Managing Oncology Costs

Claiborne E. Reeder, RPh, PhD; and Debra Gordon

Abstract

This monograph will review the burden of illness in oncology, suggest a framework for evaluating oncology costs and consequences, identify economic modeling formats in cancer care, and explore methods of cost control for cancer care.

(Am J Manag Care. 2006;12:S3-S16)

Cancer is the second leading cause of death in the United States, claiming approximately 570 280 Americans in 2005. The disease is responsible for 1 of every 4 deaths, and strikes approximately 1.37 million people per year.[1] Although survival rates for the 15 most common cancers have been improving every year since 1993, the overall number of cancer deaths has continued to increase given the country's growing population and the aging of its citizens.[2]

Overall, the incidence of age-adjusted cancer rates in the United States has remained steady since 1992 for all cancer sites combined, although the incidence of some neoplasms—including melanoma and cancers of the kidney in men and women, prostate and esophageal cancer in men, and leukemia, non-Hodgkin's lymphoma, breast, thyroid, and bladder cancer in women—has increased.[2] Broken down by sex, incidence rates have remained steady for men but increased 0.3% for women.[1]

This state of affairs will likely change, however. Indeed, the number of cancer cases in the United States is expected to double over the next 50 years to 2.6 million, the result of an aging and expanding population.[1]

Even without any significant increase in cancer incidence or mortality rates, costs have been increasing significantly. In 2004, the country spent $189.8 billion on overall costs for cancer, including $69.4 billion for direct medical costs, $16.9 billion for lost productivity caused by morbidity, and $103.5 billion for lost productivity due to mortality. Those costs were expected to increase in 2005 to $209.9 billion overall, including $74 billion in direct medical costs and $135.9 billion in indirect costs related to morbidity and mortality, about a 9.5% increase.[1]

Spending on cancer in the United States accounts for 4.7% of overall medical treatment expenditure and about 10% of Medicare spending.[3] Moreover, 41.3% of Medicare drug expenditures were for oncology/hematology drugs, paid primarily through Part B reimbursement.[4] Among cancer types, lung cancer tops the list of total expenditures, accounting for 13.3% of all cancer treatment dollars (~$9.6 billion), followed by breast cancer at 11.2% (~$8.1 billion).[3]

Although the cost of cancer treatment as a percentage of overall direct medical treatment expenditures has remained fairly consistent over the past 30 years, the National Cancer Institute (NCI) predicts these costs will begin rising at a faster rate, particularly as the population ages and the number of cancer cases increase. Additionally, the NCI notes that cancer costs will continue to rise as newer, more effective, and more expensive biologic treatments enter the pharmaceutical market.[3]

Relative to other pharmacotherapy, these new biologic treatments come with substantial costs and, in many instances, may only prolong life a few months longer than current treatments. For instance, adding the antivascular endothelial growth factor bevacizumab to a standard routine of irinotecan-5-FU/LV (IFL) for advanced colorectal cancer increased mean survival time by 4.7 months compared with those receiving IFL

Address correspondence to: Claiborne E. Reeder, RPh, PhD, University of South Carolina College of Pharmacy, 715 Sumter Street, Room 109, Coker Life Sciences Bldg, Columbia, SC 29208; reeder@cop.sc.edu.

alone, a clinically significant difference, but a small one, nonetheless.[5]

The significant costs of these new drugs often put them out of the reach of any American without health insurance and pose an economic difficulty even for those with excellent insurance. In the case of colorectal cancer, for instance, one published cost comparison found differences of $21 000 and $30 000 between regimens containing bevacizumab or cetuximab and those using only fluorouracil and leucovorin.[6] Overall, the cost of a standard regimen for treating advanced colorectal cancer has risen from about $500 to about $250 000 since the introduction of these new compounds.[7]

Meanwhile, the lung cancer drug gefitinib costs about $1800 per month and must be taken for months or even years; erlotinib, another biologic for metastatic non–small-cell lung cancer, costs about $2500 per month. Neither of these agents cure the disease; they only slow progression and extend survival time, enabling physicians to treat the cancer as a chronic condition.[8] This is a paradigmatic shift in how cancer is treated. Rather than an acute disease with a high mortality rate, cancer is increasingly being viewed as a chronic disease, with some patients possibly receiving treatment with these and other equally expensive drugs for years, even decades.

As a result, health insurers are increasingly focusing on oncology costs. One survey found that 58% of responding health plans said they planned to focus on oncology in 2005 as part of a national movement towards specialty pharmacy programs to manage costs.[9]

The "oncologic time bomb" predicted by an American Cancer Society task force in 1999 has exploded.[10]

How health insurers, patients, healthcare professionals, and employers approach these rising costs over the next decades has tremendous implications for the entire healthcare system. One survey of 139 medical oncologists at 2 large academic hospitals found that although the majority (78%) said patients should have access to effective care regardless of cost, 71% said that rising costs would result in more rationing in the area of oncology treatment over the next 5 years.[11]

Burden of Illness in Oncology

Any discussion of oncologic costs must, of course, move beyond dollars and cents. Pertinent issues include not only direct medical costs, but indirect costs, survival, quality of life, health-related quality of life (HRQOL), and psychological issues.

Understanding the scope of these costs and benefits enables policymakers, researchers, insurers, and employers to evaluate the individual and societal benefits of oncology expenditures on the prevention and treatment sides, as well as across diverse racial, ethnic, socioeconomic, and geographic differences.

Framework for Evaluating Oncology Costs and Consequences

Outcomes research. For decades, oncology outcomes have been measured in clinical terms, such as mortality or survival; progression-free survival (the time until the tumor begins to grow again); and clinical end points (tumor size, duration of response, hematological markers). With rising costs and greater treatment options, these relatively simple outcome markers are no longer sufficient.

