CHAPTER 10

Economics for pharmaceutical management

SUMMARY

Economics can help managers make difficult resource-allocation decisions by providing a framework and a set of concepts and tools for evaluating alternatives in terms of their costs and benefits. Key economic concepts include—

Scarcity: the fact that resources are always limited
Opportunity cost: the benefits that are given up in choosing one option over the next-best alternative
Marginal costs and marginal benefits: the additional costs incurred and additional benefits gained by increasing output
Incentives: the factors related to both monetary and nonmonetary rewards or to penalties that influence the behavior of individuals or organizations

Considerable debate exists about the appropriate role of government in the health sector. The "social welfare" perspective argues for broad government involvement, whereas the "market economy" perspective holds that government should become involved only when the market system fails. General support exists for the government to provide public goods, which are available for the benefit of everyone. Prominent examples include goods and services with positive externalities, such as immunization, and merit goods, such as health education, which private markets tend not to provide in sufficient quantities.

Policy makers must also be concerned with distribution issues—who pays for and who benefits from publicly supported services. Through the use of subsidies, governments can encourage the consumption of health services beyond what individuals would pay for on their own.

The private sector is actively involved and often predominant in health care and especially the pharmaceutical sector. Government involvement with the private sector is often justified as a means of correcting "market failure," which may result from equity considerations, failure of competition, information failure, and externalities. Governments are not always successful in correcting the failure.

Efficiency means getting the most output for a given quantity of resources. The tools of pharmaco-economic evaluation can help pharmaceutical managers identify the most efficient options. Different methods include cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis.

These methods are demanding and labor intensive, and although widely used in pharmaceutical access programs in high-income countries, their applicability is more limited in low- and middle-income countries. Essential medicines lists, standard treatment guidelines, generic substitution, tendering and reference pricing, and tariff and tax minimization can be more effective instruments for improving pharmaceutical purchasing and improving affordability.

Pharmaco-economic analysis can be very helpful, but should be used selectively, for instance, in assessing an entire public health program (such as childhood vaccination) or when an important product is expensive and available from only one source.

10.1 Economics as a tool for making choices

Health economics is about understanding both medical and nonmedical resource-allocation decisions that affect health under conditions of scarcity and uncertainty (Drummond et al. 2005). Pharmaco-economics is the area of health economics that focuses on the economic evaluation of medicines. Because budgets are never large enough, health managers must constantly decide which of several courses of action to follow. They may make choices among programs, among program goals or objectives, or among strategies or activities for achieving specific goals. This chapter introduces the concepts of health economic analysis and shows how these concepts can be applied to the selection of medicines.

Evidence-based medicine and pharmaco-economic analysis play a much greater role in medicine selection now than they did ten years ago, because program managers are under increasing pressure to show that they are obtaining value for their purchases or subsidies. These methods have been used most effectively within health insurance/pharmaceutical subsidy schemes in high-income countries (Birkett et al. 2001; Hjelmgren et al. 2001; Pearson and Rawlins 2005), but the basic principles are relevant to low- and middle-income countries.

As covered in other chapters, pharmaceutical management is characterized by a complex series of processes, involving (a) research and discovery, (b) product development, (c) safety and efficacy testing, (d) manufacture, (e) distribution, (f) prescription, (g) dispensing, and (h) consumption. The first four elements constitute the costs incurred before the manufacturer's distribution to wholesalers. The prices the manufacturer charges are usually many

times the marginal cost of production and are set in order to recover all of these costs and generate a profit margin. The patent system allows manufacturers to behave as monopolists, charging what the market will bear. Retail prices depend on this system and the last four processes listed. Therefore, the application of health economics methods to the selection of medicine must consider the complexity of these processes and the often conflicting roles of the different stakeholders.

Program managers can use economic analysis as a useful tool to augment, but not fully replace, experience and common sense. Economic analysis can lay out, sometimes in stark detail, the costs and consequences of different courses of action. However, real-world decision making must consider political, professional, and commercial realities. Achieving optimal value for money with every purchase or subsidy is a worthy but unattainable goal; however, judiciously and consistently applying appropriate pharmaco-economic methods will help deliver greater value for money in the longer term.

An important caveat is that health economics, done appropriately, is a rigorous, demanding discipline. Many problems with pharmaco-economic analyses arise because of limitations or biases in available clinical data, which result in unrealistic assumptions about clinical benefits and cost-effectiveness of medicines (Hill et al. 2000; Rennie and Luft 2000; Bell et al. 2006). Therefore, organizations must have access to clinicians, epidemiologists, statisticians, and economists to conduct pharmaco-economic analyses well. Because these professionals are often in short supply and expensive, many countries do not have the necessary resources. Regional cooperation is likely necessary to achieve widespread proficiency in the application of these methods.

In most low- and middle-income countries, complex health economic analyses of each individual medicine product are not necessary; rather, they are selectively applied to public health programs, such as childhood immunization, or to expensive products from a single source. In fact, formal pharmaco-economic evaluations of pharmaceutical classes should be aligned with the basic elements of pharmaceutical management policy, including maintaining essential medicines lists, establishing generic medicines policies, ensuring efficient pharmaceutical procurement and distribution systems, minimizing tariffs and taxes, and encouraging rational use of medicines.

10.2 Some basic economic concepts

Economics provides methods for evaluating choices in terms of their costs and benefits. Table 10-1 lists examples of resource-allocation decisions that can benefit from using economic tools, moving from a more macro, or health system, level to the micro level of individual products.

Highlighting a few basic economic concepts critical for understanding issues in public health may be useful. They are scarcity, opportunity cost, marginal benefits and costs, and incentives.

Scarcity. Resources are never sufficient to do everything. Choices have to be made about the best ways to use the resources that are available. Resources are not limited to money; time is a scarce resource as well, as every busy program manager knows.

