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From the Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston (M.R.R.); and the Department of Global Health Policy, University of Tokyo, Tokyo (K.S.).

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New Math on Drug Cost-Effectiveness

Peter B. Bach, M.D., M.A.P.P.

Related article, p. 1803

Nowadays, the reality of exorbitant drug pricing overshadows even the most exceptional stories of drug efficacy. It's true that we're making huge biomedical strides, yet it's also true that prices for new drugs are rising, as are prices of existing treatments.

A case in point is nivolumab, which, as Motzer et al. report in this issue of the *Journal* (pages 1803–1813), appears to extend median survival in patients with metastatic renal-cell cancer by nearly half a year. But the cost to insurers and patients of using the drug for this condition — by my estimate, around $65,000 for Medicare beneficiaries and up to twice that for commercially insured patients — can't be ignored.

The price hurts patients, limiting their access and depleting their savings. Under the current system of insurance, many patients have to pay large sums out of pocket, and research shows that when that happens, some patients will stop taking medications even if they are very effective.[1] The high costs of cancer care also drive patients into bankruptcy.

The problem is particularly acute for Medicare beneficiaries, who account for the majority of patients with cancer in the United States. For nivolumab, a drug categorized as physician-administered and thus insured under Medicare's Part B benefit, Medicare assigns 20% of the cost to the patient. Although most Medicare beneficiaries have extra insurance to cover this expense — through Medicaid, an employer-based plan, or a private-market product such as Medigap — approximately 15% do not, according to the 2011 Medicare Current Beneficiary Survey. In other words, a sizable number of Medicare patients receiving this treatment could owe about $13,000 — more than half the typical annual median income among Medicare beneficiaries, which is $24,150 (Medicare beneficiaries who lack additional coverage actually tend to have incomes below this level).

Exacerbating this problem, Medicare sets no upper limit on coinsurance under Part B (or under Part D) even though commercial plans regulated under the Affordable Care Act do have out-of-pocket maximums. Federal law prevents the maker of nivolumab (Bristol-Myers Squibb) from providing assistance to patients who cannot afford the treatment. Programs such as Genentech's for Avastin, in which beneficiaries receive the drug free once they have spent a certain amount in a calendar year, are rare.[2]

Policymakers, stymied by the rising cost of drugs, might think that an approach that relies on cost-effectiveness analyses would help the health care system deal with the high price of new treatments. After all, the United Kingdom sets standards for cost-effectiveness at about $40,000 per quality-adjusted life-year for new drugs, and overall health care spending there is a fraction of what it is in the United States.

Of course, this potential solution remains theoretical today, since Medicare cannot limit drug access on the basis of cost-effectiveness; rather, laws require Medicare to cover all cancer drugs for all uses approved by the Food and Drug Administration (FDA) or listed in recognized compendia and to pay the price the manufacturer chooses to charge. But even if Medicare could set such limits, I believe that policymakers would find limited relief from the approach.

Expensive drugs can still seem deceptively cost-effective, because of the long upward spiral we have seen in the prices of cancer treat-

ments. For example, everolimus costs about $41,000 for a course of treatment, which makes the incremental cost of nivolumab only $24,000, even though it actually costs $65,000. One need only examine the treatment histories of patients in the study by Motzer et al. to see how serious the problem of these high background costs has become. In addition to the second-line treatment that was the subject of the study, participants had already received one or two antiangiogenic therapies that can cost more than $10,000 per month, and among patients who had disease progression, many received some combination of axitinib ($11,500 per month), pazopanib ($9,000 per month), and sorafenib ($7,000 per month).

This point may seem like a finicky one, but it actually highlights a critical limitation of cost-effectiveness analysis as a tool for distinguishing the value of different treatments. Highly expensive but poorly effective treatments look good when they are marginally superior on either dimension (i.e., slightly less expensive or slightly more effective) to the treatment they are replacing. The picture can be quite different when you compare new treatments with a lower-cost alternative. Howard and colleagues illustrated that the environment that causes this paradox is worsening: the prices of new cancer drugs are increasing far faster than the benefits they offer.[3]

Even if cost-effectiveness analysis did provide a reliable way forward, there is still a budgetary problem to be considered. For some time, the rising cost of new drugs has not changed the percentage of total health care dollars devoted to drugs, since most new expensive drugs are used to treat small populations of patients and counterbalancing savings were found in replacing other brand-name drugs with far cheaper generics. Three phenomena have unsettled this equilibrium. The rate of introduction of new and expensive drugs has accelerated, with the FDA-approval rate increasing from 56% to 88% in the past 7 years.[4] Not only is the pace of conversion to generics or biosimilars (the generic version of biologic drugs) slowing, but the prices of many generic drugs are rising. And expensive drugs are now being introduced for conditions that affect millions of people rather than thousands. All this adds up to a projected 13.6% increase in total drug expenditures from last year to this year, as compared with 5% growth in overall health care spending.

