

Assessing Human and Economic Benefits of Cancer Prevention

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It is critically important to discuss and attempt to quantify the human and economic value of cancer prevention. The purpose of this chapter is to provide an overview of the ways in which this value can be defined and assessed. As will be described in much more detail in subsequent chapters, cancer prevention takes many forms. At the individual level, virtually all prevention activities involve: (1) engaging in particular behaviors (e.g., following screening and immunization recommendations, taking tamoxifen for secondary prevention of breast cancer); (2) avoiding particular behaviors (e.g., sunbathing, smoking); or (3) changing particular behaviors once they have become habitual or routine (e.g., quitting smoking, lowering dietary fat). Each of these prevention behaviors, or the lack of them, can have short- and long-term health, quality of life, and/or economic consequences.

2.1 Outcomes Assessment

In order to discuss the impact of cancer and, hence, the substantial benefits of preventing it, it is necessary to define *outcomes*. A conceptual framework articulated by Kozma and colleagues places outcomes into three categories: economic, clinical, and humanistic (Kozma et al. 1993). Economic outcomes are changes in the consumption and production of resources caused by disease or intervention, such as cancer prevention. The changes may be direct (e.g., cost of a medication) or indirect (e.g., early retirement due to reduced productivity). Clinical outcomes are the medical events that occur as a result of the condition or its treatment as measured in the clinical setting. Humanistic, or patient-reported, outcomes include condition or intervention-related symptoms and side effects, treatment satisfaction, health status, and self-assessed function and well-being, or health-related quality of life.

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The major cancer clinical trial cooperative groups in North America and Europe have recognized the importance of this outcomes triad in evaluating and improving the net benefit of cancer therapy (Bruner et al. 2004). Humanistic and economic outcomes, which are the focus of this chapter, are increasingly being incorporated into clinical trials (Lipscomb et al. 2004). In addition, the importance of outcomes assessment in cancer was reinforced with the National Cancer Institute's (NCI) establishment of its Outcomes Research Branch in 1999 (Lipscomb and Snyder 2002) and the Cancer Outcomes Measurement Working Group in 2001 (Lipscomb et al. 2005). According to the NCI, "outcomes research describes, interprets, and predicts the impact of various influences, especially (but not exclusively) interventions on 'final' endpoints that matter to decision makers: patients, providers, private payers, government agencies, accrediting organizations, or society at large" (Lipscomb and Snyder 2002).

2.2 Humanistic Outcomes

As mentioned above, humanistic or patient-reported outcomes (PROs) include a wide range of health-related concepts or constructs. According to the US Food and Drug Administration (FDA), PROs are on a continuum from the purely symptomatic (e.g., pain intensity) to more complex aspects of functioning (e.g., ability to perform activities of daily living) to much more complex concepts (e.g., quality of life) (FDA 2006). Since many cancer prevention activities are aimed at populations rather than individual patients, the term PRO in the context of this chapter may seem too narrow; however, the intent is to convey the importance of capturing individual's health and health care perceptions and experiences through self-report. The PRO that has increasingly garnered the most attention, particularly in regard to drug therapy (Willke et al. 2004; European Medicines Agency 2005), is health-related quality of life, which will be a primary focus of this section.

Quality of life is a commonly used term that usually conveys a general feeling rather than a specific state of mind. A person's quality of life, or subjective well-being, is based on personal experience and expectations, that affect and can be influenced by many factors, including standard of living, family life, friendships, and job satisfaction (Sirgy et al. 2006). Although health can impact these factors, health care is not directly aimed at enhancing them. Studies of health outcomes use the term *health-related quality of life* to distinguish health effects from the effects of other important personal and environmental factors. There is growing awareness that in certain diseases, such as cancer, or at particular stages of disease, health-related quality of life may be the most important health outcome to consider in assessing the effect of interventions (Staquet et al. 1992).

In much of the empirical literature, explicit definitions of health-related quality of life are rare; readers must deduce its implicit definition from the manner in which its measurement is operationalized. However, some authors have provided definitions. For example, Revicki and colleagues define health-related quality of life as "the subjective assessment of the impact of a disease and treatment across physical, psychological, social, and somatic domains of functioning and well-being" (Revicki et al. 2000, p. 888).

