

JANUARY/FEBRUARY 2021 VOL. 7, NO. 1

VALUE & OUTCOMES SPOTLIGHT

A magazine for the global HEOR community.

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ISPOR

Improving healthcare decisions

VALUE & OUTCOMES SPOTLIGHT

JANUARY/FEBRUARY 2021
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FROM THE EDITORS

As we enter a new phase of combating the COVID-19 virus—one where vaccine supply is increasing and mass vaccination programs are now underway—vaccine health economics and outcomes research (HEOR) is becoming critical. In 2020, the world's scientists and policy makers grappled to understand the virus, deploy tests, implement public health strategies, and develop new vaccines. In 2021, with better healthcare tools to identify, fight, and prevent the spread of the virus, we now must focus on maximizing universal access to these tools, with vaccines being a key preventive defense in our arsenal. How do we ensure that these practices and tools—particularly vaccines—are best accessed? Aside from the obvious tactic, which is to manufacture and distribute enough doses to vaccinate the entire population, achieving equitable access to and distribution of vaccines is an even more daunting challenge. Uptake of the vaccine is dependent on public trust, which as is well-documented, tends to wane in minority groups even as mounting evidence suggests that these groups are at a higher risk for viral transmission and serious negative outcomes.

As HEOR scientists, we are poised to directly address these issues and develop strategies for their mitigation. Yet the usual outcomes paradigm is not present: we need not convince decision makers that the COVID-19 vaccines have value or are cost-effective, as the societal consequences of an unvaccinated populace are clearly evident. Also, quantifying the budgetary impact of vaccine costs is not an immediate administrative priority as governments are aggressively competing to purchase doses as they become available.

In spite of this unique health economic environment, many other questions are arising and HEOR will be critical in addressing these in the coming months. For example, what are the incremental differences in cost-effectiveness between the growing number of vaccines? How does cost-effectiveness differ for subpopulations who are most at risk for increased morbidity due to demographics and/or having comorbid chronic conditions such as diabetes, obesity, cancer, and other health issues linked to more severe outcomes? How do emerging COVID-19 variants impact the effectiveness and uptake of the current vaccines? How does herd immunity, if achieved, impact cost-effectiveness? What will be the long-term vaccine costs if repeat or booster immunizations are required?

Understanding the patient perspective is crucial to addressing these questions and developing an impactful health economics strategy. We need to better understand patients' trust—or lack thereof—for vaccination; how that trust differs across race, gender, age, education, income, and geography; and how to better collaborate to build that trust and reduce vaccination hesitancy. Indeed, the world's ability to mitigate COVID-19 ultimately distills down to the fundamental principles of treatment adherence and a better understanding of human behavior—issues long known to HEOR scientists. Now more than ever, we need to listen to the patients' voices and recognize that their feelings about vaccines are often valid in the context of their life experiences.

During these difficult and challenging times, HEOR scientists are poised to make a positive impact by addressing many of the societal issues that have manifested during the COVID-19 pandemic. Working together to leverage our expertise in epidemiology, economics, modeling, patient-relevant outcomes, operations research, treatment adherence, health policy, and community health, we have a shot at making a difference!

Zeba M. Khan, RPh, PhD and
Laura T. Pizzi, PharmD, MPH
Editors-in-Chief,
Value & Outcomes Spotlight



ISPOR SPEAKS

ISPOR Through and Beyond the COVID-19 Pandemic

Nancy S. Berg, CEO and Executive Director, ISPOR

Like many organizations and companies, ISPOR spent much of 2020 in triage and transition—very rapidly planning, executing, and communicating organizational changes. We all adjusted to new dynamics in our families and at work, and to the pressures resulting from the pandemic. I am proud of the ISPOR members and staff who during difficult times collaborated not only to ensure that ISPOR got through the pandemic, but also continued to drive change in our organization. ISPOR's [Strategic Plan Update 2024](#) outlined transformative change for the Society. The Board of Directors accelerated that transformation vision in 2020 as the pandemic pushed ISPOR to be creative and to embrace new ways of disseminating knowledge, engaging members, and communicating with stakeholders. We rapidly explored innovative event platforms and created new ways of keeping members at the heart of ISPOR. Seizing opportunities to reach for an envisioned future where ISPOR is more global, more contemporary, and more responsive became an imperative. We did this because today, the role of HEOR has never been more necessary or more important.

Disciplined Research Matters

The COVID-19 pandemic and its crippling drain on healthcare systems around the world drew sober attention to inconsistencies, uncertainties, and issues that ISPOR members have been addressing for a number of years. The importance and availability of credible information was a top concern as journalists and politicians began confidently explaining terms like modeling, outcomes, and “flattening the curve.” Facebook and Twitter users suddenly became experts in herd immunity and vaccines while every family seemed to have a “mock Doc.” Throughout the pandemic, ISPOR members were reminding the world of the importance of disciplined research based on good practices as they witnessed early studies and opinions declared “research” that were occasionally withdrawn—or worse, deemed incomplete or flawed by errors. Research credibility remains at the heart of ISPOR and is one of the ways in which we continue to make an impact.

I am proud of the ISPOR members and staff who during difficult times collaborated to not only ensure that ISPOR got through the pandemic, but that we also continued to drive change in our organization.

COVID-19 brought other topics to the forefront, such as inequities in healthcare and access to quality care. As we continue to respond to a global pandemic, ISPOR and its members continue to guide solutions to these and other topics

through generating disciplined, relevant economic and health outcomes research. Recently ISPOR hosted [webinars](#) and [conference sessions](#) that discussed inequities, our publications featured articles in [Value in Health](#) and [Value & Outcomes Spotlight](#), and ISPOR is now exploring the formation of a Special Interest Group to focus specifically on the topic of health disparities. The more attention dedicated to this area, the greater impact we can make in improving healthcare decisions ... toward a healthier world.



We do not have all the answers on how to help nations balance health and economies, nor on how to overcome all budget challenges, but ISPOR can offer knowledge, experiences, and tools to support better decision making.

Finally, COVID-19 showcased the role of ISPOR members and their impact on society, which ranges from modeling used to understand and support management of the virus spread, to helping manage its containment, and to informing decisions leading to a healthy recovery. We do not have all the answers on how to help nations balance health and economies, nor on how to overcome all budget challenges, but ISPOR can offer knowledge, experiences, and tools to support better decision making. Together, ISPOR and its members have significant responsibility to society and to healthcare, and that has never been more apparent than it is today.

2020 Wrap-Up

As 2020 drew to a close, ISPOR reflected not only on the mission of the Society, but on the transformation that occurred in ISPOR's operation as a result of the acceleration of our IT strategies and digital product transformation plans. These plans ranged from rapidly converting all conferences to virtual events, adapting short courses to digital delivery, transitioning all member group meetings to virtual gatherings, to launching new on-demand webinars and new digital member communities.

In 2020, ISPOR also managed to produce a number of special events, including a joint [Summit](#) with the US Food and Drug Administration on Patient Preference Information in Medical Device Regulatory Decisions, the launch of ISPOR's first ever multistakeholder [Payer Engagement Summit](#), and a series of [COVID-19 webinars](#). Members and leaders spoke at many digital conferences on our behalf and were called on as knowledge experts for governments around the world.

We are in a pandemic, but in every challenge there is opportunity. ISPOR will continue to transform as it responds to member needs and to its mission of improving healthcare decisions globally.

Last year, we also reorganized ISPOR's operational structure, adjusted business models to support a changing world, strengthened communications, and carefully managed ISPOR's assets to ensure a strong future. A big thank you to members and their companies and institutions for continued support of their Society through volunteer leadership, event participation, and sponsorships.

Bring on the New Year

As we launch the Society's 2021 plans, we recognize that uncertainties exist around when and how ISPOR will return to face-to-face events, when we will have opportunities to interact personally with our members, and how to enrich our professional networks when we can't be together in person. Knowing this, we continue to enhance our digital programs and keep a watchful eye on the state of the pandemic as we forge ahead with all the Society's strategic plan initiatives set back in 2019, including:

- Completing the ISPOR Science Strategy and integrating it into content strategies to ensure that the Society remains focused on the topics of interest to members and their organizations. Watch for details about our new Science Strategy in the March/April issue of *Spotlight* and in upcoming member emails.
- The Board of Directors will continue assessing strategic impact and priorities as it leads work streams that are focused on

(1) exploring new membership models for ISPOR, (2) advancing our vision to create a leadership pipeline and volunteer recruitment to engage members in all career stages and from diverse backgrounds, and (3) assessing the Society's important position in lower and middle-income countries with an eye to strengthening ISPOR's impact around the world, particularly in parts of the world where healthcare needs often outweigh resources and where HEOR could be vitally important. The Board will continue to monitor the Society's strategic and financial performance, guiding us toward a vibrant and relevant future.

- ISPOR will continue to collaborate with other societies, government agencies, and decision makers in advancing its mission. For example, ISPOR recently penned a collaboration agreement with the Healthcare Information and Management Systems Society ([HIMSS](#)) to enhance information sharing between ISPOR and HIMSS members through featuring speakers at our respective conferences and facilitating dialogue around important digital health topics. ISPOR also partners with the [International Society for Pharmacoeconomics](#), the [National Pharmaceutical Council](#), and the [Duke Margolis Center for Health Policy](#) in advancing the [Real-World Evidence Transparency Initiative](#), and with [Health Technology Assessment International](#) through a joint task force on deliberative processes. Finally, a member of ISPOR's Science Team now sits on the ENCePP Steering Group (www.encepp.eu) and I am chairing the [National Health Council's 2021 Health Leadership Conference](#), one of many examples of how ISPOR gets its message to stakeholders and shares information on HEOR.

Groups and the Future

Looking to the future, we are in good hands. ISPOR's student and midcareer networks are vibrant, as are our global [groups](#). ISPOR consortia, networks, and our important chapter network continue to thrive with now 85 regional chapters and more than 135 student chapters engaged and advancing ISPOR's mission around the world.

We are in a pandemic, but in every challenge there is opportunity. ISPOR will continue to transform as it responds to member needs and to its mission of improving healthcare decisions globally. •

HEOR NEWS

1 New Year, New Price Hikes on Hundreds of Prescription Drugs (PharmaLive)

In the beginning of 2021, 70 companies raised the price of hundreds of prescription drugs by an average of 3.3%. According to an analysis by 3 Axis Advisors cited by Reuters, the average price increase is lower than 1 year ago, when the cost of drugs was raised by an average of 5.8%, and 5.2% in 2019. Pfizer, Sanofi, and GlaxoSmithKline are among those leading the way in price increases.

[Read more.](#)

2 FDA Takes Steps to Provide Clarity on Developing New Drug Products in the Age of Individualized Medicine (FDA)

On January 4, the US Food and Drug Administration (FDA) released a statement from Patrizia Cavazzoni, MD, the Center for Drug Evaluation and Research's Acting Director and Deputy Director, Operations, outlining the agency's draft guidance on investigational new drug submissions for individualized antisense oligonucleotide products. Because many of the investigators developing these products may be academics rather than biopharmaceutical or pharmaceutical companies, officials believe that they may be less familiar with the FDA's regulations, policies, and practices, and less experienced in interacting with the FDA.

[Read more.](#)

3 Trump Administration Will Let Nearly All Doctors Prescribe Addiction Medicine Buprenorphine (STAT News)

In its final days, the Trump administration announced a change in addiction medicine policy that will allow almost all physicians to prescribe buprenorphine, regardless of whether they have obtained a government waiver. Previously, doctors had to undergo an 8-hour training and receive the license, known as the "X-waiver," before they could prescribe buprenorphine. For years, addiction treatment advocates have argued that tight buprenorphine regulations prevent thousands of doctors from providing high-quality addiction care.

[Read more.](#)

4 2021-UK Market Access Prospects (Pharmaphorum)

Researcher and writer Leela Barham looks back at the year 2020 for market access initiatives in the United Kingdom, and makes some predictions for 2021. In October 2020, the United Kingdom joined 2 market access initiatives, Project Orbis (coordinated by the FDA and focused on cancer medicines) and the Access Consortium (focused on securing patient access to high-quality, safe, and effective medicines). Barham also examines the new licensing and access pathway (ILAP) at the Medicines and Healthcare Regulatory products Agency (MHRA), which brings together expertise from the MHRA, The National Institute for Health and Care Excellence, the Scottish

Medicines Consortium, National Health Service England and National Health Service Improvement, and patients. According to Barham, "2021 will reveal just how the ILAP will be operationalized and whichever product will be the first to go through the Innovation Passport stage—a new designation as part of ILAP—will help everyone understand how the criteria for the passport will apply in practice."