Today, treatment decisions must also rely on economic and humanistic costs and outcomes associated with a given treatment, including direct and indirect medical costs, the treatment's effect on the patient's overall quality of life, and any benefits to the patient and society.[12] In other words, how well do treatment options efficiently achieve desired outcomes?[13]

The importance of evaluating the cost of disease and value of treatments cannot be underestimated in today's healthcare system. With 40 million uninsured Americans, and healthcare costs making up 16% of the nation's economy (compared with 13.7% in 2000), the appropriate allocation of resources is a critical issue.[14,15]

To approach this issue in a systematic manner, researchers use outcomes research and pharmacoeconomics. Outcomes research involves the scientific and methodologically sound collection of data on the costs and consequences of various therapies. The data are then used to improve health

status as part of a process known as outcomes management.[16] Generally, 3 outcome dimensions may be considered: clinical, economic, and humanistic.[12]

Although traditional medical decision making has always included the latter 2 categories on a subjective basis dependent on the individual care provider, all 3 dimensions should be considered simultaneously when comparing treatment alternatives. Assessing the clinical, economic, and humanistic costs and benefits of a treatment regimen provides insight into the value of the respective treatments.[12]

Pharmacoeconomic approaches. Pharmacoeconomics is a component of outcomes research that brings a "systemic approach to the collection and analysis of data in decisions regarding the selection and use of pharmaceutical products and services."[12]

Pharmacoeconomics offers a set of tools to help decision makers better understand the value of treatment regimens. These methods provide a measure of the efficiency of treatments by systematically balancing the cost and consequences of treatment alternatives. There are 4 main pharmacoeconomic approaches to assess the value and efficiency of treatment interventions: cost-benefit analysis, cost-effectiveness analysis, cost-minimization analysis, and cost-utility analysis.

Cost-benefit analysis compares 2 or more interventions in terms of the total dollar cost of an intervention compared with the total monetary benefits. A cost-benefit ratio provides a measure of the "return on investment" for a given intervention or treatment. Interventions can then be compared to determine which provides the greatest dollar benefits for each dollar expended. For instance, suppose tamoxifen costs less than letrozole, but clinical studies find that letrozole is more effective as a postadjuvant breast cancer treatment in reducing the risk of recurrence (thus reducing direct and indirect costs from future medical costs and lost productivity). If the ratio of the dollar value of these benefits (decreased cost and improved productivity) to the dollar cost of treatment with letrozole is greater than the same ratio for tamoxifen, then letrozole provides the more efficient regimen.

Cost-effectiveness analysis compares the cost and consequences of 2 or more alternatives with a common therapeutic objective. In the case of tamoxifen and letrozole, the question might be not only which is the most cost effective with the greatest financially-based benefits, but which has the greater nonmonetary outcomes, such as years of life saved, hospital days avoided, tumor shrinkage, etc. The cost-effectiveness ratio would be calculated as the dollar cost per nonmonetary outcome (eg $500/years of life saved). The treatment with the lowest cost per outcome is the more efficient regimen. This is the approach used most often today, particularly in light of high-cost therapies that may or may not significantly extend life. In today's healthcare environment, a new treatment seldom displaces all other treatment options. Instead, we must decide if the added benefits of the new treatment are worth the additional costs, compared to existing treatments. This decision is aided by an "incremental analysis" where the incremental change in costs of 2 treatments is compared to the incremental change in benefits of the treatments. Incremental cost-effectiveness ratios quantify the cost per unit of benefit gained from using one treatment versus another. Generally, an incremental analysis should be included when 2 or more treatments are evaluated within a cost-effectiveness framework.

Cost-minimization analysis is used when all relevant and available treatment choices have clinically equivalent outcomes but different costs. In this instance, the approach chosen is based entirely on the lowest treatment cost. With a cost-minimization analysis, the assumption of equivalent treatment outcomes should be clearly supported by clinical evidence.

Finally, cost-utility analysis compares 2 or more treatments in which costs are measured in dollars and outcomes are measured in quality-adjusted life-years (QALYs), which adjust treatment outcomes for patient preferences. The approach that yields the lowest cost per QALY is the more efficient treatment.[17] Cost-utility analysis is particularly relevant when regimens differentially affect

quality of life during and after treatment. Consider, for example, 2 chemotherapy regimens that are equivalent in terms of their survival benefit. The 2 regimens differ, however, in terms of their emetogenic potential. It is reasonable to assume that the least emetogenic treatment would be preferred. Cost-utility analysis adjusts the outcome to account for patient preferences for the regimen with the least amount of nausea.

Interestingly, an analysis by Tengs comparing cost-effectiveness estimates with cost-utility estimates found little difference between the 2 unless the intervention had significant side effects that greatly reduced quality of life or the intervention itself greatly improved quality of life over the long term.[18]

Choosing the perspective. Before implementing an economic analysis of treatment interventions, the perspective from which the costs and benefits will be calculated must be determined. Will it be from the perspective of the individual patient and his or her family? The payer? The provider? Or society as a whole? Specification of study perspective is crucial in identifying relevant cost and outcomes.

For instance, from the patient perspective the most important outcome may be additional years of life and overall quality of life. From the provider perspective, the most important outcome may be overall reimbursement and clinical end points of treatment. However, from society's perspective, the more important outcomes may be reducing costs associated with absenteeism and decreased productivity as well as the loss of an individual's contribution to society.[19]

Once the perspective is determined, the actual measurement of costs commences. Cost can be categorized as direct medical costs, direct nonmedical costs, indirect costs (lost productivity), and humanistic costs (quality of life, patient satisfaction).

Direct medical costs. Direct medical costs include not just pharmaceutical costs, but all costs relating to treatment, including laboratory testing, physician visits, surgical costs, inpatient care, and imaging costs. Identifying direct medical costs for treatment of a specific disease can help policymakers, payers, and clinicians identify areas of focus. For instance, one study modeling the lifetime direct costs of treating metastatic breast cancer in the United States found that the combined cost of all therapies (ie, chemotherapy, hormonal therapy, and radiation therapy) accounted for just 12% of total medical costs. This suggests that focusing on other direct medical costs, specifically hospital and terminal care, would be an appropriate method for controlling or reducing costs associated with the final stages of the disease.[20]

Direct nonmedical costs. These costs typically fall on the patient and his/her family, and include items such as the cost of transportation to and from healthcare provider offices and hospitals; lodging for long-term treatment courses, such as autologous bone marrow transplants; and costs for lifestyle items like wigs and prostheses as treatment progresses. Nonmedical costs for the physician may include unreimbursed care.

