THERAPEUTIC DECISION MAKING: A COST-BENEFIT ANALYSIS

STEPHEN G. PAUKER, M.D., AND JEROME P. KASSIRER, M.D.

Abstract To help the physician decide whether or not to treat a patient who may or may not have a disease, a method has been developed for calculating a therapeutic threshold. If the probability of disease in a given patient exceeds the threshold, the preferable course of action is to treat; if the probability is below the threshold, the preferable course of action is to withhold treatment. This method is applicable in many medical and surgical settings in which some diagnostic uncertainty exists after all appropriate studies have been carried out. The technic not only exposes some of the basic principles of therapeutic decision making in the face of diagnostic uncertainty but also forms a convenient framework for analyzing the impact of "soft" clinical data on the decision-making process. (N Engl J Med 293:229-234, 1975)

THE dilemma of whether or not to administer a certain drug or carry out a certain operation in a patient without an established diagnosis is familiar to physicians. In many clinical situations considerable uncertainty exists about the presence or absence of a given disease because no further confirmatory diagnostic studies are available. Given this uncertainty, administering a treatment known to be effective for the disease under consideration will be beneficial if the disease is actually present, but may be harmful if the disease is absent. Failing to administer the treatment, on the other hand, may be deleterious if the disease is present but not if it is absent. Consider, for example, the common problem of unexplained right-lower-quadrant abdominal pain of short duration. Suppose the physician has exhausted all diagnostic studies and has concluded that acute appendicitis is quite unlikely. What are the factors involved in his decision either to operate immediately or to wait and observe the patient? The benefit of appendectomy is to cure the patient if he actually has appendicitis, but, if the patient does not have the disease, the cost is some finite risk of morbidity and mortality. Conversely, avoiding operation may exact a serious penalty if the patient actually has appendicitis (perforation, peritonitis, and sepsis), but is clearly the best course if the patient is afflicted with gastroenteritis rather than appendicitis. Physicians with excellent clinical judgment have an implicit ability to assess the integrated effect of the benefits and risks of therapeutic procedures and to relate this assessment to the likelihood of a diagnosis when they decide either to treat or to withhold a treatment. Too often, however, judgments of this type are made without detailed analysis of all these relevant factors.

In recent years, methods for dealing with such complex therapeutic decisions in an explicit and logical fashion have been developed. These methods include construction of a decision tree that describes the possible courses of action available and the consequences of each; obtaining a quantitative estimate of the probability and utility (value) of each outcome; and combining the estimates by a method that provides a measure of the "expected value," or worth, of each course of action.[1,2] Starting from these principles, a simple and clinically useful mathematical relation has been derived in this study between the *benefits* and *costs* of a treatment in a given disease and the threshold level of clinical suspicion of the disease. When the probability of a patient's illness exceeds this threshold level, the better choice is to administer treatment; when the probability is below the threshold, the better choice is to withhold treatment. The method is applicable to many problems that physicians encounter in a variety of medical disciplines and is useful in clinical situations even when an exact assessment of the benefits, costs and the probability of the disease cannot be made.

From the Clinical Decision Making Group, Department of Medicine, Tufts University School of Medicine, the Medical Service, New England Medical Center Hospital and Project MAC, Massachusetts Institute of Technology (address reprint requests to Dr. Pauker at the New England Medical Center Hospital, 171 Harrison Ave., Boston, MA 02111).

Supported in part by grants (IRO1MB00107-01) from the U. S. Public Health Service and (NIH HS 0091101) from the Bureau of Health Services Research, Health Resources Administration. U. S. Public Health Service.

