Paying for Pharmaceutical Value: The Problem of a One-Size-Fits-All Definition

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Executive Summary

It is a world, at least the US corner of it, in which any common understanding of drug value is confused by opposing incentives – to opacity and transparency, to looking at benefit broadly or narrowly, long-term or short-term: value, in short, to *whom*?

Consider the evolution of three species within the pharmaceutical ecosystem:

1. the drug industry, where a blossoming of breakthrough technologies, and billions from investors anxious to get in on the action, has created a flood of therapies for heretofore untreatable and sometimes virtually unknown

diseases – at often very high prices;

2. industrialized purchasers and purchasing agents, transformed by massive consolidation and the inexorable push to risk-sharing economics, all trying to figure out how to drive efficiency and increased value in an environment riddled with conflicting policy initiatives from the Federal and state governments;
3. patients, who are absorbing an ever-increasing share of the health care bill, either directly through cost sharing or subtracted from paychecks as higher premiums.

The industry has plenty of ways to define value. Thousands of academic and corporate health economists busily grind out cost-effectiveness analyses. CMS has designated five "compendia" as guides for reimbursable value, despite bizarrely opaque decision-making behind the compendias' choices. However, the best-known value definer is the Institute for Clinical and Economic Review (ICER), which, independent and not-for-profit, has done more than perhaps any other group to put drug value into the headlines.

ICER's analyses have many supporters and many detractors. But in spite of a formally inclusive process – public meetings and votes with clinical, payer, and patient participants – ICER's analyses, like virtually all others, put a one-size-fits-all value snapshot on a diverse, dynamic market. Or maybe *two* sizes fit all – since ICER delivers two assessments, one based on "value" and one on budget impact. But in either case, the analysis is based on an average.

In fairness, the task is not easy. For example: an anti-cholesterol PCSK9i drug is probably more valuable for a 50-year-old man with modestly high LDL-c and one previous heart attack than it is for a younger woman with perhaps even higher LDL but no previous cardiac event. He's more likely to have a near-term heart attack than she is – something both he and the insurer who pays for him would like to avoid. Likewise, as more data comes out, about both the drug and the competitors, the value of the drug changes. Indeed, as the health care system evolves – say, to a longer coverage period for beneficiaries, to covering or not covering pre-existing conditions – the weight placed on each input to the value equation will change.

And there is a second problem: if value analyses are going to be used, like clinical trials, to define which drugs patients are going to get, then arguably they should be subject to at least similarly rigorous review – a process for defining the certainty of conclusions. They are not – and given the cost of that review (for example, a whole FDA setup for cost-effectiveness), they are unlikely ever to be.

One solution is to admit the basic problem: no single valuation works. Instead, what's required is a multi-dimensional value assessment tool, or more likely set of tools, that reflects the attributes of value important to different stakeholders and the different weightings they may put on those attributes. Its logic and calculations would have to be transparent. It would have to be continually updated to match the changes in evidence. And it would require the willing participation of payers and patients (or pre-patient beneficiaries), who are now only half-heartedly involved (the latter two especially because they have no control over the system which imposes a price on them).

The US economy is all about consumer choice. But choice, particularly in health care, is expensive – mitigating against the kind of volume purchasing which lowers costs. To help people decide what they need – not what they are told they may have at a specific price – requires a different, customizable approach to value analysis.

The ICER Challenge

ICER has changed the conversation around value. It has inspired reams of discussion among policymakers and academics. Its analyses are the basis for a new formulary from CVS Health. On a few occasions pharmaceutical companies have based their prices around ICER recommendations – as **Regeneron** did with *Dupixent* (dupilumab), the first new therapy for atopic dermatitis.

However, ICER has not provided a complete solution, for a variety of reasons. The first has been mentioned: many pharma companies just do not believe that its methods are scientifically rigorous.

But there are three other related problems:

Their analyses present a drug at a moment in time, often before any actual real-world evidence is in. Yet decision-makers are in fact using the analyses to justify real-world reimbursement decisions.

The analyses reflect a specific view of value that shines a brighter light on certain attributes and shades others.

