Economic Evaluation of Immunization Strategies

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Resources used to provide health care are vast but not limitless. When clinicians are asked to participate in decisions for large groups of patients (in a managed care context, in an institution, or at the level of local health authorities), the balance between consumption of resources and the benefits of an intervention is important. Clinicians may use cost-effectiveness and cost-benefit studies to inform such decisions (but not to make them). Because of differences in methods, the presentation of results, and country-specific parameters, economic evaluations of the same vaccination strategy by different groups may have divergent results. In this article, we review methodologic issues, limitations, and ethical considerations related to economic evaluations of immunization strategies, focusing on immunizations associated with travel.

Economic evaluation is the comparative analysis of alternative lines of action that includes the effects as well as the costs of those actions. The technique was developed by economists to assist in decision-making, when a choice must be made between several courses of action. The aim of cost-benefit and cost-effectiveness analyses of vaccines is to provide a framework within which policy related to immunizations can be explored in the context of a particular health system. The precise basis for a decision based on economic evaluations will depend, however, on the context of the evaluation and whether resources must be allocated within a fixed budget.

Interventions that produce both a health benefit and cost savings are inherently cost-effective. Economic evaluation of the early vaccines, such as vaccines for diphtheria, tetanus, and pertussis, for polio, and for measles, consisted of comparing the costs of vaccination with the savings in treatment costs. For all these vaccination strategies, monetary savings are attained in tandem with improved health status, and the decision to vaccinate is straightforward. However, other vaccines produce health benefits but do not save costs. The decision to vaccinate in such instances depends on the willingness of society to pay for increased health benefits.

In the economic evaluation of an immunization program, different vaccination strategies are calculated and compared with a reference strategy, which is often the nonintervention strategy (i.e., no vaccination). Costs can be divided into medical costs related to the disease (the costs of medication, laboratory tests, consultations, and hospitalizations) and costs relating to the vaccination (the purchasing price of the vaccine and the costs of administering the vaccine and treating side effects). Societal costs are indirectly related to the treatments and vaccination and mainly consist of the costs of lost productivity due to disease [1].

The growth of travel and the increasing number of persons affected by travel-related illnesses (some of a serious nature) has focused attention on the health hazards of international travel. A special challenge when considering the cost-effectiveness or cost-benefit ratios of immunization for travelers consists in determining the effectiveness of the vaccination, which is related not only to the characteristics of the vaccine but also to the prevalence of disease in the country of destination, the reason for travel, and the behavior of the traveler.

Most economic evaluations of immunizations in travelers are cost-effectiveness and cost-benefit analyses of hepatitis A vaccination; hepatitis A is the most common vaccine-preventable disease that affects travelers to developing countries [2]. Typhoid fever rarely strikes travelers to areas of endemicity, and efficacy data on the use of typhoid fever vaccines for travelers are few [3], although more quantifiable data are available for military personnel deployed to areas in which typhoid fever is endemic [4].
ANALYTIC TECHNIQUE

A full economic evaluation deals not only with costs but also with the consequences (health benefits) of the intervention studied. Costs are always expressed in monetary units (e.g., dollars, euros, or yen). The feature that distinguishes between the different techniques of economic evaluation is the way in which health benefits are expressed: in monetary units, in natural units (cases avoided or life-years saved), or in quality-adjusted life years (QALYs).

"Cost-benefit analysis" is sometimes used loosely as a general term covering all types of economic evaluation, but, among health economists, the term is usually restricted to those forms of evaluation in which the health benefits (cases avoided or life-years saved) are expressed in a monetary value. Not surprisingly, the main controversy surrounding cost-benefit analysis is how monetary values are to be attached to benefits such as health outcomes. This is generally achieved using a "willingness-to-pay" approach—that is, by eliciting the value that might be placed by individuals on reduced morbidity or on an intervention’s impact on quality of life, when the individual is properly informed. Cost-benefit analyses force an explicit decision between costs and benefits by measuring both in the same units. An advantage of cost-benefit analysis is that it is not limited to informing resource allocation decisions within the health care sector but can also be used to compare programs in different sectors of the economy [5].

