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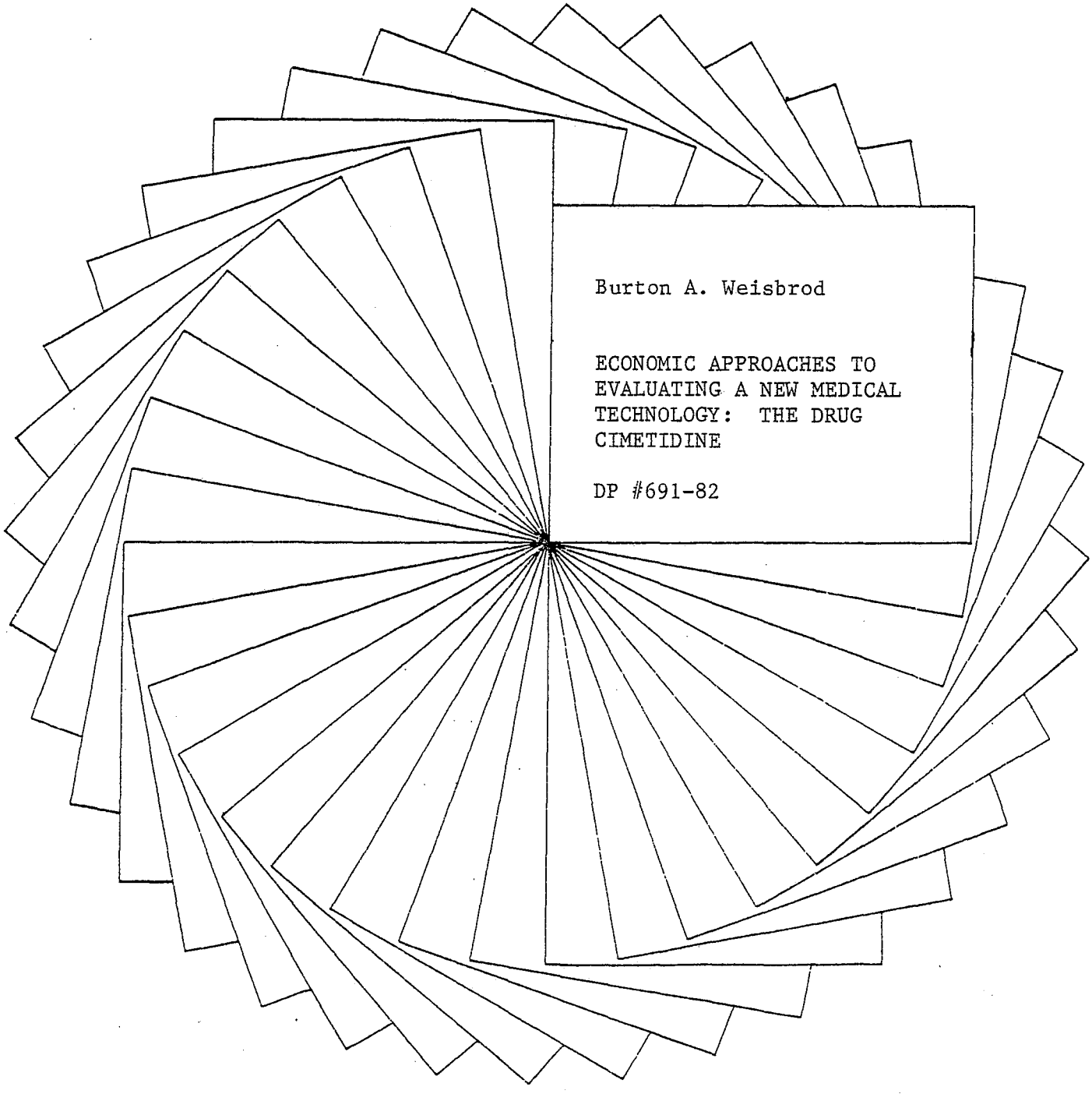

Economic Approaches to Evaluating a New Medical Technology: The Drug Cimetidine

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ABSTRACT

Economic evaluations--whether of a medical technology or anything else--are generally in one of three forms: social benefit-cost analysis, budgetary analysis, or cost-effectiveness analysis. Each is different, answering a somewhat different evaluative question from a distinct perspective.

Each of these methodological approaches has been used to evaluate the new anti-ulcer drug cimetidine. These studies are critiqued and general problems are identified. One frequent difficulty is that patients are not randomly assigned to alternative therapies, and thus there is a possibility of selection bias. A second difficulty is the specification of which alternative therapy should be used as a basis for comparison with the new technology; a commonly used alternative, a placebo, is of little relevance, since it is seldom the realistic alternative.

The desirability of incorporating economic evaluation into the medical review process is considered. The possibility of monitoring economic consequences following regulatory-agency approval and marketing of a new drug is also examined and shown to be feasible.

With specific reference to one important new medical technology, the anti-ulcer drug cimetidine, the evidence is that from a variety of economic perspectives, the drug is economically effective. Most clear are the findings that it is expenditure-reducing, primarily because it reduces the need for costly surgery.

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I. INTRODUCTION: WHY EVALUATE A NEW MEDICAL TECHNOLOGY?

The objectives of this paper are to show (1) why, and under what condition, economic evaluation of a new technology (health or other) may be useful; (2) what alternative evaluation approaches are available, (3) how those approaches have been applied to the case of one new technology, the drug cimetidine; and (4) what obstacles there are to improving the quality of economic evaluations.

Economic evaluation of a drug involves both conceptual and empirical issues. Many of these issues arise in any economic evaluation. The evaluation of technological changes in health care (such as the use of a new drug) has many unusual dimensions, but we should not lose sight of the broad framework of evaluation within which it fits.

Why is evaluation needed for a new technology? The entire market system is a complex system for evaluating economic activities. In a private market economy, a producer's profitability is a measure of the firm's private success, and profitability is also a measure of its overall economic success (allocative efficiency) if the prices it pays for resources and the prices it receives for its output reflect the values of these goods to the resource owners and consumers. These values may or may not be reflected accurately in market prices, depending on whether, for example, consumers are well informed about the usefulness of the new and old technologies.

A considerable literature has grown up on the conditions under which a firm's self-evaluation of the profitability of some change (e.g., production of a new drug) does or does not coincide with a society-wide

perspective on the desirability of that change. Most of that literature involves the search for sources of "private market failures" --when private and social costs, or values, diverge, so that the "invisible hand" cannot be relied upon to guide economic activity.[1] Some of that literature also includes the concept of "equity" in the social evaluation: Are the results of the economic change "fair"?[2]

There are several reasons to believe that when a new medical technology such as cimetidine is involved, the private profit calculus deviates materially from the social desirability calculus. For one thing, extensive government regulations constrain private behavior--from controls over approval of new drugs (by the Food and Drug Administration, in the U.S.) to controls over their use (under Medicare and Medicaid in the U.S.). A second reason, overlapping with the first, is the presence of "distortions" that tend to cause prices confronting consumers to diverge from real costs. I refer particularly to widespread private and public "insurance" for health care. Such insurance often makes access to a new medical technology free to a patient, or, at least far below real cost; this is true for drugs as well as for such expensive new technologies as renal dialysis, coronary bypass surgery, and the CT scanner. The insurance broadens access to all persons, not simply to the affluent, but it causes not only patients, but physicians, hospitals, pharmaceutical firms, developers of new technologies, and others to be less sensitive to high costs than would otherwise be the case.[3]

Given these distortions, there are reasons to question the presumption that the private marketplace--and its private-profitability signals--is an appropriate mechanism for social evaluation. Some alternatives should be sought. The next section deals with the nature of those alternatives.

