7.4

Cost-effectiveness analysis: Concepts and applications

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Introduction

Cost-effectiveness analyses (or CEAs) in health describe interventions in terms of their cost per unit of health gain that they provide. Deaths averted provides a measure of health gain but CEAs typically use measures that take account of both years and quality of life gained. Cost and effects are typically measured from the perspective of society as a whole but other perspectives are possible. Broadly speaking CEAs are used in two distinct ways: One use provides an input into a (usually public sector) decision maker about whether to alter intervention mix or change intervention coverage levels. The second is to inform broader generalizations about health policy. This chapter provides an overview of the methods currently in use to undertake CEAs and provides an extended example—based on the Disease Control Priorities Project—that illustrates both uses.

Many of the world's poorest countries spend under US$10 per person per year on health services. High-income countries spend thousands of dollars per year. Yet across this entire expenditure range questions arise about value gained for money spent on health. Most poor countries suffer huge burdens from some mix of childhood infection, malaria, maternal deaths, tuberculosis, and HIV/AIDS. Highly effective interventions exist to address most (but not all) of these conditions. If a few additional dollars per year were available, misspending those dollars on interventions offering relatively little health gain for the money would entail lost opportunities to postpone many deaths and prevent much serious disability. High- income countries, too, face choices: Could an improved mix of interventions reduce overall costs (or at least their rate of growth) while maintaining existing levels of health? Which of the effective but usually costly new interventions emerging from the R&D pipeline should public or private insurance plans cover? Rationing of healthcare is part of our future and, in many cases, our present (Maynard & Bloom 1998).

Concern, then, with value for money (or cost-effectiveness) spans income levels. Neither is the issue one principally for the private sector, for non-governmental organizations or for the public sector. Each has a potential interest. Analysts have responded to this interest over a period of several decades and produced a substantial literature on both methods and results. The purpose of this chapter is to introduce the reader to this literature. It is often said that 'Prevention is more cost-effective than cure' or 'Tertiary facilities are not cost-effective in low-income countries'. One application of CEA involves generation of the cost-effectiveness generalizations that would support or undermine such propositions. In the second major application of CEA, analysts assess options for dealing with a particular problem—options involving scale of intervention or choice of technique. Discussion in this chapter covers both these applications.

The chapter begins with a brief discussion of background and terminology, then describes methods of cost-effectiveness analysis (hereafter CEA). The chapter then illustrates use of the methods with an application that provides a sense of results.

Background

Cost-effectiveness analysis in health comprises one part of a very much larger literature on project appraisal, i.e. on assessment of the economic desirability of alternative 'projects' from a social perspective. Another important part of this literature deals with the questions of when public sector finance is most appropriate. CEAs provide relevant information to either public or private sector decision makers by indicating the cost to them of alternatives for buying better health, information that is relevant independent of the source of finance. That said, the chapter's perspective is particularly relevant to situations where public finance is justified on grounds of avoiding insurance market failures and is explicitly designed to crowd out private spending on interventions the public sector finances for all (as in all high-income countries except the US). Table 7.4.1 lists three approaches to the economic appraisal of projects or interventions and indicates their realm of applicability.

Cost-minimization analysis examines the costs of alternative approaches to achieving a quite specific objective, e.g. the cost per infant death averted or per new HIV infection averted. The purpose is to identify the least cost way of achieving the objective and to see how both cost and choice of technique vary as the magnitude of the objective varies. (For example if one had very modest goals with respect to prevention of HIV infection the least cost approach might very well be blood screening in hospitals; more substantial goals would entail addition of more costly programmes—e.g. STD treatment, condom use—to achieve the goal at minimum total cost. Note that in this example, as will often be the case, the *average* cost per HIV infection averted will rise as the target number of infections averted rises.) Cost-minimization analysis has the virtues

Table 7.4.1 Choice of economic appraisal techniques

Economic appraisal technique	Applicability for assessing			
	Options to achieve a specific objective	Options throughout the health sector	Options inside and outside the health sector	Intrinsic value
1. Cost-minimization analysis	Yes	No	No	No
2. Cost-effectiveness analysis (sometimes called cost-utility analysis)	Yes	Yes	No	No
3. Cost-benefit analysis	Yes	Yes	Yes	Yes

of specificity and of ease of communication concerning results. The disadvantage becomes apparent if there is need to compare the attractiveness of efforts to reduce infant mortality rate with those to avert HIV infections: Costs can be compared but outcomes remain incommensurable.

Cost-benefit analysis, in contrast, allows comparison of projects (or interventions or investments) across the entire economy. It does so by placing monetary values on outcomes as well as inputs. Kilowatt-hours of electricity can be compared to kilograms of rice by multiplying each by its price to obtain a total value. The simple word 'price' conceals vast complexities, however, particularly when used to measure social benefits. There is an extensive literature on the theoretical methods as well as applications in different contexts of monetary valuation of benefits. Benefits and costs occur over time—with benefits usually following costs—and alternative figures of merit (e.g. present value of net benefits or the internal rate-of-return) generate orderings of outcomes by desirability. Squire (1989) and Layard and Glaister (1994) provide excellent overviews of the methods of cost-benefit analysis and the related literature. Viscusi and Aldy (2003) review the now-extensive literature on valuation of changes in annual mortality probabilities (or on the 'value of a statistical life'). Lomborg (2007) has coordinated cost-benefit analyses for a broad range of sectors, including health (Jamison 2007) in order to create a 'Copenhagen Consensus' of where the greatest benefits would accrue to social investment.

Practical difficulties associated with monetary valuation of benefits often lead analysts to utilize the much simpler methods of cost-minimization (with the concomitant limits on applicability of the results). In addition to practical difficulties there is the more fundamental problem, in assessing health intervention options, of placing dollar value on human life (or other health outcomes). Sometimes this can be noncontroversial as when Levin *et al.* (1993) use labour productivity increases associated with reducing anaemia to derive benefit measures to weigh against the costs of anaemia control. Their findings—of high dollar benefits relative to dollar costs—can either be compared with findings for interventions in other sectors or, more important, to assess intrinsic value: If benefits exceed costs the intervention is worth doing (ignoring deadweight loss from taxation and possible public sector fiscal constraints). If one can overcome practical and other problems with cost-benefit analysis its results have the virtue of standing alone in the sense of indicating intervention desirability independently of comparison to alternatives.

In the health sector, *cost-effectiveness analysis* lies between cost-minimization analysis and cost-benefit analysis (Table 7.4.1). CEA rests on a non-financial metric that will allow comparisons across the health sector. The concepts most typically used are those of the

quality-adjusted life-year (QALY) or the disability-adjusted life year (DALY), which can be measured in many ways, but which then—by assigning, for example, a DALY value both to an HIV infection averted and to an infant death averted—allows costs per DALY to be compared for interventions addressing a broad range of problems. Even focussing analysis to within the health sector cannot be completely done by CEA, however. Some interventions that may be undertaken principally for health reasons, such as reducing ambient air pollution, have other outcomes, in this case reduced pollution-related corrosion and the amenity value of clean air. These outcomes elude the DALY metric but must explicitly be listed as inputs to the decision-making process.

This chapter focuses on CEA. That said, work on cost minimization will often in practice prove essential to CEA. Likewise empirical observations of what societies appear prepared to pay for a DALY, or more frequently to avert a death (which can be converted to DALYs), have increasingly been undertaken. These estimates of the value of a statistical life allow CEAs to be immediately translated into cost-benefit analyses. From experience it can be suggested that an explicit valuation of human life for cost-benefit analysis usually generates reactions that distract from a discussion of improving efficiency of resource allocation in the health sector. The interested reader, however, can turn to Viscusy and Aldy (2003) for a valuable review of the monetary valuation of health outcomes.

Part of the value of undertaking CEA lies in the ability to formulate generalizations—or to indicate their inapplicability. Doing so requires care and consistency concerning the definitions that underlie the generalizations, and this chapter attempts to be quite explicit. Table 7.4.2 provides a number of important definitions and distinctions that will be used later in the chapter. Perhaps the central point to note in Table 7.4.2 is the distinction between 'interventions' *per se* and the 'instruments of policy' that can encourage (or discourage) intervention or intended behaviour change. Although most CEAs concern intervention, some concern instruments of policy. More is needed concerning the latter which, after all, is what government can implement.

