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Innovations in Cancer Care: Capturing What Patients Value in the Calculus of Drug Costs

When Richard Nixon declared war on cancer in 1971, there was a sense the disease that still kills an estimated 600,000 Americansⁱ annually was a monolithic malady that scientists were close to understanding and conquering. Instead, research over the ensuing decades has revealed that cancer is hundreds, possibly thousands, of diseases with distinct causes and courses, prompting one prominent researcher to declare: *“The war on cancer will not be won in one dramatic battle; it will be a series of skirmishes.”*ⁱⁱ Many skirmishes—in the form of significant survival gains—already have been won, in part through earlier cancer detection, but mostly through treatment advances.ⁱⁱⁱ In recent years, the pace of innovation in cancer drugs has accelerated with the advent of a new generation of molecularly targeted therapies that dramatically increase the precision of cancer treatment.^{iv}

Forty-five years after Nixon declared war on cancer, another American presidency has sounded a clarion call—a moonshot—for a cure, signaling that cancer remains among the most dreaded diagnoses in the collective American psyche. Some have criticized the cancer moonshot because the idea of a single cure is “misleading and outdated.”^v Moreover, while the moonshot analogy may not mesh with scientific reality, it is useful in focusing public attention on what strategies are likely to prove more successful, such as continued investment in cancer prevention efforts and treatment innovations.

Already, investments in innovative drug therapies have paid tremendous dividends in terms of moving some cancers from fatal to chronic conditions, extending

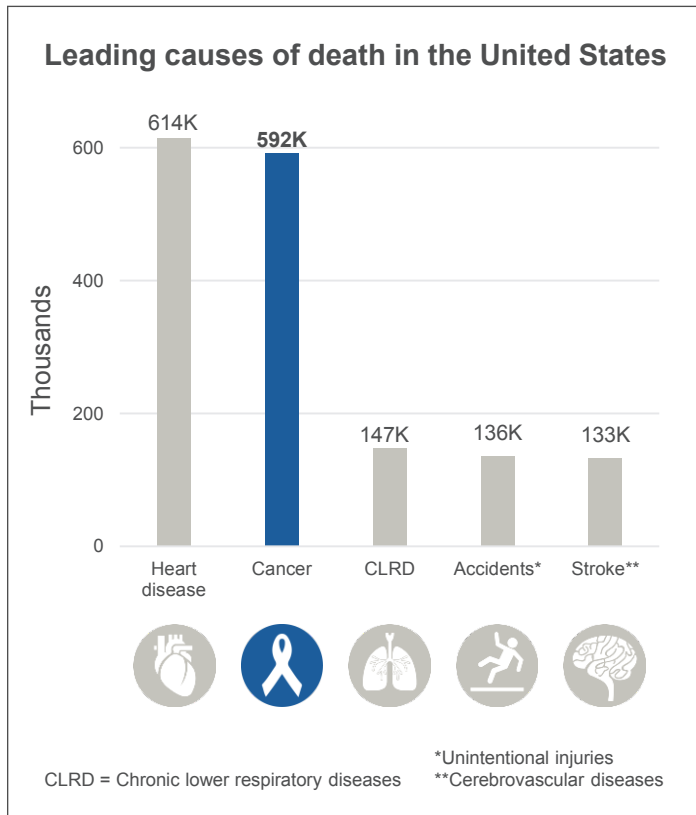
not only lives but increasing productivity. For example, Precision Health Economics (PHE) researchers estimate that the investments made from the war on cancer resulted in substantial gains in cancer survival. From 1988 to 2000, research investments resulted in 23 million additional life-years and roughly \$1.9 trillion in social value for Americans. Over the same period, roughly \$393 billion in costs to the healthcare system were incurred, suggesting that patients derived more than 80% of the total benefit.^{vi} Similarly, other PHE research comparing U.S. and European spending on cancer care found that U.S. cancer patients enjoyed greater survival gains than their European counterparts, and that these gains outweighed the higher cost growth seen in the U.S. The additional survival gains for U.S. patients net of their additional spending generated an estimated \$598 billion of additional value for U.S. patients diagnosed with cancer between 1983 and 1999 relative to European patients.^{vii}

Key Takeaways

- Gains in cancer survival over the last few decades have resulted in millions of additional life-years and trillions in social value for Americans.
- The U.S. has experienced greater health outcomes in cancer compared to those experienced in the EU, which has exceeded the additional costs of spending.
- Conventional health technology assessments fail to capture the full and true value of innovative cancer drugs to both patients and society.
- Healthy consumers value and are willing to pay more for generous policies that cover high-cost cancer treatments.
- Policymakers need to incorporate what patients value most in cancer treatment into their technology assessments and debates about drug pricing.

