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VALUE & OUTCOMES SPOTLIGHT

A magazine for the global HEOR community.

HEOR as a Signpost on the Journey to Health Equity

ISPOR
Improving healthcare decisions

VALUE & OUTCOMES SPOTLIGHT

MAY/JUNE 2024
VOL. 10, NO. 2

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A magazine for the global HEOR community.

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

ISPOR
Improving healthcare decisions

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Advancing Health Equity

Health equity and health disparity are two critical concepts that have gained significant attention in the healthcare sector. Health equity refers to the attainment of the highest level of health for all people, regardless of their socioeconomic status, race, or geographical location. On the other hand, health disparities are differences in health outcomes and their determinants between segments of the population.

Health disparities are often influenced by social, economic, and environmental disadvantages. For instance, individuals from low-income communities may lack access to quality healthcare services, nutritious food, and safe housing, which can lead to poor health outcomes. Similarly, racial and ethnic minorities often face systematic challenges in accessing healthcare, leading to higher rates of certain diseases and lower life expectancy.

Health equity refers to the attainment of the highest level of health for all people, regardless of their socioeconomic status, race, or geographical location.

As we strive for health equity, we must recognize that equality and equity are distinct concepts. The tenants of *health equality* focus on treating everyone the same, regardless of their unique needs or circumstances. While *health equity* ensures that everyone has a fair and just opportunity to attain their highest level of health, accounting for individual differences and addressing systemic barriers. Health equity, therefore, is about bridging these gaps and ensuring everyone has a fair and just opportunity to be as healthy as possible. This requires removing obstacles to health such as poverty, discrimination, and their consequences, including lack of access to good jobs with fair pay, quality education and housing, safe environments, and healthcare.

To achieve health equity, we must address the root causes of health disparities. This includes implementing policies that promote social and economic equality, improving access to quality healthcare services for all individuals, and promoting healthy behaviors in all communities. Several promising strategies have been developed and implemented to combat these disparities and attempt to bring about health equity in communities. For example, community health workers bridge gaps by providing culturally competent education, advocacy, and support by connecting patients to resources and providing them aid in navigating complex healthcare systems. Telehealth and other digital solutions have expanded patient access, especially in underserved areas, and digital health tools, such as wearable devices and phone apps, have empowered patients to manage their health proactively. Communities have begun to address social determinants of health disparities by establishing collaborations between healthcare and nonhealth sectors—such as housing, education, employment, etc—to improve overall well-being under the guiding philosophy that a person's overall health is more than just their medical state.

Telehealth and other digital solutions have expanded patient access, especially in underserved areas, and digital health tools, such as wearable devices and phone apps, have empowered patients to manage their health proactively.

As a specific example, in the United States, the Centers for Disease Control and Prevention (CDC) has declared health disparity a serious public health threat and recognized its impact on health outcomes. The CDC has developed a CORE Health Equity Strategy focused on driving research that identifies changeable drivers of disparities,

tailoring healthcare strategies to specific populations, collaborating with state health officials and minority health offices to advance health equity and establish a workforce that reflects the communities it serves.

Health equity and health disparity are interconnected concepts that highlight the need for a more inclusive and equitable healthcare system. By addressing health disparities, we can move closer to achieving health equity and ensuring that all individuals have the opportunity to lead healthy lives. Health equity isn't an abstract goal; it's a moral imperative. By dismantling barriers, promoting inclusivity, and advocating for systemic change, we can create a healthier, more equitable world. Let's ensure that every person, regardless of their background, has a fair opportunity at optimal health.

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

Health Equity and the Fierce Urgency of Now

Rob Abbott, CEO & Executive Director, ISPOR

Martin Luther King's famous "I Have a Dream" speech from 1963 was a clarion call for racial and social justice. I have lived my entire life in the long shadow of that speech. Among other things, it inspired me to dedicate my life to improving human welfare globally. One of the many phrases that King immortalized on that August afternoon was "the fierce urgency of now:"

> *We are now faced with the fact that tomorrow is today. We are confronted with the fierce urgency of now. In this unfolding conundrum of life and history, there "is" such a thing as being too late. This is no time for apathy or complacency. This is a time for vigorous and positive action.*

Whenever I am asked why I have a pervasive bias for action, I refer people to the above words. I believe that in too many matters that affect human welfare there *is* such a thing as being too late. Health equity is a good example—and an example that is rooted in many of the racial and social injustices that King fought so gallantly throughout his life. Marcia Anderson, MD, Medical Officer of Health in the Canadian province of Manitoba, executive director of Indigenous academic affairs with the Ongomiizwin-Indigenous Institute of Health and Healing, and Vice-Dean of Indigenous Health, Social Justice, and Anti-racism at the University of Manitoba, puts it well:

> *From now on, instead of "vulnerable people," I'm going to use the phrase "people we oppress through policy choices and discourses of racial inferiority." It's a bit longer but I think will help us focus on where the problems actually lie.*

It's become popular of late to speak of "social determinants of health,"[i] and while I appreciate the sentiment, I think Anderson is both more honest and more accurate in naming the underlying or foundational conditions that have created so many of the health "inequities" that exist across the globe. We know that people's living conditions—and ultimately their health—are made worse by discrimination, stereotyping, and prejudice based on sex, gender, age, race, ethnicity, or disability, among other factors. Discriminatory practices are often embedded in institutional and systems processes, leading to groups being under-represented in decision making at all levels or underserved.[ii]

I also believe that health economics, with roots in welfare economics,[iii] has a vital role to play in addressing these inequities. I'm therefore very pleased to see this themed issue of *Value and Outcomes Spotlight*, with an emphasis on health equity and the ways in which it needs to be addressed. I might add that ISPOR's new vision—*a world in which healthcare is accessible, effective, efficient, and affordable for all*—pays more than a nod to the imperative of improving health equity across the globe.

Health equity is a long-standing concern in global healthcare. While terminology varies between disciplines and countries, a common denominator is a shared interest in reducing unfair differences in health, healthcare, and financial protection from the costs of healthcare. In May 2017, a report published by the Robert Wood Johnson Foundation defined health equity as the conditions in which:

> *Everyone has a fair and just opportunity to be as healthy as possible. This requires removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to good jobs with fair pay, quality education and housing, safe environments, and healthcare.*

Equally, the Foundation defined several steps that should be taken to achieve health equity:

1. Identify important disparities which can impact an individual's health
2. Change and implement policies, laws, systems, environments, and practices to reduce inequities in the opportunities and resources needed to be as healthy as possible
3. Evaluate and monitor efforts using both short- and long-term measures
4. Reassess strategies in light of process and outcomes and plan next steps

I'm pleased to report that ISPOR is actively engaged in work that supports these steps and makes health equity an essential element in everything we do as a professional society. In

[i] Social determinants of health (SDH) are the nonmedical factors that influence health outcomes. They are the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies, and political systems. Research shows that the social determinants can be more important than health care or lifestyle choices in influencing health. For example, numerous studies suggest that SDH account for between 30-55% of health outcomes. In addition, estimates show that the contribution of sectors outside health to population health outcomes exceeds the contribution from the health sector.

[ii] Racial disparity in the United States healthcare industry, for example, has been a long-standing research topic. While quality and access has improved in the United States thanks to initiatives like the *Affordable Care Act*, there is still a gap in the quality of care different groups receive.

[iii] Welfare economics applies microeconomic techniques to evaluate the overall well-being (welfare) of a society. A key feature of the field is its assessment of the distribution of resources and opportunities among members of a particular society. This, in turn, can have a significant influence on the ways in which governments may choose to intervene to improve social welfare.

particular, we boast a Special Interest Group (SIG) centered on health equity research that is advancing equity-informative methods and data for health economics and outcomes research (HEOR) that help to reduce unfair differences in health. At the same time, a new ISPOR SIG is focused on accelerating global access to medical innovation in low- and middle-income countries. In doing so, both groups have considerable potential to address a significant social welfare gap and improve the ability of millions—and potentially billions—of people to be as healthy as possible.

Our field of HEOR is grounded in the creation of scientific evidence on the efficacy of health interventions. It is also grounded in the curation of real-world evidence that brings the patient experience and voice to bear on healthcare decision making. Put another way, our combination of patient and disease-level data, empirical approach to scientific study, and strong track record of providing useful and timely information to support decision making make HEOR a key lever to improve health equity. Consider how these powerful and persuasive capabilities might be brought together to support evidence-informed action in 3 areas:

1. Ensuring that high-quality and effective healthcare services are available, accessible, and affordable to everyone when they need them.
2. Ensuring that the structural determinants of health are more widely understood—and addressed—to improve daily living conditions for as many people as possible.
3. Ensuring that health outcomes and health service delivery are monitored to detect inequities early and to facilitate corrective action.

As the articles and stories in this themed issue of *Value & Outcomes Spotlight* make clear, HEOR is already making a difference—and is poised to do more. I am often asked to define HEOR in a way that is "relatable" to a lay audience. I like to frame my response by saying that "HEOR is about getting the best that medicine has to offer to the largest number of people at reasonable cost." I might add that in doing so, it enables more people across the world to attain their full potential for health and well-being. This is an explicit acknowledgement that HEOR has a key role to play in confronting the "fierce urgency of now" that is making health equity the norm across the world.

FROM THE REGION

A Critical Time for the Community in Porto Alegre: Mattresses on the Floor

Stephen Stefani, MD, Porto Alegre, Brazil

According to meteorologists, the sequence of extreme events began with a persistent heat wave in the Southeast and Central-West regions of Brazil. This phenomenon, combined with wind currents and humidity coming from the Amazon and the effects of El Niño, created the ideal conditions for the formation of intense rains that culminated in tragedy.

Some cities issued a red alert due to the possibility of large amounts of rain, but the volume of water exceeded 800 millimeters in more than 60% of the region. In a matter of hours, rivers and lakes violently overflowed, catching thousands of people in their homes by surprise.

I received a call in the early hours of that Sunday from one of the community leaders from a region in the extreme south of the city where I live, almost 20 km from the central region. Porto Alegre is the capital of the state of Rio Grande do Sul with a population of 1.2 million, but surrounded by cities that make up 3 times that number. The call for help came in a succinct message over the phone: "I need a doctor at the Church's community center."

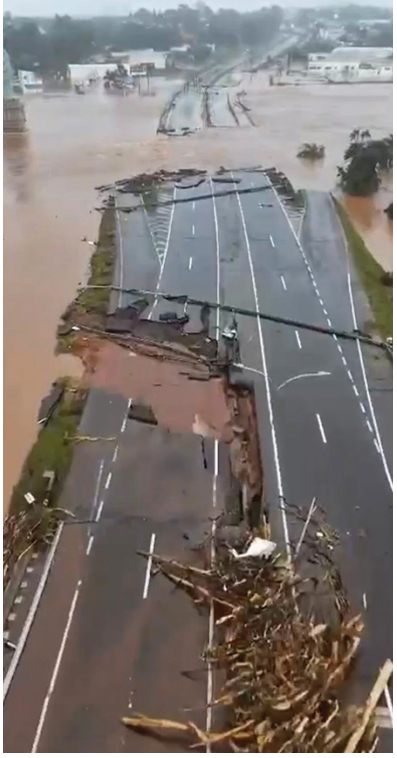
Having worked in medicine for 30+ years, it was the most shocking and saddest scene I ever witnessed. There were dozens of people (I later discovered there were 128) and an almost equal number of pet dogs and cats. People were scared and confused, lying on mattresses on the floor. Each mattress was surrounded by a few bags with personal belongings such as clothes and coats and people were taking a brief inventory of the items they were able to save from the flood.

I tried to organize an intuitive priority queue and list what the most urgent needs were. Practically one-third of the people used some chronic medication, and some only knew that it was a "white pill" for blood pressure or any other chronic disease. The only thing I was sure of was that I would need help. If, on the one hand, the pain of devastation destroys lives and families, the light of solidarity palpably represents the compassion that comes from all sides. I made a request for help to a group of friends

via WhatsApp. Within minutes, friends and colleagues arrived. Without time to exchange many words, they silently shook their heads and got to work. A few minutes later, I received a call from another colleague who was already at the local pharmacy asking what medicines he needed to buy and bring to us. And within a few hours, we had a team assembled with several volunteer professionals, established contact with the local health authorities (which were overloaded), and stocked a reasonably solid pharmacy built by donations. All people were treated and received tetanus vaccinations; in some cases we chose—despite the low level of scientific certainty—to offer prophylaxis for leptospirosis in cases that we judged to be high risk (a few days later, health authorities issued instructions that advised the same treatment approach we chose to use).

> If the pain of devastation destroys lives and families, the light of solidarity palpably represents the compassion that comes from all sides.

Perhaps most importantly, everyone was given a hand on the shoulder and an attempt to make them smile. Other shelters adopted very similar strategies, but it took us a few days to recognize that it was a system that could have been more productive with coordinated integration. Even the transfer and isolation of some patients, which in principle could make sense, could add unintended risks due to the very complex movement in a city that had up to 85% of its area compromised by flooding, lack of drinking water, or electricity. The impasse raises the need for reflection and consideration of the decisions and priorities made—driven by the urgency of the situation in an extreme context—by the professionals and volunteers involved regarding the use of scarce resources. A complex tragedy like this is not



random, nor does it have simple solutions. Somehow, it accelerates the need to address the issue in an agile and pragmatic way.

Globally, the health of the population is not determined solely by the health sector, nor are climate policies the exclusive responsibility of the environmental sector. Greater intersectoral collaboration is needed to open development paths that consider robust adaptation to climate change. This global threat to health, perhaps the greatest challenge facing the world in the 21st century, exposes the urgency of concrete and coordinated actions, both locally and globally, to mitigate its devastating impacts. This specific event affected whether through flooding, lack of electricity, or drinking water, approximately 1.5 million people. There are more than 500,000 people left homeless and 81,000 in shelters. More than 160 people died and there are still more than 100 people missing, by June. The historic center of the city, including the Centro Cultural Santander (where the meeting of the Brazilian chapter of ISPOR was held in 2023), was left standing with water levels reaching half way to the ceiling on the second floor!

The region faces a bleak scenario, without even being able to assess the real economic and social impacts in the medium- and long-term. The aftermath of this catastrophic event should add more challenges for a country that is trying to find solutions to a health system with large gaps and growing inequities. Countries need public policies that simultaneously increase climate resilience, reduce social inequalities, and improve population health. We cannot continue treating patients lying on mattresses on the floor.

> This global threat to health, perhaps the greatest challenge facing the world in the 21st century, exposes the urgency of concrete and coordinated actions, both locally and globally, to mitigate its devastating impacts.

How to Help

Devastating floods have recently impacted Porto Alegre and the surrounding areas in Brazil's Rio Grande do Sul state, severely affecting nearly 1.5 million people and creating significant health challenges, including lack of access to clean water and medical care. ISPOR's Brazil Chapter past-president, Dr Stephen Stefani, has been at the forefront of coordinating healthcare responses and ensuring the well-being of those displaced by the floods. His work in organizing these services is both impactful and admirable. For those wishing to offer assistance, resources, or support, please contact the ISPOR Brazil Chapter at secretaria@ispor.org.br

ISPOR Conferences and Events

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Barcelona International Convention Center, Barcelona, Spain

Join global healthcare leaders at ISPOR Europe 2024 for discussion and dissemination of the latest topics in health economics and outcomes research (HEOR).

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Research and Case Study abstract submissions are closing soon. Submit today!