II. EVALUATION APPROACHES

How "best" to evaluate a new medical technology such as cimetidine depends on the objective. Following a brief survey of alternatives, I shall illustrate some of them by actual evaluations of cimetidine.

A. Social Benefit-Cost Analysis

The economist's idealized evaluation framework is a comprehensive one that attempts to identify and to quantify all of the desirable consequences (that is, the "benefits") and the undesirable consequences (the "costs") of a new technology, to determine which is greater. The new technology under consideration must necessarily be compared with some "counterfactual," which is often the preexisting technology, but others may be selected--for example, a placebo. Benefits and costs are typically defined in terms of what individuals are willing (and, implicitly, able) to pay either to obtain the benefits of the new technology, or to avoid its costs. "Willingness-to-pay" is defined as economic demand, so that the intensity of anyone's liking of the new technology is gauged by what he or she would pay to obtain it; thus, economic demand reflects both the strength of preferences and the distribution of wealth. Just as with the private market for any good or service, a poor person with intense feelings may have less demand than a wealthier person with more moderate feelings about the new technology. As commonly used, the benefit-cost analytic framework is, in effect, an attempt to simulate the information that a smoothly functioning competitive private market would generate.

Both mechanisms for evaluation--the private market and benefit-cost analysis--must deal with the question of whether the consumer is suf-

ficiently well informed about the new technology and its alternatives to evaluate it. If not, then the theoretic concept is not the actual willingness to pay, whether manifest in the private market or in the econometric estimates of the benefit-cost analyst, but what the hypothetical consumer would pay if he or she were well informed. Such estimates are typically very difficult to make.

The dependence of willingness-to-pay on the distribution of wealth has led to much debate over whether this is, or is not, a problem with which benefit-cost analysis should attempt to deal. Those who deny that distributional considerations should be dealt with in a benefit-cost analysis rely upon the private-market analogy; that market's evaluation process makes no attempt to adjust for any distributional considerations; whatever is the wealth distribution that generates consumer demands, those economic demands are taken as satisfactory measures of value.[4]

Yet it can be argued that when social policy issues are at stake--such as in the areas of education, welfare, and health--it would not be appropriate to evaluate a program as having only small benefits simply because its beneficiaries were poor and, therefore, had relatively low economic demands. This position leads to the explicit inclusion of "distributional weights" in benefit-cost analysis--adjustments for effects of the income distribution on evaluation. If, for example, benefits to some particular groups of people are a goal of the program, benefits accruing to them may be given a greater weight than benefits accruing to others.[5] Such an evaluation approach attempts to make use of a social, or society-wide, perspective. The issue of whether to deal explicitly with income distributional matters highlights the underlying social orientation of benefit-cost analysis.

B. Budgetary Analysis

When a government agency undertakes an evaluation, it often uses a different approach. It is likely to be preoccupied with those benefits and costs that are incurred by the agency and in a monetary form. For example, if a new technology could be expected to increase costs to a particular agency while decreasing costs to another agency or to private individuals, the decreased costs might be omitted from the first agency's evaluation. This is often the case, and when it occurs it leads to the same types of planning failures that occur in private markets--the disregard of "external" effects. A health-planning agency, for example, might evaluate a new drug negatively if that drug were more expensive than those already available, even if a variety of favorable effects were realized by consumers and, indeed, by other government agencies. In short, agencies often engage in incomplete benefit-cost analyses--or what I term here budgetary--inflow-outflow--analyses.

A budgetary analysis may differ from a social benefit-cost analysis in two ways. (1) An agency's budgetary analysis excludes benefits and costs that are not manifest in money flows. Thus, for example, a saving of lives--which would be a benefit in the social analysis--might be omitted because there was no associated flow of funds. Even monetary benefits and costs are often excluded if they do not accrue to the agency performing the analysis, as when one governmental unit's efforts to reduce on-the-job accidents reduces medical care demands on another unit.

(2) A budgetary analysis includes sums that would be omitted from a social analysis because they reflect transfers, not real social benefits or costs. In one recent benefit-cost analysis of alternative means for treating the mentally ill, it was noted that a substantial portion of

the "experimental" program's budgetary cost was for meals and lodging, and since those costs would be incurred by someone, whether or not the treatment program was involved, that "cost" was a transfer, not a social cost.[6]

The budgetary analysis, although it omits effects that do not appear as changes in money flows and includes money flows that represent transfer payments--benefits or costs to one group being offset by corresponding, offsetting, costs or benefits to another group--does capture important benefits when they take the form of reduced expenditures. Thus, if a new technology improves patients' health, so that there is less need for surgery or other physician attention, the resulting reduction in medical care expenditures is a benefit that will appear in a budgetary analysis.[7]

Economists' preference for a social perspective notwithstanding, government agencies will continue to pursue budgetary analyses. Facing a budget constraint, and, generally, not being rewarded for benefits or reduced costs that appear elsewhere in the economic system, nor being penalized for reduced benefits or increased costs that occur elsewhere, each agency's suboptimization will lead to collectively nonoptimal results. This is one factor contributing to the soaring growth rate of health-care expenditures, up from 3.5% of GNP in the U.S. in 1929, to 4.5% in 1950, 7% in 1970, and over 9% today.

Economic evaluation is only one area in which inappropriate incentives produce inefficient and inequitable economic behavior. One hypothetical, though realistic, example of how an agency's budget perspective can lead to socially inefficient decisions may be instructive. Consider a state Medicaid official in the U.S. confronting the question of whether to include a new drug on the list of drugs approved

for reimbursement. The new drug is more costly than substitute therapies, but it is far more pleasant to take and is more effective in that it leads to a better quality of life for the patient. The official, facing a budget constraint but with no incentive to be concerned about patients--either their satisfaction or quality of life--chooses to deny approval of the new drug. The outcome would be different, however, if the drug could be demonstrated to reduce the amount of, say, surgery, which would also be a drain on the agency budget.

