SECTION 1
FOUNDATION ISSUES

CHAPTER 1

Pharmacoeconomics: Principles, Methods, and Applications

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KEY CONCEPTS

1. Pharmacoeconomics identifies, measures, and compares the costs and consequences of drug therapy to healthcare systems and society.
2. The perspective of a pharmacoeconomic evaluation is paramount because the study results will be highly dependent on the perspective selected.
3. Healthcare costs can be categorized as direct medical, direct nonmedical, indirect nonmedical, intangible, opportunity, and incremental costs.
4. Economic, humanistic, and clinical outcomes should be considered and valued using pharmacoeconomic methods, to inform local decision making whenever possible.
5. To compare various healthcare choices, economic valuation methods are used, including cost-minimization, cost-benefit, cost-effectiveness, and cost-utility analyses. These methods all provide the means to compare competing treatment options and are similar in the way they measure costs (dollar units). They differ, however, in their measurement of outcomes and expression of results.
6. In today's healthcare settings, pharmacoeconomic methods can be applied for effective formulary management, individual patient treatment, medication policy determination, and resource allocation.
7. When evaluating published pharmacoeconomic studies, the following factors should be considered: study objective, study perspective, pharmacoeconomic method, study design, choice of interventions, costs and consequences, discounting, study results, sensitivity analysis, study conclusions, and sponsorship.
8. Use of economic models and conducting pharmacoeconomic analyses on a local level both can be useful and relevant sources of pharmacoeconomic data when rigorous methods are employed, as outlined in this chapter.

Today's cost-sensitive healthcare environment has created a competitive and challenging workplace for clinicians. Competition for diminishing resources has necessitated that the appraisal of healthcare goods and services extends beyond evaluations of safety and efficacy and considers the economic impact of these goods and services on the cost of healthcare. A challenge for healthcare professionals is to provide quality patient care while assuring an efficient use of resources.

Defining the *value* of medicine is a common thread that unites today's healthcare practitioners. With serious concerns about rising medication costs and consistent pressure to decrease pharmacy expenditures and budgets, clinicians/prescribers, pharmacists, and other healthcare professionals must answer the question, "What is the value of the pharmaceutical goods and services I provide?" *Pharmacoeconomics*, or the discipline of placing a value on drug therapy,[1] has evolved to answer this question.

Challenged to provide high-quality patient care in the least expensive way, clinicians have developed strategies aimed at containing costs. However, most of these strategies focus solely on determining the least expensive alternative rather than the alternative that represents the best value for the money. The "cheapest" alternative—with respect to drug acquisition cost—is not always the best value for patients, departments, institutions, and healthcare systems.

Quality patient care must not be compromised while attempting to contain costs. The products and services delivered by today's health professionals should demonstrate *pharmacoeconomic value*, that is, a balance of economic, humanistic, *and* clinical outcomes. Pharmacoeconomics can provide the systematic means for this quantification. This chapter discusses the principles and methods of pharmacoeconomics and how they can be applied to clinical pharmacy practice and thereby how they can assist in the valuation of pharmacotherapy and other modalities of treatment in clinical practice.

PRINCIPLES OF PHARMACOECONOMICS

DEFINITIONS

1 *Pharmacoeconomics* has been defined as the description and analysis of the cost of drug therapy to healthcare systems and society.[2] More specifically, pharmacoeconomic research is the process of identifying, measuring, and comparing the costs, risks, and benefits of programs, services, or therapies and determining which alternative produces the best health outcome for the resource invested.[3] For most practitioners, this translates into weighing the cost of providing a pharmacy product or service against the consequences (outcomes) realized by using the product or service to determine which alternative yields the optimal outcome per dollar spent. This information can assist clinical decision makers in choosing the most cost-effective treatment options.[4]

There is a distinct relationship between pharmacoeconomics, outcomes research, and pharmaceutical care. Pharmacoeconomics is not synonymous with outcomes research. *Outcomes research* is defined more broadly as studies that attempt to identify, measure, and evaluate the results of healthcare services in general.[5] Outcomes research is discussed further in Chapter 2. Pharmacoeconomics is a division of outcomes research that can be used to quantify the value of pharmaceutical care products and services. *Pharmaceutical care* has been defined as the responsible provision of drug therapy for the purposes of achieving definite outcomes.[6] By accepting this as the paradigm or vision for our profession, pharmacy is accepting responsibility for managing drug therapy so that positive outcomes are produced.

Cost is defined as the value of the resources consumed by a program or drug therapy of interest. *Consequence* is defined as the effects, outputs, or outcomes of the program or drug therapy of interest. Consideration of both costs and consequences differentiates most pharmacoeconomic evaluation methods from traditional cost-containment strategies and drug-use evaluations.

PERSPECTIVES

2 Assessing costs and consequences—the value of a pharmaceutical product or service—depends heavily on the perspective of the evaluation. Common perspectives include those of the patient, provider, payer, and society. A pharmacoeconomic evaluation can assess the value of a product or service from single or multiple perspectives. However, clarification of the perspective is critical because the results of a pharmacoeconomic evaluation depend heavily on the perspective taken. For example, if comparing the value of alteplase (tissue plasminogen activator, or t-PA) with that of streptokinase from a patient or societal perspective, t-PA may be the best-value alternative because a 1% reduction in mortality rates is observed in this large population. Yet, from a small community hospital's perspective, streptokinase may represent a better value because it provides similar outcomes for less money. Once the perspective is clear, a full evaluation of the relevant costs and consequences can begin. Again, perspective is critical because the value placed on a treatment alternative will be dependent heavily on the point of view taken.

Patient Perspective

Patient perspective is paramount because patients are the ultimate consumers of healthcare services. Costs from the perspective of patients are essentially what patients pay for a product or service, that is, the portion not covered by insurance. Consequences, from a patient's perspective, are the clinical effects, both positive and negative, of a program or treatment alternative. For example, various costs from a patient's perspective might include insurance copayments and out-of-pocket drug costs, as well as indirect costs, such as lost wages. This perspective should be considered when assessing the impact of drug therapy on quality of life or if a patient will pay out-of-pocket expenses for a healthcare service.

Provider Perspective

Costs from the provider's perspective are the actual expense of providing a product or service, regardless of what the provider charges. Providers can be hospitals, managed-care organizations (MCOs), or private-practice physicians. From this perspective, direct costs such as drugs, hospitalization, laboratory tests, supplies, and salaries of healthcare professionals can be identified, measured, and compared. However, indirect costs can be of less importance to the provider. When making formulary management or drug-use policy decisions, the viewpoint of the healthcare organization should dominate.

PHARMACOECONOMIC CONTROVERSY

Surprisingly few providers are prepared to identify and measure their true economic costs. Charge data may be more readily available but usually are not reflective of the true costs of healthcare. Thus it can be challenging to translate charges into actual costs. A cost-to-charge ratio can be useful in many instances. Additionally, a common proxy used for costs of medications is average wholesale price (AWP). However, realistically, there are no providers actually paying AWP for their drugs, and AWP therefore is not an accurate proxy for drug-cost data.

Payer Perspective

Payers include insurance companies, employers, or the government. From this perspective, costs represent the charges for healthcare products and services allowed, or reimbursed, by the payer. The primary cost for a payer is of a direct nature. However, indirect costs, such as lost workdays and decreased productivity, also can contribute to the total cost of healthcare to the payer. When insurance companies and employers are contracting with MCOs or selecting healthcare benefits for their employees, then the payer's perspective should be employed.

Societal Perspective

The perspective of society is the broadest of all perspectives because it is the only one that considers the benefit to society as a whole. Theoretically, all direct and indirect costs are included in an economic evaluation performed from a societal perspective. Costs from this perspective include patient morbidity and mortality and the overall costs of giving and receiving medical care. An evaluation from this perspective also would include all the important consequences an individual could experience. In countries with nationalized medicine, society is the predominant perspective.