METHODS AND RESULTS

To focus on the therapeutic aspects of a clinical problem, a situation is considered here in which no further diagnostic information or tests are available. The following assumptions have been used in constructing a model of this problem:

1. Only a single disease is being considered: a given patient either has, or does not have, the disease.
2. A well defined, clearly beneficial treatment for the disease is available.
3. The physician must decide whether or not to administer the treatment in the face of some uncertainty about the presence or absence of the disease in a given patient.
4. A patient who has the disease and goes untreated is subjected to the loss of some finite benefit of therapy.
5. A patient who does not have the disease, but who nevertheless receives treatment, is subjected to some finite cost of therapy — for example, risk of complications. The patient who has the disease is subjected to the same cost but also gains some finite benefit from treatment.

A model with these characteristics is represented in Figure 1. Referring to the figure, one can see that the decision to be made (square node) is whether to administer therapy (treat) or not to administer therapy (no treat). In either case, there is some chance (circular nodes) that the patient either has the disease (dis) or does not (no dis).* The notation "no dis" indicates that the disease under consideration is not present; other diseases may be present. The four possible outcomes are represented by the terminal branches of the tree. The uppermost branch represents the patient who has the disease and is treated. The second terminal

*This notation corresponds to the symbols D+ and D− used elsewhere.[3]

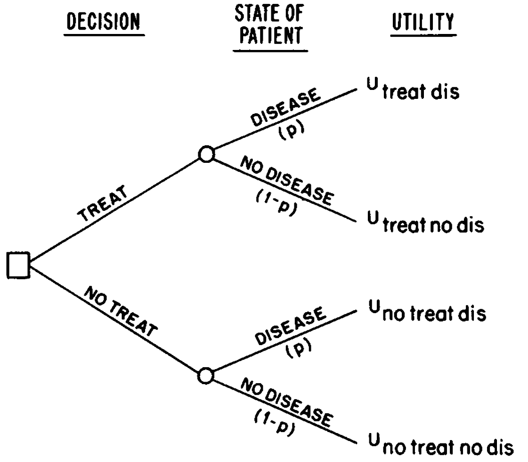

Figure 1. Decision Tree Showing Two Therapeutic Choices for Patients Who Either Have or Do Not Have a Given Disease. The square node is a decision point; the circular nodes denote a chance happening.

branch represents the patient who does not have the disease, but who, nevertheless, also receives treatment. The third branch represents the patient who has the disease, but who goes untreated. The lowermost branch represents the patient who does not have the disease, and who is not treated. The probability that the disease is present is represented as (p); thus, the probability that the disease is not present is $(1 - p)$. Each of the four possible outcomes has a certain value (usually to the patient but sometimes to society), and this relative value is denoted as the utility of the outcome (e.g., $U_{treat\,dis}$). If the four utilities are measured in consistent units (e.g., length of life, absence of pain, dollar value or even in arbitrary units), the values of the outcomes can be compared and ordered.

Assigning numerical values to probabilities and utilities of each branch makes it possible to calculate the worth, or *expected value,* of both main options — in this case, the expected value of "treat" and "no treat." For readers unfamiliar with the methods used to make these calculations, a brief summary is given here: the contribution of each of the terminal branches to the value of a particular course of action is equal to the product of the utility of that branch and the probability of its occurrence. The expected value of each decision course is calculated by summing of the products of the probability and the utility for each of its two subbranches.* For example, the expected value of the option to treat (EV_{treat}) is equal to $(p)U_{treat\,dis} + (1 - p)U_{treat\,no\,dis}$. After the expected value of each option has been calculated, the option with the higher expected value should be selected to maximize the likelihood of achieving the best outcome.[1,2]

Identification of Benefits and Costs

Ideally, one would choose to treat only patients with the disease and avoid treating those without the disease. As pointed out earlier, however, when the presence of disease cannot be ascertained with certainty, treatment will sometimes be withheld from patients who have the disease and sometimes given to patients who are free of the disease. The benefit of treatment is clearly restricted to patients who have the disease, and can be expressed as the difference between the utility of administering treatment to patients who have the disease and the utility of withholding treatment in those who have the disease (i.e., $U_{treat\,dis} - U_{no\,treat\,dis}$). The adverse effects of treatment apply to treated patients both with and without the disease. For convenience, the cost of treatment in patients who have the disease is incorporated into the utility of the uppermost branch ($U_{treat\,dis}$). Consequently, the cost of treatment as defined in this study applies to patients who do not have the disease. This cost is expressed as the difference between the utility of avoiding treatment in patients who do not have the disease and the utility of administering treatment to those who do not have the disease (i.e., $U_{no\,treat\,no\,dis} - U_{treat\,no\,dis}$).