CEAs in the literature vary substantially in their underlying methodologies and assumptions and, in consequence, comparisons are frequently difficult. Yet without comparability of substantial numbers of interventions, the relative attractiveness of individual interventions remains uncertain and generalizations are difficult or impossible. To define best practice in methods and to provide a template for comparative studies, the US Public Health Service convened a major review panel in 1993. Gold *et al.* (1996) report its conclusions. Discussion in this chapter for the most part follows the Public Health Service guidelines. Garber (1999) and Newmann (2005) provide more extensive discussions of the theory, methods,

Table 7.4.2 Interventions and instruments of policy[1]

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1. *Intervention categories*

   The term 'intervention' is used to denote actions taken by or for individuals to reduce the risk, duration, or severity of an adverse health condition. Interventions are the proximal cause of deliberate changes in risks, duration, or severity. Instruments of policy (see below) encourage, discourage, or undertake interventions. Stopping smoking, for example, is an intervention that an individual can take to reduce risk from a range of diseases; taxing tobacco products is a potential instrument of government policy to encourage this intervention. Interventions are divided into those that are 'population-based' and those that are 'personal'.[2]

   1.1 *Personal interventions* are directed to individuals and can be provided at home, at clinics (community, private, work-based, or school-based), at district hospitals, or at referral hospitals.

       a) Primary prevention aims to reduce the level of one or more identified risk factors in order to reduce the probability of the initial occurrence of a disease (e.g. medication for established hypertension to prevent stroke or MI).

       b) Cure of a condition aims to remove its cause and restore function to the *status quo ante*.

       c) Acute management consists of time-limited interventions that decrease the severity of acute events or the level of established risk factors to minimize their long-term effect (e.g. thrombolytics for acute MI or angioplasty to reduce stenosis in coronary arteries).

       d) Secondary prevention (or chronic care) consists of ongoing interventions aimed at decreasing the severity and frequency of recurrent events of chronic or episodic diseases (e.g. SSRIs for severe unipolar depression).

       e) Rehabilitation aims to restore (or partially restore) physical, psychological, or social function resulting from a previous condition.

       f) Palliation aims to reduce pain and suffering from a condition for which no means of cure or rehabilitation is currently available (this may range from the use of aspirin from headaches to the use of opiates to control terminal cancer pain).

   1.2 *Population- based primary prevention* is directed toward entire populations or population subgroups. These interventions fall into three broad categories:

       a) Personal behaviour change;

       b) control of environmental hazards; or

       c) population-oriented medical interventions (e.g. immunization, mass chemoprophylaxis, and screening and referral).

2. *Instruments of policy*

   These are the activities that can (potentially) be undertaken by governments or other entities that wish to encourage or discourage interventions, or, importantly, to expand the menu of potential intervention. We distinguish five major instruments of policy:

   2.1 Use of *information, education, and communication* (IEC) seeks to improve the knowledge of individuals (and service providers) about the consequences of their choices.

   2.2 Use of *taxes and subsidies* on commodities, services, and pollutants seeks to effect appropriate behavioural responses.

   2.3 Use of *regulation and legislation* seeks to limit availability of certain commodities, to curtail certain practices, and to define the rules governing finance and provision of health services.

   2.4 Use of *direct expenditures* seeks to provide (or finance provision of) selected interventions (e.g. immunizations), to provide infrastructure (e.g. medical schools) that facilitates provision of a range of interventions or to provide infrastructure that influences behaviour (e.g. speed bumps).

   2.5 Undertaking *research and development* (or encouraging them through subsidies) is an instrument central to the goal of expanding the range of interventions available and reducing their cost.

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[1] This table was prepared with Thomas Gaziano and Sonbol Shahid-Salles.

[2] The International Epidemiology Association's *Dictionary of Epidemiology* (Last 1988) provides a helpful discussion of different types of preventive intervention but, interestingly, has no entries for 'cure' or 'rehabilitation'. Their term 'tertiary prevention', which is not used here, seems to encompass both 'rehabilitation' and 'palliation', as we define those terms.

and uses of CEA than is appropriate for this chapter, and the interested reader is referred to those reviews.

Assessing the cost-effectiveness of intervention

This section contains a discussion of general issues associated with choosing interventions, that is, with criteria for cost-effective choice. The nature of the instruments open to government to promote cost-effective intervention was delineated in Table 7.4.2. The purpose is not to provide an account of the (many) methodological issues associated with economic assessment of intervention options; rather it is simply to describe the basic concepts being applied, raise a few particular issues, and refer the reader to the relevant literature. In addition to the comprehensive work for the Public Health Service that was just mentioned, valuable additional background may be found in Drummond *et al.* (2005).

Cost-effectiveness analysis broadly and narrowly construed

A starting point for cost-effectiveness analysis broadly construed is to observe that health systems have two objectives: (1) To improve the level and distribution of health outcomes in the population,

and (2) to protect individuals from financial risks that are often very substantial and that are frequent causes of poverty (WHO 1999, 2000). Financial risk results from illness-related loss of income as well as expenditures on care; the loss can be ameliorated by preventing illness or its progression and by using appropriate financial architecture for the system.

We can also consider two classes of resources to be available: Financial resources and health system capacity. To implement an intervention in a population, the system uses some of each resource. Just as some interventions have higher dollar costs than others, some interventions are more demanding of system capacity than others. In countries with limited health system capacity, it is clearly important to select interventions that require relatively little of such capacity. Human resource capacity constitutes a particularly important aspect of system capacity. Figure 7.4.1 illustrates this broadly construed vision of CE and, in its shaded region, the more narrow (standard) approach for which quantitative estimates are available. Jamison (2006) discusses further.

Although in the very short run little trade-off may exist between dollars and human resources or system capacity more generally, investing in *the development of such capacity can help make more of that resource available in the future.* An important mechanism for strengthening capacity, inherent in highly outcome-oriented programmes, may simply be to use it successfully—learning by doing.

In practice, however, literature on economic evaluation of health projects typically reports the cost per unit of achieving some measure of health outcome—QALYs or DALYs or deaths averted—and at times addresses how that cost varies with the level of intervention and other factors. This corresponds to the shaded box in Fig. 7.4.1. Pritchard (2004) and Newman (2005) provide valuable introductions to this literature. Cost-effectiveness calculations provide important insights into the economic attractiveness of an intervention, but other considerations—such as consequences for financial protection and demands on health system capacity—need to be borne in mind.

As previously indicated it is useful to consider two distinct uses for CEA. One is to inform broad policy generalizations and the other is to help assess the relative attractiveness of changes in the scale of implementation of an intervention or in the technique for addressing a specific problem. In either case the analyst must specify a base case and define the intervention as a change from that base. For policy generalizations it will typically be useful to include consideration of large changes; for addressing specific problems

more modest increments will be typical. The natural base case for dealing with specific problems will usually be the status quo, and what is to be considered as 'given' for the purpose of analysis will usually be substantial (although dependent on time frame). Establishing a base case for policy generalizations is less obvious. Guidelines developed at WHO (Murray *et al.* 2000) suggest using the '... null set of related interventions'. Substantial practical difficulties are likely to be associated with ascertaining the consequences of no intervention, and the utility to a policy maker of trying to imagine a starting point so different from her own may be limited. In most cases a more natural approach will be to identify base cases close to current reality for policy makers in a number of paradigmatic circumstances. Incremental cost-effectiveness assessments from those bases will then provide more naturally interpretable information. In this context it will often prove important to explicitly consider the effects of doing less than is being done in the base case, thereby generating negative costs and negative effects. Such 'negative intervention' may prove highly cost-effective.[1]

Outcome measurement: Disability-adjusted life-years (DALYs)

A critical choice in applications of economic analysis to resource allocation is that of whether to value outcomes because of their economic benefits or because of some more proximal effectiveness measure (Table 7.4.1). To provide a clearer sense of the context for CEA it is worth a brief additional discussion of approaches to monetary valuation of health outcomes. When there are good markets for products or labour, benefits can be assessed in monetary terms by using market prices to value benefits as well as to value costs. Even when willingness-to-pay valuation cannot be assessed directly because of lack of market prices, as is often true in the health sector, questions in surveys are increasingly being used to elicit information about hypothetical willingness-to-pay (or contingent valuation). Pervasive problems of consumer ignorance of effectiveness of intervention and a widespread tendency for individuals systematically to underestimate risks (Weinstein 1989) suggest that willingness-to-pay assessments will need to be used with caution when applied to health. An alternative approach—sometimes called the human capital approach—is to view health investments as instrumental to improving economic productivity; estimates of the effect of a health intervention on productivity thus provide a lower bound to total benefits. One example comes from assessing the effect on the productivity of rubber plantation workers of correcting iron deficiencies (Levin *et al.* 1993); other examples come from assessment of the effect on economic productivity of malaria control efforts. It is worth noting that both willingness-to-pay and human capital approaches inevitably imply different values to be attached to the life of different individuals of the same age in the same country—and even greater variation across countries. Phelps and Mushlin (1991) and Garber (1999) further discuss the close relation between cost-effectiveness and cost-benefit analyses.