PHARMACOECONOMIC CONTROVERSY

Controversy surrounds the issue of study perspective. Many researchers and academicians assert that society is the only relevant and the most appropriate perspective from which to conduct a pharmacoeconomic analysis. However, in the United States, these studies can be very resource-intensive in terms of time and money. Further, organizations may need to focus solely from their own perspectives to obtain the data necessary to inform timely decision making.

COSTS

3 Once a perspective is chosen, the costs and consequences associated with a given product or service can be identified and measured

TABLE 1-1 Example of Healthcare Cost Categories

Cost Category	Costs
Direct medical costs	Medications
	Supplies
	Laboratory tests
	Healthcare professionals' time
	Hospitalization
Direct nonmedical costs	Transportation
	Food
	Family care
	Home aides
Indirect costs	Lost wages (morbidity)
	Income forgone because of premature death (mortality)
Intangible costs	Pain
	Suffering
	Inconvenience
	Grief
Opportunity costs	Lost opportunity
	Revenue forgone

using pharmacoeconomic methods. A comparison of two or more treatment alternatives should extend beyond a simple comparison of drug acquisition costs. Healthcare costs or economic outcomes can be grouped into several categories: direct medical, direct nonmedical, indirect nonmedical, and intangible costs.[7] Other costs often discussed in pharmacoeconomic evaluations include opportunity and incremental costs. Inclusion of these various cost categories, when appropriate, provides a more accurate estimate of the total economic impact of a healthcare program or treatment alternatives on a specific population, organization, or patient. Table 1–1 contains examples of these costs. Again, the costs that are identified, measured, and ultimately compared vary depending on the perspective.

Direct Medical Costs

Direct medical costs are the costs incurred for medical products and services used to prevent, detect, and/or treat a disease.[7] Direct medical costs are the fundamental transactions associated with medical care that contribute to the portion of gross national product spent on healthcare. Examples of these costs include drugs, medical supplies, and equipment, laboratory and diagnostic tests, hospitalizations, and physician visits. Direct medical costs can be subdivided into fixed and variable costs. Fixed costs are essentially "overhead" costs (e.g., heat, rent, electricity) that are not readily influenced at the treatment level and thus remain relatively constant. For this reason, they are often not included in most pharmacoeconomic analyses. Variable costs, which change as a function of volume, include medications, fees for professional services, and supplies. As more services are used, more funding must be used to provide them.

PHARMACOECONOMIC CONTROVERSY

Should personnel costs be considered fixed or variable costs? In a hospital setting, one might consider whether switching from a drug that requires a three-times-daily versus once-daily administration truly saves time for healthcare personnel. Some argue that staffing is relatively constant and that such a change would not cause the hospital to reduce its overall personnel levels, whereas others maintain that such a change allows personnel to perform other activities that provide value. In times of *downsizing*, personnel often are viewed as variable costs by hospital administrators.

Direct Nonmedical Costs

Direct nonmedical costs are any costs for nonmedical services that are results of illness or disease but do not involve purchasing medical services.[7] These costs are consumed to purchase services other than medical care and include resources spent by patients for transportation to and from healthcare facilities, extra trips to the emergency department, child or family care expenses, special diets, and various other out-of-pocket expenses.

Indirect Nonmedical Costs

Indirect nonmedical costs are the costs of reduced productivity (e.g., morbidity and mortality costs).[7–9] Indirect costs are costs that result from morbidity and mortality and are an important source of resource consumption, especially from the perspective of the patient. Morbidity costs are costs incurred from missing work (i.e., lost productivity), whereas mortality costs represent the years lost as a result of premature death. To estimate indirect costs, two techniques typically are used: (1) human capital (HC) and (2) willingness-to-pay (WTP) methods. The HC approach attempts to value morbidity and mortality (primarily wages and productivity) losses based on an individual's earning capacity using standard labor wage rates.[10] This approach raises an ethical dilemma because the value of a life is related directly to income. Using the WTP approach (contingent valuation), the indirect and intangible aspects of a disease can be valued. Patients are asked how much money they would be willing to spend to reduce the likelihood of illness.[11] However, the values obtained through this method can be unreliable because of the substantial differences in valuations of life that result from the subjective nature of this approach.

Intangible Costs

Intangible costs are those of other nonfinancial outcomes of disease and medical care.[7] Examples include pain, suffering, inconvenience, and grief, and these are difficult to measure quantitatively and impossible to measure in terms of economic or financial costs. In pharmacoeconomic analyses, frequently intangible costs are identified and discussed, but not quantified formally.

Opportunity Costs

Opportunity costs represent the economic benefit forgone when using one therapy instead of the next best alternative therapy.[12] Therefore, if a resource has been used to purchase a program or treatment alternative, then the opportunity to use it for another purpose is lost. In other words, opportunity cost is the value of the alternative that was forgone.

Incremental Costs

Incremental costs represent the additional cost that a service or treatment alternative imposes over another compared with the additional effect, benefit, or outcome it provides.[13] As medical interventions become increasingly intense, costs generally increase. However, the additional outcome gained per additional dollar spent generally decreases. At some point of increasing expenditures, there may be no additional benefits or even a reduction in outcome. Thus incremental costs are the extra costs required to purchase an additional unit of effect and provide another way to assess the pharmacoeconomic impact of a service or treatment option on a population.

CONSEQUENCES

4 Similar to costs, the outcomes or consequences of a disease and its treatment are an equally important component of pharmacoeconomic analyses. The manner in which consequences are quantified is a key distinction among pharmacoeconomic methods because the assessment of costs is relatively standard.

Like costs, the consequences (or outcomes) of medical care also can be categorized. One approach is to separate outcomes into three

categories: economic, clinical, and humanistic. *Economic outcomes* are the direct, indirect, and intangible costs compared with the consequences of medical treatment alternatives.[14] *Clinical outcomes* are the medical events that occur as a result of disease or treatment (e.g., safety and efficacy end points).[14] *Humanistic outcomes* are the consequences of disease or treatment on patient functional status or quality of life along several dimensions (e.g., physical function, social function, general health and well-being, and life satisfaction).[14] Assessing the economic, clinical, and humanistic outcomes (ECHO) associated with a treatment alternative provides a complete model for decision making.

Positive versus Negative Consequences

These consequences (outcomes) can be further categorized as positive or negative. An example of a positive outcome is a desired effect of a drug (efficacy or effectiveness measure), possibly manifested as cases cured, life-years gained, or improved health-related quality of life (HRQOL). Because all drugs have adverse effects, negative consequences also can occur with their use. A negative outcome is an undesired or adverse effect of a drug, possibly manifested as a treatment failure, an adverse drug reaction (ADR), a drug toxicity, or even death. Pharmacoeconomic evaluations should include assessments of both types of outcomes. Evaluating only positive outcomes can be misleading because of the potential detriment and expense associated with negative outcomes. Thus the balancing of positive and negative consequences is important in any pharmacoeconomic evaluation.

Intermediate and Final Consequences

Consequences also can be discussed in terms of intermediate and final outcomes. Intermediate outcomes can serve as a proxy for more relevant final outcomes. For example, achieving a decrease in low-density lipoprotein cholesterol levels with a lipid-lowering agent is an intermediate consequence that can serve as a proxy for a more final outcome such as a decrease in myocardial infarction rate.[15] Intermediate consequences are used commonly in clinical and pharmacoeconomic analyses as proxies predictive of final outcomes because their use reduces the cost and time required to conduct a trial.

PHARMACOECONOMIC CONTROVERSY

The challenge with using intermediate consequences of medical interventions lies in finding appropriate interim outcome indicators that can reliably predict the long-term effects of a program or treatment alternative.

