nitude of the **1978** decline in surgery for ulcer disease.

There is little evidence of any effect on cimetidine on mortality from ulcer disease. In several studies, patients treated with cimetidine lost significantly fewer days of work than patients taking placebo, but no controlled study compares work loss among patients on different, effective treatments.

REVIEW OF BENEFIT-AND-COST ANALYSES OF CIMETIDINE

Available Analyses

We are aware of two analyses of the social resource implications of cimetidine (109, 121). Both were sponsored by Smith Kline & French Laboratories, through their office of cost-benefit studies. One study, published by the Netherlands Economic Institute in February 1977 (109), analyzed the possible effect of cimetidine on the Dutch economy. That analysis estimated that if cimetidine had been used by half of all ulcer patients in the Netherlands, the potential savings would have been **$23** million, or **21** percent of the estimated $111 million total costs of ulcer disease in 1975, We will not comment on this study, because most of the issues it raises are also raised in the second study, and the latter is a more recent analysis which focuses on the United States.

The second study, entitled *The lmpact of Cimetidine on the National Cost of Duodenal Ulcers* **(121),** was conducted by Robinson Associates, Inc., a marketing research and management consulting organization located in Pennsylvania. A summary of the methods and conelusions of the Robinson Associates study, along with our critique of the study, are presented in the section below.

The Study by Robinson Associates, Inc.

Summary of Methods and Conclusions

The Robinson Associates study **(121)** estimated that if cimetidine had been used in **80** percent of duodenal ulcer patients in the United States, 1977 national health care costs for duodenal ulcer disease would have been reduced by **$645** million **(29** percent of that study's estimated total expenditures for duodenal ulcer). An estimated **$271** million would have been saved in medical care costs. The estimated **$271** million savings is the net result of a $34 million increase in drug costs, offset ninefold by $305 million in savings in other expense categories; the bulk of the $305 million medical care savings is from estimated reductions in hospital care ($258 million) and surgeons' fees ($30 million). In addition to the **$271** million net savings in medical expenditures, the study estimated that $373 million would have been gained from increased productivity—$329 million (88 percent) from decreased morbidity, and the remainder from decreased mortality.

The Robinson Associates analysis was based on two types of estimates. First, physician experts were asked in late 1977 to estimate the likely clinical and health system effects of cimetidine compared to traditional therapy for duodenal ulcer patients. Then, applying cost figures derived principally from SRI's assessment of the costs of ulcer disease in the United States **(146),**[33] Robinson Associates estimated the potential savings in 1977 due to the average predicted changes in health status and medical care. Summing the results for each cost category, the analysis yielded the conclusions summarized in the preceding paragraph.

A detailed reconstruction of the Robinson Associates analysis is beyond the scope of this review. Below we provide a description of certain methodologic features of the analysis as a basis for our comments in the critique that follows. First, we consider the expert estimates of the clinical and health system effects of cimetidine; then, we consider the conversion of these estimates into projected annual savings.

[33] SRI's assessment was discussed in some detail in the section of this case study on the cost of illness.

Twenty-three physicians who were familiar with cimetidine served as expert consultants for the Robinson Associates analysis. Each was asked in an interview about five specified ulcer-patient types—ranging from a patient with typical symptoms and newly diagnosed ulcer to a patient hospitalized with the complication of bleeding but not requiring immediate surgery—which were intended to represent a spectrum of severity of illness in patients with duodenal ulcer. The 23 physicians first estimated the proportion of all ulcer patients represented by each type. Then they described what they believed to be the usual treatment for each patient type and any changes in that treatment that would be made in a program that would include cimetidine. Finally, they estimated clinical and health system effects (including such elements as recurrence, physician visits, hospitalizations, surgery, diagnostic tests, missed work, complications, and mortality) for each type of patient treated without cimetidine and with up to 8 weeks of cimetidine. The physicians were not asked to estimate dollar costs for any postulated effects.

The methods that were used in the Robinson Associates study to convert estimated clinical and health system effects into dollar savings were as follows. As a baseline for estimating the costs of duodenal ulcers, Robinson Associates used estimates of the costs of peptic ulcer disease in 1977 developed by SRI **(146).** Within each direct and indirect cost category, the analysts estimated from secondary sources the fraction of peptic ulcer costs attributable to duodenal ulcer disease (with the remainder attributable to gastric ulcer).