[Read more.](#)

5 Price Transparency and Variation in US Health Services (Peterson-KFF Health System Tracker)

New rules about establishing price transparency requirements for healthcare services have been released by the US Department of Health and Human Services. As of January 1, 2021, hospitals are required to make payer-negotiated rates for common services available to consumers through an online tool and for all services to be contained in a machine-readable file. A second rule requires insurers in the individual and group markets and self-funded employer plans to make rates and individualized cost-sharing estimates for certain common services available to enrollees by January 1, 2023, and for all services by the following year. However, ongoing litigation challenging the constitutionality of the Affordable Care Act and the price transparency rule aimed at hospitals could affect the implementation and impact of these new rules.

[Read more.](#)

6 CMS Issues Final Rule for Medicare Coverage of Breakthrough Technologies: 5 Things to Know

(Becker's Health IT)

The Centers for Medicare & Medicaid Services (CMS) issued a final rule on January 12, 2021 that is expected to speed up the FDA approval process for Medicare coverage of new and innovative medical devices and technologies. Among the things the final rule will do is let Medicare provide national coverage simultaneously with FDA approval up to a 4-year period.

[Read more.](#)

7 Paper Finds Gaps in Health Data Are a Barrier to Health Equity (PhRMA)

Thirty-five years after the US Department of Health and Human Services released the Report of the Secretary's Task Force on Black and Minority Health (Heckler Report), racial disparities in healthcare continue to exist, laid bare by the COVID-19 pandemic. PhRMA plans a series of its own reports in 2021 addressing this topic by identifying the challenges in data collection, solutions that have been identified, and actionable steps that can be taken.

[Read more.](#)

8 Tennessee to Become the First State to Run a Closed Medicaid Drug Formulary (Pharmalot)

Tennessee, in an effort to overhaul spending by the state program, has been granted permission by the Trump administration to maintain a closed formulary, while at the same time being able to retain Medicaid drug rebates even as state officials negotiate with drug companies for other supplemental rebates.

[Read more.](#)

9 Pandemic Propels Health Systems to Mull Insurer Acquisitions, Partnerships (Healthcaredive)

At the JP Morgan Conference, which was held virtually in January 2021, the main subject of discussion was the impact of COVID-19. Several health system executives stated that they are on the hunt for health insurer acquisitions and partnerships or advocating for such arrangements as a result of the challenges of the pandemic in-person clinical revenue. Overall, executives acknowledged that health plans helped keep them profitable.

[Read more.](#)

10 Cerner Wants to Build a \$1B Data Business as it Expands Reach Into Pharma Market (Fierce Healthcare)

Health IT giant Cerner wants to expand its data business to \$1 billion, building on its \$375-million planned acquisition of Kantar Health announced in December 2020. The company is looking to create a leading data insights and clinical research platform and wants to harness data to improve the safety, efficiency, and efficacy of clinical research across life sciences, pharmaceuticals, and healthcare at large.

[Read more.](#)

RESEARCH ROUNDUP

Section Editor: **George Papadopoulos, BSc(Hons), GradDipEpi, MAICD**, Partner & Director, Lucid Health Consulting & School of Medicine, UNSW, Sydney, New South Wales, Australia

"The impact of vaccination on the health of the world's peoples is hard to exaggerate. With the exception of safe water, no other modality has had such a major effect on mortality reduction and population growth." (Plotkin and Mortimer, 1988).

The articles in this month's Research Roundup look at the topic of vaccine health economics and outcomes research (HEOR), including the challenges and opportunities presented by COVID-19, accounting for herd immunity and the value of trust in addressing vaccine hesitancy. We, as always, trust you enjoy delving into the research presented here and look forward to highlighting research in the next edition.

Health Economics and Emergence From COVID-19 Lockdown: The Great Big Marginal Analysis

Donaldson C, Mitton C. Health economics and emergence from COVID-19 lockdown: the great big marginal analysis. *Health Econ Policy and Law*. 2020;1-5. doi:10.1017/S1744133120000304.

Summary

Despite denials of politicians and other advisors, trade-offs have already been apparent in many policy decisions addressing the COVID-19 pandemic and its social and economic consequences. The authors illustrate why it is important, from a well-being perspective, to recognize such trade-offs and provide a framework based on the economic concept of "marginal analysis" for doing so. The framework exposes crucial questions to be addressed, such as the critical value of reducing the reproductive rate of the virus and further opening of the economy and/or background infection, above which health considerations predominate. These may vary from jurisdiction to jurisdiction and the value of lives forgone resulting from the small increases in reproductive rate of the virus and/or background infection levels that may have to be tolerated as the economy is gradually opened.

Relevance

In the view of the authors, the trade-offs referred to in the paper are inevitable and for purposes of optimizing overall human welfare, they are better recognized, analyzed, and publicly debated.

Impact of Vaccines; Health, Economic and Social Perspectives

Rodrigues CMC, Plotkin SA. *Front Microbiol*. 2020;11:1526. <https://doi.org/10.3389/fmicb.2020.01526>

Summary

The development of safe and efficacious vaccination against diseases that cause substantial morbidity and mortality has been one of the foremost scientific advances of the 21st century. It is estimated that vaccines have prevented 6 million deaths from vaccine-preventable diseases annually. The importance of various organizations in global cooperation and participation was essential in the setting of the 2019 global pandemic of SARS-CoV-2, in light of the health and economic impact of COVID-19

on societies in high-, middle- and low-income countries. The review covers a brief history of vaccine development, the health benefits of vaccination, such as reduction in infectious diseases morbidity and mortality, the eradication of infectious diseases, herd immunity, and also the economic and social benefits such as the cost-effective preparedness for outbreaks.

Relevance

This excellent and comprehensive review highlights the benefits of vaccinations to society from the perspectives of health, economy, and social fabric which need to be considered in the overall assessment of impact to ensure that vaccines are prioritized by those making funding decisions.

Consideration of Value-Based Pricing for Treatments and Vaccines Is Important, Even in the COVID-19 Pandemic

Neumann PJ, Cohen JT, Kim DD, Ollendorf DA. *Health Affairs* 2021;40(1):53-61. <https://doi.org/10.1377/hlthaff.2020.01548>

Summary

Pricing in a pandemic is complicated and fraught. The authors review alternative pricing strategies (cost-recovery models, monetary prizes, and advance market commitments) for COVID-19 drugs, vaccines, and diagnostics. The authors argue that hybrid pricing strategies are undoubtedly needed in a pandemic, but even in a public health crisis, value-based pricing is important. All pricing strategies should be informed by formal health technology assessment and cost-effectiveness analysis and ideally, analyses would be conducted from both a health system and societal perspectives. Incorporating the added value of social benefits into cost-effectiveness analyses does not mean that manufacturers should capture the entire societal benefit of a diagnostic, vaccine, or therapy. Such analyses can provide important information and help policy makers consider the full costs and benefits of products and the wide-ranging ramifications of their actions. The authors identified 23 economic evaluations of COVID-19-related interventions, including 14 cost-effectiveness analyses, 5 cost analyses, and 4 benefit-cost analyses. These analyses evaluated a range of interventions, including policy measures (social distancing or lockdown orders), treatments (dexamethasone or remdesivir), screening strategies, and hypothetical vaccines. Although estimating the full value of a drug for COVID-19 is difficult, the pandemic's economic impact leaves little doubt that it would be substantial.

Relevance

The authors conclude that people may believe that the setting of a pandemic is not the appropriate venue for value-based pricing. However, robust and sound value assessments to inform product prices can help ensure that tests, treatments, and vaccines are available for this crisis and for crises yet to come.

Will COVID-19 Vaccines Be Cost-Effective—And Does It Matter?

Appleby J. *BMJ*. 2020;371:m4491. <https://www.bmj.com/content/371/bmj.m4491/rapid-responses>

Summary

A feature article in which the author poses the question of whether the COVID-19 vaccines would be considered cost-effective under the National Institute for Health and Care Excellence's (NICE) approach to measuring value and questions whether NICE's methods are appropriate. A question and challenge that could be equally applied to other similar health technology assessment bodies around the world. Many governments, including the United Kingdom, have committed to

financially support businesses and people in lockdown and many governments have already signed deals for COVID-19 vaccines in development ahead of establishing their clinical effectiveness, let alone their cost-effectiveness. NICE guidance on the approach to economic evaluation does recognize the fact that healthcare technologies might have wider benefits or costs and that these can be reported separately with prior agreement.

Relevance

COVID-19 may be unusual, but it draws attention to a debate for NICE and other similar organizations around the globe about the extent to which we want these bodies to broaden their perspective on inclusion of wider economic benefits or costs. As the author concludes, the world has painfully learned, that health (and care) and our economic lives are (and always have been) inseparable. NICE's response to the article is worth reviewing. They accept the challenges posed by the author as they rapidly create guidelines to inform frontline COVID-19 care and assess the benefits of new technologies, including the rapid approach of COVID-19 vaccines to improve its treatment. •

FROM THE JOURNALS

Constrained Optimization Modeling in Malaysia: Intervening for the Good of the People

Section Editors: Soraya Azmi, MBBS, MPH, Beigene, USA; Agnes Benedict, MSc, MA, Evidera, Budapest, Hungary

Applying a Constrained Optimization Portfolio Model to Aid Prioritization of Public Health Interventions in Malaysia

Varghese L, Ezat Wan Puteh S, Schecroun N, et al

Value Health Regional Issues. 2020; 21(5):172-180.

One of the fundamental reasons why ISPOR exists is to help governments or health payers make better decisions using available evidence that minimizes expenditure while maximizing value. While payers and decision makers in developed countries are as resource constrained as anywhere else, these countries have well-developed frameworks, including health technology assessment (HTA) organizations that support a diligent and in-depth process of selecting the treatments that can offer the best value for investment. On the other hand, many developing and lower-income countries are as yet unable to use HTA processes at the same level of sophistication due to limited expertise, lack of organizational framework

support, lack of local data, and various other reasons depending on the specific country.

The government of Malaysia provides highly subsidized care for its citizens who choose to use government facilities for their healthcare needs. As such, prudent management of the government healthcare budget is a key concern. Malaysia has begun to apply HTA processes progressively over the past decade for pharmaceutical products that are aimed at disease treatment, but the country is not yet implementing HTA in all healthcare decisions. Interventions and strategies related to public health such as vaccinations are one of the areas that tend not to be subject to HTA evaluations. This problem may be common to other developing countries as well. In situations where an HTA framework does not exist, what approaches can be used to methodically evaluate options using health economic principles?

The paper by Varghese et al illustrates one approach that can be considered—constrained optimization modeling was

used to decide between interventions. The research project was undertaken by GlaxoSmithKline in collaboration with the Malaysian Ministry of Health and a Malaysian academic institution. The paper describes a situation where health decision makers needed to make a choice between 7 health priorities in infectious diseases. These were: hepatitis B and C, rotavirus, *Streptococcus pneumoniae*, *Bordetella pertussis*, dengue, and cholera. The aim of the exercise was to identify priorities among these 7 conditions that would optimize the health outcome measure of quality-adjusted life-years (QALYs) gained while remaining within budget constraints. Unlike a cost-effectiveness analysis (CEA), a constrained optimization approach produces a link between budget and outcome and does not require an explicit threshold. However, similar to what is sometimes used in a CEA, the model used was based on a static, multicohort Markov model that was programmed in Excel running across annual time cycles. The model followed up to 15 successive age cohorts that were hypothetically vaccinated starting from year 2017 until each cohort reaches 100 years.

Table 3. For the lifetime and 20-year time horizons, the cumulative number of cases, deaths, disease management costs avoided, and QALYs gained comparing no intervention with intervention.

Outcomes avoided versus no intervention	HBIg newborns	Hepatitis C treatment	Rotavirus vaccination	Pneumococcal vaccination	Dengue vaccination	Pertussis vaccination pregnant women	Cholera vaccination
Lifetime horizon							
Cases	242 674	268 642	2 772 397	1 718 289	1 006 271	9601	224
Deaths	1134	22 626	2772	1985	2214	80	2
Disease management costs, \$US	829 745	7 581 274	345 078 808	423 526 470	337 432 782	30 439 425	448 450
GP visits	*	*	525 850	1 965 983	654 076	0	0
Hospitalizations	*	*	1 306 834	483 044	1 760 974	121 607	1792
QALYs (gained)	32 676	691 944	195 459	136 438	132 965	6284	146
Intervention costs, \$US	39 540 656	2 178 461 979	99 037 478	322 709 811	649 145 364	83 250 904	64 999 361
QALY gain/\$US invested	0.000826	0.000318	0.001974	0.000423	0.000205	0.000075	0.000002
Ranking	2	4	1	3	5	6	7
20-year horizon							
Cases	53 060	142 396	2 772 397	1 698 954	1 006 271	9601	224
Deaths	15	4866	2772	1977	2214	80	2
Disease management costs, \$US	16 262	2 048 993	345 078 808	419 523 497	337 432 782	30 439 425	448 450
GP visits	*	*	525 850	1 946 582	654 076	0	0
Hospitalizations	*	*	1 306 834	480 203	1 760 974	121 607	1792
QALYs (gained)	927	195 135	195 459	135 852	132 965	6284	146
Intervention costs, \$US	39 540 656	2 178 461 979	99 037 478	322 709 811	649 145 364	83 250 904	64 999 361
QALY gain/\$US invested	0.000023	0.000090	0.001974	0.000421	0.000205	0.000075	0.000002
Ranking	6	4	1	2	3	5	7

GP indicates general practitioner; HBIg, hepatitis B immunoglobulin; QALY, quality-adjusted life year; \$US, US dollars.
*Included directly in disease management costs.