In cost-effectiveness analysis, the problem of placing a monetary value on life or health is avoided. Incremental costs are compared to incremental health benefits, as measured in natural units, such as cases avoided, disability-years averted, lives saved, or life-years saved. The effectiveness of different procedures is then expressed in terms of cost per unit of outcome.

A particular type of cost-effectiveness analysis is cost-utility analysis, in which outcomes are measured in terms of QALYs gained. QALYs combine changes in quantity and quality of life into a single composite measure that is independent of the program or disease being assessed. This approach makes it possible to compare, for example, new vaccines for drastically different illnesses, ranging from pneumonia to long-term neurologic impairments. The quality-adjustment factors (or utilities) are weights ranging from 0 to 1 (1, optimal health; 0, health state judged to be equivalent to death). These factors should reflect aggregated preferences of individuals for the outcomes and have been measured directly among patients or the general public.

THE IMPORTANCE OF THE PERSPECTIVE

The choice of the perspective is the most important part of an analysis, because it determines which costs should be included in the analysis and how they should be valued. Whether a vaccine is cost-effective may depend on who is asked. The patient, society in general, and a third-party payer may reach different judgments about specific costs. In the comprehensive societal perspective, all costs and benefits should be identified, regardless of who incurs the costs and who receives the benefits.

Hospitalization costs, vaccine efficacy, and vaccine prices, as well as the incidence of disease, are main determinants in the cost-effectiveness equation. For a rotavirus immunization program, for example, the number and cost of hospitalizations due to rotavirus infection are of paramount importance. With the gradual decrease in hospital charges associated with rotavirus diarrhea in the United States, the value of a rotavirus vaccine has decreased [6]. Furthermore, rates of hospitalization in some groups (e.g., individuals enrolled in health maintenance organizations) may become even lower, as the care of patients with diarrhea is shifted from an in-patient to an out-patient basis. Because caregiver loss of earnings accounts for >90% of societal costs, companies contracting health services for their employees may perceive that societal costs are particularly important and may opt to pay for the vaccine themselves, to ensure continuity in the workforce. A similar argument can be applied to vaccination against hepatitis A, which is associated with low mortality and low hospitalization rates but high societal costs in terms of lost productivity, as has been shown in studies of airplane crews [7].

TARGET POPULATIONS

Cost-effectiveness analyses of immunization strategies are very sensitive to incidence and prevalence rates of disease. The risks of acquiring hepatitis A virus infection for US and European residents traveling abroad vary according to the living conditions and length of stay of the traveler and the incidence of hepatitis A in the area visited. Risks are highest for travelers who live in or visit rural areas, trek in back-country areas, or frequently eat or drink where sanitation is poor. Concentrating interventions on those segments of the traveling population that are at high risk of infection or of developing serious sequelae after infection can turn a program with an unfavorable cost-effectiveness ratio into a cost-effective intervention.

Although almost all elderly people were immune to hepatitis A virus a few years ago, for new cohorts of this age group, this will not be the case [2]. Mortality due to hepatitis A increases with age, but so does the seroprevalence of hepatitis A virus antibodies. Screening elderly travelers may eliminate the need for vaccination for many of them, thus increasing the cost-effectiveness of the vaccination. Several studies have undertaken analyses of the cost-effectiveness, as well as the efficacy and safety, of available vaccines for military
personnel and workers involved in peacekeeping missions [8, 9]. Active immunization for hepatitis A virus seems to be the most cost-effective option for frequent travelers [10, 11] and for travelers who are planning longer stays, as well as for military personnel [12], especially those in troops likely to be deployed overseas repeatedly.

THE USE OF MODELS

Most economic evaluations of immunizations are based on decision-analytic models. The main advantage of such models is that they offer a flexible and timely framework for analysis. Because incidence rates for infectious diseases may differ substantially from year to year, models may offer the advantage of more-stable estimates of incidence rate.

Models have, however, clear limitations. Pieces of information from different studies and populations are combined and used in a single model. Moreover, estimates incorporated into the analysis may be inaccurate, and, because of the complexity of many models, biases may not be apparent to readers of the study.