To estimate the proportion of costs that would be saved by cimetidine, the analysts then proceeded as follows. First, they assigned prices to each component of each cost category. For example, in the category of hospital costs, they established the cost per hospital day for patients who do not have surgery and the cost per hospitalization for patients who do undergo surgery. Next, the analysts combined these cost components with physician estimates of the management and course of patients with and without cimetidine. For example, the hospital costs for each type of patient were calculated as the sum of costs for the proportion of those patients given surgery plus costs for those not given surgery, as follows:

proportion of patients of this type who are hospitalized
x [(proportion of patients hospitalized without surgery
x number of nonsurgical hospitalizations per year
x average length of stay for nonsurgical patients
x cost per day)
+ (proportion of patients hospitalized with surgery
x cost per surgical admission)]
= total annual hospital cost per patient of this type

Similar calculations yielded an estimate of the annual costs in each cost category for each type of patient with and without cimetidine.

Next, the percentage difference in costs in each cost category due to cimetidine was calculated for each type of patient. The percentage change for each type of patient was then weighted by the proportion of all ulcer patients estimated by the physicians to be represented by that type. This yielded the percentage change in a given cost category for an "average" patient treated with cimetidine rather than traditional therapy.

The percentage change in cost per "average" patient was further adjusted to reflect: the posited extent of use of cimetidine. The physician consultants predicted that an average of 80 percent of the five patient types would be treated with cimetidine 2 to 3 years after the time of the interviews. This figure, used as the basis for dollar projections in Robinson Associates study's conclusion, is a composite of the estimated extent of use (ranging from 73 to 93 percent) for each of the five types of patients.

Next, the percentage change in cost for each cost category, as adjusted for the proportion of patients using cimetidine, was multiplied by the costs of duodenal ulcer disease assigned to that category. This provided a dollar estimate of savings in each category. Summing the dollar estimates over all cost categories yielded the total projected savings attributable to the use of cimetidine by a given proportion of patients.

In short, the Robinson Associates analysis used prices of the components of medical care only as a basis for estimating the percentage

change in cost due to cimetidine. Once derived, these percentages were applied to independent assessments of the cost burden of all duodenal ulcer disease to estimate dollar savings.

Critique

The cost-and-benefit analysis that Robinson Associates prepared for Smith Kline & French has many positive attributes. First, the study represents the kind of serious analysis of the economic effects of a new drug that is important and valuable. If society is to attend to both the economic and clinical implications of medical interventions, careful analyses of costs and benefits are essential. Second, we believe the analysts selected appropriate categories of resource costs to assess. Their direct cost components correspond roughly to the **health** system effects outlined in the benefit-and-cost model we presented earlier in this case study. Their translation of mortality and morbidity components into indirect costs is appropriate for a resource cost analysis. Third, their approach of comparing estimated net resource effects of cimetidine to resource use without cimetidine is a reasonable one. Fourth, their method of obtaining physician estimates of clinical and health system effects was an imaginative one, and it required no guesses about costs from clinicians. Finally, the report provides sufficient detail about its methods and assumptions to allow the reader to reach independent conclusions.

We believe this report deserves scrutiny, because, to our knowledge, it is the most comprehensive analysis of the resource implications of cimetidine in the United States. As a thorough economic assessment of a recently introduced drug, the study may serve as a model for future evaluations of other emerging medical practices. In the discussion of the study that follows, we have attempted to examine the analysis carefully in light of the benefit-and-cost model and data presented earlier and the guidelines for review of benefit-and-cost analyses that are presented in the next section of this case study.

We believe the Robinson Associates study substantially overestimates expected savings from cimetidine. The accuracy of the estimated savings attributable to cimetidine in the Robinson Associates study depends on at least five features: 1) the accuracy of the clinical and health system effects projected by their physician experts; 2) the relation between a percentage reduction in health services devoted to ulcer disease and savings in health resources; 3) the accuracy of the estimated total costs of all duodenal ulcer disease used as a baseline for percentage savings; 4) the applicability of projected percentage effects to the total population of patients with duodenal ulcer disease; and 5) the validity of the methods used to compute average percentage effects due to cimetidine. We question some of the assumptions and methods used in each of these five areas.

