

Case Study #11: Benefit= and-Cost Analysis of Medical Interventions: The Case of Cimetidine and Peptic Ulcer Disease

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SUMMARY

Introduction

This case study presents a conceptual model for assessing the benefits and costs of medical technology, and uses this model as a framework for analyzing the benefits and costs of cimetidine in the treatment of peptic ulcer disease.

The body of the study is organized into three major parts: 1) a description of the benefit-and-cost model; 2) a selective description of clinical features, epidemiologic patterns, and costs of peptic ulcer disease; and 3) a review of the development, dissemination, health benefits, and resource costs of cimetidine. The study ends with a critique of one major analysis of cimetidine's costs and benefits and some suggestions for further research.

The Benefit-and-Cost Model for Medical Interventions

The benefit-and-cost model stresses that an evaluation of medical technology must apply to an identifiable patient population and a specific health intervention. An intervention may have a diagnostic or a therapeutic purpose. A patient

population may be defined in terms of diagnostic category, a clinical sign or symptom, a risk factor, or a complication of disease.

The model posits two principal classes of effects: clinical effects and health system effects. The specific components of each depend on the population and intervention of interest. Clinical effects and health system effects interact and lead to an outcome, expressed in terms of health status and resource costs.

The components of the model apply to both cost-effectiveness analyses (CEAs) and benefit-cost analyses (BCAs), but the two analytic approaches have distinct purposes and measure some components in different ways. The model can also serve as a basis for identifying the structural components of a decision analysis that compares alternative medical interventions.

The model and a set of guidelines for review of health care benefit-and-cost analyses are used to organize and guide our discussion of the costs and benefits of cimetidine in peptic ulcer disease.

Peptic Ulcer Disease

Ulcers probably have multiple causes, but gastric acid and pepsin appear to be necessary ingredients. Epigastric pain (pain in the upper middle abdomen) is often a prominent symptom of peptic ulcers, but the clinical presentation is variable. Furthermore, typical ulcer symptoms may be caused by conditions other than ulcers. A definite diagnosis requires direct visualization by endoscopy or radiographic imaging of the ulcer. Specific treatments of ulcer disease are directed at reducing the presence or effects of gastric acid.

Ulcer disease is a chronic condition with spontaneous remissions and recurrences. Rates of complications and mortality from ulcers are relatively low. Excessive mortality appears to be present only in the first year or so following diagnosis. Little reliable information exists about the natural history of ulcer disease in the general population.

Peptic ulcer is a common condition that affects millions of Americans at some time during their lives. The best available epidemiologic evidence suggests that about 250,000 Americans develop new peptic ulcers each year. New duodenal ulcers are more than four times as common as new gastric ulcers. Some studies have found that the incidence of duodenal ulcer rises gradually with age; others have found that it remains fairly constant above age 35. Above age 40, the incidence of gastric ulcer appears to rise more dramatically than the incidence of duodenal ulcer. Duodenal and gastric ulcers are epidemiologically distinct. Several lines of clinical and epidemiologic evidence suggest that over the past 20 years the occurrence of new ulcers has declined, or ulcer disease is generally less severe than it was at one time, or both.

The basis for some estimates of the costs of ulcer disease and the benefits of treatment is the Health Interview Survey of the National Center for Health Statistics (NCHS). Results of the Health Interview Survey, based on self-reported conditions in a household survey, however, appear to overestimate the occurrence and consequences of ulcer disease.

We estimate that the costs of ulcer disease in 1975 were approximately \$2 billion. Just under half of this total was due to health care expenditures (direct costs), and the remainder was due to productivity losses from morbidity and mortality (indirect costs). Our estimate is based on a review of two independent analyses of the costs of ulcer disease, one by the National Commission on Digestive Diseases (NCDD) and the other by the Stanford Research Institute (SRI). The NCDD and SRI estimates of the total costs of ulcer disease in 1975, \$1.3 billion and \$2.6 billion, respectively, differ by approximately \$1.3 billion. The NCDD and SRI estimates of direct costs differ by approximately \$400 million, a difference that reflects differences in the two studies' methods and differences in their detailed assumptions and procedures. Their indirect cost estimates differ by approximately \$900 million, a difference that reflects differences in the studies' projected morbidity losses. SRI's indirect cost estimate, the higher one, is based on data from the Health Interview Survey, which is an inflated indicator of disease-specific morbidity. In both the NCDD and SRI studies, estimated indirect costs are based on a rather low discount rate—2.5 percent. Use of a smaller discount rate increases the present value of future earnings, thereby increasing apparent costs of illness due to morbidity and premature death.