Indirect costs. These costs are composed primarily of the patient's lost productivity in the workplace, home, and society as a whole, both from the illness and premature death, as well as time and productivity lost by the patient's family, friends, and others involved in the patient's care.[19]

Two approaches commonly used in estimating costs associated with lost or diminished productivity are the human capital approach and the willingness-to-pay approach. The human capital approach is based primarily on the value of wages lost from decreased productivity for those in the workforce.

For example, according to Chang et al, higher absenteeism rates for employees with cancer translated into higher costs ($373 vs $101; $P < .05$). Cancer patients also had, on average, more monthly short-term disability days than controls (5.2 vs 0.2), resulting in mean monthly costs of $698 vs $25 ($P < .05$). Additionally, cancer patients' caregivers had higher mean monthly costs of deductibles and copayments and also had more absenteeism per month than caregivers of the control group.[21]

The willingness-to-pay approach measures productivity costs based not only on

lost wages, but also on the value the patient places on their own health and well-being.[22] Willingness-to-pay basically estimates what people would be willing to pay to avoid the illness episode and its sequelae.

A market value may be used even for those not in the workforce. This market value considers what the patient would have been paid for nonworkforce activities, such as housekeeping and child rearing. Additionally, an opportunity-cost approach may be used, which considers those wages that might have been lost as a result of the patient's illness if the patient had been employed outside the home.[17]

The direct effect of cancer-related treatment on patients' daily activities may also be considered. A study of ovarian cancer patients who experienced chemotherapy-related hematologic or neurologic side effects found that indirect costs for patient and caregiver work loss and caregiver support payments were greater, in most instances, than the direct medical costs for thrombocytopenia and neurotoxicity.[23]

Humanistic costs. Humanistic costs and outcomes consider the effect of treatment on a patient's HRQOL and satisfaction with that treatment. These measures have gained acceptability in assessing the value of various cancer treatments beyond traditional clinical outcomes. Given the growing understanding that traditional mortality end points may not reflect the actual effect of cancer and its treatment on patients and that many cancers have no cure, these measures are being used as end points for clinical trials of new cancer therapies.[19,24] The humanistic value of any treatment regimen should be balanced against the clinical and economic consequences of the treatment.

Although similar, HRQOL and patient satisfaction represent different constructs. Health-related quality of life is a multidimensional construct that captures the effects of an illness or its treatment on aspects that are relevant and important to a patient's well-being. These dimensions typically include physical, emotional, and social functioning as well as symptoms.[25]

All treatments affect patients' HRQOL in a positive or negative way. For instance, any adverse events related to pharmaceutical treatment have an effect, as does the time and energy required to receive those treatments.

In addition to its use as a primary or secondary end point in clinical cancer trials, HRQOL is also used to compare the effects of interventions, to assess funding priorities at the National Institutes of Health against the overall burden of the disease, to index the relative burden of cancer for individual nations or groups of nations, and to evaluate the performance of healthcare providers and managed care plans.[13,26] Considering HRQOL issues also helps identify the effects of treatment changes on patient well-being and predict survival.[27]

Satisfaction with care measures how well a particular treatment meets the expectation of the patient. These expectations may involve aspects of quality of life or the ability to function at a particular level.[28]

Including patient preferences for a given treatment and its consequences in an outcome analysis can have significant effects. For example, a cost-utility analysis of paclitaxel in combination with cisplatin for patients with advanced ovarian cancer published in 1997 found that although first-line treatment costs with the drugs were about 4 times higher per cycle than the then-standard treatment of cyclophosphamide and cisplatin, incorporating patient treatment preferences into the model revealed a much smaller cost difference per quality-adjusted, progression-free year.[29]

Numerous tools are available to assess HRQOL from a general (generic) or disease-specific perspective across a range of illnesses. One of the most widely used generic instruments is the MOS SF-36. If one is interested in the effects of a particular aspect of a therapy or its treatment, a disease-specific HRQOL instrument is more appropriate. Numerous cancer-specific instruments, such as the FACT-Anemia and the Prostate Cancer Treatment Outcomes Questionnaire, exist. The choice of instrument depends on the patient, the disease, and the treatment under investigation.[28]

Incorporating HRQOL and Patient Preferences

Clegg et al incorporated HRQOL and

patient preferences into a cost-effectiveness and cost-utility analysis of 4 drugs for treating non–small-cell lung cancer: vinorelbine, gemcitabine, paclitaxel, and docetaxel.[30] The review found that although survival gains of a few months were modest with the new compounds, they were clinically significant relative to survival in the untreated group. The researchers also found the treatment resulted in gains in quality of life compared with best supportive care, because some of these newer forms of chemotherapy had fewer negative effects on HRQOL.

The analysis concluded that the newer drugs extended life at a cost for year of life gained (YLG) that was much lower than for other treatments.[30] This study illustrates the importance of considering the impact of treatment choice on patient quality of life and satisfaction with care. Therapies that minimize adverse events or meet patient expectations are more likely to be used and accepted by the patient. Patient acceptance translates into improved adherence, which should have a positive effect on treatment outcomes.

Economic Modeling in Cancer Care

Economic models are used to describe the essential elements, consequences, and complications of a treatment decision under conditions of uncertainty. As such, models provide estimates when data are either not available or are insufficient to make a decision. They can also be used to extrapolate existing data to predict other events.

Models are also used when the relevant clinical trials have not been conducted or the requisite data are not collected as part of the trial and to extrapolate long-term outcomes, such as survival, when only short-term end points, such as tumor size or neutrophil count, were measured.

Decision analysis. Decision analysis is a systematic approach to evaluating a problem or decision that incorporates both clinical and economic costs and consequences of the decision under conditions of uncertainty. Decision analysis enables the evaluation of complex clinical choices after weighing the risks and benefits of alternatives and the likelihood (probability) that any of these alternatives will occur. Without this approach, data for such decisions might take years to collect through clinical trials. Decision analysis is often used when competing treatment interventions, each with its own tradeoffs, are available and a specific treatment decision must be reached.

Decision analysis begins with a question, such as, "Which treatment option maximizes the outcome of interest?" The question should be framed by factors such as target patient population, diagnosis and treatments, reason for the analysis, and study perspective. For instance, is the decision analysis being conducted to determine treatment options for an individual patient or to guide policy decisions?