For each of the disease areas, the model calculated the avoided cumulative number of cases, deaths, general practitioner visits, hospitalization, and disease management costs by estimating and comparing states with and without the intervention over 2 time periods: lifetime and 20 years. The cumulative QALYs gained by each intervention are estimated equally. Finally, the interventions are ranked according to their QALYs gained per monetary unit invested in them. The ranking is dependent on the inverse of the cost-effectiveness ratio. The highest ranked intervention is budgeted for first and if budget allows, then the second ranked intervention is included and again if there is any remaining budget, the following ranked interventions are considered in the same way. In their results, the

authors reported that the rotavirus vaccination was ranked first, followed by pneumococcal vaccination, and then followed by dengue vaccination. The QALY gain/US\$ invested was 0.001974, 0.000421, and 0.000205 respectively as shown in the table (**Table 3** in the published article).

As with any model, the limitations of the analysis were the level of evidence used as inputs for the disease, their cost, and the effectiveness of the interventions. According to the authors, the data inputs were based on a literature review of published Malaysian articles from the

region. This is a common approach when specific country data are not available. The inputs were also vetted by 6 local experts since the source studies available may have had their own limitations. Among other limitations, the authors also acknowledged the simplicity of the model (1 decision tree and 5 interventions); however, on the flip side, this increased the user-friendliness of the model. Sensitivity analysis was also not performed.

This paper could be of interest to readers who want to know more about how decision-making problems may

be solved when the HTA process does not yet exist. Despite the limitations of the study, it provides insight into an evidence-based solution using economic evaluation principles. And as stated by the authors, this approach also helps to give decision makers a tool to facilitate discussions with stakeholders responsible for budget allocation while providing a degree of transparency and rationality to decision making. •

ISPOR NEWS

Value Assessment in the Age of COVID-19: 8 Takeaways From the ISPOR-IVI COVID Webinar Series

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COVID-19 has swept across the globe and disrupted healthcare access as well as the role and pace of scientific inquiry and emphasized the need for global collaboration. As the world races to develop novel technologies to diagnose, treat, and prevent COVID-19, the pandemic has amplified methodological and policy challenges for the health economics and outcomes research (HEOR) community in conducting value assessment and health technology assessment (HTA).

From July to November 2020, ISPOR and the Innovation and Value Initiative (IVI) co-led a 5-part webinar series, "Value Assessment in the Age of COVID-19: Meeting the Challenges." Experts from diverse disciplines including economics, medicine, epidemiology, public health, and patient advocacy were convened to discuss challenges and potential solutions. A wide range of topics were addressed, including methodologies, health inequity, public health, and pricing and reimbursement strategies (Figure 1).

Each webinar discussion offered numerous insights and important learnings. In reflecting across the series as a whole, several important topics rose to the top. In this article, we outline our 8 key takeaways for value assessment and HTA in the context of COVID-19 (Figure 2).

1. Economic evaluation models used in value assessment and HTA should feature a societal perspective and consider the impacts of novel health interventions for COVID-19 on the broader economy.

Quantitative economic models, most notably cost-effectiveness analysis models, are increasingly used to prioritize the use of health interventions given limited health sector resources. Existing models typically feature an individually focused health system or a "limited" societal perspective. Compared with other diseases, COVID-19 is highly contagious and has sizable impacts on the nonhealth sectors. Due to its significant social and economic impacts, economic models focusing on COVID-19 should be broadened to feature a societal perspective and reflect a comprehensive set of social costs and benefits, as proposed by the Second Panel on the Use of Cost-Effectiveness in Health and Medicine.¹⁻³ In constructing the societal perspective, modelers should consider a broader set of novel value elements, such as fear of contagion and severity of disease, as outlined in the ISPOR Special Task Force on Value Assessment Frameworks.³⁻⁴

Along these same lines, existing models typically do not consider the impacts of novel technologies on nonhealth sectors and the broader economy. As novel health interventions are likely

to generate gains in all sectors, alternative methodologies that explicitly model the impacts and interactions of novel treatments on aggregate economic indicators such as employment and gross domestic product should be considered. Computable general equilibrium models are promising alternatives, as they enable modelers to include all economic sectors to various degrees of aggregation and disaggregation, depending on which are of the most interest.⁵

Economic evaluation models are used to support a range of decisions, including those related to pricing, coverage, and utilization. Understanding the impacts of novel treatments on both health and nonhealth sectors is important, but this does not imply that innovators of novel therapies should capture the full value of system-wide gains generated, as discussed below.

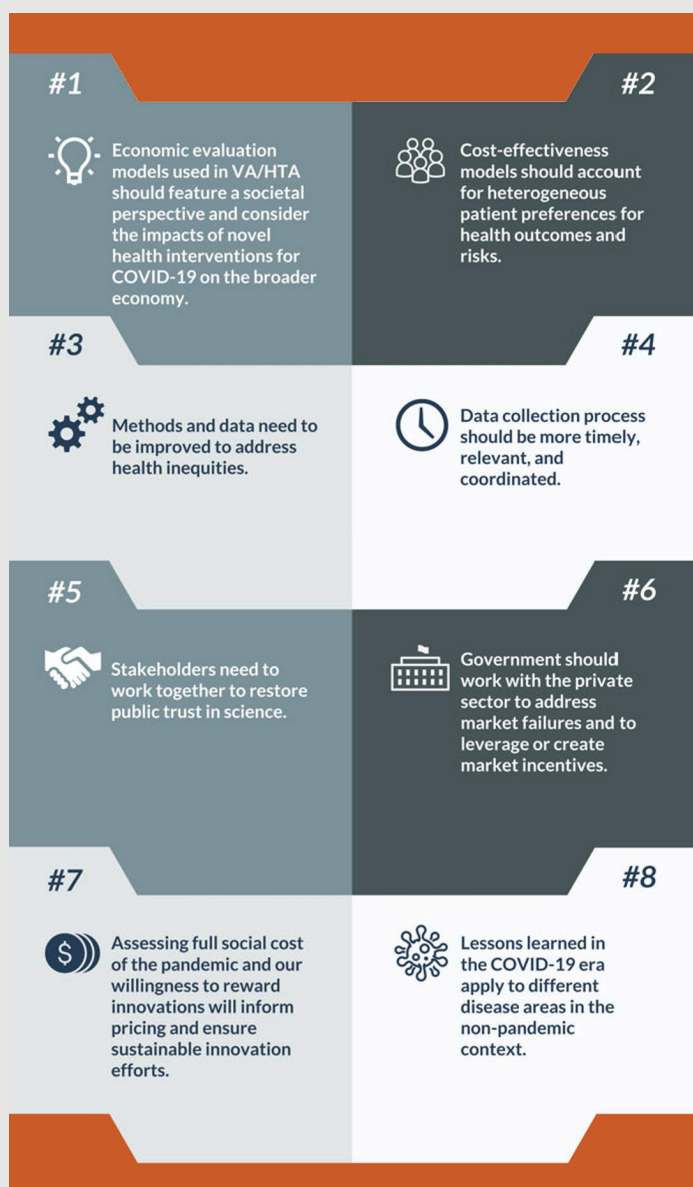
Figure 1. Overview of the webinar sessions and panelists.

1	HOW SHOULD THE COVID-19 PANDEMIC CHALLENGE CONVENTIONAL WISDOM ABOUT VA/HTA? Finn Borlum Kristensen, MD, PhD (University of Southern Denmark) Darius Lakdawalla, PhD (University of Southern California) Michelle McMurry-Heath, MD, PhD (Biotechnology Innovation Organization) Gary Puckrein, PhD (National Minority Quality Forum) Shelby Reed, PhD (Duke University)
2	COVID-19: ARE OUR METHODS UP TO THE TASK? Anirban Basu, PhD (University of Washington) Lou Garrison, PhD (University of Washington) Susan Griffin, PhD (University of York) Darius Lakdawalla, PhD (University of Southern California) Dan Ollendorf, PhD (Tufts University) Charles Phelps, PhD (University of Rochester)
3	BALANCING ECONOMICS AND ETHICS: HOW CAN VA/HTA SUPPORT EQUITABLE RESOURCE ALLOCATION? Jennifer Bright, MPA (Innovation and Value Initiative) Richard Cookson, DPhil (University of York) Amber Hewitt, PhD (Families USA) Jennifer Miller, PhD (Yale University) Laurie Zephyrin, MD (Commonwealth Fund)
4	THE ROLE OF PUBLIC HEALTH: HOW CAN VA/HTA INFORM PANDEMIC POLICY INTERVENTIONS AND PUBLIC RESOURCE ALLOCATION? Henning Tarp Jensen, PhD (London School of Hygiene and Tropical Medicine) Marcus Keogh-Brown, PhD (London School of Hygiene and Tropical Medicine) Penny Mohr, MA (Patient-Centered Outcomes and Research Institute) Yannis Natsis (European Public Health Alliance) Murray Ross, PhD (Kaiser Foundation Health Plan) Reed Tuckson, MD, FACP (Tuckson Health Connections)
5	USING VA/HTA IN PURSUING INNOVATION AND ACCESS IN A PANDEMIC Amitabh Chandra, PhD (Harvard University) Sung Hee Choe, MPH (FasterCures) Rena Conti, PhD (Boston University) Adrian Towse, MA, MPhil (Office of Health Economics) Richard Willke, PhD (International Society for Pharmacoeconomics and Outcomes Research)

VA/HTA=value assessment and health technology assessment

For complete information about the speakers and specific webinar sessions, please visit the following URL: <https://www.ispor.org/conferences-education/education-training/webinars/value-assessment-in-the-age-of-covid-19-meeting-the-challenges>

Figure 2. 8 key takeaways for VA/HTA in the pandemic context.



HTA indicates health technology assessment; VA, value assessment.

2. Cost-effectiveness models should account for heterogeneous patient preferences for health outcomes and risks.

A recent COVID-19 study by Duke University researchers used an experimental design and showed that individuals in American society have diverse preferences regarding social distancing restrictions, infection risks, and economic outcomes.⁶ These preferences and differing levels of compliance with COVID-19 public health measures reveal that preferences related to health outcomes and risks vary across population subgroups. These heterogeneous preferences matter, especially in terms of how they affect health behaviors such as vaccination uptake and other preventive measures.

Conventional cost-effectiveness analysis estimates often implicitly assume that all individuals have identical and “average”

preferences.⁷ A potential way to consider the impact of heterogeneous risk preferences on cost-effectiveness analysis is the Generalized, Risk-Adjusted Cost-Effectiveness (GRACE) framework—an augmented cost-effectiveness analysis that offers a unifying framework to account for divergent patient preferences alongside quality-adjusted life-years and the usual elements of a cost-effectiveness analysis.⁷

3. Methods and data need to be improved to address health inequities.

Evolving data from the COVID-19 pandemic highlight its disproportionate impacts in our society, with greater incidence among people of color and those with lower socioeconomic status. Health inequities have been extensively documented across disease states and countries. Value assessment and HTA methods need to be improved and tested to address questions of inequity more thoroughly.

Ensuring that data collection and evidence-generation efforts represent a diverse patient population is the necessary first step. Encouraging participation from underserved communities will allow the sources and magnitudes of disparity to be examined and provide necessary data inputs for methods that address inequity.

Distributional cost-effectiveness analysis is a promising analytical framework that allows decision makers to assess the impacts of various policies on health disparities in addition to the population-level health gains.⁸

4. Data collection processes should be more timely, relevant, and coordinated.

For models to generate insights that aid real-time decision making, data collection efforts need to be more timely, relevant, and coordinated. In the United States, due to a fragmented healthcare system, data are typically collected and stored by different stakeholders in separate data systems. Although an abundance of data already exists, the challenge is to integrate data on a common platform that promotes interoperability. More communication is needed across stakeholders to coordinate such efforts.