According to the American Cancer Society, as of January 2014, about 14.5 million Americans with a history of cancer were alive. In addition, almost 1.7 million new cancer cases are expected to be diagnosed in 2016. Cancer is the No. 2 killer of Americans—only heart disease kills more—accounting for almost one in four deaths each year (Figure 1). Every day, about 1,630 people in the United States die from cancer.^{viii}

Figure 1: 2016 U.S. Cancer Statistics 2016

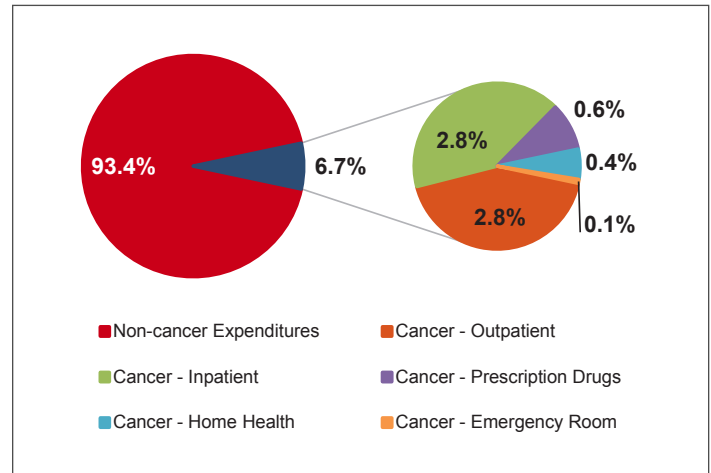


Note: Data provided for 2014 U.S. population. Cause of death based on the ICD-10 codes taken from death certificates.

Source: National Center for Health Statistics. Health, United States, 2015: With Special Feature on Racial and Ethnic Health Disparities. Hyattsville, MD; 2016.

According to the Agency for Healthcare Research and Quality (AHRQ), total spending on direct medical care for the U.S. civilian noninstitutionalized population in 2012 was \$1.35 trillion, with spending on cancer care accounting for \$87.5 billion, or about 6.7 percent of total spending (see Figure 2).^{ix} The AHRQ analysis also found that one in 20 Americans (5%) has an expense each year for cancer care. In addition, of every dollar spent on cancer care, about 9.3 cents pays for prescription drugs, 41.3 cents goes to inpatient hospital care, 42.8 cents pays for physician and other outpatient care, and the remainder goes to home health and emergency department visits.

Figure 2: Cancer spending as a share of total U.S. health care spending, 2012



Source: Cohen, SB. The Concentration of Health Care Expenditures and Related Expenses for Costly Medical Conditions, 2012, Statistical Brief No. 455, Agency for Healthcare Research and Quality, Rockville, MD; October 2014.

Compared to other industrialized nations, the United States spends more on health care, both overall and for cancer specifically. While many experts contend that higher U.S. spending delivers little in terms of better health outcomes, growing evidence suggests that higher U.S. spending on cancer care is an exception.^x As documented by PHE researchers in a study of 16 countries, those spending more on cancer care, including the U.S., had consistently lower cancer mortality between 1995 and 2007. During the same period, countries increasing spending the most showed the greatest declines in cancer-related mortality.^{xi}

Move to Define Value in U.S. Cancer Care

Despite significant gains in U.S. cancer survival rates,^{xii} the cost of cancer care, especially new drug prices,^{xiii} has become a flashpoint in the debate about appropriate health care spending. The concern is straightforward: if general health care spending and cancer-specific spending continue to rise rapidly, care will become less affordable for more and more Americans. As a result, there has been a broad move in recent years to define and assess the value of health care services in terms of better care for individual patients, improved population health, and smarter government spending.