	Submission Deadlines:	*Notifications:*
Issue Panels, Workshops, Other Breakout Sessions, Case Studies	6 June	Week of 15 July
Research	27 June	Week of 19 August

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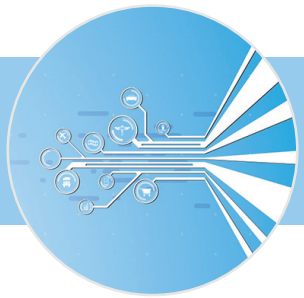
ISPOR Real-World Evidence Summit 2024* | 17 November
Barcelona International Convention Center, Barcelona, Spain



During the 17 November Real-World Evidence Summit, we will explore the use of real-world evidence (RWE) in Joint Clinical Assessment of the EU health technology assessment (HTA), with insights from the cross-border collaborations on pricing and reimbursement in the EU countries. In addition, the feasibility of HTA reassessment post market entry will be considered, drawing from lessons learned from US Medicare Drug Price Negotiation. Other major topics covered will be causal inference and external control arms for comparative effectiveness analyses, the hierarchy of RWE studies, and the role of patient registries.

*The Summit is a co-located event at ISPOR Europe 2024

Learn more at here.

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Utilizing RWE and HEOR Throughout the Product Lifecycle: From Product Positioning to Market Access and Reimbursement

Assessing Real-World Data From Electronic Health Records for HTA

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ISPOR Education

ISPOR Short Courses

Upcoming ISPOR Short Courses include:

June 5-6 | 10:00AM – 12:00PM EDT (Virtual)

Digital Real-World Evidence Generation Approaches in Rare Diseases and Oncology

After the completion of this course, participants will be able to...

- Draft a study protocol and informed consent.
- Understand drivers of an ethical approval strategy.
- Build an effective data capture strategy, comprising PROMs and the capture of other types of data.
- Understand drivers of an effective information governance strategy.

June 26-27 | 11:00AM – 1:00PM EDT (Virtual)

Leveraging Clinical Outcome Assessment Data to Maximize the Value of New Treatments Beyond Labeling

After the completion of this course, participants will be able to...

- Understand how clinical outcome assessment (COA) supports the totality of value of pharmaceutical treatments.
- Discern the value of COA data for benefit/risk evaluation.
- Recognize the value of COA data for HTA and market access decisions.
- Leverage the value of COA data for policy makers, clinicians, patients, caregivers, and advocates.

July 10-11 | 10:00AM – 12:00PM EDT (Virtual)

Causal Machine Learning for Health Economics and Outcomes Research

After the completion of this course, participants will be able to...

- Understand the strengths and limitations of employing machine learning (ML) for causal inference.
- Estimate average treatment effects from observational data using causal ML techniques, such as double/debiased ML.
- Estimate heterogenous treatment effects using popular causal ML methods, including Causal Forests and Bayesian Additive Regression Trees.
- Integrate estimates of heterogeneous causal effects into decision modeling frameworks for optimizing treatment allocation.

July 24-25 | 10:00AM – 12:00PM EDT (Virtual)

Automated Health Economic Analysis Using R Shiny

After the completion of this course, participants will be able to...

- Develop R Shiny applications for automated health economic analyses.
- Utilize graphical examination techniques for model calibration and sensitivity analysis.
- Integrate complex data input/output interfaces with customized features and formats.

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ISPOR Education

ISPOR Webinars

Upcoming webinars include:

June 11 | 12:00PM – 1:00PM EDT

Overcoming the Barriers of Open-Source Modeling

By completing this webinar, you will...

- Understand the basics of open-source modeling (OSM) and why its uptake has been limited.
- Gain clarity on the barriers to the development and use of OSM and strategies to overcome these barriers according to stakeholders.
- Recognize the most promising strategies for optimizing the use of OSM and the steps in implementing them.

June 12 | 10:00AM – 11:00AM EDT

ISPOR Top 10 HEOR Trends: What Are the Key Themes for 2024-2025?

By completing this webinar, you will...

- Gain awareness of the HEOR topics related to health, healthcare, health policy and scientific research rated as most important by ISPOR members.
- Understand the major trends influencing HEOR and ISPOR's activities related to them for both the HEOR and non-HEOR audience.
- Become informed about ISPOR activities related to each of the top 10 topics.

July 9 | 10:00AM – 11:00AM EDT

The Role of Real-World Evidence for Devices and Diagnostic Market Access in Europe

By completing this webinar, you will...

- Understand country-specific key decision pathways for medical devices and diagnostics reimbursement and learn which of these requirements can be satisfied by real-world evidence.
- Learn specific examples on how real-world evidence was used to satisfy country-specific health technology assessment hurdles.
- Understand the strengths and limitations of real-world data in the context of utility in reimbursement decision making.

July 11 | 1:00PM – 2:00PM EDT

IRA Part II: Next 15 for Medicare Drug Price Negotiations in 2025

By completing this webinar, you will...

- Be introduced to the eligibility criteria for selection of drugs for Medicare drug price negotiation.
- Receive clarity on the methods used to forecast the list of products likely subject to negotiation.
- Understand the key factors that may lead to some drugs with comparable levels of gross spending to be ineligible for price negotiations.

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HEOR NEWS

1 Inflammatory Bowel Disease Has No Borders: Engaging Patients as Partners to Deliver Global, Equitable, and Holistic Healthcare (The Lancet)

In a commentary, Christopher A. Lamb, Cate Titterton, Rupa Banerjee, Anna Gomberg, David T. Rubin, and Ailsa L Hart write that while Crohn's disease and ulcerative colitis are considered to be diseases of high-income countries, inflammatory bowel disease today is a global condition with an accelerated incidence in Asia, Africa, and Latin America, paralleling industrialization and lifestyle change. Read more

2 High Price of Popular Diabetes Drugs Deprives Low-Income People of Effective Treatment (KFF News)

Supply shortages and insurance hurdles for GLP-1 agonists have left many patients with diabetes and obesity without the medicines they need to stay healthy, and according to a KFF poll, 54% of adults who had taken a GLP-1 drug, including those with insurance, said the cost was "difficult" to afford. Read more

3 Canada's Family Physician Shortage (The Lancet)

According to the College of Family Physicians of Canada, the country's historic level of population growth has outstripped its supply of family physicians, and the result is a crisis with often severely negative health implications for as many as 6 million patients, and in some regions, as much as 30% of the population lacks access to a family doctor. Read more

4 New Guidance Aims to Reduce Bloodstream Infections From Catheter Use (WHO)

The first global guidelines to prevent the occurrence of bloodstream and other infections caused by the use of catheters placed in minor blood vessels during medical procedures include 14 good practice statements and 23 recommendations on key areas for health workers, including: education and training of health workers; techniques of asepsis and hand hygiene practices; insertion, maintenance, access, removal of catheters; and catheter selection. Read more

5 Tests Could Lead to Fewer People Having Unnecessary Chemotherapy After Surgery for Early Breast Cancer (NICE)

Patients with breast cancer may be able to forego chemotherapy by using tumor profiling tests recommended by the UK healthcare authority to guide treatment decisions after surgery, if test results indicate that a person is at low risk of cancer recurrence. Read more

6 WHO Updates List of Drug-Resistant Bacteria Most Threatening to Human Health (WHO)

According to WHO's updated Bacterial Priority Pathogens List 2024, critical priority pathogens, such as gram-negative bacteria resistant to last-resort antibiotics, and *Mycobacterium tuberculosis* resistant to the antibiotic rifampicin, still present major global threats due to their high burden. But high-priority pathogens, such as *Salmonella* and *Shigella*, are of particularly high burden in low- and middle-income countries, along with *Pseudomonas aeruginosa* and *Staphylococcus aureus*, which pose significant challenges in healthcare settings. Read more

7 Rural Hospitals Experienced More Patient Volume Variability Than Urban Hospitals During the COVID-19 Pandemic, 2020-2021 (Health Affairs)

Researchers found that changes in average daily medical volume at rural hospitals showed a dose-response relationship with community COVID-19 burden, ranging from a 13.2% decrease in patient volume in periods of low transmission to a 16.5% increase in volume in periods of high transmission. Read more

8 Japan Weighs Incentivizing Childbirth by Fully Covering Expenses (Kyodo News)

The Japanese government is considering fully covering expenses for child delivery under the public medical insurance system from fiscal 2026, in its latest effort to battle the declining birthrate. While under the medical insurance system in Japan, people basically pay 10% to 30% of medical costs out of pocket when they receive treatment for illness and injuries, but normal deliveries are not considered illnesses and therefore not covered. Read more

9 New Report Flags Major Increase in Sexually Transmitted Infections, Amid Challenges in HIV and Hepatitis (WHO)

According to a new report from the World Health Organization, new data show that sexually transmitted infections are increasing in many regions, with new syphilis cases among adults aged 15-49 years increasing by more than 1 million in 2022, reaching 8 million. The highest increases occurred in the Americas and the African region. Read more

10 Good News for India's Healthcare System (Indian Express)

National Health Accounts data show that government health expenditure as a proportion of Gross Domestic Product increased by an unprecedented 63% between 2014-2015 and 2021-2022. There was also a consistent decline in out-of-pocket expenditure as a share of the total health expenditure, dropping from 62.6% to 47.1% in 2014-2015 versus 2019-2020. Read more

HTA POLICY UPDATE

Section Editors: **Sandra Nestler-Parr, PhD, MPhil, MSc; Ramiro E. Gilardino, MD, MSc**

Welcome to the second edition of the HTA Policy Update which shines a light on the recently created Canadian Drug Agency and provides a brief update on the EU HTAR. We welcome suggestions and guest editorials for future issues. Please contact the *Value & Outcomes Spotlight* editorial office with your suggestions.

The Canadian Drug Agency: The federal government's national pharmacare agenda gives CADTH a new name and an expanded mandate

Trevor Richter, BSc, MSc, PhD, Executive Director, Global Market Access, BioCryst Pharmaceuticals, Ottawa, Canada; **William (Bill) Dempster, BA, LLB, MA**, President, 3Sixty Public Affairs, Ottawa, Canada

Health technology assessment (HTA) is set to take on a broader role in Canada, as the federal government pushes national pharmacare legislation through Parliament,[1] which has seen the creation of the Canadian Drug Agency (CDA). Although named in the pharmacare legislation, CDA is not a government organization but is a not-for-profit corporation with a board of directors comprising provincial and territorial public drug program leaders.[2]

CDA will be developed from CADTH, a nongovernmental agency renowned for the use of HTA to support health policy decision making. The new CDA mandate extends beyond CADTH's functions to focus on appropriate use of medications, pan-Canadian data collection, and expanding access to health data, including real-world evidence.[3,4]

HTA was a cornerstone of the work done by CADTH. Most notably, CADTH's pharmaceutical reviews and reimbursement recommendations have guided publicly funded provincial and territorial drug programs. While it is hoped that the CDA will leverage HTA to address its broader mandate, it is unclear how the increased emphasis on a federal health policy agenda might impact HTA programs that have primarily served provincial and territorial interests.

HTA focused on pharmaceuticals presents an acute challenge for provinces and territories in Canada, largely as a result of Canada's poor record in providing timely access to new pharmaceutical technologies. Canada ranks last in the G7 and 19th out of 20 peer countries in the Organisation for Economic Co-operation and Development in how long it takes for approved new medicines to become publicly funded for patients.[5] It is unclear how the creation of the CDA will address this challenge. Given that the provinces and territories recently established the pan-Canadian Pharmaceutical Alliance as an independent agency with a mandate to negotiate drug prices, questions have arisen about the appropriateness of the provinces and territories participating in the federally controlled CDA,[6] and the CDA has had to reassure stakeholders that reimbursement reviews will not be affected by its creation. Regardless of whether HTA programs that support access and reimbursement decisions for pharmaceuticals remain within the new CDA or elsewhere, it is crucial during this transition to maintain the integrity of Canada's existing HTA infrastructure.

While the establishment of the CDA could significantly change the landscape for pharmaceuticals in Canada, its true impact will only become clearer over time. Whether the CDA succeeds will depend on how the new federal objectives can be balanced with the needs of the provinces and territories, which rely on the robust HTA processes that have long supported Canada's healthcare decision making.

The political calendar may be the biggest factor in how far the CDA can go; the Liberal Party of Canada is far behind its rival Conservatives in the polls, and the minority government has to face voters by no later than October 2025. The race to stand up CDA before the Conservatives take over and Ottawa pulls back on national pharmacare initiatives (which happened the last time the Tories took power in 2006) has begun.

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Update on the EU Regulation for HTA

After the public consultation period, the European Commission adopted the Joint Clinical Assessment (JCA) Implementing Act of the Regulation on Health Technology Assessment in the European Union (EU HTAR; Regulation 2021/2282) on May 23, 2024. The Implementation Act on JCA provides more clarity on the process, timelines, and templates for JCAs and is an important milestone in the implementation of the HTAR. There were no surprises—timelines are tight for all elements of the JCA, and some may argue that the Implementing Act still leaves important issues unresolved.

RESEARCH ROUNDUP

Section Editor: **Aakash Bipin Gandhi, BPharm, PhD**, Health Economics and Value Assessment Business Partner, Sanofi, Cambridge, MA, USA

Health equity and decentralized trials.

Dahne J, Hawk LW. *JAMA*. 2023;329(23):2013-2014.

Summary

The article by Dahne and Hawk describes health equity in the context of decentralized clinical trials. Specifically, the article stresses the need for robust evidence and studies that would help determine whether a decentralized approach improves access to clinical trials for individuals that face health disparities. Decentralized approaches can help improve trial access by helping individuals overcome logistic barriers including transportation issues and proximity to trial sites. Further, individuals with child or caregiver responsibilities or disability can also benefit from this design. However, there is lack of robust scientific evidence that quantifies the direct impact of decentralized trials on health equity. Possible unintended consequences of using decentralized approaches also need to be considered before its selection as a primary method of improving trial representativeness. For example, decentralized approaches are highly dependent on digital technologies. However, underrepresented groups may have lower rates of technology uptake (possibly due to lack of internet access), which exacerbate health equity issues in trials instead of resolving the same.

Relevance

In light of the COVID-19 pandemic, decentralized clinical trials offer the ability to leverage digital tools to present certain trial procedures to participants. These include study recruitment postings, informed consent forms, clinical outcomes assessments, and compensation processes. While offering these advantages, decentralized trials should not be misunderstood as being the ideal process to improve trial representativeness. Formal scientific comparisons between decentralized and traditional randomized trials can help determine which design would be most effective in improving trial access for underrepresented populations.

Mapping health disparities in 11 high-income nations.

MacKinnon NJ, Emery V, Waller J, et al. *JAMA Network Open*. 2023;6(7): e2322310-e2322310.

Summary

In this article, MacKinnon et al describe differences in geographic health disparities across 11-high income nations based on results from the 2020 Commonwealth Fund International Health Policy (IHP) survey. The IHP survey is cross-sectional and represents a nationally representative sample of patients that self-report data on 10 health disparity indicators across 3 domains. These include health status and socioeconomic risk factors, affordability of care, and access to care. The countries included in the survey were Australia, Canada, France, Germany, The Netherlands, New Zealand, Norway, Sweden, Switzerland, the United Kingdom, and the United States. The study found that compared to other countries in the survey, the United States had the most geographic health disparities (5 out of 10 indicators). Of the countries surveyed, Canada, Norway, and The Netherlands did not display any statistically significant geographic disparities. Access to care was found to be the primary indicator of disparity among the surveyed countries that showed statistical significance for the presence of geographic health disparities.

Relevance

Findings from this study can help policy and decision makers introduce suitable interventions and programs that can help improve geographic health disparities.

The US health equity crisis—an economic case for a moral imperative?

Wadhera RK, Dahabreh IJ. *JAMA*. 2023;329(19):1647-1649.

Summary

The study by Wadhera and Dahabreh estimated and reported the economic burden of health inequities stratified by racial and ethnic subgroups in the US population. Specifically, the study inclusion criteria focused on adults in the United States that were ≥25 years old who had less than a 4-year college degree. The study utilized the Medical Expenditure Panel Survey and state-level Behavioral Risk Factor Surveillance System data to calculate excess medical expenditure stratified by race and ethnicity. The authors found that the economic burden of racial and ethnic inequities ranged from $421 billion to $451 billion depending on the dataset used for the assessment. A large proportion of the economic burden was associated with the disproportionately poor health among African Americans compared to the rest of the population included in the study. Further, the economic burden of education-associated inequities ranged from $940 billion to $978 billion depending on the dataset used for the assessment.