METHODS OF PHARMACOECONOMICS

5 The pharmacoeconomic methods of evaluation are listed in Fig. 1–1. These methods or tools can be separated into two distinct categories: economic and humanistic evaluation techniques. These methods have been used in a variety of fields and are being applied increasingly to healthcare.[16]

ECONOMIC EVALUATION METHODS

The basic task of economic evaluation is to identify, measure, value, and compare the costs and consequences of the alternatives being considered. The two distinguishing characteristics of economic evaluation are as follows: (1) Is there a comparison of two or more alternatives? and (2) Are both costs and consequences of the alternatives examined?[17] A full economic evaluation encompasses both characteristics, whereas a partial economic evaluation addresses only one. Pharmacoeconomic evaluations conducted in today's healthcare settings can be either partial or full economic evaluations.

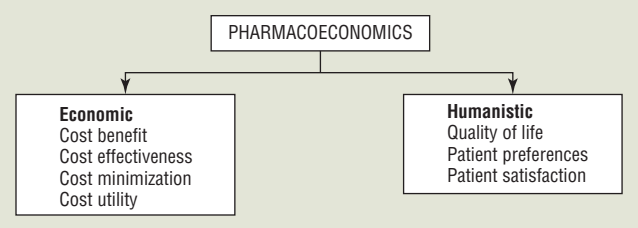

FIGURE 1-1. Components of pharmacoeconomics.

Partial economic evaluations can include simple descriptive tabulations of outcomes or resources consumed and thus require a minimum of time and effort. If only the consequences or only the costs of a program, service, or treatment are described, the evaluation illustrates an outcome or cost description. A cost-outcome or cost-consequence analysis (CCA) describes the costs and consequences of an alternative but does not provide a comparison with other treatment options.[15] Another partial evaluation is a cost analysis that compares the costs of two or more alternatives without regard to outcome.

Full economic evaluations include cost-minimization, cost-benefit, cost-effectiveness, and cost-utility analyses. Each method is used to compare competing programs or treatment alternatives. The methods are all similar in the way they measure costs (in dollars) and different in their measurement of outcomes. Although a full economic evaluation generally provides higher-quality and more useful information, the time, resources, and effort employed are also great. Thus healthcare practitioners and clinicians also find it necessary to employ various partial economic evaluations.

Application of economic evaluation methods to healthcare products and services, especially pharmaceuticals, might increase their acceptance by healthcare professionals and society.[18] The methods used most commonly by healthcare practitioners are discussed in the next sections and summarized briefly in Table 1–2.

COST-OF-ILLNESS EVALUATION

A cost-of-illness (COI) evaluation identifies and estimates the overall cost of a particular disease for a defined population.[8] This evaluation method is often referred to as *burden of illness* and involves measuring the direct and indirect costs attributable to a specific disease. The costs of various diseases, including diabetes, mental disorders, and cancer, in the United States have been estimated.

By successfully identifying the direct and indirect costs of an illness, one can determine the relative value of a treatment or prevention strategy. For example, by determining the cost of a particular disease to society, the cost of a prevention strategy could be subtracted from this to yield the benefit of implementing this strategy nationwide. COI evaluation is not used to compare competing treatment alternatives but to provide an estimation of the financial burden of a disease. Thus the value of prevention and treatment strategies can be measured against this illness cost. Various examples of COI studies are available in the literature, including the burden or cost of Alzheimer disease.[19,20]

COST-MINIMIZATION ANALYSIS

Cost-minimization analysis (CMA) involves the determination of the least costly alternative when comparing two or more treatment alternatives. With CMA, the alternatives must have an assumed or demonstrated equivalency in safety and efficacy (i.e., the two alternatives must be equivalent therapeutically). Once this equivalency

TABLE 1-2 Summary of Pharmacoeconomic Methodologies

Method	Description	Application	Cost Unit	Outcome Unit
COI	Estimates the cost of a disease on a defined population	Use to provide baseline to compare prevention/treatment options against	$$$	NA
CMA	Finds the least expensive cost alternative	Use when benefits are the same	$$$	Assume to be equivalent
CBA	Measures benefit in monetary units and computes a net gain	Can compare programs with different objectives	$$$	$$$
CEA	Compares alternatives with therapeutic effects measured in physical units; computes a cost-effectiveness ratio	Can compare drugs/programs that differ in clinical outcomes and use the same unit of benefit	$$$	Natural units
CUA	Measures therapeutic consequences in utility units rather than physical units; computes a cost-utility ratio	Use to compare drugs/programs that are life extending with serious side effects or those producing reductions in morbidity	$$$	QALYs
QOL	Physical, social, and emotional aspects of patient's well-being that are relevant and important to the patient	Examines drug effects in areas not covered by laboratory or physiologic measurements	NA	QOL score

CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; CMA, cost-minimization analysis; COI, cost-of-illness evaluation; CUA, cost-utility analysis; QOL, quality of life; QALY, quality-adjusted life-year.

in outcome is confirmed, the costs can be identified, measured, and compared in monetary units (dollars).

CMA is a relatively straightforward and simple method for comparing competing programs or treatment alternatives as long as the therapeutic equivalence of the alternatives being compared has been established. If no evidence exists to support this, then a more comprehensive method such as cost-effectiveness analysis should be employed. Remember, CMA shows only a "cost savings" of one program or treatment over another.[21]

Employing CMA is appropriate when comparing two or more therapeutically equivalent agents or alternate dosing regimens of the same agent.[21] For example, if drugs A and B are antiulcer agents and have been documented as equivalent in efficacy and incidence of adverse drug reactions (ADRs), then the costs of using these drugs could be compared using CMA. These costs should extend beyond a comparison of drug acquisition costs and include costs of drug preparation (pharmacist and technician time), administration (nursing time), and storage. When appropriate, other costs to be valued can include the cost of physician visits, number of hospital days, and pharmacokinetic consultations. The least expensive agent, considering all these costs, should be preferred. This method has been used frequently, and its application could expand given the increasing number of "me too" products and generic competition in the pharmaceutical marketplace.[22]

COST-BENEFIT ANALYSIS

Cost-benefit analysis (CBA) is a method that allows for the identification, measurement, and comparison of the benefits and costs of a program or treatment alternative. The benefits realized from a program or treatment alternative are compared with the costs of providing it. Both the costs and the benefits are measured and converted into equivalent dollars in the year in which they will occur.[8,16] Future costs and benefits are discounted or reduced to their current value.

These costs and benefits are expressed as a ratio (a benefit-to-cost ratio), a net benefit, or a net cost. A clinical decision maker would choose the program or treatment alternative with the highest net benefit or the greatest benefit-to-cost (B:C) ratio.[9] Guidelines for the interpretation of this ratio are indicated[16,21,23]:

- If the B:C ratio is greater than 1, the program or treatment is of value. The benefits realized by the program or treatment alternative outweigh the cost of providing it.
- If the B:C ratio equals 1, the benefits equal the cost. The benefits realized by the program or treatment alternative are equivalent to the cost of providing it.
- If the B:C ratio is less than 1, the program or treatment is not economically beneficial. The cost of providing the program or treatment alternative outweighs the benefits realized by it.

CBA should be employed when comparing treatment alternatives in which the costs and benefits do not occur simultaneously. CBA also can be used when comparing programs with different objectives because all benefits are converted into dollars. CBA also can be used to evaluate a single program or compare multiple programs. However, valuing health benefits in monetary terms can be difficult and controversial. The expression of some health benefits as monetary units is neither appropriate nor widely accepted. Therefore, unless the benefits of a program or treatment alternative are expressed appropriately in dollars, CBA should not be employed.[21]

CBA can be an appropriate method to use in justifying and documenting the value of an existing healthcare service or the potential worth of a new one. For example, when a clinical pharmacy service is competing for institutional resources, CBA can provide data to document that the service yields a high return on investment compared with other institutional services competing for the same resources. However, the relative magnitude of the costs and benefits for the service must be considered when making this resource-allocation decision. If a service costs $100 to implement and results in a benefit to the hospital of $1,000, and a service that costs $100,000 to implement results in a benefit of $1 million, both have a B:C ratio of 10.[21] Thus caution should be exercised when using B:C ratios and CBA as a comparison tool.