In 2015, two notable attempts were launched to initiate discussion of what constitutes value in cancer care. In the first, the American Society of Clinical Oncology (ASCO) issued a Conceptual Framework to Assess the Value of Cancer Treatment Options^{xiv} “... to

provide a standardized approach to assist physicians and patients in assessing the value of a new drug treatment for cancer as compared with one or several prevailing standards of care.” Referencing the Institute of Medicine’s (IOM’s) six elements of quality health care delivery: safety, effectiveness, patient centeredness, timeliness, efficiency, and equity, the ASCO value framework focuses on three of the six IOM elements:

- **Clinical benefit** (efficacy), encompassing one or all of the following: survival gains, slower disease progression, and improved symptom control resulting in improved quality of life.
- **Toxicity** (safety), referring to treatment side effects that diminish quality of life or a patient’s ability to complete the usual activities of daily living.
- **Cost** (efficiency), including expenses incurred by patients, payers, and society.

The framework notes that the other three IOM elements—patient centeredness, timeliness, and equity—are “essential elements of quality care” but are not as easily measured or typically reported as outcomes in clinical trials.

The second effort to quantify the value of new cancer drugs is Memorial Sloan Kettering Cancer Center’s DrugAbacus, an interactive web-based tool that incorporates measures of cost, toxicity, efficacy, novelty, research and development costs, rarity of the disease, and population health burden.^{xv} Users can adjust the six measures to generate a price for each drug and then compare that price to the actual price of 54 cancer drugs introduced since 2001. Similar to the ASCO framework, the DrugAbacus does not incorporate clear measures of what matters most to patients in cancer treatments. Unlike the ASCO framework, DrugAbacus imposes an ad hoc weighting scheme that attempts to quantify how performance on each of the six measures ought to move the price.

Historically, the so-called gold standard in judging the effectiveness of innovative cancer therapies has been overall survival (OS), but researchers increasingly are questioning whether OS is the most appropriate clinical endpoint given the sequential treatment of many cancer patients and long follow-up period and costs of clinical trials using OS as an endpoint. Instead, growing evidence, including research from PHE, indicates that progression-free survival may be a preferable endpoint

in some contexts.^{xvi} While not perfectly correlated with OS, PFS can be collected much more rapidly. This speed advantage may be quite valuable when severely ill patients are waiting for information about an experimental therapy. In a number of important cases, including those with high-unmet clinical needs, the benefits of greater speed outweigh the advantages of perfect accuracy.

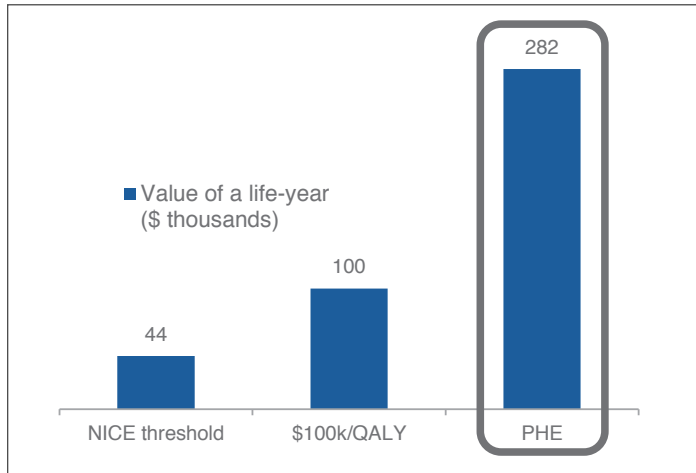
Global Approaches to Value

Many industrialized countries, notably the United Kingdom (UK), Canada, and Australia, rely on formal health technology appraisals, typically based on cost-effectiveness analysis, to assess the value of new therapies. Two metrics drive current cost-effectiveness analysis: quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs). A QALY measures disease burden in terms of both quantity and quality of life lived, while an ICER is the ratio between the difference in cost and difference in benefit of two or more medical interventions. QALYs often are used to quantify the benefit of an intervention when calculating an ICER, which is typically expressed as the incremental cost per QALY. Until recently, there has been little consideration in health technology appraisals of what patients value in cancer treatment other than extended life based on median overall survival and toxicity of side effects.