Relevance

This study displayed and quantified the extent of adverse economic consequences attributable to health inequities across racial and ethnic minorities in US populations. These findings can guide policy decision makers in targeting suitable interventions, programs, and government initiatives at the state and national levels to mitigate the economic consequences of health inequities in these populations.

Note from the Section Editor: *Views, thoughts, and opinions expressed in this section are my own and not those of any organization, committee, group, or individual that I am affiliated with.*

HEOR AS A SIGNPOST ON THE JOURNEY TO HEALTH EQUITY

By Christiane Truelove

Health equity—patients' equal ability to access the healthcare and resources they need, when they need it—continues to be a struggle everywhere in the world, 2 years after the COVID pandemic revealed the weaknesses in healthcare systems.

IN THE UNITED STATES, RACIAL AND ETHNIC DISPARITIES in health and healthcare exist across and within states, according to the Commonwealth Fund 2024 State Health Disparities report. These researchers found that Black people are more likely than Asian American, Native Hawaiian, and Pacific Islander, Hispanic, and White people to die early from avoidable causes.

A report from the National Institute on Minority Health and Health Disparities (NIMHD), part of the National Institutes of Health, states that in 2018, the economic burden of health disparities by racial and ethnic minority groups is estimated at $451 billion, or $1377 per person, and the burden of education-related health disparities at $978 billion, or $2988 per person. Like the Commonwealth Fund researchers, this NIMHD-funded study also found the disparities varied by state. The economic burden was estimated using excess medical care costs, lost labor productivity, and premature deaths.

> In 2018, the economic burden of health disparities by racial and ethnic minority groups is estimated at $451 billion.

For researchers in the health economics and outcomes research (HEOR) field, health equity may be the last thing they consider in their research, but according to Mani Keita Fakeye, PhD, health equity research lead and technical advisor at Deloitte, "Health equity transcends the entire research and health services value chain. It cuts across all strategic decision making and the whole body of knowledge, evidence, and thought," she says. "From a philosophical standpoint, our entire conceptualization of health equity has room for improvement."

The importance of understanding differences

Eliseo J. Pérez-Stable, MD is the director of NIMHD and one of the authors of the 2023 report. Pérez-Stable, who originally is from Cuba, initially took notice of health disparities when he was at the University of California, San Francisco (UCSF), as a resident, a fellow, faculty, and then director of the Division of General Internal Medicine. "In clinical work, I realized how important it was for me to take care of patients who only spoke Spanish because I'm fluent in Spanish. That was my first encounter with inequities in the healthcare system." Pérez-Stable partnered with other faculty at UCSF to develop a research program called Latino Healthcare, which eventually became the program on minority health.

At NIMHD, there is a more advanced perspective on these health outcomes differences. The term "health disparities" is used to describe differences in health outcomes that adversely affect socially disadvantaged populatons and are influenced by social and structural factors as biology, behavior and healthcare systems. These outcomes were not caused by "one's identity of being African American, or Latino, or American Indian, or Asian, but was instead in the context of where we live that led to worse outcomes." The mission of the NIMHD is "to lead scientific research to improve minority health and reduce health disparities."

Whether researchers refer to "health disparities" or "health equity," Pérez-Stable believes we're all talking about the same thing, "Health equity is the aspirational goal of everyone having optimal opportunities to attain their best health possible and then applying that principle to make sure that barriers to promote good health are removed," says Pérez-Stable.

For Fakeye, her perspective on health equity originates from her personal experience. Born in Guinea, West Africa and growing up in South Carolina, she has now spent more than a decade in Maryland after attending Johns Hopkins for her public health training. "Hopping around to many different places, it's become par for the course for me to understand different people, different types of thinking, and different values. It's been great to actually be able to meet people where they are and connect with them," Fakeye says. "Diversity is something that should bring us together."

When it comes to health equity research, Fakeye believes the research teams themselves should be diverse. "If you have a team of people who are exactly the same and think exactly the same, that team will actually be very good at doing one thing very well. But if you have a team that's diverse, that team has the capacity to do many things well—but it takes a fair amount of investment for consensus."

> "Health equity transcends the entire research and health services value chain."
>
> – Mani Keita Fakeye, PhD

"It's insufficient to just say, 'let's bring people together.'" That's an important starting point—but the *how* in health equity is just as important as the *what* in how we bring people together and who we bring to the table."

Health equity requires data

Khushbu Balsara, DDS, MPH, is a second-year postdoctoral research fellow at Johns Hopkins Bloomberg School of Public Health, Health Systems and Policy. She analyzes health outcomes and access to healthcare both in the United States

and in low- and middle-income countries. In the United States, her research focuses on Medicare and Medicaid coverage, specifically examining the recent expansion of oral health benefits for adults under Maryland's Medicaid program, and assessing the access to smoking cessation programs and lung cancer screening among Black adults in Maryland. In lower- and middle-income countries, she is involved in projects such as JHU-Hanoi HEalS and BIGRS, focusing on injury prevention, trauma care and rehabilitation, and examining ways to strengthen health systems and emergency health services.

> "We have the aspirational goal of everyone having optimal opportunities to attain their best health possible and then applying that principle to make sure that barriers to promote good health are removed."
>
> – Eliseo J. Pérez-Stable, MD

According to Balsara, one of the biggest challenges for HEOR researchers trying to examine the impact of health disparity on outcomes is access and availability of data from clinics. In her research on the expansion of oral health benefits and comparing outcomes to previous coverage, "when we went looking for the health outcomes, there were no evaluation reports to find. We are still looking at the gray literature."

The collection of data outside of the clinic also presents challenges. "We plan to do interviews, but don't know if patients are willing to come forward because of their past experiences with the healthcare system," Balsara says. Even as an educated person, she felt overwhelmed trying to navigate the US healthcare system, having come from a country where she did not have to deal with privatized health insurance.

While policy makers order changes to improve healthcare, often these new policies do not include directions on how to evaluate their impact on outcomes. Data may not be collected, or if it is collected, it is not reported. "If you were thinking about strengthening our health systems, that is one of the very big connecting bridges that will help us actually study these outcomes with a magnified view," Balsara says. "Because if there are no reports, how are we going to look at the future trend, how are we going to see how we can improve, how can we do better?"

And then there is the question of who can get access to the data needed to do health equity research, especially for researchers without generous funding to be able to purchase data from private entities. "Many early career researchers who have an interest in health equity might not be able to afford these data sets," Balsara says. "To be equitable, we need to make sure the data are visible to the public, visible to researchers, and accessible to all."

Even if data are available, their completeness, as far as the elements needed to determine health equity, is another matter. Pérez-Stable recalls speaking with representatives of one large health insurance entity during the COVID pandemic about the claims data of members. "They don't know the race and ethnicity of their claims data, so they create algorithms to impute the data," he says. "I know that artificial intelligence is here and there are people using it, but I hesitate to put all my trust in the data where you have more than half of the fundamental variables missing, and then the missing data are imputed based on an algorithm."

Although researchers can make good guesses based on census data and ZIP codes, "it all boils down to having better primary data in the electronic health record or in the clinical context," Pérez-Stable says. "I wouldn't say we haven't made progress, but different systems have different approaches to this—some are systematically doing it; others are not. While automated check-ins can have screens where a patient can answer questions about race and ethnicity and put them into the electronic record, not all practices use automated check-ins and a front desk registration person is not the right person to determine what your race or ethnicity is."

Pérez-Stable points out that individuals are not usually asked about their educational background or other proxy for socioeconomic status in the clinic, especially if they have private insurance. "Private insurance doesn't necessarily mean that you're well off, it just means you're employed with an employer who provides benefits," he says.

> "The *how* in health equity is just as important as the *what* in how we bring people together and who we bring to the table."
>
> – Mani Keita Fakeye, PhD

In 2023, the World Health Organization (WHO) released the largest global collection of health inequality data. Importantly for researchers, the repository allows for tracking health inequalities across population groups and over time, by breaking down data according to group characteristics, ranging from education level to ethnicity. According to WHO, the repository's data show that in just a decade, the rich-poor gap in health service coverage among women, newborns, and children in low- and middle-income countries has nearly halved. Moreover, by eliminating wealth-related inequality in under-5 mortality, the lives of 1.8 million children could be saved.

"The ability to direct services to those who need them the most is vital to advancing health equity and improving lives. Designed as a one-stop-shop for data on health inequality, the repository will help us move beyond only counting births and deaths, to disaggregating health data according to sex, age, education, region, and more," said Tedros Adhanom Ghebreyesus, MSc, PhD, WHO director-general. "If we are truly committed to leaving no one behind, we must figure out who is being missed."

HEOR research in the battle against health disparities

The role of HEOR researchers and health economists in addressing health disparities "is one that I've come to appreciate more from my current position as the director of NIMHD," says Pérez-Stable.

"I think a lot of people are afraid to talk about economics in science," Pérez-Stable says. "They think, 'It's money and we just do knowledge.' But in the population science perspective or the political science perspective, that's never been the case."

When it comes to addressing health equity in HEOR, ISPOR believes its members have a critical role to play. Health equity ranked 5th of the top 10 HEOR trends identified by ISPOR members in the 2024-25 report. The organization's Health Equity Research special interest group is advancing novel methods for assessing the health equity impacts of decisions on unfair differences in health and applying equity-informative cost-effectiveness analysis across markets, conditions, and payer types, as well as improving data sources used by the HEOR community to study health inequities.

ISPOR also includes health equity as a petal in its Value Flower. While she likes the depiction of health equity as a petal of the value flower, Fakeye says it should be a "more fundamental piece of the flower, like the stem."

> "To be equitable, we need to make sure the data are visible to the public, visible to researchers, and accessible to all."
>
> – Khushbu Balsara, DDS, MPH,

"We'll have a more robust understanding of what health equity is when you think about it alongside other elements like the cost of a therapy or a treatment, the effects on productivity, the effects on quality-adjusted life years, etc. These all have health equity implications," Fakeye says. "Health equity is not something to examine on the side—or through a quick subanalysis of race and gender—and you think you've checked off that box or that petal. It's intersectional."

By the Numbers: Health Equity

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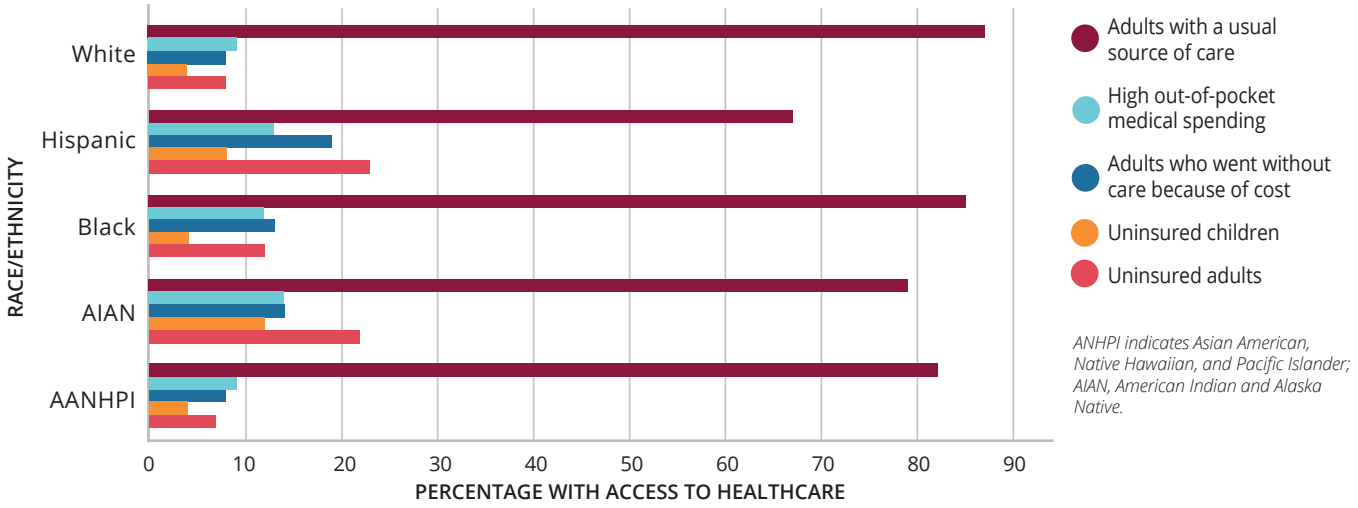
Differences in healthcare access among different racial and ethnic groups in the United States



ANHPI indicates Asian American, Native Hawaiian, and Pacific Islander; AIAN, American Indian and Alaska Native.

AHRQ's Equity Agenda Identifies 6 Priorities for Research to Reduce Health Disparities

1 **Institutional Leadership, Culture, and Workforce**
Publish publicly available white papers and toolkits on evidence-informed workforce diversity strategies

2 **Data-Driven, Culturally Tailored Care**
Share research findings with policy making entities on evidence-based collection of patient race, ethnicity, and language data by providers and payers

3 **Health Equity Targeted Performance Incentives**
Develop toolkits to assist health care organizations with integrating equity metrics into their performance management systems

4 **Health Equity-Informed Approaches to Health System Consolidation and Access**
Support the development of geographic information systems to track changes in the healthcare access, quality, and equity resulting from consolidation and other policy changes

5 **Whole-Person Health**
Expand access to secondary linked data sets analysis across federal surveys to accelerate research on health outcomes linked to social needs

6 **Whole Community Investment**
Develop new health equity research funding models with funding allocated directly to community organizations working in partnership with universities or healthcare organizations

Economic Burden of Health Inequities in the United States

"There's a **potential economic gain** of **$135 billion per year** if racial disparities in health are **eliminated**, including **$93 billion** in **excess medical care costs** and **$42 billion** in untapped productivity."

"**Health inequities** account for approximately **$320 billion** in annual healthcare **spending**. If unaddressed, this figure **could grow to $1 trillion or more** by 2040."

Deprioritized Children and Young People in Health Technology Assessment: Are Too Many Methodological Challenges Pushing Health Equity Down the Ladder in the Decision-Making Agenda?

Angeliki Kaproulia, MPharm, MSc, **Donata Freigofaite, MS**,* **Andre Verhoek, MS**, Cytel, Rotterdam, The Netherlands, and **Grammati Sarri, PhD**, Cytel, London, England, UK

Health technology assessment (HTA) submissions of medical treatments for children and young people are limited and criticized for failing to address several methodological and equity issues due to evidence scarcity.

Current HTA frameworks do not comprehensively consider the reality of the unique challenges (ethical, methods, processes) for pediatric medicinal products.

Health equity for children and young people is currently a neglected topic in HTA. Pediatric health disparities need to be formally assessed in HTA decision making for new health technologies targeting this population.

Introduction

Most health treatments used by children and young people (children and young people) are not explicitly authorized for their age group, illustrating the prevalent practice of off-label or off-license drug usage. Although children and young people account for 20% of the total European population,[1] more than two-thirds of available medicinal products lack specific labeling for pediatric use and have not undergone the testing and validation necessary to ensure their safe and effective use in children.[2] The US Food and Drug Administration (FDA) has stated that the absence of well-established pediatric use information in labeling poses serious threats to children and young people, as it may lead to inappropriate dosing and an increased risk for unsafe or ineffective treatments.[3]

The FDA and European Medicines Agency have provided clear guidance to tackle scientific and ethical issues related to the development of medicinal products for pediatric use.[3,4] Although reimbursement decision makers seem to have acknowledged the unique challenges in evidence generation for this population, these issues cannot be properly addressed without modifying the standardized framework of clinical and cost-effectiveness assessments.