Let us consider first the physician experts' opinions of the clinical courses of patients with and without cimetidine. The mean of these estimates is intended to represent an unbiased estimate of the course of duodenal ulcer disease using conventional treatment, and an unbiased estimate of the effects of cimetidine. An unbiased estimate of the former is best achieved by physicians of varied specialty backgrounds who together treat the full range of patients with ulcer disease, An unbiased estimate of the latter requires both knowledge of cimetidine's clinical effects and a neutral attitude toward the drug.

The 23 physicians whose opinions form the basis of the Robinson Associates study were **all** gastroenterologist-researchers who had participated in early clinical trials of cimetidine and whose participation in this study was solicited by Smith Kline & French (121). This selection, the authors state, ensured informed opinion about the potential effects of cimetidine—but it does not ensure individual objectivity or a balanced range of views. Of 32 physicians contacted by Smith Kline & French to participate in the study, 4 refused either because they were too busy or for unknown reasons.[34] It is possible

[34]Four others were disqualified or unavailable because of extensive travel. One of the 24 physicians who agreed to participate was not interviewed because of illness (121).

that researchers who were less enthusiastic about the drug were less eager to express their views when contacted by the manufacturer.

To enhance the credibility of subjective physician estimates, Robinson Associates cite a Danish study (66) that compared observed experience in 154 patients over 13 years with physician estimates of some of the long-term consequences of ulcer disease (proportion treated surgically and proportion of medically treated patients with varying degrees of symptoms). The Danish study found that the mean estimates of 143 physicians corresponded fairly closely to patient experience. The Danish investigators interviewed a wide range of general practitioners, medical specialists, and surgeons to obtain their mean estimates. These investigators also noted that there were some systematic biases that tended to balance one another. For example, the **65** general practitioners in the Danish study estimated that 15 percent of patients would undergo operations for ulcers, and the **50** surgeons predicted 27 percent; the observed proportion was 22 percent. Thus, this study suggests the importance of using a broadly based sample to achieve unbiased mean estimates. Just as surgeons' estimates alone might not accurately represent surgery experience, a group of research gastroenterologists seems unlikely to represent a fair cross-section of physician experience with and expectations for patients who have ulcer disease.

The effects estimated by the physician consultants in the Robinson Associates study varied widely. The projected cost consequences of using cimetidine in **100** percent of duodenal ulcer patients ranged from a savings of **67** percent based on one physician's estimates to an increased expenditure of 40 percent based on another's estimates. Seven of the physicians projected effects that yielded net losses or small savings (of less than 10 percent), while eight physicians projected effects that led to savings of 40 percent or more. If the selection was biased in favor of physicians at the "optimistic" end of the spectrum of clinical and health system effects of cimetidine, the mean cost savings estimate will be similarly biased.

Cost savings in the Robinson Associates study are estimated as a proportion of the total costs of duodenal ulcer disease. Two aspects of the Robinson Associates calculations deserve comment, and we expand on these points below. First, a given percentage reduction in health services requirements for a particular disease probably does not convert directly to an equivalent proportion of health resource savings. Second, we believe that the baseline costs of duodenal ulcer disease employed by Robinson Associates are too large, primarily because of an inflated indirect cost estimate.

An implicit assumption in applying a percentage cost reduction to the health system expenditures for ulcer disease is that savings will be realized in direct proportion to the decreased use of medical services. For example, if hospital days decline by **10** percent, then 10 percent of resources devoted to hospital care are assumed to be saved. This calculation uses average costs per hospital day rather than marginal costs of the last 10 percent of hospital days. To the extent that fixed and semivariable costs contribute to the cost of a hospital day, the marginal savings from reducing a given fraction of hospital days will be less than the average cost of those days.[35] The remaining fixed cost components will simply be redistributed over the remaining hospitalized patients, Thus, the direct conversion of percentage reduction in hospital days to percentage savings in resource costs of hospital care may be questioned.[36] Short-term resource savings might even be less than the averted marginal costs, insofar as available supply of hospital resources induces other demand.[37] If hospital beds previously occupied by patients with ulcer disease are filled by other patients (without ulcer disease) who previously would not have been hospitalized, then potential savings would be eroded further.

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[35] Fixed costs are independent of the volume of services. Semivariable costs are a function of both time and volume of services.

[36] A related problem is the frequent use of charges as proxies for resource costs of care. Charges reflect average rather than marginal costs, and for a variety of reasons, charges for particular services may differ from their average resource costs.

