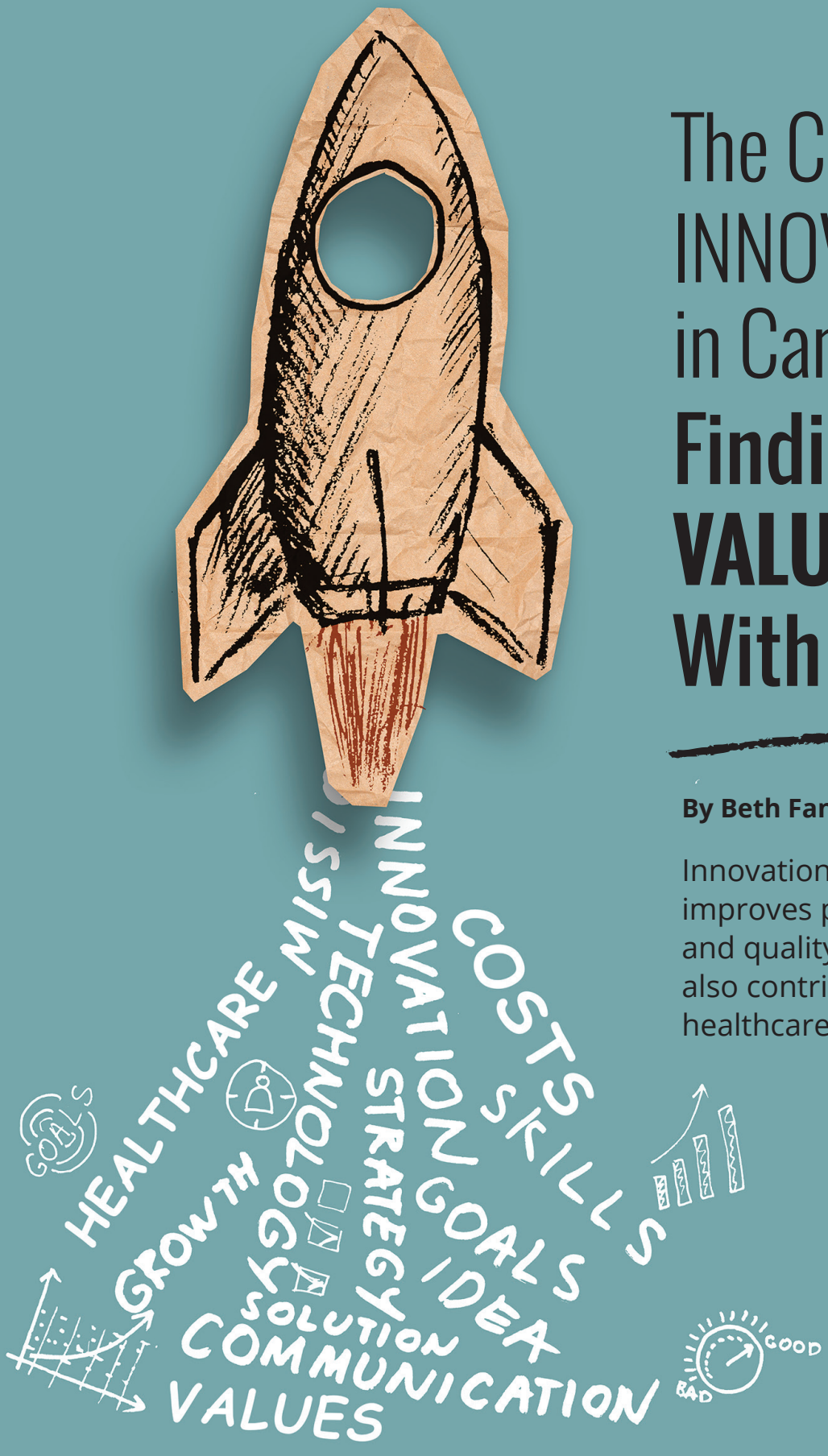

The Cost of INNOVATION in Cancer Care: Finding Our VALUES With HEOR

By Beth Fand Incollingo

Innovation in cancer care improves patients' longevity and quality of life, but it also contributes to rising healthcare costs.