More typically, however, outcomes will be assessed in deaths or disability averted, rather than dollars, and the task is to come up with some measure for making such an assessment that allows comparisons across the health sector (i.e. that allows CEA), even if intersectoral comparisons (cost-benefit analyses) remain infeasible or subject to excessive ethical debate. There is now a valuable literature on how effectiveness measures to aggregate the disability-, morbidity-, and
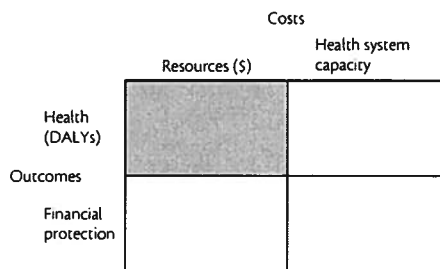
Note. The shaded box represents the domain of traditional cost-effectiveness analysis

Fig. 7.4.1 Intervention costs and effects—a more general view.

premature mortality-averting effects of interventions across the health sector might be constructed and applied. The most widely used measures are the (closely related) DALY and QALY, for disability or quality-adjusted life year. The DALY, in addition to providing the effectiveness measures for cost-effectiveness analyses, can be used with epidemiological information to assess the burden of disease in a population, as has been done for the major regions of the world (Murray *et al.* 1994; most recently updated in Lopez *et al.* 2006). Table 7.4.3 sets forth the characteristics of the main approaches to disability weighting that serve as the core of effectiveness measurement. Stouthard *et al.* (1997) provide a clear exposition of methods for disability weighting with an informative application for the Netherlands. From a practical perspective, the use of ratings based on expert judgement is probably the best that can now be done if the purpose of the analysis is to compare interventions across the sector. It is also worth noting that the construction of DALYs or QALYs requires value judgements, although they are less subject to controversy than is explicit valuation of human life. (Even measures involving mortality only, e.g. numbers of deaths averted, while they appear to be value-free, if used to measure intervention effectiveness or disease burden, rest on strong value judgements. Minimally a mortality-based measure rests on the implicit value assumption that disability is not a concern. Chapman *et al.* 2004 argue that usually, in practice, inclusion of disability weights affects relatively few cost-effectiveness analyses.)

A workable measure for effectiveness for most CEAs will be DALYs gained. The DALY gain associated with averting a death at a given age is, simply, the life expectancy at that age, with life-years gained in the future discounted back to the present (typically at a discount rate of 3 per cent per annum). Life expectancy at a given age is calculated relative to a standard low-mortality population, e.g. Japan. Unhealthy life-years are given lower weights than healthy ones, depending on degree of disability (assessed by one of the rating procedures listed in Table 7.4.3) so that the effectiveness of interventions to address morbidity or disability can be measured in terms that permit comparison with interventions that avert mortality. The QALY and DALY measures now used are particular forms of the more general concept introduced by Zeckhauser and Shepard (1976).[2] Garber and Phelps (1997) provide the basic theoretical underpinnings for cost-effectiveness analyses in health that adjust life-years for quality, and, in particular, they point to conditions allowing a dollar value to be assigned to a QALY so that, if desired, a CEA can be directly reinterpreted as a cost-benefit analysis.

Timing of outcomes can be dealt with through discounting. Johannesson (1992) provides a general discussion of discounting healthy life-years, and Cropper *et al.* (1992) report empirical assessments of time preference for saving lives. Most analysts value years of healthy life at all ages equally; this assumption can be readily relaxed, however, to give greater weight to different age. The initial variant of the QALY did provide greater relative weight to middle-aged people, but the DALY can (but need not) weight

Table 7.4.3 Alternative approaches to measuring outcomes

Approach to measurement	Cost of implementation	Possible bias	Example or application
Mortality			
Deaths averted	Very low	Highly biased against conditions involving disability; equally weights death in very old age and in middle age	Assessment of priorities in child survival (Walsh and Warren 1979)
Years of potential life lost	Very low	Highly biased against conditions involving disability	Regularly used by Centers for Disease Control and Prevention to assess burden of disease in the United States (MMWR 1992)
Disability or quality-of-life adjusted life-years (DALYs or QALYs)[1]			
Expert ratings assessment	Low	Unrepresentative experts	Ghana Health Assessment Project Team (1981)
Survey-based	Medium	NA	European quality-of-life assessments (EuroQol Group 1990)
Risk trade-offs	High	Questionable relevance of artificial gambles	Various quality-of-life assessments
Quantity-of-life trade-offs: Individual length versus quality of life	Medium/high	Probably low for patient-level decision-making	Various quality-of-life assessments
Quantity-of-life trade-offs: Across individuals	Medium	Probably low bias for social decision making	Vaccine development study (Institute of Medicine 1986); Nord (1991)

NA: Not applicable

Note: This table does not review approaches to measuring the economic benefits of changes in health status. Such measures—based, for example, on willingness to pay for reductions in the probability of adverse outcomes or on assessment of health-related determinants of labour productivity (human capital)—allow conclusions to be drawn about the inherent attractiveness of particular health interventions relative to their cost, not simply by comparison with other interventions. Tolley *et al.* (1994) and Pauly (1995) provide valuable overviews of this literature, which is briefly discussed in the text.

[1] Each of the methods for quality of life measurement—ratings, risk trade-offs, quantity-of-life trade-offs, and calibrations—can be undertaken by different groups, possibly with different results. The groups can be of 'experts': respondents to a survey or, in a clinical setting, potential patients. For the ratings method, this table comments on both expert and survey approaches: a similar breakdown could be provided for each method.

Sources: See references in final column of table.

different age groups differently. DALYs have been used for disease burden assessment and cost-effectiveness analysis in a number of recent World Bank and WHO documents (World Bank 1993; WHO 1996; WHO 2000; Murray and Lopez 1996). Lopez *et al.* (2006) report results using DALYs without age weights. Sensitivity analyses were undertaken in the initially published disease burden assessment using DALYs (Murray *et al.* 1994) and concluded that results were insensitive to age weights and discount rates over a broad range.[3]

DALYs can in principle also be weighted to reflect how equitably they are distributed in ways that are standard in project evaluation outside the health sector (Squire 1989).

Costs

Costs of inputs are generally assessed at market prices. This simple observation masks much complexity, however, both conceptually and in practice. The few paragraphs that follow highlight several important issues, but the interested reader is referred to Gold *et al.* (1996) for a more thorough treatment.

Tradeable and nontradeable inputs

For some inputs into healthcare, costs may be lower in low- and middle-income countries (for example, for semi-skilled labour). These costs are typically for inputs that cannot be traded internationally, and their existence undermines attempts to estimate costs that are not simply country-specific. Squire (1989) provides a general discussion of approaches to dealing with tradeables in project analysis through use of 'shadow prices'. His recommendations are more relevant to country-specific assessments than to cross-national comparisons.

The working conclusion of this chapter is that for tradeables (e.g. non-patented drugs, most equipment, and high-level manpower) considerations of cost variability between high- and low-income countries are of minimal significance (relative to other uncertainties).[4] For facilities and lower level manpower real costs do vary across countries, leading some analysts to conclude that costs are most usefully expressed as fractions of local per capita income—a method that assumes essentially no health sector inputs to be internationally tradeable. Barnum and Greenberg's (1993) CEA for cancer interventions is an example of an attempt to divide costs into those for traded goods and those for nontradeables. Their assessments do suggest that local costs will often be important and that those who attempt to assess the cost-effectiveness of intervention in a comparative context should pay close attention to this issue unless there is a free market for foreign exchange and the costs of nontradeables are similar to those of the comparator country. It is a matter of judgement about the extent to which costing of nontradeables undermines efforts to form generalizations across countries. One conclusion is that such generalizations are both useful and possible, but that they are best done within groups of countries with broadly similar income levels.