Opportunity cost. Choices that entail opportunity costs go beyond money alone. They take into account potential benefits that are given up in order to follow a chosen course of action—benefits that could be derived from committing resources to the next-best alternative. For example, if running a training course in inventory management means that another course in rational medicine use cannot be conducted, the forgone course is the

Table 10-1 Examples of resource-allocation decisions at different levels of government

Central government	Central ministry of health	Pharmaceutical program managers
How much should the public sector spend for all recurrent budgets?	How much should be allocated to primary, secondary, and tertiary care?	How much should be spent on pharmaceuticals, training, and storage?
How much should be allocated to the different ministries?	How much should be allocated to different program activities?	What methods can be used to plan for international pharmaceutical purchases when the value of local currency is falling?
	How much should be spent on pharmaceuticals, personnel, and other operating costs?	
	How much should be allocated to different geographic jurisdictions?	Which pharmaceutical distribution strategy will deliver medicines to health facilities most efficiently?
	How much should be allocated to urban compared to rural, dispersed populations, for whom unit costs of services are higher?	Which medicines should be purchased and at what prices; to whom should they be given?

opportunity cost of running the inventory management course. The concept of opportunity cost is helpful in evaluating alternatives by looking explicitly at the trade-offs they involve.

Marginal benefits and costs. When resource-allocation decisions are made, the question is often not whether to allocate all or nothing to a particular activity, but whether to spend a bit more or a bit less. The additional costs of doing a bit more are called marginal or incremental costs, and the additional benefits that result are called marginal benefits. The relationship between the additional costs and benefits is usually called the incremental cost-effectiveness ratio.

For example, ministries of health are rarely faced with decisions about whether or not to provide vaccinations; however, a program manager might have to decide whether to keep the clinic open for another hour at the end of the day. To make this decision, the manager would estimate the marginal cost of keeping the facility open (in terms of extra salaries, utilities, and so forth) and compare this cost to the marginal benefit (in terms of numbers of additional children who would be vaccinated during the extra hour). The incremental cost-effectiveness ratio would be expressed as the cost per extra child vaccinated. The opportunity cost of keeping the clinic open for another hour would be the activities forgone as a result: for example, resources may no longer be sufficient to conduct an educational outreach session.

Incentives. An incentive is some kind of compensation (a reward or penalty that is monetary or otherwise) that influences the behavior of individuals or organizations. For example, governments may provide a financial incentive to parents to ensure that their children are fully immunized. Governments have an incentive to provide preventive health care because it should reduce the demand for and thus the cost of providing more expensive curative care. In practice, however, patients and communities strongly demand curative care. Governments can also create incentives to influence the behavior of individuals or organizations. In charging fees, for example, they can discourage individuals from making unnecessary visits to health facilities for minor complaints. This assumed tendency to overuse facilities if they are made available free of charge is known as "moral hazard." However, many studies have shown that user fees reduce care-seeking behavior among poor patients, which may have negative health outcomes.

The carrot-or-stick approach can be extended to industry. For instance, by levying fines for the distribution of substandard products, governments can encourage pharmaceutical producers to maintain the quality of their products. By establishing certain kinds of controls and incentives, government can influence consumers and providers to choose lower-priced medicines.

10.3 Economics of the public sector

The appropriate role of the government in the health sector, as well as in the broader economy, has been debated for centuries by philosophers, economic theorists, and political thinkers. Since the 1980s, the debate has been heightened by a two-pronged dilemma. On the one hand, centrally planned economies have generally failed to ensure economic security for their populations; on the other hand, some market-focused economies have shown notable inability to ensure universal access to basic social services such as health care.

In appraising the role of government, considering the two extreme positions in this debate is useful. One can be called the social welfare perspective; it supports the vision of an active central government that provides virtually all social services and participates actively in the production of goods and services throughout the economy. This perspective assumes without question that education, health, and other social services will be fully provided by the government. What can be called the market economy perspective, at the other extreme, holds that the government should intervene only if and when the market system performs imperfectly. The economist's perspective on the appropriate degree of government involvement is to weigh benefits against costs; in other words, both governments and markets can be imperfect, and the appropriate mix needs to be assessed on a sector-by-sector basis.

Goals of public expenditure

Historically, the role of the public sector has been undisputed for certain activities. Traditionally, these areas have included maintenance of law and order and national security; investment in infrastructure, such as roads, electricity, and communications networks; and provision of certain types of goods and services. Technically, these activities are termed *public goods, externalities,* and *merit goods.* However, none of these areas is now invulnerable to change, and many governments have experimented with privatizing areas previously regarded as the sole province of the public sector.

Public goods. Services that are widely agreed to be essential and that are consumed collectively (for example, national defense and policing), certain types of utilities and amenities (such as street lighting, sewage systems, and parks), and public health services (such as aerial spraying for vector control) are termed *public goods*. Public goods are often referred to as nonexcludable, meaning that they cannot be provided to some and withheld from others, and nonrival, meaning that no competition exists for the goods; consumption by one person does not reduce its availability to others (Cowen 2008). Because of these factors, public goods are often not sold in the market, and relying on the private sector to provide them may be impractical.

In practice, these definitions have limited applicability, and in recent years, governments have explored ways to engage the private sector in some forms of public infrastructure. For example, power and water companies, which are traditional public entities, have been privatized in many countries, and new highways are often built through partnerships between the public and private sectors. Currently, the overall effects of these policies are unclear, but they do represent a clear shift in government thinking about providing public goods.

Externalities. External effects, sometimes called social costs or benefits, extend beyond the party directly involved in the production or use of a good or service (Musgrove 1996). Examples of goods with positive externalities are immunization and communicable disease control; all members of the community enjoy the benefits of immunization or treatment because their chances of contracting these diseases are reduced as a result. Because private markets tend to underprovide public goods with positive externalities, governments usually take responsibility for funding public goods or subsidizing their use.

Merit goods. Merit goods are things that are good in themselves and include, for example, providing health services for the poor. If left to the market, merit goods would be underprovided. Populations want these services to be provided, but private markets tend not to take care of this group.