Growing recognition that QALYs and ICERs are relatively blunt tools to assess value to patients has prompted other countries to begin exploring how to identify and incorporate dimensions of value beyond cost and survival gains into technology assessments. For example, in UK, Sir Ian Kennedy was commissioned by the National Institute for Health and Clinical Excellence (NICE) to recommend how NICE should incorporate the value of innovation and other benefits into technology assessments. Asked to present to the Kennedy Commission, PHE researchers outlined how innovation, disease severity, and other aspects of value could be included in technology assessments to more accurately reflect patient and societal values.^{xvii} Ultimately, the value of a life-year should be driven by the values of patients, not of payers. According to PHE research, people terminally ill with metastatic cancer place much greater value on extended survival than traditionally understood.^{xviii} In the study of 4,800 people with colorectal cancer, breast cancer, cancer of the head and neck, or lung cancer, researchers examined patients’ demand for different treatments and then estimated their willingness to pay more out of pocket for their treatment of choice. The analysis concluded that

patients valued the benefits of metastatic therapy about 25 times the average total cost—\$180,284 value annually per patient compared to \$7,321 in drug costs. Figure 3 demonstrates that patients with metastatic disease using their own money place more than twice as much value on life-extension than payers do.

Figure 3: Patients place a higher value on each life-year than many regulators and health technology assessment agencies



Source: Seabury SA, et al. Patients value metastatic cancer therapy more highly than is typically shown through traditional estimates. *Health Affairs*. 2012;31(4):691-699.

Rethinking Value in Cancer Care

Peer-reviewed research from PHE has contributed to growing evidence that conventional technology assessments fail to capture the full and true value of innovative cancer drugs to both patients and society. A full accounting of patient and social values can alter the calculus of drug costs, ensuring that new technologies are not undervalued and encouraging continued innovation that leads to better care for individual patients, better overall population health, and smarter spending.

What Patients Value in Cancer Care

Ongoing efforts to reform the U.S. health care system emphasize providing high-quality, affordable, and patient-centered care, defined by the IOM as: “... care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions.”^{xix} Every cancer case is unique; each patient experiences a different disease course and requires a personalized approach to his or her care. As researchers gain increased understanding of just how personal cancer is, there are few health care realms where the need for

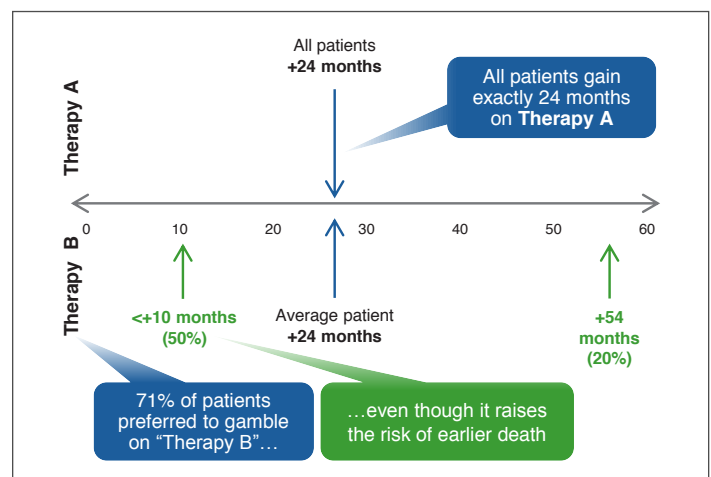
patient-centered considerations is greater than in cancer treatment.

A logical extension of the growing focus on patient-centered care is recognizing and incorporating what matters most to patients into assessments of innovative cancer drugs. Moreover, what matters can range from the value of hope in terms of extended survival to the so-called option value of living long enough to benefit from the next treatment innovation to marking an important milestone, such as the birth of a grandchild.

The Value of Hope

Assessments of the medical and economic value of cancer therapies traditionally have focused on average or median gains in patient survival, ignoring the value patients may place on therapies with a wider spread of outcomes offering potentially longer survival. As illustrated in Figure 4, PHE researchers found that more than three in four patients (77%) with melanoma, breast cancer, or other kinds of solid tumors preferred “hopeful gambles”—or the chance of getting a better than average response to treatment—instead of “safe bets” in cancer treatment.^{xx} The findings indicate that current technology assessments, often used to determine access to cancer therapies, don’t include an important source of value to patients and should either incorporate hope into the value of therapies or set a higher standard of acceptable cost-effectiveness ratios for patients in an end-of-life context.

Figure 4: 71% of patients preferred the riskier therapy, but with a chance at long-term survival



Source: Seabury SA, et al. Patients value metastatic cancer therapy more highly than is typically shown through traditional estimates. *Health Affairs*. 2012;31(4):691-699.