C. Cost Effectiveness Analysis

The terminology used in economic evaluation is often confusing. In one recent study "benefit-and-cost analysis" was coined "to encompass both cost-effectiveness and cost-benefit (or benefit-cost) analyses."[8] Another term, "risk-benefit analysis," appears to be similar to cost-effectiveness analysis (defined below), as applied in the health area. "Risks" and "benefits" are defined in terms of a nonpecuniary measure of output, with costs other than "risks" of adverse outcomes being measured in monetary terms. "Cost-benefit analyses is broader than risk-benefit analysis because risks are only a part of the total costs."[9]

In any cost-effectiveness analysis, the costs of achieving some particular "output" in alternative ways are compared. In the health area the concept of "output" that is increasingly used is "quality-adjusted life-years." Whereas, in general, no attempt is made to place a value on such a year, the implication is that its importance is equal for people in a "similar" state of health. In any event the output concept is clearly distinguishable from the willingness-to-pay basis for output assessment.

When a social benefit-cost analysis is undertaken, analysts frequently find that the outputs, or benefits, are considerably more difficult to quantify and to evaluate in monetary terms than are the costs.[10] In the case of a new drug, for example, how should we quantify and value better health, reduced anxiety, and longer life?

While economists have examined these questions conceptually, and have also developed estimates of such hard-to-measure-and-value benefits, the difficulties are considerable.[11] As a result, these forms of benefits are often omitted or simply mentioned;[12] sometimes they are dealt with explicitly but are not valued, so that the analysis includes both monetized and nonmonetized magnitudes.[13]

Given the problem of valuing benefits, an alternative is to concentrate on the costs, leaving the determination of benefits to others--such as the "political process." "Cost-effectiveness analysis" does this; it poses the evaluation-analytic problem as follows: What is the cost of achieving a particular outcome by each of a variety of means? Once the "particular outcome" is stated, the problem becomes a search for the lowest-cost solution. What is the least-cost way of maintaining a specified number of combat-ready military aircraft, given the alternatives of having more new planes, fewer new planes but more replacement parts for any disabled planes, or fewer new planes and fewer replacement parts but more mechanics to make repairs? What is the least-cost way to "save" a given number of lives, given such alternatives as increase the number of influenza vaccinations, increase the number of chest x-rays to detect lung diseases, or increase the amount of Coast Guard protection for pleasure sailors? What is the least-cost way to treat an ulcer patient--with antacids? cimetidine? surgery?

More than a decade ago the U.S. Department of Health, Education, and Welfare published a report containing a table of predicted "Costs per Death Averted, 1968-1972," which reported that the federal government spent $87 on automobile seat belt-usage programs per death "averted," $6400 on programs to reduce smoking (and lung cancer) per death averted, and $42,944 on colon-rectum cancer detection programs per death averted.[14] While such numbers are interesting and certainly thought-provoking, their policy relevance can be questioned on many grounds, only one of which I want to deal with here.

Is a "death averted" (or an ulcer patient treated) an appropriate output unit? That is, should public policy in the health area be directed to allocate resources so as to minimize the cost of such an "output" (or an ulcer patient treated)? The answer is no, for several reasons.[15] (1) A death averted (or ulcer patient treated) is not a homogeneous good; does it make no difference, for example, how long-lasting the outcome is? (2) Some diseases are causes of pain and suffering but not death; thus, an allocation of resources that focused solely on deaths would erroneously disregard, for example, arthritis. (3) The cost per death averted (or per patient treated) may depend on the magnitude of the effort--that is, on the number of deaths averted or persons treated; as between two health programs, one might cost twice as much per unit of output (say, death averted) at one scale of effort, while the relative cost could be quite different, and even reversed, at a larger, or smaller scale.

This brief summary of some of the problems with cost-effectiveness analysis illustrates that "there is no such thing as a free lunch." One cannot escape the problems (costs) of defining and measuring benefits without facing a new set of problems. It may be easier to determine

which alternative approach is least costly once someone else has specified the outputs or objectives, but great pains are required to ensure that the specification of outputs does not inadvertently bias choices. Averting deaths (however that is exactly defined) is surely a worthy goal, but if policy based on that goal were to disregard diseases that brought much pain and suffering but few deaths, it would surely be inappropriate and economically inefficient.

There is no easy solution to these difficult problems of identifying and valuing benefits and costs comprehensively. We can, however, be aware of the nature of the problems, thus reducing the likelihood that the "simplifying" assumptions of analysts--not to mention their oversights and outright errors--will go unrecognized. Table 1 shows the variety of evaluation approaches that may be used. The idealized benefit-cost analysis is society-wide, cell (i). Cost-effectiveness analysis is, typically, less comprehensive and from a narrower perspective, such as a particular government agency, cell (b).[15a]

We turn next to a review of the quantitative work evaluating the new drug technology, cimetidine. The various studies differ in both evaluation perspective and comprehensiveness.

III. EVALUATIONS OF CIMETIDINE: A REVIEW

A. Culyer and A. Maynard have undertaken a cost-effectiveness analysis of cimetidine.[16] They ask, in effect, this question: If duodenal ulcer problems are to be treated in one of two ways--by surgery or with cimetidine--which is less costly? They do not evaluate the alternative of no treatment at all. Neither do they evaluate alternative treatment therapies such as antacids. They are aware of these alter-

Table 1

A Typology of Evaluation Approaches

Perspective	Comprehensiveness		
	Budgetary Analysis	Cost-Effectiveness	Social Benefit-Cost
Government agency	a	b	c
Government generally	d	e	f
Society	g	h	i

Note: The scale (a to i) measures the comprehensiveness of evaluation approaches carried out from the perspectives of given units. Thus the most comprehensive evaluation would be a benefit-cost evaluation from the perspective of society in general.

natives, and they also recognize that "a complete evaluation should take account of the benefits as well as the costs. The justification for the more restricted cost-effectiveness approach is simply that it is often as far as one can realistically, or persuasively go because of data problems."[17]

Culyer and Maynard recognize yet another qualification noted in the preceding section, that outputs (effects) of the alternative treatment approaches may not be the same, so that "The least cost method may therefore not be the one which should be chosen, especially if higher-cost methods produce more beneficial outcomes for patients."[18]

The fact, discussed in section II, above, that an economic evaluation may be quite different depending on the perspective of the evaluator, is also recognized by Culyer and Maynard. The question of whether a new technology such as cimetidine is "worthwhile" can be examined, they note, from the standpoint of the National Health Service, the public sector as a whole, or society generally. (See our table 1.)

While they do not say so explicitly, Culyer and Maynard proceed to take a society-wide perspective in their cost-effectiveness analysis. That is, they attempt to be broad in their (social) perspective, but only partial in their comprehensiveness (examining only costs, not benefits). In terms of Table 1, they focus on cell (h).

Notably, their social perspective encompasses forms of costs for which there are no associated market prices--for example, time costs to patients for obtaining treatment, and costs of death from surgery. At the same time, the social perspective leads them to exclude such transfer payments as social security, which would have entered a governmental budgetary analysis, as we noted above.