A glance at oncology spending during a recent 6-year period provides a clear sense of that trend, which is also driven by the needs of a growing and aging global population coupled with fragmented access to cancer care. In 2016, worldwide spending for oncology—converted into US dollars—totaled $90 billion. By 2022, that number had more than doubled to $193 billion.[1]

While the vast majority of oncology dollars go to medical services,[2] significant expenses also crop up at the drug store, where over-the-counter and prescription medications used in cancer treatment are the most lucrative category for pharmaceutical companies.[3]

In the United States and in low- and middle-income countries, those costs not only affect the national bottom line but the economic well-being of patients and their families, whose financial strain or even ruin can threaten their getting the care they need.

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>
> – Dan Ollendorf, PhD, MPH

A study conducted in the United States between 1998 and 2014 showed that 42.4% of patients surveyed 2 years after a cancer diagnosis reported having spent their life savings on treatment.[4] On average, patients spent more than $92,000. That's a dangerous trend, as patients who declare bankruptcy due to the costs of cancer care have an 80% higher chance of dying than those who are not financially drained.[5]

"As large financial burdens have been found to adversely affect access to care and outcomes among cancer patients, the active development of approaches to mitigate these effects among already vulnerable groups remains of key importance," the research team for the life savings study concluded.

Emerging solutions lie in health economics and outcomes research (HEOR), a field that—through evidence from economic models, clinical trials, and real-world studies—identifies interventions that can help patients receive the most cost-effective care. But how can we make sure that the benefits of HEOR reach adults with cancer across healthcare delivery systems in low- to high-income countries, informing decision making from the preventive stage through cancer screening, diagnosis, treatment, survivorship, and end of life?

It's a complex undertaking that can only succeed through collaboration between governments, health technology assessment (HTA) experts, pharmaceutical and medical device companies, academia, healthcare systems, doctors, payers, patients, and advocates.

Weighing the Value of Cancer Drugs

In high-income countries that offer universal healthcare, the billion-dollar question is how to work within a fixed budget to choose the interventions that deserve coverage—including targeted oral drugs distributed at pharmacies, chemotherapies or immunotherapies administered in clinical settings, medical devices, imaging technologies, diagnostic and screening tests, and innovations in the way services are delivered.

In England, that exercise leads to positive recommendations for about 80% of proposed interventions, while separate assessments make room in the budget by identifying approved strategies that are no longer cost-effective, said Meindert Boysen, PharmD, an independent HTA expert and former Director of Health Technology Evaluation and Deputy CEO of the National Institute for Health and Care Excellence (NICE).

When advising the UK's National Health Service about the value of cancer interventions, he said, NICE considers not only health economics and relative clinical effectiveness but also insights from stakeholders, so that decisions incorporate "equity and social justice." Thus, the organization may deem a drug with weaker evidence cost-effective if it's likely to fill an unmet need for a small population of very sick patients without causing large-scale displacement of other promising technologies.

Still, NICE's decisions can be controversial, as was its 2024 recommendation against Enhertu (trastuzumab deruxtecan), a treatment for metastatic HER2-low breast cancer that has been approved in 13 countries, and for which about 1000 patients in the United Kingdom would have been eligible.[6] Patient advocacy group Breast Cancer NOW said the decision marked a "dark day" in the United Kingdom.

There are different challenges in America, where the US Food and Drug Administration (FDA) evaluates interventions without considering prices, which are set later by pharmaceutical companies and paid for by patients and their private or public insurers.

That strategy does little to hold down the cost of treatment, which may explain why the United States lags behind Australia, Canada, and the United Kingdom in health gains per dollar spent.[7,8] In 2020, median per capita spending on cancer care in the United States was $584, the highest among 22 high-income countries.[9] Yet, America's cancer mortality rate was just below the median within that group, with 6 countries reporting more favorable outcomes.[10]

Working to rein in the costs of American cancer care is the Institute for Clinical and Economic Review (ICER), an independent, nonprofit organization that measures the value of proposed interventions compared with existing alternatives and suggests fair prices.

This small organization reviews just 12% to 15% of the drugs approved by the FDA each year, and pharmaceutical companies don't have to comply with its suggestions. Still, Chief Scientific Officer and Director of HTA Methods and Engagement Dan Ollendorf, PhD, MPH, believes ICER's work has the potential to shave dollars off the cost of cancer care.