In addition to estimating costs for 1975, SRI projected an estimate of peptic ulcer costs in 1977. Because of unwarranted assumptions of growth in the morbidity of ulcer disease and use of more expensive resources, the problem of overestimated costs is compounded for 1977.

Cimetidine

Cimetidine represents a new class of histamine antagonists, called H_2 -receptor antagonists, which block stimulation of gastric acid secretion. The product was developed after extensive research by the Smith Kline & French pharmaceutical firm and is marketed under the registered brand name Tagamet®.

The Food and Drug Administration (FDA) approved the use of cimetidine for up to 8 weeks by patients with duodenal ulcer disease or hy-

persecretory conditions such as Zollinger-Ellison syndrome in August 1977. Use of cimetidine spread rapidly. Since March of 1978, the drug has been prescribed in approximately 60 percent of ambulatory visits for ulcer disease each month. In 1978, a conservatively estimated 1.5 million to 2 million U.S. ambulatory patients with ulcers and other symptoms of gastric acidity were treated with cimetidine. Worldwide sales to hospitals and pharmacies in 1979 probably exceeded \$400 million.

The Benefit- and-Cost Model Applied to Cimetidine

Organized according to the benefit-and-cost model presented earlier, this part of the case study describes available information about the effects of cimetidine. It deals separately with cimetidine's clinical effects, its health system effects, and its potential impact on outcome.

Numerous controlled studies of patients with duodenal ulcer confirm that cimetidine promotes healing and provides faster and more complete pain relief than placebo. Less conclusive evidence suggests the drug may be more effective than placebo for patients with gastric ulcer. An intense antacid program appears to be about as effective as cimetidine for patients with duodenal ulcers, but more evidence of this is still needed. Clinical studies have also shown that relief of symptoms is not a reliable indicator of healing. In general, European studies have found more favorable results with cimetidine than have U.S. trials.

Cimetidine used for up to 2 months appears to be a relatively safe drug. Most known side effects are minor or reversible; however, recently reported changes in the bacterial flora of the stomach and endocrinologic effects may be more significant. Available studies of maintenance cimetidine for periods up to 1 year do not alter the current assessment of the drug's relative safety. As is the case with any new drug, possible long-term consequences of cimetidine's use are not known.

Compared to an intense course of antacids, cimetidine is about equally effective and more risky, but less troublesome to patients with

duodenal ulcer. Cimetidine plus a moderate amount of antacid costs no more than a therapeutically equivalent course of intense antacid therapy. Experts now differ in their recommendations for initial therapy of duodenal ulcer, some favoring cimetidine and others antacids. A reasonable approach is to select therapy based on each individual patient's preferences and personality.

Compared to placebo, maintenance treatment with cimetidine for as long as 1 year significantly reduces the chance of ulcer recurrence during the treatment period. Once cimetidine treatment is discontinued, patients appear to relapse at the same rate as they would have without maintenance treatment. We are aware of no controlled trials comparing maintenance cimetidine to treatments other than placebo. There is little empirical evidence either that cimetidine prevents future complications of ulcer disease or that cessation of cimetidine promotes complications. At present, FDA is considering approval of cimetidine for use longer than 8 weeks in patients with duodenal ulcers who are at high risk for surgery.

In European trials, but not in U.S. studies, cimetidine-treated patients tend to consume less antacid than placebo-treated patients. Very limited empirical data are currently available on the possible effects of cimetidine on use of other medication, on diagnostic tests, and on physician visits. There are several studies under way that may shed light on these matters.

Data from NCHS show that in 1978, the first full calendar year after cimetidine was introduced in the United States, there was an unexpectedly sharp decline in the rates of surgery for ulcer disease. This drop occurred against a background of falling rates of surgery and hospitalization for ulcer disease over the previous decade. Although other explanations of the large drop in surgery for ulcer disease in 1978 are possible, the widespread use of cimetidine may have been a contributing factor.

There is little evidence of any effect of cimetidine on mortality from ulcer disease. In one short-term trial and one maintenance study, patients treated with cimetidine lost significantly