Deciding on an evaluation perspective is a crucial matter, but the methods used to estimate specific forms of benefits and costs are no less important to the outcome of the evaluation. The cost of hospitalization, for example, is far from ambiguous. Culyer and Maynard, in estimating costs of surgical treatment of duodenal ulcers (DU), present several average costs per case, calculated in different ways. When based on average cost per day for all acute hospitals, and the average number of days of hospitalization for DU surgery patients, a cost of £615 per case is derived; when a multiple regression model is used to distinguish among types of cases, the estimate for a DU surgery patient fell by nearly one third, to £419; and when there was direct observation of staff time employed to treat a DU surgical patient at a particular hospital, the resulting estimate was £386 per case.[19]

That hospital "costs" depend on the evaluation approach used was recently shown in another study, of the costs of treating mental patients. It highlights the systematic omission in hospsital cost calculations of real social costs that the hospital does not pay.[20] Specifically, there were omitted costs of the land on which publicly owned hospitals are located, and understated costs of capital depreciation resulting from the use of depreciation accounting based on historical rather than replacement costs.

Culyer and Maynard included among the forms of costs they estimated not only hospital costs but the patients' loss of earnings during the period of surgery-related hospitalization. Depending on which of two alternative assumptions they used regarding the difference in days lost from work if surgery or cimetidine therapy was employed, they derived savings from cimetidine treatment that were even greater than the savings in hospital costs (£584-£974 per case). Of particular importance is

their inclusion of unpaid housewives' time. The loss of housewives' productivity associated with surgical treatment is a real cost to the economy, but because it is not reflected in explicit payments it is often overlooked in expenditure-oriented evaluations.

It is noteworthy that work-time lost due to peptic ulcer disease varies substantially among countries. An ulcer patient with "active symptoms" is off work for an average of 12 days (per year) in the U.S., 35 days in Italy, and 45 in the Netherlands.[21] The potential absenteeism cost savings from successful treatment vary accordingly.

Culyer and Maynard acknowledge that they did not "measure the costs of pain, etc. nor of the hidden costs falling on the families of patients, nor of other costs falling on primary care services, local authority services, etc."[22] Nevertheless they did not hesitate to estimate the costs of "case fatality," the value of lives lost because of surgical treatment. Those costs were estimated using three alternative theoretic approaches which produced a very wide range of estimates: £230, £340, and £15,000 per case. The latter figure, which is derived from another author's estimate of £3 million per death avoided, is characterized by Culyer and Maynard as the "conceptually superior" method."[23] The £15,000 per case for the higher case-fatality cost of surgical treatment is enormously more important quantitatively than the other costs they estimated.

When Culyer and Maynard compare their various estimates of the greater cost of surgery with estimates of the cost of a cimetidine regimen lasting from 20 to 35 years they find the following:

Cost per case of vagotomy (surgery) and cimetidine

	Lowest estimate	Highest estimate
Vagotomy	£1,180	£16,370
Cimetidine	1,010	1,240

Since the authors prefer the risk-avoidance basis for estimating the cost of deaths from surgery, and since that approach leads to by far the highest cost estimate in the table, their conclusion is that "we have little hesitancy in judging the drug treatment to be substantially less costly than surgery for DU where the choice is clinically acceptable."[24]

These calculations assume that surgery and cimetidine are alternative ways to produce a particular output; this is the cost-effectiveness approach. The "output" is, implicitly, a DU patient who is no longer troubled by the DU. Unless the two therapies, however, are essentially equivalent in this respect, the comparative-cost estimates are of little or no value for economic planning. The authors acknowledge that their study is not a cost-benefit study, but is "a cost-effectiveness study in which the unit costed has been the case."[25] Only when the differences in benefits between the two therapies in their effects on patient welfare is essentially zero can "the results reported . . . be considered as decisive."[26]

There are reasons to wonder about how reasonable it is to assume that the outputs or benefits are virtually the same for the two therapeutic approaches. One issue is whether cimetidine substitutes for surgery or only postpones it. Insofar as the latter is the case, Culyer and Maynard's estimates overstate the cost saving from cimetidine. As one writer put it, to the extent that cimetidine only postpones surgery the question arises as to whether "those patients would have been better off if surgery had been advised at a much earlier stage."[27] And since

the enormous bulk of that saving came from the risk of mortality from surgery, it is of considerable importance to determine the extent to which cimetidine substitutes for, and the extent to which it only postpones surgery. It is really not enough to note--parenthetically at that--"(for example, whether the drug may, for some patients, only postpone the necessity for surgery is not at present known.)"[28]

In a study published before the Culyer and Maynard paper, there was some evidence that cimetidine is not 100 percent successful in eliminating the need for surgery for ulcer patients;[29] that is, for some patients it does only postpone surgery. During a double-blind trial lasting only one year, one of the 32 patients receiving cimetidine was referred for surgery, and even though this was a far lower proportion than the 15 of 36 placebo patients who required surgery (a difference significant at the .0005 level), the point is that for some patients cimetidine does not substitute for surgery. This is not to deny the possible value of postponement, since even postponement of surgery is an economic benefit. The value of the postponement depends in part on the interest rates appropriate for the economy; a cost delayed is desirable, ceteris paribus. However, the cost-saving estimated by Culyer and Maynard applies only when the "postponement" is permanent. If it were possible to distinguish patients by the probability that cimetidine would be a permanent substitute for surgery (or by the expected duration of postponement of surgery), then the Culyer-Maynard estimates would apply to the extreme group; other, smaller cost-savings would be found for populations in which varying durations of cimetidine-caused postponement of surgery were expected.

Other costs omitted by Culyer and Maynard are the pain associated with surgery and its aftermath, and the inconvenience of permanent drug maintenance.

Apart from the quantitative findings, there are at least two other useful observations in their paper. One is that only some of the social costs of either treatment approach fall upon government--the budgetary impact on the National Health Service (NHS)--while some fall on patients or other parties. Consequently, for example, because the cost of mortality falls upon the patient, surgery can appear to be the cheaper alternative to the NHS even if it is more costly from the social perspective, which includes the costs to patients.[30] This illustrates the difference between the perspectives in rows 1 and 3 of Table 1--and specifically the difference between cells (a) and (h).

The second point worth underscoring is the enormous handicap under which any economic analyst must labor when doing a retrospective analysis. Clearly, the economic evaluation should "be designed at the same time as the clinical part of the exercise, and data to be collected pari passu."[31] Otherwise, selection bias regarding who does, and who does not receive the new technology can seriously contaminate the evaluation--a point also emphasized by Geweke and Weisbrod (discussed below).

Two examples of the feasibility of integrating economic analysis with clinical trials are the studies by Rita Ricardo-Campbell et al. and by G. Bodemar and A. Walan of days of work lost by patients receiving cimetidine compared with those receiving a placebo (note that the counterfactual comparison here is not surgery).[32] In connection with the double-blind randomized trials of cimetidine, it was found that cimetidine was significantly more effective than placebo in reducing work-time lost among ulcer patients. Unfortunately, no comparison was made with surgery

or other therapies in either study, nor was there any attempt to place a monetary value on the work-time lost. In the case of DU patients, the realistic alternatives to cimetidine include antacids, anticholinergics, and surgery--not placebos. The importance of the Campbell et al. and Bodemar-Walan studies, therefore, is less in their findings than in their demonstrations of the feasibility of studying economic variables such as work-time lost through random assignment of patients.

