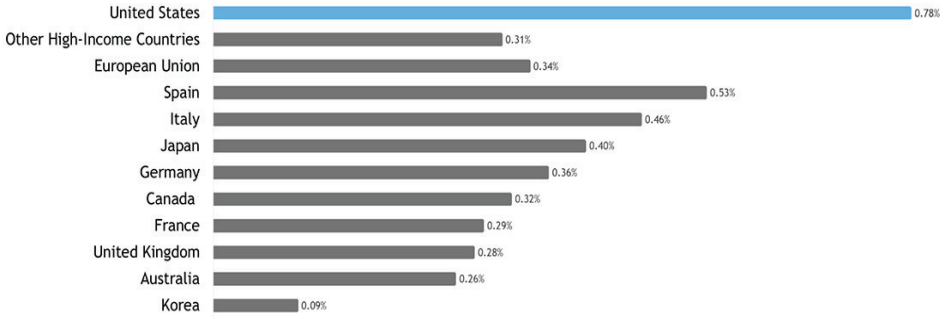
** Richard Kane, MIPP, and Sarah McKeown, MSPH, are co-first authors of this article.*
*** Note: Estimates of rebates, discounts, revenue clawbacks, and other paybacks are modeled using publicly available information on aggregate amounts and mechanisms from official government reports and statistics.*

medicines, a small amount relative to its economic size, but a far higher share of its GDP compared to other high-income countries. Japan and Germany, the second and third largest markets in the world for innovative medicines, contribute much smaller shares of their GDP to new medicines. Japan contributes only 0.40% of its GDP to new medicines, and Germany contributes only 0.36%. All other high-income countries in this study contribute a smaller share of their GDP to new medicines than the United States, including Australia 0.26%, Canada 0.32%, France 0.29%, Italy 0.46%, Korea 0.09%, Spain 0.53%, and the United Kingdom 0.28% (**Figure 1**).

The results also show that the United States contributes 60% of the spending on new medicines by high-income countries, even though its share of economic resources among these high-income countries is only 38%. Other high-income countries contribute less to biopharmaceutical innovation than the size of their economic resources would suggest. For example, France and the United Kingdom each contribute only 3% of the spending on new medicines by high-income countries, even though each of them garners 6% of the economic resources (**Figure 2**).

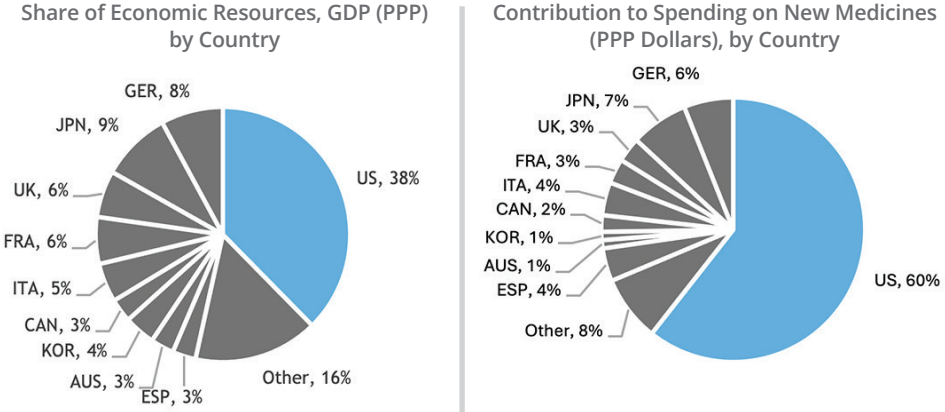
The findings of this study are consistent with prior research suggesting that the United States bears a disproportionate share of global spending on pharmaceutical innovation relative to its economic size. Earlier analyses by the Council of Economic Advisers and Neumann et al argued that higher US pharmaceutical spending plays a central role in sustaining global biopharmaceutical research and development, and our analysis supports this conclusion by estimating that the United States accounts for 60% of spending on new medicines while representing only 38% of economic resources among high-income countries.[4,5] The results are also consistent with previous studies showing that patients in Europe and other high-income countries experience delayed and more restricted access to innovative medicines because of government reimbursement decisions, health technology assessments, and budget impact analyses.[7-10]

Figure 1. Contribution to New Medicines First Launched Over the Last 10 Years as a Share of Gross Domestic Product, 2023



Note: Estimates of spending on new medicines are based on analysis of Global Data, NAVLIN, IQVIA MIDAS®, country regulatory data, and publicly available information from government reports on discounts, rebates, and revenue clawbacks. Gross domestic product data are from Global Data.

Figure 2. Share of Economic Resources vs Contribution to Spending on New Medicines



GER indicates Germany; US, United States; JPN, Japan; UK, United Kingdom; FRA, France; ITA, Italy, CAN, Canada; KOR, Korea; AUS, Australia; ESP, Spain; GDP, gross domestic product; PPP, purchasing power parity. Note: Estimates of spending on new medicines are based on analysis of Global Data, NAVLIN, IQVIA MIDAS®, country regulatory data, and publicly available information from government reports on discounts, rebates, and revenue clawbacks. GDP data are from Global Data.

What Drives the Spending Gap?

Worse patient access, not just low government-set prices, drives lower spending on new medicines as a share of GDP in Europe and other high-income countries. In the United States, new medicines approved as safe and effective are soon available for coverage and reimbursement by public health insurance. In other high-income countries, government regulatory agencies engage in further cost- and budget-based evaluations to determine whether already approved medicines should be covered by the public health insurance program and at what price.

Patients in Europe and other high-income countries experience delays in access to new medicines compared to patients in the United States due to their governments conducting cost- and budget-impact evaluations. For example, patients wait on average 25 months in France after a new medicine has been launched globally for access through public health insurance, and patients in the United Kingdom wait 30 months.[8] In addition, decisions based on those cost- and budget-impact evaluations can reduce patients' access to new medicines further through restrictions and negative coverage decisions. For example, less than half of new medicines are available through the public health insurance programs in France (40%) and the United Kingdom (46%), and patients face restricted access to the smaller share of medicines that are available.[8] One study shows that in 2024,

the uptake of new medicines publicly covered in the United Kingdom was 81% lower than in the United States, and more than 90% lower for new cancer medicines.[9,10]

Conclusion

The United States accounts for a disproportionately high share of global spending on new medicines relative to its economic size. Worse patient access, not just low government-set prices, drives lower spending on new medicines as a share of GDP in Europe and other high-income countries.

Over the past decade, concerns have grown in the United States that it bears a disproportionate share of the costs of investing in biopharmaceutical R&D. The US government has recently initiated pilot demonstrations in Medicaid and drafted proposed pilot demonstrations for Medicare that set drug prices by referencing prices in other high-income countries.[11-13] These policies could worsen access to new medicines in Europe and other high-income countries and thereby further widen the gap in spending with the United States.

However, patient access to new medicines could improve in high-income countries countries and spending gaps relative to GDP narrow if they adopt reforms similar to those agreed to by the United Kingdom in its recent pharmaceutical pricing agreement with the United States. In this agreement, the United Kingdom commits to increase spending on new medicines from 0.3% to 0.6% of GDP by the end of 2036, increase net prices by 25% "while maintaining broad patient access and ensuring rapid and equitable adoptions of those medicines," and reduce revenue clawbacks to no more than 15%.[14]

Policy makers should consider how strict pricing and coverage rules can delay patient access to new medicines and reduce incentives for innovation. Greater international cost-sharing and faster access to treatments could benefit patients, support continued drug development, and create a fairer global system.

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From Brussels to Washington: Lessons Learned From 30 Years of International Reference Pricing in Europe

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KEY TAKEAWAYS

The United States has embarked on one of its most ambitious pharmaceutical pricing reforms in decades: international reference pricing.

Europe's substantial experience in international reference pricing suggests that the devil is in the detail, and nowhere more so than in implementation rather than policy design.

President Trump's Most-Favored-Nation policy's true impact will be measured not in drug list prices, but in launch delays, market exits, and the fundamental restructuring of the pharmaceutical industry.

An Ambitious Pricing Reform

The United States is a major market for innovative drugs, with prices on average 2.78 times higher than in 33 other nations, according to a 2024 report.[1] Some, including US President Donald Trump, argue these high prices drive global pharmaceutical innovation, with the rest of the world's health systems getting a "free ride."[2] Overall, the United States represents approximately half of global pharma sales.[3]

Trump's Most-Favored-Nation (MFN) drug pricing policy is built on a simple, politically powerful idea: the United States should not pay more than patients in other wealthy countries for the same medicines. By linking its drug prices to international benchmarks, the United States has embarked on its most ambitious federal pricing reforms yet: international reference pricing (IRP).

> Most-favored-nation policy's true impact may be measured not in reduced US prices, but in launch delays or omissions, market exits, and the fundamental restructuring of the pharmaceutical industry.

Europe has been implementing IRP based on publicly visible list prices for 30 years—with mixed results. But what can Americans learn from the European experience?

The evidence from Europe and the strategic responses to Trump's MFN policy already visible from pharmaceutical executives suggest the policy's true impact will be measured not in reduced US prices, but in launch delays or omissions in ex-US markets, market exits, and the fundamental restructuring of the pharmaceutical industry. Increasingly, confidential agreements are being negotiated when a market's willingness to pay threshold for a drug falls below the referenced list price needed for a company to continue to supply it.

The US Experiment: What's Actually Happening?

Trump's MFN policy architecture encompasses 3 implementation pathways targeting high-cost drugs: the voluntary GENEROUS (GENErating cost Reductions fOr US Medicaid) model for state Medicaid programs, separate mandatory models for high-cost drugs under Medicare Parts B and D, and direct manufacturer agreements through the TrumpRx platform.

The GENEROUS model bases MFN reference prices on the second lowest country-specific manufacturer-reported net price (among 8 comparator nations), adjusted for differences in gross domestic product (GDP) per capita using a purchasing power parity method.[4] The 2 additional proposed Medicare models use international drug prices to set alternative benchmarks for calculating rebates authorized by the Inflation Reduction Act, but are not tied to MFN directly.