Numerous examples of CBAs have been published in the literature recently.[24–27] However, of all pharmacoeconomic evaluation methods, CBA is probably used the least. Although this method has the advantage of valuing indirect costs monetarily (using the HC and WTP approaches) and intangible benefits (using the WTP approach), the valuation of outcomes such as productivity and quality of life is difficult to perform reliably and meaningfully.[10,28]

Because of difficulties in measuring indirect and intangible benefits, many CBAs measure and quantify direct costs and direct benefits only. Some researchers assert that these should not be considered "true" CBAs because they do not take into account the indirect costs and benefits.[28]

COST-EFFECTIVENESS ANALYSIS

Cost-effectiveness analysis (CEA) is a way of summarizing the health benefits and resources used by competing healthcare programs so that policymakers can choose among them.[17] CEA involves comparing programs or treatment alternatives with different safety and efficacy profiles. Cost is measured in dollars, and outcomes are measured in terms of obtaining a specific therapeutic outcome. These outcomes are often expressed in physical units, natural units, or nondollar units (lives saved, cases cured, life expectancy, or drop in blood pressure).[8,13,29]

The results of CEA are also expressed as a ratio—either as an average cost-effectiveness ratio (ACER) or as an incremental cost-effectiveness ratio (ICER). An ACER represents the total cost of a

program or treatment alternative divided by its clinical outcome to yield a ratio representing the dollar cost per specific clinical outcome gained, independent of comparators. The ACER can be summarized as follows[7,13,21]:

$$\text{ACER} = \frac{\text{health care costs (\$)}}{\text{clinical outcome (not in \$)}}$$

This allows the costs and outcomes to be reduced to a single value to allow for comparison. Using this ratio, the clinician would choose the alternative with the least cost per outcome gained.[9] The most cost-effective alternative is not always the least costly alternative for obtaining a specific therapeutic objective. In this regard, cost-effectiveness need not be cost reduction but rather cost optimization.[30]

Often clinical effectiveness is gained at an increased cost. Is the increased benefit worth the increased cost? Incremental CEA can be used to determine the additional cost and effectiveness gained when one treatment alternative is compared with the next best treatment alternative.[7] Thus, instead of comparing the ACERs of each treatment alternative, the additional cost that a treatment alternative imposes over another treatment is compared with the additional effect, benefit, or outcome it provides. The ICER can be summarized as follows:

$$\text{ICER} = \frac{\text{cost}_A(\$) - \text{cost}_B(\$)}{\text{effect}_A(\%) - \text{effect}_B(\%)}$$

This formula yields the additional cost required to obtain the additional effect gained by switching from drug A to drug B.

CEA is particularly useful in balancing cost with patient outcome, determining which treatment alternatives represent the best health outcome per dollar spent, and deciding when it is appropriate to measure outcome in terms of obtaining a specific therapeutic objective. In addition, CEA can provide valuable data to support drug policy, formulary management, and individual patient treatment decisions. Globally, CEA is being used to set public policies regarding the use of pharmaceutical products (national formularies) in countries such as Australia,[31] New Zealand, and Canada.[32] These countries, along with others, including Spain, the United Kingdom, Italy, and the United States, even have their own guidelines for conducting research.

PHARMACOECONOMIC CONTROVERSY

Which ratio is the right ratio to use in pharmacoeconomic analyses? Experts differ over which ratio, ACER or ICER, is the most appropriate and useful. ACER reflects the cost per benefit of a new strategy independent of other alternatives, whereas ICER reveals the cost per unit of benefit of switching from one treatment strategy (that already may be in place) to another.[13]

COST-UTILITY ANALYSIS

Pharmacoeconomists sometimes want to include a measure of patient preference or quality of life when comparing competing treatment alternatives. Cost-utility analysis (CUA) is a method for comparing treatment alternatives that integrates patient preferences and HRQOL. CUA can compare cost, quality, and the quantity of patient-years. Cost is measured in dollars, and therapeutic outcome is measured in patient-weighted utilities rather than in physical units. Often the utility measurement used is a quality-adjusted life year (QALY) gained. QALY is a common measure of health status used in CUA, combining morbidity and mortality data.[33]

Results of CUA are also expressed in a ratio, a cost-utility ratio (C:U ratio). Most often this ratio is translated as the cost per QALY gained or some other health-state utility measurement.[8,16] The preferred treatment alternative is that with the lowest cost per QALY (or other health-status utility). QALYs represent the number of full years at full health that are valued equivalently to the number of years as experienced. For example, a full year of health in a disease-free patient would equal 1.0 QALY, whereas a year spent with a specific disease might be valued significantly lower, perhaps as 0.5 QALY, depending on the disease.

CUA is the most appropriate method to use when comparing programs and treatment alternatives that are life extending with serious side effects (e.g., cancer chemotherapy),[34] those which produce reductions in morbidity rather than mortality (e.g., medical treatment of arthritis),[30,35] and when HRQOL is the most important health outcome being examined. CUA is employed less frequently than other economic evaluation methods because of a lack of agreement on measuring utilities, difficulty comparing QALYs across patients and populations, and difficulty quantifying patient preferences. CUA is complex, and thus CUA can be limited in scope of application from a hospital or MCO perspective. Nevertheless, when comparing treatment alternatives where HRQOL is the most important health outcome being examined, CUA should be considered.

PHARMACOECONOMIC CONTROVERSY

Because QALYs and other utility measures are highly subjective, there is some disagreement among researchers regarding which scales should be preferred for measuring utility.

HUMANISTIC EVALUATION METHODS

Pharmacoeconomic evaluations also may focus on humanistic concerns. Methods for evaluating the impact of disease and treatment of disease on a patient's HRQOL, patient preferences, and patient satisfaction are all growing in popularity and application to pharmacotherapy decisions. These methods also can assist clinicians in quantifying the value of pharmaceuticals.

HRQOL has been defined as the assessment of the functional effects of illness and its consequent therapy as perceived by the patient.[36] These effects often are displayed as physical, emotional, and social effects on the patient.[17] Measurement of HRQOL usually is achieved through the use of patient-completed questionnaires. Many questionnaires are available, and most are either disease-specific or generic measures of health status.[37,38] Various overviews on HRQOL and its application to pharmacy have been published.[15,38–41] For further discussion on health outcomes and HRQOL, refer to Chapter 2.

APPLICATIONS OF PHARMACOECONOMICS

6 Healthcare practitioners, regardless of practice setting, can benefit from applying the principles and methods of pharmacoeconomics to their daily practice settings. *Applied pharmacoeconomics* is defined as putting pharmacoeconomic principles, methods, and theories into practice to quantify the *value* of pharmacy products and pharmaceutical care services used in real-world environments. Today's practitioners increasingly are required to justify the value of the products and services they provide. Applied pharmacoeconomics can provide the means or tools for this valuation.