Government activity often extends beyond these three types of goods and services. Many people look to government to create a supportive environment for the private sector by encouraging stability and ensuring the availability of basic infrastructure to enforce laws and legally binding contracts. Arguments for a more active public sector are often most forcefully made in developing countries, where levels of private investment may be low, and the private sector is consequently less well developed. Nevertheless, the governments there are sometimes much less developed and can have issues with corruption and lack of transparency.

The roles that governments can play in the pharmaceutical sector are discussed in Chapter 8 and range from total control and provision of all pharmaceutical services (increasingly rare) to minimal government intervention, with pharmacy services provided mostly by the private sector, without government support or interference.

10.4 Understanding the private sector

In contrast with the public sector, private-sector resource allocation decisions are determined largely by the interaction of buyers and sellers in the marketplace, mediated by price. Health program managers in the public sector sometimes think of the private sector as greedy, unscrupulous, unethical, and concerned only with profit at the expense of equity and quality. They often see consumers as unable to judge the quality of health services and therefore vulnerable to manipulation by the private sector. However, the private sector usually plays a significant role in the health sector in the production, distribution, and sale of pharmaceuticals as well as in the direct provision of a significant proportion of health services through private clinical practices, private hospitals, and retail drug sellers. This fact alone is an important reason for better understanding the private sector, which, some believe, has advantages over the public sector in certain circumstances and for certain activities. Appreciating both the strengths and the weaknesses of the public and the private sectors is essential to good public-sector decision making.

Markets and competition

The private sector is characterized by buyers and sellers in the marketplace negotiating the exchange of goods and services through the mechanism of price. In the pharmaceutical sector, the sellers of medicines may be manufacturers, wholesalers, pharmacies, or retail drug sellers. Purchasers may be government, private, or nongovernmental health facilities, or individual consumers. When multiple suppliers act independently and large numbers of purchasers exist, markets are described as "competitive." Through the use of prices as signals, competitive markets are able to allocate resources efficiently, making sure that resources get to the people who are willing and able to pay for them.

Suppliers enter the market when they see an opportunity to make a profit, that is, to earn revenues in excess of costs. With this incentive, they are willing to invest their own money and take a risk as they engage in new activities, expand into new markets, and respond to consumer demand. Under competitive conditions, suppliers can be expected to earn a reasonable level of profit; if they try to increase their profits above this level, another supplier will likely offer a lower price and take away their business. In this way, the price system functions as a control, or discipline, mechanism. Suppliers do not compete on the basis of price only; they may compete on quality (providing a higher quality for the same price), reliability, service, or capacity.

In practice, this type of competitive market is sometimes hard to achieve with pharmaceutical products. Because information is a public good, private markets will tend to underprovide it. The scientific advances that underlie innovative pharmaceuticals are an example of this phenomenon. Various mechanisms have been developed to encourage research and development in medicines and vaccines for neglected diseases. For example, an advance market commitment, a contract from a government or donor, guarantees a viable market for a new medicine or vaccine that would otherwise be too financially risky to develop—such as

a product that would benefit developing countries. In 2009, five countries and the Bill & Melinda Gates Foundation activated the first advance market commitment of USD 1.5 billion to speed the development of a vaccine for pneumococcal disease (GAVI Alliance 2009).

The intellectual property system, notably patents, also tries to address this shortcoming by giving innovators a time-limited monopoly in exchange for revealing the nature of their invention. Monopolies, in general, lead to higher prices and suboptimal use in the short run, but the intended trade-off (not always realized) is that this system produces a greater rate of innovation in the long run. Thus, the situation is far more complex than a simple competitive market.

In most countries, patents are now granted for twenty years, although the effective patent period of medicines is eight to fourteen years, because of the time development takes. After the patent on a medicine expires, generic suppliers are able to compete, and prices typically plummet to become much closer to the marginal cost of production. For both patented and generic products, the pharmaceutical marketplace is also distorted by the presence of public and private insurance.

In most developed countries, the government negotiates prices with pharmaceutical suppliers in an effort to provide a counteracting force (monopsony or single-buyer power) to offset the single-seller power of monopolists. Government intervention is the rule rather than the exception, especially in rich countries. The theoretically competitive model of multiple suppliers and multiple purchasers is often replaced by a more pragmatic model of multiple monopolistic suppliers of products and one or a few large purchasers (government or nongovernmental organizations) who can exercise considerable purchasing power. (See Chapter 9 on pharmaceutical pricing policies.)

Economies of scale. In competitive markets, suppliers have an incentive to produce goods and services as efficiently as possible, using the least-cost combination of inputs. In some cases, the private sector is able to generate efficiency gains because of the size and diversity of its operations. Economies of scale occur when the production of larger quantities leads to lower average costs. For example, a plant that produces 4 million tablets a day is likely to do so at a lower cost per tablet than one that produces only 10,000 a day. Beyond some level of output, however, additional machinery or equipment may need to be bought, or more resources may need to be spent in supervising production, which may increase average costs.

Economies of scope. Economies of scope result when combining a number of different activities enables them to be done at lower average cost. Private distribution networks may benefit from economies of scope by combining the delivery of pharmaceuticals with the delivery of other goods and services.

Ethics and business

As previously mentioned, both nongovernmental organizations and public-sector groups have tended to attribute unethical and unscrupulous motives to the private sector. Although examples exist of suppliers that brazenly cheat by providing substandard medicines, for example, the long-term interests of private providers do not encourage engaging in this type of activity. As long as there is the prospect of a continued, profitable relationship with a purchaser, the supplier has an incentive to retain customers by providing good-quality services.