The limitations of comparing cimetidine with a placebo treatment are uppermost in the thinking and work of Geweke and Weisbrod, who have attempted to evaluate cimetidine relative to other therapies currently in use. This work is examined later in this paper.

The recent paper by Fineberg and Pearlman reviews a number of economic studies of the cost of ulcer disease.[33] It should be noted that study of the total costs of any disease--regardless of the perspective, the comprehensiveness of the work, or the quality of the estimates--itself tells us nothing regarding the economic efficiency of using cimetidine or any other therapeutic approach. The key question for the purpose of making resource-allocation decisions is, How much would total costs be reduced and benefits increased, by using one specific therapy rather than another.

Thus, from any of the economic-evaluation perspectives discussed above, the real issue is not whether cimetidine is "effective"--relative to a placebo or even relative to an alternative therapy such as antacids, anticolinergics or surgery--but how its relative effectiveness compares with its relative costs, viewed (ideally) over the patient's lifetime. Evidence of the kind presently obtained from clinical trials--involving comparisons with placebos, and even then not examining costs--is only one component of an economic-evaluation process.

It is clear that the effectiveness of cimetidine relative to a placebo is less germane to economic evaluation than its effectiveness relative to alternate therapies. Alternate therapies have been in widespread use; they are replaced, to at least some extent, by cimetidine. Consequently, the economic evaluator wishes to know (1) how much more effective cimetidine is than these other therapies; (2) how great the "value" is of the additional effectiveness; and (3) what the differential cost is. The evaluation analysis focuses on "marginal" behavior--changes in benefits and in costs. It is worth noting that a new medical technology that was less effective than another therapy would pass an economic-efficiency evaluation (e.g., a benefit-cost test or a budgetary test) if it were sufficiently less costly than the alternative therapy with which it is being compared.

The earliest effort to evaluate the likely impact of the introduction of cimetidine on the social costs attributed to duodenal ulcer was carried out by Robinson Associates.[34] In that study, 23 of the physicians who conducted clinical trials of cimetidine for the Food and Drug Administration were asked to describe in detail their drug treatment regimens for various types of DU patients with and without the availability of cimetidine. They were asked to evaluate both regimens according to the following criteria: frequency of repeat episodes, frequency of patient visits to physician, likelihood and frequency of hospitalization, likelihood of surgery, frequency of diagnostic x-rays and endoscopies, amount of missed work, and likelihood of death from ulcer complications. These estimates were then combined with information from secondary sources of indirect and direct costs of various forms of treatment, and cost reductions resulting from the availability of cimetidine were computed for each type of DU patient. The physicians were also asked to estimate a

"penetration" rate for cimetidine--the proportion of each type of patient that would be treated with cimetidine when the drug was being used by most of the physicians in the U.S. who would eventually do so. The study estimated a reduction of $645 million, or 29 percent, in U.S. health care costs for DU. The drug cost component was estimated to increase by 40 percent, but decreases in all other components were predicted.

According to Harvey Fineberg and Laurie Pearlman

> The Robinson Associates analysis substantially overstates expected savings from cimetidine. Considering the exaggerated baseline costs of ulcer disease assumed in the analysis, the incomplete spectrum of patients included, and the distortion introduced by the method of calculating mean percentage reductions in costs, the estimated $645 million savings are probably two to three times too large. Potential bias introduced by the selection of physician informants would increase the magnitude of that overestimate.[35]

J. Geweke and B. Weisbrod, in a set of three papers, have directed attention to the effects of cimetidine on budgetary expenditures.[36] They emphasize both the incompleteness of their analyses relative to the social benefit-cost perspective, and the partial justification for focusing on expenditures.[37] "The question of whether a particular medical input--drug or other--causes medical expenditures to increase or decrease has obvious policy relevance, given the current political emphasis on 'cost containment.'"[38]

Geweke and Weisbrod compare the budgetary expenditure approach with the full social benefit-cost approach. They point out that the focus on budgetary analysis represents a simplification of the benefit-cost framework, in which benefits from a new technology consist only of reductions in costs, and, indeed, reductions in only those costs that are reflected in explicit payments for health resources.

The Geweke-Weisbrod studies are the first published efforts to use panel data to trace DU patients over time, in order to determine dif-

ferences in expenditures and resource-use patterns for specific patients treated with different therapies, including cimetidine. They have evaluated cimetidine from a government budgetary perspective, utilizing data from the Medicaid programs in the states of Texas and Michigan. They were able to follow identifiable patients for periods of two to three years, noting the level and nature of their medical care expenses for hospitalization, physicians, drugs, etc., distinguishing between those treated with and without cimetidine.

Because they studied people in real (although nonexperimental) settings, they were able to compare expenditures for patients who were treated with antacids, anticholinergics, surgery, or combinations of therapies but excluding cimetidine. Comparing expenditures of DU patients taking cimetidine with those receiving other therapies would seem to be more meaningful than a comparison with a placebo group.

One dimension of costs of treatment that is often overlooked in the evaluation process is the inconvenience, discomfort, and riskiness of a treatment mode to the patient. This is potentially important for two reasons:

1. These costs are real, although not reflected in an expenditure of money, and they may vary markedly among alternative treatment measures. Use of large quantities of antacids seven or eight times each day, for example, is clearly less convenient than taking a single cimetidine pill three or four times per day, and having surgery is clearly more anxiety-producing and dangerous than is taking of antacids or pills.

2. These differences in convenience, etc., can affect compliance with physician recommendations. A patient simply may not take the prescribed large quantities of antacids, whereas he or she may comply much more fully with instructions for the easier-to-take cimetidine. The com-

parative effectiveness (and benefits) of various therapies thus depends not on their success under ideal experimental conditions but under real living conditions.

Geweke and Weisbrod note that in many controlled experiments in the health area the only groups compared are those in which the new technology (e.g., cimetidine) is used by either all persons (the "experimental" group E_1) or none (the "control" group C). But this gives a distorted picture of actual utilization that can be expected. Thus, they suggest the addition of a third group, E_2, one for which the new technology is available but is utilized only some of the time, depending on provider judgments, as would be the case in the real world. "Clearly, the more interesting experiment is a comparison of groups C and E_2."[39]

The critical evaluation question, regardless of which of the perspectives discussed above is taken, is how treatment with cimetidine changes outcomes--benefits, costs, expenditures, health state, etc.--compared, not with placebo treatment, nor with nontreatment, but with the variety of treatments that actually would occur in the absence of cimetidine. This is what Geweke and Weisbrod have attempted to do.

The major problem with which Geweke and Weisbrod wrestled is potential "selection bias." In an idealized experiment, which they describe, DU patients would be assigned randomly to treatment with cimetidine or with other therapies. In fact this has not been done.