As the world races to develop safe and effective COVID-19 interventions, data collection efforts should be designed for both near-term regulatory approval and longer-term evidence needs. Understanding of COVID-19 is rapidly evolving and data collection efforts should generate long-term, real-world evidence that will enable assessment of novel interventions and preparation for the next pandemic.

Data collectors should also be more active in their outreach efforts, shifting away from a “if we build it, they will come” mentality. With a broad and diverse population pool as their goal, data collectors need to actively reduce barriers to patient participation.

5. Stakeholders need to work together to restore public trust in science.

As shown in many countries, public health interventions are cost-effective solutions to fighting a pandemic. But they only work when a clear message is delivered and the public trusts

government institutions and the scientific enterprise. Globally, adherence to public health guidelines has varied widely. In the United States, the lack of coordination between the federal government and state health departments has contributed to an erosion of trust. Restoring public trust should be a major initiative moving forward, requiring coordinated efforts from the media, health providers, researchers, government, and politicians.

The HEOR community can contribute to restoring the public's trust in science in several ways. When conducting value assessment and HTA, we should be more transparent about methodologies, key assumptions, and data inputs. We should acknowledge and fully examine the uncertainty in our estimates by conducting sensitivity analyses that use alternative assumptions and data inputs. Efforts should also be made to communicate our methodology and findings to nontechnical, non-HEOR audiences.

6. Government should work with the private sector to address market failures and to leverage or create market incentives.

Government can be instrumental in fighting the current pandemic and future ones, both directly and indirectly. In some instances, governments should directly intervene to address market failures, such as repurposing existing generic medications to fight COVID-19 and developing testing kits. In others, government should support rather than supplant the market mechanism. For incentivizing and distributing novel health technologies, the government should work with the private sector to leverage or create market incentives and structures. For example, instead of committing to the advance purchase of specific products in development, the government can set aside resources and signal to the market that innovations meeting certain value-based criteria will be rewarded.

In evaluating and prioritizing technologies to fight the pandemic, the government should work with the private sector to assess existing and pipeline health technologies and coordinate efforts accordingly. As the pandemic affects every facet of society, a holistic strategy is needed, building on what we know and advancing diagnoses, treatments, and vaccines. Existing value assessment and HTA tools can help evaluate the social and private returns to different innovation efforts and help the government determine whether direct or indirect interventions are required.

7. Assessing the full social cost of the pandemic and our willingness to reward innovations will inform pricing and ensure sustainable innovation efforts.

The emergency regulatory approvals of COVID-19 treatments and vaccines have stirred up debates about pricing. Traditional cost-effectiveness analyses were used to inform the pricing of remdesivir, for example, in some earlier analyses. But as noted previously, conventional cost-effectiveness analysis approaches do not fully consider the impacts of novel health interventions on the broader economy and might not be the most appropriate decision tool in the pandemic context.

To derive prices consistent with the value-based pricing framework, the social cost of the pandemic should be assessed. Recent estimates set the pandemic's cost to the United States at over \$16 trillion, taking into account lost economic growth and health loss.⁹ Effective novel interventions are likely to generate huge social benefits (inclusive of health and nonhealth gains) and decisions must be made about size and share of the reward to innovators that "save the day."

Part of the pricing debate centers on the cost-effectiveness threshold, which reflects society's willingness to pay for novel interventions. Instead of arbitrarily adjusting the existing threshold, policy makers should examine the full social cost and should scale willingness to pay based on appropriate incentives for innovations.

Improving these methods and practices can help in evaluating novel health technology and public policy interventions to fight the pandemic, ensure equitable resource allocation, and incentivize long-term scientific innovation for future pandemic preparedness.

There is little debate that every individual in our society should have access to these novel treatments, regardless of price. But with an eye toward future pandemic preparedness, the signaling effects of current pricing on future innovations must also be considered. Appropriate market incentives should be put in place for innovators to develop technologies that will provide pandemic readiness.

8. Lessons learned in the COVID-19 era apply to different disease areas in the nonpandemic context.

Lessons from the pandemic will have long-lasting impacts on value assessment and HTA methods and practices in our community. Improving these methods and practices can help in evaluating novel health technology and public policy interventions to fight the pandemic, ensure equitable resource allocation, and incentivize long-term scientific innovation for future pandemic preparedness.

Many of the challenges highlighted by COVID-19, such as lack of integrated data and health disparities, are not unique to the pandemic context. COVID-19 provided us with a unique context and a sense of urgency to "pressure-test" our methods and address the existing shortfalls in value assessment and HTA. As we emerge from the pandemic, we should also bear in mind that these learnings apply in the postpandemic era across all disease areas.

Conclusion

ISPOR and the Innovation and Value Initiative launched the webinar series to convene thought leaders from diverse disciplines to explore a range of unique methodological and

policy challenges made plain by the pandemic. While much has been learned from this confluence of stakeholder perspectives, addressing these challenges is a longstanding proposition requiring much greater collaboration across our fields. In 2021 and looking forward, ISPOR and the Innovation and Value Initiative will continue to explore initiatives with the HEOR community to advance the methods and practices of value assessment and HTA. •

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The course will be taught by Uwe Siebert, MPH, MSc, ScD, MD, UMIT, Innsbruck, Austria.

Network Meta-Analysis in Relative Effectiveness Research

24-25 February | 4-Hours Total | 2-Day Short Course

This course gives a brief overview of different decision-analytic model types and provides an introduction to Markov modeling techniques. Based in part on the ISPOR Task Force Reports on Indirect Treatment Comparisons, the fundamentals and concepts of network meta-analysis will be presented. The evaluation of networks presents special challenges and caveats, which will also be highlighted in this course. The material is motivated by instructive and concrete examples. The ISPOR-AMCP-NPC questionnaire for assessing the credibility of a network meta-analysis will also be introduced.

The course will be taught by Jeroen P. Jansen, PhD, Precision Xtract, Oakland, CA, USA; Sarah Goring, MSc, Precision Xtract, Vancouver, Canada.

Introduction to Health Technology Assessment (HTA)

3-4 March | 4-Hours Total | 2-Day Short Course

The course provides an overview of basic HTA principles including benefit assessment (biostatistics, clinical epidemiology, patient-relevant outcomes, risk-benefit assessment), economic evaluation (costing, cost-effectiveness analysis, pharmacoeconomic modeling, budget impact analysis, resource allocation), and ELSI (ethical, legal, and social implications). Using real-world examples covering both drugs and devices, the course will review the practical steps involved in developing and using HTA reports in different countries and healthcare systems.

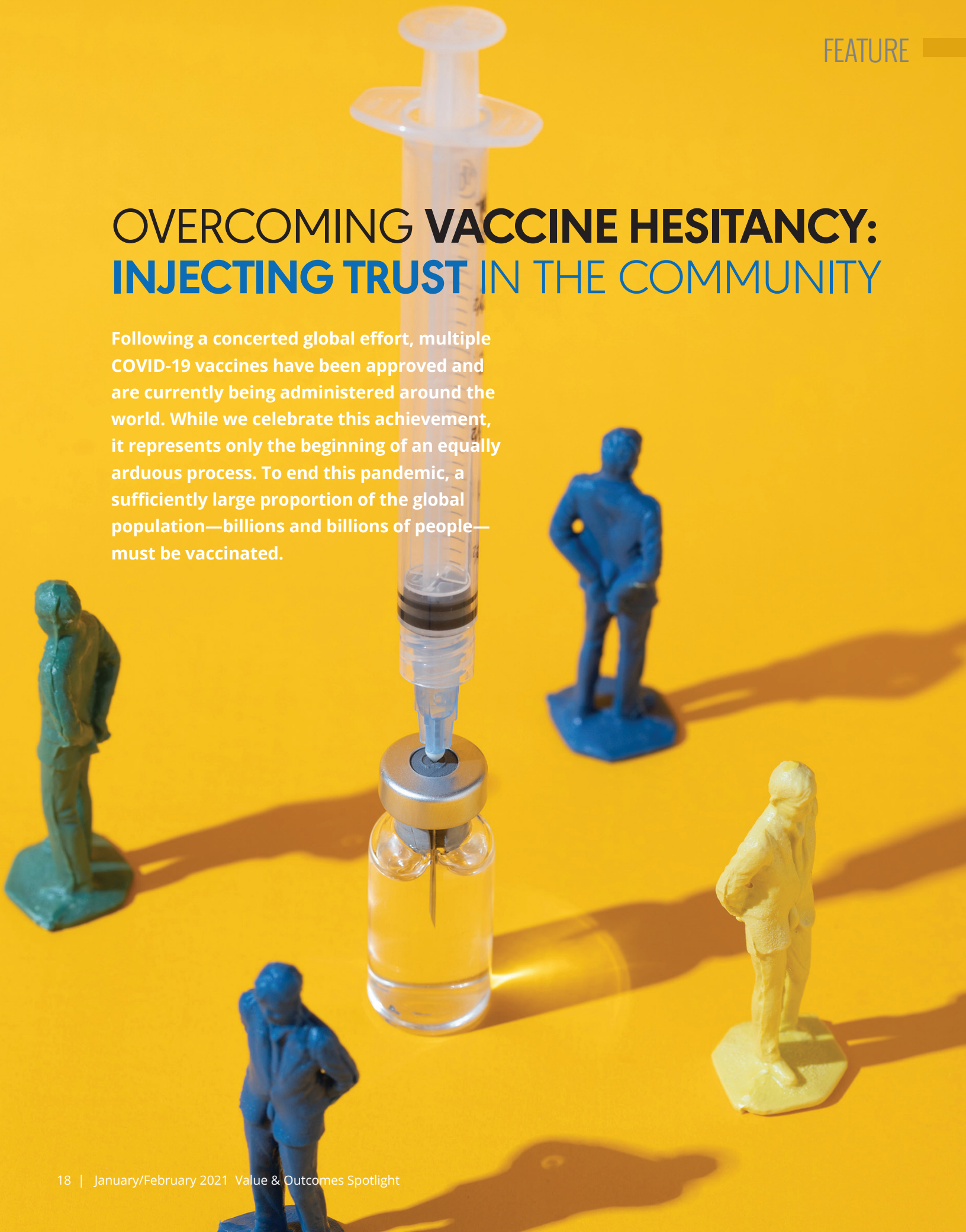
The course will be taught by Uwe Siebert, MPH, MSc, ScD, MD, UMIT, Innsbruck, Austria; Petra Schnell-Inderst, MPH, PhD, UMIT, Innsbruck, Austria.



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OVERCOMING **VACCINE HESITANCY:** **INJECTING TRUST** IN THE COMMUNITY

Following a concerted global effort, multiple COVID-19 vaccines have been approved and are currently being administered around the world. While we celebrate this achievement, it represents only the beginning of an equally arduous process. To end this pandemic, a sufficiently large proportion of the global population—billions and billions of people—must be vaccinated.



While nations struggle with manufacturing and supply-chain logistics, the growing worldwide distrust in immunization and the rise of vaccine hesitancy may prove even more challenging. Governments, public health officials, and advocacy groups must be prepared to address vaccine hesitancy to ensure adoption of novel vaccines, achieve broad population immunity, and help us return to more normal lives. Unless the origins of such wide variation in willingness to accept a COVID-19 vaccine is better understood and addressed, differences in vaccine coverage between countries could potentially delay global control of the pandemic and the ensuing societal and economic recovery.

For this article, William Schaffner, MD, Lynn Field-Harris, MPA, and Nelly Salgado de Snyder, PhD shared their thoughts on vaccine hesitancy, differences across populations, and possible ways real-world evidence may help to address vaccine hesitancy.

The Complicated Construct

Vaccine hesitancy—a patient-level reluctance or refusal to receive a vaccination—is a deeply complex and context-specific construct, influenced strongly by personal experiences and belief systems.¹ It threatens to not only reverse progress made in tackling vaccine-preventable diseases (eg, measles), but also derail efforts to control the current COVID-19 pandemic.

Despite vaccinations having long been heralded as providing one of the most cost-effective ways of avoiding disease, preventing 2 to 3 million deaths a year, public doubt and unease continues to grow. In 2019, following a 30% increase in the number of measles cases globally, the World Health Organization highlighted the dangers of vaccine hesitancy as one of the top 10 health threats joining air pollution, climate change, and HIV/AIDS.