Much of the criticism of the last decade has been directed at manufacturers of patented pharmaceuticals. The main arguments have centered on the price at which they sell their products, particularly in poorer countries, and their lack of involvement in the development of new medicines for some diseases that are major causes of morbidity and mortality in those countries (Trouiller et al. 2002). With the help of intense lobbying from advocacy groups, however, the pharmaceutical industry appears to be recognizing its wider global responsibilities and is addressing its damaged reputation. As a result, modest progress is being made in some areas to provide greater access to some previously unaffordable medicines (for example, antiretroviral medicines for HIV/AIDS) and in the development of medicines for neglected diseases. In theory, many pharmaceutical suppliers will be quite happy to sell medicines at "differential" (lower) prices in poor countries, as long as those prices are above their marginal costs of production and distribution and prohibitions against reexporting to higher-priced markets (parallel trade) are enforceable (Danzon and Towse 2003).

Encouraged by the World Health Organization and the World Bank, some research-based companies have been using differential prices to sell their products on different markets (WHO and WTO 2001). This subject is discussed in more detail in the chapter on medicine pricing (Chapter 9). Products that have been the subject of differential pricing include contraceptives, vaccines, and antiretroviral medicines (GAVI n.d.).

In addition, nonprofit organizations are developing new medicines for conditions such as tuberculosis, malaria, leishmaniasis, and trypanosomiasis. Some are part of large international initiatives (Medicines for Malaria Venture, Drugs for Neglected Diseases Initiative, TB Alliance), and much funding has come from the private sector (for example, the Bill & Melinda Gates Foundation). Several initiatives are public/private-sector partnerships, involving pharmaceutical manufacturers (see Chapter 3 on intellectual property and access to medicines). The result has been considerable blurring of the traditional barriers between the public and private sectors in pharmaceutical research, development, and distribution.

10.5 Government interaction with the private sector

Governments interact with the private sector in many different ways. In its simplest form, this interaction consists of government purchases of pharmaceuticals and supplies from private pharmaceutical companies. In theory and in relation to pharmaceutical products, much government involvement is motivated by a desire to correct "imperfect" private markets.

Market failure

A number of potential market failures exist in the medical marketplace in general, and the pharmaceutical marketplace in particular, that distort outcomes away from the efficiencies that would be expected under the simple competitive ideal—

- Insurance means that patients, and physicians as their agents, do not face the social costs of their decisions to use health care.
- Information is a public good, but the adoption of the patent system as compensation creates monopoly power, which can be abused.
- In general, purchasers do not have good information about the price and quality of the health care services they buy. This information asymmetry can work to the benefit of sellers.
- Regulatory requirements create high barriers for new manufacturers entering the market, which lessens competition.

Patients' inability to assess the quality, safety, or efficacy of pharmaceuticals means they must rely on the clinicians who prescribe them, on pharmaceutical producers to maintain production quality standards, and on governments to intervene with regulatory activities. Inspection of medicines, registration and licensing of pharmacists, and medicine registration processes are all ways in which governments attempt to protect consumers from dangerous, ineffective, and poor-quality medicines (see Chapters 6 and 19). These demanding safety standards, although necessary, make entering the market difficult for new companies.

Achieving economic efficiency in the presence of market failure is one of the principal aims of pharmaco-economics; techniques for achieving efficiency are discussed later in this chapter. Efficiency in pharmaceutical management requires that the medicines are effective and affordable, represent value for money, and are used appropriately. But governments are not concerned only with efficiency. Most also try to achieve a degree of equity in the distribution of funds and services. Lack of access to essential medicines discriminates against those with the least ability to pay, leading to avoidable mortality, suffering, resentment, and in some cases, economic decline. Governments are in the best position to correct these inequities, and access to essential medicines is now regarded by some as a human right. Because private-sector decision making is driven more by profit than by equity considerations, equity is often the first motivation for government involvement in essential medicines programs. The relatively high cost of pharmaceuticals compared to that of other goods suggests that without government involvement, the poor would be denied access to lifesaving medicines. This probability is especially high in remote areas, where cash incomes are usually lower and delivery costs higher.

Types of government interventions

In a broad sense, arguments are that government interventions are needed to correct market imperfections, ensure the safety and efficacy of medicines, and improve access and affordability. These aims can be advanced by various types of legislation; in addition, governments can influence prices by becoming large purchasers (or subsidizers) of medicines and using their extensive purchasing power. Pharmaco-economic analysis can facilitate the use of this approach as a tool for calculating social willingness to pay, as discussed below.

The term *regulation* refers to the set of tools that governments use to ensure that private-sector actions are consistent with the broader welfare of society. The objectives of regulation are usually improvements in quality, efficiency, or equity. Pharmaceutical legislation and regulation are discussed further in Chapter 6.

With pharmaceuticals, the instruments used to regulate the private sector (for example, manufacturers, distributors, pharmacies) include controls on medicine and service quality through mandatory inspection programs; controls on imports (restricting imports of dangerous products or permitting the import of only essential medicines); and registration and licensure of pharmacists. Restrictions have also been widely imposed on the prices at which pharmaceuticals can be sold. For example, in Australia, a section of the National Health Act prevents the national medicines selection body (the Pharmaceutical Benefits Advisory Committee) from listing a new product on the schedule at a higher price than the comparators unless it offers better efficacy or safety (see Country Study 10-1).

A number of issues should be considered in evaluating the potential effect of regulation: the extent of coverage (for example, does it include both public and private sectors?), the capacity of government to monitor compliance, the extent of enforcement and exemptions, and the extent to which the private sector can circumvent or evade regulations (for example, through the emergence of an uncontrolled parallel market for nonessential or banned medicines).

Country Study 10-1
Australia: Ten years of using pharmaco-economics in decision making

In Australia, the federal government subsidizes the use of pharmaceuticals through the maintenance of a "positive" formulary, called the Pharmaceutical Benefits Schedule (PBS). Recommendations to list new medicines on the PBS are made to the health minister by a Pharmaceutical Benefits Advisory Committee (PBAC), based on the importance of the medicine, the need for it in the community, its efficacy and safety compared to other medicines or treatments for the condition, and, since 1993, its cost-effectiveness. In addition, the committee considers the financial implications of adding the medicine to the formulary.

