NOVEMBER/DECEMBER 2024 VOL. 10, NO. 6

VALUE & OUTCOMES SPOTLIGHT

A magazine for the global HEOR community.

MEASURING VALUE

THE QALY TURNS 50: & WHAT HAS IT ACHIEVED WHAT IS ITS FUTURE?

ISPOR
Improving healthcare decisions

VALUE & OUTCOMES SPOTLIGHT

NOVEMBER/DECEMBER 2024
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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.

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Value Assessments: Are We There Yet?

In a value-driven healthcare system, value assessments can be used as a tool to evaluate and measure the value of healthcare interventions, treatments, and services. In this issue of *Value & Outcomes Spotlight*, the feature article by John Watkins, PharmD, MPH, BCPS, provides an excellent and comprehensive overview of the quality-adjusted life-year (QALY) and covers both strengths and weaknesses of the traditional QALY approach as well as the proposed enhancements being applied. I have highlighted some of the key insights below.

The Role of QALYs in Healthcare Decision Making

Over the past 5 decades, the QALY has served as a key metric in cost-effectiveness analysis within healthcare. It provides a standardized approach for evaluating the benefits of medical interventions by comparing the years of life that would be added by the intervention, adjusted for the quality of those years. The QALY seeks to quantify health outcomes by integrating both the quantity and quality of life into a singular measure, facilitating comparisons across diverse medical treatments and conditions. This capability allows payers, policy makers, and clinicians to make more informed decisions regarding the allocation of limited healthcare resources.

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Torbica and colleagues highlighted that the use of QALYs in formal decisions mainly occurs in Europe where there is extensive use in some countries like the United Kingdom. France and Germany are different from the rest of Europe as they do not formally use QALYs. Instead, they rely on evidence of incremental net clinical benefit to score a new drug and use these ratings in price negotiations with manufacturers. However, in cases where a manufacturer claims its drug is innovative, France may request cost per QALY studies. In Germany, an economic evaluation can be conducted if there is no agreement on price in the first year the drug is on the market.

Conversely, there are countries that are low utilizers (ie, the United States) where the use of QALYs is less prominent in formal decision making due to regulatory constraints and the nation's emphasis on individual autonomy. The US experience underscores significant historical, cultural, and institutional variations impacting QALY adoption and points to factors such as social values and administrative traditions influencing the use of economic evaluation in healthcare.

Facing the Criticisms and Limitations

Despite its utility and benefits of broad applicability to compare across treatments and interventions, the QALY framework is not without criticism. Critics argue that the QALY has limitations of not being patient-centric, which can lead to potential discrimination against certain patient populations such as older adults, individuals with disabilities, and those with chronic life-limiting conditions and rare diseases. By relying on average population perceptions, the QALY might devalue specific lives by not accurately capturing individual patient experiences, which can undermine the sensitivity of QALYs to personalized healthcare needs. Furthermore, the use of QALY thresholds in decision making, such as coverage limits in healthcare, introduces potential barriers to access. This raises ethical concerns about equity, as value thresholds do not always reflect the nuanced realities of individual health priorities and societal willingness to pay for healthcare advancements. For these reasons, QALYs should not be used in making individual patient-level decisions.

Exploring Alternative Measures
In response to these challenges, alternative metrics have emerged. The Equal Value of Life Years Gained (EVLY) and Health Years in Total (HYT) attempt to address some discriminatory limitations inherent in QALYs. EVLY assigns equal weight to life-years gained, irrespective of underlying health state, aiming to reduce age and disability bias. HYT separates changes in quality of life and life expectancy, which enhances the discrimination implications and aligns with additive health outcomes. Additionally, the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) framework seeks to address the broader impacts and preferences related to health interventions, incorporating dimensions like "mental insurance value" and potential peace of mind derived from available treatments.

The Future Outlook on QALYs
As we reflect on decades of QALY usage, we must examine its achievements and limitations and consider what the future holds for this influential tool in assessing health outcomes. As health systems around the world grapple with rising costs and increasing healthcare demands, the role of QALYs as a measurement tool will undeniably evolve. For some countries, particularly those with pluralistic health systems like the United States, formal adoption of QALYs in policy remains complex. However, there is significant value in considering QALYs as part of a multifaceted toolkit for healthcare decision making.

As health systems around the world grapple with rising costs and increasing healthcare demands, the role of QALYs as a measurement tool will undeniably evolve.

The future of QALYs may lie in its ability to adapt and integrate new dimensions of value that reflect both individual and societal health priorities. Organizations such as ISPOR are instrumental in fostering these discussions. The ISPOR "value flower" seeks to expand beyond traditional QALYs by incorporating holistic perspectives, potentially aligning metrics like QALYs with legal and regulatory requirements while addressing criticisms of bias and lack of individual customization.

Ultimately, the legacy and future of QALYs hinge on distinctive approaches encompassing multiple viewpoints, aiming to reflect diverse healthcare values. As each region tailors its use of cost-effectiveness measures, ISPOR and similar entities provide a platform for exchanging ideas and encouraging international collaboration to enrich health outcomes measurement. Through adaptive methodologies, like GRACE and others, QALYs are poised to stand the test of time, offering valuable insights into the optimal allocation of scarce healthcare resources across the globe.

So back to the question on value assessments—are we there yet? No, we're not there yet, but I'm confident that we will keep moving toward the eventual goal of reflecting value in the richest, most nuanced way possible.

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

What Is This Thing Called Value?

Rob Abbott, CEO & Executive Director, ISPOR

Economists love to talk about value. The entire field of welfare economics is premised on the belief that the behavior of individuals (and firms) regarding the allocation of scarce resources can be accurately modeled to divine the overall well-being of a society. In health economics, techniques such as cost-effectiveness analysis (CEA) are used to assess the value of a new drug or therapeutic intervention. And of course, the quality-adjusted life-year (QALY) is a key arrow in the health economist's metaphorical quiver to measure the effectiveness of healthcare interventions, even if it is oft-maligned.

> The point here is to be careful about the underlying assumptions that inform our work, and to get as close to the customer (or patient) as you can to better understand what they value in their therapeutic journey.

The only problem, or caution, here is that value in the real world is often much more nuanced and difficult to measure than we would like to admit. Peter Drucker, one of the great management theorists of the 20th century, frequently said that the needs, wants, and aspirations of customers were so complicated that they could only be answered by customers themselves. As an example, he famously described a homeless shelter, where the received wisdom about value was defined as nutritious meals and clean beds. In fact, as interviews with the shelter's homeless customers revealed, while the food and beds were appreciated, they did little or nothing to satisfy deep aspirations not to be homeless. The customers said, "We need a place of safety from which to rebuild our lives." The shelter threw out their assumptions and rules and began to work with individuals to find out what a rebuilt life means to them and how they can be helped to realize their goal. The point here is to be careful about the underlying assumptions that inform our work, and to get as close to the customer (or patient) as you can to better understand what *they* value in their therapeutic journey.

With the above context, I'm excited to introduce this issue of *Value & Outcomes Spotlight* that focuses on value assessment, and the QALY in particular. Value assessment is an evolving field that strives to assist policy makers in making decisions about which health services—drug, device, surgery, and so on—should be reimbursed and at what level. This is especially important as healthcare systems move away from traditional fee-for-service to value-based arrangements. To make it even more complicated, there is no singular approach to assessment and value definition that consistently meets the needs of all stakeholders. Payers, for example, think about value differently than patients. The former are particularly interested in managing or containing overall expenditures and demonstrating value for money, whereas the latter are interested in accessing treatments that will improve their lives both quantitatively and qualitatively. As noted earlier, the QALY is not without its critics. The *Affordable Care Act* in the United States even prohibits the Patient-Centered Outcomes Research Institute from using cost-per-QALY benchmarks. The use of QALYs by policy makers, in the United States and elsewhere, to inform coverage and reimbursement decisions is controversial. Still, there are limits to what any society can sustainably spend on healthcare, and it is useful, perhaps even vital, to gain as much insight as possible on both the quantity and quality of life that different treatment options offer patients.

So, how to move forward?

As the papers in this issue of *Value & Outcomes Spotlight* make clear, a standard measure of health outcomes that enables comparisons across different disease areas and populations is a good thing. So too, with the valuation of health states in utility measurement. The QALY is a de facto standard in this regard, but it is not perfect. We therefore need to take a clear-eyed view of it (and other assessment approaches) as underlying assumptions about social value, for instance, can result in an inequitable weighting of outcomes. Further, the quality of the data used in calculating a QALY must be high to ensure that the resulting value statements are reliable. The range of costs that are typically considered in a QALY can also be a limiting factor.

> There are limits to what any society can sustainably spend on healthcare, and it is useful, perhaps even vital, to gain as much insight as possible on both the quantity and quality of life that different treatment options offer patients.

It is perhaps most appropriate to take a step back from the QALY in and of itself and consider the broader issue of value assessment and the guiding principles that should inform any approach to try to define value. As my colleague, Peter Neumann, has pointed out, value assessment in healthcare has typically focused on pharmaceuticals rather than services and procedures, even though the latter comprise roughly 70% of health spending in the United States (versus 15% for drugs). This suggests that at a meta level, there is abundant room to apply value assessment in different areas and, in so doing, achieve broad system efficiency and affordability. As to some of the principles that might inform a refreshed approach to assessment, whether directed at drugs or services, it cannot be stressed enough the importance of gathering stakeholder

(patient, payer, and other) input throughout the assessment process. This is foundational to any exercise that seeks an accurate definition of value. Building on this, the assessment should include all aspects of the healthcare ecosystem, not simply the drug or therapy. Similarly, a broad approach should be taken to evaluating benefits and costs, and these should be considered over a long-term horizon. Finally, any value assessment should use all available evidence to inform the value decision.

ISPOR's new 2030 strategy includes a specific goal to "lead the definition, measurement and use of value for health and healthcare decision making". Supporting this goal are strategic objectives directed at refining the definition of value to explicitly reflect the emerging concept of whole health; to identify, create, and advance approaches to improve the measurement and use of value; and to drive the integration of affordability, accessibility, and equity in value-based decision making. As such, the papers collected in this issue of *Value & Outcomes Spotlight* are especially meaningful to me as we seek to grow our knowledge of the

> It is perhaps most appropriate to take a step back from the QALY and consider the broader issue of value assessment and the guiding principles that should inform any approach to try and define value.

shape of current thought on value assessment. As ISPOR CEO, I feel both a great responsibility and an opportunity to step onto this intellectual frontier and signal to our members and other stakeholders that we are actively shaping the conversation about value—something that lies at the heart of all economic decisions.

Conference Sessions Bold and Bustling in Barcelona

Photos by Christian Dusek

The ISPOR Europe 2024 conference broke all attendance records, drawing more than 6400 registrants from 120+ countries to Barcelona, Spain on November 17th-20th. The conference theme, "Generating Evidence Toward Health and Well-Being," explored the importance of scientific evidence in understanding and improving the health and well-being of people across the globe.

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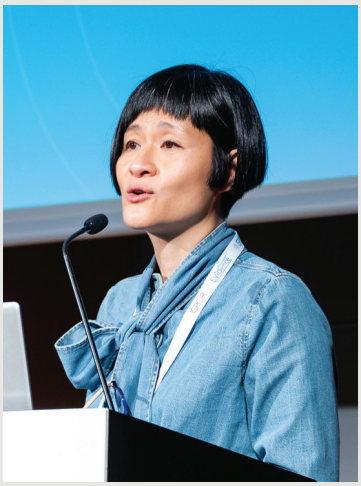


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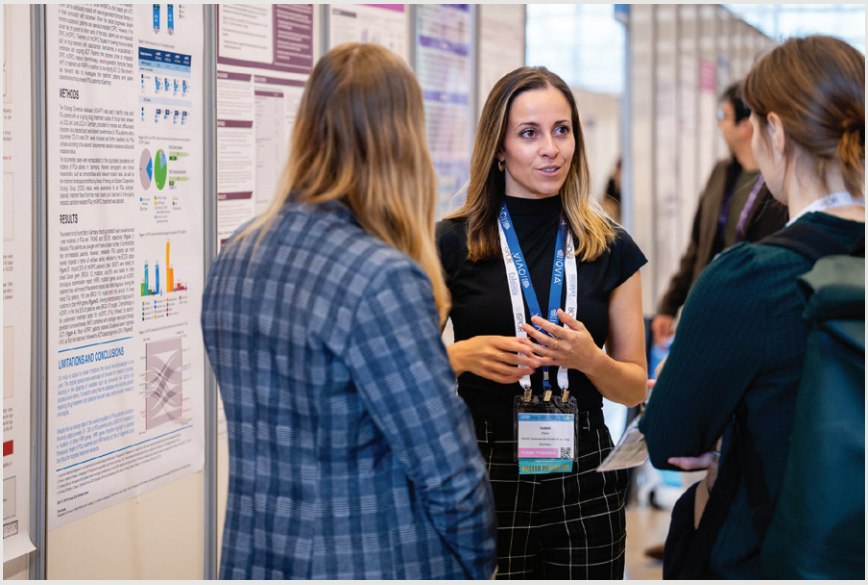


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In this edition of Methods Explained we are covering value of information analysis (VOI) based on a conversation with 2 international experts on the topic, Saskia Knies and Natalia Kunst. Saskia Knies, PhD, is coordinating advisor at the National Health Care Institute in The Netherlands (Zorginstituut Nederland), which is the first health technology assessment agency in the world to mandate VOI in its guidelines, and a member of the ISPOR Task Force on VOI. Natalia Kunst, PhD, is senior research fellow (associate professor) at the Centre for Health Economics of the University of York, co-founder of the Collaborative Network for VOI, and author and editor of several publications on VOI.

Value of Information Analysis

Section Editor: **Koen Degeling, PhD**

What is the objective of VOI and what can it be used for?
VOI comprises a toolbox of analyses and metrics that can be used to provide a range of insights. Their aim is to achieve improved health outcomes at the same or lower costs through improving resource allocation decisions, eg, whether a new healthcare intervention should be reimbursed or not. These analyses quantify the uncertainty in such decisions and provide an understanding of the consequences of making a particular decision given the information at hand and of the value of performing further research before making the decision. Within the field of health economics and outcomes research (HEOR), VOI is typically performed using decision-analytic models as part of health technology assessments, such as cost-effectiveness models or other types of health economic models.

Given the uncertainty in the model parameters that arises from the evidence used, VOI determines the probability that the best decision according to the model turns out to be suboptimal when more evidence would be available, and estimates what the consequences are of making the wrong decision. A consequence can be that patients receive a suboptimal treatment, which can either be a less effective treatment or a cost-ineffective treatment.

These insights can be used as a type of sensitivity or uncertainty analysis to improve the understanding of a decision-analytic model by providing information on the drivers of uncertainty and whether those uncertainties have an impact on the decision. Ultimately, insights from VOI are used for research prioritization, ranking the value of proposed studies, and informing stop–go decisions. They can also inform the optimal design of future research studies.

In this issue of Methods Explained, we focus on the 2 most used VOI metrics: (1) the expected value of perfect information (EVPI), and (2) the expected value of perfect parameter information (EVPPI, also known as expected value of partially perfect information). The EVPI and EVPPI provide insight into the total amount of uncertainty and how that impacts the decision, and which parameters contribute most to this uncertainty.

On a high level, how does VOI work?
Although VOI is mostly applied in model-based health economic analyses, it can theoretically also be applied in data-driven studies, such as trial-based cost-effectiveness analyses. VOI takes the uncertainty from evidence used to populate the decision-analytic model and analyzes what the probability is that the wrong decision is made based on the model outcomes, and what the consequences of making the wrong decision are. These consequences are typically quantified in terms of health or monetary outcomes, such as the net health benefit or net monetary benefit. These outcomes are then extrapolated to the relevant (patient) population over a certain time horizon. The decision maker must interpret those findings and determine whether they are comfortable making the decision based on the current evidence or whether further research needs to be performed. This can assist in making the trade-off between making the decision with (potentially high) uncertainty or reducing this uncertainty through further research, as well as the resources required to do so.

For example, based on a given willingness-to-pay threshold per quality-adjusted life year gained, the EVPI may be $2 million for a given patient population over a 5-year period. This suggests that the decision maker may choose to delay the decision if they believe that all the uncertainty in the decision can be negated through further research that costs less than $2 million. However, it is typically not feasible to conduct research that collects enough evidence to negate the uncertainty in all model parameters. Rather, a particular research study would reduce the uncertainty in only specific parameters. To that end, an EVPPI analysis can be used to investigate which parameter or group of parameters contributes most to the uncertainty in the decision. In the example, it could be that an EVPPI of $1.5 million is found for the parameters on overall survival of the intervention and comparator treatments. In other words, the value of reducing the decision uncertainty by collecting perfect information on the overall survival parameters is $1.5 million.

If it is considered feasible to negate this uncertainty in the decision for that budget, additional VOI analyses should be

performed to determine whether further research is indeed worthwhile and what the optimal study design is. This can be done by estimating the expected value of sample information and the expected net benefit of sampling.

What makes VOI different from other types of sensitivity and uncertainty analyses?

VOI is a decision-analytic method that can be described as an uncertainty analysis. While there are other sensitivity and uncertainty analyses that are well-known and often conducted as part of an economic analysis, such as one-way sensitivity analysis and probabilistic analysis (also referred to as probabilistic sensitivity analysis), there is a notable difference between these methods. A one-way sensitivity analysis provides insights into the impact of uncertainty in specific parameter(s) on the model outcomes. Probabilistic analysis is an uncertainty analysis that helps propagate uncertainty from the model input parameters to the outcomes of the model. The results of a probabilistic analysis can be used to assess the probability of cost-effectiveness for the decision options considered. VOI gives insight into uncertainty in the decision and the impact of specific parameters on this *decision uncertainty*. This is a fundamental difference, because even if outcomes are highly uncertain, there may be no uncertainty in the decision if the complete range of outcomes suggest one decision alternative is optimal (or not).