[37] The notion of hospital bed supply creating demand for more hospital services, called Roemer's Law, was originally proposed 20 years ago (130).

The total costs of duodenal ulcer disease used by Robinson Associates are based on the estimated costs of peptic ulcer developed by SRI **(146).** SRI's estimate is substantially higher than another recent, independent estimate of the cost of ulcer disease by NCDD (4), and, as we discussed earlier, we believe a more correct figure lies between the two. If Robinson Associates had based their projected savings from cimetidine use on the costs of ulcer disease as estimated by NCDD, making no other changes in their analysis, the resulting estimated savings would have been over **50** percent less. Use of NCDD's cost figures, without altering any other assumption or calculation used in the Robinson Associates study, would have produced an estimated savings of only **$307** million, in contrast to the **$645** million savings projected on the basis of SRI's figures. Use of our midpoint calculation developed in the section of this case study on the cost of peptic ulcer disease yields estimated savings of only **$476** million.

Another important source of misestimation in the Robinson Associates study is the assumption that the five patient types represent the full range of patients with duodenal ulcer disease. The most severely ill type of patient included in the Robinson Associates study is one who is hospitalized and bleeding but not in need of immediate surgery. Thus, the study omits patients who have very severe bleeding or other life-threatening complications of ulcer disease such as perforation. According to CPHA data **(42),** nearly **6** percent of patients hospitalized for duodenal ulcer disease in 1977 had perforation, and **28** percent had bleeding. The number of excluded patients who require prompt surgery may be estimated conservatively to include 90 percent of patients with perforation (or 5 percent of hospitalized patients) and between 10 and 20 percent of patients admitted for bleeding (or an additional 4 percent of hospitalized patients). Thus, approximately 9 percent of hospitalized patients, all of whom receive surgery, are excluded from the range of patients in this study.

The omission of these patients from the Robinson Associates study has substantial consequences for the study's cost estimates. For example, consider the area of hospital costs alone. Assuming traditional therapy, Robinson Associates estimate total hospital costs to be $732 million. At 80-percent cimetidine use, they estimate savings in hospital costs to be **$258** million, a 35-percent reduction from hospital costs with traditional therapy. According to the SRI figures that served as a baseline for the Robinson Associates estimates, nearly **72** percent of hospital costs for ulcer patients in 1977 were due to the estimated 20 percent of hospitalized patients who underwent surgery (146). Assuming the excluded patients, who are most severely ill, were responsible only for a proportionate share of costs for surgical cases, the proportion of total hospital costs for duodenal ulcer disease devoted to these patients would be approximately **32** percent, and the dollar amount devoted to their care would be **$237** million .[38]

Although the expert consultants were not asked about this group of most severely ill patients, we think that cimetidine would not have been expected to alter the acute management of more than a small fraction of them. Assuming that 80-percent cimetidine use would have been estimated to save as much as 15 percent (approximately **$36** million) of the hospital costs for these patients, and then applying the proportion of savings estimated for "all" duodenal ulcer patients in the Robinson Associates study to the hospital costs attributable only to the included patients, we compute the savings in hospital care to be **$209** million rather than **$258** million. [39]

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[38] Proportion of hospital costs due to surgical care of excluded patients = proportion of surgical cases excluded x proportion of total costs due to surgical cases: 0.324 = (0.09 0.20) x 0,72. Dollar amount devoted to hospital care of excluded patients = proportion of hospital costs due to excluded patients x total hospita] costs: $237 million = 0.324 X $732 million.

[39] Let :

$C \equiv$ estimated hospital costs due to all patients with traditional therapy

$C_E \equiv$ estimated hospital costs due to excluded patients with traditional therapy

$C_I \equiv$ estimated hospital costs due to included patients with traditional therapy

$S \equiv$ estimated hospital savings from all patients with 80-percent cimetidine use

$P_{SE} \equiv$ estimated proportion of costs saved by 80-percent cimetidine use attributable to excluded patients

$P_{SI} \equiv$ estimated proportion of costs saved by 80-percent cimetidine use attributable to included patients

Thus, the incomplete spectrum of patients included in the study produces an overestimate in savings of nearly **$50** million in the area of hospital costs alone. The exclusion of the most severely ill patients also incurs additional, if smaller, overestimates of savings in other cost areas. If cimetidine reduces the fraction of patients who reach the most severely ill category, however, then this source of overestimation would be reduced proportionately. The authors of the Robinson Associates report repeatedly point out that their projected percentage savings are unaffected by changes in estimated baseline costs for ulcer disease. As we have just seen above, however, the percentage savings calculated in the study are quite sensitive to the inclusion or exclusion of different types of patients with duodenal ulcer.