However, for the 155 million US citizens with commercial insurance who remain at the mercy of prices their insurers negotiate, any benefits from MFN policies remain at best indirect and emerging.[5]

In January 2026, Novartis CEO Vas Narasimhan told Bloomberg at the World Economic Forum in Davos that the policy shift represents "a pretty seismic shift in the structure of our industry," warning that "the biggest impact is going to be on future launches. Be it delayed launches, might be no launches" across Europe, Japan, and Canada.[6]

By April 2026, 17 major pharmaceutical companies had signed MFN drug pricing agreements with the Trump administration.[7] The TrumpRx platform went live in February 2026, with 43 products featured at launch.[8]

The Carrot and the Sticks of President Trump's MFN

For drug companies that do not engage in MFN deals, there are consequences. The threat of regulatory penalties (including revocation of approvals) and 100% tariffs on their drug imports has been an incentive to secure engagement from big pharma.[2,9]

For those that sign deals early, beyond the President's protection from tariffs, there is greater flexibility to shape terms, including the ability to sell directly to patients at MFN prices via the TrumpRx or company platforms; thereby preserving volume and brand presence even at lower net prices.[10,11]

Restating its claim that "foreign nations freeloading on American-financed innovation" (referring to countries that pay lower prices for medications and contribute lower revenues to industry innovation), the Trump administration has warned that disciplinary US trade policies will be imposed if foreign governments continue to keep pharmaceutical prices below what the administration considers fair market levels.[12,13]

Thus, on a global scale, MFN agreements have been leveraged to influence trade policy through the threat of tariffs.

> For the Most-Favored-Nation framework to deliver meaningful change, it would need to rely heavily on broad net price transparency. However, mandating such disclosure would be highly complex.

The emerging UK-US pharmaceutical deal neatly illustrates how international pricing dynamics can reshape domestic health technology assessment (HTA). With US policy makers adopting MFN benchmarks that explicitly reference UK prices, the United Kingdom's historically stringent cost-effectiveness thresholds risked anchoring US reimbursement at levels industry viewed as unsustainably low.

To avoid trade retaliation, the United Kingdom has agreed to raise the National Institute for Health and Care Excellence's (NICE) core incremental cost-effectiveness ratio range, signaling a greater willingness to pay for innovation and reducing the chance that the National Health Service prices become the de facto global floor for MFN calculations. In return, the agreement offers political and trade "mitigations" for the United Kingdom, including reassurances of tariff-free access and a lower risk that aggressive cost containment at home will translate into punitive measures or constrained access to future launches in the much larger US market.[14] However, it remains unclear whether these changes will be sufficient for the United Kingdom to avoid significant impact, including launch delays.

For the MFN framework to deliver meaningful change, it would need to rely heavily on broad net price transparency. However, mandating such disclosure would be highly complex and, if fully realized, the resulting price convergence could render launches in certain markets, such as the United Kingdom, economically nonviable.

Cogentia Healthcare Consulting's survey of 10 US market access industry experts, conducted before MFN policies were announced, showed that most participants expected the implementation of IRP in the United States to have a "somewhat negative" or "very negative" impact across 4 domains: drug launch prices, innovation, reference country prices, and administrative burden.[15]

Learnings From Europe

Europe is experienced with IRP, with most countries using some form of strategic IRP policies, often in conjunction with other methods such as HTAs, to align drug prices with their perceived value.[16]

Europe's history in IRP gives the following learnings:

1. Transparent and predictable methods are key

Transparency in the IRP process and predictability in the basket selection and revaluation frequency can reduce uncertainty for manufacturers. For example, the Netherlands' Medicines Pricing Act explicitly sets out the reference basket (currently Norway, Belgium, France, and the United Kingdom), the calculation method (average of reference prices), and the timetable for regular price revisions. [17,18]

2. Utilize complementary strategies

European countries such as France, Italy, and Spain use a combination of both HTA and IRP methods to support pricing. The United States could potentially leverage value-based pricing analysis from the Institute for Clinical and Economic Review (ICER) alongside IRP methods to develop a more robust pricing approach, rather than relying on a single method like IRP.

3. Select an appropriate reference basket

European countries tailor reference countries to market size and economic status and regularly review reference baskets. For example, Norway limits its IRP basket to 9 countries with similar GDP, rather than referencing all EU states.[19]

A Global Impact

While in theory IRP promises to accelerate access and curb excessive spending, Europe's experience shows a different story. In many IRP-exposed European markets, companies delay submitting new medicines by up to a year because they prefer to launch and establish prices in large, high-income markets first (eg, Germany, France, Italy, United Kingdom, and Spain), as early low-price launches can influence their entire global portfolio due to IRP.[20-22]

To preserve room for negotiation under these constraints, manufacturers have increasingly relied on high list prices with discounts (often confidential) available to European payers.

Transposed to the United States, MFN risks exporting and amplifying these dynamics. If European list prices feed directly into US benchmarks, global manufacturers will have even stronger incentives to design launch sequences around US MFN exposure. Manufacturers would likely aim for European list prices that appear to fall within an acceptable US reference band,

while pushing budget-constrained payers toward deeper confidential discounts and tighter confidentiality provisions—effectively decoupling public list prices from true transaction prices. However, as MFN evolves, the pricing anchor could be the net price.

Many stakeholders are worried that, once a system requires net prices to be reported for MFN purposes, many launches would not be commercially viable. There is the question of whether the confidentiality of commercial agreements can be shredded and how such mechanisms would be legally structured. If there is net pricing transparency globally, the result is likely to be less access to innovation for patients in less-commercially attractive markets as launches that risk the price corridor would not happen.

Some European industry leaders propose a common EU list price, paired with confidential net prices to reconcile this tension: maintain publicly visible prices that roughly align with US expectations, while safeguarding country-specific affordability behind the veil of secrecy.[23] For this approach to work, there would need to be a harmonized approach to pricing across Europe, which is not currently the case.

> Many stakeholders are worried that, once a system requires net prices to be reported for Most-Favored-Nation purposes, many launches would not be commercially viable.

Germany is currently having significant debates about the use of confidential prices but acknowledges the challenges of this within the constraints of the current system.[24] A recent example of where this has led to European list price increases is Mounjaro (tirzepatide), whose list price was increased in the United Kingdom (by 170%) because of pressure from the US administration.[25] Interestingly, the Mounjaro manufacturer applied a different launch strategy in Germany, where Mounjaro became the first drug to invoke a confidential price option, owing to their significant research and development presence in Germany as per the recently updated German Medical Research Act.[26] Behind the list price increase in the United Kingdom, confidential discounts and net prices for the NHS remain in place.

For the United States, MFN may deliver short-term savings and greater price convergence with peers. But it also raises the possibility that manufacturers will strategically deprioritize or pull out of non-US launches to protect US price realizations, thereby widening global access gaps and entrenching a more US-centric innovation model.

> If Europe becomes less attractive as an early launch region and global revenues shift accordingly, pressure could paradoxically result in the need for higher US prices to compensate for diminished earnings elsewhere.

A recent example of this is Insmed's Brinsupri (brensocatib) for non-cystic fibrosis bronchiectasis. In a May 2026 earnings call, Insmed's Chair and CEO reiterated the need for clarity on MFN policies before launching in Europe, having previously stated in February: "we want clarity on the MFN policies that are coming forward now. I think we are going to have that in the coming weeks and, at the most, months. But until that is clear, it seems to us that the prudent thing to do is to sort of [put] things on hold until we know what that is going to look like."[27,28] This suggests that in the short-term, companies will look to delay launches in Europe while waiting for greater clarity on the impacts of MFN. In the meantime, hesitancy around European launches may inadvertently fund the Chinese biotech market.[28]

Over time, if Europe becomes less attractive as an early launch region and global revenues shift accordingly, pressure could paradoxically result in the need for higher US prices to compensate for diminished earnings elsewhere—undermining MFN's original promise.[15,22] While reducing drug costs is an important goal, some argue that linking US prices to those abroad is a blunt instrument that risks doing more harm than good overall and will not achieve the stated goal. Reference pricing, by definition, can be done only when other markets have the product in question.

Perhaps a more sustainable approach would be to reinforce domestic HTA to evaluate a drug's effectiveness compared with existing alternatives, and to move towards more value-based pricing. Rather than referencing prices set abroad, the United States could ground its pricing decisions in transparent assessments of clinical benefit and cost-effectiveness that align with national priorities and societal willingness to pay.[20]

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When Worlds Converge: How Most-Favored-Nation Policy and International Reference Pricing Reshape Global Market Access Interdependencies

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KEY TAKEAWAYS

Global pricing systems are becoming more interconnected. The United States is increasingly linking drug prices to those in other developed countries, mirroring approaches used globally. Pricing decisions in one country can directly affect pricing, access, and market dynamics in others.

Pricing pressures are reshaping launch and access strategies. Greater reliance on international price benchmarks may prompt drug manufacturers to rethink where and when they launch products.

Stronger evidence is essential to defend value. As pricing and reimbursement scrutiny increases, manufacturers will need stronger evidence to reduce uncertainty and support value discussions.

Global government drug pricing and access policies have been undergoing significant changes over the past year. While some countries in Europe have implemented reforms that shift away from international reference pricing (IRP), the United States has moved toward IRP through Most Favored Nation (MFN).

This shift in US drug pricing policy creates a convergence of pharmaceutical pricing systems that once operated in distinct spheres, which could broadly impact affordability, access, and innovation. By linking US reimbursement to ex-US price benchmarks, MFN adds complexities for manufacturers, policy makers, and healthcare systems that will need to be carefully observed and managed. Increasingly, pricing decisions in one country will influence others through reference baskets (groups of socioeconomically comparable countries), benchmarking formulas, and pricing revision cycles.[1]

Complex and Colliding Pricing and Access Policies

Governments across more than 75 countries have long used IRP as one policy tool to inform or regulate medicine prices, although its role varies by market and is often applied alongside other pricing and reimbursement considerations.[2] These market-level differences in how IRP is applied create a complex landscape for pricing negotiations, necessitating continual adjustments and frequent updates to IRP models.

Key elements include:

- the basket size, or the number of reference countries included;
- whether referencing is applied at launch only or updated periodically;
- benchmark methodology, such as average, median, or lowest price;
- adjustment factors, such as purchasing power parity to account for differences in general cost of living across countries or exchange-rate considerations; and
- price level referenced (ex-manufacturer or wholesale price).

Countries frequently change how they structure their IRP policies, and some have sought amendments related to drug pricing. For example, an amendment to Germany's Medical Research Act introduced optional confidential discounted reimbursement to allow companies to keep their reimbursement price negotiations with statutory insurance funds private, so they won't affect negotiations with other countries, thereby impacting reference baskets.[3] Another amendment to the Act removes IRP as a key mechanism for price negotiations. Switzerland has also pushed toward confidential price models to ensure access to innovative medicines.[4,5]

> Market-level differences in how international reference pricing is applied create a complex landscape for pricing negotiations, necessitating continual adjustments and frequent updates to models.