The enormously successful history of vaccines may be contributing to increasing levels of hesitancy. Previously devastating diseases, such as polio and smallpox, are long forgotten, leading some patients to minimize the potential threats of vaccine-preventable diseases as they weigh the potential risks and benefits of newer vaccines.²

Furthermore, some patients may overestimate risks associated with current vaccines due to misinformation obtained through misleading or erroneous social media and other poorly vetted sources. Despite rapid spread of the current COVID-19 contagion, misinformation is spreading at an even faster rate. Misinformation creates barriers to universal vaccination, obfuscating vaccination benefits and emphasizing the adverse effects of vaccination, thus impeding patient understanding and overall buy-in.³ Not only are these sources free from editorial oversight, but users may also self-select content streams, which may contribute to ideological isolation and further limit access to accurate information.

Who Is Prone to Hesitancy?

Recent global surveys of COVID-19 vaccine hesitancy reveal large differences by country. A June 2020 survey of 13,426 people from 19

countries found that while 71.5% of participants voiced a willingness to take a COVID-19 vaccine, rates by country varied from almost 90% in China to less than 55% in Russia.⁴ A more recent global survey conducted in October 2020 of 18,526 adults in 15 countries found 73% of respondents willing to take the COVID-19 vaccine. Countries with the highest levels of vaccination intent included India (87%), China (85%), South Korea (83%), and Brazil (81%). Respondents in France reported the lowest level of vaccination intent with only 54% expressing intent to get the COVID-19 vaccination (**Figure 1**). Among those respondents who did not intend to receive the COVID-19 vaccine, risk of side effects was the most frequently cited concern in Japan, while speed of clinical trials presented the most significant worry to respondents in both Spain and Brazil.

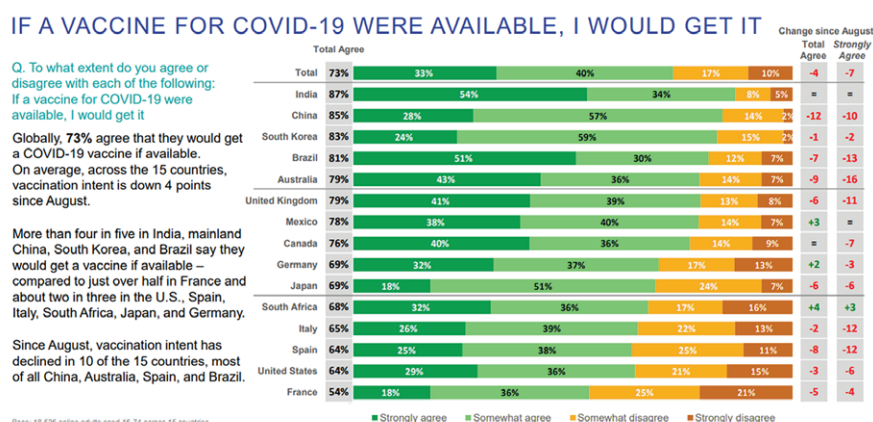
Despite vaccinations having long been heralded as providing one of the most cost-effective ways of avoiding disease, public doubt and unease continues to grow.

Finally, a low perceived risk of contracting COVID-19 was the most commonly cited concern among vaccine deniers in India and the United States.⁵

Political climate may also influence vaccine hesitancy. Soon-to-be-published research identified a highly significant positive association between support for populist parties and skepticism of vaccine importance of effectiveness.⁶ Authors argue that vaccine hesitancy and political populism are both rooted in a profound distrust in elites and experts on both ends of the political continuum.

The Kaiser Family Foundation monitors attitudes in the United States towards COVID-19 vaccinations. Its December 2020 report found that 71% of respondents would probably or definitely receive the COVID-19 vaccine, while roughly a quarter of respondents remain hesitant. Within this December report, vaccine hesitancy varied by political leaning (higher for Republicans versus Democrats) and residency (higher rates for rural versus urban residents).

Figure 1. Global survey of 18,526 adults in 15 countries regarding willingness to take the COVID-19 vaccine.



Adapted from Boyon N. Global attitudes on a COVID-19 vaccine: Ipsos survey for the World Economic Forum.⁵

Racial Differences in Vaccine Perception

Perhaps the most important revelation in the Kaiser Family Foundation's December report concerned differences in vaccine hesitancy by race. Roughly a third of Black adults (35%) stated that they definitely or probably would not get vaccinated.

[The COVID Collaborative](#), a nonprofit coalition made up of Langer Research Associates, Unidos US, and the National Association for the Advancement of Colored People, examined beliefs held by Blacks and Latinos regarding the safety and effectiveness of COVID-19 vaccines, finding 86% of Black and 66% of Latino respondents doubted vaccine safety, while 82% and 60% doubted effectiveness.

These racial differences are particularly troubling given that vaccine hesitancy affects those populations that are also disproportionately suffering the impacts of COVID-19. To prevent widening health disparities, it is critical to address vaccine hesitancy within these groups.

Deep-Seated Mistrust in the Process

"I really understand the whole issue of hesitancy," shared Lynn Fields-Harris, MPA, former executive director of Center in the Park, a community center serving a predominantly Black population of older adults in Philadelphia, Pennsylvania. "I understand not so much fear of the vaccine and fear of COVID-19, but the distrust in government and the medical community, which has been exacerbated by the pandemic, laying bare the racism and inequity systematized in this country."

"There's a great feeling that we are responsible for one another, that together we're willing to make that sacrifice for the safety of other people."

The significant mistrust held by many communities of color of public health officials, policy makers, and health providers continues today. The long history of both abuse and exclusion of people of color continues to erode patient trust, as Fields-Harris emphasized the ongoing impact of the Tuskegee Syphilis Study. [Editor's Note: *"The Tuskegee Study of Untreated Syphilis in the Negro Male" was a study conducted between 1932 and 1972 by the United States Public Health Service and the Centers for Disease Control and Prevention.*] "I feel like the struggle for communities of color is on so many levels the focus in terms of rebuilding trust," she said. "It is really going to have to be something visible. Something tangible that people can see is moving in the right direction."

William Schaffner, MD, professor of Preventive Medicine and Health Policy, Division of Infectious Diseases at Vanderbilt University, understands why some populations may be resistant to vaccines. "In the interest of equity and appropriate public health response, you reach out to minority populations to make sure that they're vaccinated, and they may respond in a way that you hadn't anticipated, saying 'Wait a minute, do you want us to go first? Oh, once again, you're experimenting on us.'" This, he noted, may lead many within this population to opt out of vaccinations, waiting instead for more safety evidence.

To help reassure Black Americans of the safety of COVID-19 vaccines, the National Medical Association, a professional society of African American doctors, conducted its own review of vaccine data, endorsing the emergency authorizations of both the Moderna and Pfizer/BioNTech vaccines.

Nelly Salgado de Snyder, PhD, spoke to COVID-19 vaccine attitudes held by Mexicans residing in Mexico versus those residing in the United States. Salgado de Snyder is a professor and senior researcher in medical sciences at the National Institute of Public Health of Mexico and currently is a Latino Research Institute Fellow at the University of Texas studying health access for Mexican immigrants in the United States. She noted that antivaccine views in Mexico are relatively rare given the country's history of successful universal vaccination campaigns. "Overall, people in Mexico are receptive to vaccines," she said. "Mexican immigrants in the United States experience far higher levels of hesitancy driven by both vaccine misinformation and by mistrust of the government. The problem with immigrants who live in the United States is that they have limited access to health information and they do not trust the government or institutions in general."

Salgado de Snyder sees the US political climate regarding immigration and undocumented workers fueling immigrants' mistrust of public health and other institutional organizations, leading to the belief that these institutions may be a threat to their well-being. She shared an example of vaccine misinformation received through social media messages. "Social media posts state, 'The vaccine is a plot! They are injecting you with the virus because they want to get rid of you and all the immigrants! You are undesirable in this country!'"

A recent Kaiser Family Foundation survey supported this view, finding 74% of Hispanic respondents in the United States feel hesitant or resistant to the vaccine.⁷ Yet, Salgado de Snyder said that hesitancy among immigrants is often higher in men. She noted that immigrant men are particularly prone to vaccine hesitancy given their concerns about lost income from time spent seeking vaccinations.

Finally, trust in public health organizations has been further eroded by the politicization of the COVID-19 pandemic. In the United States, the former administration's support for the use of hydroxychloroquine in treating COVID-19 despite there being no reliable supporting evidence of its efficacy or safety, coupled with the "warp speed" vaccine development timeline has heightened suspicions of how safe and effective the vaccines are.

Using Real-World Evidence to Open the Door to Trust

In the current battle against COVID-19, real-world evidence has helped accelerate the development of safe and effective vaccines, providing critical evidence needed for emergency use authorization. And through projects such as the Vaccine Safety Datalink, a partnership between the Centers for Disease Control and 8 health plans, and the Post-Licensure Rapid Immunization Safety Monitoring System, a part of the US Food and Drug Administration's Sentinel Initiative, real-world evidence continues to be used track the safety of new vaccines.^{8,9}

In addition to these ongoing surveillance measures, real-world evidence may also help address vaccine hesitancy by providing the necessary information about the safety and efficacy of new COVID-19 vaccines needed to help reassure patients. Possible ways that real-world evidence may contribute include:

- Conducting culturally responsive assessment of vaccine efficacy and safety within specific subpopulations, such as Black or Latino populations
- Examining safety and efficacy in patients with rare conditions (eg, sickle cell disease) or other comorbid conditions
- Addressing fertility/reproduction concerns
- Conducting comparisons of different vaccines within subpopulations. Are all COVID-19 vaccines equally safe and effective in all subpopulations?

The determinants of vaccine hesitancy differ depending on the cultural, societal, and personal beliefs; geographic region; and sociodemographic characteristics. They may evolve as misinformation spreads. Therefore, ongoing surveillance is needed so researchers can understand what information is needed to tailor evidence-based strategies to overcome the problem with sustainable interventions.

In designing research strategies to alleviate vaccine hesitancy, Schaffner emphasized the need to understand the core reasons behind individual fears. “You have to respect that it’s perfectly reasonable to be skeptical, hesitant, and concerned. You have to recognize that there are many people who may not read the paper every day or read the scientific literature.” He continued, “Once you recognize that skepticism is reasonable and is an appropriate human response, you then open up your mind and begin to ask, ‘What evidence may help settle their fears?’”

Fields-Harris agreed with this need for researchers to understand the core concerns of these communities. “I do think that mistrust is deeply ingrained. Researchers and scientists must gain an understanding of the communities so there can be some kind of engagement.”

Importance of the Right Message and the Right Messenger

Hesitancy may persist even with more culturally sensitive messages—accurate and relevant information that is free from political influence. The knowledge-deficit approach to address vaccine hesitancy has shown limited effect in changing minds given the complex mix of cognitive, emotional, cultural, social, spiritual, and political factors that influence vaccination choices.¹⁰

“Information is necessary, but not sufficient to change people’s attitudes and behavior,” said Schaffner. “You have to change their attitudes. And that’s where you need to be comforting and reassuring. I keep using these words, ‘comfort and reassurance’ more than facts. When we lead with facts often it is not the best way to start.”

Schaffner, Fields-Harris, and Salgado de Snyder emphasized the importance of the right messenger together with the right message when addressing vaccine hesitancy such as a respected, trusted source in their community. Both Fields-Harris and Salgado de Snyder highlighted the influence religious

leaders and teachers could have in alleviating vaccine hesitancy. Fields-Harris said, “Information around what the vaccine is, what the impact is, was much more readily accepted by peer-to-peer education and awareness.” Schaffner added that vaccine messaging may need to reach beyond standard public health outlets, using instead neighborhood barbershops or beauty shops. And Salgado de Snyder stressed the importance that all vaccine messaging be translated into native languages and be accessible to even a low-literacy public.

Hope for Future Community Support

Promisingly, the people we spoke to for this article were hopeful that by addressing vaccine hesitancy, wider community support for COVID-19 vaccines may drive vaccination campaigns. “My hope is that as everybody else gets vaccinated and we begin to see beneficial effects of the vaccine, some of those hesitant people will be brought in. They want to be part of the group,” said Schaffner.