Only a handful of technology submissions for children and young people undergo formal assessment through the decision-making process. This can be the result of deprioritization in the health technology assessment (HTA) scoping phase or due to a high proportion of early development failure in treatments targeting children. For example, in a review of technology appraisals for children and young people from the National Institute for Health and Care Excellence (NICE) between 2013 and 2023, the annual percentage of HTA submissions ranged from 3% to 13%.[5] In addition, the clinical and economic evidence included in HTA submissions is frequently suboptimal, lacking in both quality and quantity and failing to meet the minimum methodological standards commonly expected in adult indications.

Policy makers have taken steps to stimulate financial investment in pediatric drugs, aiming to eliminate barriers to undertaking clinical trials in children and young people by appointing pediatric specialists within federal regulatory and reimbursement bodies and funding research for children and young people.[3,4] Several challenges have also been identified in HTA submissions for children and young people in terms of evidence generation, data quality, and extrapolations in economic models. The most widely discussed methodological topics are health-related quality of life (HRQoL) for children and young people and limited data follow-up.[5]

> Although children and young people account for 20% of the total European population, more than two-thirds of available medicinal products lack specific labeling for pediatric use and have not undergone the testing and validation necessary to ensure their safe and effective use in children.

Recent discussions have focused on how to expand value drivers in HTA decision making beyond clinical and economic considerations to include societal aspects; however, incorporating these value elements has been given much less contemplation in assessments of technologies for children and young people. For example, incorporating health equity is a core strategic initiative for adult diseases, but has been largely overlooked

*Employed by Cytel at the time this manuscript was drafted.

in the decision-making agenda for novel treatments for children and young people. This omission leaves children and young people more vulnerable to experiencing health disparities as adults even though resolving health disparities early in life will have lifelong implications for the entire population (**Figure 1**).

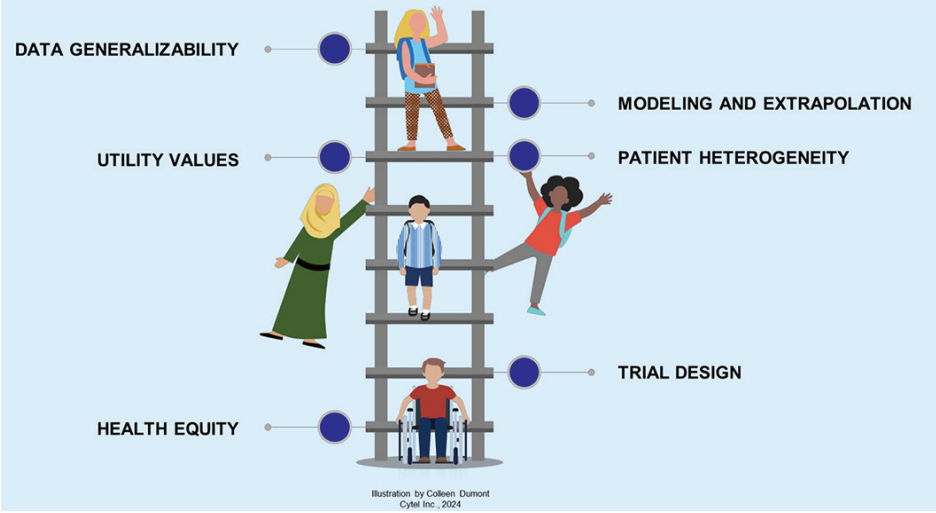
Data Generalizability

Data generalizability is a significant hurdle when building evidence packages from clinical trials or other sources for reimbursement decision making. Trial participants may not represent real-life patients who are more likely to receive newly available treatments. External validity of pediatric clinical trial data is more of a concern in submissions for treatments specifically intended for children and young people compared with adult trials, due to operational and ethical obstacles in trial recruitment. Industry has emphasized the difficulties in producing large and "high-quality" evidence in children that meets HTA standards, mainly related to pediatric disease characteristics (often in low-prevalence diseases/low numbers of children affected, need for dose-adjustment in a wider children and young people population) and high heterogeneity of pediatric patients in terms of anatomical, psychological, social, and cognitive development features.[1] Researchers also struggle to recruit sample sizes large enough to statistically power studies to account for that heterogeneity or considered mixed-age clinical trials given the combination of societal, operational, and ethical barriers in pediatric clinical trial recruitment.

> Incorporating health equity is a core strategic initiative for adult diseases, but has been largely overlooked in the decision-making agenda for novel treatments for children and young people.

In a recent review of submissions to NICE for children and young people, committee critiques focused on increased uncertainty generated by small sample sizes in clinical trials and the extent these data can be generalizable to the local UK pediatric population. The large fluctuations in individual patient profiles (due to high trial heterogeneity) and the absence of confirmatory data on a treatment's relative efficacy have been heavily criticized, increasing uncertainty in decision making. The interpretation of evidence was further complicated by the extent to which assumptions were made by borrowing adult data to resolve evidence gaps.

Figure 1. Evidence Challenges in HTA Submissions for Children and Young People



Uncertainty in Pediatric Models

The impact of methodological limitations in both generating reliable pediatric clinical data and confidently modeling the lifetime impact of health technologies on children and young people has been widely communicated.[2] These limitations focus on the use of quality-adjusted life-year as a core metric given the inadequacies in the current methods to elicit preferences and attribute values per health state in children and young people as well as the lack of flexibility in economic model structures to address submission technical challenges in this population.

HRQoL among children and young people is difficult to measure due to scarcity of adequate/appropriate techniques or algorithms to map corresponding data in adults. Furthermore, children younger than 12 years of age may require caregivers to respond on their behalf,[6] and proxy respondents might be influenced by their own perceptions.[7]

Model structure considerations such as altered time horizons, capability to account for treatment-related health states, and the need for long-term extrapolation of limited follow-up clinical data require stronger assumptions to resolve uncertainty. This is one of the largest areas of HTA critiques given the lack of trust in a treatment's efficacy (health gain benefits) claims while the need for solid safety evidence remains critical.

> Health equity is rarely discussed in HTA submissions for children and young people.

The lack of reliable data to fit model inputs is also related to comparators in the decision problem. Off-label medications (often tested in adults) are used to treat various pediatric diseases given the absence of age-appropriate options. According to NICE, for instance, a manufacturer was unable to compare its technology to potentially relevant comparators because there were no pediatric studies that allowed for network meta-analysis.[8]

Health Equity

Health equity is achieved when everyone can attain their full potential for health and well-being.[9] For children and young people, this translates into increasing access to quality healthcare that accounts for their unique developmental and societal needs.

A range of political, socioeconomic, and contextual factors can affect health disparities. Despite increasing evidence about what impacts poor health, these health inequities have persisted, and in some cases, are getting worse. Many stakeholders have strongly advocated for the need to incorporate elements of health equity more widely in reimbursement assessments. Therefore, it is surprising that this is not a higher priority for pediatric HTA submissions given that childhood adversity can affect development and have a lifelong impact on health and well-being. Health equity is rarely discussed in HTA submissions for children and young people, seemingly falling far down a long list of methodological challenges involved in HTA submissions for this group. But this lack of attention to pediatric health disparities may further disadvantage already marginalized children, potentially resulting in worse health status and poor long-term health outcomes (**Table 1**).

Recommendations

Efforts are needed to ensure the integration of new medicines into routine clinical practice beyond the promotion of drug development and clinical trials (eg, innovative trial designs) for children and young people. Processes that have an impact on market authorizations and drug reimbursements are pivotal for guaranteeing equal access to new treatments for children and young people in daily practice.[2]

Real-world evidence can be of significant help to fill in evidence gaps and provide a long-term perspective, especially in trials with short follow-up and small sample sizes (eg, rare diseases). HTA bodies can assess the effectiveness and safety of an intervention across different pediatric populations using real-world evidence.

> HTA bodies have an opportunity to restore health equity by considering health disparities at the base of evidence.

Flexibility in HTA decision making by recognizing a priori the evidentiary challenges is imperative to address health disparities effectively. These limitations are particularly pronounced in rare diseases, where issues such as the classification of disease severity across the children and young people population and, subsequently, the conduct of appropriate HTA evaluations have proven to be challenging.[8,10]

Adaptive market access pathways can enhance early access to new technologies for patients and significantly contribute to tackling health inequalities. This discussion is particularly relevant for treatments targeting disease areas of high medical need among overlooked populations such as children and young people. It may involve regulatory approval in stages, incorporation of real-world evidence alongside clinical trial data, and engagement of patients and HTA bodies in discussions.[11]

Given the lifelong impact of treatments for children and young people on the health and well-being of individuals, HTA bodies have an opportunity to restore health equity by considering health disparities at the base of evidence. For example, international consensus on methods for measuring utility could promote the use of pediatric HRQoL instruments in clinical trials.[12] In addition, eliciting social values through engagement with patients and caregivers would potentially fill in the gaps of HRQoL among children and young people.

Conclusions

While advances have been made in child-specific regulatory provisions for drug approval in the United States and European Union, reimbursement decision makers have not considered formulating changes in the methods to adjust evaluation criteria for technologies targeting children and young people, including prioritizing health equity in the evidence base.

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Table 1. Challenges and recommendations associated with methodological and equity issues in CYP HTA submissions

	Data Generalizability	Uncertainty in Pediatric Models	Health Equity
Challenges	• Patient heterogeneity • Small sample sizes	• Lack of health-related quality of life instruments and mapping algorithms specific to children and young people • Limited follow-up data • Variation in clinical practice due to off-label use	• Equity lacks attention in the context of health technology assessment submissions for treatments for children and young people • Magnification of health disparities across an already marginalized population
Recommendations	• Use of real-world evidence • Innovative trial design (eg, basket trials)[1] • Regulatory frameworks for promoting the generation of pediatric clinical data[1]	• Patient/caregiver engagement on health-related quality of life measurement • Development of framework for children and young people at local or European Union level • Use of real-world evidence	• Flexibility in health technology assessment decision-making by recognizing the evidentiary challenges (eg, rare diseases) • Use of real-world evidence • Adaptive pathways for market access

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Health Equity within Health Technology Assessments: What Progress Has Been Made?

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There is a need for a standardized health equity framework and increased collaboration to improve data generation relevant to HTA evaluations.

Some recommendations for including Health Equity are: addressing equity concerns from patient perspectives, incorporating health equity considerations into economic analyses, considering access and its impact, and ensuring transparency in the decision-making process.

Health equity-focused HTA may lead to the identification of disparities in access, outcomes, and costs, particularly for marginalized or underserved populations.

Introduction

Health technology assessment (HTA) bodies have the unique and influential role of evaluating health technologies to create policies that affect healthcare resource access and allocation.[1] HTA allows evidence-based decision making that aims to support equitable and effective healthcare systems.[2] Although various health equity-related frameworks have been developed to support the fair and systematic incorporation of health equity into HTA decision making, there is a lack of consensus on how to incorporate health equity measures.[3-5] This article delves into a review presented at ISPOR Europe 2023[6] aimed at understanding the extent of health equity incorporation in global HTA report of cystic fibrosis medicines shedding light on critical gaps and potential recommendations.

> Although various health equity-related frameworks have been developed to support the fair and systematic incorporation of health equity into HTA decision making, there is a lack of consensus on how to incorporate health equity measures.

The review included HTAs conducted by HTA bodies and independent organizations conducting these assessments (eg, Institute for Clinical and Economic Review [ICER]). National HTA bodies were identified using the International Network of Agencies for Health Technology Assessment. Identification of the HTA reports was conducted searching the following terms using the Boolean operator "OR:" cystic fibrosis, lumacaftor, elexacaftor, tezacaftor, ivacaftor. A targeted literature review was conducted to determine an appropriate, relevant framework to assess the HTA reports. The Framework for Equity by Benkhalti et al[5] was used to review included HTA submissions to evaluate the extent of health equity incorporation within these HTAs. Some considerations included stakeholders' involvement, outcome measures, and methodological approach.

Key Findings

Among the 33 HTA bodies identified, only 12 had reports on cystic fibrosis medicines, with 3 meeting the inclusion criteria. The review revealed varying degrees of health equity consideration among the included reports. While the Canadian Agency for Drugs and Technologies in Health[6] and the Institute for Clinical and Economic Review[7] demonstrated patient and advocacy group engagements, there was limited consideration of medication access and its impact on patient outcomes. For instance, CADTH allowed information to be submitted directly from patient groups on outcomes and issues important to patients and caregivers and directly engaged advocacy groups. ICER utilized formal questionnaires and reports from the US Food and Drug Administration in addition to direct patient and advocacy group engagement.[8] European HTA had patient and organization inclusion frameworks, but the extent of incorporation was not clear in the submission analyzed.

Recommendations for Improvement

Several recommendations were identified to enhance the integration of health equity in HTA assessments (**Figure**). These include addressing equity concerns from patient perspectives, incorporating health equity considerations into economic analyses, consideration of access and its impact, and ensuring transparency in the decision-making process. Additionally, there is a need for a standardized health equity framework and increased collaboration to improve data generation relevant to HTA evaluations.

It is important to note that this study may not have reflected recent advances in health equity in HTAs, as health equity improvements more recently gained rapid traction due to the COVID-19 pandemic, highlighting stark health disparities globally.[10]

> There is a need for a standardized health equity framework and increased collaboration to improve data generation relevant to HTA evaluations.

More contemporary guidance was published by ICER in 2023[11] and CADTH in 2019.[12] In this guidance, ICER established methods for US HTA with the objective of ensuring health equity gaps are ameliorated. The main recommendations included the following: (a) HTA bodies' direct engagement with patients and patient groups during scoping to better understand the experiences and perspectives of the potential impact of the intervention under review, (b) setting a minimum threshold for adequate representation of racial and ethnic populations in clinical trials, (c) deterrence from computing cost-effectiveness estimates for subpopulations determined solely based on sociodemographic status, (d) encouragement to integrate thoughtful consideration of social values over quantitative equity-informative economic evaluation as a substitute, and (e) implementation of the process to identify healthcare structural changes necessary to ensure that disparities aren't worsened with the introduction.[11]

The CADTH framework centers around patient engagement only and recommends the following: (a) engage patients, families, and patient groups to enhance the quality and applicability of the evaluations and (b) ensure that those affected by the HTA may actively contribute to the assessment. This framework is outlined using rationale and values (relevance, fairness, equity, legitimacy, capacity building), mechanisms of involvement, and diverse stakeholder involvement.[12,13]

Conclusion

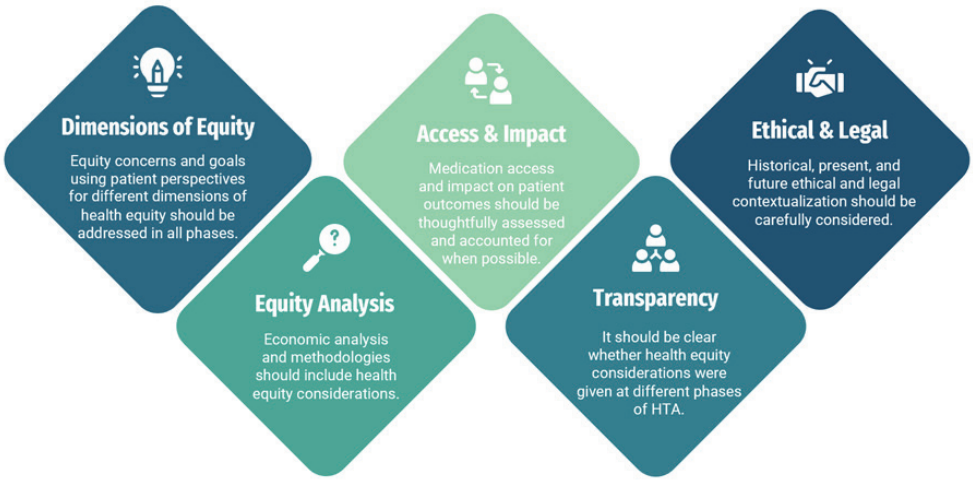
The study underscores the gaps and lack of consensus on health equity incorporation within HTA, particularly in diseases with high unmet needs like cystic fibrosis. The findings may highlight the importance of collaboration to improve health equity-related data generation and standardization in HTA guidance to improve HTAs globally. Despite limitations of this work, such as language restrictions, public availability of assessments, and disease-specific focus, the study provides valuable insights for enhancing health equity integration in HTA processes.

