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Commentary

Health Care Costs: How Do We Decide Value? When Do We Decide? How Do We Particularize the Decisions?

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How do oncologists and patients make heath care decisions? Do we use a "shared decision-making" model? Has paternalism become a thing of the past? Do we rely on the latest randomized trial data and then apply it in the same way that the trial eligibility criteria were determined? When we counsel someone about cancer care (screening, prevention, and treatment), do we include financial risks in the discussion? Costs for cancer care are rising throughout the world. This is especially noted in high-income countries [1]. Contributors to increasing costs include demographic, technological, regulatory, industrial, and governmental factors as well as individual patient and physician behaviors. Lack of knowledge of "costs" and limited reporting of "true" benefits of medical care are impediments to meaningful discussions of providing individual care and reforming health care. Individual and societal expectations are also driving the "cost curve" of health care. Financial considerations, overuse, for example, are perceived to be placing more pressure on the practice of medicine in the U.S. than in the past. Costs of new treatment development through the clinical trial process, individual and group expenditures, and public/governmental monetary outlays for cancer treatment drugs continue to rise. The research focus on "targeted therapy," like trastuzumab, and personalized cancer treatment based on the molecular characteristics of an individual's cancer may also increase the costs of new treatment development and patient care.

There is a great deal of angst regarding the future of medicine and the care of the sick based on the perception that we will not be able to afford care. The recent emphasis on "end-of-life" care has precipitated worry of "rationing," an act undertaken by policy makers, and financial means testing for medical care. Reports of personal bankruptcy resulting from critical or life-threatening medical illnesses fill the news [2]. There is also a perception of inequality in access and distribution of health interventions known to be of value, not rationing but an access to care concern and a distributive justice issue nonetheless. It is incumbent on the oncology community that we discuss, review, and assess the best means of providing care for the benefit of all citizens. The costs of cancer care have been the subject of ethical review, and the question has been asked: "How much is life worth?" [3] Evidence-based medicine, based on analysis of randomized controlled trials (RCTs), and comparative effectiveness research provide two methods that have been proposed to assist in decision making for health care. Whereas evidence-based medicine has, as a component, the patient's values and participation in the decision, comparative effectiveness research (CER) does not "particularize" an individual treatment decision. CER is defined as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition, or to improve the delivery of care." This is intended to provide assistance in health care decisions for the public, policy makers, and individuals with the goal of improving health care [4]. Other clinical decision aids, such as number needed to treat and number needed to harm, and clinical efficacy reports from RCTs have their proponents. It has been suggested that RCTs lack the necessary details for use in clinical practice [5]. Each method has supporters and detractors and no "surefire" best method is available to practicing physicians and patients to aid in clinical decision making. Countries such as the U.K. have developed formal processes for the evaluation of technologies and drug therapies to guide health care financial coverage decisions. The U.K. National Institute for Clinical Excellence provides an explicit methodology for analysis of technologies and therapeutics and includes cost-effective analysis (CEA) in the process. This method uses decision analysis methodology and data from RCTs to reach a decision on the relative benefits and costs of interventions. The

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analysis generally is described as a measure of life-years gained (LYG) or quality-adjusted life years (QALYs) for reporting purposes. Comparing two or more interventions can provide a measure of the "incremental cost-effectiveness," often expressed as a ratio, of the differing strategies for treatment, as an example, chemotherapy for human epidermal growth factor receptor (HER)-2^+ breast cancer with and without trastuzumab [4, 6–8]. Other countries, including Australia and Canada, also use cost-effectiveness measures for approving the use of drugs and technologies. In the U.S., a consensus panel defined the use of CEA and stated that "the information it provides is critical to informing decisions about the allocation of health care" [9, 10]. CER and CEA have been used effectively not only for policy decision but also to enhance individual informed decision making for clinicians and patients. In the U.S., costs have not been part of the approval decision process for the U.S. Food and Drug Administration (FDA). They require safety and effectiveness determinations for making drug approval decisions. The approval is generally for an "indication," but once approved an agent may be used as desired by practicing clinicians. Although some insurers, including the Centers for Medicare and Medicaid Services, have restrictions, the development of approved compendia based on guidelines for care make chemotherapy agent use more liberal than the FDA may have intended. Many clinicians may not be aware of drug costs in relation to benefit derived for their patients, or perhaps think these "should not be" a consideration.

It is clear that some rational process for addressing costs of care and benefit for individuals and society must be developed and generally agreed upon if we are to sustain cancer care advances. In the U.S., we have an opportunity to enhance and implement a rational approach to care decisions, but we will need leadership to develop the national will to proceed. Physician organizations, the American Society for Clinical Oncology for example, are best suited to bring this to the public and provide the necessary background and imperatives for change.