Patient and home provider time

Another important issue in cost analysis concerns assessment of the amount and value of time required of patients or caretakers. More attention to time costs is important both for improving cost analyses and because behavioural response to the availability of an intervention may be sensitive to time requirements. The importance of mothers' time, in particular, for compliance with child survival interventions has been stressed by Leslie (1989).

Yabroff *et al.* (2007) point to the potentially substantial magnitude of patient time costs in a study from the US The Public Health Service provides recommendations for subsequent work that would help redress this omission. A related issue concerns treatment of costs that will ensue from intervention success; Levin *et al.* (1993), for example, point out that substantial food costs can result from micronutrient supplementation or parasite control: Appetites improve. The existence of such costs suggests the importance, in these cases, of broadening the definition of the intervention. Meltzer (1997) provides a theoretically complete discussion of these issues.

Costs to well-being and risks to health

Some interventions impose costs in well-being, e.g. use of condoms of reduced alcohol or cigarette consumption. Others entail direct adverse health consequences through side effects of their inherent riskiness. While little effort has been made to include these costs in CEAs for low- and middle-income countries, their existence points to issues for interventions to change behaviour.

Joint costs

A final issue concerning cost analysis is that of joint costs, that is, the situation where several interventions are essentially made available with a (partially) common set of inputs. Some authors handle this in part by defining interventions in terms of natural packages; for example, Jamison *et al.* (1993) consider the preventive intervention for polio to be diphtheria–pertussis–tetanus vaccine plus polio immunization, and assess the cost-effectiveness of that package, because polio immunization would (almost always) be given with the other vaccines. Debas *et al.* (2006) also deal with joint costs in surgical interventions by packaging, in this case by considering the 'intervention' to be the operation of the surgical ward of a district hospital for a year. Future directions for CEA will likely include much attention to large packages or 'platforms', like the surgical ward both to deal with joint costs and because of greater policy relevancy.

Other issues

CEAs for comparisons across interventions use the common metric of dollar cost per DALY gained, with the understanding that incremental costs and cost-effectiveness will likely vary across locales (even after controlling for intervention quality) because of differences in individuals, in epidemiological conditions, in delivery system characteristics, in the initial degree of penetration of the intervention into the population, and in the range of available alternatives.[5] Table 7.4.4 lists many important factors that lead to variation in incremental cost-effectiveness, and, to the extent that interventions are first applied where their cost-effectiveness is highest, these factors collectively will lead to rising costs per QALY with increased application of an intervention. Figure 7.4.2 illustrates this for control of dengue; up to a point, improved case management is most cost-effective, but beyond that point, if a higher level of control for dengue is to be sought, chemical and then environmental strategies of vector control must be introduced.

Intervention specificity and targeting

This phenomenon of rising costs per DALY comes up implicitly in many analyses; the cause of the phenomenon is, frequently, the lack of intervention specificity and, also frequently, the needs for costly targeting, case-finding, or compliance monitoring.

Table 7.4.4 Factors influencing variation in cost-effectiveness

Influencing factor	Important examples
Epidemiological environment	
Prevalence of condition	Screening and referral programmes for leprosy; for cervical and breast cancer.
Incidence of condition	BCG immunization for tuberculosis; preventive measures for many injuries.
Case-fatality rate	Measles immunization; oral rehydration therapy for diarrhoea.
Transmission dynamics of infectious conditions	Treatment of sexually transmitted diseases in core versus non-core groups; vector control for malaria, dengue.
Existence of competing risks or synergisms	Measles vaccination results in amplification of cost-effectiveness by strengthening individuals in a general way. Among the very young or elderly, competing risks reduce the cost-effectiveness of some targeted interventions.
Individual characteristics	
Age	Cancer treatment: More cost-effective for younger patients
Tendency to compliance	Tuberculosis chemotherapy; antihypertensive medication
Tendency to self-refer	Sexually transmitted diseases control
Levels of risk factors	High levels of hypertension and hyperlipidemin enhance intervention cost-effectiveness
Individual variation in values	Attitude toward disability relative to risk of death; can lead to individual differences in intervention effectiveness.
System characteristics	
Local costs of non-traded inputs to healthcare system	Real costs of care-intensive interventions (such as hospitalization to ensure compliance with tuberculosis chemotherapy) are low where wages are low, because most health-care personnel are relatively immobile internationally.
Generalized systemic competence	Case management of dengue haemorrhagic fever: High cost and low effectiveness in unsophisticated systems. Cost per DALY at the margin of some interventions in a system with high level of professionalism and capacity may be much lower than in less well developed systems.
Discount rate	Hepatitis B immunization: Where discount rates are high, interventions with pay-offs well into the future become relatively less attractive, and age of the patient becomes a less significant determinant of cost-effectiveness.
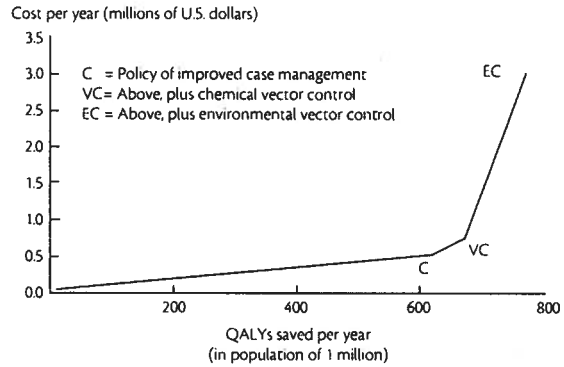
Fig. 7.4.2 Increasing cost per QALY associated with more complete control of dengue.

Intervention specificity refers to what fraction of intervention recipients would benefit assuming that the intervention is applied exactly to the individuals to whom it should be applied. Specificity will be influenced by such factors as the 'prevalence of the condition', 'incidence of condition', and 'levels of risk factors' (Table 7.4.4). Take BCG vaccination for TB as an example; many countries specify that it be applied to all newborns, but it is a benefit, *ex post*, only to that tiny fraction of children who would have died in childhood from miliary tuberculosis (TB) without it. Tuberculosis chemotherapy for sputum positives, by contrast, although costly, will virtually never be applied when unneeded; it is highly specific. Initially targeting BCG or other interventions to populations at highest risk, although inevitably at some cost, will maximize cost-effectiveness while simultaneously advancing equity objectives. Although the incremental cost per DALY gained by expanding coverage may be rising, sufficient resource availability may justify expansion.

To continue the TB example, patients who seek care, and who are then compliant with the treatment regimen, cost less than those for whom active case-finding is required or who require careful monitoring for compliance. All these factors lead to another reason for rising costs per incremental DALY gained. To take another example, oral rehydration therapy (ORT) in the hospital or clinic setting is highly cost-effective; it will only be used for severe cases of diarrhoea, and it is likely to be applied effectively by qualified medical personnel. When ORT is taken to the community, however, cost-effectiveness declines substantially, both because of a decrease in intervention specificity (mild cases will be treated unnecessarily) and because home treatment will be applied less effectively than hospital treatment in severe cases.

These points are relatively obvious, but there is often an optimistic bias toward assessing cost-effectiveness under assumptions of favourable targeting and compliance costs and of favourable intervention specificity. One might expect, as previously noted, rising marginal costs and decreasing marginal effectiveness as interventions are extended through populations; these combine to dilute cost-effectiveness. Thus favourable case cost-effectiveness estimates can be real, but their margin of applicability may be limited. In principle, it is desirable to acquire some sense of the responsiveness of intervention cost-effectiveness to a range of parameters, particularly the extent of application of the intervention. In practice, sensitivity

analysis is sometimes possible but often difficult—and comparisons are then made for 'representative' estimates of incremental cost-effectiveness to provide general guidance to decisionmakers. When there are great differences in the incremental cost-effectiveness of different interventions—as this chapter concludes there to be—this 'general guidance' can suggest important redirections of policy.

Fixed costs

When an intervention requires large fixed costs, total programme costs need to be weighed against total effects; simple assessment of marginal cost and effectiveness fails to suffice. The fixed costs involved in, to take several examples, investing in major facilities, mounting a media-based health education programme, or devising regulations and procedures can be substantial. Fixed costs need not be financial; managerial or political attention to a problem may have an important fixed cost element. When fixed cost may be important, understanding the total burden of disease is necessary for estimating potential total intervention effects. By the same token, cost-effectiveness analyses will need to include consideration of large increments in intervention. (See, for examples, Barnum et al. (1980) for analysis of simultaneous scaling up of multiple child survival interventions or Watts and Kumaranayake (1999) for a brief discussion of scaling up AIDS control interventions in Africa.)