Now, with MFN, the United States is added to the mix of nations applying IRP principles. MFN was issued by President Trump as an Executive Order in May 2025 and seeks to tie US drug prices to those in similarly developed countries.[6]

A voluntary Centers for Medicare & Medicaid Services (CMS) model called GENEROUS (GENErating cost Reductions fOr US Medicaid) model[7] adjusts Medicaid pricing based on manufacturer-reported average prices from 8 countries: the United Kingdom, France, Germany, Italy, Canada, Japan, Denmark, and Switzerland. In December 2025, CMS announced 2

proposed mandatory IRP-style initiatives aimed at reducing costs for beneficiaries:

- The Global Benchmark for Efficient Drug Pricing (GLOBE) Model, which would assess a rebate for certain drugs payable under Medicare Part B if the prices exceed those paid in economically comparable countries.[8]
- The Guarding US Medicare Against Rising Drug Costs (GUARD) Model, which would assess rebates for certain drugs payable under Medicare Part D if the prices exceed those paid in economically comparable countries.[9]

Both of these models use a 19-country reference basket for MFN benchmarking. Both GLOBE and GUARD include 2 IRP benchmarks: a default CMS-derived international benchmark that is based on international pricing data sources, and an optional manufacturer-submitted volume-weighted average net price benchmark.[10]

However, there is still uncertainty as to how GUARD and GLOBE will evolve, since both are currently pilot models and cover about 25% of the Medicare Part D and Part B population. The impact of GENEROUS, meanwhile, will depend on how many states choose to participate.

MFN's implications across the US healthcare ecosystem, particularly for products largely used outside the Medicare and Medicaid populations, remain uncertain.

Implications for Global Drug Pricing Policy

Reference pricing can influence a company's launch sequence and price corridor for a new product. If a product faces a mandated low price in a country, the company could choose to delay launching the product in that country or even avoid that market entirely to avoid causing the price to decrease in other countries that use reference pricing. In Europe, for example, lower-income countries face delays or even no access at all because pricing is anchored to countries that can afford to pay more for the product.[11]

Now, in response to the deployment of MFN in the United States, some manufacturers are delaying European launches, opting not to launch, and even withdrawing existing products from markets they believe will be lower priced because of price erosion in the United States.[12,13] Instead, manufacturers of some products—particularly more costly, innovative products—are opting to launch first in other markets such as Japan, which offers incentives for innovation and poses a lower risk of IRP spillover than European markets.[14]

Implications for HEOR, Market Access, and Commercial Teams

These dynamic developments across global healthcare environments create new and, as yet, unclear complications for different stakeholders, including health economics and outcomes research (HEOR) teams. As reference pricing increases downward pressure on prices, robust evidence becomes even more important to demonstrate product value and reduce uncertainty in pricing and reimbursement discussions.

> Greater pricing and reimbursement scrutiny will put pressure on HEOR teams to quantify incremental health benefits alongside healthcare resource-use offsets, comparator and downstream treatment cost savings, and affordability and budget impact.

In response, HEOR professionals will need to proactively adapt their strategies to mitigate the fallout from reference pricing and anticipate common evidence critiques from payers and health technology assessment bodies across markets. These critiques include inappropriate comparators, nonrepresentative populations, immature or non–clinically meaningful endpoints, limitations in indirect treatment comparisons or external controls, insufficiently reliable real-world data (RWD) sources, and uncertainty regarding long-term outcomes.

There are several key steps HEOR professionals can take to respond to this changing environment.

Build an integrated evidence-planning strategy with both access and approval in mind. The comparator strategy, patient-relevant endpoints and patient-reported outcomes, and plans for long-term follow-up will need to facilitate robust evidence generation. Where data are immature, extrapolation should be clinically anchored, transparently tested, and complemented where possible by fit-for-purpose RWD from comparable patient populations to strengthen external validity and reduce uncertainty.

Strengthen value demonstration for decision makers. Greater pricing and reimbursement scrutiny will put pressure on HEOR teams to quantify incremental health benefits alongside healthcare resource-use offsets, comparator and downstream treatment cost savings, and affordability and budget impact. Where credible, the value case should also capture broader elements such as productivity, caregiver quality of life, environmental impacts, and other societal benefits, reflecting the continued expansion of value assessment frameworks beyond traditional clinical and cost-effectiveness metrics.

Minimize uncertainty in long-term benefits by designing postlaunch evidence gathering from the outset. Where randomized controls are not feasible (for example, advanced therapy medicinal products for rare diseases), natural history studies and other external comparator approaches may be required. These must be methodologically rigorous and supported by fit-for-purpose data infrastructure. Post launch, HEOR teams can further shape long-term data collection (eg, durability extrapolation, registry strategy), and guide managed access or outcomes-based agreements by clearly defining the target population, clinically meaningful outcomes, assessment timing, data sources, governance, and the economic consequences of success or failure.

Test pricing and launch sequencing scenarios. HEOR teams should continue to assess price potential and willingness to pay for the product's target markets through comprehensive economic modeling, particularly considering the additional complexities of launch sequencing in the MFN era.

By comparing the projected commercial opportunities and associated risks of different launch sequence scenarios, HEOR professionals can inform decisions about optimal launch sequences.

Conclusion

The anticipated convergence of pricing responses to MFN has the potential to become a self-reinforcing feedback loop in which decisions in one market ripple through reference baskets and revision cycles to affect affordability, access, and incentives for innovation elsewhere.

The near-term impact of MFN remains difficult to predict. Manufacturers should be prepared to take steps to reduce payer uncertainty and defend product value.

Manufacturers and HEOR teams should also expand stakeholder engagement and prepare for more HTA-like value expectations in the United States, including expectations related to product value in terms of broader societal and caregiver impacts where relevant. The downstream effects of CMS models, adoption of confidential net pricing, and further shifts in launch timing or market-entry decisions driven by cross-country price referencing will be top of mind for all manufacturers.

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The information provided in this article does not constitute legal advice. Cencora, Inc., strongly encourages readers to review available information related to the topics discussed and rely on their own experience and expertise in making decisions related thereto.

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The Inflation Reduction Act and Medicare Drug Pricing: What It Means for Patients, Innovation, and Access

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KEY TAKEAWAYS

The Inflation Reduction Act introduces a shift toward evidence-informed pricing, where real-world evidence is increasingly being used to inform drug price negotiations and the role of health economics and outcomes research in pricing decisions is expanding.

Beyond controlling costs, it will be important to demonstrate how drug pricing reform translates into improved medication adherence, health outcomes, and overall value for patients.

Collaboration among researchers, policy makers, payers, and manufacturers is essential, with a growing need for earlier, decision-focused evidence generation aligned with new requirements.

A Turning Point in US Drug Pricing

The Inflation Reduction Act (IRA), enacted in 2022, introduced major changes to prescription drug pricing in the United States.[1] Central to the legislation is a new mandate enabling the Centers for Medicare & Medicaid Services (CMS) to negotiate prices for high-cost drugs without generic or biosimilar competition.[2]

This negotiation authority is exercised through Medicare, beginning with 10 high-spending Medicare Part D drugs (retail prescriptions) whose negotiated prices took effect in 2026 and expanding to physician-administered medicines covered under Medicare Part B starting in 2028. The program is designed to expand in subsequent years, with additional drugs selected annually for negotiation: 15 Part D drugs for 2027, 15 (including Part B) for 2028, and 20 annually thereafter.

Beyond price negotiations, the IRA introduced a series of consumer-focused provisions including a $35 monthly insulin cap, a $2000 annual out-of-pocket cap under Medicare Part D, free access to recommended adult vaccines, and inflation-based rebates.[2]

> Early experience with the Inflation Reduction Act suggests it is delivering on its most visible promise: lowering out-of-pocket costs for patients.

From a health economics and outcomes research (HEOR) perspective, the IRA marks a structural shift toward evidence informed pricing, with clinical benefit, comparative effectiveness, and real-world evidence (RWE) increasingly shaping Medicare drug prices. Emerging analyses suggest that CMS is increasingly relying on longitudinal data, comparative effectiveness research, and real-world utilization patterns in determining "maximum fair price," signaling a transition toward an evidence-intensive environment more aligned with international health technology assessment (HTA) systems.[3,4]

However, the IRA is more than a set of cost-control measures. It introduces a shift that elevates the importance of HEOR assessments—such as cost-effectiveness analyses, patient-reported outcomes, or subgroup analyses—as key inputs into pricing decisions.

What's Working: Immediate Benefits for Patients

Early experience with the IRA suggests it is delivering on its most visible promise: lowering out-of-pocket costs for patients.[5,6] Essential medications are more affordable and their costs are more predictable for Medicare beneficiaries, particularly those living with chronic conditions such as diabetes and cardiovascular disease. Most notably, the IRA introduced a cap on annual out-of-pocket spending for prescription drugs under Medicare Part D, set at $2000 starting in 2025. This cap is expected to benefit more than 3 million Medicare beneficiaries annually. Negotiated prices are projected to save patients $1.5 billion in 2026 alone.[6]

CMS estimates show that, had the prices negotiated for 2026 been in effect during 2023, aggregate net spending on prescription drugs would have decreased by an estimated $6 billion, representing a 22% reduction.[7] Furthermore, analyses of CMS negotiation materials indicate that RWE was cited across Maximum Fair Price explanation documents, although its prevalence and sources varied and the evidentiary weighting remains undisclosed.[8] For patients, affordability improvements are not only financial but also clinical. Although direct post-IRA evidence on adherence is still emerging, extensive pre-IRA literature links lower cost sharing to improved adherence and outcomes, suggesting that affordability gains may translate into health benefits.[9,10] These developments underscore the growing role of HEOR—

including adherence modeling, budget impact analysis, and distributional cost-effectiveness frameworks—in connecting affordability to patient outcomes.

The Trade-Off Question: Innovation Under Pressure

While the affordability gains are clear, they come with important questions about long-term consequences, particularly regarding pharmaceutical innovation.[11] Emerging evidence from modeling studies suggests that manufacturers may respond by shifting investment strategies. Larger pharmaceutical companies could potentially prioritize products with lower development risk and faster returns. Smaller and mid-sized biotech firms, often responsible for breakthrough advances in oncology, rare diseases, and neurodegenerative conditions, may face tougher funding environments as future revenues become less predictable.[12]

Alzheimer disease research offers a clear example of this tension.[13] Developing treatments in this space requires substantial investment, long timelines, and high clinical uncertainty. For example, recent disease-modifying therapies for Alzheimer disease have required decades of research investment with uncertain clinical success, and pricing constraints introduced by the IRA may further complicate return-on-investment expectations in such high-risk areas.[13]

> Cost-containment policies do not operate in isolation. For the health economics and outcomes research community, this creates a need to adapt how value is quantified in the context of Inflation Reduction Act negotiations.