“If people feel that taking the vaccine will have a broader impact beyond themselves, I believe they will be more inclined to do it,” added Fields-Harris. “There’s a great feeling that we are responsible for one another, that together we’re willing to make that sacrifice for the safety of other people.” •

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About the Author

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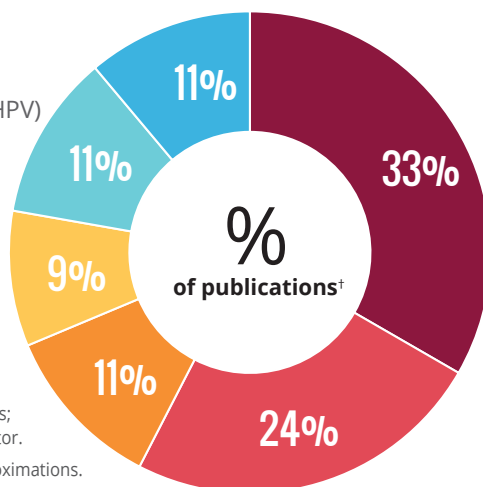
By the Numbers: Vaccines HEOR

Section Editor: The ISPOR Student Network

Number of Economic Evaluations* of Vaccination Programs Is Relatively Low¹

Vaccine group

- Influenza
- Pneumococcal
- Human papillomavirus (HPV)
- Herpes zoster
- Tetanus-diphtheria pertussis
- Hepatitis B

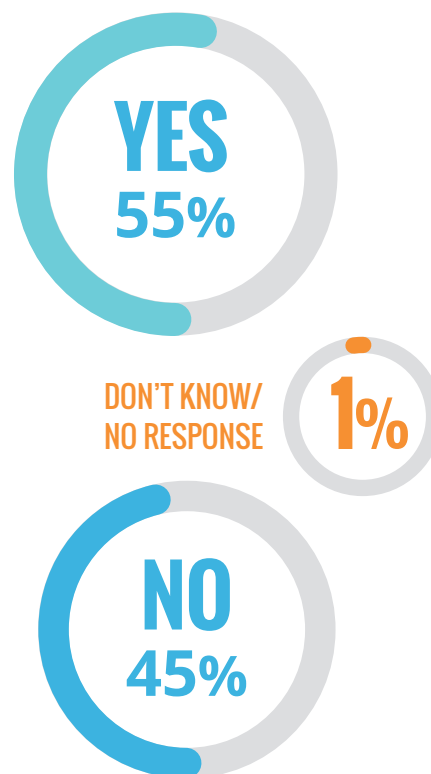


*Economic evaluations that encompass: (1) cost-effectiveness, cost-utility, or cost-of-illness analyses; (2) both pediatric and adult populations; (3) using nonvaccination as a comparator.

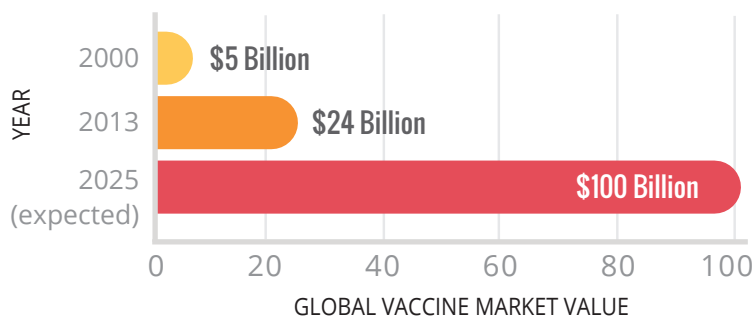
†Sum may not yield 100% due to approximations.

Countries With a National HPV Vaccination Program (n=194)

In addition to other life-saving vaccines for children, a significant proportion of countries lack national vaccination programs offering more recent vaccines (eg, HPV).²



Global Vaccine Market Expected to Reach \$100B by 2025*



*Data extrapolated before COVID-19 pandemic.

5 Proposed Tools to Improve Market Access to Vaccines³

- 1 **Pull mechanisms** as innovative procurement approach (volume guarantee contracts, public funding)
- 2 **Push mechanisms** to accelerate vaccine supply (increase production capacity and new production and supply strategies)
- 3 **Long-term commitments** may be needed to fund vaccines to stimulate capacity expansion
- 4 **Reduce risks** for producers and purchasers
- 5 **Increase predictability and coresponsibility** of stakeholders (eg, volume guarantee and/or prepayment)

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Health Technology Assessment for COVID-19 Treatments and Vaccines: Will Cost-Effectiveness Analysis Serve Our Needs?

William Padula, PhD, MS, University of Southern California, Los Angeles, CA, USA; Natalie Reid, PhD, MPH, MBA; Jonathan Tierce, CPhil, Monument Analytics, Baltimore, MD, USA

- The COVID-19 pandemic is likely to produce cost-saving treatments, vaccines, and/or cures that make the application of cost-effectiveness analysis difficult to determine the price of technology.
- Alternative economic evaluation measures such as budget impact analysis, net health benefit, and net social benefit may more accurately assess the value that COVID-19 health technologies deliver to society as a whole.
- Should the ISPOR community rethink how it uses economic evaluation methods to analyze the value and price of forthcoming COVID-19 health technologies?

With the novel coronavirus pandemic (COVID-19) impacting nearly every society worldwide, now it is more important than ever to find practical solutions that differentiate COVID-19 patient care from other infectious diseases. This involves swift research and development of health technologies, including treatments and vaccines, to fight COVID-19. However, broad access to these solutions could be several months to years away, leaving the healthcare service industry (eg, hospital facilities and providers) as our current and best solution to help patients survive. This demand for healthcare services requires health economists to shift gears, to not only focus on health technology assessment (HTA), but also on value assessment of healthcare services.

Fighting Back, but Paying the Price

Attendees of the Virtual ISPOR 2020 workshop, “Understanding Intricacies of Value Assessment—Learning How to Conduct Economic Evaluation of Health Services and What Makes This Approach Different From Health Technology Assessment,” were asked, “What will the United States spend the most money on in the healthcare sector in 2020 to fight COVID-19 pandemic?” Thirty-five percent of respondents selected that the United States would spend the most on healthcare services in the fight against COVID-19, compared to health technologies for diagnostics, vaccines, and treatments in the next year

(Table 1).^{1,2} Despite healthcare services leading the United States in healthcare spending compared to testing and diagnostics, vaccines, and pharmaceutical treatments, traditional HTAs are not typically applied to healthcare services. HTAs will only examine about 12% of the \$3.5 trillion US healthcare budget. The United States needs to refocus on value assessment of other healthcare provisions, such as healthcare services.

Willingness to Raise the Threshold

During the same Virtual ISPOR 2020 workshop, another poll of attendees explored what the willingness-to-pay threshold should be for COVID-19 vaccines and treatments. Traditional willingness-to-pay thresholds have ranged from 1x to 3x the per-capita gross domestic product, falling within \$50,000 to \$150,000 per quality-adjusted life year (QALY) gained.^{3,4} Recent empirical work by Phelps indicates that the exact willingness-to-pay threshold for the US society is between \$100,000 and \$105,000 per QALY and Vanness et al estimates that it is approximately \$104,000 per QALY.^{5,6} Relative to these values, should the threshold be higher to capture the exceptional value a COVID-19 treatment, vaccine, or cure would have on society? Or should it be a lower threshold to account for accessibility and affordability considerations? Or should it just remain the same as what good empiricism still suggests (ie, about \$100,000 per QALY)?

Table 1. Twitter Poll: “What will the United States spend the most money on in the healthcare sector in 2020 to fight COVID-19 pandemic?”

COVID-19 Healthcare Spending	(N=37)
ED/ICU/Clinical Services	35.1%
Testing & Diagnostics	24.3%
COVID-19 Vaccine	29.7%
COVID-19 Treatment	10.8%

ED indicates emergency department; ICU, intensive care unit.

Table 2. Twitter Poll: “US HTA’s willingness-to-pay has ranged from \$50,000/QALY to \$150,000/QALY, representing opportunity costs of next-best alternatives. COVID-19 is [trillions of dollars] in economic impacts and opportunity costs—we need to invest in a solution or many may die. What is the willingness-to-pay threshold for COVID-19 treatment or vaccine?”

COVID-19 Healthcare Spending	(N=82)
\$50,000/QALY	29.3%
\$100,000/QALY	22%
\$150,000/QALY	19.5%
\$180,000/QALY	29.3%

HTA indicates health technology assessment; QALY, quality-adjusted life year.

The workshop attendees who were polled showed that there is no consensus on what the willingness-to-pay threshold should be. The results are a bimodal distribution of participants indicating a desired threshold of \$50,000/QALY and others up to as high as \$180,000/QALY (Table 2).⁷ The mixture of poll results regarding willingness-to-pay thresholds is interesting, perhaps highlighting mindsets across the spectrum amongst the workshop participants: (1) those selecting a lower willingness-to-pay threshold may worry about the connection between value assessment and price of technology; (2) those on the higher end of the willingness-to-pay threshold range communicate that innovation deserves to be rewarded in the macroeconomic implications; and (3) traditionalists choosing \$100,000/QALY indicate that COVID-19 treatments should be no different than other technologies. Incidentally, a report by the Institute for Clinical and Economic Review (ICER) evaluating the value and pricing of remdesivir to treat COVID-19 primarily cited a willingness-to-pay threshold of \$50,000 per QALY for their analyses, in addition to reporting \$100,000 and \$150,000 per QALY thresholds—we assume this since this was the bolded value that ICER reported in their “Base Case Model (assuming mortality benefit)”—putting them on the lower range of opinion while also including price points in their analysis at willingness-to-pay thresholds of \$100,000/QALY and \$150,000/QALY.⁸

Weighing the Cost of COVID-19

Regardless of the willingness-to-pay threshold that societies choose (and recognize that it is a choice) to value COVID-19 vaccines, treatments, or cures, the opportunity cost of doing nothing is too high. Dollars spent on the COVID-19 pandemic are not limited to the healthcare sector. The opportunity costs of these dollars span the entire economy—from businesses and employment, to education and housing, if not more. In a 2009 article, Becker cited that a pandemic could have a partial impact of \$20 trillion on the US economy.⁹ His figure was adjusted for an “expected” risk of 1/100 of \$20 trillion, leading to an expected impact of about \$200 billion. However, now that it is 100% clear that COVID-19 is a global catastrophic event, the weighted impact of the pandemic on Becker’s figure should be 100/100 given zero uncertainty (ie, \$20 trillion).

Becker’s rationale, based on the uncertainty of an imminent pandemic combined with the size of the economy that could

be impacted, can be used to present another way of computing value. A technological solution for COVID-19 will offset a greater opportunity cost. The United States should be willing to draw 3 to 5 years of credit in order to maintain forward health and economic progress. Thus, the 3-year investment would be \$60 trillion (\$20 trillion Gross Domestic Product x 3 years). With 320 million Americans financing this investment, it would result in \$187,500 per person (\$60 trillion/320 million people). Thus, those who selected willingness-to-pay thresholds above \$150,000 per QALY were not without cause, even if such logic had not yet been applied.

Looking at the Long-Term Impact

We have now seen the impact of reduced social distancing to reopen economies. It is arguable whether this juxtaposition between public health and the economy is fully valid. One could take the perspective that full economic activity requires nearly full health, and so when economic activity jeopardizes health, there is damage to both (hence, industrial pollution regulations, Occupational Safety and Health Administration [OSHA] work safety regulations, etc). Whether we are spending money on healthcare services or moving towards vaccines or treatments that may be more efficient solutions, the debate will continue as to the fair market value of technological solutions to manage or eliminate the health risk and economic impact of COVID-19.

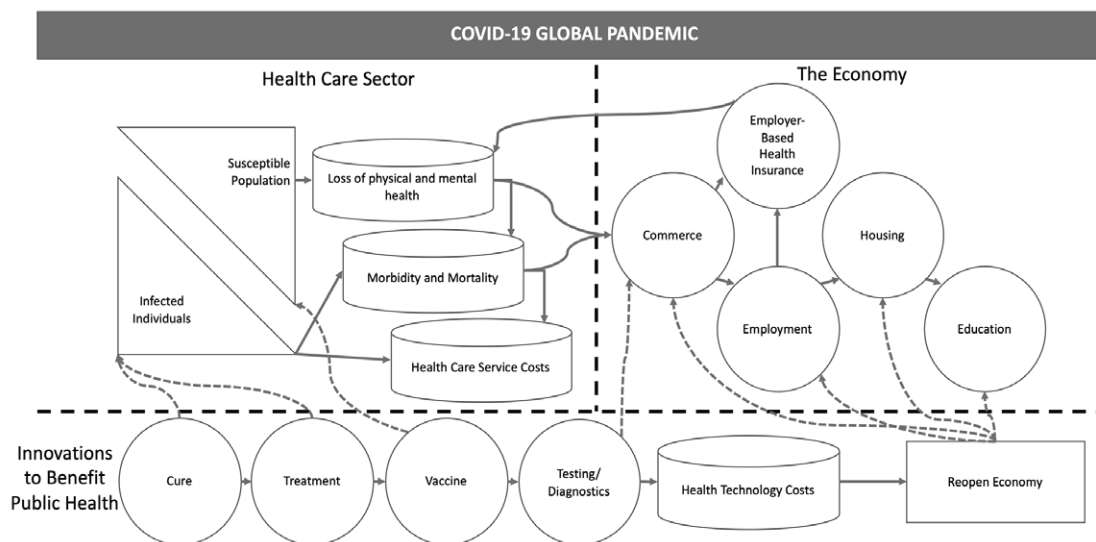
Despite healthcare services leading the United States in healthcare spending compared to testing and diagnostics, vaccines, and pharmaceutical treatments, traditional HTAs are not typically applied to healthcare services.