Disease burden assessment needs can be combined with CEA in an explicit way to help evaluate where there might be large pay-offs

to R&D investments or to focused political or managerial attention on reallocation of interventions. This requires an analysis, essentially, of whether a major disease burden persists mainly because of: (1) A lack of knowledge about the disease and its determinants, (2) a lack of tools, or (3) failure to use the existing tools efficiently. Of course, more than one factor is likely in each case. Where possible, this analysis can be quantitative. Figure 7.4.3 illustrates an analytical approach recently applied (WHO 1996). Using data on the efficacy of the available cost-effective interventions, and consulting the judgement of field experts on the proportion of the population receiving effective interventions, it is possible to estimate:

◆ What portion of the potential burden of each disease or condition is now being averted

◆ What could be averted now with better use of existing cost-effective interventions

◆ What could be averted now, but only with interventions that are not cost-effective

◆ What cannot be averted with existing interventions but would require new ones

The analysis is intended to identify where the greatest needs lie, and thereby guide assessment of priorities for different major fixed commitments such as R&D or political attention. The unit of currency employed for this analysis is, once again, the DALY. While such analyses are not intended to suggest that some spurious
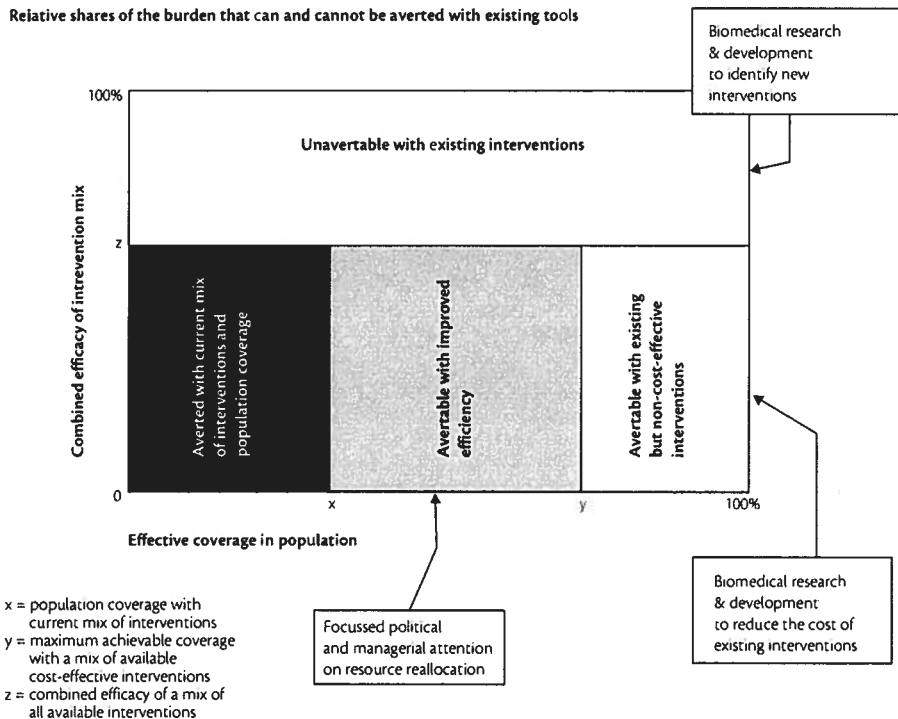

Fig. 7.4.3 Analysing the burden of a health problem to identify control and research needs.

precision can be achieved in the analysis of need, they do indicate a sense of the *relative* distribution of the effort required.

The area of the rectangle in Fig. 7.4.3 represents the total estimated disease burden in DALYs (or deaths or YLLs) from a given condition, such as diarrhoeal disease, under the counterfactual assumption that current explicit control interventions were not being applied. The horizontal axis represents the extent to which effective treatment is reaching the population—that is, how far into the population a mix of interventions is penetrating. The vertical axis represents the combined effectiveness of this mix. The subdivisions within that square represent different portions of the burden: (1) That which is being averted now by the existing mix of cost-effective interventions among the people that the intervention is reaching; (2) that which could be averted if the existing interventions were used more efficiently; (3) that which could be averted with existing tools, but not cost-effectively; and (4) that which is not avertable with existing interventions. Calculations of the relative share occupied by each subdivision can help to spell out the priorities. For example, where it is calculated that a large portion of the total burden of a certain disease cannot be averted with the existing cost-effective tools, then there is a strong case for R&D to develop new ones (if the disease burden is sufficiently large). Where it is calculated that a large fraction of the burden could be averted if existing tools were used more efficiently, *and the absolute disease burden is large*, there is a strong case for political and managerial attention to achieve fuller employment of available cost-effective interventions.

Non-health outcomes of health interventions

An additional problem in applications concerns interventions that have outcomes outside the health sector. Table 7.4.5 lists a number of important examples. CEA applied to health outcomes only will, obviously, understate the overall value of these interventions. While cost-benefit analysis would solve this problem, applicability may be difficult for reasons previously discussed. Under these circumstances a clear listing of costs, probable health effects, and non-health effects will at least inform the analysis.

Perhaps the clearest examples are control of smoking, promotion of breastfeeding, and environmental improvements. Limitation of smoking markedly reduces risk for lung cancer, ischaemic heart disease, and chronic obstructive pulmonary disease; outside the health sector it reduces (at least to some extent) property damage from fire and frees productive resources for alternative use. Breastfeeding, likewise, has multiple health effects; it enhances child immunity, reduces exposure to infection, provides balanced nutrition and, by suppressing ovulation, postpones the next pregnancy (Anderson 1990). The cost of breastfeeding, includes however, as do many health-promoting interventions, substantial amounts of mothers' time—which is not easily valued in terms, say, of wages forgone (Leslie 1992). Finally, whereas environmental interventions have beneficial health consequences, their main objectives may lie outside the health sector; World Bank (1992) provides a comprehensive discussion.[6]

Thus when interventions for health have a range of non-health outcomes, assessment of the attractiveness of these interventions

Table 7.4.5 Selected interventions with multiple outcomes

Intervention	Outcomes		
	Main health outcome	**Secondary health outcome**	**Non-health outcomes**
Provision of water supplies and sanitation	Control of diarrhoeal diseases	Control of skin, respiratory, and helminthic infections	Saving of household time; welfare improvements
Provision of soap	Control of diarrhoeal diseases	Control of skin, respiratory, and helminthic infections	Amenity
Reducing ambient air pollution	Reduced lung and vascular disease		Amenity
Reduction of vehicle speed limits	Reduced severity and incidence of crash-related injuries		Reduction in property damage from vehicle crashes; energy conservation; time costs
Control of smoking	Reduced incidence of lung cancer, heart disease, and chronic obstructive pulmonary disease	Reduced incidence of minor cancers; reduction in burn injuries	Welfare loss for current addicts, welfare gain for nonsmokers; freeing of land and labour for uses other than tobacco production
Vector control	Reduced incidence of vector-borne diseases		Improved welfare when vectors, such as mosquitoes, are nuisances
Female education	Reduced child mortality rates	Improved child growth; improved adult health	Higher levels of female productivity and earnings; improved congruence between actual and desired fertility levels
Breastfeeding	Improved child growth through improved nutrient availability and protection against diarrhoea	Protection of child against infectious disease; postponement of next pregnancy; possible long-term cognitive benefits to child	Savings in costs of infant formula and bottles; time costs for mother
Family planning services	Reduced child mortality	Reduced maternal morbidity and mortality	Economic and welfare gains from improved control of level and timing of fertility

should, ideally, quantitatively aggregate intervention effects along multiple dimensions. Likewise for clinical interventions there will frequently be joint costs (associated, for one example, with the availability of diagnostic facilities in a district hospital); again, in country-specific application, these matters can be assessed more quantitatively than they can be in a general overview.

The purpose of this section has been to introduce concepts without attempting to provide a detailed discussion of methods. In the next section an extended example of application of CEA is provided both to convey broad substantive lessons and to indicate how CEA has now become a working tool of the health policy analyst. A number of valuable handbooks on methods do exist and, as indicated earlier, this chapter is in the spirit of the US Public Health Services recommendations. Box 7.4.1 encapsulates that perspective.