4 One of the primary applications of pharmacoeconomics in clinical practice today is to aid clinical and policy decision making. Through the appropriate application of pharmacoeconomics, practitioners and administrators can make better, more-informed decisions regarding the products and services they provide. Complete pharmacotherapy decisions should contain assessments of three basic outcome areas whenever appropriate: economic, clinical, and humanistic outcomes (ECHO). Traditionally, most drug therapy

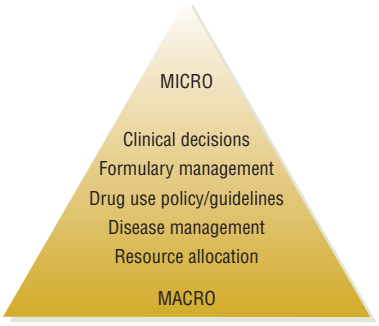

FIGURE 1-2. Decisions for pharmacoeconomic applications.

decisions were based solely on the clinical outcomes (e.g., safety and efficacy) associated with a treatment alternative. Over the past 15 to 20 years, it has become quite popular also to include an assessment of the economic outcomes associated with a treatment alternative. The current trend is also to incorporate the humanistic outcomes associated with a treatment alternative, that is, to bring the patient back into this decision-making equation. This ECHO model for medical decision making has become prevalent in current healthcare settings.[14] In today's healthcare environment, it is no longer appropriate to make drug-selection decisions based solely on acquisition costs. Thus, through the appropriate application of pharmacoeconomic principles and methods, incorporating these three critical components into clinical decisions can be accomplished.

6 Pharmacoeconomic data can be a powerful tool to support various clinical decisions, ranging from the level of the patient to the level of an entire healthcare system. Figure 1–2 shows various decisions that can be supported using pharmacoeconomics, including effective formulary management, individual patient treatment, medication policy, and resource allocation.[13,21] For discussion purposes, the application of pharmacoeconomics to decision making is divided into two basic areas: drug therapy evaluation and clinical pharmacy service evaluation.

DRUG THERAPY EVALUATION

6 Historically, pharmacoeconomic principles and methods have been applied commonly to assist clinicians and practitioners in making more informed and complete decisions regarding drug therapy. For example, pharmacoeconomics can provide critical cost-effectiveness data to support the addition or deletion of a drug to or from a hospital formulary with or without restriction. In fact, the pharmacoeconomic assessment of formulary actions is becoming a standardized part of many pharmacy and therapeutic (P&T) committees.

Selecting the most cost-effective drugs for an organizational formulary is important. However, it is equally important to determine the most appropriate way to use and prescribe these agents. Hence, developing and implementing appropriate-use guidelines or policies based on sound pharmacoeconomic data can have a great impact on influencing prescribing patterns. Further, implementing sound drug-use guidelines/policies will ensure the most appropriate and cost-effective use of pharmaceutical agents throughout the healthcare system.

The application of pharmacoeconomics also can be useful for making a decision about an individual patient's therapy. Evaluating the impact a drug has on a patient's HRQOL can be useful when deciding between two agents for customizing a patient's pharmacotherapy. Although this can be one of the most difficult applications of pharmacoeconomics, it is also one of the most important.

CLINICAL PHARMACY SERVICE EVALUATION

6 The most recent application of pharmacoeconomic principles and methods has been for justifying the value of various healthcare services, particularly pharmacy services. When a specific service is competing for hospital resources, pharmacoeconomics can provide the data necessary to justify that the service maximizes the resources allocated by healthcare system administrators. Pharmacoeconomics can be useful in determining the value of an existing service, estimating the potential worth of implementing a new service, or capturing the value of a "cognitive" clinical intervention. Practitioners and administrators can then use these data to make more informed resource-allocation decisions.

For example, suppose you want to implement a pharmacy-based therapeutic drug monitoring program. It is hypothesized that this service will improve quality of patient care and save money for the healthcare system. After negotiating with hospital administrators, the funding for this service is approved for a 1-year trial basis, after which you must document and justify the value of this practice. Theoretically, all the relevant costs and benefits of the program should be measured and, if appropriate, converted into dollars using CBA. Potential benefits can include decreased total drug costs and decreased incidence of ADRs. Potential program costs are primarily the salary and benefits for a pharmacist and additional laboratory tests to monitor patients. Data documenting that the benefit of this pharmacy service yields a high return on investment (ROI) should increase the probability of the program continuing to be funded by the healthcare system.

Unfortunately, previous reviews of the literature have revealed a disappointing number of rigorous economic evaluations of clinical pharmacy services published to date.[42–44] However, a review published in 2003 indicates that the quality of published studies finally may be increasing.[45] Historically, McGhan and colleagues[42] evaluated 35 potential CBAs or CEAs of pharmacy services published before 1978 and concluded that only 5 of these studies were legitimate CBAs or CEAs. MacKeigan and Bootman[43] reviewed 22 CBAs or CEAs published between 1978 and 1987 and concluded that CBAs and CEAs have not been adopted extensively for the evaluation of clinical pharmacy services. In 1996, Schumock and associates[44] reviewed economic evaluations of pharmacy services published between 1988 and 1995. Of the studies reviewed, only 19 were considered "full" or legitimate economic analyses, and the authors concluded that although the number of articles published has increased over the years, there is still a need for improvement in the quality or rigor of study design. Despite the relatively low number of methodologically sound studies, this review also revealed some results that demonstrate the potential value of clinical pharmacy services. Of the 109 studies evaluated, the various clinical services reviewed in this study yielded an average C:B ratio of 16:1. In 2003, these authors updated their review and included articles published from 1996 to 2000.[45] After reviewing 59 articles, these authors noted an improvement in the overall quality of the research (more studies included comparison groups and measured both costs and outcomes). Studies were conducted in hospital settings (52%), community pharmacies and clinics (41%), and community/clinic settings (18%). For the studies reporting the statistic, B:C ratios ranged from 1.74:1 to 17.01.[45]

STRATEGIES TO INCORPORATE PHARMACOECONOMICS INTO PHARMACOTHERAPY

Various strategies are available to incorporate pharmacoeconomics into pharmacotherapy. Popular strategies for applying pharmaco-

TABLE 1-3 Advantages and Disadvantages of Pharmacoeconomic Application Strategies

Strategy	Advantage	Disadvantage
Use published literature	Quick Inexpensive Subject to peer review Results can be from RCT Variety of results can be examined	Results from RCT Difficult to generalize results May not be comparative Misuse of pharmacoeconomic terms Variations in rigor/quality
Build an economic model	Quick Relatively inexpensive Yields organization-specific results Bridges efficacy and effectiveness Data collection is unobtrusive	Results dependent on assumptions Potential for researcher bias Controversial Reluctance of decision makers to accept results
Conduct a pharmacoeconomic study	Flexible Usually comparative Yields organization-specific data Reflects "usual care" or effectiveness Data from multiple sources can be used	Expensive Time-consuming Difficult to control and randomize Potential for patient selection bias Potential for small sample size

RCT, randomized controlled trial.

economics to assess the value of pharmaceutical products and services include using the results of published pharmacoeconomic studies, building economic models, and conducting pharmacoeconomic research.[46] Advantages and disadvantages of these strategies are summarized in Table 1–3.

USE THE PHARMACOECONOMIC LITERATURE

7 Quantifying the value of pharmaceuticals through pharmacoeconomics has increased in popularity. Many pharmacoeconomic analyses are published in primary medical and pharmacy literature sources. Over the past 30 or more years, the actual number of pharmacoeconomic studies published exceeded 35,000 in 1993. However, the eagerness to conduct pharmacoeconomic evaluations of drugs often exceeds the quality of these evaluations. Variations in quality and indiscriminate use of pharmacoeconomic terminology are documented in medical and pharmacy literature sources.[4,42–45,47–49] To use this literature as an aid in clinical decision making, it must be (1) critically evaluated for quality and rigor and (2) interpreted correctly. Therefore, prior to using pharmacoeconomic data to make clinical and policy decisions, decision makers should recognize the potential limitations of those data.