Summarizing these definitions:

$$\text{Net benefit (B)} = U_{treat\,dis} - U_{no\,treat\,dis}$$
$$\text{Net cost (C)} = U_{no\,treat\,no\,dis} - U_{treat\,no\,dis}.$$

In the remainder of the paper, benefit (B) will be taken to represent the net benefit of appropriate therapy, and cost (C) the net cost of unnecessary therapy.

Solution of the Decision Tree in Terms of Costs and Benefits

The expected value (EV) of both courses of action shown in Figure 1 can be calculated as follows:

$$EV_{treat} = (p)U_{treat\,dis} + (1 - p)U_{treat\,no\,dis}$$
$$\text{and } EV_{no\,treat} = (p)U_{no\,treat\,dis} + (1 - p)U_{no\,treat\,no\,dis}.$$

Applying the principles described above, one should select the course of action with the higher expected value. When the expected values of the two principal courses of action are equal, the physician should be indifferent to choosing either course. Thus, indifference to either option exists when $EV_{treat} = EV_{no\,treat}$. Substituting the equations given above makes it possible to derive an expression containing a probability value at which the physician should be indifferent to treating or not treating. This probability value at the indifference point is derived as follows:

$$EV_{treat} = EV_{no\,treat}$$

Therefore, $(p)U_{treat\,dis} + (1-p)U_{treat\,no\,dis} = (p)U_{no\,treat\,dis} + (1-p)U_{no\,treat\,no\,dis}$

And, solving for p (the probability at the indifference point),

$$p = \frac{U_{no\,treat\,no\,dis} - U_{treat\,no\,dis}}{U_{treat\,dis} - U_{no\,treat\,dis} + U_{no\,treat\,no\,dis} - U_{treat\,no\,dis}}.$$

If the probability of the disease in a given patient is greater than the probability at the indifference point, treatment is preferred; if the probability of the disease in a given patient is less than the probability at the indifference point, withholding treatment is preferred. Thus, p is a threshold probability that will be denoted hereafter as T to avoid confusing this threshold level with the probability that a given patient has the disease. Substituting B (benefit) and C (cost) for the utilities in the equation, and substituting T

*The utilities used in this paper are expected values derived from the probabilities and utilities of various outcomes in each branch.

for p, we obtain an equation relating benefits and costs to the threshold probability:

$$T = \frac{C}{B + C}. \text{ Simplifying further: } T = \frac{1}{\frac{B}{C} + 1}.$$

Since the various utilities and, therefore, the benefit and cost are functions of the disease and the treatment under consideration, it is possible to specify a value for T (the threshold) for the disease and the treatment in a given cohort of patients.* Applying the equation in a clinical setting then requires assessing the probability of the disease in a given patient and determining whether this probability is above or below the threshold value. If the probability of the disease for the given patient exceeds T, EV_{treat} exceeds $EV_{no\,treat}$, and treatment would be the preferred course of action. If the probability of the disease for the given patient is less than T, $EV_{no\,treat}$ exceeds EV_{treat}, and treatment should be withheld.

In many situations, it may be difficult to estimate the probability that a given patient has the disease in question. However, even in these cases, it is often possible to establish a range of probabilities that can be reasonably expected to include the probability for the given patient. If this entire range can be shown to lie above or below the therapeutic threshold, the appropriate course of action will be evident. Similarly, if the costs and benefits of therapy are not precisely known, it may be possible to specify a range for them, and thereby to specify a range for the threshold.