Finally, payers follow ICER primarily when it serves their purposes.

On the first point, most of ICER's reports analyze drugs shortly before or after FDA approval. That makes sense: people want to get an idea of a drug's value when it first appears on the market. But without real-world evidence, it is difficult to justify yes/no coverage decisions. And yet that is exactly what has been done by the new CVS formulary, which rejects any drug with an ICER-derived QALY (a statistical determination of value: quality adjusted life year) of greater than $100,000.

Second, ICER analyses reflect specific choices made by the reviewers – and thus a kind of "average" value (with a societal glaze). Take the three new anti-CGRP medicines for migraine prevention – the first new drugs for a condition that destroys quality of life for millions of people. ICER's report, as is their custom, focuses on a societal view of the economics – ultimately to a notion of affordability (will the use of the treatment increase drug expense by more than a set inflation amount). But there are two problems with migraine economics. In aggregate, they are largely hidden and in particular are different for different people. In an admittedly relatively old article in *Value Health*, Elisabeth Hazard and colleagues estimated that as much as 70% of the economic costs of the disease are indirect or related to productivity – in short, that there's no obvious payer writing a check for an otherwise preventable expense (as there would be, for example, with a drug that prevented a hospitalization). One can define productivity costs – coming up with an average cost for presenteeism (at work but unproductive because of the migraine) and absenteeism (missing work entirely) – but they do not make it prominently into ICER's report. And certainly it is not easy for an employer to figure this out.

Still, estimates of the impact are not unavailable; the costs they reveal are hardly negligible; and excluding them dramatically changes the value-for-money equation. For example, Richard Lipton of the **Albert Einstein College of Medicine** and colleagues estimate that excluding productivity costs cuts the value-based price of Novartis's *Aimovig* (erenumab) by 16%. Likewise, in their study of Aimovig's cost-effectiveness, Michael Sussman of **Boston Health Economics** and a group of colleagues conclude that the drug used for preventing episodic migraine likely offers less value for money unless the calculation includes productivity costs.

Meanwhile, the costs are different for different people and different employers. A migraine drug that keeps a

lawyer at the office, generating hourly fees, could be worth far more to her payer-employer than it would be to the Medicare plan for keeping her mother out of bed – though in fact the drug might be worth the same to both women, crippled by pain.

And finally, ICER's reviews – the closest the US has come to independent drug valuation – have, at best, baby teeth. Payers tend to follow ICER recommendations only when they accord with their economic incentives. And because payers participate in ICER's reviews at best tepidly, they have no real commitment to them. They certainly do not want to give up any influence they have to a third-party pricing agent – particularly since payers, patients and pharmaceutical companies will rarely see eye-to-eye on payment terms.

Step One To A Solution

A first step to solving the challenges of defining value for multiple stakeholders, and getting them to believe in and use it, is to admit the problem. Second, we need to fund and create a flexible, multi-dimensional value system, or set of systems (often called multi-criteria decision analysis, or MCDA, tools) that can be modified for the intended stakeholder and whose assessments are updated regularly. Such tools exist, albeit in somewhat simplified form – for example, the *Drug Abacus* from **Memorial Sloan Kettering** and **Real Endpoints**, and the *RxScorecard*, also from Real Endpoints. The University of Colorado has just created an entire program around the idea, its Pharmaceutical Value (PValue) initiative.

What could improved valuation tools consider? Besides the basic safety, efficacy, price and cost-offset elements, they should include metrics around strength of evidence (for example, whether a trial was conducted against an active comparator or placebo), patient-centered evidence (including patient-reported outcomes), quality of life, productivity and out-of-pocket costs for transportation and accommodation, not to mention the economic impact on caregivers.

Darius Lakdawalla at the Schaeffer Center for Health Policy and Economics at the **University of Southern California** and a group of colleagues go further, arguing for including the value, among other elements, of reducing uncertainty, fear of contagion, the cost of physical and financial risk protection, severity of disease and the increase in hope and scientific spillovers. Payers – PBMs, national insurers, regional payers, and employer coalitions – would have to be an integral part of such a broader assessment process: they need to have bought in to the evidence presented, then use the tools to transparently justify their decision-making.