Ferrans (2005) has provided a useful overview of various definitions and conceptual models of health-related quality of life. Definitions may differ in certain respects, but an important conceptual characteristic they share is multidimensionality. Essential dimensions of health-related quality of life include:

- › Physical health and functioning
- › Psychological health and functioning
- › Social and role functioning

In addition, disease- and/or treatment-related symptomatology (e.g., pain), general well-being, and spiritual well-being are sometimes assessed. The latter is more likely to be included in measures developed for conditions that have the potential to impact not only quality of life but length of life as well (e.g., cancer). For example, the four-dimensional model that provides the framework for the cancer-related quality of life questionnaires developed at the City of Hope National Medical Center includes spiritual well-being along with physical, psychological, and social well-being (Grant et al. 2004).

2.3 Measuring Health-Related Quality of Life and Other Patient-Reported Outcomes

Although PROs such as health-related quality of life are subjective, they can be quantified (i.e., measured) in a uniform and meaningful way. The quality of the data-collection tool is the major determinant of the quality of the results. Psychometrics refers to the measurement of psychological constructs, such as knowledge, attitudes, and well-being. It is a field of study concerned with the proper development and testing of instruments (e.g. questionnaires) so that confidence can be placed in the measurements obtained. Two of the most commonly assessed psychometric properties are reliability and validity. Briefly, reliability refers to the consistency, stability, or reproducibility of scores obtained on a measure; validity reflects whether the instrument actually measures what it is purported to be measuring. More thorough discussions of these properties are provided elsewhere (Streiner and Norman 2003; Frost et al. 2007). Anyone planning to use PRO measures in cancer prevention research or clinical practice should confirm that there is adequate evidence to support the reliability and validity of the measures chosen.

Cullen and colleagues, in their review the short-term quality of life impact of cancer prevention and screening activities, addressed ways in which outcomes have been assessed through the use of new and existing measures (Cullen et al. 2004). Since many of the outcomes were exclusively psychological states (e.g., anxiety, relief) or symptoms, they cannot be considered assessments of health-related quality of life. Measures of health-related quality of life should include, at a minimum, the three essential dimensions (i.e., physical, psychological, social) recognized as comprising it. Nevertheless, the review by Cullen and colleagues and another by Mandelblatt and Selby (2005) provide important insight into the research that has been conducted to assess the short-term patient-reported

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consequences of clinical preventive services such as chemoprevention, genetic testing and counseling, and screening. Knowledge of these consequences is critical in attempting to understand and act upon the factors that may affect participation in prevention-related activities. Although it remains an empirical question, it appears that the predominantly transient negative consequences of participating in cancer prevention activities would be readily offset by the positive long-term outcomes (e.g., avoidance of quality of life losses resulting from cancer-related morbidity). As asserted by Badia and Herdman (2001), preventive interventions are unlikely to lead to gains in quality of life, but should prevent or delay reductions in quality of life over time.

A specific example of PRO assessment in the context of cancer prevention is provided by the National Surgical Adjuvant Breast and Bowel Project (NSABP) Study of Tamoxifen and Raloxifene (STAR) P-2 Trial (Land et al. 2006). The STAR P-2 Trial was designed to evaluate the relative efficacy of the two study drugs in reducing the incidence of invasive breast cancer in high-risk post-menopausal women. The investigators used a number of measures to compare patient outcomes by treatment arm, including the Center for Epidemiological Studies Depression Scale (CES-D), the Medical Outcomes Study (MOS) Sexual Activity Questionnaire, a 36-item symptom checklist, and the MOS 36-Item Short-Form Health Survey (SF-36). This battery of multiple instruments and scales enabled the investigators to assess the PROs they felt were most relevant in the target population. The health-related quality of life end points were the physical (PCS) and mental component summary (MCS) scores of the SF-36. The SF-36 will be discussed in more detail below.