Examples of the Use of the Benefit-Cost Equation

Whether or Not to Operate for Suspected Appendicitis

Case description. A 15-year old boy has right-lower-quadrant pain that has persisted for two days, with progressive increase in severity. He is anoretic, but has not experienced nausea or vomiting. He has had two loose bowel movements each day. His temperature is 38°C by rectum, and abdominal examination shows diffuse voluntary guarding, most marked in the right lower quadrant, but no palpable masses. Urinalysis is normal, and the white-cell count is 15,000, with a slight shift to the left.

Assume that the physician assesses the probability of acute appendicitis to be 0.3 and the probability of acute gastroenteritis to be 0.7 on the basis of the above data. Should immediate operation be performed, or should the patient be observed further?

Analysis. In this analysis, the assessment of benefits and costs will be based on the risk of death, although it would have been possible to incorporate other factors such as discomfort and the dollar cost of surgical treatment. In this example, therefore, utilities are measured in terms of survival.

Assumptions made.

1. Operative mortality of laparotomy is 0.1 per cent. Survival with surgery is thus 99.9 per cent.[4]
2. The mortality rate of appropriately treated appendicitis with perforation in the general population is approximately 4 per cent.[5,6] The exact figure for mortality of untreated appendicitis in a comparable cohort of healthy boys of this age is unknown, but, for the purposes of this analysis, we have assumed a 50 per cent probability of perforation if operation is delayed and a mortality of 2 per cent for perforation; thus, the overall mortality is 1 per cent for deferring necessary operation, and survival without immediate operation for this cohort is 99 per cent.

Calculations.

$$\text{Benefit (B)} = U_{treat\,dis} - U_{no\,treat\,dis} = 99.9\% - 99\% = 0.9\%$$

$$\text{Cost (C)} = U_{no\,treat\,no\,dis} - U_{treat\,no\,dis} = 100\% - 99.9\% = 0.1\%$$

$$B/C = 9$$

$$\text{Thus, threshold (T)} = \frac{1}{\frac{B}{C} + 1} = \frac{1}{9 + 1} = 0.1.$$

Conclusion. In this case, the probability of appendicitis (estimated at 0.3) is above the threshold of 0.1, and immediate operation is the preferred choice. It should be noted, of course, that the benefit of appendectomy in patients with appendicitis includes not only the prevention of death but also the avoidance of adhesions, abscesses and sepsis.[6,7] Similarly, operation exacts costs other than death in patients without appendicitis, including pain and a variety of medical and surgical complications.[6,8,9] One could recalculate the B/C ratio taking these additional benefits and costs into consideration. If the lower limit of the B/C ratio were found to be 4, for example, the therapeutic threshold would be 0.2, and operation would still be the appropriate choice.

Whether or Not to Administer Anticoagulants for Suspected Pulmonary Embolism

Case description. A 30-year old asthmatic woman who takes oral contraceptive agents is seen because of right-sided pleuritic chest pain and dyspnea. She had experienced an anaphylactic reaction several years earlier at the time intravenous pyelography was carried out. Examination shows diffuse wheezing and an accentuated pulmonic component of the second heart sound. There is no evidence of phlebitis. X-ray study of the chest shows only hyperaeration. Arterial-blood gases on room air show oxygen tension of 60 and carbon dioxide tension of 30 mm Hg and a pH of 7.50. Lung scan shows a defect in the right-lung field.

Assume that the physician estimates that the probability of acute pulmonary embolism is between 0.4 and 0.6, on the basis of the above data. Because this woman had a previous anaphylactic reaction to x-ray contrast material, pul-

*The cohort as defined here is a group of patients with common risk characteristics such as age and cardiovascular status. Other elements such as the risk of anesthesia or operation in a specific hospital and personal attitudes of the patient should also be considered when tailoring the benefits and costs to the cohort.

monary angiography is considered too risky. Should long-term (six months) anticoagulation be undertaken or not?