Quantitative modeling studies suggest IRA-related pricing provisions may reduce the long-term economic value captured from innovative therapies, particularly in therapeutic areas with long development timelines and extended product life cycles.[14] In practice, manufacturers may adapt by prioritizing indications with shorter time-to-market or modifying life-cycle management strategies.

The inclusion of small-molecule oncology therapies such as ibrutinib in the first wave of IRA negotiations illustrates this dynamic. As small molecules are subject to negotiation earlier in their life cycle than biologics, manufacturers may face compressed revenue windows, which could influence portfolio strategies. Early industry responses suggest a potential shift toward biologics or therapies with longer exclusivity periods, raising questions about future investment in certain classes of oncology treatments. It is important to note, however, that these projections are based on early evidence and modeling assumptions, and the full impact of the IRA on innovation and investment behavior will become clearer as real-world data emerge over time.

These dynamics underscore that cost-containment policies do not operate in isolation. For the HEOR community, this creates a need to adapt how value is quantified in the context of IRA negotiations. For example, standard cost-effectiveness models may under-value therapies for conditions like Alzheimer disease if they do not account for benefits such as delaying disease progression, reducing caregiver burden, or providing financial risk protection. Expanding HEOR frameworks to explicitly capture these elements through scenario analyses, severity weighting, or inclusion of broader societal outcomes can help ensure that high-risk innovations are more accurately reflected in negotiated prices.

Access and Equity: Uneven Gains

Another key insight from early research is that the benefits of the IRA are not evenly distributed. Medicare beneficiaries see clear reductions in out-of-pocket costs, but patients outside Medicare may not benefit directly. This creates the potential for widening access gaps across the healthcare system.[11]

Equity challenges also emerge in how coverage is implemented across plans. For example, widely used anticoagulants such as apixaban and rivaroxaban illustrate how lower negotiated prices do not automatically translate into better patient access.[15] While Medicare's maximum fair price is expected to reduce overall costs, formulary placement and cost-sharing differences may still affect what patients pay. For patients requiring long-term anticoagulation, even modest increases in out-of-pocket costs can lead to missed doses or treatment discontinuation that can increase the risk of stroke and hospitalization.[16] Early analyses of the first 10 drugs selected for negotiations (including widely used therapies in cardiovascular and metabolic disease) also suggest that access and savings may vary across therapeutic classes and patient subgroups, emphasizing the importance of distributional analyses.[17]

> Evidence generation will need to shift from primarily post-launch, payer-focused analyses to earlier, negotiation-driven strategies that produce evidence tailored to specific populations and pricing decisions.

At the same time, the IRA is accelerating the use of RWE to monitor these effects. As mentioned earlier, reviews of CMS negotiation documentation indicate that a substantial proportion of cited evidence includes observational studies and Medicare claims analyses, demonstrating how RWE could have a potential role in comparative effectiveness assessment and pricing decisions.[8,18] A recent review presented at ISPOR 2025 highlighted emerging shifts in spending distribution and beneficiary financial exposure under IRA provisions,[19] underscoring the need for ongoing claims-based monitoring to assess equity impacts across income and risk strata.

Collectively, these dynamic developments demonstrate the need for HEOR studies that align with the evidentiary needs and timelines of IRA price negotiations. In practice, this includes generating RWE using Medicare claims and observational data to assess comparative effectiveness and/or treatment patterns. Simulations

that assess the impact of formulary placement or drug switching could also inform decision making. Such analyses can help identify how the IRA's effects on access, clinical outcomes, and out-of-pocket burden vary across patient populations, which can help facilitate equitable pricing and coverage decisions.

Looking Ahead

The IRA is likely to reshape not only pricing but also evidence generation and decision-making processes across the US healthcare system. Several policy directions merit consideration:

- Establish transparent evidentiary standards, including clear guidance on acceptable comparative effectiveness evidence, real-world data quality, and the role of cost-effectiveness thresholds in price-setting.[3,20]
- Ensure negotiated prices translate into lower patient cost sharing and improved access by aligning plan design and limiting cost-shifting.[15]
- Evidence generation will need to shift from primarily postlaunch, payer-focused analyses to earlier, negotiation-driven strategies that produce evidence tailored to Medicare populations and CMS pricing decisions.

These strategies reflect the need for policies to evolve alongside emerging evidence, carefully balancing affordability, patient access, and impact on innovation to ensure sustainable improvements in health outcomes.

The Bottom Line

The Inflation Reduction Act is already reshaping the US pharmaceutical landscape. It has delivered meaningful, immediate relief to patients, yet its long-term success will depend on thoughtful and adaptive policy stewardship. The path forward from an HEOR perspective is to ensure that negotiated prices reflect not only costs, but also meaningful differences in clinical benefit, patient outcomes, and overall value for patients.

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Optimize Health in Chronic Disease Populations by Putting Patient-Important Outcomes First

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KEY TAKEAWAYS

For patients with chronic disease, treatments targeting biomarkers or symptom control are typically more accessible than those targeting outcomes necessary for the functioning most important to the patient. Focusing treatment development on these under-addressed outcomes will further optimize health.

Further progress toward health optimization for chronic disease patients requires that treatment development and testing begin by targeting patient-important outcomes.

Prioritizing the inclusion of patient-important outcomes will ensure that the development and testing of new treatments is based not only on whether they are safe, but whether they facilitate optimal health.

Chronic Disease Treatment Should Aim for Health Optimization

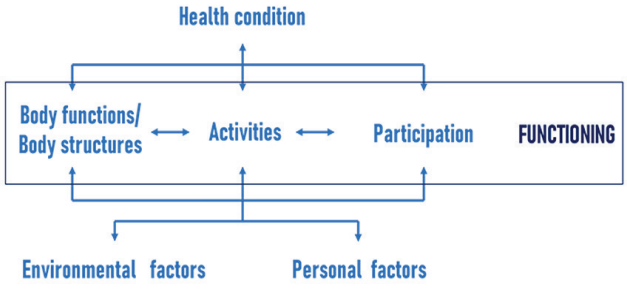
In the 20th century, the principal pathway for improving the health of societies was reduction of mortality and disease. While this approach resulted in major gains, societies are now increasingly challenged by chronic and noncommunicable diseases, which generate substantial and insufficiently addressed burdens of comorbidity and disability.[1] Although estimates vary across jurisdictions, the prevalence of chronic conditions has risen to historically high levels, affecting approximately 20% of children younger than 18 years[2] and more than half of adults older than 60 years,[2] while their incidence continues to grow across low-, middle-, and high-income regions alike.[2,3] Because chronic diseases are long-lasting and widely distributed, their consequences extend beyond patients to caregivers to health systems and societies as a whole. This means that, while it is still necessary for societies to aim for acute-care survival targets, such targets are no longer sufficient on their own.

In the 21st century, health scientists must devote more efforts toward an under-recognized goal: to ***optimize*** individual health ***despite*** the persistence of chronic disease. When the threat of mortality is minimized, The International Classification of Functioning, Disability and Health (ICF) provides a way to reframe treatment targets around optimization for everyone.[4] The ICF is more in keeping with the 1948 World Health Organization (WHO) Charter definition of broad health ("a state of complete physical, mental, and social well-being"[4]) than its preceding companion-classification of diagnoses, found in the International Classification of Diseases.[5] Health in the ICF is conceptualized not by the absence of disease pathology, but by the presence of an individual's functioning (**Figure 1**).

Functioning is the optimal health aim represented in the ICF classification (used to classify not categorical and functional outcomes). This classification maps onto outcomes of perceived health, caregiver burden, and social participation, which are emphasized in many health technology assessments. Functioning, in the WHO's ICF language, is the result of a synergy between one's body functions, (like moving limbs, breathing, or concentrating), daily activities, (like learning, eating, or walking), and participation in life roles (such as relationships, schooling, or work). In the ICF framework and classification, functioning is further supported (or hindered) by an individual's environment (communities and society) and personal factors (like income, resilience, or education). Taken together, these components mean that an individual's health is defined by what they can do, or need to do, in a situation, place, or time; ***not solely*** by whether a disease is absent or present.

Adoption of the ICF reframes therapeutic success (ie, good outcome) as the ability of individuals to achieve and sustain functioning, even when disease is present. Disability (ie, the opposite of functioning) is empirically observed in multiple chronic diseases, including heart disease, diabetes, arthritis, and multiple sclerosis. Disability occurs when patients achieve biomarker or symptom control, yet still have difficulty functioning due to mood, concentration, mobility, going to school or

Figure 1. The Framework of the World Health Organization's International Classification of Functioning, Disability and Health (ICF)[4]

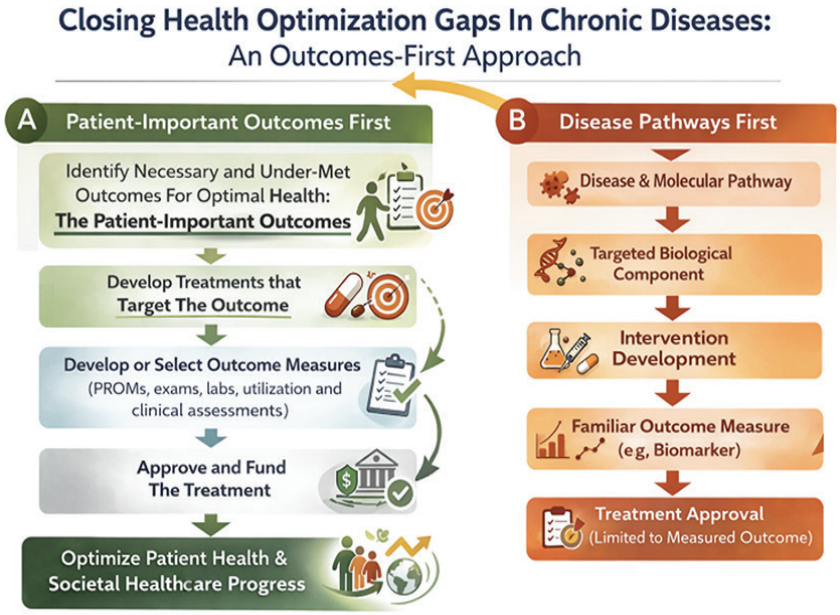


work, maintaining relationships, or taking care of their families.