Two other sets of assumptions in the Robinson Associates study also affect the calculated savings. The first of these is the relative dollar values assigned to the components of each cost category (e.g., how much less expensive is a hospital stay for nonsurgical than for surgical patients?). The second set of assumptions is the estimated proportion of all included patients in each of the five patient types. The data underlying these assumptions can be expected to vary over some range. To accommodate such variation, one could, for example, estimate a confidence interval about physician estimates of the proportion of patients of each type.[40] The Robinson Associates study would have been strengthened by explicit sensitivity analysis, testing the effect on the conclusions of systematic alteration of key assumptions.

(continued from p. 53)

Given:

- C - $732 million (from Robinson Associates study)
- C_E - $237 million (from preceding footnote)
- C_I - $C - C_E = \$(732 - 237 \text{ million}) = \$495$ million (by definition, $C = C_I + C_E$)
- P_{SE} - 0.15 (assumption; see text)
- P_{SI} - 0.35 (from Robinson Associates study)

Then:

S - $C_E \times P_{SE} + C_I \times P_{SI}$

- ($237 million) (0.15) + ($495 million) (0.35)
- $209 million.

[40] This is separate from the question of bias in the mean estimate, i.e., whether a group of gastroenterologist-researchers would perceive the world of ulcer patients to be made up of as high a proportion of "initial diagnosis patients" (type 1) as would a group of general practitioners or less specialized internists.

The method used by Robinson Associates to compute the expected reduction in costs caused by cimetidine use has another subtle, but potent, effect on their estimate. Assume for the moment that the interviewed physicians did constitute a representative sample of informed opinion about the effects of cimetidine. It would be desirable, then, for the overall estimated percentage reduction in costs to be a statistically unbiased measure of individually perceived percentage reductions. Take a simplified case. If physician A provides estimates of cimetidine's effects that produce a 70-percent decrease in resource consumption, and physician B provides estimates that produce a 50-percent decrease, we would like the overall estimated reduction to be midway between the two, or **60** percent. Since we presumably trust each physician's judgment equally, each perceived percentage reduction should contribute equally to the overall estimate of percentage reduction. However, the method used by Robinson Associates to compute percentage reduction in costs has the effect of placing greater weight on the percentage reduction estimates of physicians who perceive ulcer disease as more severe and requiring higher levels of resources.

Mathematically speaking, this distortion occurs because the ratio of estimated means is not the same **as** the mean of estimated ratios. To see how this distortion can arise, again consider two simplified examples. First, physician A and physician B are asked about the consequences of ulcer disease with and without cimetidine for a given type of patient. The effects are translated into various categories of resource cost, such as hospital care. Physician A estimates effects that lead to a total annual cost of **$1,000** without cimetidine and **$500** with cimetidine use. Physician B estimates effects that lead to a cost of $100 without cimetidine and **$50** with the drug. In each case, the estimated percentage reduction is 50 percent. Proceeding as Robinson Associates did, we can compute an average cost without cimetidine and an average cost with cimetidine.

$$\text{average cost without cimetidine} = \frac{\$1,000 + \$100}{2} = \$550$$

$$\text{average cost with cimetidine} = \frac{\$500 + \$50}{2} = \$275$$

Then the "average" percentage reduction attributed to cimetidine, as computed by Robinson Associates, would be the difference between these average costs divided by the cost without cimetidine, or:

$$\frac{\$550 - \$275}{\$550} = 0.50$$

In this case, both physicians projected the same percentage reduction, and the calculated percentage reduction agrees with both of them. So far, this approach appears sound.