Health equity-focused HTA helps identify disparities in access, outcomes, and costs, particularly for marginalized or underserved populations, further addressing health inequities that haven't been fully uncovered and promoting social justice. The inclusion of health equity leads to better informed, ethical, and optimal decision making and resource allocation. Finally, these transparent efforts would assist in building connections in communities with historic mistrust in healthcare systems and prevent any unintended impact of introducing an intervention that widens health disparities.[14]

> Health equity-focused HTA helps identify disparities in access, outcomes, and costs, particularly for marginalized or underserved populations.

All stakeholders in the healthcare ecosystem should commit to action to ensure progress, albeit incrementally, towards optimal implementation of health equity considerations in HTA. Overall, by addressing existing gaps and implementing recommendations, stakeholders can promote fair and equitable access to healthcare technologies, ultimately improving health outcomes for all populations.

Figure. Potential recommendations based on excluded domains from the framework[5]



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The Value of Technology to Reduce Barriers to Clinical Trial Diversity and Facilitate the Development of Patient-Centric Medicine

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Many patient subgroups, often those facing the greatest health challenges, are not fairly represented in the clinical research process.

Lack of diversity in clinical trials has implications on the generalizability of results to the real-world population, leading to treatment gaps, unsafe dosing recommendations and reduced access to innovative medicines in underrepresented groups.

Digital technologies such as telemedicine, digital health apps and remote consultations have the potential to reduce barriers to trial involvement and facilitate increased representation if implemented appropriately within clinical trials.

Introduction

Historically, participants of clinical trials have not been fully representative of the target patient population, with women, ethnic minorities (eg, Black, Asian, Hispanic), people with disabilities, and those under age 18 years and over age 75 years being consistently under-represented. This means that many patient subgroups, often those facing the greatest health challenges for whom clinical trials could provide life-saving therapies, are not being fairly considered during the clinical research process. This lack of diversity in clinical research can significantly impact our understanding of the effectiveness and safety of a treatment in the underrepresented subgroups and can result in a body of clinical knowledge that is not generalizable to the real-world patient population. Therefore, this issue can be considered both medical and moral.

However, increasing digitalization of clinical trials and advances in technology offer the opportunity to run more patient-centric trials and increase the representation of a wider patient population in clinical research.

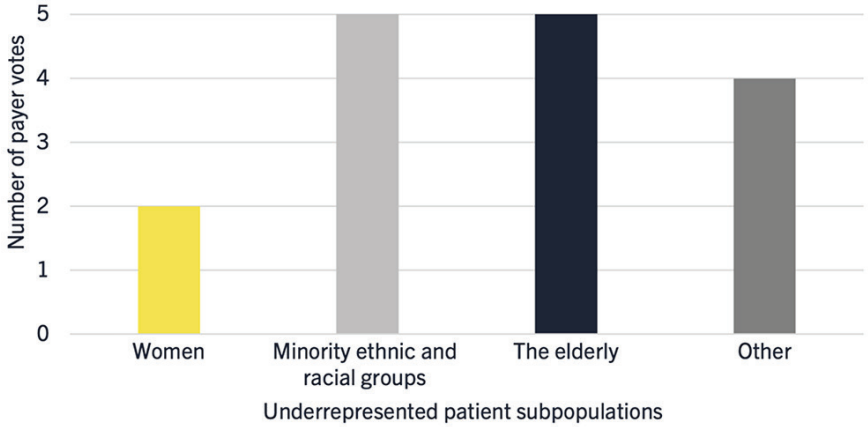
An online research program utilizing the Lightning Insights platform was conducted with the aim to explore how advances in technology can increase patient-centricity in clinical trials, reduce the burden of trial participation, and increase access to a broader, more diverse pool of patients. Research was conducted with health technology assessment (HTA) and budget-holding stakeholders (herein termed payers) in the United States, United Kingdom, Germany, and France. Telephone interviews were also conducted with specialist oncologists (key opinion leaders) in the United States, United Kingdom, and Germany. The research explored stakeholder perceptions of the barriers to clinical trial diversity, the key implications of a lack of trial diversity on both patients and society, and how technology can enable clinical trial cohorts to be more representative of real-world patient populations.

Underrepresented patient cohorts in clinical trials

In discussion with key stakeholders across Europe and the United States, there was a clear consensus that patient cohorts involved in clinical research in oncology often lack diversity. Indeed, 91% of all respondents believed that clinical trials typically are not representative of all patient subpopulations, with only one payer (from France) considering clinical research carried out in public hospitals to be representative of all types of patient subpopulations.

In particular, minority ethnic and racial groups and the elderly were highlighted as being underrepresented in clinical trials (**Figure 1**), which is consistent with

Figure 1: Payer perceptions of traditionally underrepresented patient subpopulations in clinical trials



**Affiliation at the time this paper was drafted.*

the literature. For example, a recent analysis of oncology trials revealed that only 4% to 6% of participants in the United States are Black and 3% to 6% are Hispanic, despite representing 15% and 13% of cancer populations, respectively.[1] Similarly, it has been reported that while individuals over the age of 70 years represent 50% of cancer patients, this cohort has historically represented just 13% of cancer trial participants.[2]

> This lack of diversity in clinical research can significantly impact our understanding of the effectiveness and safety of a treatment in the underrepresented subgroups.

Interestingly, key opinion leaders did not generally consider that women are an underrepresented group in oncology clinical trials, unless they were categorized as elderly, single parents, or those of a low social economic demographic. While the lack of representation of women in clinical trials has been well documented, this may be consistent with the positive trend of increasing representation of females in trials in the United States outlined in a recent report from the National Academies of Sciences, Engineering and Medicine.[3] However, specifically in the field of oncology, this trend appears to have plateaued.

Barriers to clinical trial diversity

As illustrated in **Figure 2**, multiple factors are considered to be barriers to diversity in clinical trials. In particular, logistical and practical barriers to trial enrollment (such as access to transport, mobility, and support networks) were viewed as having a high influence on clinical trial diversity by the majority of payer and key opinion leader respondents.

The lack of inclusion of minority ethnic and racial groups is also interlinked with wider socioeconomic factors that contribute to individuals' ability to take time off work, travel to clinical trial sites, and incur out of pocket costs. Language and communication barriers were considered a large determinant in the lack of ethnic diversity, influencing medical mistrust from patients and the willingness of principle investigators to recruit certain patients. Key opinion leaders also noted communication difficulties as a consideration when recruiting the elderly, alongside the increased likelihood of frailty, comorbidities, and lower performance status.

Other groups considered to be underrepresented included "less fit" patients and those with comorbidities. As with elderly patients, there may be barriers to willingness to participate in clinical trials here, as well as potential bias from researchers to include "fit" patients who are more likely to respond favorably during the trial.

Implications of a lack of diversity in clinical trials

Lack of diversity in clinical trials has a very real impact on how advances achieved through clinical research are translated to treating patients in the clinical setting. Respondents in the research noted that lack of diversity has implications on the generalizability of results to the real-world patient population and can lead to treatment gaps, unsafe dosing recommendations and reduced access to innovative treatments in underrepresented groups. Furthermore, it may cause medical mistrust in minority populations who are not represented in clinical trials, potentially having a knock-on effect on treatment compliance.

> Lack of diversity in clinical trials has a very real impact on how advances achieved through clinical research are translated to treating patients in the clinical setting.

There is valuable discussion to be had around how randomized controlled trial (RCT) outcomes translate to real-world patient populations.[3] Driven by advances in technology and catalyzed by the COVID-19 pandemic, the landscape for conducting clinical trials is evolving, with stakeholders potentially more receptive to consider alternative methodologies that increase patient centricity and accelerate patient access to innovative new medicines.[4]

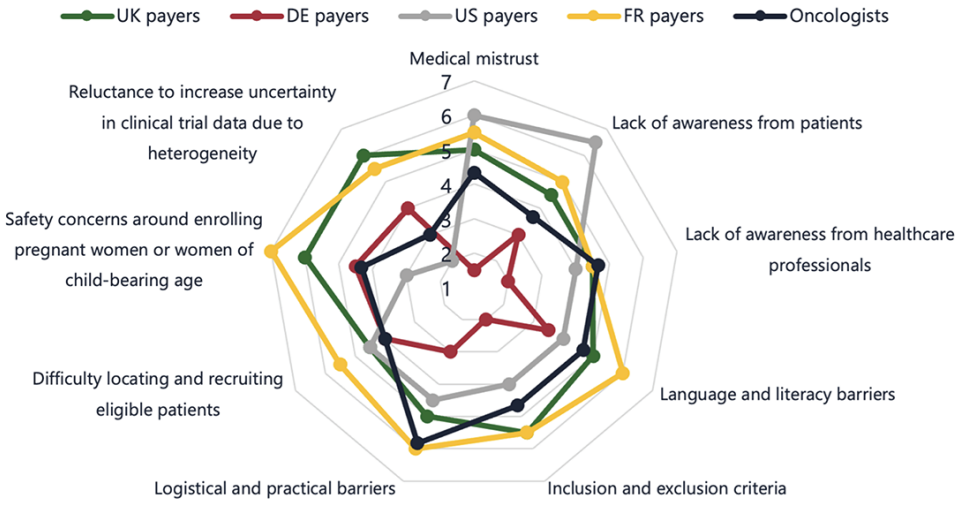
The role of technology in reducing barriers to clinical trial diversity

Technology has the potential to facilitate increased representation of all relevant patient subgroups in clinical trials in several ways, for example:

- Faster and more efficient identification, recruitment, and enrollment of patients

Figure 2: Stakeholder perceptions on barriers to diversity in clinical trials.

(1 = low influence on trial diversity; 7 = high influence on trial diversity)



DE indicates Germany; FR, France, UK, United Kingdom, US, United States.

- Recruitment of patients across multiple global locations
- Increasing patient centricity and patient engagement within clinical trials to reduce patient dropout

Telemedicine and access to remote consultations with physicians were considered by all stakeholders to be highly influential in their potential to improve trial diversity as well as being easy to implement (**Figure 3**). The COVID-19 pandemic has led to an increase in telemedicine, with a noted improvement in routine clinical practice management. This can be extrapolated to the clinical setting, where remote patient recruiting and consenting and video conference assessments can remove the need for participants to travel to the clinical trial site and report to the investigator, reducing time and costs and increasing convenience for the patient. At-home/portable diagnostics, smartphones, and wearables (using digital health apps) were rated as highly influential by key opinion leaders, but their implementation was considered more challenging, if, for example, traditionally underrepresented patient subpopulations (eg, the elderly) have limited access to these technologies and lack education on how they should be used.

> Advances in technology must be implemented appropriately within clinical trials to reduce barriers to trial involvement and increase representation.

Furthermore, virtual cohorts are digital nonidentical synthetic data records that preserve the statistical properties of the original data. They may be used for the simulation of clinical trials to augment datasets and detect effects in underrepresented groups in a study.[5] However, stakeholders were generally unfamiliar with the use of synthetic data in clinical trials and lacked trust in the reliability of artificial intelligence algorithms to create virtual cohorts. Therefore, it is clear that no single solution exists to increase diversity in clinical trials, and education is a key component to be implemented alongside exciting, new technologies to ensure their full potential is realized.

Other strategies that can increase diversity in clinical trials

Outside of technology, other strategies could be implemented to increase representation in clinical trials. Regulatory requirements can have a role in encouraging sponsors to ensure increased representation in clinical trials. Currently, there are limited formal procedures to ensure that the demographics of the trial cohort are considered objectively when evaluating the data package in Europe or the United Kingdom. However, in the United States, draft guidance has been published to support pharmaceutical companies to ensure minority patients are represented in clinical trials, and some trials are now allowing extended periods of enrollment to certain minorities to meet this requirement.[6] Furthermore, recent updates to the Institute for Clinical and Economic Review value assessment framework aim to promote equality in clinical trials through assessing the demographic diversity of participants in clinical trials.[7] Across markets, however, regulations to enforce diversity, such as quotas, may be considered pragmatically challenging and potentially unethical.

Finally, stakeholders across countries emphasized the importance of engaging with patients to support increased diversity in clinical trials. For example, community outreach and social media programs aimed at educating patients about the importance and benefits of clinical trials, as well as increasing role models and representation of underrepresented groups among clinical trial staff are considered key ways to increase patient's willingness to participate in clinical trials.

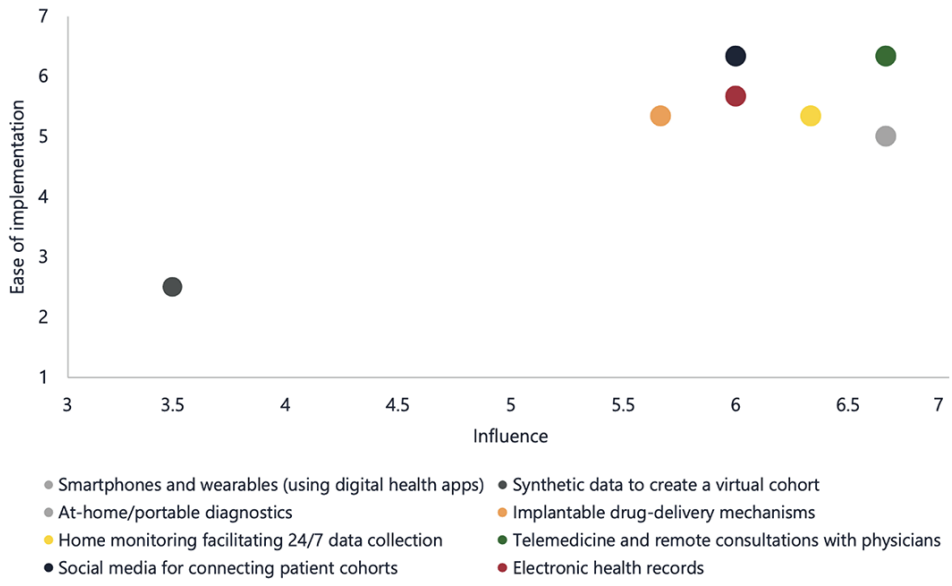
This speaks to a general shift in the pharmaceutical industry to prioritize the patient and encourage patient involvement in every stage of clinical research, with massive potential to improve representation and real-world patient outcomes.

Conclusion

Insights generated through consultation with payer and clinical stakeholders in key global markets confirm the well-documented historical underrepresentation of certain patient subpopulations in clinical trials. This has implications on the generalizability of results to real-world populations, impacting clinical outcomes, access to equitable healthcare, and potentially

Figure 3: Assessment of technologies according to their potential influence and ease of implementation for improving clinical trial diversity.

(Influence: 1 = low potential to influence the clinical development process and 7 = high potential to influence the clinical development process. Ease of implementation: 1 = difficult to implement and 7 = easy to implement)



exacerbating health disparities that exist within communities. Advances in technology must be implemented appropriately within clinical trials, alongside education programs, regulatory requirements, and sustained patient-engagement to reduce barriers to trial involvement and increase representation. This should be implemented through updating regulatory frameworks to include assessments of clinical trial diversity, offering hybrid participation options for site visits, and using communication and marketing tools that will resonate with diverse patient populations.

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Are We Leaving No One Behind? Health Technology Assessment as a Pathway to Social Justice

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Health technology assessment (HTA) agencies are starting to include health equality and/or equity principles in HTA appraisal frameworks.

Health equality and/or equity principles within HTA appraisal frameworks remain broad, subjective, and unquantifiable, calling for objective data analysis to quantify health equality and/or equity.

Manufacturers should proactively assess the impact and value of their new health technologies on health equality and/or equity and include related value propositions in their HTA dossiers, or work with payers to implement schemes to ensure equal and equitable access to healthcare.