Analysis. The danger for a patient with pulmonary embolism is re-embolization, with its associated morbidity and mortality.[10] Long-term anticoagulation is associated with a relatively low mortality in this age group but is complicated by notable morbidity.[11,12] We shall calculate the upper bound of the benefit/cost ratio (and thus the lower bound of the threshold), basing it on utilities calculated from mortality data alone. We shall then calculate the lower bound of the benefit/cost ratio (the upper bound of the threshold) basing it on utilities calculated from morbidity data alone.

Assumptions made.

1. Without treatment, there is a 50 per cent chance of re-embolization.[10,13]
2. Of patients with re-embolization, 50 per cent die:[10,13]; thus, without treatment, 25 per cent of patients will die from re-embolization.
3. Long-term anticoagulation is associated with a 5 per cent morbidity rate (requiring hospitalization) and a 0.01 per cent mortality rate.[11,12,14]
4. With a prior pulmonary embolism and with anticoagulation, there is a 15 per cent chance of re-embolization[10,13-15] and thus a 7.5 per cent chance of death from re-embolization.
5. The morbidity of a major complication from anticoagulation is considered equivalent to the morbidity of a non-fatal episode of re-embolization.

Calculations. For anticoagulation without pulmonary emboli (treat no dis), 99.99 per cent of patients survive, and 95 per cent of such patients are free of morbidity. For untreated pulmonary embolism, morbidity is 50 per cent, and mortality is 25 per cent (survival is 75 per cent). For treated pulmonary embolism, 7.5 per cent of patients die of re-embolization; therefore, 99.99 per cent × 92.5 per cent, or 92.5 per cent survive; 85 per cent × 95 per cent or 81 per cent are free of morbidity from either re-embolization or anticoagulation.

a. Calculations based on mortality data alone:

$$\text{Benefit (B)} = U_{\text{treat dis}} - U_{\text{no treat dis}} = 92.5\% - 75\% = 17.5\%$$

$$\text{Cost (C)} = U_{\text{no treat no dis}} - U_{\text{treat no dis}} = 100\% - 99.99\% = 0.01\%$$

Thus, B/C = 1750 and T = 0.00057

b. Calculations based on morbidity data alone:

$$\text{Benefit (B)} = U_{\text{treat dis}} - U_{\text{no treat dis}} = 81\% - 50\% = 31\%$$

$$\text{Cost (C)} = U_{\text{no treat no dis}} - U_{\text{treat no dis}} = 100\% - 95\% = 5\%$$

Thus, B/C = 6.2 and T = 0.139

Conclusion. The B/C ratio lies between 6.2 and 1750, thus setting the threshold of treatment (T) between 0.139 and 0.00057. In view of the fact that the estimated probability that the patient has a pulmonary embolism (0.4 to 0.6) exceeds the upper limit of 0.139 for the threshold, anticoagulation is the appropriate choice. For this particular patient, the calculation of the lower limit of the threshold was not needed, but, if the probability of pulmonary embolism had been considerably less, the value based on morbidity alone might have been required.

Discussion

Therapeutic decisions in the face of diagnostic uncertainty can be approached de novo by use of the basic principles of decision analysis, but certain advantages accrue from the application of the simple equation $T = \frac{1}{\frac{B}{C} + 1}$ derived in this study. The value of applying this equation to the management of patients and to the teaching of the principles of therapeutic decision making is considered here.