To use decision analysis, there must be a criterion for the optimal decision, whether that is maximizing survivability, life expectancy, quality of life, or cost effectiveness.[31] Decision analysis is often used as a tool to estimate average or expected cost in a pharmacoeconomic evaluation.

Data for decision analysis models are obtained from a variety of sources, including clinical trials, meta-analyses, administrative or medical databases, and expert opinions. In addition to specifying the sources of economic and clinical data, decision analysis models should also make all assumptions transparent to the reader.

Assumptions for a decision analysis may include estimates for length of life, medical costs, levels of disability, and effect on quality of life.[32]

Decision analysis models are often presented in the form of a "decision tree" with symbols such as squares, circles, or triangles indicating key decision points. Square nodes are "decision nodes," because the branches represent a potential option or choice. Circular nodes are "chance or probability nodes," because each branch represents future outcomes that are beyond the control of the decision maker and are uncertain.[33] Chance nodes have probabilities of occurrence associated with each possible outcome. Finally, the triangle node represents the end point or outcome cost.

A simple decision tree is depicted in the **Figure**. This decision tree depicts a choice between 2 chemotherapy agents, both of which are effective in treating the cancer. In

this example, Drug X has a lower incidence of nausea than Drug Y (30% vs 40%). Drug X is also slightly more efficacious than Drug Y, but also more expensive. Dollar amounts displayed at the terminal nodes (triangles) represent the total cost of treatment, including drug cost, for the particular arm of the decision tree. When the average or expected cost is calculated, Drug X is shown to have a lower average cost per patient treatment ($3080 vs $3124).

In the oncology arena, decision analysis has been used to model a variety of treatment decisions, such as the use of bone marrow transplants, colony stimulating factors, prostatic-specific antigen testing, and screening mammography. When complete, these decision analysis models provide not only an "optimum" solution but also a clear delineation of the underlying structure and assumptions used. Decision analysis models can be modified as new or additional information about treatment options becomes available.

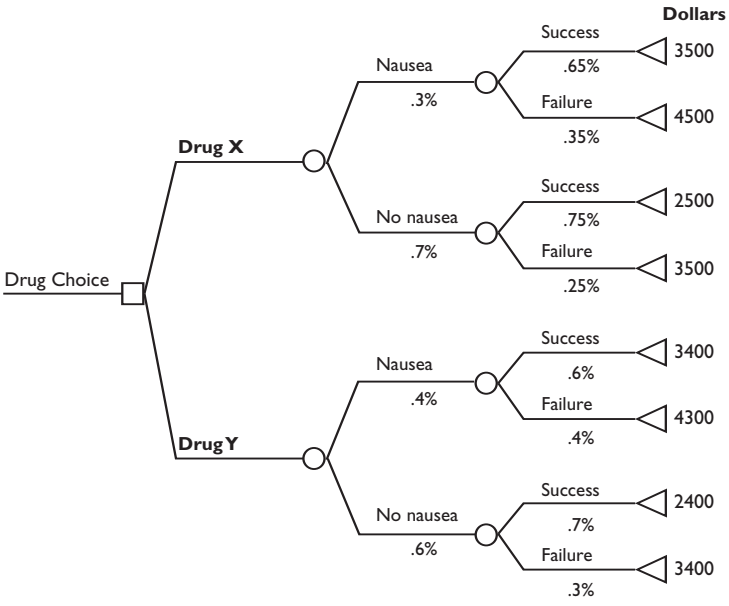
Decision analysis may use static or dynamic models. A static model is best used when the event in question has a relatively well-defined start and end points that occur within a finite period of time, such as the development of community-acquired pneumonia. The onset, progression, and treatment of this acute condition is well defined (the condition is typically "cured" within a few weeks) and thus well-suited to a static model.

A dynamic model, on the other hand, is more useful for chronic conditions, such as heart failure or even cancer, in which the patient improves but then has a recurrence. In this case, the patient is in various health states over a long period of time. Conditions such as these are more amenable to dynamic models, like Markov models, where the model is more fluid and the patient is allowed to move among various health states as the illness improves or progresses.

Examples of Economic Models

In Lee et al, researchers used a Markov decision analysis to determine the cost effectiveness of postmastectomy radiation therapy (PMRT) in high-risk premenopausal breast cancer patients (those with positive

Figure. Decision Tree for 2 Chemotherapy Agents



lymph nodes). They derived clinical data for the model from a large meta-analysis of adjuvant systemic therapy trials for breast cancer with and without PMRT and estimated cost data from other literature.[34]

The model estimated the number of recurrences, relapse-free and overall survival, and costs over a 15-year period using a discount rate of 3%. Cost-effectiveness ratios were calculated per incremental QALY and YLG. One- and two-way sensitivity analyses were performed to determine the sensitivity of results to clinical and economic assumptions.

The analysis found that PMRT reduced the risk of relapse by 31%, projecting a 15-year relapse-free survival rate of 52% with PMRT and 43% without. PMRT increased overall survival from 48% to 55%, resulting in an incremental 0.29 YLG per patient. Fifteen-year costs also increased from $40 800 to $48 100, which translated into a cost per additional YLG of $24 900. Based on their analysis, the authors concluded that PMRT offered "substantial clinical benefits" in a cost-effective manner.

Another example comes from Sanders et al, who used decision analysis to assess the cost effectiveness of a potential vaccine for human papillomavirus (HPV) as a way to prevent cervical neoplasms. Cervical cancer is one of the most common malignancies in

women, diagnosed in about 13 000 women per year and responsible for the death of about 4000 women per year.[35]

Researchers built a decision tree to evaluate length of life and cost for vaccinating adolescent girls against high-risk types of HPV. The target population was all adolescent girls in the United States, with a base case of 12-year-old girls (sexual activity before age 12 is considered rare). This assumption was tested in a sensitivity analysis.

The analysis assumed universal vaccination, although during the sensitivity analyses the researchers did evaluate the cost effectiveness of targeting only high-risk girls. The model included data on incidence of HPV infection; low- versus high-risk HPV types; rates of HPV progression; cancer surveillance, treatment, and progression; benign hysterectomy (assuming such women were protected from cervical cancer); HPV vaccine characteristics; and the effects of HPV infection and cervical cancer on quality of life and costs.