The tool(s) would allow each of these value elements to be weighted differently by different stakeholders – but the weighting itself would be visible and thus so would be the underlying assumptions of that particular stakeholder about the value of each metric.

As these transparent tools become part of the assessment process, there should be two simultaneous changes in the way evidence is gathered and evaluated. First, payers would be increasingly pressured to use the systems, transparently justifying their choices for preferring one drug over another or their decisions to restrict their use. If the tools are available, and if payers have been part of the process of developing them, beneficiaries and employers (and governments, for that matter) could reasonably demand to see their evaluations.

Second, pharmaceutical companies would have to adjust their development programs to the metrics of the value-assessment system: any arguments for a quality-of-life advantage, for example, would have to be justified with trial

or real-world evidence. If they argue for straightforward access, they would likely have to show superiority not to placebo but to standard of care. In the beginning, companies might have to run such trials after approval but the FDA could begin to work with value-assessment systems early on, as part of the initial approval process and to weigh in on the inclusion, measurement and possible integration of the novel elements of value.

A more customizable and transparent value assessment system will by no means solve all problems when it comes to drug value. The fact is certain government regulations make value assessment irrelevant – in cancer for example. CMS in effect mandates coverage of oncology drugs – just so long as a drug's use makes it into one of the five privately-owned compendia (and by and large commercial plans follow suit). The rule entrenches opacity: there is virtually nothing from the compendia organizations themselves on how the drugs are chosen. And nothing about potential conflicts of interest – such as whether financial incentives influence the compendia in their choices of which drugs to include.

The result, spending on cancer drugs has ballooned. In the US spending has doubled in the last five years, according to **IQVIA**, to $50bn – significantly more than the $15bn spent on drugs for the higher-mortality problem of cardiovascular disease. All this oncology spending is very tightly focused – 80% of the total, says IQVIA, on fewer than 10,000 patients. Research dollars have followed. According to **Cello Health BioConsulting** (formerly Defined Health), oncologics make up by far the biggest share of the industry pipeline – roughly eight times the share of cardiovasculars. Many of these oncology programs are barely differentiated from each other (for example, the 45 PD-1 and PD-L1 antibodies Cello has identified in development programs). But all of these oncologics – if the current situation persists and if granted approval – are likely to be generously reimbursed. There are consequences to the disproportionate oncology spend: to compensate for spending they cannot control, pharmacy directors clamp down on spending they can, such as spending on new therapies for COPD and heart disease, diseases no less deadly than cancer.

A second problem: while a flexible value assessment system can get us closer to an agreed-upon cost for any individual user, buyers and sellers in the largely for-profit US reimbursement system will still disagree on value, around general or very specific populations. Patients will still want access to a drug that has some, but not yet all, the data required for regular reimbursement. Payers will not want to pay for this drug – expensive for them and an incentive for the manufacturer not to complete the studies in the first place (the FDA found this out in spades when it approved drugs with the recommendation that manufacturers do additional studies – which of course manufacturers by and large never did).

That is why, along with more flexible value assessment tools, we need the flexibility – now often prevented by payer infrastructure, habit and legal constraints – to create contracts between buyers and sellers that pay for value delivered, not just promised. Value-based contracts are often the necessary next step for defining value in the real world.

The first task is for all players to reach a common understanding that reducing value to a single analysis, let alone a single number, cannot reflect the reality of a diverse, constantly changing, scientifically uncertain health care world. It is equally true that the alternative we are arguing for – a toolkit for defining value differently for different stakeholders – will not solve all our problems with drug purchasing. It is absurd to think that any quantitative evaluation will perfectly resolve disputes in a world where decisions are often deeply personal. But combining a set of tailored, regularly updated value assessments with risk-sharing contracts that allows us to deal with evidentiary

uncertainty by paying for what works will get us closer to a health care system that provides the choice Americans demand aligned to the value the choices provide.