A primary consideration when evaluating and interpreting a study is the ability to generalize or transfer the results to other healthcare settings and countries. It can be difficult to generalize and transfer the results of a published study primarily because of wide variations in practice patterns, patient populations, and costs among healthcare systems and countries. Further, differences in study perspectives, data sources, and analytic styles may present a challenge for practitioners attempting to extrapolate or relate exact cost savings or cost ratios to their own practice settings. To enhance the ability to use pharmacoeconomic results published in the literature, consider the following points:

1. What is the technical merit of the study?
2. Are the results applicable to local decision making?
3. Do the results apply generally in different jurisdictions with different perspectives?[50]

TABLE 1-4 Basic Criteria for Evaluation of Pharmacoeconomic Literature

Objective
What is the question(s) being considered?
Is the question clear, defined, and measurable?
Perspective
What is/are the perspective(s) of the analysis?
Is the perspective appropriate given the scope of the problem?
Pharmacoeconomic method
What pharmacoeconomic tool was used?
Is it appropriate given the problem?
Is it actually what was conducted?
Study design
What was the study design?
What were the data sources?
Is the evaluation suitable if carried out in a clinical trial?
Choice of interventions
Were all appropriate alternatives considered and described?
Were any appropriate alternatives omitted?
Are the alternatives relevant to the perspective and clinical nature of the study?
Is there evidence that the alternatives' effectiveness has been established?
Costs and consequences
What are the costs and consequences (outcomes) included?
Are the costs and outcomes relevant to the perspective chosen?
Do they include negative outcomes (failures, ADRs)?
How were they valued?
Were costs and consequences measured in the appropriate physical units?
Discounting
Was the study performed over time?
Were costs and consequences that occur in the future discounted to their present value?
Was any justification given for the discount rate used?
Results
Are the results accurate and practical for medical decision makers?
Were the appropriate statistical analyses performed?
Was an incremental analysis performed?
Sensitivity analysis
Are the cost ranges for significant variables tested for sensitivity?
Are the appropriate and relevant variables varied?
Do the findings follow the anticipated trend?
Conclusions
Are the conclusions of the study justified?
Is it possible to extrapolate the conclusions to daily clinical practice?
Sponsorship
Was there any bias due to the sponsorship of the study?

ADRs, adverse drug reactions.

Various guidelines, criteria, reviews, and consensus-based recommendations for evaluating, conducting, and reporting pharmacoeconomic literature have been published.[7,17,31,32,51–60] These guidelines and criteria have been combined and summarized into 11 categories most pertinent to pharmacotherapy.[54] A summary of these 11 criteria and pertinent questions for each category are given in Table 1–4. Each evaluation criterion is briefly discussed next.

STUDY OBJECTIVE

A clear statement of the purpose of the study should be given. This objective should be clear, concise, well defined, and measurable.

STUDY PERSPECTIVE

The researcher must select one or more perspectives (e.g., patient, provider, payer, or society) from which the analysis will be conducted.[9] This perspective should be appropriate given the scope of the pharmacoeconomic problem identified. An evaluation can be conducted from single or multiple perspectives as long as the costs and consequences identified are relevant to the perspective(s) chosen.

PHARMACOECONOMIC METHOD

It should be clear which pharmacoeconomic method was employed (CEA, CMA, CBA, or CUA), and this method should be appropriate given the problem (e.g., CMA is appropriate if comparing two alternatives equivalent in therapeutic outcome but not if the alternatives differ in therapeutic outcome). Also, a researcher can claim that a specific method was employed (e.g., CEA) but actually employ another method (e.g., CMA).

STUDY DESIGN

Pharmacoeconomic evaluations can be prospective or retrospective. Although prospective designs usually are preferred, retrospective evaluations can be rich with information and reflective of usual care. Many pharmacoeconomic evaluations today are conducted as a part of randomized, controlled clinical trials. Two cautions for interpreting pharmacoeconomic data collected in this manner include (1) costs can be protocol-driven, not necessarily reflective of using a drug in common practice,[61] and (2) control of subjects and decreased complications can yield greater costs and benefits than those observed in common practice.[51]

CHOICE OF INTERVENTIONS

All relevant treatment options that are available should be described completely or mentioned. The treatment alternatives and dosages being compared should be those used in common practice, and evidence of their effectiveness should be established. Because pharmacoeconomic methods are tools to aid in choosing among treatment alternatives, assessing the cost of a single alternative is considered a partial economic evaluation.

COSTS AND CONSEQUENCES

All the important and relevant costs and consequences for each program or treatment alternative should be identified. The costs and consequences identified must be relevant to the study perspective(s) and measured in suitable terms using the appropriate physical units. Costs should include direct, indirect, and intangible costs. Consequences should include the positive and negative clinical and humanistic outcomes associated with the program or treatment alternative. All these costs and consequences must be valued credibly, with the data sources clearly identified.

DISCOUNTING

The comparison of programs or treatment alternatives should be made at one point in time; thus any costs and consequences not occurring in the present must be addressed. *Discounting*, or adjusting for differential timing, is the process of reducing any costs and consequences that may occur in the future back to their present value. If a study is performed over time (more than 1 year), or if future cost savings are projected, discounting should be done using an appropriate discount rate. The rate recommended by most investigators is typically 3% to 8% per annum, representing annual inflation or bank interest rates. However, the modal rates used in pharmacoeconomic evaluations appear to be 5%.

Researchers often disagree about which discount rate to use, as well as about whether to discount costs and health benefits (simultaneously) using the same discount rate(s).

STUDY RESULTS

A full discussion of the study assumptions and limitations and how to interpret the results in the context of different practice settings[17] should be provided. This discussion should include all relevant issues of concern to potential users of the study. The results should show that the appropriate statistical analyses were performed. Also, it may be appropriate to express the study results in terms of increases, that is, to use incremental cost analysis (additional cost of gaining an additional benefit by using one drug over another).

SENSITIVITY ANALYSIS

It is imperative that researchers test the sensitivity of study results using sensitivity analysis. Using this method, practitioners and researchers can deal with data uncertainties and assumptions and their effect on study conclusions. *Sensitivity analysis* (SA) is the process of testing the robustness of an economic evaluation by examining changes in results. Specific variables such as percent effectiveness, incidence of ADRs, and dominant resources can be varied over a range of plausible values and the results recalculated. The four general approaches to SA are simple SA, threshold analysis, analysis of extremes, and Monte Carlo simulation analysis.[62] SA is of paramount importance because of the very common need for investigators to use assumptions and estimates for unknown variables.[49]

STUDY CONCLUSIONS

Researchers should assist the reader in extrapolating study conclusions to clinical practice. The conclusions drawn from the study results should be justified (internal validity) and able to be generalized (external validity).[54] Also, conclusions drawn from results that were *statistically* significant may or may not be *clinically* relevant, and vice versa.

SPONSORSHIP

Similar to evaluating the quality of a clinical trial, sponsorship of a pharmacoeconomic study should be considered when evaluating the quality and usefulness of that study.[52] The quality of studies conducted or funded by different companies or organizations will vary by sponsor, company, product, or evaluation, and the potential for bias should be neither ignored nor assumed. For example, many of the studies sponsored or conducted by the pharmaceutical industry to date have been academically rigorous as well as informative. A clear understanding of how to evaluate, critique, and use the pharmacoeconomic literature appropriately will minimize any potential effects of this criterion on clinical decision making.

CONTROVERSIES WITH PHARMACOECONOMIC LITERATURE

Over the years, the literature has highlighted the misuse of pharmacoeconomic terms, inconsistent reporting, and disagreement on the methods used for pharmacoeconomic analyses. Because pharmacoeconomics is a fairly new discipline that lacks strong consensus with respect to its methods and technically appropriate applications, the disagreement between leading researchers in this field has been widespread and evident.[60] Unfortunately, this has led to some external skepticism, as well as the inability of clinicians to use the findings of these analyses as extensively as they could to inform their local decision making.[60] Creating and implementing a standardized system for conducting and reporting results of pharmacoeconomic analyses are critical to minimize or eliminate some of these controversies. A review of national guidelines for various countries was published and revealed some areas of emerging standarization.[63] Such a standardized system would enhance clinicians' and decision makers' comprehension of the available data, as well as provide increased assurance that the results reported are methodologically sound.