There are hundreds of PRO instruments currently available (Bowling 1997; McDowell 2006), some of which have been developed for use in people with cancer (Bowling 2001; Donaldson 2004) or for individuals undergoing cancer screening (Mandelblatt and Selby 2005). The Psychosocial Effects of Abnormal Pap Smears Questionnaire (PEAPS-Q) (Bennetts et al. 1995) and the Psychosocial Consequences Questionnaire for abnormal screening mammography (PCQ-DK33) (Broderson et al. 2007) are examples of PRO measures specifically developed for cancer-related clinical preventive services. However, the vast majority of available PRO measures were developed for use in people already experiencing disease and/or disability. The value of these measures in the context of cancer prevention is that they provide quantitative evidence of the losses in functioning and well being that may be avoided by effective prevention strategies. A primary distinction among PRO instruments, particularly measures of health-related quality of life, is whether they are specific or generic.

2.3.1

Specific Measures

The pioneering work of Karnofsky and Burchenal in the 1940s that produced the Karnofsky Performance Scale recognized the need to assess the patient's functional status in the context of cancer chemotherapy (Karnofsky 1949). This tool, which was designed for clinician assessment of observable physical functioning, is still used today. It was one

EORTC QLQ-C30	FACT-G
Physical functioning	Physical well-being
Role functioning	Social/family well-being
Cognitive functioning	Emotional well-being
Emotional functioning	Functional well-being
Social functioning	
Fatigue	
Global quality of life	
Nausea and vomiting	
Pain	

Table 2.1 Domains/dimensions addressed by the FACT-G and EORTC QLQ-C30

of the first steps in the development of patient-centered and, ultimately, patient-reported outcome measures. Since then, a considerable amount of time and effort has been invested in the development of cancer-specific instruments for use in clinical trials and routine patient monitoring. Another of these instruments is the Q-TWiST (Quality-Adjusted Time Without Symptoms and Toxicity), which addressed both quality and quantity of time following cancer treatment (Gelber et al. 1993). Other examples are the EORTC QLQ-C30 (Aaronson et al. 1993) and the Functional Assessment of Cancer Therapy-General (FACT-G) (Cella et al. 1993). The European Organization for Research and Treatment of Cancer (EORTC) has worked extensively in the area of instrument development (www.eortc.be/home/qol). In addition, the developers of the FACT-G have a broad array of cancer-specific instruments available (www.facit.org). Table 2.1 lists the dimensions covered by the EORTC QLQ-C30 and the FACT-G. Each of these instruments was designed to be supplemented with additional modules or scales aimed at specific cancer patient subgroups.

Cancer-specific instruments such as these are intended to provide greater detail concerning particular outcomes, in terms of functioning and well-being, uniquely associated with a condition and/or interventions to treat or prevent it. Disease- or condition-specific instruments may be more sensitive than a generic measure to particular changes in health-related quality of life secondary to the disease or its treatment. For example, the Functional Assessment of Cancer Therapy (FACT) subscales, such as the neurotoxicity subscale (FACT-NTX), address specific concerns (e.g., finger numbness, difficulty buttoning), which would not be addressed in a generic instrument. In addition, specific measures may appear to be more clinically relevant to patients and health care providers since the instruments address issues directly related to the disease (Guyatt et al. 1993). However, a concern regarding the use of only specific instruments is that by focusing on the specific impact of a disease or its treatment, the general or overall impact on functioning and well-being may be overlooked. Therefore, the use of both a generic and a specific instrument may be the best approach. This was the approach taken by the developers of the UCLA Prostate Cancer Index, which covers both general and disease-specific (e.g., sexual, urinary and bowel function) concerns (Litwin et al. 1998).

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2.3.2

Generic or General Measures

Since primary cancer prevention involves avoiding the occurrence of disease, general measures may be more applicable in that context. Generic, or general, instruments are designed to be applicable across a wide variety of populations, across all diseases or conditions, and across different medical interventions (Patrick and Deyo 1989). The two main types of generic instruments are health profiles and preference-based measures.

Health Profiles. Health profiles provide multiple outcome scores representing individual dimensions of health status or health-related quality of life. An advantage of a health profile is that it enables clinicians and/or researchers to measure the differential effects of a disease state or its treatment on particular dimensions. The most commonly used generic instrument in the world today is the SF-36 (www.sf36.org), which was used as a component of the STAR P-2 Trial discussed above. The SF-36 includes eight multi-item scales (Table 2.2) which address a wide array of dimensions (Ware and Sherbourne 1992). Each of the scale scores can range from 0 to 100, with higher scores representing better functioning or well-being. It is brief (it takes about 10 min to complete) and its reliability and validity have been documented in many clinical situations and disease states (Ware 2000). A means of aggregating the items into physical (PCS) and mental component summary (MCS) scores is available (Ware 1994). However, the SF-36 does not provide an overall summary or index score, which distinguishes it from the preference-based measures.