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Expensive treatments for hepatitis C and elevated low-density lipoprotein cholesterol levels are both forecast, at current prices, to cost the health care system tens of billions of dollars, and around the corner are other large-market, expensive drugs for other widely prevalent conditions. So even if we set a threshold of $100,000 per life-year as a standard for a good value, drugs that treat large populations could end up eviscerating the budgets of health programs.

For this reason, the Institute for Clinical and Economic Review (ICER) incorporates the effect of a new treatment on an insurer's budget alongside estimates of cost-effectiveness when determining its value-based pricing benchmarks. Hence the organization's recent appraisal of the heart-failure drug sacubitril–valsartan (Entresto, Novartis), in which the analysis suggested that a price of $9,500 per year was appropriate on the basis of cost-effectiveness thresholds, but because the condition was highly prevalent, a price of at most $4,200 per year was determined to be affordable.[5]

Hand clapping for science is now inextricably linked to hand wringing over affordability. Drug prices are increasing more rapidly than their benefits, and the growth in spending on drugs has started to outstrip growth in other areas of health care. Addressing this problem requires realizing that cost-effectiveness assessment — a step that we are not even ready for in the United States — has limitations when one considers the price of the comparator and the impact on overall budgets.

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From the Memorial Sloan Kettering Cancer Center, New York.

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A Delicate Balance — Pharmaceutical Innovation and Access

William W. Chin, M.D.

Related article, p. 1803

As an endocrinologist, a former dean at Harvard Medical School, and a one-time head of research and clinical investigation at a biopharmaceutical company, I've seen many encouraging advances in medicine, plenty of discouraging false starts, and myriad areas where answers remain unknown. But today, as chief medical officer and executive vice president of Pharmaceutical Research and Manufacturers of America (PhRMA), I am seeing a therapeutic golden age like no other in my four-plus decades in medicine.

I believe ongoing biopharmaceutical advances hold great promise for us all, and they lie at the center of a national debate over the cost and value of health care in general and new medicines in particular. This debate demands our attention, because whereas it is essential to accelerate scientific and medical progress, it's also critical to ensure that patients have affordable access to the care they need, want, and deserve. For the sake of patients, we need to strike a delicate balance in policies that achieve both biopharmaceutical innovation and access.

The study by Motzer et al. in this issue of the *Journal* (pages 1803–1813) provides a good example of current innovation, showcasing two important drugs that offer options to patients with renal-cell carcinoma and other cancers. More important, the study reflects a broader, deeper pattern that cuts across diseases. New therapeutic approaches such as immunooncology, for example, have helped increase the 5-year survival rate across all cancers by 42% since 1975, according to the National Cancer Institute. Hepatitis C is now curable in more than 90% of treated patients, and progress in endocrinology has expanded our arsenal of weapons against diseases such as diabetes, obesity, osteoporosis, and hypertension. Motzer and colleagues highlight just 2 of the more than 500 new medications that have been approved in the United States since 2000.

Yet even with these new options for treating or curing disease, the proportion of health care spending devoted to retail prescription medications remains about the same as it was in 1960. Moreover, despite the pipeline's promise, drug spending is projected to remain at about 14 cents out of every health care dollar between 2015 and 2024, even when nonretail medications, such as those administered by physicians, are included.[1] Medications also generate benefits that cascade through our health care system, by improving patients' productivity and quality of life, extending lives, and averting more costly hospital and institutional care.

It's possible to deliver so many new medications to patients while still managing costs because the United States relies on competitive markets to set prices and encourage innovation — a system that, as I see it, is working well. After approval by the Food and Drug Administration, a new medication enters a market that is increasingly characterized by competition from other brand-name and generic drugs in the same therapeutic class. This market then does its work. Payers demand demonstration of value and drive patients to the lowest-cost options using aggressive cost-containment strategies: tiered cost sharing, prior authorization, step therapy, and incentives for prescribers to adhere to preferred clinical pathways. Drug purchasing is dominated by a few very large and sophisticated payers. By the end of 2015, the top four