The researchers found that although a prophylactic vaccine against high-risk HPV types was more expensive than current practice, it resulted in greater quality-adjusted life expectancy. They predicted that such vaccination would avoid more than 224 255 cases of HPV; 112 710 cases of squamous intraepithelial lesion, a precancerous condition; 3317 cases of cervical cancer; and 1340 deaths related to those cancers. Their sensitivity analyses found the vaccine would be cost effective, even assuming booster shots every 3 years and an efficacy as low as 40%.[35]

Methods of Cost Control in Cancer Care

During the late 1990s and early part of this century, the growth of managed care organizations began to decline. Simultaneously, health insurance premiums began to skyrocket for both employers and employees, rising by 13.9% in 2003 (the highest increase since 1990), 11.2% in 2004, and 9.2% in 2005. Since 2000, premiums for family coverage have increased 73% compared with inflation growth of 14%.[36]

Tools such as pharmacoeconomics, decision analysis, clinical guidelines, and outcomes research help health plans and employers determine which therapies are most effective and under which conditions they are most efficient. The challenge of health plans becomes one of indemnifying and implementing programs to achieve the cost-effective use of treatment regimens. Options available to control cost by encouraging appropriate use include cost sharing, consumer-driven health plans, diagnosis-related groups (DRGs), capitation, and use of specialty pharmacies to better manage oncology drug costs.

Cost sharing. In an effort to control plan premiums, employers are passing more of the premium cost to employees through higher copayments, coinsurance rates, and deductibles. In 2005, 56% of covered employees had to meet a deductible before coverage began, 36% had a separate deductible or copayment for inpatient care, and 10% had coinsurance for inpatient care (3% had both).[36] Additionally, in 2004, 97% of covered employees shared part of the cost for office visits, and 89% shared part of the cost for prescription drugs, typically in a tiered cost-sharing plan. Whereas most plans had 3-tiered pharmacy benefits, a few have gone to 4 or more. Oncology drugs administered in a specialist's office, however, are usually covered under the medical benefit.[37]

Consumer-driven health plans. These plans typically combine high-deductible plans with health savings accounts. The idea is to involve patients more in selecting their care and evaluating the quality of that care by requiring that they initially pay more out of pocket for that care. To help consumers in decision making, employers and health plans are providing data on the cost, quality, and efficiency of care. These data are being provided for the purpose of motivating consumers to use the most cost-effective and efficient providers and treatments.[38] Although just 16% of employers say they think these plans will rein in high healthcare costs, the number of employers offering these plans is expected to grow in the next few years.[36]

Mini-medical plans. An increasing number of employers are instituting so-called

"mini-medical" health insurance plans that limit coverage to a few physician visits per year, some pharmaceuticals, laboratory work, and other tests. But with annual payouts limited to $10 000 or less, they leave patients with no coverage for major illnesses, like cancer.[39]

Prior approval/utilization review. An increasing number of health plans have instituted utilization review and/or prior approval requirements for high-cost oncologic drugs, including those injectable and infusion drugs typically covered under the medical benefit. Prior authorization and utilization review programs may also be implemented for some oral and self-administered drugs covered under the pharmacy benefit. Requirements for prior approval may include diagnosis, previous therapies, and adherence to accepted clinical guidelines. In some health plans, a specialty pharmacy program handles any authorizations directly.[40,9]

Medicare Modernization Act

For years, oncologists have been the gatekeepers for many costly oncology drugs, purchasing injectable drugs from a small group of oncology drug distributors for administration in their office. They were then reimbursed based on the average wholesale price (AWP) for those drugs, plus a substantial markup for administrative costs (nursing care, storage, infusion, inventory management). In many instances, this led to significant profit for the practice, which often received substantial discounts off AWP from the distributor.[8] Oncology practices began to rely on this revenue stream to maintain the financial solvency of the practice.[9]

With the implementation of the Medicare Modernization Act (MMA) in 2005, this reimbursement method changed substantially. A provision within the MMA altered the way Medicare reimbursed oncologists for drugs administered in the office, including oncology drugs. Today, physicians are reimbursed based on the average sales price (ASP) for the drug plus 6%. To determine ASP, drug manufacturers are required to submit quarterly information on the total number of units purchased, wholesale acquisition cost, nominal sales price net of volume discounts, prompt pay discounts, cash discounts, free goods that are contingent on any purchase requirement, charge-backs, and most rebates. This information is used to determine the ASP for reimbursement.[41]

The MMA also required the establishment by January 1, 2006, of a "competitive acquisition program" in which physicians may choose to receive drugs and biologicals from competitively selected contractors. The contractors would collect applicable deductibles and coinsurance, with Medicare payments provided only for drugs and biologicals actually administered to eligible beneficiaries.[41]

Specialty Pharmacies

As Medicare moves to remove control of cancer drugs from oncologists' offices, so too are private health plans, with about 30% reporting that they planned to follow Medicare's lead in drug reimbursement and administrative fees.[9]

Consequently, more health plans are turning to specialty pharmacies, which have entered the market to provide oncology drugs. Specialty pharmacies typically deal only with drugs that require special handling or administration, have significant acquisition costs, reimbursement challenges, complex dosing requirements, and/or complicated clinical management. They ship medications throughout the United States to providers or patients and provide therapeutic oversight through case management and nursing services and, in some instances, 24-hour pharmacist services.[40]

In 2003, Michigan Blue Cross and Blue Shield contracted with 3 specialty pharmacies to offer a voluntary purchasing program for specialty drugs like oncology treatments administered in physician offices. The plan negotiates special discounts with the pharmacies and pays half the cost of the drugs. This initiative resulted in savings of more than $23 million on injectables (including noncancer drugs) in 1 year.[8] Health plan officials stated that flexibility and open communication with the plans' oncologists, rather than an adversarial perspective, was key to the program's success.