An application: The disease control priorities project

This section summarizes the findings of a range of condition-specific analyses, principally relevant to low- and middle-income countries, that were undertaken initially for the World Bank's 'Health Sector Priorities Review' (Jamison *et al.* 1993) and then updated and substantially extended in the 'Disease Control Priorities Project' (DCPP) (Jamison *et al.* 2006; Laxminarayan *et al.* 2006).[7] Earlier in this chapter it was noted that dividing interventions into two broad categories—population-based primary prevention and personal—was conducive to discussing policy tradeoffs and this section is so divided. (Table 7.4.2 defined what is included in each of these categories.) The first subsection deals with population-based interventions, and the following subsection deals with personal ones. Unless otherwise specified, the assessments are of incremental cost-effectiveness from an implicitly defined typical starting point and they are designed to reach generalizable conclusions as well as to inform decision-making in a specific context. The DCPP reached a number of substantive conclusions and those are discussed to give a sense of the input CEA can make to informing policy.

Population-based primary prevention

Population-based interventions for primary were organized into three separate strategies in the DCPP—those designed to change personal behaviour, to control environmental hazards, and to deliver preventive medical services into the population (e.g. to immunize, to provide mass chemoprophylaxis to a population). In reviewing health policies, or intervention alternatives, it will often be useful to do so within each of these three broad strategies because of commonalities of logistics, policy instruments, and approaches within each. (This is true despite the frequently great diversity of conditions to be addressed within any one intervention strategy.)

Before turning to the summary of findings, the issue of joint costs (and multiple outcomes) of interventions is discussed in light of conclusions from the DCPP. The analysis upon which the DCPP was based was structured by diseases (or adverse health conditions more generally), and the issues addressed in the individual analyses thus concern the nature, cost, and effectiveness of the interventions available for dealing with each condition or its risk factors. In many cases, of course, any given intervention will address multiple conditions and, indeed, may well have important effects outside the health sector altogether.

Looking across findings of the individual chapters in the DCPP, it is clear that multiple effect and joint cost problems do complicate the task of assessing cost-effectiveness in many important instances; that said, it is more generally true that these problems are relatively minor or can be dealt with by reasonable approximations and simplifications in the analysis.

A few general conclusions on each public health approach emerged from the DCPP:

Personal behaviour change

Some personal behaviour changes that are favourable for health outcomes tend to occur naturally as incomes rise; these include, at least for many cultures, improved hygienic behaviours, increased energy intake and quality in the diet, and decreased crowding. Improvements in these behaviours are typically important for the pre-epidemiological transition diseases and can often be affected by educational interventions even though the main force driving improvements—income increases—is beyond the domain of health policy.

Other behaviours are likely either to be less dependent on income levels (for example, breastfeeding behaviour, sexual practices) or to be adversely influenced by income increases, at least for a period of time (for example, dietary excess, sedentary lifestyles, smoking, alcohol consumption). Most of these are risk behaviours for post-transition conditions. Although the natural course of development may well improve these behaviours, the Review found scope for affordable government policy to influence them. Regulatory policies and, particularly, taxation policies for tobacco, alcohol, and fatty meats show great promise for inducing behavioural change and, currently, are very much underused. Education of elites and the public are complementary instruments, not least because they generate the political will and popular support for regulation and taxation. The extremely high cost-effectiveness of smoking control makes it, perhaps, the top priority for governmental action.

Environmental hazards control

Rising incomes help with improving water supply and sanitation and that is likely to be important in prevention of a broad range of infectious and parasitic diseases. Specific investments in water supply and sanitation are unlikely, however, because of high costs to be justified in terms of health benefits alone. Vector control, however, is at least marginally cost-effective for a number of conditions (malaria, onchocerciasis, dengue) in some environments. Use of insecticide-impregnated bed nets appears particularly attractive for control of malaria-carrying mosquitoes. Industrialization introduces new hazards into the environment (lead, mercury, and the like) that can produce severe lifetime disability if not effectively controlled. Cleaner fuels and improvements in ventilation of indoor fireplaces and cookstoves can substantially reduce risks for chronic obstructive pulmonary disease (COPD); and occupational and transport safety measures are important in many specific instances. In principle, protective measures can be delivered through environmental intervention; and water fluoridation for prevention of caries is one example. Another problem is that of lead toxicity resulting from excess use of lead-based paints and combustion of gasoline with high lead content.

Box 7.4.1 US Public health service recommendations on CEA

In 1993, the US Public Health Service convened a 'Panel on Cost-Effectiveness in Health and Medicine'. The Public Health Service asked the Panel to assess the current state-of-the-art of cost-effectiveness analysis (CEA) in health and to provide recommendations for the conduct of future studies. Gold *et al.* (1996) bring together the Panel's conclusions, and their Appendix A provides a summary of recommendations. The following extracts provide the highlights of that summary.

Purpose of CEA

◆ CEA evaluates a given health intervention through the use of a 'cost-effectiveness ratio'. In this ratio, all health effects of the intervention (relative to a stated alternative) are captured in the denominator, and changes in resource use (relative to the alternative) are captured in the numerator and valued in monetary terms.

◆ CEA is an aid to decision making, not a complete procedure for making resource allocation decisions in health and medicine, because it cannot incorporate all the values relevant to such decisions.

Costs

◆ The major categories of resource use that should be reflected in the numerator of a C/E ratio include costs of health-care services; costs of patient time expended for the intervention; costs associated with caregiving (paid or unpaid); other costs associated with illness such as childcare or travel expenses; and costs associated with non-health impacts of the intervention (e.g. on the education system or the environment).

◆ Time spent seeking care or undergoing an intervention is a resource and a component of the intervention. It should be valued in monetary terms and incorporated in the numerator of a cost-effectiveness ratio. For individuals in the labour force, wages are generally an acceptable measure of time costs.

◆ In aggregating resource costs across time, CEAs should be conducted in constant dollars that remove general price inflation.

◆ 'Transfer payments' (e.g. cash transfers from tax payers to welfare recipients) associated with a health intervention redistribute resources from one individual to another. While administrative costs associated with such transfers are included in the numerator of a C/E ratio, the transfers themselves are not, since, by definition, their impact on the transferer, and the recipient cancel out.

Outcome measurement

◆ Incorporation of morbidity and mortality consequences into a single measure should be accomplished using QALYs. In general, since lives saved or extended by an intervention will not be in perfect health, a saved life year will count as less than one full QALY.

◆ In general, community preferences for health states are the appropriate ones for use. If distinct subgroup preferences are identified that will markedly affect a C/E ratio, the study should provide this information and conduct sensitivity analyses that reflect this difference.

◆ The health-related quality of life of those whose lives have been saved or extended by a health intervention may be influenced by characteristics such as age, gender, or race. This may affect the analysis in ways that are ethically problematic. In these instances, sensitivity analyses should be conducted to indicate explicitly how the results are affected by these characteristics.

Discounting

◆ Costs and health outcomes should be discounted to present value with the shadow-price-of-capital (SPC) approach to evaluating public investments. This rate (often termed the *social rate of time preference*) can be approximated by the real rate of return on long-term government bonds, and a real, riskless discount rate of 3 per cent is now appropriate. Because of the large number of previous CEAs that have adhered to a discount rate of 5 per cent, analysts should perform sensitivity analyses using 5 per cent. The discount rate should be subject to review, and possible revision, over time in light of significant changes in the underlying economic data.

◆ Costs and health outcomes should be discounted at the same rate.

Uncertainty

◆ At a minimum, univariate (one-way) sensitivity analyses should be conducted in order to determine where uncertainty or lack of agreement about some key parameter's value could have substantial impact on the CEA's conclusions.

◆ Where possible, where parameter uncertainty is a major concern, a reasonable confidence interval should be estimated based on either statistical methods or simulation.

Early research—reviewed in Pollitt (1990)—indicates that lead toxicity may be far more important than previously thought as a determinant of slow development and impaired mental functioning.

Immunization, mass chemoprophylaxis, and screening

Interventions that can be characterized under the headings immunization, mass chemoprophylaxis, and screening all share certain common characteristics: (1) They involve the direct administration or application of a specific technical intervention to individuals on a one-by-one basis; (2) they are directed to certain target populations; and (3) the coverage of the target population is important to produce the desired effect. Technically, each of these intervention strategies is highly efficacious when correctly applied to a compliant subject, but their actual effectiveness in low- and middle-income countries is strongly conditioned by the local administrative, managerial, and logistical capabilities, as well as by traditional cultural constraints.