The Option Value of Innovation

Standard cost-effectiveness analysis measures a cancer drug's value in terms of QALYs gained at today's life expectancies, ignoring gains from the possibility that a therapy will enable a patient to survive long enough to benefit from a future breakthrough therapy.

For example, Tamoxifen, which was approved in 1992, provided option value for patients with breast cancer by slowing tumor growth. In 1998, Herceptin, which effectively treats breast cancer by blocking uncontrolled cancer cell growth, was approved. Ignoring option value implies that Tamoxifen provided 1.26 additional years of life expectancy, according to a PHE study.^{xxi} However, after adjusting for option value, the additional life expectancy provided by Tamoxifen increased to 1.57 years. Alternatively, consumers were willing to pay \$200,339 for Tamoxifen, but once option value is considered, willingness to pay increased to \$247,913. Thus, although Tamoxifen's clinical benefits were far from perfect, it provided option-value for patients who lived to see Herceptin's approval. Similarly, the introduction of tyrosine kinase inhibitors (TKIs) in 2001 to treat chronic myeloid leukemia (CML) led to substantial survival gains that enabled patients to live to see new, more effective therapies several years later.^{xxii}

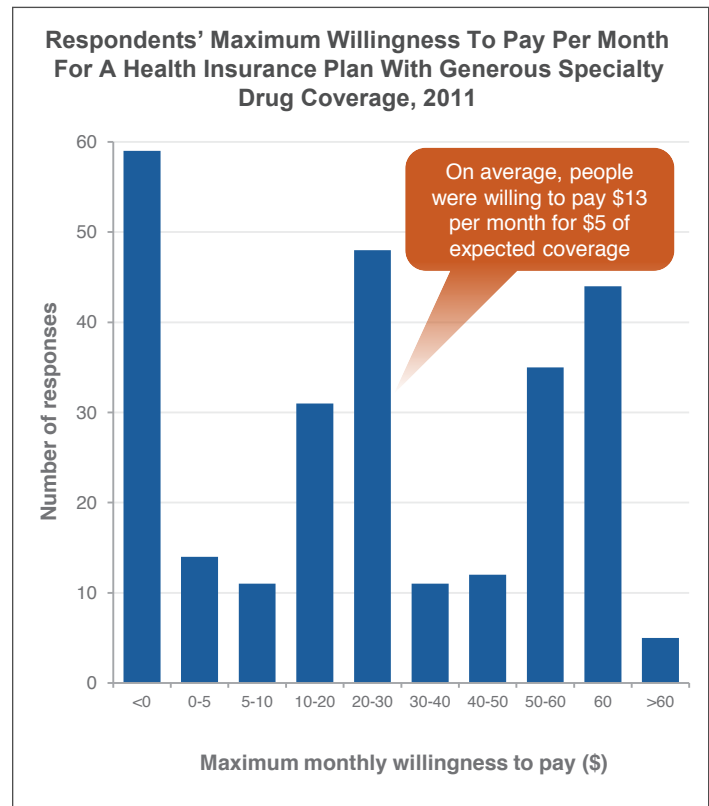
The Value of Generous Insurance

The substantial value of high-cost cancer therapy extends from cancer patients to the healthy consumers that pay the bulk of health insurance premiums that finance treatment. PHE researchers measured the value that healthy people place on more generous coverage of high-cost specialty drugs for cancer and other diseases that they may contract in the future.^{xxiii} As illustrated in Figure 5, the study found American adults were estimated to be willing to pay an extra \$12.94 on average in insurance premiums per month for generous specialty-drug coverage—in effect, \$2.58 for every dollar in out-of-pocket costs that they would expect to pay with a less generous insurance plan.

Generous coverage of cancer drugs may also partially offset spending on other health care services, PHE researchers found when they examined the effect of TKI use on non-pharmaceutical spending for patients with CML. Use of TKIs was associated with a 30 percent reduction in non-pharmaceutical spending for CML patients—\$26,406 for TKI users vs. \$38,194 for non-users^{xxiv}—and offset about 40 percent of the incremental

pharmaceutical cost of using TKI therapy. The true cost of cancer therapy, net of all savings, is thus lower than it appears at first glance.