The data generated from a model must be interpreted within the limitations of the model and its assumptions. With regard to travel immunizations, the incidence of disease in the country of destination is the most critical factor in most models. Use of incidences specific to the destination may enhance the value of the model.

DEALING WITH UNCERTAINTY

Economic evaluations of vaccines require the analyst to combine information about the incidence of the disease to be prevented, the probabilities of sequelae, the clinical effectiveness of the vaccine, and costs incurred. Costs incurred may include those for treatment of the disease and its sequelae, administration of the vaccine, and treatment of potential adverse effects. Sensitivity analysis is the main method by which analysts test for uncertainty. It involves changing the value of variables that are known to be uncertain or that change over time. A plausible range for variation can be determined by review of the literature or by consulting experts. Another approach is to use scenario analysis. Typically, the scenarios will include a base-case (best-guess) scenario, the most optimistic (best-case) scenario, and the most pessimistic (worst-case) scenario. Finally, another approach is to undertake a threshold analysis. In threshold analysis, the critical value(s) of a parameter or parameters central to the decision are identified, and the analyst assesses which combination of parameter estimates could cause the threshold to be exceeded and make the program unacceptable.

WHAT IS CONSIDERED COST-EFFECTIVE?

There is no single and valid criterion for the cost-effectiveness ratio below which an intervention should be adopted. A threshold value of $50,000 per life-year saved is often quoted in the medical literature. Laupacis et al. [13] found in 1992 that technologies that cost <$20,000 per QALY were almost universally accepted as appropriate; technologies that cost $20,000–$100,000 per QALY were provided routinely, but there might be no consensus about their appropriateness; and technologies that cost >$100,000 per QALY were generally deemed to be inappropriate. Similarly, the Committee to Study Priorities for Vaccine Development [14] placed candidate vaccines in 4 groups or levels (level I, most favorable and saves money and QALYs; level II, more favorable, with costs <$10,000 per QALY; level III, favorable, with costs of $10,000–$100,000 per QALY; and level IV, less favorable, with costs >$100,000 per QALY).

LIMITATIONS AND ETHICAL ISSUES

Although economic evaluation provides an argument for targeting specific groups, it also emphasizes the differences between public policy and individual preference [2]. The value and benefits that individuals would attribute to various methods of prevention are linked to their perception of the threat of disease and its likely impact on their lives. Some people are at greater risk or have lower thresholds for taking any health risk [15].

The general ethics of economic assessment of technologies rests on the fundamental presupposition that having information is a precondition for making good choices and that “good” is what results in the greatest good for the greatest number. Of primary concern from a policy viewpoint is the fact that cost-effectiveness analyses do not usually incorporate the importance of the distribution of the costs and the consequences (health gains) among different patient or population groups into the analysis. Yet, in some cases, the identity of the recipient group (e.g., individuals with lower socioeconomic status, elderly individuals, and working mothers) may be an important factor in assessing the social desirability of an immunization program. Although it is sometimes suggested that differential weights be attached to the value of outcomes associated with special recipient groups, this is seldom done. Rather, an equitable distribution of costs and consequences across socioeconomic or other defined groups in society is viewed as a competing element in decision-making, in addition to that of efficient deployment of resources.

Another point of controversy involves the question of when an aggregation of modest benefits to larger numbers of people should be allowed to outweigh more-significant benefits to fewer people. Within the model, all QALYs are considered to be equal, without regard for the nature of the health benefit.
that is measured. Thus, the number of QALYs gained when many people receive a small health benefit as a result of a reduction of a minor form of illness can be the same as the number of QALYs gained when a very small number of deaths are averted.

Finally, economic evaluation techniques assume that resources freed or saved by preferred programs will be used in alternative worthwhile programs. This assumption warrants careful scrutiny: if the freed resources are consumed by other ineffective or unevaluated programs, then not only are no savings gained, but overall health care system costs will actually increase, without any assurance that additional improvements in the health status of the affected populations will result.

References