Now consider the following variation. Physician A estimates effects that cost **$1,000** without cimetidine and $400 with cimetidine, a 60-percent reduction in costs. Physician B estimates effects that lead to a cost of **$100** without cimetidine and **$60** with the drug, a 40-percent reduction. The average estimated reduction is:

$$\frac{0.60 + 0.40}{2} = 0.50$$

or **50** percent. Calculated by the method of Robinson Associates, the percentage reduction IS:

$$\frac{(51{,}000 + \$100) - (\$400 + \$60)}{\$1{,}000 + \$100}$$

$$= \frac{\$1{,}100 - \$460}{\$1{,}100}$$

$$= \frac{\$640}{\$1{,}100} = 0.58$$

Thus, the calculated reduction of 58 percent is much closer to the perceived reduction of physician A, who viewed ulcer disease in this type of patient as more severe and costly than did physician B.[41]

The estimation method used by Robinson Associates confounds the estimate of perceived effects of cimetidine, on the one hand, with variability in the perceived severity and overall management of ulcer disease, on the other. If the Robinson Associates study had taken the mean of physician estimates with traditional therapy as the baseline from which percentage reductions were calculated, there might be a stronger case for an approach like that used. However, the calculated percentage reductions were applied to an independently determined baseline cost. This reinforces the argument for seeking an unbiased measure of expected percentage reduction, namely the mean of the physicians' percentage estimates.

The practical consequences of this distortion are substantial. A series of bar graphs provided in the Robinson Associates report (their tables **34** through **43,** pp. **54-63)** shows percentage changes in cost based on the estimates of each of the **23** physician informants. A separate figure in the report depicts the distribution of physician percentage estimates for each of nine cost categories and overall costs. On the basis of the bar graph for the distribution of physician estimates of overall cost savings, we calculate that the mean of the estimated percentage reductions by the 23 physicians was approximately **24** percent (see table 20). By contrast, the "mean" shown in the Robinson Associates bar graph and used in the analysis was a percentage cost reduction of 34 percent (at 100-percent cimetidine use).

This suggests that the "average" percentage reduction used in the Robinson Associates

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[41] Symbolically the difference between the method in effect used by Robinson Associates to calculate a "mean" percentage cost reduction and the mean of the percentage reductions estimated by the physicians can be expressed as follows

n ≡ number of physician experts
TC_i ≡ cost calculated from physician i estimates of effects with traditional treatment (without cimetidine)
CC_i ≡ cost calculated from physician i estimates of effects with all patients receiving cimetidine treatment

Then:
$TC_i - CC_i$ ≡ cost savings calculated from physician i estimates
$\frac{TC_i - CC_i}{TC_i}$ ≡ percentage cost reduction calculated from physician i estimates

Robinson Associates estimates "mean" percentage cost savings as an "average of total costs":

$$\frac{\sum_{i=1}^{n} (TC_i - CC_i)}{\sum_{1=1}^{n} TC_i} \times 100 \qquad (1)$$

The mean of percentage savings estimated by physicians is:

$$\frac{\sum_{i=1}^{n} \left(\frac{TC_i - CC_i}{TC_i} \right)}{n} \times 100 \qquad (2)$$

In general, eqn. 1 # eqn. 2, although the two may give the same result in exceptional circumstances.

Table 20.—Percentage Cost Savings Estimated From Robinson Associates Study

Physician number	Percentage savings[a]
1	68%
2	62
3	62
4	55
5	50
6	48
7	47
8	42
9	36
10	35
11	28
12	27
13	19
14	13
15	12
16	11
17	8.5
18	8.5
19	3
20	0
21	– 9[b]
22	– 24[b]
23	– 40[b]
Total	562%
Mean percentage cost savings = 562/23=24.4%	

[a]Gauged from the height of the bar graph for each physician in Robinson Associates table 43
[b]Estimated cost increase

SOURCE Robinson Associates, Inc, *The Impact of Cimetidine on the National Cost of Duodenal Ulcers*, 1978(121)

analysis was approximately 42 percent larger than the mean of the estimated percentage reductions provided by the physician experts.[42] (Similar discrepancies of varying degree are found with each category of cost shown in the Robinson Associates bar graphs.) Basing overall percentage cost savings on the mean of percentage reductions estimated by the 23 physicians would reduce the projected savings at 80-percent cimetidine use by approximately $190 million, from **$645** million to approximately $455 million.

In summary, we believe the Robinson Associates analysis substantially overestimates 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 reduction in costs we believe 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.

Despite our criticisms of the Robinson Associates study, we believe its basic thrust is probably correct. Cimetidine does appear to save more medical resources than it costs. The $305 million savings in medical costs that Robinson Associates estimates from the use of cimetidine are approximately nine times the estimated $34 million direct costs of the drug. Thus, even if the drug costs were tripled and the estimated savings reduced by two-thirds, use of cimetidine would still appear to be an economically sound investment. Also, the estimated savings in health resources omit potential gains in productivity from use of the drug.