The PBAC analyzes the relative clinical performances and costs of both the potential new medicine and comparable medicines already listed on the PBS. The PBAC bases its decisions on the principle that if a medicine is no better than a comparable product, it should not cost more. If the product is superior to existing therapies but more expensive (a common situation), and funds are available, any extra expenditure should represent "value for money." Costs are not limited to each product's acquisition cost, but can include savings in other areas—for instance, decreased use of other medicines or fewer consultations, tests, and hospital admissions.

Incremental cost-effectiveness ratios for the new medicine compared to existing medicines are then developed. These economic data inform decision making, but no formal "threshold" exists for what is cost-effective. Other issues, including clinical need and social values, are influential. Decisions projected to cost more than 10 million Australian dollars (AUD) per year must be approved by the cabinet of the federal government.

More than ten years' experience in using pharmaco-economic evaluations in PBAC decision making has resulted in several observations. The processes have survived multiple technical and ethical challenges, notably but not exclusively from industry. A government productivity commission criticized the PBAC about the level of disclosure in its decision making. In 2002, the Department of Health and Aging began publishing summaries of PBAC's positive recommendations on its website, but so far full details of the assessment process are still not provided.

No evidence suggests that Australia has been denied access to important medical advances by the demand that a new medicine demonstrate "value for money," with the PBS subsidizing a comprehensive range of medicines for patients. The PBS is a positive formulary, in that the PBAC does not seek to limit choice or restrict the numbers of medicines within a classification. However, pressures on the system are real; for example, patient advocacy groups with particular clinical needs continue to seek relaxation of decision-making criteria that affect them.

As in most other countries, the costs of medicines are a concern, and the viability of the PBS has been questioned. To curtail growth in pharmaceutical costs, the PBAC increasingly relies on restricting subsidies by defining eligibility criteria that target patients in whom the new medicine has been demonstrated to be cost-effective. During the decade in which the PBAC has used pharmaco-economic analyses, expenditure on the PBS has risen from about AUD 1 billion per year in the early 1990s to about AUD 6 billion in 2005. This increase does not mean that the use of economic information in decision making has been a failure—rather, it suggests that the other side of the cost equation, the demand side, has been less well managed. Prescribers often ignore restrictions, and the use of new medicines for indications and patient populations in which the medicine has not been shown to be cost-effective has contributed to the rapid growth in PBS costs.

Using pharmaco-economic analyses in decision making is not a panacea for rising pharmaceutical budgets. However, such techniques do make the trade-offs between the costs and benefits of the medicine more transparent. Although considerable progress has been made in the technical aspects of the conduct of pharmaco-economic analyses, progress on managing prescribing practices has been notably less successful. The challenge ahead is how to use the available information on cost-effective medicine use to influence how medicines are prescribed and used in the Australian community.

Source: Birkett et al. 2001; Hailey 2009.

When regulations are in place, they should be regularly evaluated to determine whether they are achieving the desired effects or, as is frequently the case, the government intervention has had unforeseen and negative consequences.

Legislation designed to improve the affordability of medicines is harder to implement when the government does not subsidize medicines and thus is unable to use its extensive purchasing powers. For example, since 1997, South Africa has tried to regulate medicine prices in the private sector, but it has met stiff resistance from stakeholders, including pharmaceutical manufacturers, wholesalers, and retail pharmacists (Republic of South Africa 1997). To achieve greater control over prices and improve affordability and access, the South African government plans to introduce a form of national health insurance before 2014 (*ANC Today* 2009).

The capacity required to implement and monitor the effects of regulations—and the costs of monitoring them—needs to be carefully weighed against the proposed benefits.

Challenges to government interventions

Arguments in favor of government involvement often contrast private-market failure with "perfect" government intervention, but this result is never achieved in practice. The private market may fail, but government intervention also fails sometimes. Governments in all countries at all levels of development are subject to threats to their effectiveness. Informed decisions about public involvement in essential medicines programs must acknowledge the sources of government ineffectiveness, including inefficiency in service delivery, inequities in revenue collection, interest-group pressures, lack of good governance, and widespread corruption.

Inefficiency in service delivery arises from a lack of individual incentives for good performance, bureaucratic inflexibility, and political pressure to create employment. Overexpenditure on staff and underexpenditure on pharmaceuticals, for example, could result in having idle staff who are unable to meet the needs of patients. Inefficiencies in government accounting systems that cause lengthy delays in payments may result in suppliers' raising their prices or deciding not to bid at all on government contracts.

Inequities in revenue collection can result in a reduction in health services, which is felt most acutely by lower-income groups, which are most dependent on them. If the more affluent members of society succeed in avoiding taxes and other government levies, the financial burden for government activity falls on those with fewer means and options.

Even honest, well-meaning politicians and officials are subject to interest-group pressures. Political supporters, members of the same ethnic group, and concerned business organizations can influence bureaucrats to allocate services and resources in ways that do not promote equity. Generally, the more affluent are able to exert such pressures; ironically, the less well-off may lose directly and indirectly—by paying more in taxes as well as by receiving fewer services.

Finally, lack of good governance and corruption can be revealed in self-interested manipulation of the medicine selection process, corruption in the award of tenders, nepotism in the appointment of key staff, sales of medicines on the outside by health staff, and other destructive practices. Indeed, the World Bank has identified corruption as one of the greatest obstacles to a country's economic and social development (see http://www.worldbank.org/anticorruption).

10.6 Efficiency concepts

Efficiency concepts form the basis for understanding the use of pharmaco-economic analysis. Whereas effectiveness concerns the degree to which services are provided or outputs are produced (for example, how well does a medicine work in practice?), efficiency can be understood as getting the most output for a given quantity of resources committed or, alternatively, achieving a given level of output at minimum cost. In this field, efficiency is usually referred to as "cost-effectiveness" (Drummond et al. 2005).