"Patients in the United States, especially those who are privately insured, feel the impact of high list prices in their coinsurance and copayments," Ollendorf said. "The closer we can get a manufacturer's announced list price to align with our assessment of a therapy's value, the better off all stakeholders will be."

Through an 8- or 9-month evaluation process that involves multiple stakeholders, ICER suggests launch prices for drugs that are nearing regulatory approval. It also spotlights nonevidence-based price hikes made by pharmaceutical companies, like those that resulted in combined additional spending of $276 million in 2023 for targeted cancer drugs Darzalex (daratumumab, indicated for multiple myeloma) and Cabometyx (cabozantinib, indicated for advanced renal cell carcinoma, hepatocellular carcinoma, and differentiated thyroid cancer).[11]

There are signs that ICER's efforts are having an effect. An estimated 59% of US payers include ICER data in their formulary decisions,[7] and recent research suggests that therapy prices tend to be lower at launch if an ICER assessment is released before the manufacturer announces a price.[12]

Establishing Value Thresholds

With an array of healthcare systems come divergent methods for evaluating the cost-effectiveness of cancer treatments.

ICER assesses the value of interventions according to a threshold of $100,000 to $150,000 per quality-adjusted life year (QALY) or equal-value life year (EVLY) gained. NICE also employs the QALY, but with a lower threshold of $28,471 to $42,857 per unit, which can lead to different decisions about value.[7]

A study that compared what the 2 organizations decided about 11 cancer drugs found that they agreed on the cost-effectiveness of 7 of the medications.[7]

"Most new cancer drugs were not cost-effective in either the United States…or England," the authors wrote. "Furthermore, NICE's capacity to negotiate price discounts and access schemes result(s) in much lower cost per QALY valuations and more favorable recommendations than those of ICER for similarly assessed cancer drugs."

While the QALY is a popular way to measure net health gain, there are alternative formulas designed to better incorporate quality of life and avoid bias, including the ISPOR value flower.[13] Still, striving for equity is a common goal no matter which algorithm is used.

To keep a level playing field for people with other conditions, ICER doesn't inflate its value threshold when assessing oncology interventions. Ollendorf is convinced that doesn't harm patients with cancer, though, as ICER still finds some of the highest prices in oncology care to be justified—as it did for Kymriah (tisagenlecleucel), a single-dose CAR-T cell immunotherapy whose introductory price was $475,000.[14,15]

"If a CAR-T drug turns a fatal blood cancer into a survivable one, you're adding a lot more years of life," he said.

NICE uses different rationales, Boysen said, relying on 3 thresholds for value depending on disease severity.

"They're calculated on the basis of what you might otherwise experience as a healthy person and what you're losing because of where you are in your cancer care," he said. "Then there's a fourth, even higher threshold for ultra-rare genetic diseases that are generally not cancer."

> "Neither clinical nor HEOR data are static phenomena. This is a dynamic and evolving evidence base that needs to be tracked, and with artificial intelligence, we may get even better at doing that."
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> – Meindert Boysen, PharmD

While The Netherlands factors in the lost productivity of patients who can no longer work due to their cancer, the United Kingdom does not, Boysen added, as that "might value younger people who are producing over and above people who are older and mostly consuming."

Grappling With Insufficient Evidence

A key obstacle for healthcare decision makers is that oncology treatments often receive accelerated approvals based on single-arm studies.

"Without knowing their impact on progression-free or overall survival," Ollendorf said, "there's a lot of uncertainty about the benefits these interventions are bringing."

In the United States, that often leads to insurers paying for therapies that turn out not to be beneficial. According to an analysis by Harvard University researchers, only 43% of the cancer drugs that gain accelerated FDA approval eventually demonstrate a benefit on overall survival or quality of life.[16]

ICER does an informal 1-year checkup on interventions it's reviewed, inviting manufacturers to supply additional information about effectiveness. And the FDA can rescind

a therapy's approval or indication based on the results of confirmatory trials. But according to Ollendorf, it's not unusual for the agency to keep a treatment on the market if it meets other metrics, such as improving quality of life or helping to fill an unmet medical need.

"The United States has more cancer drugs on the market than most other high-income countries," Ollendorf said, "because regulators elsewhere may have taken a more conservative view of the evidence."