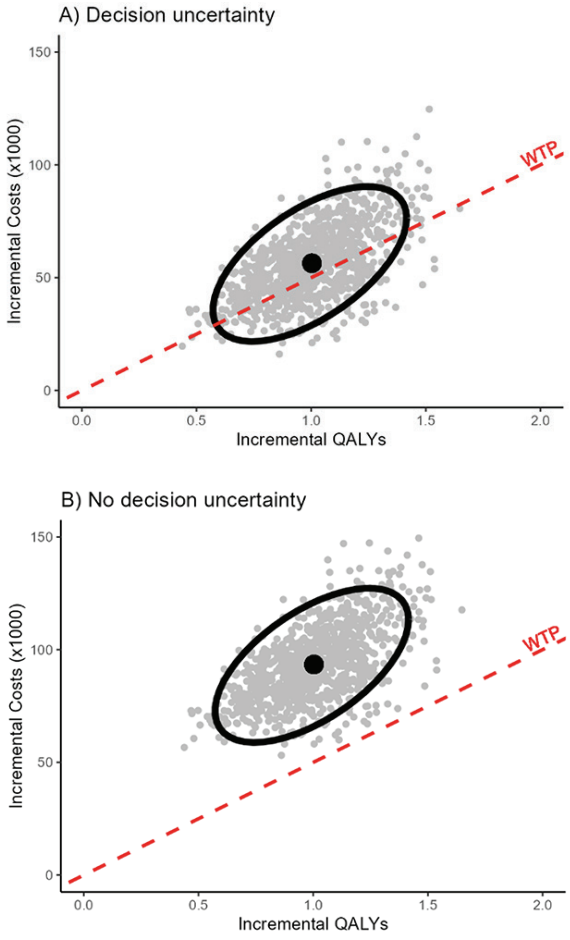
The difference between uncertainty in outcomes and decision uncertainty can be illustrated using the incremental cost-effectiveness planes presented in **Figure 1**. This figure shows 2 scenarios for a hypothetical cost-effectiveness analysis of a novel intervention Treatment A compared to Treatment B. Both scenarios presented in Figure 1 have the same amount of uncertainty in the outcomes, as demonstrated by the spread of the probabilistic analysis iterations (gray points) and corresponding confidence interval (black ellipse). There is substantial decision uncertainty in the left plot (**Figure 1A**) because the point estimate (black dot) suggests that Treatment A is not cost-effective and many iterations (gray points) are located above the willingness-to-pay threshold, but a substantial number of iterations suggest it may actually be cost-effective (a meaningful number of gray points are below the willingness-to-pay threshold). In the right plot (**Figure 1B**), however, there is no decision uncertainty because all iterations are located above the willingness-to-pay threshold, indicating that intervention Treatment A is not cost-effective.

This example illustrates that a probabilistic analysis only gives insights into the uncertainty around the outcomes and the probability of being cost-effective, whereas VOI quantifies the decision uncertainty and, therefore, is an important extension. Additionally, sensitivity analyses and probabilistic analyses do not give insights into the consequences of making the wrong decision, whereas VOI does quantify this impact on the net outcomes.

What steps are involved in performing VOI?

The reports of the ISPOR Task Force on VOI give an excellent overview of the steps involved with performing the different VOI analyses.[1,2] In summary, a prerequisite to perform VOI is a clearly defined decision problem and a health economic model

Figure 1. Incremental cost-effectiveness planes illustrating how the same amount of uncertainty in the outcomes can result in (A) substantial decision uncertainty and (B) no decision uncertainty, where the gray points represent the iterations of the probabilistic analysis, the black dot the mean outcomes, the black line the 95% confidence interval around that estimate, and the red dashed line the willingness to pay per quality-adjusted life year gained.



that is considered appropriate to inform decision making. A probabilistic analysis needs to be performed, including the assignment of appropriate probability distributions that describe the uncertainty in the model parameter values. The EVPI per patient can be calculated directly from the output of a probabilistic analysis and, hence, does not require additional analyses than typically performed. The EVPI per patient should be extrapolated to the total patient population over a specific time horizon.

The EVPPI can be obtained through a double-loop Monte Carlo simulation. This is comparable to performing a probabilistic analysis a few hundred or a thousand times, which can be computationally demanding and is not always feasible. Therefore, several approximation techniques have been developed to estimate the EVPPI based on the output of a standard probabilistic analysis. An example of this is the Sheffield Accelerated Value of Information tool.[3]

To what extent have these methods been used in practice?
Performing probabilistic analysis has become standard practice due to increased awareness and increases in computational power. As a logical extension of probabilistic analysis and due to the availability of guidance and increased awareness, the uptake of VOI has been increasing. Although initial applications have mostly been academic, a wealth of practical applications can nowadays be found in literature.

A key facilitator for the uptake of methods within the field of HEOR is inclusion in health economic evaluation guidelines. Therefore, an important milestone in the adoption of VOI is the inclusion of the EVPI and EVPPI as mandatory analyses in the 2024 update to the guidelines of the National Health Care Institute in The Netherlands.[4] With this, the number of VOI analyses and consideration thereof in reimbursement decisions is expected to increase.

What are the remaining challenges in the adoption of VOI?
There are clear guidelines and practical examples that explain how VOI can be performed, although the HEOR community may not yet be familiar with the methods, what they can do, and how valuable the results can be.

An important challenge in the adoption of VOI likely is the interpretation of the results, as it may not be possible to clearly define what EVPI or EVPPI values are acceptable or when a decision may be delayed. Decision makers need to consider the results of VOI in the totality of information that is available to them, but this may be considered somewhat subjective in a context where consequences are high.

A frequently asked question is whether it is worthwhile to perform VOI if there is little uncertainty in the outcomes of the health economic analysis. The perception that performing VOI is only relevant when there is a large amount of uncertainty may also hamper the uptake. However, this is not necessarily true. There can be relatively little uncertainty in the outcomes, but the potential impact of that uncertainty on the decision can be high. The opposite can be true as well.

An important barrier to the use of VOI in practice may also be the disconnect between the funders of most research and the funders of healthcare. Currently, even when the funders of healthcare decide that the underlying evidence is too weak to reimburse a specific intervention, they may not be able to mandate further research to be performed by others.

What are some key references for further reading?
The reports of the ISPOR Task Force on VOI are a great starting point for those interested in learning more about the VOI toolbox and how they may use it in their research.[1,2] Also, a book on VOI has recently been published.[5] For a practical example of VOI, the study by Natalia Kunst et al on the clinical effectiveness and cost-effectiveness of population-based newborn screening for germline TP53 variants is an interesting read.[6]

We welcome your feedback on this article and any suggestions for methods to be covered in future editions. Send your comments and suggestions to the Value & Outcomes Spotlight Editorial Office*.*

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FROM THE REGIONS

Advancing HEOR Around the World: Insights From the Saudia Arabia, Maghreb, and Kazakhstan Chapters

The ISPOR Outstanding Chapter Award program recognizes ISPOR regional chapters' outstanding contribution and leadership in advancing ISPOR's mission in global regions: Asia Pacific, Latin America, and Europe, Middle East, and Africa. The ISPOR Saudia Arabia, Kazakhstan, and Maghreb chapters have been recognized for their exemplary achievements in advancing health economics and outcomes research (HEOR) in their regions.

These awards are based on a thorough review of chapters' impact on HEOR and health policy in their regions through activities, including education, research and engagement, and contribution to ISPOR strategic initiatives, as described in their annual reports.

Large-Sized Chapter

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President, ISPOR Saudi Arabia Chapter

ISPOR: Can you share examples of an innovative project or initiative your chapter launched this year that had a significant impact on the HEOR community in your region?

Hana Al-Abdulkarim: This year has been incredibly successful for the Saudi Arabian chapter. We have been fully dedicated to advancing ISPOR's mission and vision by organizing and hosting a wide range of activities. Locally, we have held several events, inviting experts from the region to speak or attend. Regionally, we have collaborated with the Gulf Health Economics Association and the Arab Health Economics Network on various initiatives, including chairing a workshop entitled, "Strategic Priorities and Collaborative Opportunities in Health Economics for the Gulf Region." The workshop focused on discussing opportunities and challenges in adopting and implementing health economic evaluations to address the increasing healthcare challenges in the Gulf Cooperation Council Countries, specifically in the United Arab Emirates. Following the workshop, our chapter team developed a manuscript summarizing the discussions, which we plan to publish as a perspective paper.

In addition, we are proud to announce our partnership with the Arab Health Economics Hub, which aims to build capacity among health economists, health policy makers, healthcare professionals, researchers, and economic and development planners in the Arab region. This collaboration also supports the optimization of health systems at both micro and macro levels in alignment with the internationally agreed sustainable development goals of universal health coverage in the region. As part of this partnership, we organized the 1st and 2nd Annual Arab Health Economics Meeting in Cairo, Egypt.

Furthermore, our chapter conducted a closed session on health technology assessment (HTA) with a group of regional and European experts to leverage the European HTA experience. Beyond our local and regional activities, we had the privilege of participating in 2 regional events, including SIPHA on January 23-25, 2024, which was a significant accomplishment for our chapter. Mai Alsaqa'aby, a member of our chapter, served as one of the scientific committee members and developed a session consisting of 4 talks about health economics. Additionally, we organized a regional event entitled "An Introduction to Patient-Reported Outcomes and their Role in HEOR" in collaboration with HEOR experts from Lebanon and Canada. Additionally, the chapter participated in Seha annual conference in Abu Dhabi, where Dr. Yazed spoke about the socioeconomic burden of select rare health conditions, such as spinal muscular atrophy, in Saudi Arabia. The chapter is also participating in the Emirates Health Economics Society where Dr. Yazed will talk about the impact of healthcare privatization on access, quality, and efficiency. Moreover, he will lead a discussion to explore the status of real-world healthcare data generation in the Gulf Cooperating Council countries and this discussion will involve multiple stakeholders representing the 6 Arab Gulf countries.

ISPOR: What collaborative efforts have you led to strengthen the connection between HEOR professionals across different sectors?

HA-A: *Medical community outreach:* We have established connections with several medical societies, including the Saudi Diabetes and Obesity Society, the Saudi Community Medicine Society, the Saudi Pharmaceutical Society, and the Rare Diseases Society. Additionally, we have re-established the media committee to reach out to the public and promote our activities and events through various social media platforms such as X, LinkedIn, and others. We have also created our own database of contacts for individuals who have attended our events and those holding different positions in the healthcare sector in order to invite them to our events and share information about our workshops via email. Furthermore, we are in the process of signing a memorandum of understanding with the Saudi National Health Institute (SNIH), which is the leading scientific and research funding body for healthcare researchers in Saudi Arabia.

Cross-sector healthcare outreach: This year, our chapter conducted a Cross-Sector Healthcare conference aimed at fostering collaboration among professionals from various sectors, including the insurance sector, the public health authority, the Saudi FDA, the Health Transformation Program, the Saudi Health Council, rare diseases societies, and the National Institute for Health Research. The goal was to raise awareness around HEOR, enhance communication, improve engagement of the chapter members, share best practices, and address common challenges in healthcare.

We host the international healthcare economics forum in collaboration with Alfaisal University every year. In the upcoming meeting we will be delving into the future of healthcare, focusing on technology, artificial intelligence, and digitalization. This year's keynote session will unveil the recently published ISPOR framework for defining digital health interventions.

Partnerships: We are collaborating with various sectors, including Princess Nora University, the SNIH, the Public Health Authority, and King Saud University College of Pharmacy.

Community outreach: We conducted an awareness campaign for multiple sclerosis to educate the community about the disease. The campaign was held at Dr. Soliman Alhabib Hospital, one of the largest private hospitals in Riyadh. Our initiative included translating scientific articles into Arabic, a crucial step that significantly enhances access to scientific knowledge and directly contributes to improving healthcare outcomes in the community. The Arabic content is disseminated on various media channels in plain, easily understandable language.

ISPOR: How do you envision your chapter's contributions influencing the future of HEOR in your country or region?

HA-A: I envision our chapter's contribution to HEOR as a multifaceted approach that significantly influences future healthcare policies and practices in Saudi Arabia.

Our commitment to public health is unwavering, as evidenced by our efforts to raise awareness about HEOR. This initiative empowers individuals and communities to take control of their health, leading to improved health outcomes and reduced long-term healthcare costs.

Supporting future HEOR experts: We are focusing our educational efforts on students and graduates through introductory HEOR workshops, such as building budget impact models and cost-effectiveness models, and critical appraisal of health economic and scientific studies to provide them with the basic skills that can help them in a future career. Additionally, our chapter board members ensure that students are involved in various subcommittees as volunteers to support the chapter's vision and mission and gain experience in project management within a nonprofit organization, such as the media, logistics, event management, and public relations committees.

Data-driven insights: Our focus on evidence-based decision making is not just a priority, but a cornerstone of our work. By prioritizing local real-world data collection and analysis, we are able to generate valuable insights into population health trends, shaping health policies and resource allocation. This approach should reassure you of the soundness of our decisions and the confidence we have in our work.

Equity in healthcare access: Our society can advocate for equitable access to healthcare services, particularly for underserved patient populations. An important example is the access challenges faced by patients with rare diseases, who are often denied access to expensive orphan drugs. We have been working for the past 2 years on highlighting and addressing this gap through panel sessions that bring all stakeholders to the same table. Later this year, we will have a workshop to discuss access challenges for patients with spinal muscular atrophy. We hope these efforts will help promote policies that ultimately improve overall health outcomes by ensuring that all individuals receive the care they need.

Innovative health solutions: Emphasizing research and development in health technologies and interventions can lead to more cost-effective solutions. By collaborating with academic institutions and private sectors, we can foster innovation that improves patient care and enhances our healthcare system's economic sustainability. Moreover, we can emphasize innovative concepts that can address affordability and uncertainty concerns, such as managed entry agreements.

Collaboration across sectors: Encouraging partnerships between government, private sectors, and nonprofits can create a more integrated approach to health economics. Collaborative efforts can lead to shared resources and innovative solutions that benefit the healthcare ecosystem.

I truly believe that we have succeeded in making ISPOR Saudi Arabia recognized as the hub for HEOR experts to network and collaborate and for candidates seeking the next step in their career. Through all these efforts, the ISPOR Saudi Chapter can significantly shape the future of health economics in our country, leading to a more efficient, equitable, and sustainable healthcare system.

Medium-Sized Chapter

Alima Almadiyeva, MD, MSPH
Deputy Chair
Salidat Kairbekova National Research Center for Health Development
Nur-Sultan, Kazakhstan
President, ISPOR Kazakhstan Chapter

ISPOR: Can you share examples of an innovative project or initiative your chapter launched this year that had a significant impact on the HEOR community in your region?

Alima Almadiyeva: The board of the Kazakhstan chapter organized many events during this year. However, the most notable included a project, "Time to Reimbursement for Novel Cancer Medicines Approved in 2013-2022 in Kazakhstan," which revealed exciting results of observation on the decision-making processes during those almost 10 years. We are preparing to publish those results in the coming months.

The second event was a conference with the participation of world-known international experts from the United States and Europe. This global collaboration is a testament to the growing influence of our chapter and the importance of our work not only for healthcare in Kazakhstan but also for the region of Central Asia and Commonwealth of Independent States. Since health systems in post-Soviet countries have undergone drastic changes and still need to be continuously developed, the discussions raised during the conference were more than just beneficial. Due to global challenges and constant uncertainties, low- and middle-income countries like Kazakhstan are in deep need of rational and comprehensive tools, like health technology assessment (HTA) and health economics and outcomes research (HEOR). We also acknowledge that capacity building is a considerable step forward in value-based healthcare. Thus, the conference held in Astana this year brought us together with other prominent experts from various countries.

ISPOR: What collaborative efforts have you led to strengthen the connection between HEOR professionals across different sectors?

AA: The ISPOR chapter in Kazakhstan has members with various backgrounds. Many are opinion leaders, so seminars and webinars are held annually because of the region's thirst for knowledge. To support our colleagues, we disseminate insights and global trends from the last ISPOR roundtables and conferences, such as patient-centered research, various evidence-based approaches, and value assessment. Colleagues cooperate in the framework of joint activities, including involvement in preparing legislative acts in health.

Collaborating before and during the conference held in Astana was also important. People serving in other sectors of the economy were engaged. We invited specialists from the Ministry of Health, National Committees and Commissions, the Ministry of Justice, the Ministry of Digital Development, the innovations and aerospace industry, patient organizations, health managers, and individuals with backgrounds in health, economics, or related fields. Some professional associations, such as the Association of Clinical Pharmacologists and the Association of International Pharmaceutical Manufacturers, participated in the discussions. Indeed, there is still much work to complete, especially on capacity building and education on HTA and HEOR, which is a way to increase the level of engagement of colleagues from other countries in Central Asia.

ISPOR: How do you envision your chapter's contributions influencing the future of HEOR in your country or region?

AA: The more people in our region learn about HTA and HEOR, the more HEOR evolves. Further efforts will be focused on research activities. Some topics from health policy and patient-reported outcomes will kick off our schedule of events for the following years. We also prepare to organize our regional conferences annually. These efforts should improve the understanding among stakeholders and improve decision making considerably.

Small-Sized Chapter

Samir Ahid, PhD
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Fès-Meknès, Morocco
President, ISPOR Maghreb Chapter

ISPOR: Can you share examples of an innovative project or initiative your chapter launched this year that had a significant impact on the HEOR community in your region?

Samir Ahid: This year, the ISPOR Maghreb Chapter—with the collaboration of the Moroccan Society of Health Economics product (SMEPS)—successfully launched 3 significant initiatives that have greatly impacted the HEOR community. First, the 10th National & 3rd African Conference on Pharmacoeconomics and Pharmacoepidemiology, held in Rabat, emphasized the critical role of the patient's voice in healthcare decision making. The congress brought together experts from 15 countries, fostering dialogue between patients, healthcare professionals, and policy makers to promote patient-centered approaches in health policy.

In January, the 3rd edition of the post-ISPOR Scientific Day covered the latest developments in health economics, policy, and health technology assessment (HTA). This event provided a platform for sharing knowledge on improving healthcare decision making and financing, addressing Africa's unique health challenges.

Additionally, the ISPOR Maghreb Chapter, with the collaboration of SMEPS and in partnership with Euromed University of Fez and AstraZeneca, launched the HTA Charaka initiative. This groundbreaking partnership aims to elevate Moroccan capabilities in HTA through educational sessions and workshops. The initiative supports Morocco's healthcare system reform

by promoting evidence-based decision making and improving access to innovative treatments for patients. This collaboration brings together the academic expertise of Euromed University, ISPOR Maghreb Chapter, and SMEPS's research capabilities and AstraZeneca's leadership in biopharmaceuticals to create a powerful synergy, advancing healthcare in Morocco.

ISPOR: What collaborative efforts have you led to strengthen the connection between HEOR professionals across different sectors?

SA: The ISPOR Maghreb Chapter has been actively fostering collaboration between HEOR professionals across different sectors through strategic partnerships and initiatives that encourage interdisciplinary engagement. By promoting open dialogue between academia, industry, and government, the ISPOR Maghreb Chapter has strengthened networks that support evidence-based decision making in healthcare.

We have facilitated cross-sector collaborations through educational initiatives, workshops, and capacity-building projects that address both the technical and practical aspects of HEOR. These efforts have enabled professionals to share insights, apply innovative methodologies, and work together toward common goals, such as improving healthcare access and outcomes. Additionally, our partnerships with international and local stakeholders have further expanded the exchange of knowledge and resources, fostering a unified approach to tackling the region's healthcare challenges.

ISPOR: How do you envision your chapter's contributions influencing the future of HEOR in your country or region?

SA: The ISPOR Maghreb Chapter is dedicated to shaping the future of HEOR by promoting evidence-based decision making and fostering the integration of HEOR into policy and practice. Our efforts aim to build a stronger foundation for evaluating healthcare technologies, improving access to innovative treatments, and optimizing resource allocation in healthcare systems.