Several types of efficiency concepts exist, with a variety of definitions that are characterized by some lack of agreement. Generally, e*conomic efficiency* refers to economic systems that can provide more goods and services to society without using more resources. *Scale efficiency* occurs when the production costs are reduced because of higher production volume. *Productive efficiency* in a health system refers to maximizing health outcome for a given cost, or the minimizing cost for a given outcome. Because types of efficiency relate to the pharmaceutical sector, this chapter takes a pragmatic approach by referring to the concepts of allocative efficiency and technical efficiency. *Allocative efficiency* is the broad concept of undertaking the best combination of activities to achieve the greatest net benefit to the community; for example, should we spend money on preventing cardiovascular deaths or childhood illness? Or should we spend money on education or health? *Technical efficiency* is concerned with determining the right quantities of different inputs and the least-expensive combination of inputs to achieve a given outcome; for example, what is the most cost-effective way to reduce cardiovascular deaths? The concepts of allocative and technical efficiency are closely linked and in real life cannot be separated.

Allocative efficiency

Allocative efficiency has relevance to pharmaceuticals, not least because medicines can consume 25 to 65 percent of entire health budgets in some low-income countries (WHO

2010). In some countries, 20 to 30 percent of pharmaceutical expenditure is for products that have no relevance to the main health problems of the population—clearly an inefficient allocation of scarce resources, which might be better used in public health programs or education (WHO 2010).

Decisions affecting allocative efficiency are most often made at the policy level, for example, deciding whether to allocate additional funds to the ministry of health or the ministry of education. Within the ministry of health, decisions involve how much to spend on primary, secondary, and tertiary care or whether to spend additional program funds on controlling tuberculosis or treating sexually transmitted infections. Such allocative decisions can have unintended and undesirable effects; a decision to reduce spending on pharmaceuticals and supplies in order to pay salaries could lead to inefficiency if staff are then underused because of other shortages (for example, a surgeon who cannot perform operations because the operating-room equipment has not been maintained or because anesthetics are in short supply).

Technical efficiency

Technical efficiency means obtaining the maximum physical output from the physical inputs in pursuit of a particular goal, such as reducing deaths from HIV/AIDS by increasing the number of individuals receiving and adhering to effective antiretroviral medicines. Technical efficiency includes not only the cost-effectiveness of the medicines, but also the system that selects, procures, distributes, and dispenses the medicines to consumers.

Selection of medicines should consider the medicines' comparative efficacy and cost-effectiveness, measured in terms of the money spent in achieving an adequate and sustained suppression of the AIDS virus, for example.

In procurement, the use of competitive international tendering has advantages. As discussed in Chapter 9 on medicine pricing, improving the efficiency of the tendering process can result in substantial price reductions. Determining the appropriate quantities of medicines to buy also affects efficiency: overstocking brings risks of expiry, and stockouts reduce program output and lead to expensive emergency orders.

In pharmaceutical distribution, when not enough transportation is available or vehicles are often inoperative, personnel may be underused. The same output could be achieved with fewer personnel, or output could be dramatically increased with a slightly greater expenditure on vehicle maintenance. A program manager might consider the costs and benefits of changing from using a fleet of program vehicles to contracting delivery to a commercial transportation firm in an effort to increase efficiency.

Rational use of medicines has the potential to improve efficiency; for example, prescribing excessive courses of antibiotics is inefficient, because the same outcome could be achieved using fewer. Similarly, a subtherapeutic medicine dose fails to achieve the desired clinical outcome and wastes resources because the patient is likely to return for further treatment. Polypharmacy leads to lower rates of adherence to treatment and is inefficient; resources are consumed, but the desired clinical outcome is not achieved.

Program managers can control only some of the factors that affect technical efficiency. For example, program managers may not have control over the allocation of funds among different line items, such as personnel and fuel, making it difficult to use inputs in the most efficient combinations. Incentives and management structures are important. If a more efficient use of resources leads to tangible benefits for health workers, they are more likely to make more efficient choices. If they are penalized (for example, if underspending a budget leads to less money being allocated next year with no offsetting incentives), health workers are unlikely to behave in an efficient and cost-saving manner.

Information is important in increasing technical efficiency: managers and health care providers who have information about the costs of alternatives are more likely to make efficient use of their resources than those who do not. Formulary manuals, standard treatments, and therapeutic guidelines are intended to provide such information to health workers. Relatively simple performance indicators have been developed using information that should be available to most supply system managers; such indicators can be used to monitor supply system efficiency on a routine basis (see Chapter 48).

Health care decision makers can use information on efficiency to improve the current situation and make better plans related to performance, costs, and staff utilization. In addition, efficiency is an important economic concept because demonstrating that existing resources are being used efficiently provides powerful support to requests for additional resources. But achieving both allocative and technical efficiency depends on access to information on both costs and outcomes of competing treatment programs. Exploring the relationships between costs and benefits lies at the center of economic evaluation.

10.7 Economic evaluation of pharmaceutical products

Although concepts of efficiency are vital to all aspects of pharmaceutical management, including procurement, distribution, and dispensing, as well as to the selection of essential medicines for formularies and reimbursement lists, pharmaco-economics is defined as the analysis of the costs and benefits of medicine therapy to health care systems and society (ISPOR 2003).

The essential characteristic of pharmaco-economic analyses is that they involve *comparisons*—usually a new medicine is compared with the best existing treatment; therefore, decisions are almost always made "on the margin." The best analyses are those that are based on high-quality clinical studies (Birkett et al. 2001).

The term *economic evaluation* refers to a set of analytical tools that can help identify which of several alternative treatments offers the greatest benefit compared with its cost. These analytical tools can help address questions such as: What medicines should be included on the formulary? What are the patient outcomes of various treatment modalities? How do two options for providing pharmacy services compare?