Figure 5: Respondents' maximum willingness to pay per month for a health insurance plan with generous specialty drug coverage

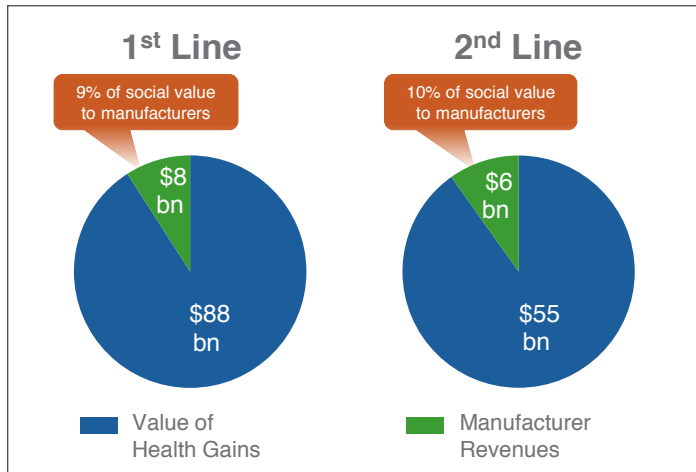


Source: Romley JA, Sanchez Y, Penrod JR, Goldman DP. Survey results show that adults are willing to pay higher insurance premiums for generous coverage of specialty drugs. *Health Affairs*. 2012;31(4):683-690.

Social Value vs. Drug Manufacturer Profits

While new cancer drugs can be extraordinarily expensive, growing evidence shows the value of survival gains from innovative cancer drugs accrues mostly to patients and society, not drug companies. For example, a PHE analysis of the cost of using TKIs to treat CML demonstrated that the social value generated was nearly 10 times greater than the cost of therapies. More specifically, first-line CML therapy using TKIs generated \$88.1 billion in social value, while earning manufacturers \$8.2 billion.^{xxv} Similarly, for second or third-line CML therapy using TKIs, manufacturers earned \$5.7 billion, compared to \$55.1 billion in value of survival gains generated for society. In other words, approximately 90 percent of value was retained by patients in the form of survival gains, while 10 percent of costs were recouped by drug companies for both first-line and second-line CML therapies (see Figure 6).

Figure 6: Patients with chronic myeloid leukemia captured about 90% of the value of innovation over the last decade



Source: Yin W, Penrod JR, Maclean JR, Lakdawalla DN, Philipson T. Value of survival gains in chronic myeloid leukemia. *Am J Manag Care.* 2012;18(11):S257-S264.

Critics often focus on the cost of innovative treatments at approval,^{xxvi} but the value of new treatments can take time to accrue as additional indications are added and more patients can benefit. In cancer, novel treatments are often initially approved for metastatic disease or treatment of small populations with high levels of unmet need, but expansion to adjuvant care settings or earlier disease stages may contribute even more benefits. In a study of docetaxel and paclitaxel, PHE researchers found that the value of a new treatment may increase over time as evidence is collected, use expands to new indications and earlier stages of disease, and more patients benefit from access.^{xxvii} PHE’s findings indicate that drug pricing and manufacturers’ profits can be quite different when viewed over time rather than as an immediate cost.

Conclusion & Implications

Health systems all over the world continue to shift towards paying for value, not just volume. The success of all these efforts hinges on our ability to accurately measure value to patients. However, a growing body of research, spearheaded by PHE researchers, indicates current technology assessments—primarily those relying on QALYs, ICERs, and OS—consistently undervalue the benefits of new cancer drugs to patients and society. The same body of research points towards new approaches for capturing the real value of such therapies.

Rising U.S. health care spending continues to pose a conundrum for policymakers. The solution lies in targeting our spending towards high-value interventions, to ensure that society gets what it pays for. From that perspective, singling out innovative drugs to treat complex diseases like cancer might do more harm than good. Pharmaceutical spending contributes modestly to total healthcare spending on cancer, and a body of evidence documents the substantial value patients place on innovative therapies. A serious discussion is needed about the relative value of spending on a range of healthcare goods and services, not just innovative pharmaceuticals.

Just as there is a move to incorporate evidence-based practice and patient-centered care to ensure the greatest return possible on investments in health care, the United States needs to consider how to incorporate what cancer patients value most into technology assessments and discussions of drug pricing. Otherwise, we run the risk of knowing the price of everything and the value of nothing.

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