Through our educational initiatives and collaborative projects, we are building local expertise in HEOR and equipping professionals with the tools needed to address the evolving healthcare needs of the region. By strengthening connections between academia, industry, and policy makers, we aim to create a sustainable framework for healthcare innovation that benefits both patients and health systems. Ultimately, our contributions will help advance more efficient, patient-centered healthcare that aligns with global best practices and supports long-term system reforms.

HEOR NEWS

1 Effects of Comprehensive Smoke-Free Legislation on Smoking Behaviors and Macroeconomic Outcomes in Shanghai, China: A Difference-in-Differences Analysis and Modeling Study (The Lancet Public Health)

In assessing the impact of Shanghai's public smoking ban on individual smoking behaviors and quantifying its effect on macroeconomic outcomes, experts found smoking prevalence decreased in Shanghai by 2.2 percentage points (95% CI 2.1-2.3), equivalent to an 8.4% reduction in the number of current smokers. They theorize that if there were a national ban, it would result in a 0.04-0.07% increase in the national gross domestic product in China between 2017 and 2035, outweighing the economic costs of smoking ban enforcement. Read more

2 Measles Cases Surge Worldwide, Infecting 10.3 Million People in 2023 (WHO)

There were an estimated 10.3 million cases of measles in 2023, a 20% increase from 2022, according to new estimates from the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC). Inadequate immunization coverage globally is driving the surge in cases. Read more

3 Worldwide Trends in Diabetes Prevalence and Treatment From 1990 to 2022: A Pooled Analysis of 1108 Population-Representative Studies with 141 Million Participants (The Lancet)

More than 800 million adults live with diabetes worldwide, and in most countries, especially in low- and middle-income countries, diabetes treatment has not increased at all or has not increased sufficiently in comparison with the rise in prevalence. Read more

4 Teleconsultation on Patients With Type 2 Diabetes in the Brazilian Public Health System: A Randomized, Pragmatic, Open-Label, Phase 2, Non-inferiority Trial (TELECONSULTA diabetes trial) (The Lancet Regional Health Americas)

The primary objective was to test the hypothesis that teleconsultation is non-inferior to face-to-face consultation in terms of glycemic control, and the results show the non-inferiority, underscoring the transformative potential of telemedicine in addressing the complexities of diabetes management within the framework of a universal healthcare system. Read more

5 Real-World Cost-effectiveness of Multi-gene Panel Sequencing to Inform Therapeutic Decisions for Advanced Non-small Cell Lung Cancer: A Population-Based Study (The Lancet Regional Health Americas)

The study in British Columbia, Canada, which aimed to determine the population-level cost-effectiveness of publicly reimbursed multi-gene panel sequencing compared to single-gene testing for advanced non-small cell lung cancer (NSCLC), found a moderate to high probability that panel-based testing to inform targeted treatment for NSCLC would be cost-effective at higher thresholds. Read more

6 Is it Possible to Pay for More Equitable Health Outcomes? (Health Affairs)

Blue Cross Blue Shield of Massachusetts uses a pay-for-equity program that is focused on equity and quality simultaneously, with the priority being reducing differences by maintaining at least the baseline for the group receiving the highest quality care, while improving care for groups receiving the poorest care. Read more

7 Wealth and Mortality Among Late-Middle-Aged Individuals in Norway: A Nationwide Register-Based Retrospective Study (The Lancet Regional Health Europe)

In looking at high-quality register data on wealth and mortality for the entire population of Norway, researchers found results suggesting that wealth is an important predictor of mortality even after individuals' observed and unobserved characteristics are accounted for, with the most disadvantaged groups being nonpartnered men and women at the lower end of wealth distribution. Read more

8 Evidence That Regulatory and Market Forces Are Driving Adoption of Biosimilars (Health Affairs)

Evidence suggests that the maturing postapproval biosimilar marketplace is flourishing, with the entry of biosimilars for adalimumab (Humira) offering a case study that demonstrates these recent market and policy dynamics. Read more

9 Small-Molecule Drugs Offer Comparable Health Benefits to Biologics at Lower Costs (Health Affairs)

When comparing the incremental quality-adjusted life-year (QALY) gains, incremental costs, and incremental cost-effectiveness ratios (ICERs) of small-molecule drugs and biologics approved by the FDA from 1999 to 2018, researchers found small-molecule drugs tend to be associated with lower additional costs ($4738 versus $16,020) and more favorable cost-effectiveness ($108,314 per QALY versus $228,286 per QALY). Read more

10 Evaluating the Effects of the World Health Organization's Online Intervention 'iSupport' to Reduce Depression and Distress in Dementia Carers: A Multi-center Six-Month Randomized Controlled Trial in the UK

In evaluating iSupport, a self-guided online intervention designed by the World Health Organization (WHO) to reduce mental health problems in dementia carers, researchers found virtually no difference in mean distress and depression scores between those using iSupport and those in usual care. Read more

MEASURING VALUE

THE QALY TURNS 50:

WHAT HAS IT ACHIEVED + WHAT IS ITS FUTURE?

By John Watkins, PharmD, MPH, BCPS, Managed Care Perspectives, LLC

For almost half a century, the principal measure of value (net health gain) in cost-effectiveness analysis (CEA) has been the quality-adjusted life year (QALY). Several organizations have offered frameworks that include additional value dimensions not captured by the QALY. In 2018, an ISPOR Special Task Force assembled a more comprehensive list known as the "ISPOR value flower" graphic.[1] QALYs are calculated by health economists around the world, but most countries don't use them in formal decision-making processes. Even its strongest proponents acknowledge the QALY's shortcomings. Willke and colleagues recently summarized the position of ISPOR's scientific leadership. They "emphasize that the QALY can provide useful information for decision making, with appropriate use it will not be discriminatory, and it should be available for use in combination with other summary measures of health benefit."[2]

History and Present Use

The general concept of cost-utility analysis had been discussed since the late 1960s. George Torrance and colleagues first published a description of the methodology in 1972,[3] and the term "QALY" was first used in a peer-reviewed publication by Zeckhauser and Shepard in 1976.[4] Since then, it has traveled around the world, yet according to Michael F. Drummond, MCom, DPhil, Professor Emeritus, Centre for Health Economics, University of York, England, United Kingdom, only a small number of countries actually use QALYs in health technology assessment (HTA) and decision making. Others use them alongside the formal decision-making processes of their governments. In the United States, for example, the Institute for Clinical and Economic Research (ICER) routinely includes CEA in its reports, presenting both QALY- and equal value life year (EVLY)-based cost-utility ratios. Use of the QALY by federally funded payers to determine coverage is explicitly forbidden by law, but some private payers use ICER's work to inform formulary and coverage policy decisions and to negotiate price.

Use of the QALY in formal decisions is mostly confined to Europe. In 2020, Torbica and colleagues surveyed its use in 36 Organisation for Economic Co-operation and Development (OECD) countries, finding that Australia, Belgium, Canada, Czechia, Estonia, Finland, Hungary, Iceland, Ireland, Israel, Mexico, The Netherlands, New Zealand, Norway, Poland, Portugal, Slovakia, Slovenia, Sweden, and the United Kingdom made extensive use of QALYs, whereas Austria, Chile, Denmark, France, Germany, Greece, Italy, Japan, South Korea, Latvia, Lithuania, Luxembourg, Spain, Switzerland, Turkey, and the United States were low utilizers.[5]

> "Only a small number of countries actually use QALYs in health technology assessment (HTA) and decision making. Others use them alongside the formal decision-making processes of their governments."
>
> – Michael F. Drummond, MCom, DPhil

France and Germany do not formally use the QALY, Drummond notes, having adopted systems that score new drugs based on their evidence of incremental net clinical benefit, similar to ICER's Evidence Ratings. They use these ratings in price negotiations with manufacturers in lieu of formal CEA although France consults cost-utility modeling in situations where the manufacturer is claiming that the drug is innovative. Australia, Canada, and New Zealand follow the English model developed by the National Health Service (NHS) and the National Institute for Health and Care Excellence (NICE). Other countries outside Europe that make some use of QALYs in HTA include Colombia and Taiwan. Federico Augustovski, MD, MSc, PhD, Director, Health Technology Assessment and Health Economics Department and Professor of Public Health, University of Buenos Aires, Argentina, adds, "Local value sets for preference assessment instruments (ie, EQ-5D) for local QALY estimations were derived in several countries in the region (Argentina, Brazil, Chile, Colombia, Ecuador, Perú, and Trinidad and Tobago)." Some of these were not reviewed by Torbica because they are not OECD countries. The level of detail Augustovski describes shows that thoughtful work supporting QALY calculation is happening in countries that have not officially incorporated CEA in their formal HTA process.

Factors Affecting Adoption

Torbica and colleagues studied factors associated with formal adoption of QALYs in decision making. "It appears that…culture, values, and institutional context have an influence on the use of HTA and economic evaluation in healthcare, either directly or indirectly."[6] The most important predictor of QALY use was the presence of a national single payer health system. Such systems exclusively control market access and thus have strong price negotiating leverage. A fixed budget, which calls attention to tradeoffs and marginal costs, is another factor, as is transparency. Most such systems provide access to records, which is not the case with private payers. Torbica et al's path model showed direct association between QALY use and institutional context (type of health system and administrative tradition). Social values (efficiency, equity, personal responsibility, etc) appeared to influence indirectly through the institutional context.[7]

Cultures have differing concepts of health, illness, medicine, and the balance between individual autonomy and overall welfare of society. Countries like England highly value horizontal equity and have a greater sense of social solidarity. In principle, everyone in England can access care, but high-cost drugs and medical technologies strain limited resources, resulting in queuing for procedures such as advanced imaging and surgery. This form of rationing can harm patients if it results in lengthy delays to essential care. The United States emphasizes individual autonomy, with each patient free to choose the treatment they believe is best for them. Society focuses on the needs and wants of individuals, which limits the government's ability to control prices and creates access barriers for lower income individuals, de facto rationing on ability to pay. Neither result is desirable.

Breslau and colleagues reviewed 53 HTA guidelines to determine which of 21 societal and novel value elements they identified were included (average 5.9 elements per guideline). Only 4 value elements—productivity, family spillover, equity, and transportation—appeared in more than half the guidelines examined.[7]

Societies of European origin believe it is possible to control disease. Expressions like "I have cancer" or "my diabetes" implies ownership and therefore ability to manage the disease.

As one patient with cancer said, "It has a *name*! We can fight it." Other cultures see patients assuming a more passive role in illness. It is something that happens to them, something they can't control. QALY use in Asia is challenged by nonallopathic medical systems whose practitioners do not perform randomized controlled trials, making it difficult to obtain clinical data required for QALY calculations. Swami and Srivastava described the role of culture, value, and politics in doing HTA in India, a country technologically advanced, but very different in culture from the West. Healthcare practices include traditional medicine, such as Ayurveda, homeopathy, Unani, yoga, and Siddha, along with allopathy. Home remedies are often used due to their low cost.[8]

Culture is impacted by history. Alexis de Tocqueville, an astute early visitor to the United States, identified major differences: the vastness of the land, its isolation from the rest of the world, the absence of a system of landed aristocracy, the federal system of government, the power of an independent judiciary, and the "religious aspect of the country" but lack of a state religion.[9] US immigrants were self-selected individuals who often risked their lives on the journey. They came for various reasons: escape from persecution or political disruptions, economic opportunity, adventure, and the promise of land ownership. They brought an optimistic self-reliance that the frontier forged into a culture of independence. Americans may eventually accept a national health system, but they will demand choice.

Pluralistic health systems are less likely to have a robust HTA process that uses QALYs. Private health systems have less well-defined budgets, and plurality reduces the contracting leverage of any one payer. US antitrust law prohibits payers from collaborating in price negotiations with manufacturers. The legal and regulatory framework can impact HTA by mandating coverage of particular treatments or restricting use of CEA to determine coverage. Private payers' budgets are not subject to public scrutiny, and private for-profit payers must also consider stockholder interests. The ISPOR Working Group on HTA in Pluralistic Healthcare Systems offered 5 recommendations to address these specific challenges: establish a national focus for HTA, develop a uniform set of HTA methods guidelines, ensure that HTAs are produced in a timely fashion, facilitate the use of HTA in the local setting, and develop a framework to encourage transparency in HTA.[10]

Benefits and Uses

The QALY is a standard measure of the net health benefit derived from an intervention. It facilitates comparisons within and across disease states and treatment types. "QALYs represent time alive scaled to reflect health state desirability. Though they have some limitations, they are useful because they combine mortality and morbidity into a single metric, reflect individual preferences, and can be used as a standard measure of health gains across diverse treatments and settings," explains Peter J. Neumann, ScD, Director of the Center for the Evaluation of Value and Risk in Health at Tufts Medical Center, Boston, MA.[11] The QALY combines an objective clinical measure (years of life gained) with a subjective one (utility) based on individual values and preferences. The resulting estimates of cost per QALY gained can be used to compare different interventions, regardless of similarity. Users can compare an intervention to a specific threshold beyond which the intervention is considered to be of low value. Government and private payers can use QALY calculations when negotiating prices.

QALYs are not specific to healthcare and can be used to study tradeoffs with other investments that benefit the public, such as education, infrastructure, and social services, highlighting the marginal cost to society, which might otherwise be overlooked. Societal perspective is important in the United States, where there is relatively little public awareness of budget constraints and the marginal cost of tradeoffs may not be immediately apparent. For example, with employer-sponsored insurance, it is unlikely that the public will connect layoff of workers to rising insurance premiums when the market is simply responding to increased labor cost by replacing expensive employees with automation or outsourcing jobs to countries offering lower-cost workers.

> "It appears that culture, values and institutional context shape attitudes of policy makers towards economic evaluation and HTA in general, and QALY in particular."
>
> – Aleksandra Torbica, PhD

Zeckhauser first proposed QALY calculations to inform societal allocation of scarce resources. The scope was broad, including "energy planning, national health insurance…occupational health and safety regulation, indeed national defense policy," all of which affect both quantity and quality of life (QOL). "Disinterested citizens" argued over these matters primarily because they lacked information regarding consequences of proposed actions, rather than because they held different values. As an economist, Zeckhauser believed that more accurate predictions would focus arguments on issues that can be resolved and lead to effective action. "The guiding principle should be to select the measure(s) that would predict the choices that an informed individual would make for himself."[12] Individuals would estimate the utility of each possible action, seeking to maximize utility. This principle is reflected in ISPOR's mission to advance HEOR excellence to improve decision making for health globally.

Broad applicability is a major strength of QALY-based methods and an argument for their use. Highway accidents provide an example that directly impacts healthcare, since they can cause emergency medical treatment, permanent disability, reduced utility, and death. Interventions that reduce vehicle

accident injuries would thus have a direct impact on life and the demand for medical care. A National Highway Traffic Safety Administration report illustrated the application of utilities in this field, helping policy makers appreciate marginal cost impacts across highway engineering and healthcare.[13] The US Environmental Protection Agency has used QALYs to analyze the health impact of air pollution regulations,[14] while the Centers for Disease Control and Prevention use them to analyze the cost-effectiveness of prevention interventions.[15] The federal government makes use of QALYs in these areas but is prohibited from applying them to Medicare.

Criticisms

Despite these benefits, valid criticisms of QALY-based allocation decision making in healthcare and implementation challenges explain why so few countries have adopted formal CEA in coverage decision making. A fundamental objection is that health state utilities are population-based and not patient-centric. Patient advocates argue that QALYs discriminate against the elderly, disabled, and those with chronic life-limiting conditions. Utilities are based on the general public's perceptions, measured by surveying uninvolved individuals who are well-informed about experience utility and have enough information about the health state to visualize a patient experiencing it. However, individual patient experiences vary widely and may not match the population-level valuation. Daniel Kahneman observed a discrepancy between self-evaluated utilities and those assigned by the stated preference-based methods used in the surveys. These valuations, he argued, are decision-based processes and fail to take into consideration the hedonic aspects of the patient's experiences.[16]

> "QALYs represent time alive scaled to reflect health state desirability. Though they have some limitations, they are useful because they combine mortality and morbidity into a single metric, reflect individual preferences, and can be used as a standard measure of health gains across diverse treatments and settings."
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> – Peter J. Neumann, ScD

Proponents counter that experienced utility-based methods do not require respondents to make a sacrifice. Since there is no opportunity cost, individuals respond as they would in an ideal state—we all want the best if it's free. QALY-based methods offer no way to make a more nuanced evaluation of treatment impact on an individual's health state. A patient's value equation changes over time as they reach goals and set new ones. For patients with cancers, "the experience of living through the side effects of treatment changes the value as you go along," says retired oncologist Richard McGee, MD. Population estimates do not consider ethnic and demographic characteristics, occupation, and individual circumstances. For example, to return to work, an injured athlete, military member, or first responder must meet higher physical performance standards than most others who can still do their jobs despite reduced physical function. QALYs do not take this into consideration. Self-assessed utility varies across individuals, depending on their circumstances, life goals, and relationships. There is no one-size-fits-all. The Generalized Risk Adjusted Cost-Effectiveness (GRACE) method described below attempts to address this shortcoming of the QALY.

Age discrimination is a concern for patient advocates and pharmaceutical manufacturers. To address this question, Xie and colleagues analyzed 4445 studies from the Tufts CEA Registry published between 1976 and 2021. Of these, 661 (15%) were in populations over age 65. A comparison of ICERs between the 2 groups found "no systematic differences in published ICERs using QALYs."[17] However, it is still true that QALY calculations favor those most likely to benefit from treatment. While this may be the most efficient way to allocate scarce resources, there will be circumstances where it is less fair to individuals who can expect some, but not as much, benefit.

Patients and the public also react to the arbitrary nature of cost-utility thresholds, which in the United States currently range from $50,000 to $150,000 per QALY. These are proposed as coverage limits, but usually no satisfactory rationale for the specific numbers is given.* The concept of "willingness to pay" seems odd when those making the treatment decision (provider and patient) do not actually pay the cost, and the payer who does has no role in the decision. To an economist, these thresholds represent the value of the treatment in light of tradeoffs and marginal cost; to the budget holder, they represent limits designed to maintain affordability; to the patient, whose focus is on the need for care, they are a barrier to access. In the United States, most people react negatively to authorities telling them what to do.

Given these objections, it should be clear that the output of cost-effectiveness analysis is intended to guide population-level decisions about pricing and funding, not individual treatment decisions, which should be the result of shared decision making by provider and patient. Payers may use CEA to inform coverage policy, but these policies are always subject to individual case-based review, recognizing that every patient is unique and may have factors requiring an exception to the general policy.