Health equality and/or equity as a path to development

While the right to good health is considered a basic human right, many populations suffer from poor health. Globally, cross-group comparisons suggest health inequalities, which imply unequal distributions of health states across populations.[1-3] Evidence indicates high prevalence of health inequities, which occur when health inequalities are the result of unjust, systematic, and avoidable factors related to the social determinants of health (SDH).[4] Health inequities between groups may stem from differences in demographics, socioeconomic status, educational status, healthcare access, environmental exposure, etc. The promotion of health equality and equity has been recognized by global institutions, such as the World Health Organization and the United Nations, as a means to address unfair differences in health across populations.[4] Specially, the United Nations' Sustainable Development Goals highlight improving access to quality healthcare and essential medicines across populations as a key objective to ensuring health equality and equity.[5]

The use of health technology assessment (HTA) has been identified by global institutions as a potential means to advancing health equality and equity. While HTA reviews have been intended historically to ensure an optimal use of finite healthcare resources, there is a growing recognition that HTA can also reduce health disparities across populations.[6] However, the extent to which HTA agencies actively consider health equality and/or equity promotion as a component of their assessments is relatively uncharacterized, increasing the need for research into this area.

Evaluation of health equality and/or equity considerations in HTA policies

The objective of this research was to identify HTA appraisal frameworks in high- and middle-income countries (HICs, MICs) to assess whether considerations of health equality and/or equity are included as core principles of the HTA decision-making process. To accomplish this objective, we selected Europe as a region in which most HICs have established HTA entities, and Latin America and Asia as regions in which HICs and MICs are in the process of establishing HTA entities. We identified a total of 20 countries with established formal HTA entities: 5 each in Western Europe, Northern Europe, Latin America, and Asia. We reviewed the HTA appraisal frameworks from each country and identified those in which health equality and/or equity were considered as part of the decision-making criteria. We also reviewed initiatives by the Centers for Medicare & Medicaid Services (CMS) and the Institute for Clinical and Economic Review (ICER) in the United States. CMS, the public insurer for the aged and disabled population, is a critical player given its high purchasing and influencing power across all insurers in the United States. Moreover, ICER is also a critical player given its increasing influence over CMS and international collaboration on HTA processes.

> Efforts to advance health equality and/or equity, which have been on the global health agenda for the past 25 years, are now being incorporated into national decision-making processes.

Global efforts to advance towards health equality and/or equity goals

Equality and/or equity as criteria for HTA decision making

We identified the appraisal frameworks of formal HTA agencies in Argentina, Brazil, Chile, China, Colombia, England, Finland, France, Germany, Iceland, Italy, Kazakhstan, Malaysia, The Netherlands, Norway, Peru, South Korea, Spain, Sweden, and Taiwan **(Table 1**). Among these, we identified 8 countries (Argentina, Chile, China, England, Finland, Norway, The Netherlands, and Sweden) in which HTA appraisal frameworks include health equality and/or equity within the criteria used to evaluate health

Table 1. Use of health equality and/or equity principles for HTA decision making

CHN	Asia	Middle-income	✓ Yes	Prioritization of health technologies
KAZ	Asia	Middle-income	× No	N/A
KOR	Asia	High-income	× No	N/A
MYS	Asia	Middle-income	× No	N/A
TWN	Asia	Middle-income	× No	N/A
ARG	LatAm	Middle-income	✓ Yes	Prioritization and evaluation of health technologies
BRA	LatAm	Middle-income	× No	N/A
CHL	LatAm	High-income	✓ Yes	*Evaluation of health technologies*
COL	LatAm	Middle-income	× No	N/A
PER	LatAm	Middle-income	× No	N/A
FIN	Northen Europe	High-income	✓ Yes	Prioritization of health technologies
ISL	Northen Europe	High-income	× No	N/A
NLD	Northen Europe	High-income	✓ Yes	Prioritization of health technologies
NOR	Northen Europe	High-income	✓ Yes	Prioritization of health technologies
SWE	Northen Europe	High-income	✓ Yes	Prioritization of health technologies
DEU	Western Europe	High-income	× No	N/A
ESP	Western Europe	High-income	× No	N/A
FRA	Western Europe	High-income	× No	N/A
GBR	Western Europe	High-income	✓ Yes	*Evaluation of health technologies*
ITA	Western Europe	High-income	× No	N/A

Abbreviations: ARG: Argentina; BRA: Brazil; CHL: Chile; CHN: China; COL: Colombia; DEU: Germany; ESP: Spain; FIN: Finland; FRA: France; GBR: England; HTA: Health technology assessment; ISL: Iceland; ITA: Italy; KAZ: Kazakhstan; KOR: South Korea; MYS: Malaysia; PER: Peru; N/A: Not applicable; NLD: Netherlands; NOR: Norway; SWE: Sweden; TWN: Taiwan.

Table 2. Health equality and/or equity principles in place and means of promoting health equity and/or equity across HTA decision-making

COUNTRY	REGION	INCOME CLASSIFICATION	CRITERION IN PLACE	MEANS OF PROMOTING HEALTH EQUALITY AND/OR EQUITY
USA	Americas	High-income	Health equity	Considers patient population in the clinical trial and metrics to quantify unmet need
CHN	Asia	Middle-income	Impact on equity	N/A *(confidential information)*
ARG	LatAm	Middle-income	Impact on equity	Weights the probability of impacting health equity across the population
CHL	LatAm	High-income	Equity in access	Considers impact of access across socioeconomic statuses and geographic locations
FIN	Northen Europe	High-income	Equality issues	N/A *(confidential information)*
NLD	Northen Europe	High-income	Equal access	Ensures equal access among both adult and patient populations
NOR	Northen Europe	High-income	Equity and solidarity	Considers the distribution of health effects & outcomes across the population subgroups
SWE	Northen Europe	High-income	Need and solidarity	Assesses the technology based on population needs and the promotion of solidarity
GBR	Western Europe	High-income	Equity issues	Considers health equality when drafting recommendation guidelines

Abbreviations: ARG: Argentina; CHL: Chile; CHN: China; FIN: Finland; GBR: England; HTA: Health technology assessment; N/A: Not applicable; NLD: Netherlands; NOR: Norway; SWE: Sweden; USA: United States of America.

technologies. The health equality and/or equity principle is mostly used to guide decision making on the prioritization of health technologies to be evaluated by HTA agencies from the pool of available technologies awaiting evaluation. In a few instances, the principle is also used to guide decision making during the technical appraisal of the health technology under evaluation.

Furthermore, we observed that the criteria in place used to incorporate health equality and/or equity in the decision-making process and the means for promoting health equality and/or equity were subjective, broadly defined, lacked specific metrics for quantification, and varied greatly across countries (**Table 2**). Among the criteria in place, equity was explicitly mentioned in Argentina, Chile, China, England, and Norway, emphasizing the commitments by these countries to not only improve health outcomes but also reduce social injustice and provide the resources needed for disadvantaged populations. In particular, in Chile, the decision-making policy directly linked the equity criterion to the determinants of health. In China and Finland, the means of promoting health equality and/or equity were confidential and not publicly disclosed.

> Health equality and/or equity principles within HTA appraisal frameworks remain broad, subjective, and unquantifiable, calling for objective data analysis to quantify health equality and/or equity.

In the United States, as there is no national HTA process or agency, we identified the appraisal framework and decision-making initiatives of ICER. We found that ICER has announced the Value Assessment Framework (VAF) initiative to evaluate changes in its methodology for the assessment of technologies in order to advance health equity goals. The initiative involves the evaluation of potential changes to the current methodology by an advisory board, followed by updates to the VAF in the future. In 2023, ICER announced that the VAF will focus on 2 HTA methods related to health equity: analyses of clinical trial diversity and racial/ethnic subpopulations and quantitative measures to guide discussion and voting on unmet need (**Table 2**).

Governmental efforts to advance health equity in the United States

Given the lack of national HTA process or agency in the United States, we also identified efforts by CMS to enable the inclusion of value in its decision-making process and promote equity, including the agency's "Framework for Health Equity 2022-2032".[7,8] The framework aims to promote health equity, increase healthcare access, and improve health outcomes among CMS beneficiaries. The program is based on 5 priorities that include assessing existing health disparities and developing solutions to address them (eg, increasing access

to healthcare services and coverage) (**Figure 1**). The framework focuses on data collection and analysis to support evidence-based decision making, resource and capacity building to improve equal access to infrastructure and equipment, and patient support and empowerment of populations.

Moreover, CMS has also implemented performance-based payment programs to improve health equity. The Enhancing Oncology Model is a 5-year program intended to improve the quality of healthcare, while decreasing the associated costs and reducing health disparities related to SDH.[9] To accomplish these goals, the program implements payment incentives and disincentives for participating clinicians, which include monthly enhanced oncology services payments, performance-based payments, and performance-based recoupments. This is in line with existing payment policies that CMS is implementing to address SDH. Participants are required to develop health equity plans that address SDH in order to reduce health disparities among beneficiaries.[9,10]

Another CMS program is the ACO REACH model (Accountable Care Organization Realizing Equity, Access, and Community Health).[11] This model was developed to test innovative payment approaches to better support the delivery of care and patient coordination in underserved communities. Participants are required to identify underserved communities and implement initiatives to reduce health disparities among beneficiaries of the model.

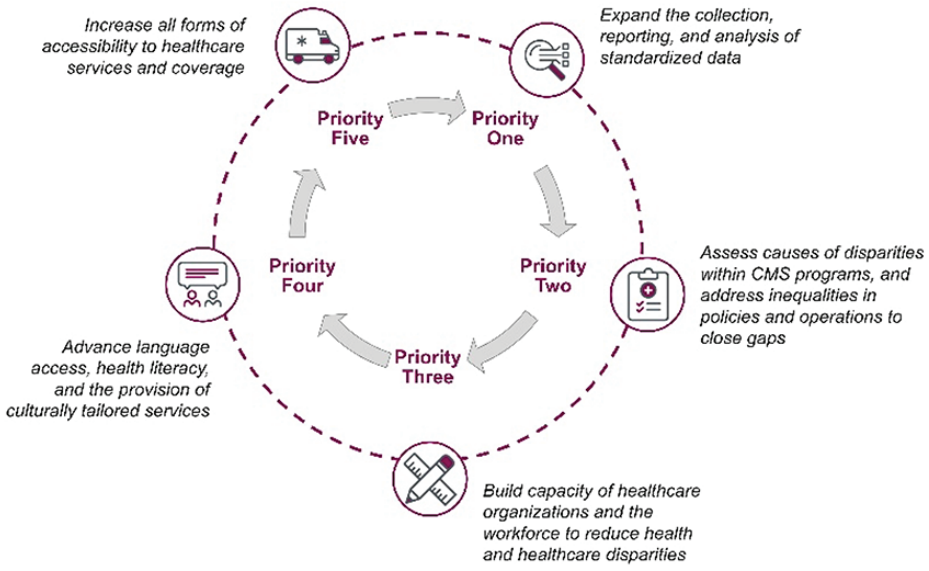
The way forward—strengthening health systems and value communication

This research shows that efforts to advance health equality and/or equity, which have been on the global health agenda for the past 25 years, are now being incorporated into national decision-making processes. With HICs leading the movement, countries are moving towards evidence- and equality- and/or equity-based decision-making frameworks that consider the impact of SDH on access to new health technologies and the impact that these technologies may have on efforts to advance health equality and/or equity. As countries with established HTA agencies refine their HTA processes, and countries with emerging HTA agencies define their HTA processes, there is room for improvement towards equality- and/or equity-based decision making.

Nonetheless, health equality- and/or equity-based criteria for HTA decision making remains broad, subjective, and/or undefined in the appraisal framework of several HTA agencies selected in this research. This lessens the impact of the criteria on the final HTA decision-making process. It is imperative that HTA agencies should consider incorporating equity considerations into frameworks for assessing cost-effectiveness by mandating the use of analytical methods that consider equity within a health system (eg, distributional cost-effectiveness analysis). HTA bodies should also define and implement analytical parameters, such as the Health Equity Index, to objectively quantify health equality and/or equity at baseline and the impact that new health technologies will have on the health equality and/or equity of the population. HTA agencies must also develop frameworks to help manufacturers address data gaps (eg, in clinical trial data and in economic evaluations) that may limit the ability to make this quantification. Global collaboration among HTA agencies, academics, and policy makers could help advance these efforts. Nonetheless, practical challenges for the implementation of the above-mentioned strategies, driven by differences in patient populations and health system structures, will need to be overcome.

As national efforts to support health equality and/or equity advance, it is imperative that HTA agencies consider policies that request manufacturers to consider health equality and/or equity in their HTA submissions. Such policies may drive manufacturers to consider the impact that their new health technologies would have on health equality and/or equity in the healthcare systems of each country or region, and the data required to demonstrate it. This impact should become a component of value-added services that can target SDH to reduce health inequality and/or inequity, and of the value proposition of new health technologies, in line with value propositions on disease burden, unmet need, and clinical, humanistic, and economic value. This value proposition on health equality and/or equity should be incorporated into the value story, value communication, and overall value strategy of new health technologies throughout their life cycles. Furthermore, the quantification of economic gains to health systems resulting from reduced health inequalities and/or inequities due to access to the new health technologies could provide additional support to

Figure 1. CMS framework for health equity priorities



CMS indicates Centers for Medicare and Medicare Services.

innovative payment methods seeking to advance health equality and/or equity and to economic value claims that present the direct and indirect benefits of the new health technologies. This would be the most critical in countries that follow a societal perspective for their HTA decision making, such as Sweden and other countries in the North-European region.

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Methods for Estimating Healthy Life Expectancy

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Healthy life expectancy (HLE) represents the number of years people can expect to spend in good health across their lifetime. The UK government has targets for increasing HLE and reducing geographical inequality in HLE.

Two methods used for calculating HLE are the widely adopted Sullivan method and multistate Markov models.

While data requirements for multistate Markov models are more complex, they can produce more accurate HLE estimates for specific cohorts.

Introduction

Healthy life expectancy (HLE) is an important public health metric that measures not only how long people live, but also how well they live, providing valuable information that can guide health policy decisions. In this article we explore 2 methods—the Sullivan method and multistate Markov models—which are both widely used for HLE calculations but vary in their data requirements, calculation complexity, and applicability.

What is HLE?

HLE measures the expected number of future years spent in "good health" from any given age.[1] For calculating HLE, good health is assumed to be a binary concept (ie, an individual is either in good health or not).[2] This contrasts with other measures (eg, quality-adjusted life expectancy), which use a more granular definition of health.

Considered alongside life expectancy, HLE can provide an indication of overall population health levels as well as highlighting disparities between different population groups, such as groups defined by geography or deprivation.[3] The UK government's 2022 Levelling Up White Paper included the following as 1 of its 12 missions: to increase national HLE by 5 years by 2035 and to narrow the HLE gap between the least and most advantaged areas in the United Kingdom by 2030.[4] This HLE gap currently stands at 14 years.[5] HLE is also an important concept in other high-income geographical areas such as the United States, Canada, and the European Union.[6]

How is HLE measured?