Preference-Based Measures. For health-related quality of life scores to be most useful as an outcome in economic analysis, they need to be on a scale anchored by 0.0 (i.e., death) and 1.0 (i.e., perfect health). The values for the health states represented on the scale reflect the relative desirability or preference level for individual health states as judged by population- or patient-based samples. Although one can undertake direct preference measurement, a number of preference-based instruments are already available for which the health state preferences have been derived empirically through population studies. Examples include the Health Utilities Index (HUI) (www.healthutilities.com), the Euro-QoL Group's EQ-5D (www.euroqol.org), and the SF-6D (www.sf36.org). The SF-6D was developed to provide a preference-based overall summary or index score for data collected with the SF-36 (Brazier et al. 2002). The domains addressed by each of these instruments are listed in Table 2.2.

Quality-Adjusted Life Years (QALYs). The preference-based instruments described above are administered to assess respondents' self-reported health status, which is then mapped onto the instrument's multiattribute health status classification system producing a health-related quality of life score on the 0.0–1.0 scale. Scores on this scale, which may represent the health-related consequences of disease or its treatment, can be used to adjust length of life for its quality resulting in an estimate of *quality-adjusted life years* (QALYs). QALYs integrate in a single outcome measure the net health gains or losses, in terms of both quantity and quality of life. The metric of life-years saved (LYS) is not sufficient since death is not the only outcome of concern; health-related quality of life changes can occur with or without changes in life years. The QALY approach assumes that one year in full health is scored 1.0 and death is 0.0. Years of life in less than full health are scored as less

Table 2.2 Domains included in selected generic instruments

SF-36	
Physical functioning Role limitations due to physical problems Bodily pain General health perceptions Vitality Social functioning Role limitations due to emotional problems Mental health	
Quality of well-being scale (QWB)	
Mobility Physical activity Social activity Symptoms/problems	
Health utilities index (HUI)	
HUI2	HUI3
Sensation	Vision
Mobility	Hearing
Emotion	Speech
Cognition	Ambulation
Self-care	Dexterity
Pain	Emotion
Fertility	Cognition
	Pain
EQ-5D	
Mobility Self-care Usual activity Pain/discomfort Anxiety/depression	
SF-6D	
Physical functioning Role limitation Social functioning Mental health Bodily pain Vitality	

than 1.0 QALY. For example, based on a review by Tengs and Wallace, a year of life with small-cell lung cancer after the disease has progressed is equal to 0.15 QALY (Tengs and Wallace 2000).

QALYs can be a key outcome measure, especially in diseases such as cancer, where the treatment itself can have a major impact on patient functioning and well-being. Although the QALY is the most commonly used health outcome summary measure, it is not the only

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one (Gold et al. 2002). Other conceptually equivalent outcomes include *years of healthy life* (YHL), *well years* (WYs), *health-adjusted person years* (HAPYs), and *health-adjusted life expectancy* (HALE). As observed by Ubel, without an outcome measure such as QALYs, it would be impossible to compare the relative cost-effectiveness of life-prolonging versus life-enhancing interventions, much less interventions that do both (Ubel 2001). The remainder of this chapter discusses the economic issues and methodologies relevant to cancer prevention.

2.4

Economic Outcomes and Cancer

Prevention of cancer renders an economic benefit for society by reducing the amount of resources necessary for the treatment of cancer. The NCI reports that cancer treatment accounted for \$41 billion in 1995, just under 5% of total U.S. spending for medical treatments (NCI 2004). By investing in cost-saving cancer prevention modalities, more resources may be available for the overall health care system. Johnson and colleagues estimate that 53% and 13% of the medical expenditures for persons with lung cancer and chronic obstructive pulmonary disease are attributable to smoking, respectively (Johnson et al. 2003). Substantial medical resources would become available, if smoking were reduced.