The effort and investment of finding a solution to COVID-19 is deserving on ethical and even moral grounds alone, since the alternative is continued loss of life in the United States and worldwide. While the success and timing of treatments and vaccine technologies coming through the pipeline is uncertain, it is certain that any technological solution for COVID-19 is a dominant strategy (ie, costs less and generates greater health benefits) compared to our only current options. Pouring unlimited dollars into ventilation and critical care for those that are sickest, keeping our economy shut down, and promoting self-isolation is not efficient. Isolation hurts the economy, education, and safe housing, not to mention the counteractive deterioration in physical and mental well-being caused by societal withdrawal and sedentariness from sheltering in place (Figure 1).

Final Thoughts

Between the many economic evaluations that have been published or are likely to come recommending different price points for COVID-19 technology, it is unclear whether cost-effectiveness analysis is the most appropriate solution to finding the price point. Any successful vaccine or effective treatment will dominate all current solutions—healthcare services and social distancing. A dominant strategy cannot provide a pathway to

Figure 1. Impact diagram of health technologies on the COVID-19 global pandemic to repair burdens on the healthcare sector and the economy.



determine price, as most price points will still be cost saving. The COVID-19 situation highlights the tensions between pricing, value, affordability, and ethics of healthcare services and technologies. Perhaps other measures of economic evaluation with which ISPOR members are familiar, including budget impact, net health benefit, and net social benefit are the alternatives we need to consider first to guide decision makers towards high-value solutions at the right price.

The COVID-19 situation highlights the tensions between pricing, value, affordability, and ethics of healthcare services and technologies.

Ultimately, traditional HTA-oriented cost-effectiveness analysis is best suited for comparing reasonably similar treatment choices within a reasonably narrow band of considerations within therapeutic areas. When applied to pandemic situations, the whole society and economy becomes part of the consideration. This is where the medical costs now include, and can even be dwarfed by, the costs of damage to the economy. Yet, the outcomes, not just years of life saved, but numbers of lives saved and impact on population growth, become unwieldy for traditional cost-effectiveness metrics. This is a very different context for valuing and pricing of technologies that can effectively address the underlying cause of the pandemic. The ISPOR community is well equipped with the methods to address the growing needs of value assessment related to COVID-19 and needs to leverage its diversity and expertise to develop a consensus for methodologies and recommendations on how to fairly value and price solutions for technology manufacturers that ensure affordability, accessibility, and innovation. •

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Demystifying ICER's Equal Value of Life Years Gained Metric

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- In this article, the authors seek to shed light on ICER's equal value of life years gained metric: why it was developed, what it represents, how it is calculated, and its impact on ICER's assessments.
- While the concept of ICER's equal value of life years gained metric is relatively straightforward, the description of how to calculate it is not very clear. To that end, the authors present 3 different methods for calculating this metric.
- In general, the authors conclude that treatments with greater life extension and where the quality of life of surviving patients is low will see the greatest potential benefit from the equal value of life years gained metric compared to the quality of life years metric.

In December 2018, the Institute for Clinical and Economic Review (ICER) introduced the equal value of life years gained (evLYG) metric and has since incorporated it in its 2020-2023 Value Assessment Framework to be a component of all their new health technology assessments (HTAs).^{1,2} This article seeks to shed light on ICER's evLYG metric: why it was developed, what it represents, how it is calculated, and its impact on ICER assessments.

Why the evLYG?

The quality-adjusted life year (QALY), which incorporates the potential of treatments to both improve quality of life and extend life, has been the preferred metric for many HTA agencies worldwide. Since it began drug evaluations in 2014, ICER has utilized the QALY as its primary outcome measure, following the United Kingdom's National Institute for Health and Care Excellence.

However, in the United States, the QALY has been viewed historically with suspicion by healthcare payers, patients, and advocacy groups. These stakeholders have presented both methodological and ethical arguments against the use of QALYs. These arguments call out the inherent subjectivity of quality-of-life estimates and thresholds and raise concerns about the potential to limit patient access to treatments. In addition, concerns have been raised that the QALY discriminates against the elderly, disabled, and terminally ill by assigning a lower

value to their lives than others. According to the National Council on Disability, "QALYs are built on a faulty premise that life with a disability is inherently worse than lives without a disability."³ This was the basis for banning the use of QALYs by Medicare in the Affordable Care Act.⁴ While ICER defended the use of QALYs in their evaluations, they also developed the evLYG metric as a supplement to the QALY in response.¹

What Is the evLYG?

The evLYG values all gains in life years at the full value of a healthy life year, such that regardless of age, disability, or illness, all life year gains are valued equally. ICER utilizes a value of 0.851 for the value of a healthy life year based on the age- and gender-adjusted utility of the healthy US population.⁵ Arguably, the name ICER chose for this outcome is a misnomer, as it implies that there is no quality-adjusted component; however, that would be an incorrect assumption, as evLYs do include improvements in quality of life. A more descriptive term would have been quality-adjusted equal value of life years. **Figure 1** summarizes the key characteristics of life years (LYs), QALYs, and evLYs.

When ICER introduced the evLY, they did not provide a clear example or set of calculations for how to incorporate the evLY metric into cost-effectiveness analyses. Accordingly, **Figure 2** attempts to illustrate the evLY concept and what it adds to the standard QALY outcome. The

Figure 1. Summary of key characteristics of outcomes.

	LY	QALY	evLY
Length of life	Life extension is valued at its full value (ie, 1 year of life = 1)	Life extension is valued at the utility of the health state, which varies depending upon the state	Life extension is valued at the value of a healthy life (ie, utility of 0.851)
Quality of life	Improvements in quality of life are <u>not</u> included	Improvements in quality of life are included	Improvements in quality of life are included

evLY indicates equal value of life years; LY, life year; QALY, quality-adjusted life year.

Figure 2. Equal value life years.

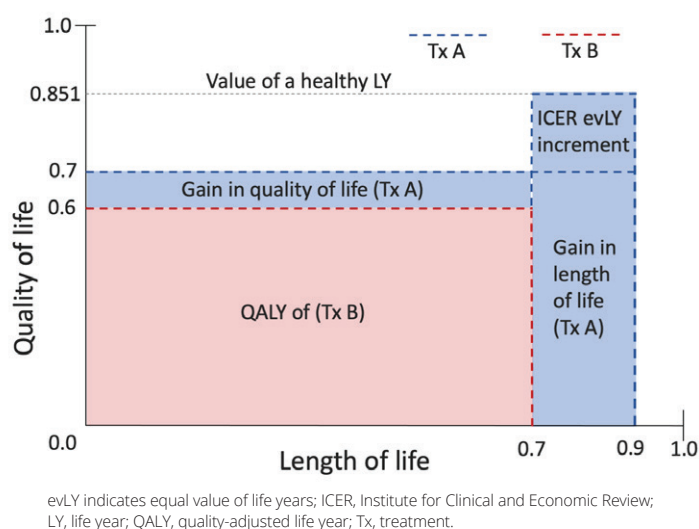


figure represents a single cycle in a cost-effectiveness analysis, where the x-axis represents life years (maximum value of 1, assuming a 1-year cycle) and the y-axis represents quality of life (maximum value of 1).

The evLY adds the increment above the gain in length of life (in the figure, this area is defined by $[0.851 - 0.7] \times [0.9 - 0.7] = 0.0302$). This increment is calculated and added to each treatment with a life year gain relative to the comparator with the lowest life years (which becomes the reference). The evLYG is the difference between the entire blue-shaded area minus the red-shaded area in **Figure 2**.

How Is the evLY Calculated?

ICER provides a stepwise description of their method to calculate evLYs in Appendix E of their recent evidence reports. Unfortunately, the steps are not very clear. In particular, step 3 is confusingly worded and contains an error in which the average quality of life is described as $LYs \div QALYs$ when it is correctly calculated as $QALYs \div LYs$. Additionally, the method that ICER describes is only one possible method for calculating evLYs.

Figure 3 shows 3 possible methods to calculate the blue shaded area (evLYs) using 2 rectangular figures, which all yield the same result. **Figure 4** shows the formulas for how to calculate these areas in a spreadsheet using each of the 3 methods that we developed. These formulas can be utilized to calculate evLYs for each cycle in a cost-effectiveness analysis.^a The values are summed to obtain the cumulative values and discounting may be applied just as for LYs and QALYs.

Note that the evLY for the treatment with the lowest LYs will equal the QALYs for that treatment, with the exception where the LYs for a treatment are not consistently the lowest across all cycles and in microsimulations due to individual patient variation. evLYs will always be lower than LYs and generally higher than QALYs, with the exception where a treatment that extends life reduces quality of life by an amount that exceeds the evLY increment. Utilizing health state utilities greater than ICER's 0.851 healthy utility value will result in the application of an evLY decrement; however, a higher value for a healthy life could be utilized.^b

Figure 3. Methods for calculating evLYs.

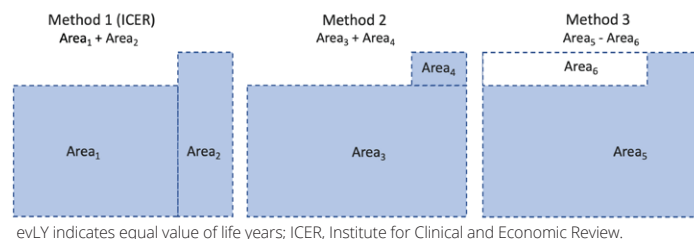


Figure 4. Calculating evLYs.

Treatment A Outputs		Treatment B Outputs	
LY_A	0.9	LY_B	0.7
QALY_A	0.63	QALY B	0.42
evLY Calculations			
Tx A – Method 1	= QALY_A/LY_A*LY_B+0.851*(LY_A-LY_B) = 0.6602		
Tx A – Method 2	= QALY_A+(0.851-QALY_A/LY_A)*(LY_A-LY_B) = 0.6602		
Tx A – Method 3	= 0.851*LY_A-((0.851-QALY_A/LY_A)*LY_B) = 0.6602		
Tx B	= QALY_B = 0.42		
evLYG Calculation			
evLYG	= evLY(Tx A)-evLY(Tx B) = 0.6602-0.42 = 0.2402		

evLYG indicates equal value of life years gained; evLY, equal value of life years; LY, life year; QALY, quality-adjusted life year; Tx, treatment.

What Is the Impact of evLYG on ICER's Assessments?

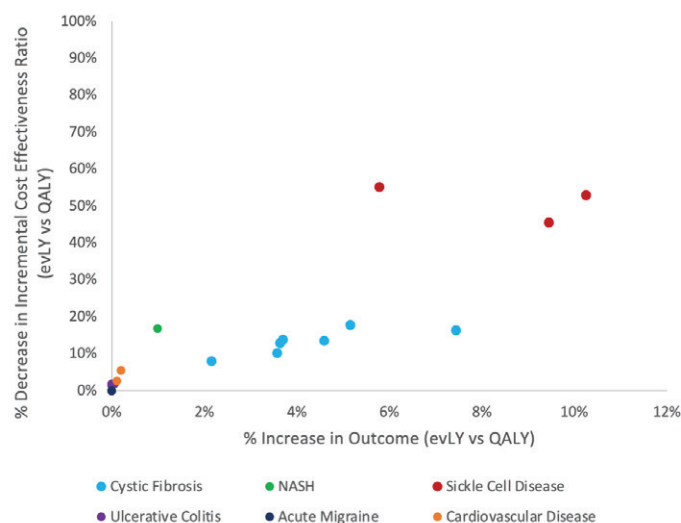
As of July 2020, ICER's evLYG metric has been used as an outcome measure in 6 assessments (2 completed and 4 in process). ICER reports evLYs in addition to LYs, QALYs, and total costs in the disaggregated results. Incremental cost-effectiveness ratios for evLYs are also included, in addition to those for LYs and QALYs. Since evLYs result in larger values than QALYs for life-extending treatments and since the evLYs for comparators with lower LYs yield the same evLY values as QALYs, this results in larger incremental differences and consequently lower incremental cost-effectiveness ratios for evLYs than for QALYs. **Figure 5** shows the impact of evLYs on these 6 assessments. Points at or near the origin reflect no essential difference between the 2 metrics. Points to the northeast represent higher evLYs and lower cost-effectiveness ratios. The degree that cost-effectiveness ratios improve (decrease) depends on the percent increase in QALYs and the relative QALY differences between the individual comparators.