Interpretation of the Benefit-Cost Equation

The relation between the net benefit and cost of treatment and the minimal level of suspicion of the disease (threshold probability) required to recommend therapy is plotted in Figure 2. As defined by the equation, when benefits and costs are known, the ratio between them defines how certain a physician should be of a diagnosis before recommending treatment. At one extreme, if the benefit of treatment is zero, the threshold (T) is one, and, since the probability of the disease cannot exceed one, therapy would never be selected. At the other extreme, if the cost of inappropriate treatment is zero, the threshold is zero, and treatment would be selected if there is even a slight chance that the disease is present. Similarly, when the benefit/cost ratio is high, treatment is the appropriate choice even when the suspicion of the disease is quite low (for example, penicillin for suspected streptococcal pharyngitis), and when the ratio is low, treatment is appropriate only when the diagnosis is virtually certain (for example, amphotericin B for suspected systemic mycosis). The

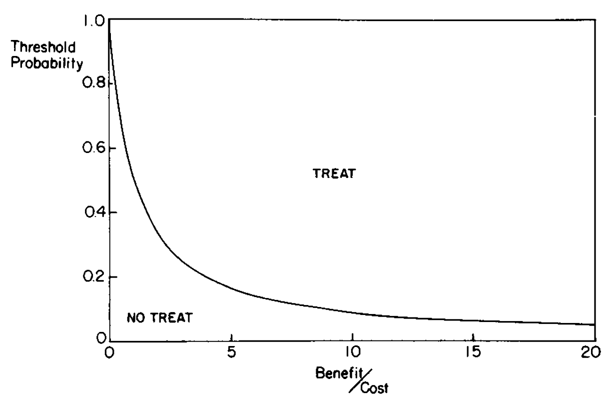

Figure 2. Relation between Benefit and Cost of a Treatment and the Threshold Probability.

For a given benefit/cost ratio, treatment is preferred when the probability of disease in an individual patient exceeds the threshold value.

non-linear relation between the benefit/cost ratio and the threshold probability is of some interest. The characteristics of this relation are such that the therapeutic decision is decreasingly sensitive to the ratio as the ratio increases — i.e., small differences in the ratio at low benefit/cost ratios (e.g., 0.5) have much more impact on the decision than comparable differences at high ratios (e.g., over 10).

This approach to therapeutic decision making can be illuminated by quantitative analysis of one of the examples described earlier. In Example 1, we assumed the probability of acute appendicitis for the young boy with abdominal pain to be 0.3, and that of gastroenteritis to be 0.7. If we can visualize a cohort of 1000 such patients, 300 would have acute appendicitis, and 700 would not. If the entire cohort were subjected to operation, the complications of perforation would be avoided, but one patient would die (0.1 per cent anesthetic deaths). On the other hand, if none of the group were subjected to operation, approximately 1 per cent of the patients with appendicitis, or three patients, would die of complications of perforation. Since the mortality rate is higher in the group not operated on, the better decision is immediate operation in a patient with a 0.3 probability of appendicitis. The threshold probability above which immediate operation is the better choice was calculated in Example 1 at 0.1. If the probability of appendicitis in this cohort had been 0.1 (100 patients with appendicitis and 900 patients with gastroenteritis), the mortality rates in both the group operated on and that not operated on would be equal (one patient per 1000), and the physician recommending treatment for a patient with this chance of the disease should be indifferent to either immediate operation or watchful waiting.

"Sensitivity Analysis" with the Benefit-Cost Equation

In the practical application of this type of analysis, one can be hampered by the necessity of assigning fixed numerical values to the probabilities and the utilities of the outcomes. Although one would prefer objective data upon which to base these assignments, one must often rely on subjective assessments, which necessarily introduce some "softness" into the values of the probabilities and the utilities. Nonetheless, the lack of solid data on which to base the assessment of probabilities and utilities should not be a deterrent to use of the approach described here. Clinicians frequently incorporate subjective data assessments into their decision-making processes. They may point out, for example, that even though they are unable to make an exact assessment of the probability of a disease in a given patient, the probability is no lower than 0.1 and no higher than 0.3. They often go on to conclude that it makes little difference whether the probability is 0.1 or 0.3 because in either case the decision whether or not to administer a treatment is the same. The process of testing whether variations in probabilities or utilities influence a given decision is known as "sensitivity analysis."[1,2] Sensitivity analysis merely involves substituting the values that bound a range and determining the appropriate course of action for the values assigned. If the decision is not altered throughout the estimated range of variation, the decision is said to be "insensitive" to this variation. If the decision can be altered within the range of variation of the probabilities and utilities, the decision is said to be "sensitive" to this variation, and additional data gathering may be necessary.