Alternative Measures

Use of QALY-based decision making in federally funded programs is restricted by law in the United States. Section 504 of the Rehabilitation Act of 1973 "forbids organizations and employers from excluding or denying individuals with disabilities an equal opportunity to receive program benefits and services."[18] The Affordable Care Act adds language

prohibiting "use of a cost-effectiveness analysis threshold and QALYs in PCORI comparative effectiveness studies, which has been understood as a prohibition on support for PCORI's conducting conventional cost-effectiveness analyses."[19] The Inflation Reduction Act authorizing Medicare to negotiate drug prices states that the Department of Health and Human Services Secretary "shall not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill." In other words, the use of health outcomes evidence based on QALYs in the process of negotiating a maximum fair price is not permitted.[20] In 2023, HR-485, the Protecting Health Care for All Patients Act, which would have banned use of the QALY "and other similar measures" in decision making for federally funded programs, was passed by the House but failed in the Senate.[21] With Republicans in charge, a similar bill may be introduced when Congress convenes in January. The language ("other similar measures") is vague and subject to interpretation.

To address this barrier, ICER now reports cost-utility ratios from both equal value of life years (EVLY) gained and QALY calculations. The EVLY, as defined by ICER and labeled evLYG in their publications, assigns a "healthy population" level utility of 0.85 to any additional life years achieved by the intervention. The evLYG measures QOL improvements or decrements versus the comparator during the rest of the lifespan, but any extended life receives the same weight, no matter the underlying utility. This avoids discrimination against the elderly, disabled, or terminally ill. ICER analyses generally show only a modest difference between QALY and evLYG results because most drugs ICER reviews extend life modestly at best; however, this will not be true for gene therapies and other drugs expected to extend survival. Lacking evidence from long-term follow-up, both QALY and evLYG lifetime gains are hypothetical at this point. Otherwise, the evLYG is subject to the same criticisms as the QALY, and it fails to capture treatment benefit that improves utility without extending survival.

Health years in total (HYT) is another QALY alternative measure proposed by Basu, Carlson, and Veenstra in 2020. This new measure uses the same inputs but differs from the QALY in that "the HYT framework separates life expectancy changes and QOL changes on an additive scale." Rather than the multiplicative combination in the traditional QALY, HYT have the same axiomatic foundations as QALY and perform better than both QALY, in terms of the discriminatory implications, and EVLY, in terms of capturing QOL gains during added years of life. HYT are straightforward to calculate within a CEA model.[22] The authors hope that the HYT will be more readily accepted in the United States: "The lack of separability in QALY imparts its discriminatory property," Basu points out. However, given the trend toward broader US legal restriction, the HYT may yet face challenges. Neither EVLY nor HYT solve the challenge of achieving distributional equity.

Following the ISPOR Task Force Report, a new approach, GRACE, which helps align HTA practice with realistic preferences for health and risk, was proposed by Lakdawalla and Phelps in 2020.[23] "The disability community has pointed out mathematical limitations of the QALY," explains Lou Garrison, PhD, Professor Emeritus at the University of Washington, Seattle, WA, and Special Task Force co-leader. "We don't have a universal exchange rate between quality and quantity of life, such that a certain percentage increase in quality of life is equivalent to so many life years for everyone. Obviously, every individual has his/her own exchange rate, but people aren't voting with their own dollars in the health economy. So we don't have unfettered market transactions to measure this value. But, given information on disease probability, QALY loss, and other costs, and given the value that a patient places on a year of healthy life, conventional CEA predicts what that patient should be willing to pay in insurance premiums or taxes. That's the intuition behind conventional CEA, but the mathematics and the methodology are limited since conventional CEA doesn't fully capture the value of reducing uncertainty.

"We don't have unfettered market transactions to measure this value. But, given the value that a patient places on a year of healthy life, conventional CEA predicts what that patient should be willing to pay in insurance premiums or taxes."

– Lou Garrison, PhD

"In my view, perhaps the most important part of GRACE is what we could call 'mental insurance value'— the peace of mind you get from knowing something can be done about your health condition. For example, in November 2019, before COVID, if asked, you might have said you were feeling pretty good. Then in March of 2020 you were told you might die by June and there might be nothing we could do about it: your utility fell. But when we learned that the mRNA platform could produce a vaccine in 9 months, utility levels went up for billions of people." That peace of mind is what GRACE captures, Garrison says. It's also an example of scientific spillover, another important value element—since that the new mRNA platform can be applied to produce other vaccines.

"I think it's situated in the broader project of building a microeconomic foundation for cost-effectiveness analysis," Darius Lakdawalla, PhD, Professor of Pharmaceutical Development and Regulatory Innovation at the University of Southern California, Los Angeles, CA, explained. "GRACE attempts to generalize those foundations and give analysts more choice by looking at how the structure of preferences and the shape of the utility over health impacts and influences the implications of cost-effectiveness analysis. And so, it's

our hope that it can be useful. It actually gives you a way to perform cost-effectiveness that aligns with US law because there are well-fitting utility functions that correspond to nondiscriminatory cost-effectiveness, which is required now under the IRA [Inflation Reduction Act] and the ACA [Affordable Care Act]. The ISPOR value flower showed us a number of empirical anomalies that needed explanation, and GRACE shows you how the shape of preferences can help unlock some of these anomalies. When you have a more explicit approach to thinking about utility, it also provides a means to update the measurement of preferences with more modern methods, so you can use prospect [aversion to loss] theory and quantifying and implementing cost-effectiveness analysis in the framework of GRACE."[24]

> "The ISPOR value flower showed us a number of empirical anomalies that needed explanation, and GRACE shows you how the shape of preferences can help unlock some of these anomalies."
>
> – Darius Lakdawalla, PhD

GRACE attempts to modify traditional CEA to incorporate other dimensions of value. It is a work in progress within the broader space of generalized CEA, which was recently reviewed by Padula and Kolchinsky, who suggest that with further development we could have "off-the-shelf" resources to help inform, for example, maximum fair price in the context of Medicare drug price negotiation. Additional novel value elements could be incorporated.[25] Generalized CEA can potentially help in distributional cost-effectiveness analysis. The QALY is agnostic to an individual's socioeconomic status or vulnerability, and in some situations might actually favor the wealthier individual. GRACE provides some flexibility to support distributive justice and allow future researchers to better align with what consumers want.

Unanswered Questions

This summary of the QALY leaves many questions unanswered. What is the underlying purpose of healthcare versus health insurance? How should it be funded? From whose perspective should resources be allocated, and how can we make decisions for a public that does not share a common worldview?

When offered truly lifesaving innovations, how much *should* we be "willing to pay?" What percentage of gross domestic product is the practical upper limit of the healthcare "budget" we can afford? How do we balance long- versus short-term perspectives?

How societies answer these questions will determine the future of CEA and the QALY. What role should ISPOR and its members play in guiding this conversation to find solutions? There is no single "right" answer. Each country or region must find its own way. However, there is wisdom in a multitude of counselors. ISPOR can provide a venue where diversity and honest discussion are encouraged and we learn from the ideas of others.

** The $50,000/QALY threshold used in the United States was originally based on the cost of maintaining a renal dialysis patient. No convincing argument for these numbers has ever been offered.*

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By the Numbers: Value Assessments

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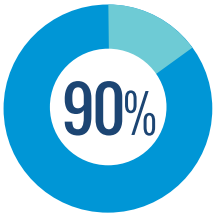
Stats Behind the Quality-Adjusted Life Year (QALY) Debate



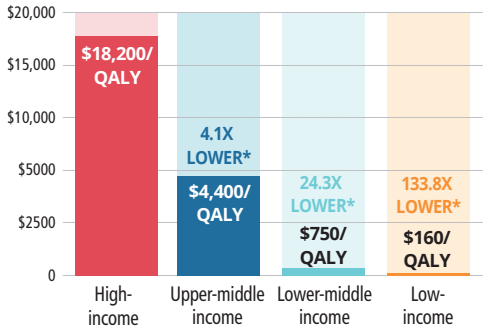
QALYs are used in 90% of global health systems to compare healthcare interventions.

1 QALY = 1 YEAR OF LIFE IN PERFECT HEALTH

88 studies reviewed identified **9 major criticisms of QALYs**

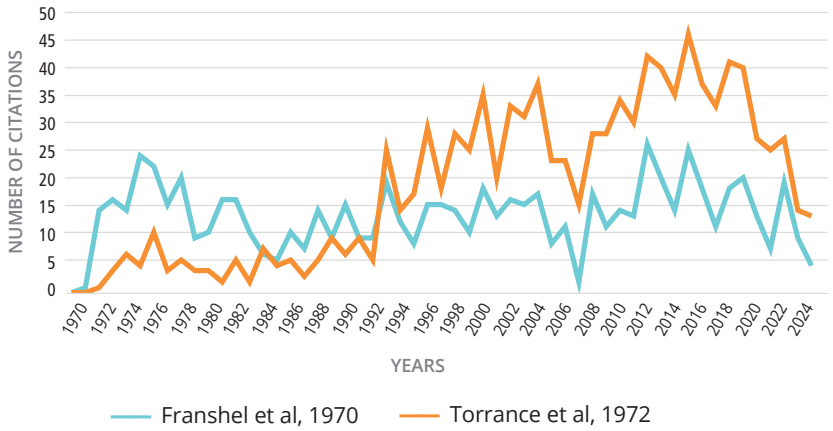
1. methods for measuring health states
2. methods for measuring utilities
3. non-health benefits/effects
4. severity
5. health equity
6. aggregation of outcomes
7. aggregation of individuals
8. ageism
9. disability discrimination

Cost-Effectiveness Thresholds Per QALY According to Country Income Level



*Comparisons of Median Thresholds Compared to High-Income Countries

Trends in the Adoption of 2 Seminal QALY Publications



Pros and Cons of the QALY

Advantages and Criticism of Quality-Adjusted Life Years (QALYs)

- Comparability
- Compositeness: quality and quantity of life

METHODS
- Methods for measuring health states
- Methods for determining and measuring utilities
- Exclusion of nonhealth benefits

NEUTRALITY CRITICISM
- Severity
- Benefit aggregation
- Health equity

DISCRIMINATION CRITICISM
- Ageism
- Disability discrimination

Enhancing Access to Innovative Medical Technologies Through Early Value Assessment in the United Kingdom

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Early value assessment aims to accelerate access to innovative medical technologies by evaluating technologies that could address unmet needs.

The National Institute for Health and Care Excellence (NICE) publishes evidence-generation plans for conditionally recommended technologies; once generated, NICE will assess this evidence to determine whether the technology should be routinely adopted within the National Health Service.

Our understanding of how innovative medical technologies can improve patient care and healthcare systems will continue to evolve as conditionally recommended technologies integrate into the National Health Service and more data are generated.

Overview of innovative MedTech in the United Kingdom

In February 2023, the UK Department of Health and Social Care published the government's 5- to 10-year plan to support the use of innovative medical technologies (MedTech) to support patient care and clinical outcomes.[1] Innovative MedTech include digital health technologies, such as therapies and systems that can improve patient health or increase healthcare system capacity.[2,3] Examples of innovative MedTech include mobile treatment apps, wearable devices, telemedicine platforms, imaging systems, electronic health records, surgical instruments, and artificial intelligence–powered diagnostic tools.

> By providing patients with access to healthcare regardless of location, innovative technologies that deliver treatment could potentially reduce waiting lists, decrease the number of hospital visits, and reduce costs associated with face-to-face healthcare consultations.

Innovative MedTech have the potential to address several unmet needs in healthcare by improving the efficiency and capacity of healthcare systems, as well as by allowing patients to be diagnosed, receive treatment, and be monitored remotely. By providing patients with access to healthcare regardless of location, innovative technologies that deliver treatment could potentially reduce waiting lists, decrease the number of hospital visits, reduce costs associated with face-to-face healthcare consultations, and help to address inequality by providing a treatment option for patients who are unable or unwilling to travel for in-person appointments.[3,4]

The National Institute for Health and Care Excellence (NICE) is a nondepartmental public body sponsored by the Department of Health and Social Care in England. NICE publishes a wide range of guidance on how to improve health and social care, including appraisals on the clinical and cost-effectiveness of new health technologies.[5] In June 2022, a new early value assessment (EVA) process was introduced to accelerate the assessment of innovative MedTech by NICE. The aims of EVA include:[3]

- Allowing patients and the National Health Service (NHS) in England to benefit from earlier access to promising innovations that address unmet needs;
- Facilitating adoption of new innovative MedTech and supporting evidence generation for new technologies; and
- Verifying that innovative MedTech deliver the expected benefits and ensuring these technologies provide value for money for the NHS.

This article provides an overview of the NICE EVA program, including published EVA guidance, evidence gaps highlighted during the assessments, and next steps for conditionally recommended technologies.

EVA for innovative MedTech in the United Kingdom

Innovative MedTech that address unmet need(s) within an NHS priority area, lack sufficient evidence for a full NICE appraisal, and are currently being used in the NHS or are planned for uptake within the next 6 months may be suitable for EVA.[3,6] The initial priority topics identified for EVA were mental health, cardiovascular, early cancer detection, and technologies that boost healthcare capacity.[6] During the EVA process, NICE assesses the available evidence for a single technology or a number of similar technologies and makes one of the

following recommendations based on potential benefits and harms to patients, carers, and the system (including costs):[3]

- **Conditionally recommended for use while further evidence is generated:** For technologies that are likely to address an unmet need and where any risks or uncertainties can be sufficiently mitigated.
- **Recommended in research only:** For technologies where there is considerable uncertainty about whether an unmet need would be addressed or about whether potential benefits outweigh potential risks.
- **Not recommended for use:** For technologies that are not expected to address an unmet need and/or may be harmful even in a research context.

Published and ongoing EVAs

As of August 29, 2024, 16 EVA health technology evaluations (HTEs) have been published and 4 are currently in development. Each evaluation has a reference number on the NICE website, with the prefix "GID-HTE" applied while the evaluation is ongoing and the prefix "HTE" applied when the EVA guidance has been published. As summarized the **Figure**, digitally enabled therapies to treat mental health disorders (anxiety and low mood [HTE3 and HTE9], depression [HTE8], agoraphobia [HTE15], and psychosis [HTE17]) are the most common EVA topics currently, followed by digitally enabled therapies for other conditions such as chronic obstructive pulmonary disease (HTE18 and GID-HTE10030), weight management (HTE14), and low back pain (HTE16).[4,7]

A total of 120 innovative MedTech have been included in the evaluation scope across the 16 published EVA guidance documents, of which 57 have been conditionally recommended for use while further evidence is generated.[4] Recommended innovative MedTech were expected to address an unmet need within the NHS.[4]

- Diagnostic technologies may be quicker and more accessible than in-person diagnostics, reducing wait time for diagnosis and allowing patients to begin treatment or make lifestyle changes earlier.
- Digitally enabled therapies could provide an alternate or additional treatment option to existing therapies, reduce disease symptoms, improve patients' ability to function in everyday life, reduce wait times for in-person treatment, and free up NHS resources to increase capacity elsewhere.
- Innovative technologies could boost healthcare capacity by improving knowledge sharing, increasing efficiency and consistency throughout the NHS, and reducing pressure on hospitals.

> Although early data for conditionally recommended innovative MedTech suggest these technologies could advance patient care and/or improve health and social care systems, many uncertainties are not currently addressed by available evidence.

In some instances, patients may find the flexibility, comfort, and convenience of digitally enabled therapies preferable to in-person appointments. The EVA guidance for KardiaMobile 6L (AliveCor), a 6-lead, handheld electrocardiogram device that can be used during home visits by health professionals (HTE10), noted that patients preferred KardiaMobile 6L due to it being easier to use and less intrusive than standard electrocardiogram devices, which require patients to attend medical centers.[8]

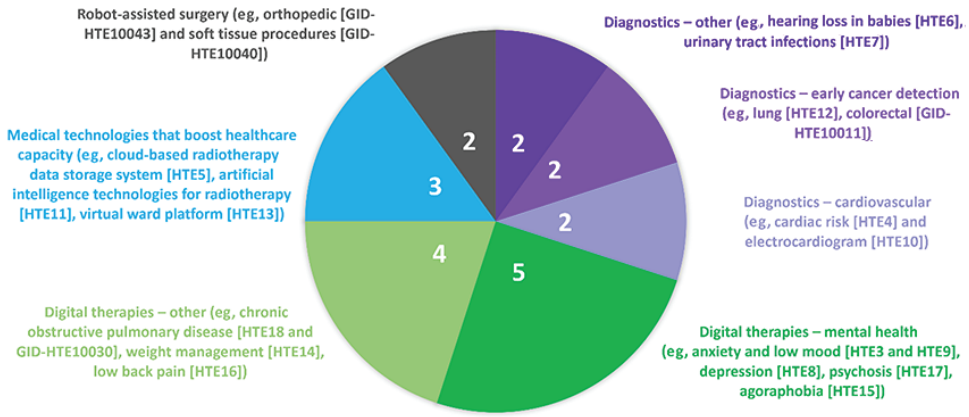
Although early data for conditionally recommended innovative MedTech suggest these technologies could advance patient care and/or improve health and social care systems, many uncertainties are not currently addressed by available evidence. These can include safety concerns, patient uptake, patient adherence to digitally enabled therapies, set-up costs, and costs associated with training individuals (including NHS staff, patients, and caregivers) on how to use the technologies.[4] These data gaps could be addressed by conducting real-world studies.

Additionally, some technologies may pose equality issues. For example, the EVA guidance for technologies to manage nonspecific low back pain (HTE16) noted that digitally enabled therapies may be unsuitable for people who do not have the appropriate devices (eg, smartphones or tablets), have limited Internet access, or cannot read or understand health-related information (eg, individuals who do not speak English).[9] Individuals who are unfamiliar with digital technologies, have visual impairments, or have problems with manual dexterity may have limited benefit from digitally enabled therapies.[9]

From recommendation to clinical practice

There is currently limited clinical evidence on the effectiveness of

Figure. Topics across all published and ongoing NICE innovative MedTech EVAs as of August 29, 2024[4,7]



Abbreviations: EVA, early value assessment; MedTech, medical technologies; NICE, National Institute for Health and Care Excellence. Published EVAs are given the identifier "HTE" while EVAs in development have the identifier "GID-HTE."

innovative MedTech in the UK/NHS setting. As part of the EVA process, NICE develops evidence-generation plans for conditionally recommended innovative MedTech that highlight key evidence gaps and suggest methods to address them.[3,6]

In a draft proposal set out by NICE and NHS England in May 2024 introducing a new integrated pathway for introduction of medical technologies into the NHS, EVA is described as a "bridge" to the full NICE appraisal that identifies additional evidence needed for full appraisal, facilitates early access to promising new technologies, and enables the technology developer to collect the necessary evidence in the NHS setting.[10] Moreover, NICE and NHS England expect EVA guidance to benefit clinicians and commissioners by allowing them to prepare for new MedTech that address patient need and clinical demand and are likely to be adopted into the NHS.[10] Public engagement on the draft proposal ended on August 15, 2024, and a report will be published in the future addressing the issues raised during the consultation.[10]

> Early value assessment is described as a "bridge" to the full NICE appraisal that identifies additional evidence needed for full appraisal, facilitates early access to promising new technologies, and enables the technology developer to collect the necessary evidence in the NHS setting.

