Non-governmental drug assessments

Aiming for a 'grand bargain' on drug prices in the US

For decades, the pharmaceutical industry operated in the US under an unofficial social contract. In exchange for government-funded basic science and several years of exclusive market access, drug companies would price their products responsibly. In the early 1990s, Roy Vagelos, then the chairman of the world's largest drug maker, Merck & Co, exemplified this restraint by pledging to keep price increases below the country's annual level of economic inflation. The free market, loosely moderated by the good judgement of strong industry leaders like Dr Vagelos, was able to achieve success for shareholders and patients alike.

Unfortunately, the recent era of profit maximisation by both payers and manufacturers has frayed the pharmaceutical social contract, and political pressure is escalating on all sides of the US health system. Insurers blame drug makers for high launch prices and double-digit annual increases, drug makers blame insurers for placing administrative and financial barriers on patients seeking to access these treatments, and for the first time, clinicians are vocalising concerns over the dysfunctional market dynamics that hinder patient care and propel US drug prices ever higher.

Despite spending nearly twice as much per person on health care, the US leads other wealthy nations in the rate of deaths that could have been prevented by modern health care. This low-value paradox is rooted in several factors distinct to the US health system – including extensive pricing power for drug makers, decentralised reimbursement spanning a variety of public and private payers, and a culture that tends to prioritise medical advancement over cost-effectiveness. And while federal legislators have conducted public hearings to shame egregious examples of price gouging, the US remains the only industrialised nation without a governmental health technology assessment agency guiding coverage decisions and pricing for new drugs.

With the social contact no longer intact, and with the country hesitant to over-engineer a government solution to a free-market problem, the fundamental question remains: how can the US ensure it receives reasonable value for the prices it pays for drugs?

Influence without governmental authority

A little more than 10 years ago, I founded the Institute for Clinical and Economic Review (ICER) as an experiment to determine how health technology assessment could function in this uniquely American environment. My aim was to provide a fair and objective analysis of evidence as the starting point for bringing all stakeholders – patients, doctors, drug makers, insurers and others – together to help patients gain sustainable access to high value care. ICER functions outside of the US government, but more critically, outside any conflicts of interest stemming from either the pharmaceutical or insurance industries. We are an independent, non-partisan research organisation, and our drug assessments are funded entirely by non-profit foundations. Although we also evaluate medical devices, diagnostic tests, and other healthcare services, ICER is now commonly referred to as the nation's independent watchdog on drug pricing.

Even without official governmental authority, ICER's drug assessments are sharply focused on translating evidence into real-world decisions. We complete our review of each therapy near the date of its US Food and Drug Administration approval – late enough to incorporate the most robust clinical trial data available, and early enough to inform the pricing and coverage decisions that need to happen in the US shortly after approval. Through rigorous, public analyses of clinical data, we develop policy recommendations and establish each medicine's 'value-based benchmark price,' an independent reference point frequently used by both public and private payers to guide pricing negotiations and structure coverage policy. A 2016 survey by America's Health Insurance Plans found that 75% of health plans were using ICER reports regularly.

Public payers are following suit. The US Department of Veterans' Affairs, which provides federally-funded health care for more than nine million military veterans, last year announced its plans to integrate ICER reports into its formulary management and pricing negotiations. ICER assessments are similarly adopted by state-funded Medicaid programmes, which provide insurance coverage for nearly 70 million low-income individuals, children, the elderly and people with disabilities. For example, New York's Medicaid programme announced this year it would strive to negotiate supplemental rebates on drugs where the best available pricing still exceeded ICER's value-based benchmark price.

Effective incentive structures require both 'sticks' and 'carrots.' And over the past 12 months, manufacturers have begun to see ICER's evidence reviews not just as a weapon payers can use to extract additional discounts, but as an independent endorsement that can foster a mutually beneficial market for an appropriately priced medicine.

In advance of one of 2017's most anticipated drug launches, pharmaceutical companies Sanofi SA and Regeneron Pharmaceuticals Inc approached ICER with the high-minded goal of establishing a 'grand bargain' with US payers regarding their new product Dupixent, a treatment for atopic dermatitis. The manufacturers were willing to launch Dupixent with a US net price within ICER's value-based benchmark price range – more than 40% below what financial analysts had forecasted – under the assumption that a defensible price would drive payers to loosen coverage criteria so that all patients who needed this medicine would have easier access to it. It worked.