Economic benefits rendered by improving health go beyond the costs associated with medical treatments. The economic benefits of cancer prevention include decreases in the frequency of health-related disruptions in productive activity, such as lost work days. By promoting health, cancer prevention reduces the need for assistance with personal care services and allows greater intangible benefits, like dignity, autonomy, and individuality. Simply put, prevention is better than cure because, as stated by Thomas Adams, a seventeenth century physician, it saves the labor of being sick.

Although the economic benefits of cancer prevention are widely acknowledged, especially by NCI, there is a paucity of evidence regarding these benefits. The information regarding economic outcomes that is available is rarely translated for and applied to evidence-based medical decision making. As a result, cancer prevention is often inefficiently utilized. Researchers who study the economic outcomes of cancer prevention provide valuable information to individuals and institutions, who may fail to consider the full scope of the economic benefits (Fryback and Craig 2004). For example, the vaccination of girls against human papillomavirus (HPV) may be justified on grounds of improved health and cost savings; however, the case for boys, who may be future carriers of the cancer-causing virus, require deliberation over whether the marginal benefits is worth the high cost in terms of cancer resources (Elbasha et al. 2007).

Decision makers at the individual, institutional, or governmental levels require evidence on economic outcomes of cancer prevention to improve their ability to make informed choices with regard to prevention activities, thereby maximizing limited resources. In this section, we describe core concepts in economic outcomes research and provide examples to illustrate their importance.

2.5

Defining and Measuring Economic Outcomes

Every cancer prevention strategy entails a change in the use of scarce resources, also known as an economic outcome. If we were to list the resources necessary to produce an intervention and the resources saved due to the intervention, we would have a description of the net bundle of resources attributable to the intervention. This bundle is known as the intervention's *opportunity cost*. Once the intervention is undertaken, the opportunity to use these resources differently is lost. Consideration of the economic outcomes associated with interventions is important for individuals and institutions that practice evidence-based medicine.

Economic outcomes, changes in resources due to an intervention, may be categorized by system, path, and flow. Resources from the medical system, such as physician time, medications, and hospital beds, are distinguished from non-medical resources, such as community, familial, and personal goods. For example, fuel consumption by an ambulance is a medical outcome, whereas fuel for personal transportation to a clinic is a non-medical outcome. Medical and non-medical resources are differentiated, because each system faces different budgetary constraints.

Economic outcomes are also separated by their path, whether they are directly related to an intervention or indirectly related through a change in health caused by the intervention. For example, a nicotine patch may be consumed as part of a smoking cessation intervention, therefore a direct economic outcome of the intervention. The patch may change smoking-related behaviors, such as smoking breaks at work. Changes in productivity are indirect economic outcomes of the intervention. The direct and indirect outcomes are components of the smoking cessation program's opportunity cost. The concept of indirect and direct economic outcomes is unrelated to the accounting term "indirect costs" referring to overhead or fixed costs.

Economic outcomes represent an inflow of resources through consumption or an outflow of resources through production. Patients directly consume medical resources over the course of an intervention, but patients are also producers of resources. Smoking cessation programs change the consumption of resources, such as cigarettes, nicotine replacement medications, and counseling. These programs may also affect the productivity of individuals, either by making their lives more productive, or by extending their productive lives. When considering the economic benefits of cancer prevention, the effect on the consumption of current resources may be small compared to the benefits in terms of productive activities. Economic outcomes can be characterized as medical or non-medical, direct or indirect, and an inflow or outflow of resources.

Unit of Economic Outcomes. Economic outcomes are best measured in natural units. Natural units often appear in the form of number of hours, quantities of a specific medication, or distance traveled. Natural units describe the changes in the inflow and outflow of resources related to the intervention. Clinical-economic trials, which are randomized controlled trials that prospectively collect economic endpoint data, provide the strongest evidence on economic outcomes, because these trials randomly assign alternatives to participants to identify causality. In a prospective substudy of a randomized clinical

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trial, Sculpher and colleagues (Sculpher et al. 2000) evaluated alternative drug therapies, reititrexed and fluorouracil with folinic acid, for advanced colorectal cancer based on the number of trips made to and from the hospital and the time lost from usual activity over the therapy period. In their study, they examined medical records for medical resource consumption data and self-report data to assess travel mode, distance, and time. This is an excellent example of a clinical-economic trial that collected economic endpoint data in natural units. These natural units can be translated into monetary values according to the perspective of the decision maker.