As of August 29, 2024, NICE has published 14 evidence-generation plans (1 for each published EVA except HTE4 and HTE7). The plans included recommendations on study designs, priority outcomes for data collection, possible data sources (such as general practitioner electronic records or existing databases), and relevant stakeholders (such as patient organizations and clinical experts who could help with data collection and analysis).[3,4,6] Technology developers must contact NICE within 6 months of plan publication and annually thereafter during the period of evidence generation (2 to 4 years). Any substantial risks with evidence collection, new safety concerns, or significant changes to the technology must be reported to NICE as soon as possible. At the end of the evidence-generation period, the technology developer will submit its evidence to NICE for review and assessment of whether the innovative MedTech should be routinely adopted within the NHS.[4]

> Our understanding of how patients and the NHS can benefit from adoption of new innovative MedTech will continue to evolve over the next few years as additional studies are conducted to address evidence gaps and uncertainties flagged by NICE for the conditionally recommended technologies.

Conclusions

The number of EVA evaluations is expected to increase in the future as the innovative MedTech industry continues to develop and integrate into existing healthcare systems. Our understanding of how patients and the NHS can benefit from adoption of new innovative MedTech will continue to evolve over the next few years as additional studies are conducted to address evidence gaps and uncertainties flagged by NICE for the conditionally recommended technologies.

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Seeing the Bigger Picture: How Capacity Constraints Impact Value

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Incorporating capacity constraints is essential for accurate economic evaluations in ophthalmology.

By considering reduced treatment delays, cost savings, and improved quality-adjusted life-years (QALYs), decision makers can optimize resource allocation.

Emerging therapies that address capacity constraints bring significant benefits, reducing delays and improving patient outcomes.

Prioritizing cost-effectiveness and patient well-being in disease areas with limited capacity is crucial for efficient healthcare resource utilization.

Introduction

Cost-effectiveness analysis is a key component of health technology assessment, which evaluates whether a new treatment provides value relative to existing health technologies available to patients. This analysis typically involves estimating the downstream effects of introducing the new treatment on healthcare costs and patient outcomes. Traditional cost-effectiveness analysis implicitly assumes that there is unlimited capacity in the healthcare system and does not consider capacity constraints that may impede or limit the implementation of treatments. In many chronic disease areas, including ophthalmology disorders, implementing effective treatment can be capacity-intensive because it often requires frequent specialized administration or monitoring. As a result, the timely provision of these treatments is capacity-dependent. In the presence of capacity constraints, treatment delays may lead to worsened health outcomes for patients.[1]

> In the presence of capacity constraints, treatment delays may lead to worsened health outcomes for patients.

New treatments that alleviate capacity constraints would not be adequately valued if the positive impact on health outcomes of avoiding treatment delays is ignored, given that traditional cost-effectiveness frameworks do not explicitly consider the impact of capacity. Considering these capacity constraints and their impact on patients and healthcare systems when assessing the cost-effectiveness of new treatments in these disease areas may therefore be important to gauge an accurate assessment of relative value. This article explores the impact and importance of adding capacity constraints to cost-effectiveness analysis, illustrated using a case study of a simulation model for 2 treatments for neovascular age-related macular degeneration (nAMD) and diabetic macular oedema (DMO).

Healthcare capacity constraints in ophthalmology

Most healthcare systems have to operate with constrained capacity, which includes limited availability of hospital beds, doctors, nurses, medicines, and other resources required to deliver care to patients. Ophthalmology is one of the areas that is most affected by capacity constraints due to the increasing prevalence of retinal conditions, aging population, and the uptake of resource-intensive treatments that require frequent administration as often as once every 4 weeks.[2]

> Most healthcare systems have to operate with constrained capacity, which includes limited availability of hospital beds, doctors, nurses, medicines, and other resources required to deliver care to patients.

Capacity constraints are a worldwide issue. As of September 2022, nearly 10% of National Health Service (NHS) waiting lists were in ophthalmology, with 657,222 people in England waiting for their first NHS ophthalmology appointments.[3] Treatment delays caused by capacity constraints can have a significant impact on health; it is estimated that every month, approximately 22 people in the United Kingdom suffer from severe or permanent sight loss due to treatment delays in NHS eye clinics.[4] While the Royal College of Ophthalmologists set a 2-week referral target,[5] nearly four-fifths of optometrists report delays of 12 months or more for secondary care referrals, follow-up appointments, or treatments for their patients.[1] Recognizing the exceptional strain on NHS capacity, the National Institute for Health and Care Excellence (NICE) published productivity objectives that include more durable therapies in ophthalmology that allow fewer interventions and appointments.[6]

The issue of capacity constraints is not unique to the United Kingdom. A survey of 49 retina specialists in Spain concluded that proper implementation of anti-VEGF treatment regimens is complicated by healthcare resource limitations.[7] In France, an audit of intravitreal injection management in one ophthalmology department revealed a large increase in demand for intravitreal injections.[7] Internationally, there is a lack of ophthalmologists to deliver eye care services.[8]

Why consider health system capacity in economic evaluation?

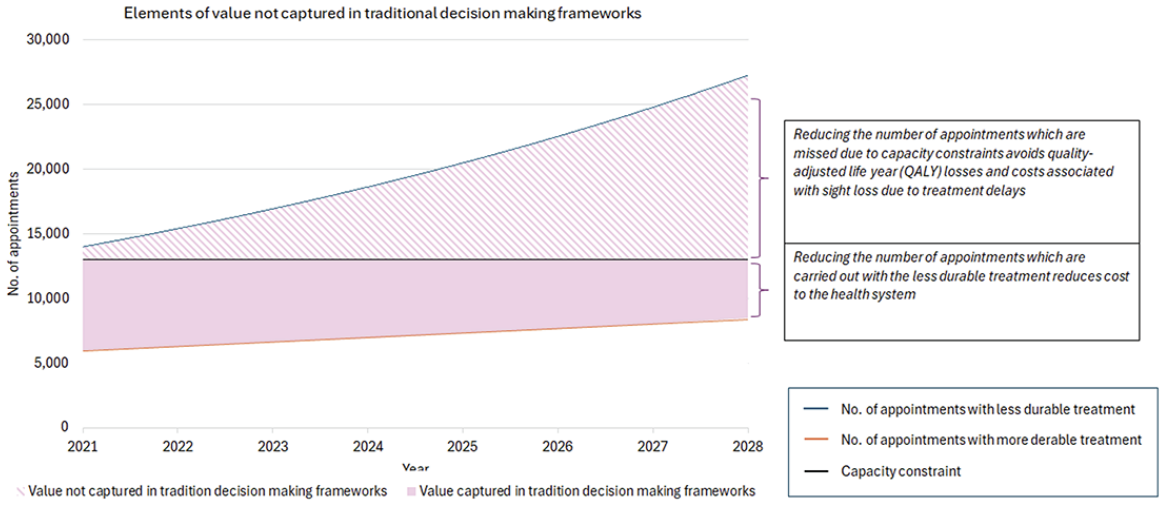
The emergence of sight-saving therapies with more durable outcomes and associated with more efficient use of resources (ie, longer treatment-free intervals between injections) offers an alternative. However, the traditional decision-making framework using cost-effectiveness analysis is not able to capture the value of reducing the strain on ophthalmology clinics, leading to undervaluation of treatments that can alleviate health system burden. This is illustrated using the conceptual example in the **Figure**. Economic evaluations that are able to quantify capacity constraints and incorporate them into cost-effectiveness analyses are needed in order to capture the true costs and benefits of treatments in disease areas where capacity constraints are an important consideration for healthcare decision making.

Ophthalmology case study to include capacity constraints in economic evaluation

To illustrate what impact capacity constraints could have on the cost-effectiveness of treatments for retinal conditions in the United Kingdom, a patient-level simulation model was developed.[9] The model simulated a cohort of patients treated using a more durable therapy with a higher per unit drug cost (drug A) versus a less durable therapy with a lower per unit drug cost (drug B) in the context of a typical NHS eye hospital. Drug A can extend the interval between 2 treatments to up to 16 weeks for around 60% of patients, while drug B can extend the treatment intervals to up to 12 weeks for around 40% of patients. These treatment types were chosen to illustrate how not considering the impact of capacity constraints could lead to different decisions about resource allocation and prioritization of treatments. The characteristics of simulated patients, their treatment regimens, and intervals were informed using published literature and expert opinion to reflect real treatment options available in clinical practice. Clinic capacity was simulated by setting a limit on the number of intravitreal injection appointments available each week over a 5-year period. This number determined when demand for appointments exceeded the routine capacity available at the hospital. In this case, either the patient visit was delayed or provided as a more expensive out-of-hour service once a maximum allowed delay time was reached. After consulting experts, it was assumed that the maximum allowed delay time was 2 weeks for first appointments for nAMD, 4 weeks for nAMD follow-up appointments and DMO first appointments, and 6 weeks for DMO follow-up appointments. The model then estimated the number of patient visits, the number and duration of delays, the cost of treatment, and the loss of quality-adjusted life-years (QALYs) due to treatment delays. Technical details of the model can be found in the published study.[9]

Over 5 years in a resource-constrained hospital, the number of injections required for treating patients with the less durable drug B exceeded the capacity of the hospital and therefore caused treatment delays, while the number of injections required for treating patients with durable drug A did not exceed capacity. Compared with drug B, drug A resulted in the avoidance of 18,910 treatment delays, incurred about £2 million (GBP) extra costs due to higher drug acquisition cost, and avoided the loss of 106 QALYs, resulting in an incremental cost-effectiveness ratio of £19,574/QALY, which is considered good value for money according to NICE's cost-effectiveness threshold in the United Kingdom. If the reality of capacity constraints had been ignored, decision makers may have prioritized

Figure. Conceptual example of capacity constraints in economic evaluation. The number of appointments required with a less durable treatment is represented by the blue line, and the number of appointments with the more durable treatment by the orange line. When considering the reality of overburdened health systems, the number of patients who can be treated in any given year is constrained, and any who cannot be treated immediately are placed on a waiting list. As such, the value of a more durable treatment that reduces the demand for appointments includes health system cost savings (solid shaded area), as well as avoidance of quality-of-life losses and costs associated with sight loss due to treatment delays (the pattern shaded area).



drug B over drug A due to cost savings, leading to worse health outcomes for the population.

Discussion

This simulation study offered key insights on the inclusion of capacity constraints into economic evaluations. As expected, the introduction of a treatment option with more durable treatment effect reduces the total number of injections required, and therefore reduces the number of delayed appointments. Aside from the immediate cost savings from reduced service use, our framework allowed us to capture the benefit of avoiding delayed treatment to patients, which in our case was captured through additional QALYs accumulated over the 5-year model horizon. The cost and QALY impact were sensitive to several supply-side parameters, including the number of available clinic appointments, allowed treatment delay, and increase in demand over time, as well as some demand-side parameters, such as treatment discontinuation. As with any simulation exercise, the results are subject to uncertainty and should be interpreted with caution, although the study conclusions remained consistent when tested using sensitivity analyses.

> Economic evaluations that are able to quantify capacity constraints and incorporate them into cost-effectiveness analyses are needed in order to capture the true costs and benefits of treatments in disease areas where capacity constraints are an important consideration for healthcare decision making.

No published studies have considered capacity constraints in the cost-effectiveness analysis of a treatment for nAMD and DMO. Some studies in other disease areas have incorporated capacity constraints into economic evaluations. For example, in oncology, pathology laboratory capacity constraint would result in a loss of net monetary benefit and reduced cost-effectiveness of a test-treat intervention.[10] These studies and our study suggest that it is important to consider the impact of capacity constraints on patients and health systems when assessing the value of treatments. Ignoring the cost and QALY impact of delayed treatments can lead to inefficiencies in the allocation of scarce healthcare resources. The case study has shown that the inclusion of capacity constraints can change the conclusion of a cost-effectiveness analysis. Although less durable drug B is on the face of it "cheaper" than durable drug A in terms of the price per treatment, it was associated with considerable QALY losses arising from treatment delays. As a result, when taking capacity constraints into consideration, the more durable drug A was in fact considered cost-effective compared to drug B according to well-established thresholds such as the one adhered to by NICE in the United Kingdom.

Conclusion

Incorporating capacity constraints in economic evaluations is essential to comprehensively evaluate the value of treatments. By doing so, healthcare decision makers can make informed choices that prioritize both cost-effectiveness and patient outcomes in disease areas with capacity limitations.

Capacity constraints should be considered explicitly as part of health technology assessment in therapeutic areas with limited capacity, as cheaper treatment options may not necessarily be the most cost-effective if they impose additional burden on resource-scarce systems, and the overall health benefits of more durable treatments may be undervalued. Decision makers understand the context of limited budget resources but may not fully appreciate the consequences of limitations in other healthcare resources like workforce and clinic capacity. Recognizing the "true" value of treatments in the real-world setting where health systems have limited resources is critical to ensure cost-effective and sustainable healthcare systems.

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Value Assessment of Combination Digital Health Technologies Under New NICE Evidence Standards Framework

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Despite rapid growth and significant benefits to patients and healthcare systems, access to and reimbursement of digital health technologies have proven difficult.

NICE's Evidence Standards Framework starts addressing this gap by providing a comprehensive health technology assessment framework for DHT developers and assessors.

Robust clinical and economic data that reflect the technology accuracy, UK clinical setting for the target population, improved outcomes and costs, and resource use in the NHS were main decision drivers.

Higher risk technologies require more rigorous evidence.

Background

Digital health technologies (DHTs) are defined by the World Health Organization (WHO) as "the field of knowledge and practice associated with the development and use of digital technologies to improve health"[1] and have been increasingly used in clinical practice.[2] DHTs cover a wide range of technologies, such as mobile apps, genomics, artificial intelligence (AI), machine learning (ML), wearable devices, and telemedicine.[3,4] The implementation of DHTs has the potential to provide significant benefits both to patients and healthcare systems. Specifically, the combined use of drugs/medical devices with a digital component (combination DHTs [cDHTs]), such as an insulin pump monitored by an application or an ingestible sensor embedded in a tablet, has seen a rising trend in the healthcare industry.[3,5,6]

One of the current challenges in the DHTs landscape is related to the lack of established and well-characterized regulatory/assessment frameworks and reimbursement pathways. Some progress has been made with several countries (such as France, Germany, and the United Kingdom) establishing reimbursement pathways for DHTs, although with significant variability.[4]

To address the challenges of assessing these innovative technologies under the traditional frameworks, the National Institute for Health and Care Excellence (NICE), the Health Technology Assessment (HTA) body in the United Kingdom, published the Evidence Standards Framework (ESF) for the assessment of DHTs in March 2019 (updated in August 2022). The ESF aims to ensure that new DHTs are clinically effective and add value to the healthcare system, and that these are assessed consistently across the National Health System (NHS). This framework is mostly directed at decision makers and companies who develop the DHTs that will later on be considered for use and commissioning in the health system. However, it does not have a mandatory statute and it does not constitute a NICE evaluation process.[7-9]

NICE's ESF describes the type and level of evidence that different categories of DHTs (defined in 3 tiers, based on the DHT's potential risk to the user and to the system) should be able to demonstrate and comprises 21 nonmandated standards across 5 areas: (1) design factors, (2) describing value, (3) demonstrating performance, (4) delivering value, and (5) deployment considerations. The majority of the standards (17 out of 21) are applicable to all DHTs, regardless of tier.[8,9]

Figure 1. Five groups of evidence standards and their applicability to different tiers

Abbreviations: ESF, evidence standards framework; NICE, National Institute for Health and Care Excellence. Reference: NICE ESF[9]

This article evaluated the evidence alignment of recently assessed cDHTs with the ESF, as well as identified key assessment criteria employed by NICE, providing insights into the use of the ESF for stakeholders involved in the development and assessment of cDHTs.

Methodology

In order to identify the cDHTs assessed by NICE since the publication of the ESF, a search was conducted using the HTA Accelerator™, a comprehensive database that includes publicly available HTA reports. The search was conducted on March 28, 2023, and restricted to assessments published since 2019 (later updated on July 22, 2024, restricted to assessments published since March 28, 2023). The inclusion criteria consisted of device interventions assessed by NICE.

> The implementation of DHTs has the potential to provide significant benefits both to patients and healthcare systems.

Search results were then hand-selected to include assessments of cDHTs only. Supporting data were extracted for the intervention details, clinical and economic evidence, agency critique, and recommendations. For completeness, a hand-search of published information on NICE's website for each cDHT was also conducted. Lastly, the available information from each appraisal was compared against each of the 21 standards of NICE's ESF.

Results

In the first search (March 2023), 75 assessments were identified, and 25 assessments were identified in the second search (July 2024), with a total of 9 cDHTs meeting the inclusion criteria, of which 5 received a positive recommendation (with restrictions).* See **Table 1**.

Clinical evidence

All assessments included a systematic review identifying relevant clinical evidence on the cDHTs under evaluation, with randomized controlled trials (RCTs) available for 6 of the 9 assessments (with ongoing RCTs for one of them), and observational/survey data only for the remaining 3 assessments (of which one had ongoing RCTs). Most (8 out of 9 assessments) of the identified evidence included UK-based data. In addition, NICE established an evidence generation plan for 2 of the assessments, which provides information on the main evidence gaps, ongoing studies, and how these gaps can be addressed by real-world evidence (RWE).

Although RWE can be used to demonstrate that cDHTs can meet their claimed benefits in the UK clinical practice, only 3 assessments included this.

Economic evidence

All 9 assessments included an economic analysis, with 7 including a cost-effectiveness analysis, one a cost minimization model, and one a cost comparison analysis, whereas only 3 included a budget impact analysis. Although a budget impact analysis is applicable to all DHTs, a cost-effectiveness analysis is applicable to DHTs with higher financial risk only (those with substantial implementation costs). The potential cost-effective use of NHS resources was noted; however, uncertainties were highlighted in terms of the clinical data (namely the lack of robustness and high risk of bias, uncertainty in the size, and longevity of claimed benefits, lack of data in the United Kingdom or the target population), model inputs or resource use, making it difficult for NICE to draw firm conclusions about the benefits of routine use of the technologies in the NHS. Further data collection relevant to the NHS setting, as well as price reductions, were the most common recommendations.

ESF standards requirements

Among the 21 ESF evidence standards, the ones most commonly aligned to were the availability of clinical evidence and economic analyses, as well as defining the level of professional oversight, the target population, and current and proposed treatment pathway.

> One of the current challenges in the DHTs landscape is related to the lack of established and well-characterized regulatory/assessment frameworks and reimbursement pathways.

Conversely, evidence to support other requirements, such as considering environmental sustainability, establishing good data practices in the DHT design, providing a budget impact analysis, and ensuring transparency about deployment requirements, was sporadically available.