Sensitivity analysis is a useful technic, but for all but the simplest decision trees, it can be a time-consuming and tedious task. For decision trees of even moderate complexity, a computer is often needed for this type of analysis. By contrast, sensitivity analysis using the benefit-cost equation is rather straightforward and requires little calculation. In the first place, if the benefit/cost ratio is known for a cohort of patients suspected of having a given disease and for a given treatment, it may not be necessary to have a close approximation of the probability of the disease in a specific patient. If the probability in this patient is anywhere above the therapeutic threshold, treatment is the appropriate choice; if it is anywhere below the threshold, treatment should not be undertaken. Secondly, if the precise value for the ratio is not known, but, if one is confident that it lies within a certain range, both the highest and the lowest threshold probabilities will be determined. For example, a physician who believes that the benefit/cost ratio for cholecystectomy in a certain cohort of patients with suspected cholecystitis is not lower than 2 and not greater than 5 should recommend operation if he believes the probability of cholecystitis in a given patient to be greater than 0.33, and he should not recommend operation if he believes the probability to be less than 0.17. For the patients for whom he assesses the probability of cholecystitis to be between 0.17 and 0.33, he might find it possible to acquire more data to define the benefit/cost ratio better.

In some cases there will be imprecision in the physician's assessment of both the benefit/cost ratio and the patient's probability of having the disease. In such cases, the upper and lower limits of both the probability and the ratio can be plotted on Figure 2. These outer bounds for the ratio and the probability of disease will delimit an area of uncertainty within which the correct values for the given patient (presumably) lie. If this area lies wholly within either the "treat" or the "no-treat" regions of the figure, no further analysis is needed, and the best choice has been specified. If the area overlaps both regions, further definition of the patient's status or of the benefit and cost of therapy is needed. If it is not possible to further refine the data, it would probably be reasonable to select the course of action subtended by the largest portion of the area of uncertainty.

Assessment of Benefits and Costs

In the examples given earlier, the probability of survival or the probability of freedom from morbidity was used as a measure of the utility of the outcomes, but many other measures of utility may be used — e.g., years of disability.

When values are assigned to benefits and costs, utilities must be evaluated in a consistent manner (i.e., in comparable units), so that meaningful differences can be established between them. Thus, if several different measures are involved, a common combined unit of utility must be employed.

In general, the values chosen for the benefits and costs are more dependent upon the disease and treatment under consideration than upon the individual characteristics of the patient. However, if the clinical status of the patient or if the circumstances of administration of therapy vary notably from the "typical" or "average" case, benefits and costs (or both) must be adjusted to conform to a cohort of patients with similar risks and benefits. Several examples should suffice to illustrate this point: the cost of appendectomy is considerably higher for a patient with severe heart disease than for a young, otherwise healthy person; the cost of laparotomy is presumably higher when less experienced and less expert surgeons have responsibility for the patient; the cost of operation is also increased when the patient is extremely frightened by the prospect of an operation. The appendectomy example given earlier is an illustration that shows how the benefit/cost ratio can be tailored quantitatively for a given cohort. Data from the literature on the age-specific mortality rate of perforated appendix were not available; thus in the assessment of the cost of perforation for this example, the mortality rate in the cohort of young, healthy boys was taken to be 2 per cent rather than the 4 per cent figure quoted for all age groups.