> "From the moment something suspicious is found through self-examination or screening, patients need to be in a system where their path to diagnosis is clear and undisrupted."
>
> – Mimi Choon-Quinones, PhD

In response to the rise in accelerated submissions, NICE has revamped its Cancer Drugs Fund, helping create a route for the conditional approval of oncology treatments that don't meet usual standards for cost-effectiveness.[17] The fund collects real-world evidence about these drugs following their approval—typically for around 2 years, although this is not a strict limit—to assess whether they should remain in use.

"Countries like The Netherlands, Italy, and France have also looked extensively at collecting real-world evidence after accelerated approvals," Boysen said. "They recognize that neither clinical nor HEOR data are static phenomena. This is a dynamic and evolving evidence base that needs to be tracked, and with artificial intelligence, we may get even better at doing that."

Applying HEOR Principles in Low-Income Countries

Experts in high-income countries often bring HEOR-related initiatives and other medical interventions to their neighbors in low- or middle-income countries as a means of helping people affected by cancer while supporting a stable world economy. Mimi Choon-Quinones, an attorney and healthcare researcher, orchestrates those strategies in Africa.

As founder and board chair of Partners for Patients, an all-volunteer nongovernmental organization, Choon-Quinones has coauthored the Pan-African Parliament's healthcare legislation, policies, and model laws and cocreated the continent's 55-country framework to strengthen its healthcare systems.

Her efforts have hatched a range of pilot programs, from a pediatric vaccinology initiative that cures most cases of Burkitt lymphoma to a course that teaches hungry patients to grow food so they'll be strong enough to endure cancer treatment.

Eventually, Choon-Quinones expects those initiatives to make excellent HEOR use cases, as they demonstrate high value for a low investment.

Her work has highlighted the cost-effectiveness of catching cancers early, before advanced treatment is needed, a concept that rings true worldwide.

"What we've learned through all of our research, roundtables, ad boards, interviews, and surveys on the continent is that what costs the system the most money is a lack of timely diagnosis," said Choon-Quinones, who is also a senior vice president with the International Myeloma Foundation. "From the moment something suspicious is found through self-examination or screening, patients need to be in a system where their path to diagnosis is clear and undisrupted."

Breast cancer is the second-leading cause of oncologic mortality in Ghana and is especially problematic there because women are the country's primary earners, Choon-Quinones said. That's why Partners for Patients is opening 6 early detection cancer research centers in Ghana, and pharmaceutical companies are signing memoranda of understanding with the country's government to support diagnostic services, referrals, and discounted breast cancer treatments.[18]

> "Rather than waiting for companies to come up with new technologies, maybe we should specify the kind of solution we need for a disease like breast cancer and then ask them to start investigating."
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Partners for Patients has also built capacity in Ghana by training medical staff throughout the military to conduct and support oncology clinical trials, Choon-Quinones said. The organization runs a "mini medical school" that brings in physicians from high-income countries to foster medical upskilling and enhance scientific knowledge.

The Future of HEOR in Cancer Care

Looking ahead, HTA experts hope to see the introduction of interactive economic models of treatment paradigms for specific cancers, similar to the IQVIA Core Diabetes Model.[19] ICER recently developed a platform of its own, the subscription-based ICER Analytics, which contains nearly 60 economic models that users can customize to reflect their experience. Choon-Quinones believes such engines could save global healthcare systems billions of dollars.

The experts are also enthusiastic about other emerging tactics, including the following:

- Increased and earlier efforts to incorporate patient goals and values into decision making about cancer interventions.
- Joint scientific advice, a strategy that enables pharmaceutical companies to seek guidance from HTA firms and regulators about the design of their phase III trials, with the goal of generating more patient-relevant outcomes.
- New payment strategies that could help healthcare systems handle costs for expensive treatments like CAR-T therapy through the better management of money and risk over time.
- Finally, the HEOR leaders suggested some changes to the way cancer care is studied and delivered.

"Rather than waiting for companies to come up with new technologies, maybe we should specify the kind of solution we need for a disease like breast cancer and then ask them to start investigating," Boysen said.

Choon-Quinones added that instituting universal healthcare should be prioritized.

"When patients are healthy and you invest in them, national economies exponentially grow," she said. "The countries that say they have universal healthcare should take down the facade and go deeper. And the countries that don't have it should recognize that it's a great place to start, because it ultimately saves a lot of people."

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