The emerging empirical evidence cited in the section of this case study on health system effects supports the belief that use of cimetidine probably saves medical resources. In the coming years, more evidence will probably accumulate about the costs, risks, and benefits of cimetidine compared to alternatives. We may learn, for example, about newly recognized adverse effects of the drug or about rebound in the number of ulcer patients undergoing surgery or about the development of safer, equally effective and acceptable treatments. The comparative cost effectiveness of cimetidine for patients with ulcer disease in the long run is a matter of continuing empirical study,

Our discussion of the Robinson Associates study illustrates some of the difficulties of designing and conducting economic analyses of newly introduced medical practices. The work of the Robinson Associates analysts must be viewed in the context of the information available at the time it was done. The Robinson Associates study was undertaken before there was widespread clinical experience with cimetidine, and the analysts faced a dearth of empirical findings relating directly to resource costs. Given the information available at that time, the analysts might have considered the following procedure. First, define prototypical pa-

42 $\frac{0.34 - 0.24}{0.24} = 0.416$

tients that represent the full range of patients with ulcer disease, including the most severely ill. Second, obtain from a broad, representative group of physicians baseline estimates of the course of disease using traditional therapy. Third, check how closely these estimates correspond to other estimates of the total cost of duodenal ulcer disease, examine critically assumptions that underlie the estimates of the health system effects in each major cost category, and reach consensus estimates. Fourth, present to physicians familiar with cimetidine the consensus-estimated clinical courses for each patient type with traditional therapy; ask them to assume the consensus represents actual patient experience; and then ask them to estimate what changes, if any, would follow from the introduction of cimetidine. Finally, calculate the mean of the estimated percentage cost reductions and apply it to appropriately estimated costs of illness.

Guidelines for Review of Health Care Cost Analyses

Presented below are guidelines in the form of a series of questions that may aid in the design and review of cost-benefit and cost-effectiveness studies. These guidelines cover matters of definition and purpose, analytic methods, and conclusions. They are presented here in concise form and presume familiarity with the rationale and basic components of benefit-and-cost analyses in health care (see, e.g., 89).

Objectives of the Analysis

1. What is the purpose of the analysis? Is it a) to assess the optimal management of individual patients with a particular clinical condition; b) to measure the clinical and economic importance of particular clinical problems; c) to compare alternative strategies for addressing a particular health problem in a particular population; d) to compare alternative investments in health programs; or e) to compare health and other social resource investments?
2. Are the interests and potential biases of the analyst and client acknowledged? Are measures taken to guard against potential bias?

Specification of the Problem

1. Is the population of interest appropriately defined (e.g., a population with a particular diagnosis, or having a particular clinical symptom, or undergoing a particular test or treatment)? Is the population consistently defined throughout the analysis?
2. Does the analysis specify the interventions of interest and address them consistently throughout the analysis?
3. Are the conditions of use (e.g., ideal v. average) specified and consistently treated in the analysis?

Methods of Analysis

1. Are the analytic methods selected appropriate to the objectives of analysis? (e. g., CEA v. BCA, use of decision-analytic framework, etc.)
2. Is the time frame of analysis appropriate to the objectives (e. g., is patient lifetime a more suitable focus than a cross-section of patients for a limited time?)
3. Are clinical effects and other benefits appropriately specified? Are the methods of assessment explained? Are incremental benefits the basis for analysis?
4. Are cost estimates complete and appropriately categorized? Has double counting been avoided? Are induced costs and savings considered? Are marginal resources costs the basis for analysis? Are methods fully explained?
5. Are benefits and costs aggregated properly across the population and intervention of interest? Is the analysis restricted to a few uses of multipurpose intervention?
6. Are benefits and costs appropriately aggregated over time? Is discounting employed? Is the discount rate appropriate?
7. Are projected effects justified? Are the estimates based on empirical data or opinion? Are uncertainties recognized? Are the sources of all estimates clearly explained? Are estimates unbiased? Are assumptions acknowledged, fully exposed, and justified? Are estimates based on evidence from the same population and intervention that are the subjects of analysis? Are extrapolations and interpolations reasonable?