In 3 assessments (nonalcoholic steatohepatitis, cystic fibrosis, and sickle cell disease), evLYs were greater than QALYs, while in the other 3 assessments, there were virtually no differences in the outcomes. Despite reductions in the incremental cost-effectiveness ratios as large as 50% for sickle cell disease, these differences did not materially affect any assessments, as the QALY-based incremental cost-effectiveness ratios were sufficiently high, such that even the greatly reduced evLY incremental cost-effectiveness ratios were still well above the

^a Note that treatment B is the treatment with lower life years and is therefore the reference for this evLY analysis.

^b Note that ICER used an alternative value of 0.92 in the cystic fibrosis assessment for this reason. However, this raises the question of whether the evLYs are then underestimated in analyses in which a value of 0.851 was used, since the purpose of evLY is to ensure that all gains in life years are valued equally; however, ICER's deviation from this practice for cystic fibrosis violates this principle.

Figure 5. evLYs in recent ICER assessments.



evLY indicates equal value of life years; ICER, Institute for Clinical and Economic Research; NASH, nonalcoholic steatohepatitis; QALY, quality-adjusted life year.

thresholds. Across all 6 assessments, the average increase from QALYs to evLYs was 2.2% (range: 0.0%–10.3%) and the average decrease in the evLY incremental cost-effectiveness ratios compared to the QALY incremental cost-effectiveness ratios was 11.0% (range: 0.0%–55.3%). Acute migraine yielded no difference, as treatments were assumed not to extend life.

In general, treatments with greater life extension and where the quality of life of surviving patients is low will see the greatest potential benefit from the evLY metric compared to the QALY

metric. This would potentially include certain treatments for cancer (particularly those affecting younger patients) and gene therapies for debilitating, deadly diseases, while diseases where treatments only, or primarily, improve quality of life (eg, migraine, depression among cancer patients) will see minimal or no benefit. While it is still too early to tell what the full impact of evLYs will be on ICER's assessments, it appears that the impact may be attenuated by limited life year gains and incremental cost-effectiveness ratios that are already well above (or potentially below) ICER's thresholds. The real test case will be how ICER handles an assessment when the evLY makes a substantive difference compared to the QALY. •

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Value Assessment That Puts Patients at the Forefront

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- The authors take an in-depth look at living with a life-changing disease, and how the treatments of those diseases focus too narrowly on clinical outcomes.
- More needs to be done to hear the patient voice to determine what matters most to patients.
- Several new patient-centered approaches to value assessment that will help reduce the current overabundance of low-value care are highlighted.

Healthcare decisions regarding treatment options and plan coverage need to be well-informed—by both clinical endpoints and nonclinical patient experience data—as these decisions have a wide-ranging impact not only on patients and their families, but the entirety of our healthcare system. Unfortunately, there are large gaps in evidence of the effectiveness and value of healthcare that is delivered to patients around the country. This is in part because experiences and outcomes that matter to patients are often excluded from data collection processes intended to help inform the value of health services and interventions. This disproportionate focus on clinical outcomes in health technology assessments can lead to highly problematic and unintentional consequences.

Assessments meant to determine the value of such treatments could be missing crucial elements that define what it is like to live with a life-changing disease. For example, in the cancer treatment community, the measurement of outcomes such as overall survival, time spent in the hospital, and other clinical endpoints are favored over those that comprehensively measure patient quality of life—if quality of life, or patient experience measures are even captured adequately or at all. As a result, assessments meant to determine the value of such treatments could be missing crucial elements that define what it is like to live with a life-changing disease.

used in health technology assessments, was used in making healthcare decisions. Only one-quarter of patients surveyed by researchers believed that the QALY was a good way to measure value in healthcare and many expressed concerns about how it would be used by payers, policy makers, and other decision makers in determining access to treatment.¹

Hearing the Patient's Voice

Encouragingly, policy makers and the value assessment community are beginning to recognize the necessity of the patient voice and why it is important to measure outcomes that matter to patients (ie, patient-centered outcomes) and ensure they are included in determinations of value. In June 2020, the US Food and Drug Administration (FDA) announced a pilot program to communicate patient-reported outcomes from cancer clinical trials to complement existing labeling and patient information about cancer treatments.² This initiative, [Project Patient Voice](#), is an important first step towards stimulating a broader conversation about value within the chronic disease community.³ Other projects such as the Cancer Support Community's [VOICE \(Valued Outcomes in the Cancer Experience\)](#) tool are designed to measure patient priorities and understand discrepancies between what matters most to patients and what patients believe they can control.⁴

On the academic side, researchers, with the support of the PhRMA Foundation,

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Further, traditional assessments might be using measures that are not well understood by patients. A recent cross-sectional study of cancer patients and survivors found limited awareness and minimal understanding among the patient community about how quality-adjusted life years (QALY), a common measure

are developing and advancing methods of value assessment in healthcare and are beginning to broaden the view of value across the system to support the identification and removal of low-value care. From this research, exciting new approaches are emerging to generate evidence that informs value-based

decision making and tackles different challenges in healthcare delivery.

Including Novel Value Elements in Economic Evaluations

Conventional value assessment models often fail to successfully engage patients and fully capture their unique perspectives during healthcare value discussions. To address the shortcomings of traditional value assessment models, the [Patient-Driven Values in Healthcare Evaluation](#) (PAVE), a partnership between the University of Maryland's School of Pharmacy and the National Health Council, has been working to develop more patient-centered approaches to value assessment by engaging directly with patients to understand and quantify the value elements that matter most to them.^{5,6} Their most recent study engaged patient stakeholders from diverse medical backgrounds in an iterative process to develop a core set of value elements that can be incorporated into economic evaluations of healthcare interventions. Notably, approximately 75% of the value elements researchers identified were generally not used in existing value frameworks.⁷

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PAVE's patient-driven approach to value assessment can be seen through their recent partnership with the COPD Foundation, a leading patient-focused organization that provides a voice to the concerns and needs of patients with chronic obstructive pulmonary disease (COPD). PAVE researchers are working hand-in-hand to identify outcomes important to patients diagnosed with COPD and incorporate these novel value elements into economic evaluations in a way that can be quantified.⁸ PAVE is also partnering with the Asthma and Allergy Foundation to identify outcomes that matter to families of children with severe allergies and is working to ensure that patient advocacy organizations are aware of the tools being developed to empower patients to amplify their voices in value assessment discussions.

Moving Past Conventional Cost-Effectiveness Methods

The [Center for Pharmaceutical Value](#) (pValue), established at the University of Colorado's Anschutz Medical Campus, aims to apply and test novel methods for value assessment that incorporate multicriteria decision analysis (MCDA) to inform coverage decisions in the United States.

MCDA, which has been used in other sectors outside of healthcare for many years, offers a structured and transparent method to account for all criteria important to a decision. With its ability to clearly view evidence involved in the decision process, MCDA can help identify and address evidence gaps, which may be particularly relevant in the rare and ultra-rare disease space where researchers often encounter sparse evidence.⁹

pValue's research aims include the development of a patient-centered outcomes inventory table to bring structure and

importance to patient-centered outcomes not incorporated in traditional value assessment using rare disease as the initial case examples. pValue also aims to assess stakeholder perception of value based through multistakeholder engagement efforts. The flexibility associated with using MCDA alongside traditional methods for value assessment, such as the ability to strategically select and weigh inputs that matter most to stakeholders, will support those making coverage decisions to do so based on evidence relevant to their respective member populations.

Enhancing Cost-Effectiveness Methods

Recognizing that common value tools may not fully capture patient and societal well-being, the [Center for Enhanced Value Assessment](#) (CEVA) at Tufts Medical Center expands upon traditional measures of value by exploring the integration of nontraditional elements in value assessment. These include patient-centered factors such as the value of hope, family spillovers, and medication adherence. Other factors such as the risks and uncertainties associated with treatment, the financial burden on patients, the impact of the treatment on worker productivity, scientific spillovers, and equity will also be explored.

CEVA researchers plan to engage multiple stakeholders—patients, health insurers, and therapeutic area leaders—to characterize these nonstandard elements and present this information to stakeholders, alongside standard value elements and cost-effectiveness information, in the form of case studies.¹⁰ CEVA's output from these case studies could inform coverage and reimbursement decisions by payers that better align and meet the needs of their respective member populations.

Reducing Low-Value Care

A substantial amount of the US healthcare budget is spent on services and procedures deemed “low value” and medically unnecessary. Eliminating spending on care that offers little-to-no value to patients would not only facilitate the shift towards a value-driven health system but would also result in immediate and substantial system savings to facilitate the reallocation of resources towards services that provide high value to patients. As such, it is important to focus on how much and how well we spend budgets across the entire spectrum of care delivery.

This is the philosophy advocated by the [Research Consortium for Healthcare Value Assessment](#), or Value Consortium for short, which has brought together healthcare researchers to collaborate, share findings, and develop research strategies that would address inefficiencies in healthcare. The Value Consortium focuses on identifying low-value clinical services (ie, care that offers little-to-no value to patients) and tracking the use of and spending on such services. Their objective is to arm employers, providers, health systems, and state agencies with data and tools to understand how much of their spending is allocated towards low-value care and how wasteful spending can be reduced.¹¹ The absence of readily available data for payers, such as state agencies or employers, to understand their spending on low-value care is a challenge the Value Consortium aims to tackle. Value Consortium researchers have conducted major analyses of private payer claims data to identify the prevalence and utilization of 20 low-value services and have also developed a publicly available [online tool](#) that stakeholders can use to

monitor and track low-value care services in their respective states.^{12,13} The Value Consortium has also announced a new project that will begin to explore how healthcare resources can be used more wisely in the aftermath of COVID-19 in order to help hospitals and other providers cut waste and support a more robust, evidence-based understanding of value in healthcare.¹⁴

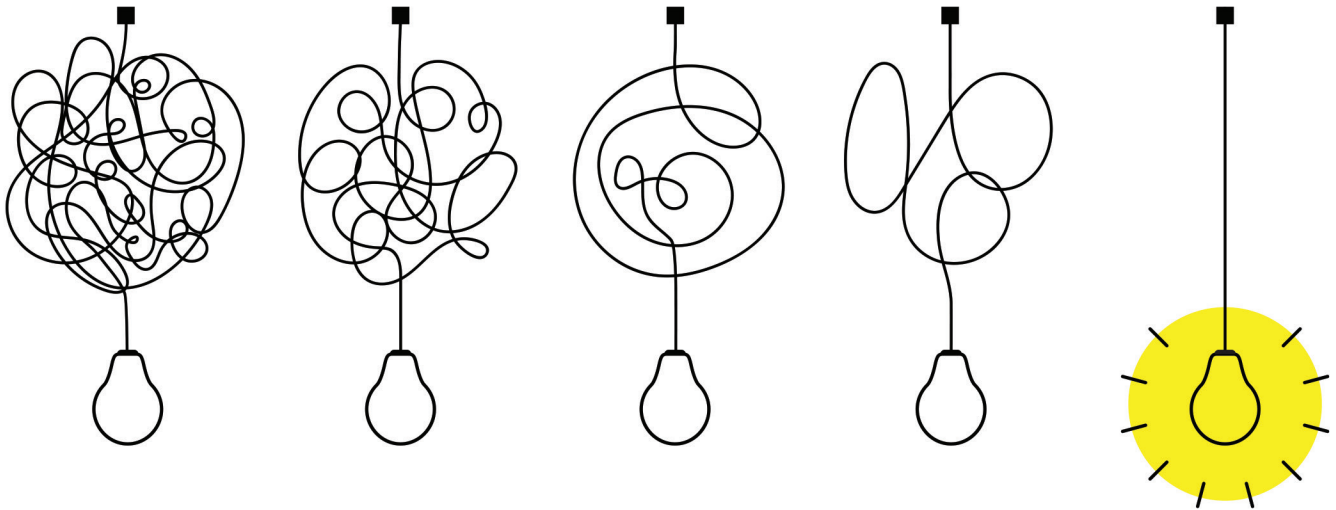
The flexibility associated with using MCDA alongside traditional methods for value assessment... will support those making coverage decisions to do so based on evidence relevant to their respective member populations.

Looking Ahead

The movement within the scientific research communities and the federal government to include the patient voice in healthcare decision making is gaining momentum. These initiatives are innovative approaches that move beyond the status quo of healthcare value measurement and assessment. The shift towards a value-driven health system requires transparent approaches that keep the patient front and center and will ensure payers make informed coverage decisions that reflect the unique characteristics of the members they represent. In doing so, these decisions will have a more sustained, positive impact on our healthcare system's budgetary strains. Beyond their innovative efforts, these research groups are forging a path to the end game in healthcare: a healthy patient population that receives the highest quality of care and delivers the most valuable outcomes. ■

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