There are various methods to calculate HLE, with the appropriate choice guided by the available data.[1] However, the most used methods are variations or extensions of 2 principal methods that we describe in this article:

1. **Sullivan method**: a prevalence-based approach using cross-sectional data at a point in time. A variation of this method is to apply health weights at each age reflecting the aggregated level of disability or illness in the population, instead of estimating the proportion of individuals in good health.[7]
2. **Multistate Markov models**: an incidence-based approach requiring longitudinal data over time. Extensions include multistate models that relax the Markov assumption of dependence only on the present state and make allowance for the duration of illness (semi-Markov models).[8]

A comparison of methods

Sullivan method

The Sullivan method is the most widely adopted for calculating HLE,[6] employed across national statistics, epidemiological research, and public health assessment. It is a prevalence-based method relying on information about the proportion of patients in good health at different ages in the population. For example, in its latest HLE release for the period between 2018-2020, the Office for National Statistics used data from the Annual Population Survey and the 2011 Census.[2]

The data inputs required to calculate HLE using the Sullivan method are:

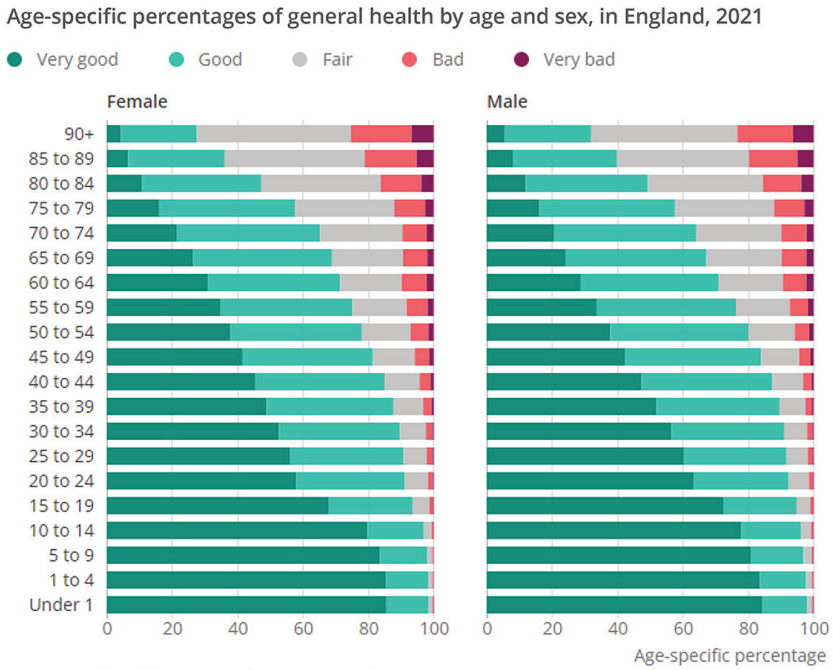
- Mortality rates for each age band; and
- Proportion in good health ("health prevalence") within each age band (**Figure 1**)

The steps in the calculation process are:

1. Graduate the mortality and health prevalence rates if necessary. Graduation is a statistical technique used to produce rates that are a smooth function of age.[9] Various graduation methods are available, from assuming a simple relationship to a published actuarial table (eg, a multiplicative scaling) to complex methods such as fitting spline functions.[10] Whether graduation is necessary, and the choice of graduation method, depends on the quality of data being used and the need for precision in the resulting HLE estimates.

2. Construct a life table from the mortality rates. A life table is a tool widely used in actuarial science to analyze the mortality of a population. It tracks a hypothetical cohort of "lives" across different age bands (typically single years of age), recording the number surviving to each age.

Figure 1. Percentages of general health for males and females, 2021 Census. Health prevalence is taken as the proportion in "Good" or "Very good" health



Source: Office for National Statistics – Census 2021

3. Multiply the number of lives in each age band by the health prevalence rate to estimate the number of healthy lives in that age band. This effectively creates a second life table tracking only those in good health.

4. In each age band, prospectively sum the number of (a) lives and (b) healthy lives over all future age bands and divide by the number of lives in the age band to estimate the (a) life expectancy and (b) healthy life expectancy. This calculation typically includes values for the current age band.

The Office for National Statistics provides more detailed, step-by-step instructions on how to construct a life table[11] and a spreadsheet template for carrying out steps 2-4 above.[12]

The outputs are *period* life expectancy and healthy life expectancy, measuring a snapshot of the population's health at the point in time to which the mortality and health prevalence rates relate. Future changes in mortality and morbidity ("cohort effects") are not automatically accounted for, although these can be built into the calculation separately by projecting the mortality and health prevalence rates based on the user's expectation of future trends. While period HLE provides a metric of overall population health at a given point in time, allowing for cohort effects can provide more meaningful HLE estimates at the individual level.

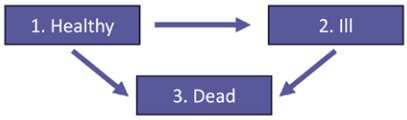
Markov models

Multistate Markov models are an incidence-based method defined by a system of states that represent the different health states an individual could occupy at any given time. Individuals move through the states over time, with this movement between states modeled by a set of transition probabilities. The Markov property (or "memoryless" property) means that the probability of an individual transitioning to a new state depends only on their current state and not on their history.

To model HLE, a 3-state illness-death model is used, containing transitions between healthy, ill, and dead states (**Figure 2**). In this example, we ignore recoveries (transitions from the ill state to the healthy state), although other versions of this model allow for these.[13]

Markov models can be regression-based (fitted to longitudinal data on patient health trajectories) or non-regression-based (with transition probabilities based on other sources such as published literature). For regression-based models, the calculation proceeds as follows:

Figure 2. Illustration of multiple state model for estimating healthy life expectancy



1. Estimate the transition probabilities between each pair of states. This can be done using packages such as msm[14] in R which fits a multistate Markov model using maximum likelihood estimation.

2. Construct the survival curve for the healthy state. Here, "survival" refers to staying in the healthy state. The survival curve measures the probability of remaining in the healthy state for a given length of time.

3. Estimate the area under the survival curve. Since HLE is the expected length of time spent in the healthy state, it can be estimated as the area under the survival curve (**Figure 3**), eg, using the *AUC* function in R.

Continuous-time Markov multi-state model

In a continuous-time Markov model, the transitions can occur at any time. For these types of models, steps 2 and 3 can be completed simultaneously in R by using the ELECT package[13] on the msm-fitted model to estimate the area under the survival curve via numerical integration.

Discrete-time Markov multistate model

In a discrete-time Markov model, the transitions can only occur at specific, evenly spaced points in time. In this case, steps 2 and 3 are completed separately and can be implemented outside of R (eg, in a spreadsheet):

- *Choose a starting age x*. The total probability of remaining in the healthy state until age *x*+*n* is the product of the individual probabilities of remaining in the healthy state for each age, from age *x* to age *x*+*n*. Calculating this probability for all terms *n* produces the survival curve for the healthy state from age *x*.

- HLE at age *x* is then estimated by summing these probabilities for all ages greater than or equal to *x*.

Lessons learned

In recent analysis, we have found similar estimates of both life expectancy and HLE when comparing these methods, demonstrating their interoperability and offering flexibility for researchers.[15]

The choice of method should be informed by the available data and purpose of the calculation. The Sullivan method can be applied using more widely collected input data and provides a good estimate of HLE based on the makeup of the population at the time of data collection.

While data requirements are more complex, the Markov multistate models can provide a better estimation of expected health over the lifetime of a cohort based on current mortality and morbidity conditions. A second advantage is that the *msm* package can be used to fit hidden Markov models, which may be relevant if the observed data contain misclassifications of an individual's true state.

Implications for stakeholders

Healthy life expectancy is a vital instrument for evaluating population health, facilitating the assessment of health inequalities across demographic groups—such as those distinguished by geography, deprivation, sex, or ethnicity—and measuring the effectiveness of health interventions, ranging from public policies to medical treatments. The UK government has set out to reduce health inequalities by 2030, and tools like HLE are a way to measure progress and hold them to account. The pharmaceutical industry can also apply these methods to estimate life expectancy and HLE improvements generated by their products (eg, by leveraging clinical trial data).

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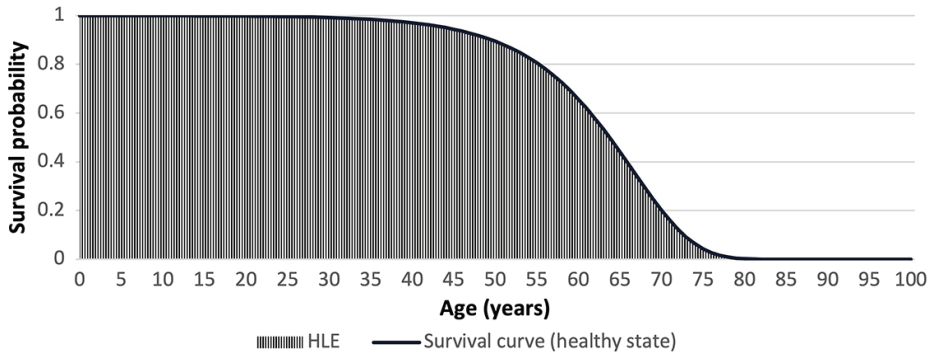
Figure 3. Example survival curve for the healthy state. HLE is the area under the curve



HLE indicates healthy life expectancy.

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How Health Technology Assessments Need to Evolve to Support Health Equity Goals

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Despite increasing ecosystem focus on health equity, health technology assessment (HTA) organizations do not include standardized metrics to assess broader impact from a health equity perspective.

Evolving approaches include recognizing HTA's role in health equity advancement, building legal and conceptual frameworks, addressing data gaps, engaging diverse patients, and diversifying workforces.

Each HTA organization should develop a standardized and locally relevant approach, practice clarity and consistency in health equity goals, reward equity-focused interventions, and consider innovative approaches to data.

Introduction

In recent decades, abundant research has quantified the breadth and impact of observed disparities in health outcomes across race, ethnicity, gender, geography, and other demographic factors. Governments, healthcare providers, payers, and suppliers are increasingly prioritizing addressing the root causes and manifestation of health inequities. In the United States, new regulatory and payment guidelines both reflect and drive this focus. The Centers for Medicare & Medicaid Services, Food and Drug Administration, and the National Committee for Quality Assurance have set forth new requirements related to payment, data and analytics, and research and development (eg, data reporting mandates) that affect payer, provider, and life sciences organizations. These requirements change the direct incentives for greater health equity focus and engagement, and the health ecosystem is honing its focus accordingly to develop action plans to address regulatory requirements. In a survey of 500 health equity executives across provider, payer, life sciences, government, and nonprofit and community organizations, 98% of respondents report expecting health equity's prioritization within their organization to increase or remain the same in the next year.[1] In addition, 92% report expecting financial investments in health equity efforts to rise.[1] As health equity grows in salience across the health ecosystem, greater scrutiny is applied to the clinical and nonclinical factors influencing health outcomes.

> As health equity grows in salience across the health ecosystem, greater scrutiny is applied to the clinical and nonclinical factors influencing health outcomes.

While most health technology assessment (HTA) organizations have well-established clinical and economic metrics and methodologies for measuring the comparative value of new technologies, they largely do not include metrics to assess broader impact from a health equity perspective.[2] The following review of this area provides insights into how HTAs are evolving to consider and potentially reward the broader impact that some new health technologies can have. Incorporating health equity-oriented measures and methodologies into HTAs can provide incentives for greater investment in technologies targeting areas where significant health inequities persist, including access, affordability, and social determinant of health barriers.

Considerations in evolving HTAs to advance health equity goals

While there is broad consistency in HTA methods related to evaluation of clinical and cost impact or effectiveness, consistent representation of health equity-oriented measures has not been achieved. For example, although some HTAs currently include measures related to treatment interaction effect by race, a standardized framework for assessing health equity impact by race does not exist.[2] As health equity prioritization increases overall, stakeholders are exploring how to evolve HTA methodologies to support these broader goals. Through a landscape review of current HTA methodologies developed by the Institute for Clinical and Economic Review (ICER, United States), the Pharmaceutical Benefits Advisory Committee (Australia), the Canadian Agency for Drugs and Technologies in Health (CDA, Canada), the Federal Joint Committee (Germany), and the

> Although some HTAs currently include measures related to treatment interaction effect by race, a standardized framework for assessing health equity impact by race does not exist.

National Institute for Health and Care Excellence (United Kingdom), approaches to health equity measures, including disease disparities, clinical trial diversity, equitable clinical efficacy, implicit bias, and implications for equitable access, were examined. Additionally, a scan of thought leadership and other guidance published by these HTA organizations, research institutions, and other organizations involved in HTAs (eg, patient advocacy groups) was conducted to understand emerging approaches to health equity considerations. The findings from the landscape review of HTA methodologies and scan of emerging practices were summarized, and the following 6 approaches regarding the evolution of HTAs in the context of health equity emerged.

1. Recognize HTAs' role in health equity advancement: To ultimately improve health equity and address disparities, ICER has recommended that HTAs go beyond providing a technical analysis of interventions. As evaluators of these technologies, HTAs are uniquely positioned to understand the settings in which these interventions will be deployed and the impact on communities. With this information, HTAs can shed light on the structural aspects of the healthcare system that are barriers to health equity and identify possible policy interventions.[3]

2. Establish legal frameworks to adjust HTAs: In a guide on establishing HTAs, the World Health Organization recommends that legal frameworks be established that would allow for HTAs to be adjusted to evolving policy and societal changes.[4] This would allow for increased agility in changes to HTAs and pave the way for health equity considerations and other critical healthcare dimensions to be included in HTA methodologies.

3. Develop and align conceptual frameworks for health equity incorporation into HTA: Given the impact of HTAs on patient access and innovations, future evolution of HTA methodologies must support clear, transparent processes and fair decision making, which includes equity considerations. Researchers at the University of Toronto developed a practical tool to identify aspects of health equity across 5 phases of HTAs: scoping, evaluation, recommendations and conclusions, knowledge translation and implementation, and reassessment.[2] This tool has been used by the CDA to incorporate health equity concerns. Governing bodies could leverage similar tools and resources as they examine their HTA methodologies and contemplate which health equity aspects should be included to achieve a conceptual framework grounded in equitable decision making.[5]

> Clear, achievable, and objective health equity goals must be defined so that manufacturers can plan early in product lifecycles, allocate appropriate research budgets, and deliver the required evidence.

4. Identify and address data gaps related to omitted subpopulations: When evaluating the data used in HTAs, organizations should carefully identify any limitations in the data, particularly with regards to underrepresented or omitted subpopulations.[3] This includes establishing thresholds for adequate representation in clinical trials and confirming that the data can capture the heterogeneity and intersectionality of treatment impact. Resources should be identified to fill data gaps prior to conducting a value assessment and appropriate time should be allocated to collect representative data.

5. Engage diverse patient groups: Advisory bodies and researchers are increasingly recognizing the need to directly engage with diverse patient groups and include impacted communities in value assessments, as demonstrated by recent guidance developed by ICER.[3] Additionally, to close data gaps, stakeholders and representatives from groups that have been historically excluded from studies must be consulted to achieve adequate representation of various perspectives across racial and ethnic populations.

6. Diversify the HTA workforce: Representation of diverse backgrounds should go beyond patient engagement efforts and extend to those who do the work of HTA, including diversity in those who award and receive funding. As recommended by the Innovation and Value Initiative, diversity should extend to professional association leaders, journal editors, research sponsors, payers and purchasers, researchers, and patient organizations.[6] A diversified HTA workforce is better positioned to improve HTA equity-oriented practices.

Advancing health equity in HTA practice

The lack of consistent health equity guidance and evaluation frameworks creates uncertainty for manufacturers in where to best invest and what data are critical to optimize access. In order to advance practice and foster bidirectional alignment between payers or HTA organizations and manufacturers, we identified action steps to advance HTA health equity practice informed by our research and lessons learned from working in the field. Measures include involving stakeholders from diverse backgrounds in the assessment process, identifying data gaps and novel data requirements, creating equity-focused criteria to evaluate technologies, providing a platform to highlight structural aspects necessary to achieve optimal and equitable outcomes, and creating standardization to provide clarity and consistency in approaches.

1. Develop a standardized approach: Despite the growing recognition of the importance of health equity in HTAs, a globally accepted, validated approach to incorporating it is yet to be identified and implemented. Efforts should be made to standardize guidelines, parameters, and metrics specific to health equity in HTAs, enabling manufacturers to develop a unified health equity approach and invest in health equity-oriented products and data.