Thus, they are concerned about the possibility that those DU patients who have used cimetidine may be systematically different from those not receiving it--for example, in terms of severity of illness or need for surgery--and/or the physicians prescribing cimetidine may be better informed, not only about cimetidine's availability but about other aspects of medical care, so that their patients would have better treat-

ment, and different benefits, costs and expenditures, than would the patients of their less-informed counterparts.

Geweke and Weisbrod attempted to adjust for selection bias in a variety of ways. The one they judge to be most useful involved a multiple regression analysis in which DU patients' disease severity—measured by history of days of hospitalization for DU and prior expenditures for DU treatments--was controlled (in a statistical sense) in order to estimate the effect on medical-care expenditures of utilizing cimetidine.[40]

While this work utilized data for both Texas and Michigan, the authors regard the Michigan data as preferable, both because of its larger sample size and its better quality (more complete data on diagnosis). Their empirical work began with the accounting records for all Michigan Medicaid recipients for the full calendar years 1977 through 1979. Information for each recipient is organized by claim, and for each claim there are one or more lines describing in some detail the nature of the treatment and the amount billed, whether to Medicaid or another party. For each individual, basic demographic information and dates of Medicaid eligibility are available. For physician and hospital claims there is always an associated primary diagnosis, and in some cases a secondary diagnosis. The lines for hospital claims specify procedures undertaken and the associated dates, but do not segregate drug billings from other charges. Medicaid drug claims originate with pharmacists, and include all legend, generic, and over-the-counter drugs billed to Medicaid. Dates filled and amounts billed are available in all cases. From this massive data file records were assembled for those 2850 individuals who (a) were continuously eligible for Medicaid over the three

years; and who (b) had at least one primary or secondary diagnosis of duodenal ulcer during the period.

When the actual average values for the previous period (months 2-8 prior to the intervention) were utilized in the statistical analysis--$60 per person for health-care expenditures on DU treatment, and one day of hospitalization for DU care--the regression results are as presented in Table 2.. To a rough approximation, the results in Table 2 may be summarized by pointing out that except for the comparison in month 1, group E--the cimetidine users--shows higher expenditures for other drugs, hospitalization, and physician visits than does the control group, C (although the differences for the highest-expenditure class, hospitalization, are not significant). The greater expenditures for C than E in month 1 are attributable to the nature of the intervention of group C. For one-third of the C sample, the intervention consisted of hospitalization or a physician visit rather than a digestive-disorder drug claim; hospitalization always entails greater expenditures than a monthly drug regimen, and a physician visit often does. It is therefore not surprising that this control group displays much higher expenditures in the first month than does the cimetidine group E.

The numerical comparisons reveal a less obvious point as well: the month 1 disparity is so great that it overwhelms the difference for the total of the following eleven months. When the twelve months following the intervention date are taken as a whole, per capita expenditures for group E are far lower, only 30 percent of those for group C. The differences are statistically significant over the whole range of the independent variables.

It might be contended that the comparison of actual expenditures of the C and E groups provides a biased result. Geweke and Weisbrod con-

Table 2

Expenditures per Case, Groups E and C, Assuming Mean Values of Pre-Sample Hospitalization, 1 day, and Pre-Sample Expenditure for Duodenal Ulcer, $60 ($x_1 = 60$, $x_2 = 1$)

Type of Expenditure	Expenditure C	Expenditure E	"t" Statistic
	(1)	(2)	(3)
		Month 1	
Cimetidine	$ 0.00	$25.07	--
Other drugs	2.98	2.78	0.78
Hospital	557.69	24.02	12.08****
Physician	92.94	29.18	9.82****
Total expenditure	653.60	81.04	12.29****
		Months 2-6	
Cimetidine	0.00		--
Other drugs	4.01	5.31	-2.48**
Hospital	24.65	51.82	-1.47
Physician	12.43	15.74	-0.74
Total expenditure	41.09	72.87	-2.44**
		Months 7-12	
Cimetidine	0.00	10.14	
Other drugs	2.95	3.77	-1.69*
Hospital	19.70	21.56	-0.10
Physician	3.80	13.37	-2.34**
Total expenditure	26.45	48.84	-1.13
		Months 1-12	
Cimetidine	0.00	54.36	
Other drugs	9.93	11.86	-1.87*
Hospital	602.04	97.40	9.62****
Physician	109.17	57.65	5.78****
Total expenditure	721.14	221.26	8.91****

Note: Single asterisk denotes significance at 10 percent level; double, 5 percent; triple, 1 percent, and quadruple, 0.1 percent.

sidered, therefore, the possibility that the appropriate comparison should be based not on the actual expenditures of the groups but on what their expenditures would have been in the idealized, random-assignment case.

It seems plausible that the new technology, cimetidine, has been used as most new medical technologies are used--sometimes substituting for higher-expenditure technologies (e.g., surgery) and sometimes for technologies that involve lower expenditures. This does not imply that such a new technology is being used inefficiently, any more than the drilling of a "dry hole" implies that the oil driller was inefficient. If geological knowledge were sufficient to determine with certainty the presence of oil, or if medical knowledge were sufficient to determine with certainty which particular therapy was least costly (given the effectiveness) then all error could be avoided. In realistic situations, however, decision-makers confront the familiar dilemma involving type I and type II statistical errors. In the case of cimetidine, this means that if the new technology were to be employed only when it was virtually certain to substitute for more costly surgery, the result would be an inefficiently low utilization rate for cimetidine. Even when it is not certain that surgery can be avoided permanently by the use of cimetidine, the key issues are the probability and duration of postponement. As the estimates in Table 2 indicate, hospital and physician costs associated with surgery (col. 1) are indeed very large compared with the average costs of cimetidine therapy (col. 2). Efficiency calls for the use of average, expected values, of the type in Table 2; the state of knowledge necessitates probabilistic statements about outcomes.

Because of these uncertainties, Geweke and Weisbrod also estimated expenditures for alternative control groups. This work may be summarized

as follows: Suppose that in the absence of cimetidine therapy, interventions would have consisted of a fraction, d, of drug therapy and the balance, 1 - d, of other kinds of therapy, including surgery. Suppose further that with the introduction of cimetidine, a fraction, m, of the nondrug interventions (surgery and physician visits) would be shifted to cimetidine. This implies that cimetidine decreases surgery and physician visits from what they would be with previously available drugs. These suppositions, combined with their estimates in table 2, enabled Geweke and Weisbrod to estimate the total per patient expenditure levels for various values of m. With cimetidine available, the average twelve-month total expenditure level per patient, for all patients (not just those using cimetidine), was estimated to equal \$772 - \$613m. If m exceeds .084--that is, if the new technology, cimetidine, reduced the need for surgery and physician visits by 8.4 percent or more--then the twelve-month expenditure level after the introduction of the new drug would be expected to be lower than that which would have prevailed without it, \$721. The latter figure is the average, twelve-month expenditure for all non-cimetidine-using patients--those using other drugs, which are relatively inexpensive, and those using surgery, which is far more expensive than cimetidine. The expenditure effect of cimetidine thus depends on the degree to which it substitutes for the lower-cost, and for the higher-cost alternatives.