Other health plans reimburse oncologists who choose not to order through the special-

ty pharmacy program at the same rate as if the drugs were purchased through the plans' specialty pharmaceutical provider (SPP), or they permit the doctor to order drugs through the SPP and receive an administration fee.[9]

However, there are concerns over the growing use of specialty pharmacies to handle oncology drugs, including the quality of drugs provided, the SPP's ability to provide the best price and provide drugs on demand, the possibility of drug waste as unneeded medications spoil, and possible malpractice issues if oncologists administer products they did not personally purchase.[42]

Provider Reimbursement

In the past 20 years, government and private health insurers have moved from reimbursement-based payment systems to prepaid systems through the use of DRGs and capitation. Under DRGs, hospitals are paid a predetermined amount based on the patient's diagnosis; under capitation, physicians and/or outpatient centers are paid a set fee per patient per month based on the characteristics and size of the expected patient population. Hospitals and physicians are expected to provide all contracted services from the aggregate of capitation payments.

The effect of DRGs on the oncology realm can be seen primarily in the area of hospital services. For instance, a comparison of hospital lengths of stay (LOS) at Mount Sinai Hospital in New York City in the late 1990s found significantly reduced preoperative and postoperative LOS after DRGs were implemented for colorectal cancer surgeries. The reduced LOS was not related to any change in patient characteristics. In fact, the patients presented with slightly more advanced tumors. The difference, the researchers concluded, was that the DRG provided an incentive for the hospital to implement changes that reduced complications and other morbidities that could extend LOS, including operative blood loss, extensive procedures, and postoperative complications.[43]

Capitation

Some managed care organizations have tried to use capitated models to control oncology costs. In these arrangements, the provider assumes the bulk of the financial risk in providing services to patients, thus limiting the plan's financial risk.

The capitation approach raises special concerns for oncology. The philosophy underpinning capitation is that the larger the capitated patient population, the lower the provider's risk. But certain cancers have extremely low incidence rates, making the development of a fair capitation rate difficult. Additionally, the area of oncology calls for the use of unique technologies that are constantly changing, complicating equitable rate setting. With low incidence of disease, the observed variability in treatment across providers increases, as does the risk in treating a particular patient or subset of patients.[44]

Some contracts might handle this problem by excluding, or carving out, specific high-cost treatments, such as autologous bone marrow transplants, expensive new drugs, or special populations (eg, children), from the capitation rate calculation. Instead, services for the specific treatments or groups of patients might be paid on a fee-for-service basis. Other contracts might establish upper and lower limits of cost (risk corridors) outside of which a fee-for-service approach is instituted or other risk-sharing arrangements are used. These are similar to stop-loss or outlier provisions, which are more commonly offered under DRGs or global pricing case rates.

Other challenges in implementing capitation for oncology services include the variability in episodes of treatment for patients (newly diagnosed vs recurrent); adverse selection and retention (ie, the "best" practices will attract the sickest patients requiring the greatest levels of care); and variability of incidence within populations that require separate risk adjustment.

For these and other reasons, capitation for oncology services never gained large acceptance in the payer or provider communities. Instead, health plans attempt to manage costs for office services through discounted fee-for-service contracts and for outpatient services through discounted fee-for-service or diagnosis-based global pric-

ing, an adaptation of the inpatient DRG option.

Recent Economic Literature on Cancer Treatment

With each newly approved and typically expensive biologic drug, concern about the economics of cancer care grows. Abstracts on the economics of cancer treatments presented at the 2005 American Society of Clinical Oncologists meeting illustrate the continued movement toward an outcomes-based, pharmacoeconomic approach to evaluating cancer treatment.

Hassett et al evaluated the number, nature, and costs of serious adverse events affecting breast cancer patients receiving chemotherapy outside clinical trials.[45] The researchers used a database of medical claims for those with employer-provided health insurance to identify a cohort of women 63 years of age and younger with newly diagnosed breast cancer. Of 8749 women with breast cancer, 2352 (27%) received chemotherapy. Approximately half (51%) of the women treated with chemotherapy visited the emergency department or were admitted at least once within 6 months of diagnosis compared with 23% of women not receiving chemotherapy.[45]

The chemotherapy patients spent twice as long in the hospital and were more likely to have adverse events than the control group. The mean per patient expenditure over the 6-month observation period was $28 674 for chemotherapy recipients compared to $16 578 for the control group. This study shows the high cost of serious adverse drug events and suggests a role for oncology specialists, care managers, and health plans in reducing chemotherapy-related complications for younger, insured breast cancer patients.[45]

Pavlakis et al evaluated the cost effectiveness of pemetrexed to docetaxel for treating non–small-cell lung cancer.[46] Rather than focusing on direct medical costs, the outcome used was reduction in toxicity-related hospitalizations. Although median survival was similar for both treatments (8 months), researchers found an incidence of hospitalization due to adverse drug events of 7.1 admissions per 100 patients for pemetrexed versus 24.3 admissions per 100 patients for docetaxel. The incremental cost effectiveness to avoid 1 toxicity-related hospitalization was $15 754, suggesting a distinct advantage for pemetrexed.[46]

Cosler et al used risk and efficacy estimates from a meta-analysis of 14 randomized clinical trials (RCTs) to evaluate the economic impact of the use of prophylactic granulocyte colony-stimulating factors (pG-CSFs) to reduce the risk of febrile neutropenia in patients receiving chemotherapy. The analysis included direct US cost estimates for hospitalization and outpatient care. Researchers found that, relative to standard care, using pG-CSF reduced overall costs associated with moderately myelosuppressive chemotherapy.[47]

With 2 similar drugs with comparable outcomes, cost often becomes the determining factor in which to use. In evaluating such a case, Ben-Hamadi et al used data from 2 RCTs for epoetin alfa (EPO) and darbepoetin alfa (DARB) for the treatment of chemotherapy-induced anemia. Their analysis concluded that a 33% reduction in the price or dosage of DARB would be required to equal the cost of treatment with EPO.[48]

Younis et al compared 2 drug regimens for adjuvant chemotherapy in lung cancer: vinorelbine and cisplatin (VP) with paclitaxel and carboplatin (PC). The authors assumed comparable survival and similar quality-of-life outcomes for the 2 regimens. Based on this assumption, cost-minimization analysis was used to select the most efficient adjuvant chemotherapy. Younis et al incorporated the direct costs of the drugs, supportive medications, laboratory investigations, and health resources at a Canadian cancer center. Indirect costs, including patients' potential loss of income based on average wages for the region and participation rates, were estimated and included in the study. The analysis found that the higher direct costs associated with the PC regimen, primarily based on the cost of the drug were offset by other factors, such as less resource use and indirect patient costs.[49]

Meanwhile, the VP regimen had higher indirect costs, reflecting a higher opportunity cost from the longer chemotherapy

schedule required. When total treatment costs (direct and indirect) were compared, there was little difference between the 2 regimens. The VP regimen had an overall cost of $11 950, whereas the PC regimen had a total cost of $12 367 (Canadian dollars).[49] This study illustrates the importance of incorporating both direct and indirect costs when comparing treatment regimens.