In economics, price is cost plus marginal profit, but outside of economics, price is often confused with cost and charges. Price represents the market value of a good, if sold. If the objective of the study is to predict revenue (or expenditure), natural units are to be translated using market values (i.e., prices). Market values fluctuate over time or region, according to market forces. If the objective is to predict cost of an intervention, natural units are to be translated according to the cost of producing those resources. The cost of producing resources may also depend upon market price of the inputs necessary for resource production. For example, a mammogram may cost a provider organization \$50 to produce, but they set a price of \$75, because that is what the market will bear. The difference between price and cost, \$25, is the marginal profit for the health organization. The inclusion and extent of marginal profit in the translation of natural units into monetary values depends on the perspective of the decision maker. The reasonable amount of profit on a mammogram for a clinic is up for interpretation.

A charge is a payment of a claim, the rightful reimbursement for the provision of goods and services according to a contract. It is neither a price nor a cost, because of its dependence on the contractual relationship between institutions. For example, managed care organizations often shift funds between services, overcharging for specialist visits to subsidize mammography under the same contract. Unlike prices, the charge for one resource may depend on the charges for other resources under the same contract. This dependent relationship makes it difficult to interpret endpoints measured through charges. However, it is well-documented that charges exceed cost in most circumstances. The economic outcomes may be represented in monetary terms, such as costs, prices, and charges, depending on perspective. However, it is important the perspective of the translation (i.e., unit of analysis) match the perspective of the decision maker, so that they may practice evidence-based medicine.

Perspective of Economic Outcomes. The monetary value of an economic outcome depends on the perspective of the decision maker (e.g., individual, institutional, societal). Individuals face different prices (or costs) than institutions, so they translate natural units into monetary values differently. The societal perspective considers the economic outcome borne by all individuals, and uses market value to translate natural units into monetary values. For example, the monetary value of an hour of a physician's time may be equal to a copayment from a patient's perspective, an institution-specific wage from a managed care organization's perspective, or a market wage from the societal perspective.

Differing perspectives may lead decision makers to disagree on policies regarding cancer prevention. Smoking cessation programs have medical and non-medical economic outcomes. Medical outcomes attributable to certain programs may entail a monetary loss from the perspective of a managed care organization. After incorporating the non-medical

outcomes, the programs may appear to save resources from the societal perspective. Disagreement between governmental and institutional decision makers over the economic consequences of smoking cessation programs are related to the translation of natural units into monetary values. Furthermore, societal and institutional perspectives often disagree about the inclusion of institutional profit in the translation.

2.6

Evaluative and Descriptive Analyses in Cancer Prevention

The economic benefits of cancer prevention are commonly described as a matter of investment in health (Wagner 1997). By investing medical resources in cancer prevention today, substantial economic benefits may accrue in the future. The purpose of evaluative analyses in cancer prevention is to examine the economic and health outcomes of alternative interventions, so that decision makers may better understand the potential impact of cancer prevention. There are four forms for economic evaluation: cost-minimization, cost-effectiveness, cost-utility, and cost-benefit. In addition, there are also descriptive studies that present economic outcomes of alternative interventions and disease, but do not directly compare health and economic outcomes. Descriptive analyses include cost-of-illness, cost identification, and cost-consequence studies. In this section, examples of evaluative and descriptive analyses in cancer prevention are provided.

Economic Evaluations. To promote evidence-based medical decision making, economic evaluations present the economic and health outcomes of alternative interventions. If an intervention costs more and is less effective than another intervention, the choice between the two interventions is clear. However, in many cases, the dominance of one intervention over another may depend on the relative importance of economic and health outcomes. For example, an intervention may cost more and be more effective or cost less and be less effective relative to another intervention. Economic evaluations verbally or quantitatively summarize the evidence to inform such difficult decisions.