Although targeting biomarkers is important for transforming previously fatal diseases into chronic ones, once patients are living with chronic diseases such as diabetes, heart and stroke diseases, or even cancer remission, other outcomes also become important to target. A biomarker associated with marginal mortality gains is rarely a valid target for optimizing these patients' health. Yet most new drug approvals introduce marginal mortality gains at high costs, which divert health system capacity away from the resources that make possible individual health progress,[7] such as promising or evidence-based lifestyle, mental health, or rehabilitative interventions. Thus, ***solely*** targeting surrogate or biomarker endpoints excludes treatment innovation that advances optimal health outcomes.

As an alternative to a biomarker-defined good-outcome strategy, developers, interventionists, and clinicians can pursue outcomes that have been endorsed by patients as priorities, then identify and assess new treatments with those outcomes in mind. In other words, optimization of health deserves more scientific and treatment effort than it receives right now.

Figure 2. PIO-First Versus Mechanism-First Treatment Approaches



PROM indicates patient-reported outcome measure.

Policy Can Create Optimal Health by Using Patient-Important Outcomes

Patient-important outcomes (PIOs) provide a roadmap to attaining the optimization goal. When it comes to chronic disease, health optimization is possible through a focus on the necessary outcomes that remain unmet or under-met. The scientific and policy solutions that will push forward progress in health optimization for chronic disease patients universally require that treatment development and testing (eg, through trials) begin by targeting a PIO (**Figure 2**). This alternative is preferable to the status quo, in which treatment success is defined by outcomes like biomarkers or mortality.

We define a PIO as an outcome that is essential to health optimization but is being insufficiently addressed. While the definition of a PIO might have evolved over time, the way we define it means it is not equivalent to a patient-reported outcome measure (PROM). Although many PROMs can assess outcomes of importance to patients, not all PROMs measure the under-addressed outcomes patients require to achieve optimal health. For example, in patients with diabetes, outcomes such as vision, weight, mobility, fatigue, and diabetes-related distress are high-priority PIOs[8]; some of these are best measured using PROMs, while others are more appropriately measured with clinical tools, exams, tests, or functional assessments.[8] Core outcome sets and standard sets across multiple chronic conditions represent a useful starting point for identifying specifically which PIOs should be measured for various chronic disease populations.

Among many core and standard outcome sets, the outcomes that are repeatedly prioritized as patient-important from the ICF health component of ***body functions*** include fatigue, appetite, motivation, emotions, and pain; from ***activities and participation,*** they include daily routines, walking, mobility, [schooling] and employment; and from ***environment,*** they include social support, formal healthcare supports and health access.[9-11] Given their importance, these outcomes and other PIOs can—and should— be the endpoints of most clinical trials for new treatments.[12] Typically, they are not.

Regulators, aware of the issue, have attempted solutions in the form of the US Food and Drug Administration's (FDA's) guidance for industry in the use of PROMs to support labeling claims and The European Medicines Agency (EMA) shortly thereafter.[13] These policy initiatives were followed by an initial decline, followed by steady growth in new drug applications and approvals that included validated PROMs as primary or secondary endpoints.[10] Despite this increased uptake, PROMs often remain grounded in investigator-defined conceptions of desirable outcome or positioned as secondary endpoints. The positioning of PROMs in trials suggests they are perceived as exploratory rather than as key targets for therapeutic development.[14] Policy should aim to achieve optimal health through treatments that target PIOs, rather than encouraging the use of PROMs that don't align with patient priorities.

Scientific funding agencies in the United States (eg, the Patient-Centered Outcomes Research Institute [PCORI]) and Canada (eg, Strategy for Patient-Oriented Research) also introduced major initiatives intended to make health research more patient-oriented, primarily through the promotion of patient engagement. Over time, these

efforts contributed to the establishment of new research norms characterized by structured checklists, guidance frameworks, and accountability mechanisms, designed to promote rigorous patient involvement throughout the research process. These engagement strategies improved patient experiences within clinical trials for areas such as recruitment, representation, and retention;[15] however, their role in developing treatment innovations that target PIOs remains uncertain. Thus, emerging standards for patient-oriented research must more intentionally and systematically redirect therapeutic targets toward PIOs, using patient engagement to achieve that objective, rather than patient engagement being a goal in and of itself.

Implications for Policy Makers

Regulatory and scientific funding policies will be unable to make progress on the health optimization problem simply by introducing process changes in the development-to-payment pipeline, or by using PROMs *or* patient engagement, without also incorporating clear mandates that treatments fill empirical gaps of patient-defined needs for good results. We recommend a bold but promising solution through the introduction of regulatory guidelines that specifically outline the importance of testing treatments that target empirically identified PIOs.

> An individual's health is defined by what they can do, or need to do, in a situation, place, or time. It is not defined by whether a disease is absent or present.

For example, patient-focused drug development strategies from the FDA and EMA have articulated the need for patients to be "involved" at all stages of development and testing, without ever articulating that patient-oriented treatments can only be defined as such if they target unmet but necessary (ie, patient-important) outcomes.[16] In particular, chronic disease categories that have succeeded in demonstrating marginal mortality gains with new treatments should be disincentivized from seeking additional approvals for treatments that ignore PIOs. Doing so might slow the speed of new development in the short-term, but in the long-term, will advance solutions toward much-needed health optimization innovations.

Funding organizations like PCORI or the National Institutes of Health can also improve the criteria for rigorous patient engagement in research, going beyond process-based patient consultation or collaboration to prioritizing the inclusion of patient-defined good-outcome measures. Doing so will ensure that new treatments are developed and tested, based not only on whether they are safe or clinically effective, but whether they facilitate optimal health for all. We recommend that funding be allocated to the [most rigorous] studies that ask the question, "Is this treatment making a difference to the outcomes chronic disease patients have empirically endorsed?" as a new requisite for excellence in patient-oriented research. In short, moving forward with the 21st century aim of health optimization requires treatment strategies that support PIOs, not the other way around.

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Elephant in the Room: How Social and Traditional Media Analytics Help Uncover Actionable, Patient-Reported Gaps in Lymphoma Care

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KEY TAKEAWAYS

Social media monitoring can uncover unsolicited but clinically relevant patient insights that structured data collection methods and clinical trial patient-reported outcomes typically fail to capture.

These unsolicited insights can inform health economics and outcomes research by identifying psychosocial burdens with the potential to influence clinical outcomes.

Analysis of traditional and social media can reveal opportunities to improve public awareness of official treatment guidelines, particularly recommendations for psychosocial support.

Silent (R)evolution

For decades, health technology assessment (HTA) and health economics and outcomes research (HEOR) have been on an evolutionary journey. Their origins are rooted in the era of evidence-based medicine, where the randomized controlled trial (RCT) was—and often remains—the gold standard for clinical and economic data. HTA bodies traditionally relied on this structured data to determine efficacy and cost-effectiveness.[1]

However, decision makers soon recognized that what works in the highly controlled, narrow population of an RCT does not always translate to the complex, heterogeneous reality of clinical practice. This led to a significant shift toward embracing real-world evidence (RWE) from claims, registries, and electronic health records to understand long-term effectiveness and safety in broader populations.[2] Alongside this shift, another emerged: the realization that a deeper understanding of the patient journey—the complete experience of a patient, from symptoms through treatment and daily management—was also a critical contributor to health outcomes. It became clear that value was not just about clinical endpoints but also about the holistic patient experience.[3,4]

This focus on the patient journey fueled the push for patient centricity, with HTA bodies and organizations like ISPOR formalizing the integration of structured patient-reported measures.[5] Yet, even these data have limitations, often failing to capture the full picture of a patient's psychosocial burdens, which can influence outcomes.[6-9]

This brings us to the present challenge. A vast source of unsolicited RWE remains largely untapped: raw, authentic, and (relatively) unbiased patient voices from social media and public forums.

On the (Patient) Journey

These unsolicited data are generated every day as patients and informal caregivers discuss their health experiences, fears, and unmet needs on social media and in public, online discussion forums. To build a 360-degree view of the patient journey, we designed a dual-pronged methodology to analyze public communications over a 24-month period (October 2022 to October 2024), focused on hematologic malignancies.[10]

The formal public narrative was captured by traditional media analysis, resulting in 531 unique mentions related to "lymphoma" across the Czech press, online news, television, and radio using the Newton Media archive. The unstructured patient-reported voice was captured using a social media listening tool from Newton Media to monitor related keywords on platforms, including Facebook, X (formerly Twitter), Instagram, YouTube, TikTok, and Reddit, as well as Czech discussion forums and user discussions on news portals.

> A vast source of unsolicited real-world evidence remains largely untapped: raw, authentic, and relatively unbiased patient voices from social media and public forums.

This combined methodology allows us to map the true patient experience, integrating the top-down information disseminated by media and healthcare experts and the bottom-up, real-world concerns reported by patients and caregivers.

What makes malignant hematologies particularly relevant for this approach is the high level of disease-related psychosocial distress experienced by patients with lymphoma and its largely "invisible" nature. Not seeing any obvious symptoms, others might not appreciate a lymphoma patient's chronic health condition, and this misperception might lead the patient to feel isolated

and lacking social validation of their suffering.[11] This invisibility stands in stark contrast to the lived reality of the disease: prolonged treatment regimens involving multiagent chemotherapy, immunotherapy, or stem cell transplantation impose cycles of response and relapse that generate persistent fear of recurrence,[12-14] while cancer-related fatigue—driven by both disease biology and myelosuppressive treatments—is associated with impaired quality of life.[15,16]

> By analyzing both social media and traditional media, we uncovered a profound, clinically relevant gap between an established need for psychosocial support and a lymphoma patient population unaware of its availability.

By applying this dual-pronged analytical methodology to patients with lymphoma in Czechia, we uncovered a significant "elephant in the room": a profound, clinically relevant gap between an established need for psychosocial support[17,18] and a patient population unaware of its availability. The patients' perspective provided insights into the immense psychosocial and financial toll of the disease. Fear was identified as a negative modifier of quality of life, evolving from fear of diagnosis to fear of relapse. Patients also reported significant financial toxicity and treatment-related fatigue. Overall, this approach proved to be an effective tool to identify unmet needs that traditional data collection methods may miss.

The Lived Patient Experience

The SML analysis provided an unfiltered view into the patient experience, revealing the true drivers of their quality of life and economic burden. Patient discussions were not limited to the classic B-symptoms (bodily symptoms beyond localized lymph nodes) such as fever, night sweats, and unexplained weight loss. Many also reported that severe, unexplained fatigue was a primary limiting factor. Alcohol-related pain in lymph nodes was another example of a symptom that led some patients toward their diagnosis. However, some patients' comments noted no visible symptoms, in which case the disease was discovered by chance.