The term "net benefit" as is used in this paper corresponds to the general use of that term to describe the value of a drug or a surgical procedure in patients with proved disease. One sometimes speaks of a treatment as being beneficial if it can help some patients with the disease (neglecting the patients who have complications from the treatment), but when one speaks of net benefit, one includes these complications, as is true of the definition used in this paper.

Decision making based on an analysis of costs and benefits is not a new approach: management and military decisions have been subjected to such analysis for some years. In medicine, cost-benefit analyses have been applied to screening programs and population surveys.[16-20] The approach described here differs from other medical cost-benefit analyses previously reported in that it is a general formulation that can be applied either to individual patients or to population groups. It would be possible, for example, to apply this method to an analysis of the value of a mass treatment program with dollar cost as the utility measure. In such cases, there is often little argument about the assignment of costs and benefits, and the incidence of the disease in the population under consideration can be used as a measure of probability.

References

1. Raiffa H: Decision Analysis: Introductory lectures on choices under uncertainty. Reading, Massachusetts, Addison-Wesley, 1968
2. Schwartz WB, Gorry GA, Kassirer JP, et al: Decision analysis and clinical judgment. Am J Med 55:459-472, 1973
3. McNeil BJ, Keeler E, Adelstein SJ: Primer on certain elements of medical decision making. N Engl J Med 293:211-215, 1975
4. Greene NM: Anesthesia, Principles of Surgery. Second edition. Edited by SI Schwartz, RC Lillehei, GT Shires, et al. New York, McGraw-Hill Book Company, 1974, pp 443-460
5. Ackerman NB: The continuing problems of perforated appendicitis. Surg Gynecol Obstet 139:29-32, 1974
6. Hobson T, Rosenman LD: Acute appendicitis: when is it right to be wrong? Am J Surg 108:306-312, 1964
7. Barnes BA, Behringer GE, Wheelock FC, et al: Treatment of appendicitis at the Massachusetts General Hospital (1937-1959). JAMA 180:122-126, 1962
8. Chang FC, Hogle HH, Welling DR: The fate of the negative appendix. Am J Surg 126:752-754, 1973
9. Yajko RD, Steele G Jr: Exploratory celiotomy for acute abdominal pain. Am J Surg 128:773-776, 1974
10. Dexter L, Dalen JE: Pulmonary embolism and acute cor-pulmonale, The Heart, Arteries and Veins. Third edition. Edited by JW Hurst, RB Logue, RC Schlant, et al. New York, McGraw-Hill Book Company, 1974, pp 1264-1278
11. Manchester B: The value of continuous (1 to 10 years) long-term anticoagulant therapy. Ann Intern Med 47:1202-1209, 1957
12. O'Sullivan EF: Duration of anticoagulant therapy in venous thromboembolism. Med J Aust 2:1104-1107, 1972
13. Thomas DP: The anticoagulant therapy of venous thromboembolism, Pulmonary Thromboembolism. Edited by KM Moser, M Stein. Chicago, Yearbook Medical Publishers, 1973, pp 271-279
14. Barritt DW, Jordan SC: Anticoagulant drugs in the treatment of pulmonary embolism: a controlled trial. Lancet 1:1309-1312, 1960
15. Murray G: Anticoagulants in venous thrombosis and the prevention of pulmonary embolism. Surg Gynecol Obstet 84:665-668, 1947
16. Schweitzer SO: Cost effectiveness of early detection of disease. Health Serv Res 22-32, 1974
17. Jick H: Drugs: remarkably nontoxic. N Engl J Med 291:824-828, 1974
18. Ahlvin RC: Biochemical screening: a critique. N Engl J Med 283: 1084-1086, 1970
19. Sagel SS, Evens RG, Forrest JV, et al: Efficacy of routine screening and lateral chest radiographs in a hospital-based population. N Engl J Med 291:1001-1004, 1974
20. Cost-benefit analysis of newborn screening for metabolic disorders. N Engl J Med 291:1414-1416, 1974