

METHODOLOGY

Economic Evaluation of Treatment Strategies in Gastroenterology

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INTRODUCTION

Given the increased pressures on health-care budgets, there is a growing interest in the methods for assessing the value for money of health-care interventions. Economic evaluation compares the costs and consequences of alternative health-care treatments and programs (see Fig. 1). It builds on the data comparing the relative clinical effectiveness of treatments, which normally comes from randomized controlled trials. The costs considered typically include direct medical costs, such as drugs, medical services, and hospitalizations. However, some studies adopt a broader perspective and consider patients' out-of-pocket expenses, costs falling on agencies outside the health-care sector, or productivity changes, if patients have to take time off work to receive care or can return to work if their condition is resolved (1).

Some economic evaluations are based solely on a single clinical study, where resource use and quality of life data are gathered alongside a clinical trial. However, it is much more common to undertake economic evaluations based on decision-analytic modeling, where clinical, cost, and quality of life data are brought together, or synthesized, from a number of sources.

Since clinicians are increasingly likely to encounter value for money issues, either in their clinical practice or their research, this short article for the Red Section outlines the basic forms of economic evaluation and gives a few examples from the field of gastroenterology.

BASIC FORMS OF ECONOMIC EVALUATION

The simplest form of economic evaluation is *cost analysis* or *cost-minimization analysis*, where only the costs of the al-

ternative strategies are compared. Of course, this approach can only be used in situations where there is common agreement, or evidence from research studies, that the alternative strategies are clinically equivalent.

An example of a cost analysis is the study by Ladabaum *et al.* (2). Their objective was to reappraise the *Helicobacter pylori* test-and-treat strategy for un-investigated dyspepsia, as compared with empirical proton pump inhibitor (PPI) therapy, in the light of the decreasing prevalence of *H. pylori* infection, peptic ulcer disease, and peptic ulcer disease attributable to *H. pylori*.

Using a decision-analytic model, populated with data from the literature, they found that the two strategies yielded similar clinical outcomes at 1 yr (assessed in terms of active peptic ulcer disease). Therefore, in their view, a simple comparison of costs was justified. They found that cost per patient was also similar between the two strategies, \$545 for the test-and-treat strategy and \$529 for empirical PPI therapy.

They concluded that as *H. pylori* prevalence, the likelihood of peptic ulcer disease, and the proportion of ulcers due to *H. pylori* decrease, empirical PPI therapy would become cheaper. However, given the modest cost difference, the test-and-treat strategy may still be favored if patients without peptic ulcer disease derive long-term benefit from *H. pylori* eradication.

In another cost-minimization analysis, Ladabaum *et al.* (3) assessed whether the combination of an educational session and availability of office-based *H. pylori* testing increased the use of the test-and-treat intervention (TTI) and whether there was any related improvement in patient outcomes. This study was conducted alongside a prospective trial in six primary care centers, three with TTI and three designated as usual care controls.

It was found that *H. pylori* testing was performed more often in TTI patients (81% vs 49%, $p = 0.004$). However, gastroenterology referral rates, endoscopy, or upper GI radiography rates were similar between the groups ($p = 0.91$), as were primary care visits per patient ($p = 0.92$). TTI patients were less likely to receive repeated antisecretory medication prescriptions ($p = 0.003$). Symptomatic status at 1 yr and satisfaction with care also did not differ between the groups, justifying the cost-minimization approach. Median annualized disease-related expenditures per patient were \$454 for TTI and \$576 for usual care patients ($p = 0.17$). The authors concluded that the combination of an educational

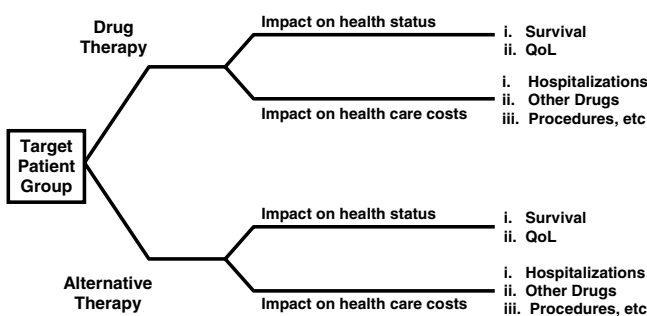


Figure 1. Components of economic evaluation.

session and availability of office-based *H. pylori* testing may increase acceptance of the test-and-treat strategy by primary care providers, but that more research is required to assess whether this strategy yields significant improvements in clinical and economic outcomes, as compared with usual care.

Although cost-minimization analysis may suffice on some occasions, the situations where alternative therapies are truly clinically equivalent are quite rare. For example, a *H. pylori* test-and-treat strategy would not be equivalent to PPI therapy if *H. pylori* eradication reduces gastric cancer rates in the future.