Four methods of economic analysis are commonly distinguished and are described here in increasing order of methodological and practical difficulty (Drummond et al. 2005).

1. *Cost-minimization analysis (CMA):* calculating the cost of two or more alternatives that have the same outcome to identify the lowest-cost option
2. *Cost-effectiveness analysis (CEA):* measuring both costs and benefits of alternatives to find the strategy with the best ratio of benefits, measured in therapeutic (clinical) or program effects, per money unit of expenditure
3. *Cost-utility analysis (CUA):* same as cost-effectiveness analysis, except that benefits are measured in "utility" units, which in theory can be compared across different disease states
4. *Cost-benefit analysis (CBA):* comparing the costs and benefits of an intervention by translating the health benefits into a monetary value, so that both costs and benefits are measured in the same unit

The distinctions among these four methods mainly concern the benefits of intervention.

Cost-minimization analysis

In cost-minimization analysis, the benefits have to be measured in the same or equivalent units, and all the alternatives considered need to produce the same quantity of benefits. The choice (which appears deceptively simple) is to identify the lowest-cost alternative, and the analysis is limited to calculation of the costs. For example, if two medicines have the same therapeutic benefits, have the same safety profile, and are of equivalent quality, the medicine with the lower cost would be selected.

In practice, CMA can be more demanding than it appears. The first challenge is to define an acceptable degree of therapeutic equivalence before comparing the costs of two regimens. Generally, *noninferiority* is the term used to define equivalence (Djulbegovic and Clarke 2001). In other words, a new treatment should be no worse than an existing medicine. A noninferiority boundary is set during the statistical analysis, to represent the tolerable maximum level of inferiority that will be allowed (for example, 10 percent); the statistical confidence interval around the difference between the two treatments must lie below this level. The costs of the medicines can be compared on that basis. Because the costs of medicines tend to vary somewhat with dose, the doses at which the products can be considered equivalent must be determined. These equivalent-effective doses are then used to establish the relative price of the new product. The costs of administration must also be included. An oral medication replacing an intravenous form with identical efficacy and safety will have the advantage of not requiring nursing time and injection equipment.

Cost-effectiveness analysis

With cost-effectiveness analysis, the unit of output of the alternatives is the same, but the quantities of output, or effectiveness of the strategy, differ. The outcomes are often described in natural units; for instance, resolution of pneumonia or cases of malaria prevented must be consistent for the treatments being compared. CEAs of this type are useful in judging technical efficiency. Sometimes the outcome measured is deaths avoided or life years gained by the use of a new treatment compared with an existing therapy. The challenge is to identify the option with the lowest cost per unit of benefit gained. For example, different vaccination strategies (fixed point, outreach, campaign) may reach different numbers of children and have varying levels of effectiveness, but cost-effectiveness analysis can help identify the one that has the lowest cost per fully immunized child.

Cost-effectiveness must be considered alongside therapeutic effectiveness. Generally, but not always, the new treatment is considered superior to the old one. Occasionally, it is less effective but much cheaper. If the budget is fixed, purchasing the lower-cost medicine may enable more patients to be treated and more lives to be saved, although the medicine is less efficacious. When working with a fixed budget, comparing the cost-effectiveness ratios of each medicine with no treatment is important. Usually, the medicine with the lowest ratio of cost to units of health gained is preferable. If the budget is not fixed and some growth is possible, the incremental cost-effectiveness ratio, which compares the new (more effective) medicine with existing treatment, should be used to commit additional funds.

CEA's main challenge is to compare different therapies: Is 5,000 dollars per heart attack avoided or 50 dollars per symptom-free period for asthma patients a better deal? Or is spending 1,000 dollars per life-year gained by reducing disability from a stroke or 5,000 dollars per life year gained for a breast cancer survivor better? In the latter instance, although the "outcomes" seem to be the same, they are not,

Table 10-2 Using economic analysis methods to make choices

Type of analysis	Medicine therapy choice: antibiotic A versus antibiotic B for treating childhood pneumonia	Transportation scheme choice: program fleet versus contracted private firm
Cost minimization	Of two medicines with equal effectiveness, which is the least expensive?	Assuming that both options are identically effective, which is the least expensive?
Cost-effectiveness	Two medicines have different degrees of effectiveness: What is the cost per child cured using antibiotic A versus antibiotic B (allowing for different efficacy of drugs A and B)?	The two options have different performances with respect to on-time delivery: What is the cost per medicine kit delivered using program transport versus a contracted firm? (Perpetually late deliveries are factored in as a smaller level of desired output.)
Cost utility	What is the cost per QALY saved of treating childhood pneumonia with drug A versus treating tuberculosis with short-course chemotherapy? (Note: This method is controversial for comparing medicine therapies.)	Because the outcome of interest is the same in both cases (that is, medicines delivered on time), no need exists to use a specially constructed measure of output.
Cost benefit	What is the cost-benefit ratio (value of costs per value of life saved) for treating childhood pneumonia versus the cost-benefit ratio for saving lives through improved road lighting? (Note: This method is normally not used to compare alternative therapies.)	Because the outcome of interest is the same in both cases (that is, medicines delivered on time), no need exists to use a specially constructed measure of output.

because quality of life will differ between stroke and breast cancer survivors. For this reason, health economists have sought different metrics that enable them to make comparisons across different disease states.

Cost-utility analysis

Cost-utility analysis is cost-effectiveness analysis conducted with the program outcomes measured in utility units. The most common utility measures are the quality-adjusted life-year (QALY) and the disability-adjusted life-year (DALY), which is more commonly used in studying developing countries (Drummond et al. 2005).

The DALY is a measure of health outcome used to compare interventions with different types of output (Murray 1994). This approach is useful for making decisions about allocative efficiency because it enables comparisons of treatments for different conditions, such as malaria, depression, and heart disease. DALYs combine mortality and morbidity (or disability) into a single measure by weighting the life-years saved by the amount of disability associated with a specific outcome.