This is the kind of granular, real-world data that structured clinical trials might fail to capture using electronic patient-reported outcomes. Similarly, the analysis of traditional media found that symptoms are most often mentioned in the context of personal stories.

The Unseen QoL and Economic Burden

On social media, patients expressed specific fears and worries about managing treatment, particularly if they were elderly and lived alone or were parents of young children. These experiences were also reflected in the traditional media, which noted that patients are often isolated during treatment and highly dependent on support from family and friends for daily needs like care, food, and transportation. While patients find psychological comfort in peer support groups and hope in treatment progress, there were few mentions in traditional media regarding professional psychological support or where to find it, and those few mentions tend to come from low-reach sources like community newspapers.

> The failure to address the psychosocial needs of patients with lymphoma is a failure in care delivery that has a demonstrable impact on survival and, by extension, on health outcomes and related costs.

And despite Czech treatment guidelines recommending psychological support as part of early palliative care to improve quality of life and treatment compliance,[19] this fact is not reaching patients. We found only limited mentions of this support in any public-facing media, and patient forums were filled with individuals who said they had been seeking this support but were unable to find it. Patient organizations that could fill this role were generally missing from those conversations.

The Value of SML for HEOR

The failure to address the psychosocial needs of patients with lymphoma is a failure in care delivery that has a demonstrable impact on survival and, by extension, on health outcomes and related costs.[20,21]

This study demonstrates that social media listening, especially when combined with traditional media analysis, represents a useful HEOR tool for gathering patient-reported data and insights that might be further analyzed for their potential to inform healthcare and health policies. It allows researchers to move beyond the confines of structured data to identify real-world, emergent patient concerns—such as lack of access to psychosocial support—that can improve quality of life and potentially clinical outcomes.

This approach allowed us to identify critical gaps in the lived patient experience. Therefore, social media listening should be embraced as a vital tool to help guide policy, improve awareness, and build a more responsive and effective patient support ecosystem.

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Empathy by Design: Insights From Patients, Advocates, and Medical Writers to Advance Patient-Centered Communication in Medical Writing

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KEY TAKEAWAYS

Both patients/patient advocates and professional medical writers consider empathy to be important in medical writing.

Incorporating patient-centered tone, suitable readability, and patient-first language can enhance the perceived empathy of scientific materials, potentially improving comprehension and impact for diverse audiences.

In the absence of an established empathy metric, using readability tools and applying patient-first language are interim approaches for evaluating and enhancing empathy in medical writing.

The Case for Empathetic Medical Writing

While there is no single definition for "empathy" in healthcare,[1,2] it is often described as the ability to recognize a patient's perspective and experience and to convey such understanding back to the patient.[3] The perception of empathy has been linked to improved patient satisfaction, treatment adherence, clinical outcomes, and clinical competence.[4-6] However, most studies assessing empathy in healthcare focus on interpersonal interactions (ie, face-to-face encounters in which both verbal and nonverbal cues can guide an exchange).[4]

Medical writing, by contrast, is inherently a one-way conversation intended to convey accurate, clear, and reliable information to support informed decision making by patients, clinicians, regulators, and researchers.[7-9] Yet a focus on objectivity and technical accuracy in medical writing may create distance between the writer and the reader just as it does in face-to-face clinical encounters.

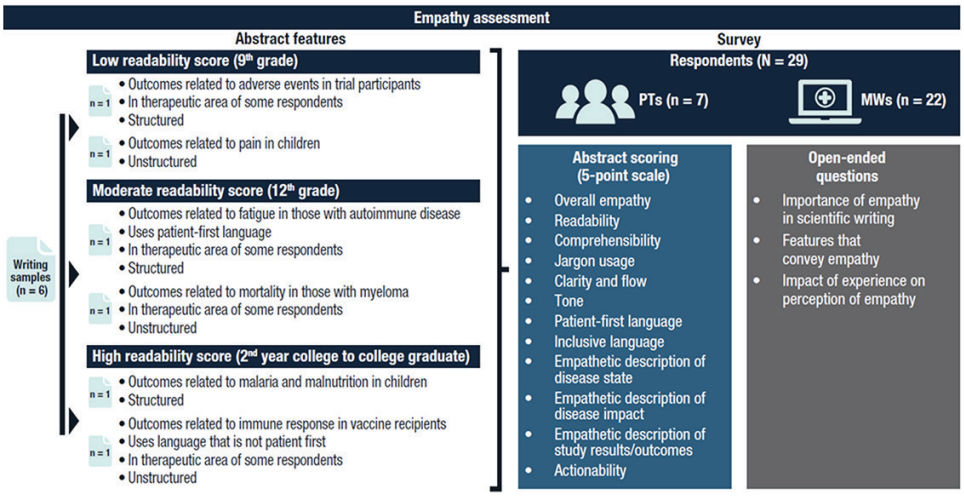
Despite its demonstrated value in healthcare, there is currently no standardized, objective way to assess empathy in medical writing. We can make the case for why empathy in medical writing matters, but the lack of a measurement framework prevents us from determining whether empathetic communication is being achieved.

We conducted a study to assess the extent to which patients/patient advocates and professional medical writers perceive empathy as important to scientific writing and to identify features they associate with the perception of empathy. Patients/advocates and medical writers were consulted to capture perspectives from 2 critical points in the communication process: that of individuals shaping the content at its inception and those engaging with and interpreting the final material. This dual-stakeholder approach intended to explore how empathy is both embedded during the writing process and perceived by an intended audience.

Assessing Empathy in Scientific Writing

Two study groups (a group of patients/advocates and a group of medical writers) participated in an online survey in which they answered open-ended questions related to the importance of empathy in medical writing (**Figure 1**). Respondents also scored 6 scientific writing samples, which consisted of published, peer-

Figure 1. Study Design



MW indicates medical writer; PT, patient/patient advocate.

reviewed scientific abstracts, ranging in readability level from 9th grade to college graduate. Writing samples were scored using a 5-point scale for 12 features: overall empathy, readability, comprehensibility, jargon usage, clarity and flow, tone, patient-first language, inclusive language, empathetic description of the disease state, empathetic description of the disease impact, empathetic description of the study results/outcomes, and actionability of the information. The writing samples were also evaluated using 7 additional standardized readability metrics. A definition for empathy was not provided at any point in the survey.

Perception of Empathy: Patient and Professional Perspectives

A total of 29 respondents with experience in 5 therapeutic areas participated in the study (**Table 1**). All patients/advocates were aged 40 years or older, while most of the writers were aged between 30 and 49 years. Most respondents were female (75.9%), held a master's degree or higher (86.2%), and reported reading scientific or health-related information daily (79.3%).

> While scientific objectivity remains essential to clinical decision making, empathetic framing may help ensure that clinical evidence is interpreted within its human context, thereby promoting better patient care.

All patients/advocates and writers considered empathy to be at least somewhat important to medical writing, with 57.1% and 72.7%, respectively, rating empathy as very important or extremely important. When asked to rate which 3 of the measured features were most important to convey empathy in medical writing, patients/advocates frequently selected comprehensibility (60%), readability (40%), clarity and flow (40%), the use of patient-first language (40%), and an empathetic description of

Table 1. Survey Respondent Demographic Characteristics

Characteristic, n (%)	PTs (n = 7)	MWs (n = 22)	Total (N = 29)
Age category, y	(n = 7)	(n = 21)	(N = 29)
18-29	0	1 (4.8)	1 (3.4)
30-39	0	12 (57.1)	12 (41.4)
40-49	2 (28.6)	8 (38.1)	10 (34.5)
50-59	4 (57.1)	0	4 (13.8)
≥60	1 (14.3)	0	1 (3.4)
Gender identity			
Female	3 (42.9)	19 (86.4)	22 (75.9)
Male	3 (42.9)	2 (9.1)	5 (17.2)
Transgender	1 (14.3)	0	1 (3.4)
Prefer not to respond	0	1 (4.5)	1 (3.4)
Education			
Some college, but no degree	2 (28.6)	0	2 (6.9)
Bachelor's degree	2 (28.6)	0	2 (6.9)
Master's degree	1 (14.3)	1 (4.5)	2 (6.9)
Professional or doctorate degree	2 (28.6)	21 (95.5)	23 (79.3)
Respondent identified as			
Patient	2 (28.6)[a]	5 (22.7)	7 (24.1)
Patient advocate	5 (71.4)[a]	1 (4.5)	6 (20.7)
Caregiver	2 (28.6)	2 (9.1)	4 (13.8)
Therapeutic area			
Hematology/oncology	1 (14.3)[b]	8 (36.4)	9 (31.0)
Infectious disease	1 (14.3)	7 (31.8)	8 (27.6)
Autoimmune disease	4 (57.1)	3 (13.6)	7 (24.1)
Endocrinology	0	2 (9.1)	2 (6.9)
Rare disease	2 (28.6)[b]	2 (9.1)	4 (13.8)
Reading activity			
Daily	3 (42.9)	20 (90.9)	23 (79.3)
Weekly	2 (28.6)	2 (9.1)	4 (13.8)
Monthly	2 (28.6)	0	2 (6.9)
Most common types of scientific reading material[c]			
Peer-reviewed scientific journal articles	6 (85.7)	22 (100)	28 (96.6)
Articles from health-related news websites or magazines	6 (85.7)	14 (63.6)	20 (69.0)
Government health websites (eg, CDC, NIH)	5 (71.4)	14 (63.6)	19 (65.5)

[a]Two respondents identified as both a patient and patient advocate.
[b]One respondent had experience with both oncology and rare disease.
[c]Respondents could check all options that applied; the top 3 most-selected options are reported.
CDC indicates Centers for Disease Control and Prevention; NIH, National Institutes of Health; MW, medical writer; PT, patient/patient advocate.

a study's results/outcomes (40%) (**Figure 2**), while writers most frequently selected an empathetic description of a disease's impact (80%), the use of patient-first language (75.0%), and an empathetic description of a study's results/outcomes (45%).