BUILD AN ECONOMIC MODEL

8 Studies that *model* the economic impact of a pharmaceutical product or service on a defined population are increasing in popularity. Modeling studies use existing clinical and/or epidemiologic data to project future outcomes.[64] Use of economic models can provide support for various clinical decisions, especially those which are time-contingent.[46] Identifying assumptions regarding the treatment alternatives being compared, the patient outcomes under study, and the probability of those outcomes occurring can provide the basis for an economic simulation to assist in the medication decision-making process.

These studies can use data from various sources available within (internal) and from outside (external) a specific healthcare organization. Common approaches to modeling are to modify and adapt existing models or to develop a distinct model to answer a specific question.[65] Typically, economic modeling in today's practice settings employs *clinical decision analysis*, which has been defined as an explicit, quantitative, and prescriptive approach to choosing among alternative outcomes.[66,67] The tool used in decision analysis is a decision tree. A decision tree provides a framework to display graphically primary variables, including treatment options, outcomes associated with those treatment options, and probabilities of the outcomes. The researcher can then algebraically reduce all these factors into a single value, allowing for comparison.

Many examples of decision-analytic models are available in the literature, spanning many therapeutic areas, including the treatment of depression,[68] migraine,[69] type 2 diabetes,[70] and community-acquired pneumonia (CAP).[71] In fact, by 1996, more than 80 published articles had been identified that applied decision analysis to questions regarding pharmaceutical products.[72] This simple decision-analysis approach is well suited for comparisons of treatment alternatives with relatively immediate consequences, for example, treating a patient with CAP. However, chronic conditions or diseases such as chronic hepatitis C are difficult to model using simple decision trees for various reasons, including time-dependent clinical outcomes, and thus may require alternate modeling techniques.

Markov models are another method of decision analysis that provides an alternative way to arrange the decision process so that clinical outcomes and time-dependent risk changes are managed efficiently. The Markov model is designed to simulate the most important aspects of a disease and can be used to estimate the long-term clinical, humanistic, and economic dimensions of the disease.[73] There are examples of Markov models available in the literature, including estimates of the cost-effectiveness of interferon-α therapy for the treatment of chronic hepatitis C infection.[74–76] Although Markov models can be stand-alone models, they often are combined with simple decision trees to predict the long-term effects of therapies.[73] These models can be complex; thus clinicians who attempt to use these data or perform their own Markov modeling should become familiar with these techniques.[73,77]

Using an economic model can help the clinician to forecast the impact of medication-use decisions on a patient, institution, or healthcare system. Also, as new drugs are marketed that can displace older agents, an economic model can expedite the reappraisal process for formulary management and drug-use policy decisions.[78] For building an economic model to assist in clinical decision making, various published studies and a review can be considered.[72,79–83] Further, guidelines for economic modeling are available, and healthcare practitioners considering using modeling techniques should refer to them.[84–86]

CONDUCT A PHARMACOECONOMIC EVALUATION

8 Clinicians may need to conduct a pharmacoeconomic evaluation if there is insufficient literature, if published results cannot be extrapolated to clinical practice, or if building a model is not appropriate. Before conducting a pharmacoeconomic evaluation, clinicians should be familiar with the similarities, differences, and appropriate application of pharmacoeconomic methods (discussed earlier in this chapter).

The decision to conduct a local pharmacoeconomic study is not without its own costs. Because both time and monetary resources are consumed by these evaluations, specific pharmacy products and services for pharmacoeconomic evaluation should be targeted. Thus this strategy should be reserved for pharmacy decisions that may have a significant impact on cost or quality of care.

Conducting pharmacoeconomic research in a hospital or managed-care environment can be challenging. Lack of institutional resources, small sample sizes, difficulty randomizing, inability to compare with placebo, and difficulty generalizing results all may be limitations. For example, when asked to determine and recommend the most cost-effective antihypertensive agent for a formulary management decision, clinicians can lack monetary and time resources to conduct a scientifically rigorous study.

Conducting a pharmacoeconomic evaluation should be guided by the criteria for quality economic evaluations.[8,17,32,51–59] A 10-step process identified by Jolicoeur and associates[87] and 4 additional steps that I have added can provide readers with guidance for conducting a local pharmacoeconomic study.[88] This process contains 14 fundamental steps for conducting a pharmacoeconomic evaluation in a healthcare system and can be applied to virtually any therapeutic area or healthcare service. Although some of these steps are similar to the evaluation criteria detailed earlier in this chapter, they will now be discussed briefly in the context of conducting an evaluation.

STEP 1: DEFINE THE PHARMACOECONOMIC PROBLEM

A broad problem might be, "Which antiemetic regimen represents the best value for the prevention of chemotherapy-induced emesis (CIE)?" However, a more succinct and measurable problem would be, "Which regimen is the best value for preventing acute CIE in patients receiving highly emetogenic chemotherapy?"

STEP 2: ASSEMBLE A CROSS-FUNCTIONAL STUDY TEAM

The study team can provide early buy-in and additional resources for a pharmacoeconomic evaluation. Team members vary depending on the analysis but can include representatives from medicine, nursing, pharmacy, hospital administration, and information systems.

STEP 3: DEFINE THE APPROPRIATE STUDY PERSPECTIVE

Choose a study perspective(s) most relevant to the problem. For example, if the problem is as listed in step 1, then the perspective of the institution or healthcare system may be most appropriate.

STEP 4: IDENTIFY TREATMENT ALTERNATIVES AND OUTCOMES

Treatment alternatives can include pharmacologic and nonpharmacologic options but should include all clinically relevant alternatives. The outcomes identified should include both positive and negative clinical outcomes.

STEP 5: IDENTIFY THE APPROPRIATE PHARMACOECONOMIC METHOD TO EMPLOY

Pharmacoeconomic methods to choose from include CMA, CBA, CEA, and CUA. Employing the incorrect method can adversely

affect medication decisions influencing both cost and quality of care.

STEP 6: PLACE A MONETARY VALUE ON TREATMENT ALTERNATIVES AND OUTCOMES

Placing a monetary value on treatment alternatives and outcomes includes not only drug administration and acquisition costs but also the cost of positive and negative clinical outcomes (e.g., determining the cost of ADRs and treatment failures). This can be measured prospectively or retrospectively or estimated using comprehensive databases or expert panels.

STEP 7: IDENTIFY RESOURCES TO CONDUCT STUDY IN AN EFFICIENT MANNER

Resources necessary will vary by study but can include access to medical or computerized records, average medical personnel wages, and specialty medical staff.

STEP 8: IDENTIFY PROBABILITIES THAT OUTCOMES MAY OCCUR IN THE STUDY POPULATION

What are the probabilities of the outcomes identified in step 4 actually occurring in clinical practice? Using primary literature and expert opinion, these probabilities can be obtained and may be manifested as efficacy rates and incidence of ADRs.

STEP 9: EMPLOY DECISION ANALYSIS

The use of decision analysis can assist in conducting various economic evaluations, including CEA. Although not necessary for all pharmacoeconomic evaluations, decision analysis and decision trees can provide a solid backbone or platform for the decision at hand. Using a decision tree, treatment alternatives, outcomes, and probabilities can be presented graphically and can be reduced algebraically to a single value for comparison (i.e., cost-effectiveness ratio).

When comparing antiemetic agents for the development of a policy for CIE prevention, CEA can be employed. Many of these agents differ with respect to effectiveness, safety, and cost. By performing a thorough CEA, these variables can be reduced to a single number (cost-effectiveness ratio), which will allow for a meaningful comparison. The treatment alternative with a better cost-effectiveness ratio than the others (i.e., lower cost per unit of outcome) would be selected and promoted for use.