For example, diagnosis and treatment of African trypanosomiasis costs 15 dollars per DALY saved; treatment for zinc deficiency costs 73 dollars per DALY saved; and measles vaccination costs 4 dollars per DALY saved (Laxminarayan et al. 2006). By contrast, interventions such as cancer treatment and environmental control of dengue fever both cost thousands of dollars per DALY saved. The 1993 *World Development Report* (World Bank 1993) was the first major analysis to use this outcome measure.

QALYs are similar to DALYs in that they calculate program benefits in terms of life-years saved, except that in the case of QALYs, the years are weighted by the "quality" of those years when they are lived in less-than-perfect health. Like DALYs, QALYs also allow comparison of interventions with different outputs. QALYs are controversial because individual qualities of life and preferences are difficult to compare. Furthermore, survey-based quality-of-life scales are not perfect measures, nor are they easily translated into QALYs.

Cost-benefit analysis

In cost-benefit analysis, both costs and outcomes are measured in financial units. Cost-benefit analysis is rarely undertaken in the health sector because of the difficulty and equity implications of assigning a monetary value to life-years saved (Drummond et al. 2005). Its main advantage is that it allows the comparison of programs with different outcomes—for example, investment in health versus investment in education.

Table 10-2 shows how each of these tools can be applied to make a range of choices, for instance, between alternative medicine therapies or alternative transportation schemes.

Steps for conducting a cost-effectiveness evaluation

Conducting a cost-effectiveness evaluation has six key steps.

Step 1. Define the objective. For example, in terms of program output—

- Which medication regimen should be the therapy of choice for the treatment of childhood pneumonia?
- What is the best approach to transporting essential medicines to health facilities?

Step 2. Enumerate the different ways to achieve the objective. For example—

- Short-course chemotherapy with more expensive medicines (option 1), versus traditional long-course chemotherapy with cheaper medicines (option 2)
- Purchase of program vehicles for delivery of medicines to health facilities (option 1) versus a contract with a private transport firm for delivery of medicines (option 2)

Step 3. Identify, measure, and value the benefits of each option. In the step 2 medicine-choice example, benefits could be measured in DALYs, which would require measures of therapeutic effectiveness and epidemiological data on the course of illness without treatment. For the transport example, an indicator of performance could be used, such as on-time delivery of pharmaceutical consignments to a health facility.

In the clinical arena, the benefits of competing treatments are usually measured in controlled clinical trials. The highest level of clinical evidence to use in economic analysis is a systematic review and meta-analysis of all available high-quality trials that compare interventions. Failure to use high-quality clinical data often leads to suboptimal pharmaco-economic analyses.

Step 4. Identify, measure, and value the costs of each option. All the inputs required for each option should be identified and the costs determined. Capital as well as recurrent costs should be included. Box 10-1 lists different types of costs that should be considered (see also Chapter 41). During this process, defining a relevant timeframe for these analyses is important. For instance, the efficacy of statins in the prevention of heart attacks and strokes has to be measured over years, not weeks or months.

Step 5. Calculate and interpret the cost-effectiveness of each option. The incremental cost-effectiveness ratio is the difference in total cost between the intervention and comparison options, divided by the difference in the number of units of output. Better overall efficiency is indicated by a lower cost per unit of output.

Step 6. Perform sensitivity analysis on the conclusions. Sensitivity analysis measures how various assumptions made in the course of estimating costs and outputs affect the conclusions. Sensitivity analysis deals with uncertainty in assumptions that underlie the analysis or with problems of imprecise measurement. In practice, sensitivity analysis identifies the values or assumptions about which uncertainty exists; determines their likely range of values; and recalculates study results based on a combination of the "best guess," most conservative, and least conservative estimates of these key values. The question of interest is whether the conclusions of the analysis would be changed with these extreme values.

Although certain costs or benefits cannot be measured accurately, it may be possible to show that the results of the analysis do not change over any reasonable range of cost or benefit. Alternatively, the difficulties in measurement may indicate that the results are very sensitive to error in measurement and that caution should be used in interpreting the results of the study. Sensitivity analysis is easy to do and is essential to properly use and defend study results.

Conducting pharmaco-economic evaluations

As noted, conducting full pharmaco-economic analyses that deal adequately with all of the sources of uncertainty is very demanding of time and resources. For the analyses to be valid and error-free, they must draw on the skills of epidemiologists, biostatisticians, and economists. Given the need to integrate a variety of information of varying quality, pharmaco-economic analysis can be prone to errors—and even manipulation—that can make any product look more economically attractive than it really is. To guard against this possibility, systematic checklists (see Drummond et al. 2005) are helpful for critical review. The principles of economic analysis are best understood by further reading and through exercises that involve the calculation and interpretation of cost-effectiveness ratios (see References

Box 10-1
Types of costs

Recurrent cost: The cost of goods that are consumed or used up over the course of a year (for example, staff, pharmaceuticals, fuel).

Capital cost: The cost of goods that are intended to last for longer than a year (such as buildings, vehicles, medical equipment).

Annualized capital cost: Capital cost per year of useful life for a building, vehicle, or other capital item.

Fixed cost: Cost that does not change with the level of output (for example, building, equipment, salaries to a certain extent).

Variable cost: Cost that changes, depending on the amount of services delivered (for instance, pharmaceuticals and supplies).

Total cost: The sum of recurrent costs and annualized capital costs.

Average cost per unit: Total cost divided by the number of units produced (for example, cost per patient treated, per immunization given, per cure dispensed).

Marginal cost: The cost of producing or providing one additional unit.

and Further Readings). In addition, the World Health Organization has published *Introduction to Drug Utilization Research* and *Drugs and Money: Prices, Affordability and Cost Containment* (WHO 2003; Dukes et al. 2003), which contain practical advice and exercises in cost-effectiveness analysis and a review of cost-containment measures. ■

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★ = Key readings.

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