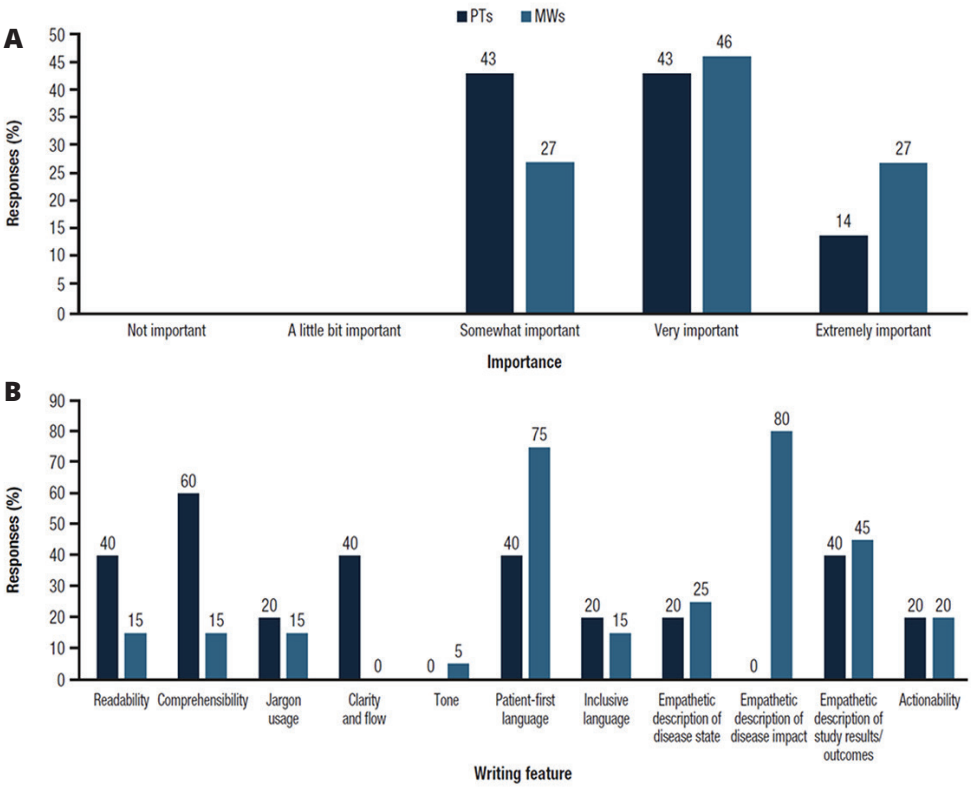
In the review of the writing samples, multiple features were strongly associated with the perception of overall empathy; however, the perception of an empathetic tone exhibited the strongest and most statistically significant correlation for patients/advocates (**Figure 3**). For writers, patient-first language exhibited the strongest and most significant correlation with empathy. For both groups, an empathetic description of a disease's impact and jargon usage were also strongly and significantly correlated with the perception of empathy in the writing samples. When comparing readability scores from 8 standardized metrics with scores for empathy, the SMOG (Simple Measure of Gobbledygook) Index showed the strongest and most significant correlation for both groups.

Interpreting the Findings: Measuring What Matters

While empathy in healthcare is commonly framed as the ability to understand a patient's personal experience, this definition arguably falls short when applied to written medical communication. In this context, empathy must also encompass an understanding of how readers (whether patients, providers, or policy makers) receive, interpret, and respond to the information. This may involve recognizing the cognitive demands of complex literature, the emotional weight of health-related topics, and the impact of how information is framed, structured, and delivered. Ultimately, to meaningfully assess empathy in medical writing, a standardized metric is needed, and developing such a metric first requires a clear understanding of which features readers associate with empathetic communication.

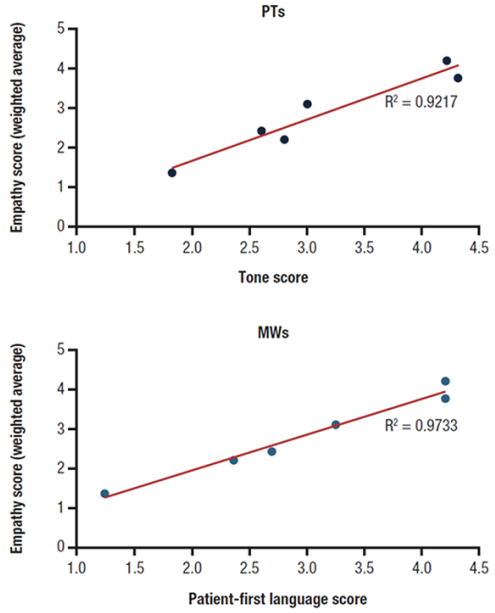
Across both patients/patient advocates and medical writers, empathy was deemed as at least somewhat important, if not extremely important, to medical writing. However, the features

Figure 2. (A) Overall Importance of Empathy and (B) Features Identified as Important to Convey Empathy in Medical Writing



MW indicates medical writer; PT, patient/patient advocate.

Figure 3. R^2 Coefficient and *P* Values Comparing Empathy Scores With Standardized Metric Readability Scores and Writing Feature Scores in the Medical Writing Samples



	PTs (n = 7)		MWs (n = 22)	
	R^2	*P* value	R^2	*P* value
Standardized metric				
Flesch-Kincaid Readability (Grade Level)	0.8638	0.007	0.6146	0.065
Automated Readability Index	0.7778	0.020	0.5620	0.086
Flesch Reading Ease	0.7756	0.021	0.5049	0.114
Gunning Fog Index	0.7992	0.016	0.5463	0.093
The SMOG Index	0.9380	0.001	0.7136	0.034
Original Linsear Write Formula	0.3230	0.239	0.1756	0.408
Linsear Write Grade Level Formula	0.7430	0.027	0.5144	0.109
New Dale-Chall Readability Formula	0.7562	0.024	0.6650	0.048
Respondent-rated features				
Readability	0.7171	0.033	0.7323	0.030
Comprehensibility	0.7748	0.021	0.7758	0.020
Jargon usage	0.9071	0.003	0.9041	0.004
Clarity and flow	0.8081	0.015	0.7248	0.032
Tone	0.9217	0.002	0.8371	0.011
Patient-first language	0.7732	0.021	0.9733	<0.001
Inclusive language	0.8003	0.016	0.9458	0.001
Empathetic description of disease state	0.8712	0.007	0.9560	0.001
Empathetic description of disease impact	0.9070	0.003	0.9544	0.001
Empathetic description of study results/outcomes	0.8648	0.007	0.9560	0.001
Actionability	0.6758	0.045	0.7269	0.031

MW indicates medical writer; PT, patient/patient advocate; SMOG, Simple Measure of Gobbledygook.

considered most important for achieving empathetic communication differed between the 2 groups. Of the 11 features evaluated, patients/advocates prioritized features related to text accessibility (ie, readability, comprehensibility, and clarity and flow), whereas writers most often emphasized features associated with emotional framing. Both groups identified patient-first language as important, though patients/advocates selected this feature nearly half as often as writers. Both groups identified an empathetic description of a study's results/outcomes relatively equally. But only writers identified an empathetic description of a disease's impact, a feature not selected by any patients/advocates, as most important. Overall, these findings suggest that while both groups value empathy in medical writing, they may recognize it differently, with patients/advocates valuing accessible, easily understood writing, and writers emphasizing empathetic framing.

> Overall, creating communications that resonate with all reader types should ultimately serve a single purpose: benefiting patients.

Although patients/advocates identified text accessibility–related features as most important in conveying empathy, the writing sample scoring data revealed a more nuanced relationship. When evaluating medical writing samples, tone exhibited the strongest and most significant correlation with perceived empathy above features of text accessibility. While still significant, features of text accessibility (ie, readability, comprehensibility, or clarity and flow) showed weaker correlations. This suggests that while patients/advocates may look for accessible language to convey empathy, in practice, their perception may be more strongly influenced by tone.

Among writers, the use of patient-first language demonstrated both perceived importance and the strongest, most significant correlation with empathy scores for the writing samples. This alignment implies that features writers are trained to use in medical writing may stand out more prominently in their perception of empathy.

While features such as readability can be readily quantified using established metrics, others, such as tone, are inherently more difficult to consistently measure. Advances in machine learning and natural language processing offer promising solutions to analyze the more nuanced aspects of medical writing. By combining these technologies with insights from diverse reader groups, it may be possible to develop a standardized metric for evaluating empathy in medical writing.

Overall, creating communications that resonate with all reader types should ultimately serve a single purpose: benefiting patients. When medical writing speaks effectively to patients, healthcare professionals, researchers, and regulators alike, it holds the potential to foster understanding, alignment, and trust across the continuum of care. For patients, empathetic writing should not simply inform; rather, it should connect with and respect their perspective. For researchers, empathetic writing can highlight the impact of patient outcomes and encourage more inclusive, ethically grounded study designs. And for regulators, it may help shape policies that resonate with public understanding and prioritize patient needs.

HEOR Professionals and Other Key Populations

As the primary audience of biomedical journal content, public health professionals and clinical practitioners warrant special consideration in the discussion of empathy in medical writing.[10] Compassion fatigue, the gradual erosion of the capacity to express empathy due to prolonged exposure to suffering, is widely documented in healthcare and is associated with burnout.[11,12] However, studies suggest that empathy may be protective against burnout by reducing depersonalization and promoting a greater sense of personal achievement.[13] In this context, maintaining awareness of the individuals represented in clinical data is particularly important.

Incorporating empathetic language into medical communications may reinforce the patient-centered intent behind clinical science by reminding healthcare professionals that the outcomes reported in tables and figures ultimately reflect the lived experiences of individuals. While scientific objectivity remains essential to clinical decision making, empathetic framing may help ensure that clinical evidence is interpreted within its human context, thereby promoting better patient care. Health economics and outcomes researchers also warrant special consideration in the discussion of empathy in medical writing, given their central role in evaluating value, outcomes, and healthcare decision making. While HEOR analyses often focus on quantifiable measures, such as cost-effectiveness, return on investment, and comparative value, the field has increasingly embraced patient-centered approaches that seek to both understand and measure the outcomes that are most important to patients.[14-16]

Incorporating empathetic framing into medical communications may help reinforce the connection between analytical findings and the personal health journeys they represent, ensuring that patients remain visible behind the economic models used to inform decisions. Furthermore, the HEOR community's expertise in measuring complex and sometimes more intangible outcomes uniquely positions them to explore whether perceived empathy in medical communication can be quantified and how it may influence patient healthcare experiences or treatment-related behaviors.

In short, empathy in medical writing should not be an afterthought. This research represents a first step toward developing a metric to evaluate, inform, and enhance the inclusion of empathy in medical writing. Overall, incorporating the features shown here to influence its perception, particularly tone, readability, comprehensibility, and patient-first language, may help writers craft communications that both inform and connect, fostering greater trust and understanding for the benefit of patients. In the absence of an established empathy metric, existing readability tools, specifically the SMOG Index, and the

consistent use of patient-first language offer practical starting points while more direct measures continue to be developed.

