

and practices of many decades. The transformation must come from within. Only physicians and provider organizations can put in place the set of interdependent steps needed to improve value because ultimately value is determined by how medicine is practiced.”⁵

The collective efforts now under way to address cancer-drug costs and benefits are preliminary but should not be undervalued. Perhaps a lesson from tennis leg-

end Arthur Ashe is apt: “Start where you are, use what you have, do what you can.”

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

From RCY Medicine, Philadelphia.

This article was published on November 18, 2015, at NEJM.org.

1. Schnipper LE, Davidson NE, Wollins DS, et al. American Society of Clinical Oncology statement: a conceptual framework to assess the value of cancer treatment options. *J Clin Oncol* 2015;33:2563-77.
2. Schnipper LE, Smith TJ, Raghavan D, et al.

American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the Top Five list for oncology. *J Clin Oncol* 2012;30:1715-24.

3. Schnipper LE, Lyman GH, Blayney DW, et al. American Society of Clinical Oncology 2013 Top Five list in oncology. *J Clin Oncol* 2013;31:4362-70.

4. Levit L, Balogh E, Nass S, Ganz PA. Delivering high-quality cancer care: charting a new course for a system in crisis. Washington, DC: National Academies Press, 2013.

5. Porter ME, Lee TH. The strategy that will fix health care. *Harvard Business Review*. October 2013 (<https://hbr.org/2013/10/the-strategy-that-will-fix-health-care>).

DOI: 10.1056/NEJMp1508387

Copyright © 2015 Massachusetts Medical Society.

Measuring the Value of Prescription Drugs

Peter J. Neumann, Sc.D., and Joshua T. Cohen, Ph.D.

Escalating drug prices have alarmed physicians and the American public^{1,2} and led to calls for government price controls. Less visibly, they have also spawned a flurry of private-sector initiatives designed to help physicians, payers, and patients understand the value of new therapies and thus make better choices about their use. Programs recently introduced or advanced by nonprofit organizations, including leading medical professional societies, represent an important innovation in the United States, but they have also revealed numerous analytic and implementation challenges.

The most prominent players include the American College of Cardiology and the American Heart Association (ACC-AHA), the American Society of Clinical Oncology (ASCO), the Institute for Clinical and Economic Review (ICER), Memorial Sloan Kettering Cancer Center (MSKCC), and the National Comprehensive Cancer Network (NCCN). Their initiatives have different missions — for example, ASCO, MSKCC, and NCCN focus on cancer drugs,

and ICER’s purview is broader and not specific to pharmaceuticals. But each organization’s framework accounts for factors underlying value, such as the quality of clinical data supporting the therapy’s use, the magnitude of its treatment effects, the likelihood of severe adverse events, and the product’s costs, ancillary benefits, cost-effectiveness, and effects on the health system budget (see table).

Several lessons are emerging. First, the move to value-based frameworks for assessing drugs and other interventions is a positive step. Anger over rising drug prices may be understandable, but it has led some observers to call for setting prices to reflect research, development, and production costs for drug firms, a strategy we believe is misguided. By instead focusing on a drug’s benefits, value-based approaches can encourage firms to produce more of what people want — products that improve health — and thereby further stimulate innovation. Consider the purchase of an automobile. Consumers don’t ask dealers about a car’s

manufacturing costs. Instead, they decide whether to buy a particular car by comparing its price and features to those of other vehicles, in the process spurring companies to develop ever better alternatives.

Second, whereas the governments of many countries use their regulatory and buying power to control drug prices, these U.S.-based initiatives represent private-sector solutions. They are a response to three realities in the United States: increasing prescription-drug costs, political opposition to giving Medicare authority to negotiate drug prices, and the fact that most Americans have private health insurance. The initiatives reveal potential for private organizations to challenge the patent-protected monopoly power enjoyed by drug manufacturers, though the groups are advisory in nature and simply provide information for the marketplace.