Outside evidence suggests that the appropriate value of m is much larger than 8.4 percent--that is, cimetidine can be expected to reduce DU surgery by more than that figure. A recent study of the incidence of surgery for duodenal ulcer, before and after the introduction of cimetidine, estimated that surgery was reduced 39 percent by the introduction of the new drug.[41] Taking m = .39 as an initial estimate, Geweke and

Weisbrod obtained an aggregate per patient twelve-month expenditure level of $534 with the introduction of cimetidine, compared with $721 without it. The new drug was thus estimated to have reduced expenditures over a one-year period by 26 percent.

The reduction in DU surgery attributable to cimetidine is a critical matter. Fineberg and Pearlman analyzed data on ulcer surgery over time, and concluded that an "unexpected" decline in ulcer surgery occurred in 1978, the year cimetidine was introduced in the U.S. The sharp decline of ulcer surgery--some 11,000 to 26,000 fewer procedures (about 12-30 percent fewer) than a trend extrapolation predicted--was especially noteworthy because there was no decline in abdominal surgery in general. Even if the effect of the new drug on the frequency of surgery was only half the 39 percent estimate by Wylie et al., or even if it was at the low end of the range estimated by Fineberg and Pearlman, the drug reduces expenditures on DU substantially.

Whichever approach Geweke and Weisbrod considered, the empirical results show that treatment with cimetidine is an expenditure-reducing alternative compared to previously existing therapeutic interventions (other drugs and surgery). It is, obviously, not expenditure-reducing in those cases in which costly surgery would <u>definitely</u> never be required and previously existing drugs would suffice, but the knowledge required to make this distinction, and hence to avoid "dry holes," is not available. The extent to which the use of cimetidine reduces expenditures depends on the extent to which it substitutes for surgery, on the one hand, or more conventional, low-cost drug therapies, on the other. There is an optimum pattern of cimetidine usage, and it is at neither the extreme of indiscriminate usage for all peptic ulcer patients, nor at

another extreme, such as usage restricted to extremely severe cases for which surgery is otherwise imminent.

While one of the approaches used by Geweke and Weisbrod shows the new technology to reduce DU expenditures by some 70 percent, and the other approach estimates the reduction at a smaller, but still, substantial, 26 percent, they emphasize that "unless the probability of surgery being required is very low--8 percent or lower--even our more conservative approach predicts expenditure savings attributable to cimetidine."[42] They also reiterate that while they examined only the expenditure implications of cimetidine therapy, the "nonmarket" effects--the advantages to patients from avoiding the pain, anxiety, and risks of surgery--are also relevant.

V. LESSONS AND CONCLUDING COMMENTS

Many of the problems confronting economic analysts of any new drug technology would be avoidable, at relatively low cost if economic evaluation were built into the randomized clinical-trials process. In its absence, economists have been forced to make assumptions about the expected usage of the new drug (or other new medical technology)--specifically whether users and nonusers constitute random, or biased, samples from the population of duodenal ulcer patients. Because of concern about selection-bias contaminating results, statistical corrective measures have been employed. These measures would be unnecessary if the needs of evaluation had been taken into account at the time of clinical trials.

Whatever the source of data, economic evaluation can proceed from a number of perspectives. From an overall economic-planning point of view,

a social benefit-cost analysis is clearly preferable to either a cost-effectiveness or a budgetary analysis. Concerns about conceptual purity should not blind us, however, to the purpose of any evaluation--to facilitate intelligent decision making. If the issue is whether or not to allocate more resources toward utilization of some new technology, it makes little or no difference whether it is 50 percent or 500 percent more efficient than its alternative, for even the lower figure indicates a socially efficient change. Thus, for example, the omission from an evaluation of the greater convenience of using cimetidine compared to antacids or surgery is of no consequence if--or insofar as--the other variables considered already show an excess of benefits over costs for cimetidine therapy.

There are advantages and disadvantages of the various evaluation approaches. Briefly, the point is that alternatives to an all-encompassing benefit-cost analysis have been developed for a reason--because it is costly to obtain data. When the costs and benefits of undertaking a more comprehensive benefit-cost analysis are considered, it may turn out that a conceptually less desirable alternative is actually preferable. The variety of evaluations of cimetidine, and the shortcomings of each, point up the important trade-offs between comprehensiveness, practicability, and cost of the study. Incomplete information, both about short-term and even moreso about long-term effects of a new technology, combine with difficult value-laden problems of how to place monetary values on pain, suffering, and life itself, to make the evaluation of health-care technologies enormously complex. A "useful" evaluation--since it will inevitably be incomplete--should (1) make clear the nature of its shortcomings; (2) not hesitate to present nonmonetary, quantitative measures of costs and benefits, leaving it to the user to

decide upon their importance relative to other consequences; and (3) understand, and make clear to the nonprofessional reader, that attempts to state benefits and costs in money terms do not reflect a morbid preoccupation with money--far from it--but simply the unavoidable need to make the varied effects of a new technology commensurable with each other. To judge the "desirability" of a new technology we need somehow to add all its favorable effects and its unfavorable effects, to find which total is greater.

In the case of cimetidine, the clinical evidence of its effectiveness compared to placebo is of little relevance for an economic evaluation which seeks to determine whether the drug's favorable effects and costs make it superior, in value terms, to the alternatives it would replace. Placebos are, in general, not among the realistic alternatives. A variety of economic assessments have been undertaken. Each is incomplete. Each has theoretic shortcomings. Yet the evidence is growing that this new medical technology is more than worth its cost (as measured by its price).

The evaluative studies for cimetidine have contributed not only to knowledge about the economic evaluation of that drug, but also about the problems of, and the opportunities for making such evaluations of other medical innovations. Building economic evaluation into the process of random-assignment clinical trials is a high priority, as is the expansion of random assignment to groups utilizing nonplacebo alternatives. In addition, increased consideration should be given to monitoring of costs and benefits after a drug is marketed (along lines utilized in the Geweke--Weisbrod studies) as part of a continuing process of approval and evaluation of new medical technologies.

We have much to learn about how to blend theoretic ideals with feasible methods, and learn we must. The stakes are high--for private innovators, the research community, government agencies, and the society at large.

Notes

[1]See, e.g., R. Musgrave and P. Musgrave, Public Finance in Theory and Practice (New York: McGraw-Hill Book Company, 1980), pp. 54-74; also B. Weisbrod, in collaboration with Joel F. Handler and Neil K. Komesar, Public Interest Law (Berkeley: University of California Press, 1978), Chap. 3.