Two years earlier when these same companies had launched their injectable cholesterol medicine, Praluent, ICER's assessment suggested that the annual list price of $14,600 would need to be discounted by 45%-62% to reach common thresholds for long-term cost-effectiveness, and an 85% discount would be required to allow US payers to

afford to treat the potentially large patient population. These discounts did not occur, and payers implemented techniques to steer patients away from Praluent and toward inexpensive generic statins. In 2018, armed with new long-term outcomes data demonstrating an improved mortality benefit for Praluent, the companies approached ICER with the hope of striking a grand bargain similar to what they achieved with Dupixent in 2017. In exchange for matching ICER's updated value-based benchmark price, the drug makers are now able to pressure payers to lower the barriers to access for the sub-population of patients who experienced the greatest benefit in the clinical trial.

These win-win opportunities for patients and the health system are important public examples of the direct impact of ICER's work, as well as high-profile models for other drug makers to contemplate.

Enhancing ICER's methodology

With health technology assessment still a relatively new concept for the US, ICER continues to evolve its methods. Last November, following a nine-month public process, we finalised a modified version of our value assessment framework to use when reviewing certain treatments for serious ultra-rare diseases. The modified framework applies to therapies that, based on approved indications and planned clinical trials, will be eligible to treat no more than approximately 10,000 US patients. We have used this modified framework for our recent reviews of Luxturna, a gene therapy for inherited blindness, and Hemlibra, a treatment to prevent bleeding in certain patients with haemophilia A.

When assessing treatments for these ultra-rare diseases, ICER now provides context around potential evidence limitations – including the feasibility of conducting randomised controlled trials, validating surrogate outcomes measures, and obtaining long-term data on safety and the durability of clinical benefit. The ultra-rare disease reviews include cost-effectiveness results for a broader range of willingness-to-pay thresholds ($50,000-$500,000 per quality-adjusted life year gained), but ICER continues to calculate value-based price benchmarks using our standard range of $100,000-$150,000 per QALY. Also, if the treatment has a significant effect on broader societal costs – such as patient or caregiver productivity, education, or disability – ICER includes these costs in a separate analysis presented alongside our standard health system perspective cost-effectiveness results.

Incentivising pharmaceutical innovation while ensuring affordable access to life-improving medicines creates a natural tension in any health system, and this tension is magnified by the evidentiary and ethical challenges associated with diseases that affect very small populations. Our modified framework for ultra-rare diseases establishes a transparent process of incorporating these additional considerations, assessing the effectiveness and value of each therapy, and recommending a price that aligns with the full benefit a patient will receive. Given the pharmaceutical industry's growing focus on ultra-rare diseases, ICER's modified framework represents a major milestone toward helping US patients gain access to the therapies they need at a price they and the country can afford.

In addition to our modified framework for ultra-rare diseases, ICER continues to hone our processes. We recently formalised a data-in-confidence policy that ensures our assessments reflect the latest evidence, and we launched a pilot to increase transparency by providing manufacturers the ability to review each of the inputs and calculations included within our economic models. At the same time, we are expanding our scope to review all noteworthy new drugs, provide more frequent evidence updates on entire therapy classes, and for the first time, highlight significant price increases that have no new clinical evidence to justify them. As we take these important steps toward becoming a more influential component of the US health system, ICER remains grounded in the core characteristics that have carried us to this point: independence, a dispassionate reliance on evidence, public transparency, and a commitment to convene and understand the perspectives of all affected stakeholders.

Moving the US toward a value-based system

High drug pricing has never been the real enemy of health technology assessment. What we truly oppose is asymmetric information. There are instances when the US is receiving great value for the medicines it purchases, and there are other instances when the health system is getting ripped off. Attempting to determine which scenario is which – without an objective and credible assessment of cost-effectiveness – is nearly impossible. But that is beginning to change, as that national conversation around drug pricing slowly shifts to one about drug value. Based on recent ICER assessments, we now understand that new treatments for tardive dyskinesia may be overpriced by 85%, but that the far pricier CAR-T therapies – one-time treatments that extend the lives of people with certain forms of lymphoma and leukemia by an average of four to eight years – appear to stay within common thresholds for cost-effectiveness.

The US health system is learning the power of these assessments, and Americans are increasingly willing to discuss the nuanced ethical issues that surround drug pricing, access and value. Although some organisations in the pharmaceutical industry – and some private insurers as well – may operate without a strong sense of the social contract that historically moderated US drug pricing, I am buoyed by the value-based approach now being pursued by drug makers like Sanofi and Regeneron. If manufacturers voluntarily price their medicines to be cost-effective, as determined by an independent and fair drug assessment, US payers should reciprocate by reducing barriers to access for eligible patients. Payers would receive good value for their money, manufacturers would receive larger sales volume, and patients and clinicians would receive easier access to the innovative medicines that can make a meaningful difference to their lives. More than a good deal, it is a grand bargain.

This article was written by Steven D. Pearson, MD, MSc, founder and president of the Institute for Clinical and Economic Review in Boston, Massachusetts, US.