Conclusion

Several forces have converged to increase the importance of oncology and oncology treatment for the payer and care management communities. The increased prevalence of cancer, improved survival, more effective and expensive treatments, and off-label use of many therapies have all highlighted the need to better manage oncology care and cost.

Historically, health plans have typically offered a rather generous oncology benefit. However, as the number and cost of new oncology therapies, especially biologics and genetically engineered agents, continue to grow, health plans will be challenged to find ways to continue the benefit in an accessible, affordable manner. Cost sharing by the patient in the form of higher copayments, deductibles, and coinsurance rates is almost certain to increase. Use of evidence-based drug formularies, prior authorization programs, specialty pharmacies, and benefit limits will be combined with data on the cost effectiveness of oncology regimens to craft a benefit that is accessible and affordable to the patient population.

Meanwhile, use of data from pharmacoeconomic and outcomes research studies has enhanced our understanding not only of the effective use of expensive oncology medicines, but also the efficient use of these agents. As the armamentarium of oncology treatments continues to grow, the need to understand the conditions under which these agents bring the most value must also be discerned. That is, providers must be able to determine the circumstances under which a particular drug or therapeutic regimen delivers a desired outcome at the lowest total cost.

Part of this decision-making process involves the use of practice guidelines from the National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO). Although such guidelines are designed to facilitate clinical decision making, it is difficult to avoid the issue of cost and efficiency of treatment given today's limited healthcare resources relative to the demand for care. Yet, it is unclear how oncology practice guidelines will incorporate evidence on the economic and humanistic dimensions of care.[50,51]

From a clinical perspective, it is easy to argue that treatments that improve quality of life and patient satisfaction add value and should be considered in reimbursement decisions. The far more difficult challenge, however, will be inclusion of relative treatment efficiency as a coverage criterion.

Nonetheless, organizations engaged in oncology practice guideline development recognize the need to discuss these issues. Evidence that the clinical-economic interface is a reality can be seen in the use of practice guidelines in reimbursement decisions. For instance, insurers are increasingly using NCCN practice guidelines in making coverage decisions, determining reimbursement levels, and implementing and managing quality assurance programs. Meanwhile, ASCO includes economic and humanistic data in its guideline development process, including cost-effectiveness and quality-of-life data as well as survival and toxicity data as part of primary and secondary outcomes.

However, the extent to which these economic factors will be formally incorporated into practice guidelines remains unclear. What is certain is that appropriate treatment must consider the efficient use of scarce resources. The economic question that should be addressed in developing practice guidelines is one of appropriate and efficient use of treatment regimens. The question is not whether to use or prohibit use of a treatment, but rather to understand, based on clinical, humanistic, and economic evidence, when to use it and under what specific circumstances.

REFERENCES

1. American Cancer Society. United States cancer statistics, 2002. Incidence and mortality. Available at: http://www.cdc.gov/cancer/npcr/uscs/index.htm. Accessed January 11, 2006.

2. Edwards BK, Brown ML, Wingo PA, et al. Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. *J Natl Cancer Inst.* 2005;97:1407-1427.

3. Cancer Trends Progress Report—2005 Update. Available at: http://progressreport.cancer.go. Accessed January 5, 2006.

4. Medicare Payment Advisory Commission. Report to the Congress: Medicare payment policy. Washington, DC: MedPAC; March 2001.

5. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med.* 2004;350:2335-2342.

6. Schrag D. The price tag on progress—chemotherapy for colorectal cancer. *N Engl J Med.* 2004;351:317-319.

7. Marcus AD. Price becomes factor in cancer treatment. *Wall Street Journal.* September 7, 2004:D1, D7.

8. Appleby C. Payers' costly battle against cancer. *Biotechnology Healthcare.* 2005;19-25.

9. MCOs' oncology strategies focus on provider issues for 2005. *Specialty Pharmacy News.* 2005;2:1-3.

10. Congialose CB, Blair, AE, Borchardt JS, et al. Purchasing oncology services. *Cancer.* 2000;88: 2876-2886.

11. Nadler ES, Eckert B, Neumann PJ. Do oncologists believe new cancer drugs offer good value? Abstract presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla. Abstract 6011.

12. Kozma CM, Reeder CE, Schulz RM. Economic, clinical, and humanistic outcomes: a planning model for pharmacoeconomic research. *Clin Ther.* 1993;15: 1121-1132.

13. Reeder CE, Kozma CM, McCollam AR. Overview of pharmaceutical outcomes, pharmacoeconomics, and quality of life. In: Ito SM, Blackburn SA, eds. *Principles and Practices of Managed Care Pharmacy.* Alexandria, Va: Academy of Managed Care Pharmacy; 1995: 103-112.

14. Smith C, Cowan C, Heffler S, Catlin A. National health spending in 2004: recent slowdown led by prescription drug spending. *Health Aff.* 2006;25:186-196.

15. Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group. National Health Expenditures. http://www.cms.hhs.gov/NationalHealthExpendData/02_NationalHealthAccountsHistorical.asp#TopOfPage. Accessed February 2, 2006.

16. Johnson N, Nash DB. Outcomes for P&T committees: where are we going? *P&T.* 1993:449-455.

17. Bennett CL, Lee T. Economic analysis of cancer treatment. In: Abeloff M, Armitage J, Niederhuber J, Kasta M, McKenna WG, eds. *Clinical Oncology,* 3rd ed. Edinburgh, UK: Churchill Livingstone; 2004:395-401.

18. Tengs TO. Cost effectiveness versus cost-utility analysis of interventions for cancer: does adjusting for health-related quality of life really matter? *Value Health.* 2004;7:70-78.

19. Schulman KA, Yabroff KR. Measuring the cost-effectiveness of cancer care. *Oncology (Williston Park).* 1995;9:523-530,533; discussion 533-528.