2. Practice clarity and consistency in health equity goals: Clear, achievable, and objective health equity goals must be defined so that manufacturers can plan early in product life cycles, allocate appropriate research budgets, and deliver the required evidence. In designing these health equity goals,

governing bodies and HTA entities must translate broad health equity concepts and create concrete, measurable goals for which manufacturers can collect data.

3. Reward equity-focused interventions: Governing bodies and decision makers could reward or prioritize interventions that improve health equity and discourage those that exacerbate health inequities. Interventions that improve health equity could be incentivized in the form of less restrictive access or better pricing. For example, increasing the acceptable cost per quality-adjusted life year or the budget impact threshold could be considered for therapies that provide data related to improvements in health equity outcomes. Interventions that exacerbate health inequities could be disincentivized with reduced access or tougher price negotiations, especially in crowded therapeutic areas where there are alternate options.

4. Consider innovative approaches to data: HTA organizations and payers should consider accepting innovative ways of demonstrating impact on underserved populations, including the use of new data and metrics, real-world evidence, and advanced modeling techniques that can quantify potential differentiated impact on underserved and marginalized populations.

Conclusion

There is a clear opportunity to update HTA methodologies to holistically consider health equity enablers and address systematic disparity drivers. More work is needed to mobilize HTA stakeholders (eg, professional societies and trade associations focused on health economics and/or HTA practice, manufacturers, researchers, payers, and providers) and align on core health equity objectives. Variability in health equity goals exists by market, with some focused more on racial or ethnic populations, while others are more focused on economic or geographic disparities. Evolving HTA methodologies to reflect the social, cultural, and ethical goals of the health system overall is critical. While consistency in overall approach is recommended, specific application within each market or HTA organization is likely required. Additional research and investment are needed to identify leading practice methodologies and align goals. Future efforts should include participation and perspectives from HTA entities, professional associations, research sponsors, payers and purchasers, researchers, and the communities of patients being served. Together, these diverse stakeholders can align on a realistic, actionable path forward to close disparities and achieve health equity.

The views reflected in this article are the views of the authors and do not necessarily reflect the views of Ernst & Young LLP or other members of the global EY organization.

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Q&A

Interview With Lionel Collet:
President, Haute Autorité de Santé, France

Lionel Collet, president of France's Haute Autorité de Santé (HAS), explains the role of the independent public authority, which extends beyond health technology assessment (HTA) to clinical practice guidelines and certifying hospitals, and its unique position as a separate body outside of the Ministry of Health. He describes France's early access procedure under which HAS has evaluated 200 products during the past 2 years, accepting 80%, weighs in on the move to introduce EU-wide HTA legislation in 2025, and outlines HAS's goal of addressing the complexities of mental health in its next strategic plan leading up to 2030.

"Maintaining independence is paramount because we must never be beholden, in any way, to either industry interests or governmental influence."

– Lionel Collet

PharmaBoardroom: Could you elaborate on the unique role and responsibilities of the Haute Autorité de Santé (HAS) compared to similar bodies in other countries?
Lionel Collet: When I stepped into my role at the HAS one year ago, it became apparent that the agency's scope and functions are quite distinct from other healthcare assessment bodies, particularly in comparison to traditional health technology assessment (HTA) agencies. Not solely focusing on HTA, HAS encompasses a broader spectrum of responsibilities. Yes, evaluating healthcare technologies for regulatory purposes, particularly for reimbursement, is a significant aspect of our work, but it is not the only facet. For example, we also engage in developing clinical practice guidelines and certifying healthcare facilities.

These core missions were established back in 2004 through legislation governing healthcare insurance. HAS holds a unique institutional setup in France as a public independent authority, distinct from being just another health agency, while my role as president is directly appointed by the President of the Republic. This means that once appointed, the president and members of the institution, including myself, operate independently from executive authority. Each member of the college, which comprises 8 members including the president, is appointed, and our 6-year mandates are irrevocable, ensuring our autonomy in decision making.

This setup is vital to safeguarding the impartiality and integrity of our decisions. Moreover, in France, laws dictate that members of such independent authorities cannot seek or receive instructions from any other authority, including the government ministry. Thus, our status remains entirely separate from the Ministry of Health, ensuring autonomy and impartiality in our assessments and recommendations. It is crucial to understand this distinction, as in France, there are only 8 such independent public authorities, with HAS being the sole representative within the healthcare sector. This aspect of HAS's institutional framework was certainly surprising and noteworthy to me upon assuming my role.

PB: Why is it essential for organizations like yours to maintain independence in carrying out your tasks?
LC: Maintaining independence is paramount because we must never be beholden, in any way, to either industry interests or governmental influence. When our primary goal is determining reimbursement, we must ensure that our assessments, particularly regarding a medication's therapeutic value, remain unassailable against anything other than scientific criteria.

Independence ensures that our focus remains steadfastly scientific in assessing technologies and medications for the benefit of all. Here, scientific integrity is one of our core values. Upon my arrival, I witnessed first-hand the caliber of individuals within the institution. While our team of 450 staff members is substantial, it is not extensive considering the scope of responsibilities, especially concerning hospital visits and the diverse array of tasks we undertake. Despite this, our institution remains remarkably efficient.

> It is striking to note that mental health surpasses even cancer and cardiovascular diseases combined in terms of healthcare insurance expenditure, highlighting the critical need to address mental health issues.

An important observation is that many French citizens are unaware of the significant contributions we make to their lives. When someone takes a reimbursed medication or benefits from early access to an innovative treatment, it is because of our evaluations. Similarly, when a patient receives optimal care from their physician, it is often guided by our clinical practice recommendations. We directly impact the daily lives of French citizens; a responsibility we take very seriously.

PB: As HAS's 2024 strategic plan draws to a close, what are the main aims of the organization's next strategic plan up to 2030?
LC: Upon assuming my role, one of our primary focuses has been developing a strategic plan for the upcoming 5 years. While the specifics are still in development, one certainty is our commitment to fostering innovation and maintaining our capacity to assess emerging technologies. However, I hope that within this strategic plan, we can pinpoint a particular area where France, and by extension HAS, must take a stance.

In our current deliberations, a central focus is on the state of mental health and psychiatry within France's healthcare system. It is striking to note that mental health surpasses even cancer and cardiovascular diseases combined in terms of healthcare insurance expenditure, highlighting the critical need to address mental health issues. Despite its significant impact, mental health remains somewhat taboo, contributing to disparities in healthcare outcomes. Individuals with mental illness face a shortened life expectancy, partly due to delayed diagnoses.

Addressing these complexities is a key priority for HAS, entailing the development of clinical guidelines, promoting appropriate medication usage, and evaluating mental health care across healthcare and social service settings. However, mental health faces unique challenges, including the absence of biomarkers and the type of ground-breaking therapeutic advancements seen in other medical fields. While there have been some advancements, such as serotonin reuptake inhibitors, significant innovation has been lacking for decades. This poses a challenge for HAS in evaluating truly innovative medications in psychiatry. Nevertheless, there is optimism regarding the evolving landscape, with discussions underway about potential biomarkers for bipolar depression, hinting at the possibility of future therapeutic progress in the field.

PB: French patients must wait an average of 443 days between a drug achieving regulatory approval and being made available, according to IQVIA's WAIT Indicator. This puts it far behind not only the likes of Germany (47 days) and Switzerland (148) but also Bosnia (262), North Macedonia (305), and Albania (376). What do you see as the root cause of this issue and how can stakeholders come together to improve it?
LC: We must be clear here; the WAIT Indicator alludes to the time elapsed between a product receiving market authorization and its subsequent reimbursement. Essentially, it signifies the duration of the evaluation process. Regarding this, France stands out positively within Europe.

If we analyze the time from market authorization to completion of HTA, France typically takes around 187 days, whereas Germany requires 221 days. If we are looking at the time taken for early access, the same is true: the average assessment takes around 77 days in France, which is faster than the legal requirement of 90 days.

Even when considering all medications and not just innovations, France tends to evaluate medications swiftly. It is crucial to note that the mere issuance of market authorization does not guarantee a product's availability in the market. There are instances where despite having authorization, products are not introduced due to various reasons.

Firstly, the medication's therapeutic value might be deemed insufficient by our assessment. Secondly, there could be prolonged negotiations regarding pricing between pharmaceutical companies and the relevant authorities, which may delay or even prevent the product's market entry.

Therefore, when interpreting French data, it is essential to focus on the moment when HAS provides its evaluation. Subsequently, market availability depends significantly on the actions and decisions of pharmaceutical companies.

PB: What is your view on the gap between the assessments conducted by HTA bodies in Europe and the availability of those medicines under conditional reimbursement?
LC: In France, we have a procedure called "early access to medicines." This law has been in place since 2021, but previously, there was another mechanism known as Temporary

Authorization for Use (ATU), to simplify matters. Over the past 2 years, we have evaluated over 200 products under the early access scheme, which are presumed to be true innovations. We have accepted 80% of these products. The remaining 20% were not accepted because they did not meet all the criteria. The criteria are very precise. Therefore, if a pharmaceutical company has a genuine innovation and applies for early access in France, meeting the criteria 4 out of 5 times, it means that immediately afterward, the product can be available at the industry's price, as pricing negotiations occur later. This is crucial to remember.

> The quality of real-world data, often derived from cohorts or registries, presents challenges. However, last year, the HAS and the transparency commission addressed these concerns, clarifying their position on alternative study designs.

So, firstly, HTAs do not hinder innovation. Secondly, they expedite patient access to innovation. I am not critical at all. I believe our American friends have other reasons for not wanting to adopt similar measures.

PB: When assessing medication efficacy, how do you address the challenge of conducting studies with real-world data?
LC: Real-world data is an area of significant focus, particularly in post-approval studies conducted after drugs have been evaluated. One of our primary concerns with real-world data studies is their often-inadequate scientific robustness. These data lack the comparative purpose we seek, which poses limitations. However, the evaluation doctrine, known as the transparency committee doctrine, evolved in February 2023 to allow for departures from traditional protocols, such as randomized studies, to permit indirect comparisons.

Quality remains a crucial criterion in these evaluations, and many studies lack the necessary standards. The quality of real-world data, often derived from cohorts or registries, presents challenges. However, last year, the HAS and the transparency commission addressed these concerns, clarifying their position on alternative study designs. Subsequently, a case involving a drug prompted a reevaluation, resulting in a shift from a ASMR5 to a ASMR4 rating, Essentially, the drug was reevaluated positively based on real-world data, this underscores the ongoing importance of robust evaluation practices amidst evolving methodologies.

PB: The move to EU-wide HTA legislation in 2025 has been described as positive for the bloc's smaller countries that were short of capabilities in this area, but potentially an added layer of bureaucracy for larger countries with well-established frameworks like France. What is HAS's take on the challenges and opportunities of this new legislation?
LC: The 2021 European Regulation, effective from January 1st, particularly focuses on oncology medications and innovative therapies, raising questions about potential duplications in evaluation processes. While the regulation explicitly states that the Common Clinical Assessment (CCA) at the European level should not be replicated by individual countries, exceptions may arise if additional compelling data surfaces between the CCA and national evaluations, warranting supplementary analysis rather than a complete redo. However, our involvement may be necessary for medical-economic evaluations, though we will not duplicate the entire process. France is expected to participate in assessing these submissions, each requiring two evaluators to draft the document.

Although the evaluation criteria, currently undergoing public consultation, may delve deeper than our current practices, concerns linger about the need for increased resources and potential delays in other areas, particularly routine medication evaluations. Despite these challenges, the European regulation offers a positive step towards standardizing scientific review processes across member states, while ensuring each country maintains autonomy over reimbursement decisions based on its own evaluation criteria.

Also, I strongly believe France has a crucial role to play in shaping the future of European healthcare, especially in ensuring a comprehensive and holistic approach to healthcare evaluation and regulation. At the heart of this endeavor lies our agency's commitment to providing expertise that promotes patient-centricity, transparency, and excellence in healthcare standards.

Within the framework of European regulations, such as the coordination group outlined in the recent legislation, our agency actively participates to ensure that France's perspectives and priorities are represented. This includes involvement in subgroups focusing on critical aspects like common clinical evaluation methods, where our agency contributes expertise and insights.

> I strongly believe France has a crucial role to play in shaping the future of European healthcare, especially in ensuring a comprehensive and holistic approach to healthcare evaluation and regulation.

The overarching goal is to foster a unified vision of health technology assessment across Europe, recognizing that health challenges transcend national borders. While advocating for a Europe-wide approach, we remain mindful of maintaining the sovereignty of national healthcare systems, allowing for flexibility tailored to each country's unique needs and circumstances.

PB: When we interviewed your predecessor, she discussed some of the strains on the French healthcare system. What are your thoughts on this matter?
LC: Like many countries worldwide, we are grappling with a shortage of healthcare professionals. However, our challenges

extend beyond staffing issues. The escalating costs of healthcare, a trend mirrored in France since the establishment of health insurance post-World War II, underscore the financial strain on our system. In France, safeguarding health is enshrined as a constitutional principle, reflecting our commitment to national solidarity. Yet, this solidarity comes with a price tag, as the expenses associated with medical products and treatments continue to soar.

> With a considerable budget, our role is not to drive down prices for industry, but to discern what deserves funding.

In this context, the sustainability of our healthcare system is a pressing concern for the future. As an indirect player in this arena, our evaluations play a crucial role in determining the scope of coverage provided by our system of national solidarity. Through rigorous assessments, we strive to navigate the complexities of healthcare expenditure, ensuring that our resources are allocated effectively to support the health needs of our population.

PB: When you mention certification of hospitals, do you evaluate the public and private sectors? And how do these evaluations differ between the public and private healthcare sectors?
LC: Our evaluations are grounded in a comprehensive set of criteria aimed at assessing the quality of healthcare services and ensuring patient safety and dignity. These criteria, numbering over 130 in our reference framework, cover 3 main domains: patient-centered, healthcare professional-centered, and facility-centered aspects. Regardless of whether the institution is public or private, the evaluation process remains consistent, emphasizing uniform standards across the healthcare landscape.

Upon evaluation, institutions are certified based on their fulfilment of these criteria, with the possibility of receiving commendations or recommendations for improvement. However, the ultimate decision regarding certification status lies with the public authorities, who determine the allocation of resources based on the evaluation outcomes.

While certification may confer certain benefits, the exact implications may vary and are subject to government policies and priorities. Ideally, certification serves as an incentive for institutions to strive for excellence and continuous improvement in healthcare delivery.

PB: Many perceive France as having one of the finest healthcare systems worldwide. It is often seen as a model where everything is covered. Where do you believe France stands today?
LC: In my view, the French are fortunate to have such an excellent healthcare system. Unlike Americans or some British citizens who may struggle to afford treatments, in France, accessibility is relatively high. Even medications priced at €300,000 to €400,000, are accessible if needed.

However, despite occasional complaints from the French about the system, it is imperative to maintain its quality. This entails ensuring well-equipped facilities and trained professionals. While optimism exists about overcoming challenges, securing adequate financial resources is crucial. With a considerable budget, our role is not to drive down prices for industry, but to discern what deserves funding.

PB: Is there any message you would like to convey to your colleagues in Europe, the United States, and worldwide regarding your work, considering the emerging interest in HTA and healthcare system reforms?
LC: Firstly, at the European level, it is essential to highlight the valuable collaboration within the Head Agency Groups (HAG), where presidents of HAS and other HTAs from across Europe convene. As the co-chairman, alongside the Portuguese president and Swedish co-chairman, we engage in monthly video meetings, fostering continuous communication and exchange. Strengthening ties among all HTAs across Europe while maintaining independence is crucial, especially with upcoming regulations. We must enhance understanding of each other's practices and initiatives.

Regarding countries in the South, we have a unique opportunity to assist in the implementation of HTA frameworks. Collaborating with Southern and Middle Eastern countries, we aim to support their HTA efforts, recognizing the global significance of this endeavor. This is not solely a French concern but of global interest.

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