The four types of economic evaluations (cost-minimization, cost-effectiveness, cost-utility, and cost-benefit) measure economic outcomes in monetary units, but each handles health outcomes in different ways. In cost-minimization studies, health outcomes are not measured, but assumed. For example, if two prevention interventions are known to have equivalent health outcomes, a study may examine which use the least amount of medical resources to minimize the cost to the health care system. Cost-effectiveness, cost-utility, and cost-benefit evaluations measure health outcomes, but using different units. Health outcomes in cost-effectiveness analyses are measured in natural units, such as number of life years saved. Cost-utility analyses use QALYs and cost-benefit analyses use monetary units, such as dollars. It can be difficult to translate health outcomes into QALYs or monetary units, so the typical form of economic evaluation is a cost-effectiveness analysis.

To summarize the evidence, cost-effectiveness and cost-utility analyses separate out the difference in cost and effectiveness between interventions and examine their ratio, known as an incremental cost-effectiveness ratio (ICER). This ratio measures the amount of resources required for each unit of health outcome (i.e., the amount of dollars required to

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increase life expectancy by one day). The ratios can be difficult to interpret because a positive value may signify an increase in cost and an increase in effectiveness, or a decrease in cost and a decrease in effectiveness. An intervention that saves money may have the same ratio as one that requires additional resources, so it is important to look at both the ratio and budgetary implications of the choice.

Cost-effectiveness analyses of cancer screening are commonplace, particularly in the cervical cancer literature (Eddy 1990; Kulasingam and Myers 2003; Goldie et al. 2004). Brown and Garber examined three cervical screening technologies (ThinPrep, AutoPap, and Papnet) among a cohort of 20–65-year-old women from the societal perspective (Brown and Garber 1999). Outcomes of interest, including life expectancy and lifetime direct medical cost, were compared among the three technologies and between each technology and conventional Pap at various intervals. The authors found that, depending on the technology and frequency of screening, these technologies increased life expectancy by 5 h to 1.6 days and increased cost by \$30–\$257 (1996 U.S. dollars) relative to conventional Pap. In this case, small increases in life expectancy are related to small increases in cost. When used with triennial screening, each technology produced more life years at a lower cost relative to conventional Pap used with biennial screening. In other words, conventional Pap used with biennial screening is dominated by each technology used with triennial screening. Among the new technologies, AutoPap dominated ThinPrep, but Papnet cost \$43 more and produced 0.11 additional days of life expectancy. The incremental cost-effectiveness ratio, \$391 (\$43/0.11) per day of life saved, suggests that if society values a day of life more than \$391 then Papnet may be preferred over AutoPap. The analysis does not account for nonmedical or indirect costs and examines only life expectancy, excluding the potential burden of cancer in terms of quality of life.

Compared to cost-effectiveness analyses, cost-utility analyses have the advantage of being able to combine multiple health and clinical outcomes into QALYs. Two cost-utility analyses of cervical cancer screening have estimated health outcomes in terms of QALYs (Goldie et al. 1999; Mandelblatt et al. 2002). Goldie and colleagues assess alternative screening strategies in HIV-infected women and Mandelblatt and colleagues examine combinations of conventional Pap and HPV testing at various intervals among a longitudinal cohort of women beginning at age 20 and continuing until age 65, 75 or death. In breast cancer screening, Tosteson and colleagues compared digital and film mammography and found that using all-digital mammography is not cost-effective (Tosteson et al. 2008).

Due to their complexity in measurement and modeling, economic evaluations may be difficult to interpret and assess in terms of study quality. Their summary of the evidence is similar to a quantitative literature review, yet they often involve the prospective collection of primary data, particularly use and cost outcomes (e.g., clinical-economic trials). Guidance for the *Journal of Clinical Oncology*, put forth by Levine and colleagues (2007), identifies five key questions, which readers may ask when reviewing a study: (1) Is the question being evaluated relevant? (2) Does the study compare the appropriate alternative interventions? (3) Is the quality of the data high (e.g., economic endpoints in a clinical trial)? (4) Does the study interpret both the efficiency (i.e., cost-effectiveness) and budgetary implications? (5) Lastly, was the study sponsored by organizations without potential conflicts of interest? Like with clinical trials, a negative response to any of these questions requires greater care in the interpretation of the evidence.