NICE recommendations

The 5 assessments receiving a positive recommendation demonstrated promising benefits for patients and potential cost savings for the NHS, although considerable uncertainties in the clinical and/or economic evidence were highlighted. Thus, these cDHTs were conditionally recommended for use in the NHS, with the collection of further evidence (such as robust evidence generation on the cDHTs clinical benefits, as well as on its testing, interpretation and accuracy, real-world data collection, data collection on resource use, and data relevant for the UK practice) being a common condition in all assessments.

The 4 assessments receiving a negative recommendation were deemed as not having sufficient evidence to support its routine use in the NHS. Recommendations for further research have been made for all assessments,

* Of note, 1 of the assessments captured in the search (HTE 11, Artificial intelligence technologies to aid contouring for radiotherapy treatment planning: early value assessment) was excluded due to the fact that it assessed 11 artificial intelligence (AI) technologies, which consisted of standalone softwares that did not meet the inclusion criteria for a cDHT. However, 2 out of the 11 technologies assessed (MRCAT Prostate plus Auto-contouring and RayStation) combined the AI functionality with a device, which could therefore fit into the cDHT category. The HTE11 guidance issued a positive recommendation for 9 of the 11 technologies (including the 2 cDHTs above) to be used in the NHS while further evidence is generated.

Table 1. Data extracted for cDHTs assessed by NICE since the publication of the ESF

Combination DHTs assessed by NICE									
Assessment	**Lead-I ECG**	**Zio XT**	**QAngio XA 3D QFR and CAAS vFFR**	**DyeVert Systems**	**Synergo**	**MRI fusion biopsy systems for diagnosing prostate cancer**	**KardiaMobile**	**Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes**	**Devices for remote monitoring of Parkinson's disease**
Guidance no.	DG35	MTG52	DG43	MTG60	MTG61	DG53	HTE10	TA943	DG51
Recommendation	**NEGATIVE** *- 2019 -*	**POSITIVE W/ RESTRICTIONS** *- 2020 -*	**NEGATIVE** *- 2021 -*	**NEGATIVE** *- 2021 -*	**POSITIVE W/ RESTRICTIONS** *- 2021 -*	**NEGATIVE** *- 2023 -*	**POSITIVE W/ RESTRICTIONS** *- 2023 -*	**POSITIVE W/ RESTRICTIONS** *- 2023 -*	**POSITIVE W/ RESTRICTIONS** *- 2024 -*
Evidence standards framework criteria									
1- The DHT should comply with relevant safety and quality standards									
2- Incorporate intended user group acceptability in the design of the DHT (patient involvement in design, development, or testing)									
3- Consider environmental sustainability									
4- Consider health and care inequalities and bias mitigation									
5- Embed good data practices in the design of the DHT									
6- Define the level of professional oversight									
7- Show processes for creating reliable health information									
8- Show that the DHT is credible with UK professionals									
9- Provide safeguarding assurances for DHTs where users are considered to be in vulnerable groups or where peer-to-peer interaction is enabled	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
10- Describe intended purpose and target population									
11- Describe the current pathway or system process									
12- Describe the proposed pathway or system process using the DHT									
13- Describe the expected health, cost, and resource impacts compared with standard or current care or system processes									
14- Provide evidence of the DHT's effectiveness to support its claimed benefit									
15- Show real-world evidence that the claimed benefits can be realized in practice (pilot in UK setting)									
16- The company and evaluator should agree a plan for measuring usage and changes in the DHT's performance over time									
17- Provide a budget impact analysis									
18- For DHTs with higher financial risk, provide a cost-effectiveness analysis									
19- Ensure transparency about requirements for deployment									
20- Describe strategies for communication, consent, and training processes to allow the DHT to be understood by end users									
21- Ensure appropriate scalability (load testing)									

Caption: Green, complies with ESF; Red, does not comply with ESF; Orange, unclear if it complies/partially complies with ESF.
cDHT indicates combination digital health technology; DG, diagnostics guidance; DHT, digital health technology; ESF, evidence standards framework; HTAA, HTA Accelerator; HTE, health technology evaluation; MTG, medical technologies guidance; N/A, not applicable; NICE, the National Institute for Health and Care Excellence; TA, technology appraisal guidance.
Note: for standard 18 (cost-effectiveness analysis), cDHTs were marked as compliant with the ESF framework (green) if a cost-effectiveness/cost-utility analysis was conducted, regardless of whether these could be defined as having higher financial risk or not

namely referring to accuracy and failure tests, patient experience studies, data collection assessing the impact of implementing a cDHT, and more robust clinical evidence generation.

Conclusion

The publication of the ESF is expected to fill a gap in the innovative and challenging setting of DHTs by supporting both developers and evaluators with a HTA framework and a risk-proportional set of evidence standards.

Although a high variability has been observed in terms of evidence, the availability of robust clinical and economic data, reflecting the cDHT's accuracy, use in the UK setting and the target population, and its potential for improved outcomes and costs/resource use in the NHS, were common elements among the positively recommended technologies.

Nine cDHTs assessments have been published by NICE since the ESF publication, which supported the current analysis. Overall, the analyzed assessments were partially aligned with the recent framework, although some standards (mostly related with the DHT design, deployment, and environmental sustainability) were only sporadically available, which may be due to the sensitive nature of such information. Moreover, while most of the assessments started after the publication of the ESF, it is plausible that the technology development did not fully incorporate the ESF standards into account.

Although a high variability has been observed in terms of evidence, the availability of robust clinical and economic data, reflecting the cDHT's accuracy, use in the UK setting and the target population, and its potential for improved outcomes and costs/resource use in the NHS, were common elements among the positively recommended technologies. Where feasible, RCTs were the gold-standard study designs for the clinical assessment of cDHTs; however, alternative study designs were also considered acceptable in some assessments, with the collection of RWE being encouraged as part of evidence-generation recommendations. Finally, developers should also consider the level of risk under which the cDHT would be assessed when developing their evidence-generation plan, as higher risk tools will require a more rigorous evidence package.

This analysis provides useful insights into the current use of ESF and key criteria involved in successful cDHTs assessments. Moreover, it highlights the variability in the available evidence for cDHTs and the need for close collaboration between stakeholders to ensure clear requirements for the successful integration of cDHTs into healthcare systems are achieved.

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Quality of Patient Engagement Activities in Health Economics and Outcomes Research: Insights From the ISPOR Community

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Patient engagement is a foundational component of patient-centered research, and there is growing interest in measuring and evaluating the quality of patient engagement activities.

A survey conducted among ISPOR members indicates there are areas that can be improved with regard to patient-engagement activities and the evaluation of the quality of those activities.

Education and communication are required to ensure that the HEOR community is ready and able to work with patients as research partners.

Education and communication regarding the value of patient engagement will help the HEOR community to better comprehend the necessity to invest in, and the potential benefits to be derived from, patient engagement, thereby helping to mitigate funding as a barrier for patient-engagement activities.

Introduction

Patient centricity is increasingly recognized as important in health economics and outcomes research (HEOR) and is one of the ISPOR 2024-2025 Top 10 HEOR Trends.[1] Patient engagement is a critical component of patient-centered research and is defined as "the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise."[2] However, simply stating an activity is "patient-centered" or involves "patient engagement" does not provide enough information for readers and researchers to assess the quality of patient engagement. There is growing interest in measuring and evaluating the quality of patient-engagement activities.

> However, simply stating an activity is "patient-centered" or involves "patient engagement" does not provide enough information for readers and researchers to assess the quality of patient engagement.

For example, the Patient-Centered Outcomes Research Institute (PCORI), in addition to updating their Foundational Expectations for Partnerships, recently released a call for applications to measure and test engagement approaches.[3,4] Industry is also increasingly recognizing the importance of adopting patient-centric approaches and making their efforts more focused on meeting patients' needs and preferences.[5]

ISPOR's Patient-Centered Special Interest Group (SIG) aims to facilitate the engagement and partnership with patients (and families and caregivers) in all stages of health-related research and care delivery in order to improve healthcare access and patient outcomes.[6] To achieve this goal, the SIG surveyed its members as well as those of closely related SIGs (eg, Clinical Outcome Assessment and Rare Disease) with the objectives of understanding member experiences with patient engagement, encountered challenges and facilitators to engagement, and assessing engagement quality.

> There appears to be a lack of understanding regarding the definition and fundamental role of patient engagement in patient-centered or patient-focused research.

In this article, we present the survey results and discuss the implications of these findings for the HEOR community.

Survey of ISPOR membership: Measuring and evaluating the quality of patient engagement activities

The survey was developed by the leadership team of the Patient-Centered SIG and underwent review by ISPOR members, including those with experience working in patient-centered outcomes research. The survey was emailed to members of ISPOR's Patient-Centered, Clinical Outcome Assessment, and Rare Disease SIGs in August 2023. The survey comprised 23 questions, covering the following dimensions through a combination of closed- and open-ended responses:

- Member experiences with engagement activities
- Facilitators encountered
- Challenges encountered
- Experience with assessing engagement quality.

Respondent demographic and research work-setting descriptors were also collected. Responses were collected anonymously. The initial email was sent with 2 follow-up reminders to encourage responses.

Results

The distribution of perspectives covered by survey participants (n=103, see **Figure 1**) was generally similar to the overall ISPOR membership.

The survey respondents identified their primary geographic region of interest as follows: Global (36.9%), North America (31.1%), and Asia Pacific (including Oceania) (14.6%). The remaining responses collectively comprised Western Europe, Central and Eastern Europe, the Middle East, and Latin America (17.5%).

Member experiences with engagement activities

Survey results showed that a large majority of respondents (76.7%) indicated their current work to be "patient-centered," while the remaining respondents either felt unsure or did not consider their work to be patient-centered. Nearly three-quarters of respondents (73.8%) reported they had engaged patients in their research at some point.* Of the 74 respondents, most (77%) reported that they currently engaged patients in their research.

> It is important for the HEOR community to recognize the distinction between patients as participants in studies and patients as active partners in development and design.

The survey provided insights into the primary attributes of patient-centered research, as perceived by the majority of respondents. These include a focus on outcomes that are important to patients (79.6%), and the collection of patient experience, preferences, or opinions through methods such as focus groups and interviews (73.8%). The most essential attribute of patient-centered research, involving patients as research partners, received only 45.6% of the votes. **Figure 2** illustrates these findings.

The survey findings highlighted the most frequently reported, important aspects of patient engagement in research. Specifically, "Representativeness/diversity of patients (including patients as research partners)" emerged as the most crucial aspect, cited by 70% of respondents. "Studies guided by patient experience data from surveys, focus groups, and interviews" (58.3%), and "Including patients throughout all stages of research from ideation or planning through to dissemination/post-market surveillance" (57.3%) followed.

Figure 1. Professional areas of practice of survey respondents

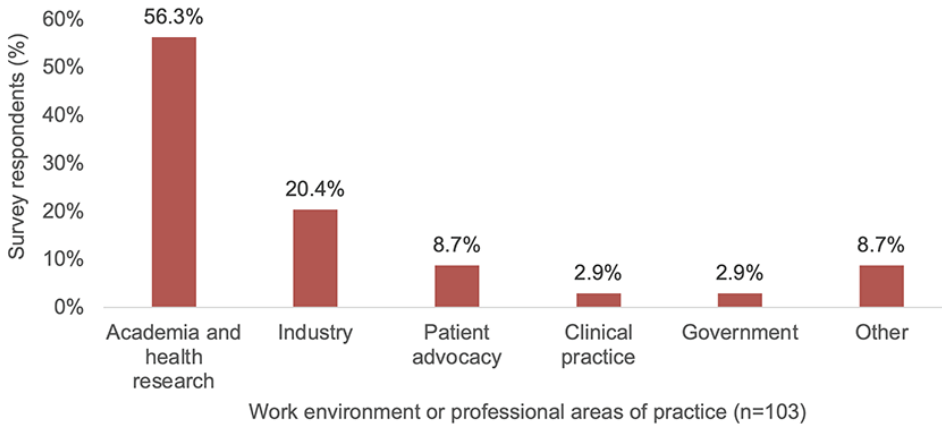
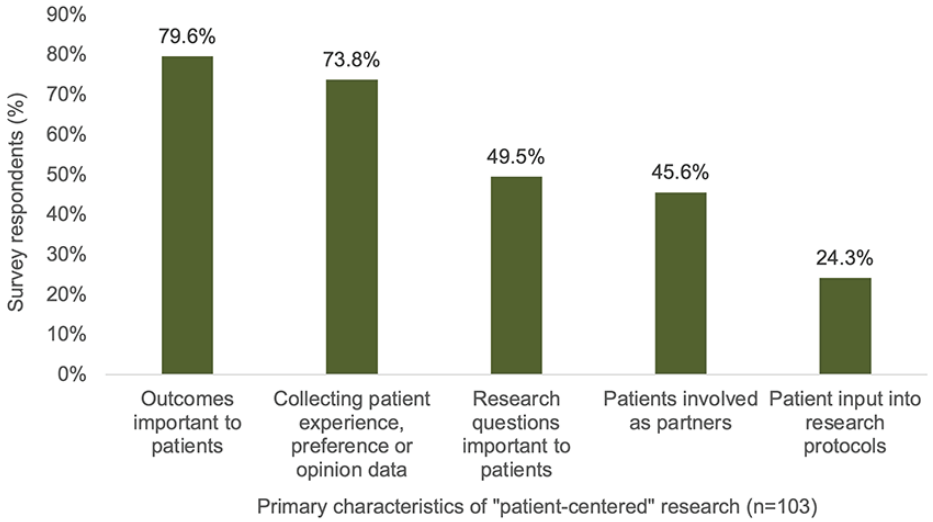


Figure 2. Primary characteristics of "patient-centered" research; respondents could select up to 3 responses



Note: The full wording of these response options in the survey were as follows: "Focused on outcomes important to patients," "Collecting patient experience, preference or opinion data through methods such as focus groups, interviews, or preference elicitation methods," "Focused on research questions important to patients," "Patients involved as partners (ie, coinvestigator, advisor, consultant)," and "Patient input into research protocols."

* Based on the National Health Council's glossary, a patient was defined in the survey as *"Someone having or at-risk of having a medical condition(s), whether or not they currently receive medicines or vaccines to prevent or treat a disease. The term "patient" is also used broadly to include persons with an illness, their care partners and family members, and representatives of the patient community, or patient organizations."*

Facilitators encountered
The survey revealed several key facilitators to engaging with patients in research. These results are shown in **Figure 3**.

Challenges encountered
Respondents also identified prevalent barriers encountered when engaging patients in research endeavors. These results are shown in **Figure 4**.

Experiences with assessing engagement quality
The survey highlighted the prevalent use of principles or guidance to inform engagement activities with patients, with 77.2% (n=57 responding to this question) utilizing such frameworks. Commonly reported principles or guidance included the US Food and Drug Administration's Patient-Focused Drug Development Guidance documents (43.9% of the n=41 responding to this question),[7] the Patient Focused Medicines Development Patient Engagement Quality Guidance and the UK Standards for Public Involvement (both 22.0%),[8,9] and the PCORI engagement rubric (19.5%).[10]

Frequently reported engagement methods were surveys (67.9% of the n=53 responding to this question), interviews (66.0%), focus groups (54.7%), patients on advisory panels/committees/work groups (50.9%), and patient consultants/advisors (41.5%). Virtual engagement was selected by the majority of respondents (92.5%) given multiple selection options.

Furthermore, the survey explored the evaluation and assessment of the quality of patient-engagement activities. Just under half of respondents (45.3% of the n=53 responding to this question) reported conducting evaluations, with the most frequently reported methods including participant interviews and focus groups (42.3%), formal internal protocols (34.6%), and the use of publicly available resources, questionnaires, or tools (26.9%). These findings provide valuable insights into the diverse approaches and practices surrounding patient engagement in research activities.

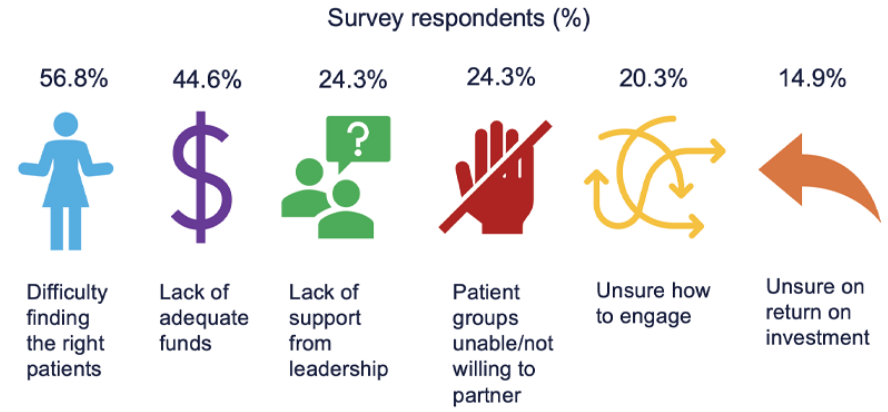
Of the 24 respondents answering the question, 16 (66.7%) reported that they asked patient research partners to assess the quality of their personal engagement experience as part of evaluation. The reported methods were "Participant interviews and focus groups" (56.2% of the n=16 responding to this question), "Formal, internal protocol in place" (25.0%), and "Use publicly available resources/questionnaires/tools" (18.8%). The remaining respondents stated that they did not do this.

Survey respondents (n=93) identified the top 3 attributes of good-quality patient engagement activities, with "Trust" ranking highest at 57.0%, followed closely by "Transparency" at 53.8%, and "Representativeness/diversity" at 48.4%. Regarding the long-term outcomes of good-quality patient engagement in research, respondents (n=93) emphasized "Findings that change patient health" as their top choice at 52.7%. This was followed by "Better quality studies" at 23.7%, and "Increased patient trust in science" at 16.1%. These insights provide valuable perspectives on the perceived effectiveness and impact of patient engagement in research endeavors.

Figure 3. Facilitators encountered when engaging patients (n=74); respondents could select multiple responses

Note: The full wording of these response options in the survey were as follows: "Patient groups (Patient Advocates, Patient Organizations [nonprofit], Patients or Caregivers) are willing and able to partner," "Patient enthusiasm/motivation," "Organization supports/is in favor of the work," and "Researcher familiarity with or experience with engagement."

Figure 4. Barriers encountered when engaging patients (n=74); respondents could select multiple responses



Note: The full wording of these response options in the survey were as follows: "Difficulty finding the right patients," "Lack of adequate funds for patient engagement," "Lack of support from leadership for engagement," "Patient groups (Patient Advocates, Patient Organizations [nonprofit], Patients or Caregivers) are not able or not willing to partner," "Unsure how to engage," and "Unsure of Return on Investment."

Insights and future directions

The survey results indicate there are areas that can be improved with regard to patient-engagement activities and the evaluation of the quality of those activities. Despite the majority of respondents considering their research as patient-centered, it is essential to address existing misconceptions and promote authentic patient-centered research. Specifically, there appears to be a lack of understanding regarding the definition and fundamental role of patient engagement in patient-centered or patient-focused research.

> Addressing the difficulties of finding representative patients with lived experience and securing sufficient funding are vital to advancing patient-centered research.