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A More Structured and Predictable Framework: Aligning Regulatory and Health Technology Assessment Processes in Europe

Niklas Hedberg, MSc, Co-Chair, European Union Member State Coordination Group on Health Technology Assessment (HTACG)

Q&A

"As high-quality assessment reports are produced, published in English, and made openly available, they may increasingly serve as a reference point beyond Europe, shaping how other systems approach health technology assessment."

– Niklas Hedberg

Europe's long-anticipated shift to a unified health technology assessment (HTA) framework is no longer theoretical; it is now being tested in practice. As the results from the first Joint Clinical Assessments begin to emerge, Niklas Hedberg describes a system balancing ambition with reality, aligning 27 Member States while managing expectations from industry, patients, and payers. At the same time, deeper questions around evidence, speed, and global competitiveness continue to shape its trajectory, positioning the framework as both a technical reform and a structural shift in how Europe evaluates and adopts innovation.

PharmaBoardroom: What are your key reflections on the first phase of Joint Clinical Assessments under the European Union (EU) Health Technology Assessment Regulation?

Niklas Hedberg: The first point is to manage expectations, as we are still at an early stage, and the experience base remains limited, particularly in terms of what can be shared publicly. We have completed a number of Joint Scientific Consultations, but these are confidential given the commercially sensitive nature of early stage data. On the Joint Clinical Assessment side, we are now close to endorsing the first reports [*Editor's note: The first Joint Clinical Assessment report was published June 9*].

At this point, the system is still taking shape, and it would be premature to draw firm conclusions. Much of the work so far has focused on establishing procedures and processes, rather than on outputs, which is a natural phase when building a new framework of this scale. The more meaningful insights will come with time and accumulated experience.

The most important development over these first 16 months has been the transition from a largely voluntary system, built over almost 2 decades under EUnetHTA [the European Network for Health Technology Assessment], to a mandatory framework under the EU Health Technology Assessment Regulation (HTAR). This shift has required a sustained effort to build trust across stakeholders, and we are now moving toward building confidence, demonstrating that we can deliver something of value for patients, healthcare systems, and society. That confidence must extend beyond HTA bodies to include companies, clinical experts, patient representatives, and payers, particularly as these assessments begin to inform national and regional decisions.

Looking ahead, the system will expand gradually, starting with oncology and ATMPs [advanced therapy medicinal products] followed by orphan medicines, and then a broader scope by 2030. Over time, I would expect a more integrated approach, where horizon scanning feeds into Joint Scientific Consultations, and those consultations help guide evidence generation for both regulatory and HTA purposes. If that alignment is achieved early, the evidence base underpinning Joint Clinical Assessments should improve, making it easier for payers to use these outputs in practice.

PB: To what extent are stakeholders aligned today around the direction of the EU HTA framework, and where do differences in expectations still remain?

NH: When speaking with stakeholders, particularly those working at a European level, there is a clear sense that there is only 1 direction of travel. Without a functioning HTA system, we would be left operating in a fragmented and uncertain environment, so there is broad agreement that this is the path to follow. That said, there have always been different views on how best to move forward, and those views have evolved over time.

If we look back 15 years or more, much of the momentum for a more converged European system came from industry itself, with companies often asking why there was no equivalent of the European Medicines Agency on the HTA side. What became clear over time was that this would require a far more substantial legislative effort than many initially expected.

> We have seen the more experienced health technology assessment bodies take a leading role in methodological discussions, bringing their experience to the table and, in effect, creating a platform for others to learn from.

Today, we hear a more critical tone from some parts of the industry, although it may still be too early to draw firm conclusions. Some of that criticism relates to the perceived strength of the link to decision makers and whether the framework is sufficiently binding in practice. Ultimately, however, this will be tested through implementation, and it is at that stage that we will need to demonstrate that the system is delivering and build the confidence that stakeholders are looking for.

PB: How has the new framework approached the challenge of bringing together different national HTA systems across Europe?

NH: From our perspective, this has been a valuable and, in many ways, constructive exercise. We have seen the more experienced HTA bodies take a leading role in methodological discussions, bringing their experience to the table and, in effect, creating a platform for others to learn from. That dynamic has helped to bridge differences in maturity across systems. At the same time, it is fair to acknowledge that, for companies, particularly smaller ones, the process can appear demanding, and in some cases more complex than anticipated.

However, most of these requirements are not new. They already existed at a national level, often in isolation and with limited coordination. What we have done is bring them together within a single European framework. The work on Population, Intervention, Comparator, and Outcomes, the so-called PICO framework, is a good example of this. Where previously there may have been 20 or more national PICOs, we are now working toward consolidating them into a more coherent European approach. That process is still evolving, but it introduces a level of coordination that was not there before and, over time, should reduce fragmentation rather than increase it.

> We are seeing contributions from across Member States, which is an important signal that this is becoming a genuinely European process.

Another important shift relates to the demand for faster access to new therapies, which has come from both patients and industry. In response, regulatory and HTA processes are now more closely aligned, meaning that much of the work has to be carried out in parallel rather than sequentially. The overall volume of work may not have increased significantly, but the way it is organized has changed, and this creates real challenges, particularly for smaller companies that may not have the same internal capacity. It is not possible to design separate systems for different types of companies, but we are making a conscious effort to engage more directly and provide targeted support where possible.

Looking ahead, once the system is fully operational beyond 2030, this approach should lead to greater efficiency overall. The Joint Clinical Assessment will be conducted once at a European level rather than repeated across multiple countries, while national elements such as pricing and health economic evaluation will remain in place. At the same time, continued dialogue through the HTA Stakeholder Network will be essential, both to strengthen trust and to refine how clinical expertise and patient expertise are integrated into the process. That ongoing exchange is already proving valuable in improving understanding on all sides.

Over time, this should also contribute to greater alignment in clinical practice across Europe. As clinical guidelines begin to take account of Joint Clinical Assessment timelines, unnecessary variation between countries is likely to diminish, even if some differences will always remain. At the same time, as high-quality assessment reports are produced, published in English, and made openly available, they may increasingly serve as a reference point beyond Europe, shaping how other systems approach health technology assessment.

PB: How is the EU HTA system building the capacity to handle full-scale implementation as all centrally authorized medicines come into scope?

NH: The starting point is that the system must operate on equal terms. We cannot introduce a framework that creates inequality, so the assumption has to be that we will be able to manage the

full scope as it expands. Much of the discussion around capacity has therefore focused on Joint Scientific Consultations, where activity is being built up progressively. There is clear feedback from companies that this should move faster, but at the same time there is a need to maintain quality. At this stage, the direction is broadly right, even if the pace remains a point of discussion.

There is also a structured approach to how this is being developed. The HTA Coordination Group publishes an annual work program alongside a report on what has been delivered, allowing stakeholders to follow both ambition and output. While the number of consultations and assessments has so far been relatively limited, the early experience has been positive, particularly in terms of the breadth of participation. One of the initial concerns was that the system might be dominated by a small number of more experienced agencies, but in practice we are seeing contributions from across Member States, whether through assessors, experts, or stakeholder engagement, which is an important signal that this is becoming a genuinely European process.

> There is a clear recognition that real-world evidence will become more important, even if questions around data quality, methodology, and its role alongside clinical trial evidence still need to be resolved.

At the same time, there is a balance to be maintained as the system scales. Numbers will need to increase, but expanding too quickly would risk undermining quality. For now, the priority is to establish a robust and credible foundation, even if that means a more gradual build-up than some stakeholders would prefer.

PB: In areas such as advanced therapies and rare diseases, how is the framework approaching the use of real-world evidence alongside more traditional clinical data?

NH: There are several layers to this. At a methodological level, we provide clear guidance on the type of evidence we would prefer to see and how it should be analyzed, but we also recognize that this is not always available, particularly for newer technologies. In those cases, we expect companies to explain their choices, justify the use of alternative data, and set out how the analysis has been conducted. That inevitably introduces a degree of flexibility, which some stakeholders perceive as a lack of predictability, but it reflects the reality of working with emerging evidence where not everything can be defined in advance.

More broadly, the role of real-world evidence remains an open question. Companies are understandably keen to use real-world data to support earlier access, but that position can become more complex when longer-term data do not fully support the initial assumptions. In that sense, building trust in real-world evidence is an issue not only for HTA bodies, but also for industry. Payers have perhaps moved further in using these data, although even there the overall approach is still evolving and not entirely settled.

At the same time, there is increasing interest in how real-world evidence can be integrated more systematically over time. It can already be discussed within Joint Scientific Consultations, and there is ongoing work on how reassessments might incorporate such data across the product lifecycle. From an HTA perspective, we are actively engaged in this area, including through initiatives such as DARWIN EU, where the HTA community is represented. There is a clear recognition that real-world evidence will become more important, particularly in areas such as oncology, advanced therapies, and rare diseases, even if questions around data quality, methodology, and its role alongside clinical trial evidence still need to be resolved.

PB: What role can the European HTA framework play in strengthening Europe's competitiveness while maintaining equitable access to innovation?

NH: These are, of course, personal reflections, but one of the more striking contrasts at present is the speed at which policy can shift in other regions. If we look at developments such as Most-Favored-Nation pricing in the United States, the pace of change is extremely rapid, and with that comes a high degree of unpredictability. Europe has taken a different approach, building over several decades an HTA system grounded in evidence, methodology, stakeholder engagement, and value-based decision making. That process has been slower, but it has also created a more structured and predictable framework.

At the same time, it is important not to expect that the HTAR will resolve every challenge, particularly those linked to pricing and the broader global context. Some of these issues are inherently complex and will remain so. What the Regulation can do is strengthen the quality of the evidence base and provide a more consistent foundation for decision making across Europe. In that sense, its role is not to act as a barrier, but to support a system in which innovation can be assessed and adopted in a credible and transparent way, even if that means being less responsive to short-term external pressures.

PB: As the system evolves toward 2030, how should companies be thinking about their approach to the EU HTA framework?

NH: The advice is relatively straightforward, even if the implications are more demanding in practice. Companies need to engage closely with the available guidance, including methodologies and templates, and ensure that these are properly understood, sometimes with the support of those familiar with working within agencies or European institutions. There are also increasing opportunities for engagement through webinars and targeted outreach—including for smaller companies—which are intended to support understanding of the system and how it is evolving.

More fundamentally, preparation needs to begin earlier. The shift towards parallel regulatory and HTA processes means that these activities can no longer be approached sequentially. Regulatory strategy, evidence generation, and market access planning need to be aligned from an early stage across the organization. This reflects a broader change in how the system is designed to function, with the aim of improving patient access by making these processes more coordinated and efficient.

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