What Patients and Providers Should Understand About Economic Evaluations in Oncology

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“Everything should be made as simple as possible, but not simpler”—Albert Einstein

Cancer is the second most expensive disease in the United States, next to heart disease, with estimated annual costs of \$263.8 billion in 2010: \$102.8 billion for direct medical costs (total of all health expenditures); \$20.9 billion for indirect morbidity costs (cost of lost productivity due to illness); and \$140.1 billion for indirect mortality costs (cost of lost productivity due to premature death).¹ With \$1.1 billion allocated for comparative effectiveness research in the United States, there has been increasing promotion of initiatives to inform clinical and health policy decisions made by physicians, payers, and regulators to help determine treatment guidelines; coverage policies; the therapeutic value of new interventions relative to standard of care; and ultimately, the best allocation of increasingly scarce resources that will provide benefits to individual patients and society.

In this regard, economic evaluations are important for providing data on the costs and consequences of interventions beyond the safety and efficacy information obtained in clinical studies. These economic evaluations are usually performed in one of three ways: retrospective analyses, decision analyses modeling, and analyses performed alongside clinical trials. As with different clinical trial designs, each of these methods has its own merits, flaws, and challenges. Retrospective databases are attractive sources of relatively easily available data that may represent what happens in actual clinical practice. However, issues mainly related to selection bias hinder the results and challenge one's abilities to use such information when defining policies. The use of decision analyses, in which data from clinical trials, literature, and expert opinions are combined in sophisticated mathematical models, is also attractive in predicting costs and outcomes of interest for various stakeholders under different scenarios.² However, the results are also difficult to translate into clinical practice and are commonly not understood by stakeholders. Analyses performed alongside clinical trials, on the other hand, mitigate issues related to selection bias and provide utilization patterns, costs, and outcomes of the trial.³ However, these analyses are notoriously burdensome to perform, clinical trials are usually not sufficiently powered for cost-effectiveness analyses,⁴ and efficacy and costs may change when an intervention moves from a randomized controlled trial to the community setting.

In addition, when a method to perform economic analysis is chosen, the form (or forms) of evaluation should be stated. These consist mainly of cost-effectiveness (CEA), cost-benefit (CBA), cost-utility (CUA), cost-minimization, and cost-of-ill-

ness analyses. In CEA, the relationship between costs and outcomes for different interventions is examined, and results are reported in cost per unit of effect (cost per life-year gained, for instance) or in effects per unit of cost (eg, life-years gained per dollar). In other words, the costs are in dollars, and the outcomes, in nonmonetary units, are usually expressed as survival. The term cost-effectiveness is actually often misused to refer to any economic evaluation, when it actually is a particular type of economic evaluation. A limitation of CEA is its inability to compare interventions with differing outcomes. For example, interventions aimed at increasing life years gained cannot be directly compared with those that improve physical functioning.⁵ Although survival is the outcome of utmost interest in oncology clinical trials, we have come to learn that other outcomes, such as quality of life, are equally essential. Thus, in CUA the intervention consequence is measured in both quantity and quality of life (cost per quality-adjusted life-year gained, for instance), taking into account utility or preferences, usually from a patient's perspective. In a health utility index, for example, being dead carries a utility of 0 and being in perfect health, 1.

In CBA, a monetary value is placed on both costs and outcomes, and the final result is reported as a monetary value, or net benefit.⁶ An advantage of CBA is that when costs and benefits are quantified in monetary terms, the hard task of measuring and valuing nonmonetary benefits, such as health gain or patient preferences, is avoided. Furthermore, from these descriptions, it is important to note that the adequate measurement of costs, outcomes, utilities, and preferences, in the case of CUA, is the basis of any economic evaluation.

In this issue, Guirguis⁷ proposes a fairly simple methodology to evaluate the value of oncology drugs in the metastatic setting that is neither a classic CEA nor CUA. In the proposed method, mean wholesale prices of drugs were divided by the median outcome the intervention provided, and then adjusted for the presence of adverse events, quality-of-life benefits, and different outcomes (eg, overall survival [OS] *v* progression-free-survival [PFS]), without a formal utility measurement method.

Several relevant shortcomings related to costs, outcomes, and utilities measurements are present in his methodology, however, and should be brought to the reader's attention. For example, the method does not use an objective evaluation of quality of life or health utilities. Better survival outcomes in oncology may also be associated with increased toxicities resulting from interventions, and these have to be quantified at the

best of our abilities. To simply discount arbitrary values is not ideal. Second, the cost analysis only factors in drug acquisition cost. Thus, it is unclear which perspective the “cost/survival” ratio is estimated for. The author infers making societal or drug approval decisions based on costs solely from a payer perspective. Finally, throughout the article, several parameters are not validated and are simply arbitrary. This applies to the author’s definitions of low, average, and high “cost/survival” thresholds, for example. Arbitrary values are open to heavy criticism and/or interpretation, as any author, payer, or technology developer could choose their own parameters, making objective comparisons across different diseases, drugs, and technologies more challenging. Finally, the author makes little distinction between PFS and OS (except for an arbitrary discount of 15% when PFS is used over OS), the calculation of which has major implications in policy making, as most payers would have different thresholds for treatments that increase survival versus delaying progression of disease (especially if there is no demonstrable improvement in patient well-being).

Nevertheless, this article brings to the attention of medical oncology practitioners several hurdles policy makers encounter: the high price of oncology drugs, the price-value dissociation, and the lack of acceptance of economic analyses by individual patients and providers. The high price of oncologic interventions is usually justified by their high value to individual patients and the cost of innovative science and drug development. However, some of these interventions have benefits that can be measured in only weeks (or even days) of added life. Thus, an alternative view is that the high prices may not be justified by the value or benefits these interventions provide when viewed from the perspective of the health care system as a whole.⁸ Furthermore, in the United States, the Food and Drug Administration and the Centers for Medicare & Medicaid Services do not explicitly adopt economic analyses data in their approval and coverage processes. Similarly, private payers are also hesitant to publicly disclose their decisions as based on costs, although costs in some form are usually assessed when approving the use of interventions for individual patients by methods such as claims review and different copayment tiers.¹⁰ Finally, although some patients may understand why and how economic

analyses affect them, they may not accept medical decisions based on economic evaluations.

Furthermore, a key question then becomes how to leverage the attention devoted to the high cost of cancer care and develop a model for economic evaluations in oncology that can be easily explained to patients, providers, and society; that adequately measures the outcomes it aims to assess; and that can be further adopted by payers and policy makers. A better understanding of health economics methods and results by patients and providers may be a first step toward the widespread acceptance of economic evaluations. For this to happen, either the methods should be simplified or methods that are directly related to individual patients may have to flourish. Thus, the author must be complimented for aiming to simplify economic analysis of interventions in oncology. However, his methods do not yet accomplish that goal. To that end, we would like to urge oncology societies and journals to promote education on health economics evaluations and invite readers to share their opinion through discussion blogs at the ASCO Web site.

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