In situations where one treatment strategy generates more benefits than another, the extra benefits need to be weighed against the extra costs. In *cost-effectiveness analysis*, the incremental costs are compared with an appropriate measure of incremental benefit, such as symptom-free days, cases detected, or life-years gained. An example of a cost-effectiveness analysis is the study by El-Serag *et al.* (4), comparing the cost-effectiveness of NSAID therapy alone with seven other treatment strategies to reduce the risk of NSAID-related clinical UGI events (*e.g.*, symptomatic ulcer, perforation, and obstruction) among chronic users of NSAIDs. Using a decision-analytic model, the seven strategies were assessed in terms of their *incremental cost per clinical UGI event prevented*, compared with conventional NSAID treatment over 1 yr.

The authors found that use of a COX-2 selective NSAID and co-therapy with PPIs were the two most cost-effective strategies. However, the incremental cost of these therapies was high (>\$35,000) in persons with a low risk of a clinical UGI event with conventional NSAIDs (*e.g.*, 2.5% per year or less). Also, because small changes in costs or assumed efficacy of the drugs could change the conclusions, the incremental cost-effectiveness ratios between any two strategies were presented for a wide range of values for costs and rates of clinical UGI events.

Whereas cost-effectiveness analysis may suffice for the economic analysis of some treatment choices, it is common to find that there are many dimensions along which clinical success or failure could be assessed, and many health states that patients could end up in. Here, in order to make an overall assessment of the clinical or social value of the interventions, a composite measure is required. A popular measure in economic evaluations is the quality-adjusted life-year (QALY), which combines the improvements from therapy in terms of life expectancy and quality of life. The estimation of QALYs is not without controversy, but the measure has been fairly widely accepted by those that undertake or use economic evaluations.

Economic evaluations that use QALYs as the measure of consequences are called *cost-utility analyses*, which are essentially a variant of cost-effectiveness analysis. An example of this type of study is that by Arguedas *et al.* (5). They examined different screening strategies for hepatocellular carcinoma, including no screening, alpha fetoprotein (AFP) alone, AFP plus abdominal ultrasound, AFP plus ab-

dominal three-phase CT, and AFP plus abdominal magnetic resonance imaging. The study used a Markov model, where members of a cohort were divided among several mutually exclusive health states and movement of the cohort across these states was modeled over time. The health states were defined to capture the salient characteristics of the disease and the treatments under consideration. They included compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and orthotopic liver transplantation. Each of the states had an associated cost and health state utility value. The latter was used to calculate the QALYs associated with each strategy, based on the time members of the cohort spent in each state.

The results showed that screening with AFP plus three-phase CT was the most cost-effective strategy, having an incremental cost-utility ratio of \$25,232 compared with no screening. Sensitivity analysis (a way of allowing for uncertainty in the estimates) showed that the results were most sensitive to the annual incidence of hepatocellular carcinoma, the proportion of tumors amenable to treatment, and the screening test characteristics and cost.

Another recent cost-utility analysis is that by Saab *et al.* (6). They compared the costs and clinical outcomes of three strategies for primary prophylaxis of variceal bleeding: (i) treatment with a β -blocker without undergoing upper endoscopy; (ii) upper endoscopic screening, with those found to have large varices treated with a β -blocker; and (iii) no prophylaxis.

This study also used a Markov model, the health states including cirrhosis with and without variceal bleed, and treatment with β -blockers. The health state utilities were obtained from an expert panel of gastroenterologists and hepatologists experienced in the management of patients with hepatic cirrhosis.

The results showed that universal prophylaxis with a β -blocker was preferred because it was consistently associated with the lowest costs and highest QALYs.

Of course, the results of cost-utility analyses cannot be interpreted without knowing the threshold willingness-to-pay for a QALY. In those jurisdictions, such as the United Kingdom, where economic evaluation plays a formal role in decision making, thresholds of £20,000–£30,000 per QALY gained have been suggested (7). In the United States, authors typically refer to the incremental cost per QALY ratios of treatments that are fairly widely available. Mentions of thresholds in the range of \$50,000–\$100,000 per QALY gained are fairly common (8).

The broadest form of economic evaluation, *cost-benefit analysis*, seeks to quantify all the costs and consequences in monetary units. Then a given treatment would be considered worthwhile if the monetary value of the consequences exceeded that of the costs. However, while attractive in principle, cost-benefit analyses are only occasionally undertaken in the field of health care, owing to the problems of measuring and valuing all of the consequences of health improvements in money terms, by estimating individuals' *willingness-to-pay*.

(See Kleinman *et al.* (9) for an example of a willingness-to-pay study in gastroesophageal reflux disease.)

A much more common approach is to use a *cost-effectiveness acceptability curve* to explore the probability of the treatment being cost-effective, given particular threshold values of willingness-to-pay. For example, in a systematic review and economic analysis of eradication therapy in the treatment of *H. pylori* positive peptic ulcer disease, Ford *et al.* (10) assessed the probability that the various strategies (*e.g.*, intermittent PPI, maintenance PPI, and *H. pylori* eradication) would be cost-effective at different values of the willingness-to-pay for a month free from dyspepsia.

CONCLUSIONS

Economic evaluation now plays a formal role in decisions about the reimbursement or use of new health technologies in a number of countries, especially in the case of listing of new pharmaceuticals on the national or local formulary (1). Its role in countries like the United States, where there are extensive patient copayments, is much less certain, but is likely to be the subject of increasing debate (11).

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