Evidence on economic outcomes is not meant to dictate the choice among alternative interventions. It is only one consideration among many possible considerations. Economic evaluations are conducted to assist policy makers in their deliberation over access to cost-effective cancer prevention strategies by providing evidence on the potential impact of the alternative strategies. In the absence of evidence-based policy, cancer prevention resources may not be allocated efficiently according to the perspectives of the decision makers.

Descriptive Studies. Cost-of-illness studies compare economic outcomes by disease and cost-identification studies examine the difference in economic outcomes across alternative interventions. Taplin and colleagues (Taplin et al. 1995) conducted a cost-of-illness study and evaluated the direct cost of treating colon, prostate, and breast cancer. Their results suggest that the direct cost of cancer treatment increases with stage of diagnosis. Tsao and colleagues estimated that the cost of treating a patient with stage III or stage IV cutaneous melanoma is roughly 40 times the cost of treating a stage I patient (Tsao et al. 1998). Although increasing medical cost by stage may not be surprising, Ramsey and colleagues found that even after controlling for stage, direct costs were lower among persons with screen-detected versus symptom-detected colorectal cancer in the 12 months following diagnosis (Ramsey et al. 2003). The findings of these cost-of-illness studies supports the premise that primary and secondary cancer prevention may result in substantial economic benefits, potentially saving economic resources from the managed care perspective.

Cost-identification studies can improve medical decision making by dispelling perceptions of cost savings. Esser and Brunner reviewed 33 studies that examine economic outcomes of granulocyte colony-stimulating factor (G-CSF) in the prevention and treatment of chemotherapy-induced neutropenia (Esser and Brunner 2003). Contrary to conventional opinion, they found little evidence that G-CSF is cost saving as primary or secondary prophylaxis, and only minor cost savings in patients undergoing bone marrow transplant. This tertiary prevention review is particularly notable because of reports that G-CSF expenses amount to 10% of the total budget of US hospital pharmacies with limited observed clinical benefits.

Evidence from cost-identification studies may also emphasize the importance of cancer prevention as a cost containment strategy. Loeve and colleagues conducted a cost-identification study for endoscopic colorectal cancer screening and found that endoscopic colorectal cancer screening has the potential to be cost saving (Loeve et al. 2000). They stated that similar analyses of screening programs for breast and cervical cancer have not demonstrated potential cost savings under any reasonable assumptions.

Some cost-identification studies have focused on the travel and time costs of cancer prevention. O'Brien and colleagues estimated direct health service costs and the indirect cost of time off work among chemotherapy patients using patient and nurse survey data as well as administrative data from 107 participants (O'Brien et al. 1993). Houts and colleagues asked 139 patients receiving outpatient chemotherapy to keep diaries of nonmedical expenses resulting from their disease and its treatment, and documented the economic experiences of these patients (Houts et al. 1984). These small, local cost-identification studies reveal a need to better understand the nonmedical economic outcomes using a patient-centered approach. Information on out-of-pocket savings in the long-run due to cancer prevention might be useful to motivate individuals at risk, and lead them to make more informed decisions regarding their health behaviors and use of medical services.

2

Cost-consequence studies entail a simple tabulation of health and economic outcomes of interventions. This rare and informal type of economic analysis is like a cost-identification analysis except that it includes health outcome information. The findings of a cost-consequence study are presented without summary statements about cost-effectiveness, which distinguishes it from economic evaluations.

2.7 Conclusion

The purpose of this chapter was to introduce the reader to ways of quantifying the human and economic value of cancer prevention activities. The human and economic costs of cancer to individuals, families, communities, and society are substantial (Brown et al. 2001). It is imperative that personal and financial investments in cancer prevention be made; however, since healthcare resources are limited, those available must be used efficiently and equitably. To justify investments in cancer prevention, it is essential to have data about the relative costs and outcomes of prevention activities. Resources should be used for programs that produce the greatest benefit for the greatest number of people. The lack of good information about input–output relationships in health care has led to enormous variations in costs and practice patterns. The creation of more useful data and the more informed use of data currently available can enhance the public's health, patient care, and the quality of health care resource allocation decisions at many levels (e.g., individual, health plan, society).

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