In particular, it is important for the HEOR community to recognize the distinction between patients as participants in studies and patients as active partners in development and design. Activities such as collecting patient experience, preference, or opinion data through qualitative methods such as focus groups, interviews, or preference elicitation methods are patient participation in research and not authentic patient engagement in research. This distinction appears to be unclear to many survey participants, highlighting the need for educational initiatives among the HEOR community. In addition, the finding that representativeness and diversity are among the most crucial aspects of engagement aligns with community efforts.[4] However, the fundamental characteristic of patient-centered research—which involves including patients as partners throughout all stages of research—received only 57.3% of the votes.

In addition, patient organizations and individual patients currently play a crucial role in facilitating patient-centered research. Active participation of other key stakeholders should be promoted. Addressing the difficulties of finding representative patients with lived experience and securing sufficient funding are vital to advancing patient-centered research. Many participants cited funding as an important barrier, highlighting the need for better understanding of the value of patient engagement. This understanding can help the HEOR community appreciate the necessity of investing in patient engagement and the broader benefits it can bring to patient-centered research. This also relates to another survey finding regarding representativeness and diversity; adequate funding is an important aspect of reaching patients for engagement, particularly those who may be historically underrepresented in research.

The assessment of patient-engagement quality also appears to be an area needing greater attention. Awareness about the need for assessment, existing assessment tools, and needed research to enhance what is available should be advanced. Greater awareness of existing tools[7,8,9,10] can support their uptake in practice and help us to understand how they can be further improved and built upon.

Our hypothesis was that these 3 SIGs would naturally attract individuals who are more knowledgeable about the topic; thus, starting with these SIG members would provide a valuable baseline. We acknowledge that the results may not be generalizable to the entire ISPOR membership or the broader HEOR community.

The low response rate to certain questions, particularly those related to principles or guidance informing patient engagement and the assessment of its quality, suggests that a proportion of survey respondents may not be aware of available resources or standard practice and/or lack hands-on experience with patient engagement, making them unable or unwilling to answer these questions. Despite our inability to pinpoint an accurate reason, this candid depiction highlights the need for further efforts to engage and educate stakeholders on these topics. Such endeavors could pave the way for more informed and comprehensive responses in future surveys.

Conclusion

This snapshot of the HEOR community's views and experiences with patient engagement and patient-centered research provides valuable insights about the need for further efforts within the HEOR community to understand and enhance patient engagement practices. This can be achieved through education, effective communication, and community capacity building among all HEOR stakeholders.

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Futureproofing Healthcare Financing in Six Association of Southeast Asian Nations Countries (ASEAN-6)

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ASEAN-6 countries are grappling with challenges related to demographic shifts and a rise in noncommunicable diseases, resulting in a need to pivot more toward preventive healthcare and strengthening of primary care.

Some ASEAN-6 health systems are struggling to improve care with a lack of available fiscal space.

Efficiency improvements and innovative financing mechanisms, such as risk-sharing agreements, are potential opportunities to generate fiscal space to help achieve SDG3 and universal health coverage.

Introduction

The United Nations Sustainable Development Goal for good health and well-being (SDG3) sets targets for various aspects of healthy living and healthcare systems.[1] It proposes a world where healthcare is a human right, aiming for universal health coverage (UHC) for at least 80% of the population, regardless of socioeconomic status or geographic area, by 2030.

While certain countries in the Southeast Asia region have achieved several SDG3 targets, many are still on the road to achievement. They also face challenges funding healthcare and UHC with limited government fiscal space (the budgetary room allowing governments to provide resources to a public purpose without impacting financial sustainability), limited or absent social health insurance, and high out-of-pocket payments. In particular, there is a predicted annual fiscal gap of US$371 billion across low- and middle-income countries (**Table 1**), hampering UHC. To achieve UHC, countries need to overcome serious health financing challenges and establish sufficient and sustainable funds, protection from financial risks, and efficiency improvements in selecting and delivering available goods and services. In August 2023, the Asia-Pacific Economic Cooperation (APEC) health financing forum highlighted the urgency of creating sustainable funding, particularly in light of the recent COVID-19 pandemic, the threat of future pandemics, and the rising levels of noncommunicable diseases (NCDs) and comorbidities.[2] We aimed to explore UHC-related challenges faced by 6 Association of Southeast Asian Nations (ASEAN) countries (ie, Indonesia, Malaysia, the Philippines, Singapore, Thailand, and Vietnam), as well as several health financing methods that may help achieve UHC and the broader SDG3 goals.

Research methodology

Our investigation included mixed methodologies, including a semistructured literature review and a web Delphi exercise (using the Welphi platform www.welphi.com). The Delphi was designed to gather insights from key stakeholders regarding critical healthcare and healthcare financing challenges in the target countries. The 3-round Delphi used an analytical framework consisting of (1) 35 healthcare-related challenges and (2) 25 statements pertaining to

Table 1. Fiscal gap of government expenditure on healthcare in the countries of interest

Country	GDP ($)	Domestic general government health expenditure (% of GDP)	Domestic general government health expenditure fiscal gap (% of GDP)	Government health expenditure fiscal gap ($)
Indonesia	$1.1 trillion	1.88%	3.12%	$37.0 billion
Malaysia	$373 billion	2.18%	2.82%	$10.5 billion
Philippines	$394 billion	2.49%	2.51%	$9.9 billion
Singapore	$397 billion	3.17%	1.83%	$7.3 billion
Thailand	$506 billion	3.07%	1.93%	$9.8 billion
Vietnam	$366 billion	2.11%	2.89%	$10.6 billion

Note: The fiscal gap in percentage terms was determined by subtracting the domestic general government health expenditure as a percentage of GDP (World Bank, 2020) from the ideal percentage of GDP allocated to health expenditure (WHO benchmark figure of 5%). The corresponding monetary value was calculated by multiplying the GDP percentage fiscal gap by the country's GDP (World Bank 2021). These calculations provide insights into the gap between current health expenditure and the desired level of investment in healthcare for each country. The medical savings account system in use ensures that Singapore already meets the WHO benchmark and that their fiscal gap is lower than that presented here. GDP indicates gross domestic product.

financial mechanisms for increasing fiscal space. The stakeholders (eg, healthcare experts, members of the pharmaceutical industry, researchers and academics, health economists, and decision makers) from each of the target countries were asked to comment on and propose new healthcare challenges and potential financial mechanisms

> To achieve UHC, countries need to overcome serious health financing challenges and establish sufficient and sustainable funds, protection from financial risks, and efficiency improvements in selecting and delivering available goods and services.

(round 1) and then rate their level of agreement/disagreement with the factors in their country context using a Likert scale (rounds 2 and 3). A total of 45 stakeholders completed all 3 rounds. This methodology allowed us to identify challenges facing national healthcare systems and gauge local appetite and willingness for potential financing mechanisms and reform.

Key healthcare challenges in ASEAN-6

We analyzed healthcare-related challenges across 5 areas: (1) general and UHC-related challenges, (2) financing challenges, (3) implementation challenges, (4) supply-side challenges, and (5) demand-side challenges. Specific detail on country responses can be seen in the accompanying report[3] but in general, shared difficulties were felt across the region, including issues such as aging populations and increasing levels of NCDs. These factors impact both healthcare financing and demand. Older individuals often require more costly and complex care due to a higher prevalence of NCDs and comorbities,[4] while the shrinking taxable workforce means less money for healthcare services. Further challenges identified across the nations include access inequalities, reduced health literacy in patients and healthcare workers alike, high proportions of informal workers, limited effectiveness of information technology in the healthcare system, and raw material cost increases. Effective management of these issues requires integrated health systems and a shift in focus from secondary to primary care, as suggested by the UN 2023 High-Level Meeting on UHC.[5] The optimal approach for primary healthcare is a blended provider payment mechanism with capitation (ie, a healthcare plan that provides payment of a flat fee for each patient it covers) at the core, linking the population with services. The involvement of performance-based payments for specific activities can also be beneficial.[6] Singapore is a leader here with a focus on preventive care and a shift to capitation-based payments.[7] Countries should concentrate on achieving full population coverage with affordable packages of services centered on prevention and delivered via effective primary care services. While they should look to build additional primary care infrastructure and address human resource gaps, they should also invest in effectively adopting digitalization in the healthcare space. Importantly, these steps should not be limited to the Ministry of Health; UHC is not the responsibility of health ministers alone. Our environment, socioeconomic status, and genetic predisposition all play a role in health and, as such, healthcare should not be thought of as "in silo" but should be considered in an interlinking manner with other aspects related to the social determinants of health. Action is required across government and must involve ministers of finance, environment, labor, and education, among others.

Increasing fiscal space for healthcare

Healthcare improvements are not possible without the generation of funds, and as countries progress toward UHC, fiscal space becomes a key factor in its success. It can be created by increasing healthcare expenditure efficiency and generating additional funds through various methods. Using the Delphi process, we assessed 45 stakeholders' opinions on different mechanisms for increasing fiscal space. Again, specific results can be seen in the accompanying report.[3] Unsurprisingly, efficiency in healthcare—the ability to deliver high-quality healthcare services while streamlining processes, minimizing waste, reducing costs, and optimizing resource allocation system[8]—proved popular among the stakeholders. There was an overarching level of agreement for each of the 10 efficiency mechanisms, suggesting they are an effective way to build fiscal space for healthcare (**Table 2**). Stakeholders also considered 8 "traditional" financing mechanisms, including taxation policies, health insurance, and social protection. "Sin taxes" proved popular, assuming revenue gains were earmarked for healthcare. Unsurprisingly, when you consider that if all countries increased excise taxes on tobacco, alcohol, and sugary beverages by 50% worldwide, more than 50 million premature deaths could be averted over the next 50 years and more than USD $20 trillion of additional revenue could be generated.[9] In contrast, partially privatizing the health system and introducing medical savings accounts received limited agreement despite the latter's success in Singapore.[10]

> Healthcare should not be thought of as "in silo" but should be considered in an interlinking manner with other aspects related to the social determinants of health.

Lastly, our analysis looked at 6 innovative financing models, including annuity models, risk-sharing agreements and health and social impact bonds. Risk-sharing agreements (ie, performance-based contracts using agreed-upon financial- or outcomes-based measures) were attractive to respondents from all countries. The use of annuity bonds (financial models that can provide a regular income stream in exchange for a lump sum or periodic payments) and social impact bonds (which leverage private capital to fund health, social, and development programs based on achieved outcomes) seemed less attractive to some, perhaps due to lack of familiarity. These mechanisms could play a valuable role in enhancing the fiscal space for healthcare in ASEAN countries. Furthermore, the focus on measurable outcomes ensures incentives for high performance, building accountability within the health sector. However, these rely on robust data collection facilities that require significant investment if not already in place. The private sector can also be engaged to raise UHC resources,

both via foreign investment and blended financing. However, mechanisms for blended financing need to be strengthened, and legislation must be in place that allows for their development and implementation. Furthermore, local stakeholders should be fully engaged in a collaborative design approach to ensure the feasibility of any innovative financing mechanism in local contexts.

Conclusion and implications

The pursuit of UHC is fraught with significant financing and resource allocation challenges, alongside major demographic changes, including aging populations and the increasing prevalence of NCDs. While some countries have made considerable progress toward achieving the targets set out in SDG3, many are still grappling with limited fiscal space and high out-of-pocket payments. Our research highlights a need for a significant transformational change toward more integrated healthcare systems, focusing on prevention and primary care services.

> A holistic approach from stakeholders within education, health, finance, and environment would ensure health improvements are sustainable, addressing health beyond the individual patient and incorporating the social determinants of health.

Addressing the identified healthcare challenges requires a multifaceted approach, including stakeholders beyond the Ministry of Health. Efforts need to be made on the ground to improve health literacy as well as understanding and accessing available health system services. A holistic approach from stakeholders within education, health, finance, and environment would ensure health improvements are sustainable, addressing health beyond the individual patient and incorporating the social determinants of health.

Ultimately, achieving UHC in ASEAN-6 countries will depend on the ability of countries to mobilize sustainable funds, protect against financial risks,

Table 2. Financing mechanisms and average agreement levels across ASEAN-6 countries

Financing Mechanism	Average level of agreement (%)
Traditional Financing Mechanisms	
Increase VAT/consumption tax with gains allocated to healthcare	76
Introduce (or increase pre-existing) "sin taxes" for various products with gains earmarked for healthcare	98
Subject luxury goods (eg, jewelry, expensive watches, and clothing) to a special tax, the revenue of which will be allocated to healthcare services	52
Introduce (or increase pre-existing) environmental tax, the revenue of which is allocated to health services	75
Introduce or increase earmarked taxes (eg, employee and/or employer insurance contributions)	66
Introduce medical savings accounts (MSAs) or increase contribution rates of pre-existing MSAs	61
Introduce modest user charges or increase statutory fixed fees at point of use and/or increase or introduce copayments for prescription drugs	54
Partially privatize health service provision to increase competition and reduce cost	60
Innovative Financing Mechanisms	
Earmark gains in GDP growth to healthcare	82
Introduce a tax on inbound medical tourism	64
Introduce annuity models for expensive medicinal products	60
Introduce health/social impact bonds as options to fund a specific area of healthcare, for example, secondary prevention	65
Introduce risk-sharing agreements	90
Introduce (or increase pre-existing) windfall corporation tax on private healthcare insurers' profits, the revenue of which is ring-fenced for healthcare services	72
Efficiency Mechanisms	
Use of international reference pricing in pricing negotiations to achieve affordable medicine prices	78
Increase funding in primary prevention (eg, cancer screening, disease detection, cardiovascular disease monitoring) and improve key stakeholders' engagement to increase efficiency	96
Improve efficiency by allowing people to purchase supplementary health insurance	82
Reallocation of resources whereby reduced spending in one area is reallocated to healthcare	51
Introduction or expansion of the national essential medicines list to cover more therapeutic areas	95
Encourage generic substitution of prescription medicines	89
Establish independent monitoring of health agencies	95
Improve health workforce knowledge	96
Improve health system digitalisation and effective regulation	100
Invest in citizen and patient awareness programs	100
Implement tools for efficient resource allocation based on the clinical and cost-effectiveness of a medical technology	96

Abbreviations: GDP, gross domestic product; VAT, value-added tax.
Note: The average agreement levels are those calculated in Round 3 of the Delphi process.

and implement efficient healthcare delivery systems. The engagement of the private sector, combined with innovative financing models and a collaborative design approach, will be crucial in generating fiscal space and ensuring access to effective healthcare for all citizens.

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An Ecological Study of the Association Between Social Determinants of Health and the Incidence and Prevalence of Cancer at the County Level

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Because social determinants of health (SDoH) are such a complex set of interconnected concepts, it is important to assess SDoH metrics as a broader construct as opposed to individual variables.

Assessment of SDoH factors at the community level can help to elucidate the influence of broader community-based factors on individual outcomes; these metrics plus detailed, patient-level healthcare data could provide additional insight on effects that SDoH assert on patient interactions with the healthcare system.

Increasing availability of SDoH and individual healthcare data provides opportunities for researchers to gain a more holistic understanding of patient health and the factors that drive it.

Introduction

Cancer is one of the leading causes of mortality and morbidity worldwide, and estimates from the World Health Organization suggest that the incidence of cancer will continue to rise.[1] Over the past few decades, major advancements in cancer treatment have improved survivorship and completely changed treatment paradigms across a variety of cancers.[2-3] Further, increased understanding of the underlying causes of cancer, including genetic, environmental, and behavioral influences, have led to improved cancer prevention activities (such as human papillomavirus vaccination programs in cervical cancer or increased focus on regular screening in colorectal cancer).[2] Although cancer prognosis continues to improve for many, globally 1 in 6 deaths are still attributed to cancer each year.

> Although clinical trials have shown vast improvements in survivorship over the past decades, these benefits are not always realized in real-world populations, especially disadvantaged groups.

Given the inevitability of cancer within populations, positive outcomes are effectively defined by comparison (eg, lower incidence, longer survival, higher rates of remission). Although clinical trials have shown vast improvements in survivorship over the past decades, these benefits are not always realized in real-world populations, especially disadvantaged groups.[2-3] Social determinants of health (SDoH), including behavioral, environmental, and socioeconomic factors (such as accessibility of healthcare, which can be influenced by economic status, transportation, and health literacy), have been increasingly shown to influence both cancer risk and postdiagnosis outcomes.[2-4] On the global stage, worse outcomes are commonly observed in poor and low-income countries where patients generally have access to fewer resources. Similar trends have also been reported in the United States with worse outcomes linked to disadvantaged social or economic status.[1-4] Although SDoH have always influenced patient outcomes, the extent of their role in both the diagnosis and management of various conditions has only more recently become an area of focus.

Research methodology

This analysis investigated the relationship between county-level incidence and prevalence of cancer and SDoH to evaluate disparities that may influence cancer risk. Annual county-level incidence (new cancer diagnoses) and prevalence (any cancer diagnosis) rates were calculated over the 2020 calendar year based on the presence of ICD-10 diagnosis codes in the claims record. The study sample was composed of patients in the Mertive™ MarketScan® Commercial and Medicare Databases with medical and pharmacy eligibility for the entire year and 6 months prior. Patients with ≥1 cancer diagnoses in the last 6 months of 2019 were considered prevalent cases and excluded from the incidence analyses. Due to calculation of the incidence and prevalence of disease in the MarketScan Databases, the analysis reflects cancer risk among a sample of patients with employer-sponsored insurance. Unlike the broader US population, all individuals in this analysis had access to at least the federally mandated minimum levels of preventive care, via employer-sponsored commercial, Medicare Supplemental, or Medicare Advantage plans. This point does not remove all disparities in healthcare access, but it does address one notable barrier to care in the United States.[2] County-level SDoH data were derived from the Robert Wood Johnson Foundation County Health Rankings data and ascribed to the patient sample in the MarketScan Database based on county of residence.

This county-level assessment of the association between cancer rates and

SDoH factors allows for a more socially focused analysis compared to individually linked SDoH data and may help to identify broader, persistent disparities in populations that specific individuals may not exhibit.[3] For conditions like cancer, which are known to be influenced by environmental factors (eg, pollution), behavioral factors (eg, health literacy, willingness to seek care), and economic status, this ecological analysis provides a different perspective, potentially allowing for external, neighborhood influences to be investigated.