Figure 1–3 contains an example of a decision tree illustrating how the probabilities of various outcomes can be organized. To calculate the ACER for drug A using "averaging out and folding back," these steps are followed:

1. Multiply the cost of path 1 by the probability of no ADE ($250 × 0.89). Repeat for path 2 ($400 × 0.11).
2. Add these two numbers and multiply by the probability of success ($266.50 × 0.93 = $247.80).
3. Repeat the two preceding steps for paths 3 and 4, and then add the resultant values ($247.80 + $50.50 = $298.30).
4. Add the cost of the drug to this value ($298.30 + $60), and divide by the probability of a success (93%, or 0.93); thus $358.30/0.93 = $385.
5. Repeat this process for drug B using paths 5 through 8.

Using the values in Table 1–5, another way to calculate the ACER for these treatment options is to multiply the cumulative probabilities (*P*) by the cumulative costs for each path, then sum the costs for each path 1 through 4 (for drug A) and 5 through 8 (for drug B), and then divide by each drug's respective effectiveness for acute CIE. On completion, the ACERs for drugs A and B are $385 and $369, respectively. Therefore, despite the 33% increase in the cost of drug B over drug A, its increased efficacy for acute CIE and its decreased incidence of ADRs actually make it a more cost-effective option.

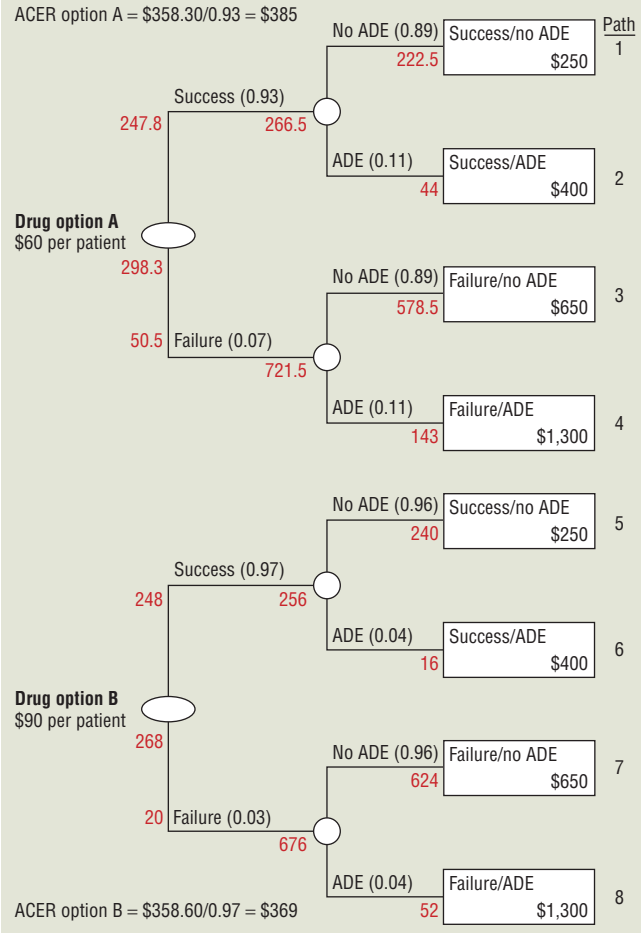

FIGURE 1-3. Example of a pharmacoeconomic decision tree comparing two drugs. *Option B* is a drug that is more specific for the target receptor in the body, is more effective, and produces fewer adverse effects than does *option A*. However, because drug *B* is more expensive than drug *A*, the cost of the added benefits must be analyzed using pharmacoeconomic techniques. This figure was completed using the safety and efficacy values for drugs *A* and *B* from Table 1–5. Values in color are calculated numbers, only included to illustrate the process of "averaging out and folding back." (ACER, average cost-effectiveness ratio; ADE, adverse drug event; P, probability [a decimal fraction between 0 and 1 indicating the likelihood of a particular event occurring in a given period].) *(Data from Sanchez LA, Lee JT. Applied pharmacoeconomics: Modeling data from internal and external sources. Am J Health Syst Pharm 2000;57:146–158.)*

STEP 10: DISCOUNT COSTS OR PERFORM A SENSITIVITY OR INCREMENTAL COST ANALYSIS

Costs and consequences that occur in the future must be discounted back to their present value. Sensitive variables must be tested over a clinically relevant range and results recalculated. If appropriate, an incremental analysis of the costs and consequences should be performed.

TABLE 1-5 Comparison of Costs of Two Drug Options for Preventing Acute Chemotherapy-Induced Emesis

Path	Drug Cost ($)	Chemotherapy Cost ($)	Laboratory Cost ($)	Extra Therapy Cost ($)	Delay in Clinic Cost ($)	Hospital Cost ($)	Cumulative Cost ($)	Cumulative Probabilities	Cost of Path ($)
Drug A									
1	60	200	50				310	0.827	256.37
2	60	200	100	100			460	0.102	46.92
3	60	200	100	200	150		710	0.062	44.02
4	60	200	150	300	150	500	1360	0.007	9.52
Cost of option									$356.83
Drug B									
5	90	200	50				340	0.931	316.54
6	90	200	100	100			490	0.038	18.62
7	90	200	100	200	150		740	0.028	20.72
8	90	200	150	300	150	500	1390	0.001	1.39
Cost of option									$357.27

STEP 11: PRESENT STUDY RESULTS

Results should be presented to the cross-functional team and the appropriate committees. Presentation style and content can vary depending on the audience.

STEP 12: DEVELOP A POLICY OR AN INTERVENTION

Take the study results and develop a policy or an intervention that can improve or maintain quality of care, possibly at a cost savings.

STEP 13: IMPLEMENT POLICY AND EDUCATE PROFESSIONALS

Spend adequate time and resources strategically implementing the policy or intervention. Educate the healthcare professionals most likely to be affected by this policy using various strategies, including verbal, written, and online communication.

STEP 14: FOLLOWUP DOCUMENTATION

Once the intervention or policy has been implemented for a reasonable period of time, collect followup data. These data will provide feedback on the success and quality of the policy or intervention.

For additional information and hands-on practice conducting a pharmacoeconomic evaluation in the real world, practitioners should consider a recently published case study. In 2003, Okamoto[89] published a case study on conducting a pharmacoeconomic evaluation using 16 steps that readers also may find useful. In this case, clinicians are challenged to conduct a faux economic analysis from an MCO (provider) perspective to support a review of inhaled corticosteroids for formulary management purposes.

CONCLUSIONS

The principles and methods of pharmacoeconomics provide the means to quantify the value of pharmacotherapy through balancing costs and outcomes. Providing quality care with minimal resources is the future, and the future is here. By understanding the principles, methods, and application of pharmacoeconomics, healthcare professionals will be prepared to make better, more-informed decisions regarding the use of pharmaceutical products and services, that is, decisions that ultimately represent the best interests of the patient, the healthcare system, and society.

ABBREVIATIONS

ACER: average cost-effectiveness ratio

ADR: adverse drug reaction

AWP: average wholesale price

B:C ratio: benefit-to-cost ratio

CAP: community-acquired pneumonia

CBA: cost-benefit analysis

CCA: cost-consequence analysis

CEA: cost-effectiveness analysis

COI: cost of illness

CMA: cost-minimization analysis

CUA: cost-utility analysis

ECHO: economic, clinical, and humanistic outcomes

HRQOL: health-related quality of life

ICER: incremental cost-effectiveness ratio

MCO: managed-care organization

QALY: quality-adjusted life year

SA: sensitivity analysis

WTP: willingness-to-pay

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