The recently enacted Patient Protection and Affordable Care Act will expand health care coverage to an estimated 32 million currently uninsured individuals by 2019. This increase in health care need comes as the "baby boomer" generation will be reaching Medicare benefits age. These two coincident occurrences are expected to have the potential to further strain heath care budgets and access unless adequate, rational policy relief is forthcoming. Physicians must play a leadership role in attempting to curtail costs while providing value in health care. In this issue of ***The Oncologist***, Hedden and colleagues provide a thoughtful assessment of trastuzumab use in the treatment of primary and metastatic breast cancer [11]. Their intent was not only to review clinical efficacy addressing the usual parameters of disease-free survival and overall survival but also to examine, in a formal, systematic critical way, QALYs and LYG in relation to economic parameters. They provide a range of costs for trastuzumab use and accept that it is cost-effective [12]. They chose to examine cost–benefit in a "real-world" scenario and relied on previously published RCT data for assessing the impact of trastuzumab over a projected 28-year time frame even though there are limited data for trastuzumab benefits beyond 5 years. Data for recurrence estimates were derived from results of published RCTs in similar populations of patients with primary and metastatic breast cancer. Cost data were obtained from the British Columbia Cancer Agency database. The use of Markov methodology allowed for decision modeling over time, and a variety of clinical outcomes states were considered. Transitions to differing health states were then applied to a hypothetical population of women with primary and metastatic breast cancer using previously published clinical trial data to inform the scenarios and transitions of the Markov model. Expert "opinion" for the modeling was minimized. A variety of sensitivity analyses confirmed the initial QALY and LYG data for trastuzumab use in patients with HER-2^+ breast cancer.

The clinician may rightly ask "What monetary value is used to declare something cost-effective?" And who decides? The "floor" for defining "cost-effective" monetarily is not universally standardized. It is encouraging that trastuzumab, a lifesaving treatment, is deemed cost-effective.

This is not the first CEA of trastuzumab use for breast cancer and it is unlikely to be the final version. Other reports include studies from North America, Europe, Australia, and China and a systematic review from Taiwan [12–24]. An estimate of recurrences avoided in relation to cardiac events has also been reported [14]. These have used methods to assess QALYs and LYG, as well as "societal costs." Generally, analyses do not include all costs, indirect and direct. Markov modeling has been the most common method of assessing outcomes, and differing choices for state transitions do not allow for crosscomparison of cost-effectiveness outcomes. With the exception of an analysis from the U.K., all reports conclude that trastuzumab use, especially in the adjuvant setting, is cost-effective for for the treatment of patients with HER-2^+ breast cancer [25].

The U.K. report concluded that the cost-effectiveness of trastuzumab remains "uncertain" and requires further research on the "duration of treatment effect" and "late toxicities." These data would be useful for most RCTs. Often, RCTs lack sufficient data for supporting clinical decision making [5].

For the Canadian system, drug prices are negotiated with pharmaceutical companies based not only on price but also on volume of drug use; therefore, it is likely that trastuzumab acquisition costs are less in Canada than in the U.S. Drug pricing, especially for new cancer agents, is a focus in the U.S. Tradeoffs for health care based on price are likely to occur [3]. CER may help in decisions about cancer care but only if an alternative treatment option is available. Until we have such data, unique expensive agents for treating patients with cancer should be reviewed with formal, critical systematic analyses of cost-effectiveness based on survival or quality of life as a measure of patient benefit. Oncologists need to become part of the ethical decision process to assure appropriate care is provided for all.

Hedden and colleagues are to be commended, not only for providing a meaningful analysis supporting a beneficial treatment for breast cancer patients, but also for reminding all prac-

titioners of the need for critical thinking regarding the costs of cancer care.

Recent publications have emphasized the need for "high-value, cost-conscious care" [26]. Physician involvement in these efforts must be considered carefully and critically, and practice efforts must be aligned with these efforts to change our practice.

The recent update of the *American College of Physicians Ethics Manual* succinctly states our responsibilities: "parsimonious care that utilizes the most efficient means to effectively diagnose a condition and treat a patient respects the need to use resources wisely and to help ensure that sources are equitably distributed." This is a matter of ethics, beneficence, and justice [27].

Until better or the "best" treatment for HER-2/Neu$^+$ breast cancer is developed, trastuzumab is the most and only demonstrated cost-effective treatment. When new treatments become available through research, CER will be needed to further guide treatment choices and inform patients and physicians.

Physicians can begin to change now by asking the "high-value" questions [28].

As we strive to eliminate cancer and its attendant suffering for our patients in daily practice, have cost, access, and availability become part of our thinking?

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