20. Berkowitz N, Gupta S, Silberman G. Estimates of the lifetime direct costs of treatment for metastatic breast cancer. *Value Health.* 2000;3:23-30.

21. Chang S, Long SR, Kutikova L, et al. Estimating the cost of cancer: results on the basis of claims data analyses for cancer patients diagnosed with seven types of cancer 1999 to 2000. *J Clin Oncol.* 2004;22: 3524-3530.

22. Luce BR, Elixhauser A. *Standards for the Socioeconomic Evaluation of Health Care Services.* New York, NY: Springer-Verlag; 1990:57-60.

23. Calhoun EA, Chang CH, Welshman EE, Fishman DA, Lurain JR, Bennett CL. Evaluating the total costs of chemotherapy-induced toxicity: results from a pilot study with ovarian cancer patients. *Oncologist.* 2001;6:441-445.

24. Turini M, Redaelli A, Gramegna P, Radice D. Quality of life and economic considerations in the management of prostate cancer. *Pharmacoeconomics.* 2003;21:527-541.

25. Radice D, Redaelli A. Breast cancer management: quality-of-life and cost considerations. *Pharmacoeconomics.* 2003;21:383-396.

26. Brown MM. Health care economic analyses. *Curr Opin Ophthalmol.* 2003;21:527-541.

27. Detmar SB, Muller MJ, Schornagel JH, Wever LD, Aaronson NK. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. *JAMA.* 2002;288:3027-3034.

28. Drummond MF, O'Brian B, Stoddart GL, et al. *Methods for the Economic Evaluation of Healthcare Programmes.* 2nd ed. New York, NY: Oxford University Press; 1997.

29. Ortega A, Dranitsaris G, Sturgeon J, Sutherland H, Oza A. Cost-utility analysis of paclitaxel in combination with cisplatin for patients with advanced ovarian cancer. *Gynecol Oncol.* 1997;66:454-463.

30. Clegg A, Scott DA, Sidhu M, Hewitson P, Waugh N. Rapid and systematic review of the clinical effectiveness and cost-effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non-small cell lung cancer. *Health Technol Assess.* 2001;5:1-195.

31. Cantor SB, Fahs MC, Mandelblatt JS, Myers ER, Sanders GD. Decision science and cervical cancer. *Cancer.* 2003;98:2003-2008.

32. Parmigiani G. Measuring uncertainty in complex decision analysis models. *Stat Methods Med Res.* 2002;11:513-537.

33. Secic M, Lang T. *How to Report Statistics in Medicine: Annotated Guidelines for Authors, Editors and Reviewers.* Philadelphia, Pa: American College of Physicians; 1997.

34. Lee JH, Glick HA, Hayman JA, Solin LJ. Decision-analytic model and cost-effectiveness evaluation of post-mastectomy radiation therapy in high-risk premenopausal breast cancer patients. *J Clin Oncol.* 2002;20: 2713-2725.

35. Sanders GD, Taira AV. Cost-effectiveness of a potential vaccine for human papillomavirus. *Emerg Infect Dis.* 2003;9:37-48.

36. Kaiser Family Foundation and Health Research and Educational Trust. Employer Health Benefits: 2005 Summary of Findings: Menlo Park, Calif; 2005.

37. Kaiser Family Foundation and Health Research and Educational Trust. Employer Health Benefits, 2004 Annual Survey Exhibit 7.1. September 2004. Available at: http://www.kff.org/insurance/7148/index.cfm. Accessed January 30, 2006.

38. McGivney WT, Mullen J. Cancer and managed care in the 21st century. *Am J Manag Care.* 2005;11(suppl 17):S509-S521.

39. Fuhrmans V. More employers try limited health plans. *Wall Street Journal.* January 17, 2006:D1.

40. Kaa K, Haenni B, Lopez T. Balancing payer policies with oncology practice management. *Hematology Oncology News & Issues.* 2002:12-13,16-17, 34.

41. Centers for Medicare & Medicaid Services. *CMS Legislative Summary*. April 2004 Summary of H.R.1 Medicare Prescription Drug, Improvement, and Modernization Act of 2003; Public Law 108-173. Available at: http://www.cms.nhs.gov/MMAUpdate/downloads/PL108-173Summary.pdf. Accessed February 2, 2006.

42. Holcombe DG. Is oncology compatible with specialty pharmacy? *Community Oncology.* 2005;2:173-181.

43. Schwartz MH, Tartter PI. Decreased length of stay for patients with colorectal cancer: implications of DRG use. *J Healthc Qual.* 1998;20:22-25.

44. Kurowski B. Cancer carve outs, specialty networks, and disease management: a review of their evolution, effectiveness, and prognosis. *Am J Manag Care.* 1998;5:SP71-SP89.

45. Hassett MJ, Pakes J, O'Malley AJ, Newhouse JP, Earle CC. Chemotherapy-related serious adverse events and health care expenditures among commercially insured women with breast cancer. Presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla.

46. Pavlakis N, Mitchell PL, Stynes G, et al. Cost-effectiveness of pemetrexed for previously treated advanced non-small cell lung cancer. Presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla.

47. Cosler LE, Eldar-Lissai DC, Dale J, Crawford G, Lyman H. Economic analysis of pegfilgrastim in patients receiving cancer chemotherapy. Abstract presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla. Abstract 60410.

48. Ben-Hamadi R, Duh MS, Henckler A, McKenzie S, Fastenau J, Tak Piech C. Cost-effectiveness of once weekly epoetin alfa and darbepoetin alfa in treating chemotherapy-induced anemia. Abstract presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla. Abstract 6093.

49. Younis T, Skedgel C, Sellon M, et al. Economic evaluation of two adjuvant chemotherapy regimens in lung cancer: vinorelbine and cisplatin versus paclitaxel and carboplatin. Abstract presented at: American Society of Clinical Oncology; May 13-17, 2005; Orlando, Fla. Abstract 6076.

50. American Society of Clinical Oncology. Clinical Guidelines. Available at: http://www.asco.org/ac/1,1003,_12-002009,00.asp. Accessed January 24, 2006.

51. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Available at: http://www.nccn.org/professionals/physican_gls/default.asp. Accessed January 24, 2006.