Most immunization interventions are highly cost-effective; and many of them address highly prevalent conditions. Measles and tetanus vaccination appear particularly cost-effective and worthy of relatively greater attention within immunization programmes. Far more could be efficiently spent on immunization than is now being spent; and, even though costs of delivery tend to rise as more

marginal populations are reached, extending immunization programmes to virtually universal coverage is likely to prove both cost-effective and a practical way of significantly improving the health of the poor.

One particularly promising application of mass chemoprophylaxis lies in the administration of anthelmintic medication and micronutrient supplements to school-age children. Here cost-effectiveness appears quite high for conditions that, although of extremely high prevalence, have only recently been seen to be of substantial importance for intellectual and physical development. A programme of chemoprophylaxis for school-age children could, like the Expanded Programme on Immunization (EPI) for younger children, be expected to serve as the starting point for an ultimately much expanded capacity to deal with the health needs of this age group.

Perhaps the most significant cancers for which treatment may be cost-effective (breast, cervical) are ones for which early screening and referral are important; so, as noncommunicable diseases become increasingly significant, this strategy will become increasingly relevant. The emerging strategies for treatment of acute respiratory infections in children all rely heavily on community-based programmes for early detection and quick referral; with increased experience, improvements in capacity for cost-effective screening and referral programmes can be expected to develop.

Personal interventions

Facilities to provide personal intervention vary continuously in size, in the degree of complexity (and range) of the conditions that they address, in the sophistication of their facilities and equipment, and in the training and skill of their staff. For conducting comparable CEAs it is useful, nonetheless, to use generally accepted terminology in categorizing facilities into three groups—clinic-level, district hospitals, and referral hospitals—while recognizing that categorization involves much simplification and that the appropriate classification structure will vary substantially from country to country. Table 7.4.6 indicates (in a very general way), for each of these three levels of facility, examples of the kinds of interventions they might address and what capacity such a facility might have for primary modes of diagnostic and therapeutic intervention.

One lesson that emerged from the DCPP is that currently CEA is severely constrained by the paucity of data relating to the effect and cost of clinical interventions in low- and middle-income environments. In the absence of such analyses, it is perhaps natural for low- and middle-income countries to import, to the extent that resources permit, the methods of case management used or being developed in high-income countries. The key phrase here is, of course, 'to the extent that resources permit'. Available resources permit importation of high-cost interventions for only a tiny proportion of a population of a low- or middle-income country. In order to extend access to services for the rapidly emerging epidemic of acquired immunodeficiency syndrome (AIDS) as well as for the impending epidemic of noncommunicable diseases, radically lower cost methods of case management will need to be developed from the rich range of technologies and procedures that now exist, or that are coming into being.

Several additional observations can be made:

♦ Curative care for tuberculosis and sexually transmitted diseases appears extremely cost-effective; further, such care is not now being provided to anything like the extent it should be, given

the high burden of morbidity and mortality resulting from these conditions. Surgical treatment of cataract is also highly cost-effective.

♦ The extremely diverse range of clinical interventions of moderate cost-effectiveness (medical management of angina or diabetes are examples as is surgical management of cervical cancer) suggests that country-specific analyses of these conditions are required and that facilities capable of competently handling diverse conditions will need to be developed.

♦ The cost is sufficiently high for some clinical interventions to imply that even if they are effective (as is the case with coronary artery bypass grafting to deal with angina), their marginal cost-effectiveness (in this case relative to medical management) is so poor that their use should be actively discouraged until other, more cost-effective interventions can be delivered to their appropriate potential.

♦ Control of pain from terminal cancer could benefit perhaps 1.5 million individuals annually at acceptable costs; current legislation and standard practices greatly limit what is done in relation to what potentially could be done.

♦ Rehabilitation (in particular from leprosy, poliomyelitis, and injury) shows promise of being extremely cost-effective; but very little attention has been accorded rehabilitation, and little is known about how best to provide services on a population basis or what might be expected in terms of effectiveness and cost.

♦ Expanding access of populations to surgical services at the district hospital level appears highly cost-effective.

Again, as with the discussion of population-based primary prevention, one theme that emerges from this review of personal intervention cost-effectiveness is that of complexity and diversity. Many interventions are clearly not cost-effective, and public policy should make every effort to discourage their use. But the available evidence does suggest that a broad range of interventions, addressing a similarly broad range of conditions, *will* prove cost-effective. Many of these interventions are not now being used to anything like the extent that they should be. Likewise, much of what is currently undertaken by the clinical system is misdirected (toward interventions of low cost-effectiveness) or simply inefficiently used. Redirection of substantial resources from interventions of low cost-effectiveness toward those with very high cost-effectiveness is clearly possible; a central task of health policy must be to design implementation strategies and government policy instruments that can promote these potential efficiency gains. At the same time, however, given our at best modest understanding of how to promote efficiency, there will often be a strong case for additional resources (appropriately directed).

Lessons from the disease control priorities project

Five very broad conclusions can be drawn from the DCPP—one methodological and the other four substantive. The methodological conclusion is that it is feasible, on a broad scale, to assess systematically intervention cost-effectiveness in the health sector in a way that can provide broad policy guidance. The effort required is substantial, but results that allow broad intrasectoral assessment of intervention priorities can be obtained.

One substantive conclusion is that the available evidence points to great variation, across interventions, in marginal cost-effectiveness.

Table 7.4.6 Personal intervention: Level of facility and mode of intervention

Level of clinical facility	Typical conditions addressed	Intervention mode	Therapeutic		
		Diagnostic	Medical	Surgical	Physical or psychological therapy
Clinic (private, community, and school- and work-based)	Minor trauma; simple injections; support of population-based interventions; uncomplicated childbirth; family planning	Clinical	Short list of essential drugs (about 20)	Sutures	Important potential role for supervising physical therapy
District hospital	Complicated childbirth; fractures and burns; complicated infections; cataract; hernia; appendicitis; diabetes, hypertension, and similarly complex condition	Clinical; basic laboratory; basic radiologic facilities	Long list of essential drugs (about 200)	Capacity of dealing with abdominal surgery, many fractures, caesarean sections, some rehabilitative surgery	Design and management of more complex regimens of physical and psychological therapy
Referral hospital	More complicated medical and surgical conditions	More advanced laboratory and radiologic facilities	As above, but also specialized drugs, chemotherapy, and radiotherapy	As above but also capacity for more complicated surgery of head and chest	Support capacity for district hospitals

Laxminarayan *et al.* (2006) summarized this evidence by grouping interventions into ranges of marginal cost per DALY for different interventions in South Asia and sub-Saharan Africa. The challenge ahead is that of designing and implementing instruments of government policy that will greatly expand use of cost-effective while decreasing use of interventions that provide very little value for money.

Garber and Phelps (1997) calculate that under a reasonable range of assumptions it will make economic sense to pay for QALYs up to a cost of about twice the level of per capita income; this leads to a second substantive conclusion, which is that, in many countries, quite a broad array of specific additional intervention is likely to prove attractive by any reasonable economic standard. (Such intervention could either be financed by reallocation from non-cost-effective interventions within the health sector, or from new resources to the sector.)

The third substantive conclusion concerns the extent to which population-based preventive as opposed to personal strategies tend to be more cost-effective. Although there are some patterns (in particular, smoking control and primary prevention by way of immunization accounts for many highly cost-effective interventions), the general conclusion is that there is no especially strong reason to believe that population-based prevention or public health interventions to have superior cost-effectiveness.

The fourth substantive conclusion from the DCPP is that few cost-effective interventions in low- and middle-income countries require more specialized facilities than those available at district hospitals. Thus, even though one cannot argue in general in favour of prevention over cure or public health over clinical intervention, one *can*, at least tentatively, conclude that district hospitals and lower level facilities potentially offer almost all attractive interventions. A strong caveat here is that relatively few advanced surgical interventions were assessed. Many of the more cost-effective ones can be done in a district hospital but some may require referral facilities.

Conclusion

Multiple methods—cost-minimization analysis, cost-effectiveness analysis and cost-benefit analysis—can provide decision makers with insights into resource allocation in health. Methods for undertaking these analyses are now mature (although, of course, controversy continues on specific points). Extensive efforts over many years have yielded a large harvest of results. Among the methods in use CEA appears most relevant for many purposes, but little additional effort may be required to recast results in terms of cost-minimization or cost-benefit analyses. In short CEA and its relatives are tested, working tools for the analyst.