[2]See, e.g., Musgrave and Musgrave, pp. 85-105; Charles Wolf, Jr., "A Theory of Nonmarket Failure: Framework for Implemenation Analysis," Journal of Law and Economics, 22 (April 1979), 107-139; B. Weisbrod, "Collective Action and the Distribution of Income: A Conceptual Approach," The Analysis and Evaluation of Public Expenditures: The PPB System, Joint Economic Committee, U.S. Congress (Washington, D.C.: GPO, 1969), pp. 177-98 (reprinted in R. Haveman and J. Margolis, eds., Public Expenditures and Policy Anaysis [Chicago: Markham, 1970]).

[3]John Godderis and B. Weisbrod, "Medical Progress and Health Care Expenditures: The Uneasy Marriage," Viewpoints (Nutley, N.J.: Hoffman-LaRoche, Inc., 1980).

[4]Arnold C. Harberger, "Three Basic Postulates for Applied Welfare Economics," Journal of Economic Literature, 9 (Sept. 1971), 785-797.

[5]Weisbrod, "Collective Action..."

[6]B. Weisbrod, "Benefit-Cost Analysis of a Controlled Experiment: Treating the Mentally Ill," Journal of Human Resources, 16 (Fall 1981), 523-548.

[7]J. Geweke and B. Weisbrod, "Assessing Technological Change: The Case of a New Drug," University of Wisconsin-Madison, mimeo, 1982.

[8]Harvey V. Fineberg and Laurie A. Pearlman, Benefit-and-Cost Analysis of Medical Interventions: The Case of Cimetidine and Peptic Ulcer Disease (Washington, D.C.: Office of Technology Assessment, United States Congress, September 1981), Case Study #11, p. 6.

[9]Rita Ricardo-Campbell, "Risk-Benefit/Cost-Benefit: Improving Government Regulation of Approval of New Drugs," presented at the World Congress on Health and Economics, Leyden University, the Netherlands, September 9, 1980, mimeo., p. 13.

[10]Analytically, there is no distinction between a benefit and a cost, since "benefits" can be negative as well as positive, as can "costs." A negative benefit--that is, an adverse effect--is equivalent to a (positive) cost. In common parlance, however, costs are thought of as the resources that are expended on the project and benefits are the outcomes; the statement that benefits are more difficult to measure is thus a view that outcomes are more difficult to measure than are resource costs.

[11]E. Mishan, "Evaluation of Life and Limb: A Theoretical Approach," Journal of Political Economy, 79 (July 1971), 687-705; M. W. Jones-Lee, The Value of Life: An Economic Analysis, (Chicago: University of Chicago Press, 1976); R. Zeckhauser, "Procedures for Valuing Lives," Public Policy, 23 (fall 1975), 419-464.

[12]U.S. Department of Health, Education, and Welfare, Office of the Assistant Secretary for Program Coordination, Selected Disease Control Programs (Washington, D.C.: HEW, September 1966), p. 9.

[13]B. Weisbrod, "Benefit-Cost Analysis of a Controlled Experiment."

[14]Selected Disease Control Programs, p. 12.

[15]To the credit of the report that presented the numbers, most of the following issues were, at least, recognized.

[15a]Under some conditions a budgetary analysis is the equivalent of a cost-effectiveness analysis. This is the case when (1) the alternative therapies being compared have "equal" results, and (2) all budgetary inflows and outflows measure real costs (outflows) and real benefits (inflows). These conditions, however, do not generally hold.

[16]A. Culyer and A.K. Maynard, "Cost-Effectiveness of Duodenal Ulcer Treatment," Social Science and Medicine, Vol. 15c, no. 1 (1981), pp. 3-11.

[17]Ibid., p. 4.

[18]Ibid.

[19]Ibid., p. 6.

[20]Weisbrod, "Benefit-Cost Analysis of a Controlled Experiment."

[21]G. Bodemar, Ricci Gotthard, M. Strom, A. Walan, B. Jonsson, and P. Bjurulf, "Socioeconomic Aspects of Treatment with Cimetidine in Peptic Ulcer Disease," in Further Experience with H_2 -Receptor Antagonists in Peptic Ulcer Disease and Progress in Histamine Research, Proceedings of the Symposium held at Capri, October 18-20, 1979 (Amsterdam-Oxford-Princeton: Excerpta Medica, n.d.), pp. 59-67.

[22]Culyer and Maynard, p. 6.

[23]Ibid., p. 8.

[24]Ibid., p. 9.

[25]Ibid.

[26]Ibid.

[27]Dr. H. R. Wulff, quoted in Fineberg and Pearlman, p. 38.

[28]Culyer and Maynard, p. 8.

[29]G. Bodemar and A. Walan, "Maintenance Treatment of Recurrent Peptic Ulcer by Cimetidine," Lancet, February 25, 1978, pp. 403-406.

[30]Ibid., p. 10.

[31]Ibid.

[32]Rita Ricardo-Campbell, Martin Eisman, William M. Wardell, and Roger Crossley, "Preliminary Methodology for Controlled Cost-Benefit Study of Drug Impact: The Effect of Cimetidine on Days of Work Lost in a Short-Term Trial in Duodenal Ulcer," Journal of Clinical Gastroenterology, 2 (1980), 37-41; Bodemar and Walan.

[33]Fineberg and Pearlman, pp. 18-23.

[34]Robinson Associates, The Impact of Cimetidine on the National Cost of Duodenal Ulcers (Bryn Mawr, Pennsylvania: Robinson Associates, 1978).

[35]Fineberg and Pearlman, pp. 55-57.

[36]J. Geweke and B. Weisbrod, "Some Economic Consequences of Technological Advance in Medical Care: The Case of a New Drug," in R. B. Helms, ed., Drugs and Health (Washington, D.C.: American Enterprise Institute for Public Policy Research, 1981), pp. 235-271; "Clinical Evaluation vs. Economic Evaluation: The Case of a New Drug," Medical Care (spring 1982), forthcoming; "Assessing Tecnological Change: The Case of a New Drug," mimeo, University of Wisconsin-Madison, 1982.

[37]Geweke and Weisbrod, "Some Economic Consequences of Technological Advance in Medical Care," pp. 235-237.

[38]Ibid., p. 236.

[39]Ibid, p. 242.

[40]The equation $y = b_o + b_1x_1 + b_2x_2$ where x_1 is total health-care expenditures related to duodenal ulcer treatment, and x_2 is days of hospitalization for duodenal ulcer, in the second through eighth month

preceding the "intervention" data; y is one of several kinds of expenditures--on drugs, hospitalization and physicians--following the intervention date. Separate estimates were made for the groups E (cimetidine) and C (noncimetidine). The estimates of predicted expenditures for the two groups were then compared for specific values of the x_1 and x_2 variables.

[41]John H. Wylie, J. Alexander-Williams, Terrance L. Kennedy, Charles G. Clarke, Peter R.F. Bell, Raymond M. Kirk, and Colin MacKay, "Effect of Cimetidine on Surgery for Duodenal Ulcer," Lancet, June 13, 1981, pp. 1307-1308.

[42]Geweke and Weisbrod, "Assessing Technological Change," p. 15.