Results

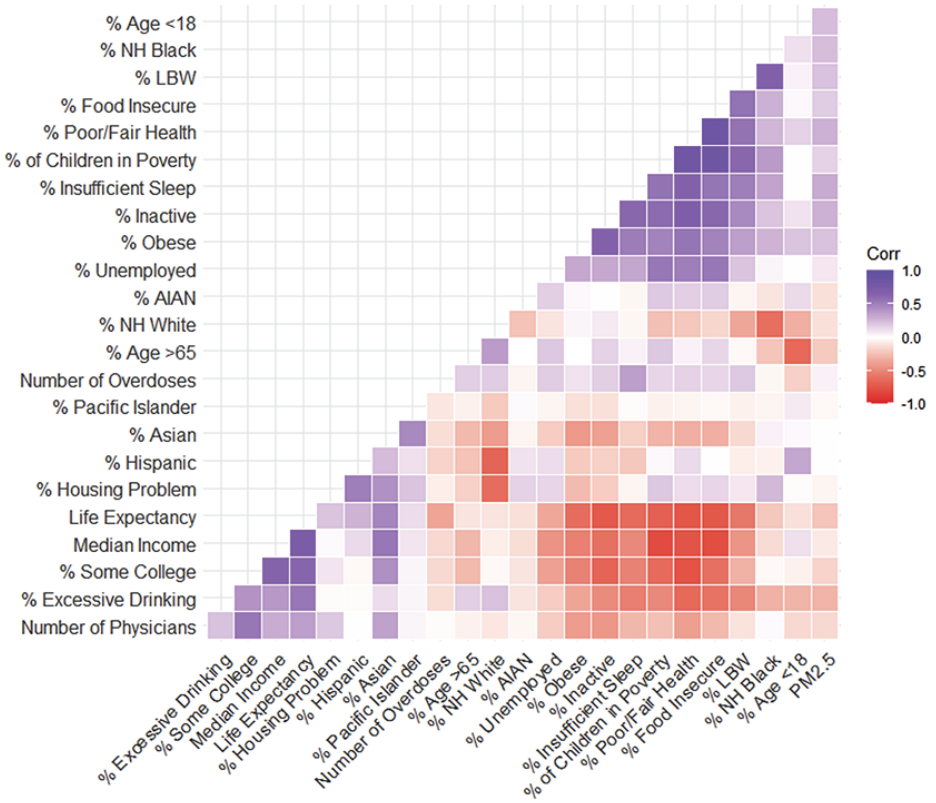
Analyses included 13.6 million patients residing in 2528 counties in the United States. Within the county-level SDoH data, strong correlations between specific variables were observed in the sample (**Figure**). For example, there were strong positive correlations between poor health, food insecurity, and child poverty, while there were strong negative correlations between poor health, median household income, and some college education. Multivariate models using Akaike information criteria stepwise linear regression identified associations between multiple demographic and SDoH variables and increased risk of cancer at the county level.

Increased cancer prevalence was significantly associated with (in order of strength) increased age, increased proportions of adults reporting poor to fair health (health status), lower rates of childhood poverty, worse air quality, lower rates of severe housing problems, increased proportions of adults aged 25 to 44 years with some college education, and higher rates of obesity in adults (**Table 1**). Increased incidence of cancer was associated with increased age, increased proportions of adults reporting poor to fair health (health status), lower rates of childhood poverty, increased proportions of adults aged 25 to 44 years with some college education, lower rates of severe housing problems, higher rates of obesity in adults, and higher rates of drug overdoses (**Table 2**).

Implications

This study investigated predictors of cancer risk at the county level by combining cancer incidence and prevalence rates calculated in the MarketScan Research Databases with

Figure. Correlation Between Social Determinants of Health Variables



Abbreviations: AIAN, American Indian or Alaskan Native; Corr, correlation; LBW, low birthweight; NH, non-Hispanic; PM, particulate matter.

Table 1. Prevalent Cancer: County-Level Risk Factors

INCIDENCE	Variable Source	Estimate	Lower 95% CI	Upper 95% CI	*P* value
Percentage of adults with obesity (BMI ≥30)	RWJF	13.65	6.47	20.83	0.000
Number of births per 1000 among females aged 15-19	RWJF	4.38	-0.52	9.28	0.080
Percentage of adults aged 25-44 years with some college education	RWJF	17.48	12.26	22.70	**<0.001**
Percentage of children living in poverty	RWJF	-42.17	-50.82	-33.52	**<0.001**
Air pollution—average daily density of particulate matter	RWJF	37.19	10.89	63.50	0.006
Percentage of households with ≥1 severe housing problem*	RWJF	-26.85	-37.79	-15.90	**<0.001**
Percentage of adults reporting poor/fair health	RWJF	65.84	46.89	84.78	**<0.001**
Percentage of individuals living in an urban environment	MSN	0.77	-0.13	1.67	0.094
Percentage of males	MSN	-12.46	-25.00	0.08	0.052
Mean age	MSN	212.66	206.59	218.72	**<0.001**

Abbreviations: BMI, body mass index; CI, confidence interval; MSN, MarketScan; RWJF, Robert Wood Johnson Foundation.

** Problems include overcrowding, high costs, lack of kitchens, or lack of plumbing.*

SDoH data obtained from the Robert Wood Johnson Foundation. Arguably, cancer rates were derived from the subset of the county that may have some of the fewest access barriers to healthcare—at least from an insurance perspective—as the population is composed of patients with employer-sponsored insurance. Thus, all individuals in the data are guaranteed to either be employed, previously employed (for Medicare), or have at least one employed family member. It's important to note that the MarketScan-derived sample still includes a diverse cohort given that companies employ individuals in a variety of different roles that are associated with different income levels. SDoH factors from the broader community were then attributed to individuals, who may or may not embody the broader characteristics of their county. Although findings within this population may not generalize to patients with other types of insurance or the uninsured, the focus on patients with employer-sponsored insurance may also help to identify associations between SDoH variables and cancer risk that do not manifest in more heterogenous populations, potentially due to health insurance being one of the largest barriers to healthcare access.

Results from this study identify many of the same factors that have previously been associated with increased cancer risk, including overall health status, air pollution, and economic factors, highlighting the major contribution of geography (eg, neighborhood attributes) on patient health outcomes.[2-4] However, both of our models also identified a series of less intuitive predictors—namely inverse relationships between cancer and childhood poverty (eg, higher poverty is associated with lower cancer rates) or housing problems and a positive relationship between higher education and cancer. Higher median income was also associated with higher cancer incidence. These findings likely point to a complex and interconnected set of relationships between SDoH and cancer risk. For instance, the overall SDoH data show an inverse relationship between childhood poverty and life expectancy, and although our models did not include life expectancy, older age was consistently the greatest risk factor for cancer; thus, there could be an interplay between age/life expectancy and childhood poverty leading to the relationships observed here. The same associations with age are not observed for housing problems or higher education in the SDoH data. In these cases, the positive association between cancer and college education (both models) and median household income (incidence model) could point to differences in healthcare access, even within this commercially insured sample, as patients who may have higher barriers to healthcare access—either due to health literacy, transportation, out-of-pocket costs, or locality of care providers—may see healthcare providers less frequently and would thus have fewer opportunities for a cancer diagnosis.

Table 2. Incident Cancer: County-Level Risk Factors

INCIDENCE	Variable Source	Estimate	Lower 95% CI	Upper 95% CI	*P* value
Percentage of live births with low weight births	RWJF	-14.41	-34.32	5.49	0.156
Percentage of adults with obesity (BMI ≥30)	RWJF	7.66	1.90	13.42	**0.009**
Percentage of adults aged 25-44 years with some college education	RWJF	10.30	6.51	14.09	**<0.001**
Percentage of children living in poverty	RWJF	-17.53	-24.93	-10.13	**<0.001**
Percentage of households with ≥1 severe housing problem*	RWJF	-8.07	-15.46	-0.67	**0.033**
Number of drug overdoses per 100,000	RWJF	7.34	5.38	9.29	**<0.001**
Percentage of adults reporting poor/fair health	RWJF	42.22	29.06	55.39	**<0.001**
Median household income, in thousands	RWJF	2.98	0.19	5.77	**0.037**
Mean age (MSN)	MSN	101.02	96.80	105.23	**<0.001**

Abbreviations: BMI, body mass index; CI, confidence interval; MSN, MarketScan; RWJF, Robert Wood Johnson Foundation.

* *Problems include overcrowding, high costs, lack of kitchens, or lack of plumbing.*

Conclusions

Overall, this county-level analysis was able to identify previously reported relationships between cancer risk and SDoH factors, demonstrating the feasibility of this approach for population-level analyses. Further, assessment of cancer risk based on claims data derived from an employed population with employer-sponsored insurance provides a slightly different context than other studies, as employment has previously been described as one of the major influences on healthcare access in the United States.[2] Additional research, potentially combining additional claims-based metrics such as county-level healthcare resource utilization trends, could help to further elucidate how SDoH influences healthcare engagement and patient outcomes in the United States.

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Q&A

A Closer Look at Switzerland's National Regulatory Authority

Raimund Bruhin, MPA
Executive Director, Swissmedic

Raimund Bruhin discusses Swissmedic's participation in cross-border regulatory initiatives such as the Access Consortium and Orbis and its efforts to support the Global South in developing regulatory standards. Bruhin also addresses the regulatory challenges posed by new technologies, such as Advanced Therapy Medicinal Products (ATMP) and Swissmedic's strategic objectives, especially in digital transformation and further international cooperation.

"Swissmedic's core responsibilities lie in the authorization, licensing, and surveillance of medicines, as well as the market surveillance of medical devices."

– Raimund Bruhin

PharmaBoardroom: Can you give us an overview of your role and Swissmedic's specific responsibilities?
Raimund Bruhin: Swissmedic is the national regulatory authority for therapeutic products in Switzerland, with the legal mandate of ensuring the quality, safety, and efficacy of medicines, vaccines, and medical devices. Unlike some other regulatory bodies, Swissmedic's mandate does not include procurement, pricing, or reimbursement for medicines, nor the antibiotic strategy; these fall under the responsibility of the Federal Office of Public Health. Swissmedic's core responsibilities lie in the authorization, licensing, and surveillance of medicines, as well as the market surveillance of medical devices.

PB: The pandemic placed significant demands on actors across the pharmaceutical value chain, including regulatory authorities. What lessons have you drawn from this challenging time that continue to impact Swissmedic's work today?
RB: The pandemic was a formative period that reinforced the importance of swift and effective communication—both nationally and internationally—and demonstrated that international collaboration, particularly in times of crisis, brings substantial added value. An example of this is our close cooperation with the International Coalition of Medicines Regulatory Authorities (ICMRA).

Second, the crisis taught us organizational flexibility and regulatory agility, serving as essential preparation for new challenges. We introduced the rolling submission process, which, while resource-intensive, allowed us to maintain focus, prioritize, and optimize processes during crises. This measure enabled us to be among the first 3 countries worldwide to authorize mRNA vaccines.

Third, we established internal task forces and optimized our crisis management to direct resources toward managing the pandemic while continuing our daily operations without disruption. These challenging times demanded extraordinary dedication and teamwork from our employees, who tackled daily challenges while

finding creative solutions to increase efficiency and maintain high-quality work. Both individuals and the organization exceeded expectations.

PB: What can you tell us about Swissmedic's participation in the Access Consortium? How does this initiative affect Swissmedic and the companies that rely on Switzerland as their primary approval market?
RB: The Access Consortium, founded in 2007, has developed into a significant international collaboration, bringing together regulatory authorities from Switzerland, Canada, Australia, Singapore, and the United Kingdom to accelerate the approval of medicines across multiple continents.

Initially, establishing a common foundation was challenging due to differing regulatory processes and requirements in the participating countries. However, sufficient harmonization has been achieved over time, and since 2018, notable progress has been made by including new active substances alongside generics, resulting in a substantial increase in approvals.

> The pandemic was a formative period that reinforced the importance of swift and effective communication—both nationally and internationally—and demonstrated that international collaboration, particularly in times of crisis, brings substantial added value.

A standout feature of this collaboration is true work-sharing, where partner authorities assess specific modules of the scientific documentation. This sharing of work enables shorter processing times and minimizes the submission gap, leading to quick and efficient approvals. The scientific exchange within the Access Consortium, including joint pipeline meetings, allows us to continually expand our expertise. Additionally, the newly introduced "Promise" pathway offers companies an optimized, faster approval pathway within the consortium.

For companies choosing Switzerland as their primary approval market, the Access Consortium offers considerable time savings and enhanced flexibility by providing access to a broad market of more than 150 million potential patients. This close international cooperation enables the rapid, targeted approval of medicines while fostering knowledge exchange and technological innovation.

PB: Could you elaborate on the international collaborations that Swissmedic maintains and how they strengthen Switzerland's position in the global healthcare and pharmaceutical sectors?
RB: Recently, we cohosted the ICMRA 'Rare' Symposium on Orphan Diseases in Lugano with the EMA and FDA. This gathering brought together experts from around the world to discuss and reassess the definition and regulation of orphan drugs. A key topic was distinguishing between truly rare diseases and so-called "orphan-like" diseases, which may require new criteria to update regulations in this area. ICMRA would be well suited to address this, as it is widely recognized that such topics can only be effectively tackled through international collaboration.

Our participation in the EMA's Open Initiative during the pandemic was also highly significant. This project enables regulatory authorities to attend meetings of the Committee for Medicinal Products for Human Use. During the COVID-19 pandemic, this was crucial, as the exchange on vaccine evaluation and adverse drug monitoring became central to our work. At Swissmedic, we emphasize, "We are not an island," and international dialogue is essential for effectively managing global health crises.

Through initiatives like ICMRA, we stay up to date with developments and can contribute our regulatory expertise at the global level. This allows us to help shape new standards and procedures that influence the global pharmaceutical market. In the area of rare diseases, in particular, we have seen that global collaboration is essential to meet patient needs.

Other supranational organizations in which we actively participate include the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), the International Pharmaceutical Regulators Programme, and the Pharmaceutical Inspection Co-operation Scheme. We are also increasingly involved in the medical device sector, including the International Medical Device Regulators Forum.

All these collaborations give us access to global networks and allow us to help shape standards and regulatory frameworks for innovations and new technologies worldwide, which in turn benefits Switzerland's therapeutic product industry.

PB: What is the Orbis Initiative and how does it strengthen Switzerland's position in the global pharmaceutical sector?
RB: Through the Orbis Initiative, we work closely with the FDA, engaging in scientific exchange to conduct parallel approvals of cancer drugs, significantly reducing approval times. While resource-intensive, this initiative shortens the submission gap and brings substantial benefits to patients by granting faster access to life-saving therapies.

Our participation in international initiatives like Orbis enhances Switzerland's global influence by providing rapid access to innovative treatments.

PB: Swissmedic also shares its expertise with regulatory authorities in developing countries and has launched the Marketing Authorization for Global Health Products procedure for this purpose. What global role does Swissmedic play today?
RB: Swissmedic has established itself as a leading international regulatory authority, deeply embedded in the global networks mentioned. A key component of our global role in supporting the Global South in developing regulatory standards is the Marketing Authorization for Global Health Products procedure. This initiative allows us to share our expertise and knowledge with regulatory authorities in low- and middle-income countries, as well as with the World Health Organization (WHO). We invite these authorities to participate in the assessment of medicines, especially those targeting diseases that disproportionately affect

the Global South. The goal is to promote international standards and support these countries in building their own regulatory capacities.

Since 2014, we have been active in this area on behalf of the Federal Council, working closely with WHO to improve access to essential medicines. We are also supporting the development of an African Medicines Agency, similar to the EMA, for African countries. This commitment helps African and Asian countries establish a robust regulatory system, allowing them to meet high international standards, ensuring safety and quality in the therapeutic products market.

Thus, Swissmedic is not only a national player but also plays a prominent role in the global health landscape by promoting the exchange of knowledge, best practices, and improving access to essential medicines internationally.

PB: What does it mean for Swissmedic to be one of the first 3 WHO-listed regulatory authorities in the world?
RB: This recognition has primarily resulted in greater global visibility for Swissmedic within the health sector, due to WHO's extensive publication of this achievement. This acknowledgment has further solidified Swissmedic's position as a globally respected authority.

Since this recognition is still recent, it is too early to discuss long-term effects. However, it's likely that Swissmedic will increasingly serve as a reference for other countries. In collaboration with WHO, we offer a training program to help other regulatory authorities build and enhance their competencies, and interest in these trainings may continue to grow. Additionally, we have received requests from partner authorities seeking our support in their own WHO listing assessments, which further strengthens our expertise and international network.

> For companies choosing Switzerland as their primary approval market, the Access Consortium offers considerable time savings and enhanced flexibility by providing access to a broad market of more than 150 million potential patients.

We anticipate that Swissmedic's decisions will increasingly serve as a basis for decision making by other regulatory bodies, the WHO Prequalification Program, and procurement agencies. This recognition from WHO is not only an endorsement of our past work but also an incentive to expand our role as a leading international regulatory authority and actively contribute to improving global health.

PB: The new generation of innovative medicines, such as cell and gene therapies, are posing challenges for regulators around the world. What role does your department for Advanced Therapy Medicinal Products (ATMP) play in this area?
RB: The development of innovative therapies, particularly in the field of ATMP, presents exciting new challenges for Swissmedic. To meet these demands, we have established a specialized department that allows us to quickly and safely approve these advanced medicinal products, as well as continuously refine our expertise and processes in this highly innovative field.

> Our participation in international initiatives like Orbis enhances Switzerland's global influence by providing rapid access to innovative treatments.

Swissmedic is prepared to support cutting-edge technologies and expedite the approval of these products. This initiative sends a strong signal to the industry: we have the competencies needed to regulate and promptly approve these novel therapies and we are committed to taking a leading role in this area. This includes cell and gene therapies, CAR-T cell therapies, mRNA-based vaccines, and tissue engineering.

In summary, Swissmedic is well-equipped to address the challenges in the ATMP field and is ready to help shape the future of drug regulation.

PB: What strategic goals do you have for the coming years and what developments should we watch for in Swissmedic?
RB: Swissmedic has ambitious goals for the years ahead. Our overarching objective is to remain "Fit for Mission," meaning we must continue to fulfil our legal mandates despite rapid technological advancements. At the same time, we aim to be "Fit for Future" by promoting innovative regulatory approaches, especially in the ATMP sector. We want to strengthen our skills and knowledge and shape global regulatory frameworks for the benefit of our patients and stakeholders in Switzerland.

Swissmedic is driving its digital transformation forward. Our goal is to soon adopt state-of-the-art digital technology and become a data-centric authority. For example, in August 2024, we successfully introduced a new cloud-based medical device database. This is one step toward becoming one of the top 5 digitally advanced regulatory authorities. This modernization is essential not only for interoperability with other regulatory authorities but also for effective collaboration with the industry.

Another key aspect of our strategy is promoting global harmonization and cooperation, particularly in the pharmaceutical and medical technology sectors. We are actively committed to international collaboration and work closely with other regulatory authorities to shape evidence-based future approvals. This includes contributing to global policy development, especially regarding innovative technologies such as artificial intelligence applications in the pharmaceutical and manufacturing processes.

To summarize, our strategic goals for 2023 to 2026 focus on protecting human and animal health through high-quality, safe, and effective therapeutic products. We strive to be perceived as a trustworthy authority by the public while supporting the development of novel therapies to accelerate access to innovative treatments. With these objectives in mind, we are working to shape the regulatory framework of the future and sustainably improve healthcare.

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