That said, much remains to be done that goes beyond specific individual applications, important as those remain. Parallel analyses of a broad array of interventions provide information more than in proportion to the number of interventions. Much of what has caught political attention in CEA has resulted from these larger efforts, although only few exist. Further investment in large comparative studies—taking a number of paradigmatic environments as the base case—will both generate valuable insights directly and serve as solid starting points for more tailored, country-specific efforts.

Notes

1. An example of negative intervention may be useful. Many countries now place individuals with severe mental illness in specialized mental hospitals that provide very long-term (and hence

expensive) care. An increasingly advocated alternative would be short-term inpatient care in general hospitals combined with long-term medical management on an outpatient basis. Scaling back or closing mental hospitals would gain dollars at the cost of DALYs. From the perspective of a national decisionmaker assessing the cost-effectiveness of closing down existing facilities is likely to prove more salient than would an exercise that hypothesizes no intervention as the base case and concludes that the health system should have avoided building mental hospitals in the first place. The widespread existence of mental hospitals for long-term care makes generic analysis of the desirability of closing them down valuable (perhaps for several paradigmatic environments).

2. Most procedures for measuring QALYs result in an interval scale of measurement with a scale unique up to an affine transformation. That is if q_1 is a utility function resulting from the measurement process then q_2 will equally well represent that measurement process if $q_2 = a + b\,q_1$, $b > 0$. Incremental cost-effectiveness analysis utilizing interval scales will preserve cost-effectiveness ratios under permissible transformations of the utility function. Any attempt at assessing cost-effectiveness in a more absolute way, e.g. not with respect to a stated starting point, will require a scale of measurement that is stronger in the sense that it will need to be unique up to a similarity transformation ($q_2 = b\,q_1$, $b > 0$) if cost-effectiveness ratios are to be preserved. Such a scale is called a ratio scale, which has a natural zero that interval scales lack. Use of QALYs or DALYs to measure burden of disease requires a ratio scale of measurement. The existing literature on utility measurement in health lacks an axiomatic formulation of the conditions under which such a scale will exist and, until such a formulation is undertaken, the theoretical foundation for disease burden measurement will remain shaky. See Krantz *et al.* (1971) for a thorough discussion of measurement theory, including a discussion of conditions under which two differently established interval scales on a set of outcomes can be used to generate an underlying ratio scale. These are conditions that indicate when, in the health context, utility measures generated by time trade-off method and the standard gamble method on the same set of outcomes would suffice to justify a ratio scale.

3. Existing disease burden studies (and cost-effectiveness analyses) discount life years lost from the life expectancy at the age of death to the present. For reasonable discount rates, this implies that the QALY or DALY loss associated with a death just after birth lies within 20–30 per cent of the loss associated with a death at age 20. This ratio differs substantially from the factor of 2 to 4 the limited number of empirical assessments have obtained (e.g. Institute of Medicine 1986). At the same time, deaths before birth are treated as having no loss—at patent variation with human reaction and social willingness to pay to avert late fetal death. This issue is also quantitatively important in that there are about 3.3 million stillbirths annually (over 1 million of which are in the 12 h before the expected time of birth). A conceptual approach to dealing with these two problems, and a related complete recalculation of the global burden of disease, appears in Jamison *et al.* (2006).

4. Garber (1999) discusses the question of what cost to assign pharmaceuticals (or devices) that are covered by patent. Patents confer temporary monopolies on the patent holders that allow prices to be set at levels often far above the marginal cost of production and packaging. This provides incentives for new product development. If a CEA uses the market price of a patented drug as its measure of cost then, clearly, it cannot properly be considered an incremental CEA. Garber (1999) argues that if the CEA is undertaken from a consumer perspective the practical approach will nonetheless be to use market prices (or whatever price can be negotiated by an influential purchaser) for costs. Pharmaceutical companies often adopt 'tiered' pricing regimes that result in lower prices in low-income countries. This will be profit-maximizing from the company's perspective and will result in patented drug prices in developing countries being much closer to the marginal cost of production—thereby attenuating the problem Garber raises. For this reason CEA's from a low-income country perspective should not treat patented drugs as tradeables.

5. Practical work in CEA often devotes substantial effort to defining and structuring the set of alternatives (Garber 1999, pp. 13–17). One result will often be to demonstrate that one or more alternatives are in some sense dominated by other alternatives under consideration. What techniques should be chosen early (i.e. under very tight budget constraints) and which ones added later can be assessed. Finally only in the context of considering closely related options can the attractiveness of a more costly but better technique be assessed. An example concerned an analysis of the attractiveness of coronary artery bypass grafts (CABG) in Brazil, which concluded that CABG for disease in the left main coronary artery was a 'good buy' because the cost per QALY was only about 25 per cent of Brazil's GDP per capita. This, however, was the cost per QALY of CABG relative to doing nothing. Medical management and (now) angioplasty are less costly but nonetheless somewhat effective alternatives to CABG. The right way to think about CABG is in terms of how much more it would cost than one of these alternatives and how many more QALYs it would buy. It is likely that considered as incremental to alternatives the cost per QALY for CABG would be far higher than the original estimate. The cost-effectiveness of any one intervention, then, can be highly sensitive to the range of alternatives being considered.

6. The extent to which environmental interventions are justified on health grounds varies. While some discussions of air quality, for example, place importance on the amenity value of clean air other emphasize health consequences. A particularly important example of the need to consider non-health outcomes, in the context of very poor environments, concerns improving water supplies (from collection of surface water, say, to wells serving a community). Unclean and inadequate water supplies undoubtedly contribute substantially to risks of diarrhoeal and other disease—diseases killing millions of people every year. Increased quantities of cleaner water will have important health benefits. Improving water supplies is, however, very costly and, in most circumstances, would appear non cost-effective relative to public health or clinical interventions to reduce child mortality. That is they would appear non cost-effective if there were no other benefits. Other benefits include time savings (usually for women) in fetching water and the amenity value (beyond the sanitary value) of the cleaner bodies, clothing, and dwellings that improved water supplies facilitate. A cost-benefit analysis, if it were feasible,

would place a monetary value on all benefits that would allow combining them. If CBA cannot be done in an acceptable way, can CEA help to inform decisions? This is probably best done through sensitivity analysis. If all the non-health benefits can be given monetary values, one can calculate the dollar value per QALY that would be required for a satisfactory rate of return to the investment in water supplies. A high value would suggest that the water supply intervention was unattractive. Alternatively one can calculate the cost of the intervention that would make the cost per QALY of improved water competitive with alternatives for reducing child mortality. If the calculated cost is much less than the actual cost this would suggest that primary justification for the water supply investment should be for its other benefits, not its health benefits, even if the other benefits cannot be valued in monetary terms.

7. In many ways the DCPP is very much in the spirit of several previous assessments (e.g. Walsh & Warren 1979), which provided an assessment of priorities for control of communicable childhood diseases in developing countries. Other recent works in this comparative spirit, but emphasizing effectiveness, include Amler and Dull (1987) and the US Department of Health and Human Services (1991), which reviewed a broad range of preventive intervention policies for the United States, and, more for clinical preventive services, the US Preventive Services Task Force (1989) review of the effectiveness of 169 interventions. The state of Oregon in the United States rank ordered over 700 interventions, using cost-effectiveness and other criteria, for the purpose of rationing limited public resources to provide healthcare for the poor; Strosberg and others (1992) discuss many facets of the Oregon plan. Jha *et al.* (1998) assessed the relative cost-effectiveness of 40 potentially important interventions in the West African context. The Harvard 'life saving' project assessed cost per life saved of several hundred preventive options (Tengs 1996). Udvarhelyi *et al.* (1992) provide a comprehensive review of medical cost-effectiveness and cost-benefit studies from the perspective of their methodological adequacy. All these approaches to the analytic evaluation of health practices fall within the general area of CEA. Once somewhat comparable cost-effectiveness assessments are available for a range of interventions then analyses focusing on only a limited set of interventions can be put into the context provided by existing studies. For example, careful analysis for the sub-Saharan Africa context of malaria control (Goodman *et al.* 1999) and HIV-1 transmission interruption (Kumarayake & Watts 2000) both benefit from and contribute to an increasing understanding of intervention cost-effectiveness in Africa.

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