Third, the frameworks reveal numerous analytic challenges. Value is an elusive target, and there’s no consensus about what dimensions should be taken into account. For example, only the

Summary of Therapy Value Frameworks.*		
Organization	Factors Considered	Description
American College of Cardiology–American Heart Association (ACC–AHA)	Clinical benefit vs. risks Magnitude of net benefit Precision of estimate based on quality of evidence Value (cost-effectiveness)	Magnitude of treatment effect ranges from class I (“benefit [greatly exceeds] risk,” “procedure or treatment is useful or effective”) to class III (“no benefit, or harm,” “procedure or treatment is not useful or effective and may be harmful”). Precision of treatment effect ranges from level A (“data derived from multiple randomized trials or meta-analyses”) to level C (“only consensus opinion of experts, case studies, or standard of care”). Value corresponds to cost-effectiveness thresholds (high: less than \$50,000 per QALY; intermediate: \$50,000 to \$100,000 per QALY; low: more than \$150,000 per QALY). The framework lists the clinical benefit and value designations without combining them.
American Society of Clinical Oncology (ASCO)	Clinical benefit Overall survival Progression-free survival Response rate Toxicity Bonus factors Palliation Time off all treatment Cost per month	A therapy can be awarded up to 130 points. Clinical benefit (≤ 80 points) reflects end point and magnitude of benefit, with preference given to evidence on overall survival if available. Toxicity (± 20 points) reflects the rate of grade 3 to 5 toxic effects with treatment relative to standard of care. Bonus point score reflects palliation (10 points if therapy improves symptoms) and increased time off all treatment (≤ 20 points). The framework doesn’t combine each drug’s point score and cost.
Institute for Clinical and Economic Review (ICER)	Incremental cost-effectiveness plus care value components Comparative clinical effectiveness Other benefits and disadvantages Contextual considerations Budget impact	Cost-effectiveness ratio must not exceed a threshold ranging from \$100,000 to \$150,000 per QALY. Selection of final threshold is based on: (a) comparative clinical effectiveness, reflecting “judgments of the health benefit magnitude” and “strength of a body of evidence”; (b) other benefits and disadvantages, including such outcomes as factors influencing adherence or return to work; and (c) contextual considerations, including “ethical, legal, or other issues” (e.g., high burden of illness, availability of alternative treatments). Budget impact is acceptable if a drug’s introduction is compatible with an annual health care budget increase of GDP growth plus 1%. ICER reverse-engineers a “value-based price benchmark” that independently satisfies both the cost-effectiveness and budget-impact criteria (see text).
Memorial Sloan Kettering Cancer Center	Efficacy (survival) Toxicity Novelty Research and development cost Rarity Population health burden	Framework assigns values to each domain. Efficacy is assessed as improvement in overall survival, if available. Efficacy score also reflects evidence quality. Toxicity is a drug’s impact on probability of severe side effects and treatment discontinuation. Novelty is scored as 1 (novel mechanism of action), 0.5 (“known target but different mechanism of targeting”), or 0 (“next-in-class”). Research and development cost corresponds to the “number of human subjects enrolled in the approval trials for the first indication.” Rarity is the 2015 projected disease incidence. Population health burden is the annual years of life lost to the targeted disease in the United States. “Fair price” is the product of the scores, each of which is scaled by a user-adjusted weight.
National Comprehensive Cancer Network (NCCN)	Efficacy Safety Evidence quality Evidence consistency Affordability	Each area is scored on a scale of 1 to 5, with 1 indicating least favorable and 5 most favorable. The framework presents the scores separately. There is no explicit synthesis. Stakeholders judge acceptability on the basis of their overall impression of the listed factors.

* GDP denotes gross domestic product, and QALY quality-adjusted life-year.


MSKCC framework awards credit for the novelty of a drug’s mode of action. Moreover, the frameworks use different strategies for weighting various dimensions and deriving an overall “score.” ICER assesses a drug’s value on the basis of its budget impact and

cost per quality-adjusted life-year (QALY), then makes modifications to account for factors such as clinical effectiveness, other benefits and disadvantages, and contextual considerations, such as the treated condition’s severity and the availability of alternative

treatments. NCCN presents information on various factors but leaves synthesis to the user. MSKCC provides an online, interactive tool that allows users to adjust the weights for various dimensions, such as a drug’s efficacy and toxicity, and derive a

“fair” price in accordance with their own preferences.

Although some of these approaches are designed to incorporate user preferences, the overall score or recommended price produced may be inconsistent with those preferences. For example, ASCO’s approach awards up to 80 points for a drug’s effect on survival (or, in the absence of that information, its effect on surrogate end points such as response rate). On the basis of the drug’s toxicity, it adds or subtracts up to 20 more points, and then adds up to 30 more points depending on the drug’s palliative benefits and whether it statistically increases the time that patients can remain off all therapy. But summing arbitrarily derived values associated with different dimensions does not necessarily produce a coherent overall score. An analogy would be a scheme to measure a car’s value by adding its safety rating — on a scale of 1 to 10 — to its passenger capacity and gas mileage. A meaningful score should instead account for how much gas mileage buyers would sacrifice to gain an additional seat and how much safety they would sacrifice to increase gas mileage.

 An audio interview with Dr. Neumann is available at NEJM.org

Fourth, the frameworks either ignore a drug’s overall budget impact (ACC–AHA) or handle it inadequately. NCCN rates “affordability” on a scale of 1 to 5 without explaining the basis for those scores. ASCO lists cost as one of the factors considered but does not combine it with its point score. ICER adjusts a drug’s price benchmark to meet cost-effectiveness requirements. It also limits each drug’s budget impact to no more than \$904 million annually (an amount that ICER estimates would hold growth of total drug

costs below the growth rate of the gross domestic product plus 1%, taking into account the number of new drugs approved each year). Although ICER discusses various ways to address budget impact, including reducing spending on other priorities, it has in practice focused on price reductions. For example, its recent evaluation of PCSK9 inhibitors approved for controlling cholesterol levels called for reducing their price from more than \$14,000 to \$2,177 per year.³ ICER deserves credit for explicitly introducing budget constraints into value assessments, but reducing a drug’s price to satisfy a specific budget criterion isn’t always appropriate. For example, ICER’s budget criterion might dissuade companies from developing drugs designed to help large portions of the population.

In our view, value-based frameworks highlighting overall cost-effectiveness are most attractive because cost-effectiveness provides a common scale for comparing products. However, cost-effectiveness analysis is an incomplete tool and doesn’t convey all of a drug’s salient characteristics. More work is needed to determine how best to consider factors such as adverse events and ancillary benefits that matter to patients alongside cost-effectiveness ratios. Online tools that help stakeholders assign weights to drug characteristics — akin to the MSKCC approach — would be welcome.

Moreover, in practice cost-effectiveness analysis does not adequately address budget impact, because it focuses on individual therapies, not broader system-wide effects. The case of Sovaldi (sofosbuvir) — the effective but expensive hepatitis C drug — has highlighted this dilemma.

Published studies found sofosbuvir “acceptably” cost-effective (i.e., \$50,000 to \$100,000 per QALY), but already strained budgets could not easily expand to accommodate the costs of making the drug available to several million Americans. Ideally, when faced with new, cost-effective products, policymakers would reduce spending on lower-value services so that higher-value ones could be accommodated. Although efforts to identify low-value interventions, such as the Choosing Wisely program, are under way, more are needed. Even if we identify lower-value services, actually reducing spending on them is exceedingly difficult because doing so would threaten income streams for physicians, hospitals, and product manufacturers.

These emerging approaches for assessing drug value are welcome in a health system sorely in need of strategies for obtaining more health for the resources expended. The frameworks will require refinement, however, before they’re ready to be broadly applied.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center, Boston.

This article was published on November 18, 2015, and updated on November 20, 2015, at NEJM.org.

1. DiJulio B, Firth J, Brodie M. Kaiser Health Tracking Poll: August 2015. Kaiser Family Foundation; August 20, 2015 (<http://kff.org/health-costs/poll-finding/kaiser-health-tracking-poll-august-2015>).

2. Experts in Chronic Myeloid Leukemia. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood* 2013;121:4439-42.

3. New cholesterol drugs are vastly overpriced, analysis says. *New York Times*. September 9, 2015.

DOI: 10.1056/NEJMp1512009

Copyright © 2015 Massachusetts Medical Society.