terventions for a particular disease, however, BCA is necessary for comparing health care with other socially desirable uses of resources.

If one chooses to develop a decision analysis comparing the use of a particular intervention with its alternatives, the benefit-and-cost model can serve as a useful basis for identifying pertinent structural components: chance events (e.g., important results of the principal and subsequent interventions), choices (e.g., use of other health system components), and outcomes (e.g., net benefits and costs). The decision-analytic approach is a prescriptive model for choosing among alternative treatment strategies. Even if technically correct in all assumptions and computations, a decision analysis does not necessarily predict the management strategies employed by physicians. In estimating the cost effectiveness of a given intervention, it is equally, if not more, important to apply a descriptive model (i. e., to base estimates on changes in management strategy that occur in practice). The distinction between prescriptive and descriptive assessment is analogous to the differentiation between efficacy (effects under ideal conditions) and effectiveness (effects under average conditions) noted in reports from OTA (112).

Any benefit-and-cost analysis encounters numerous conceptual and practical difficulties. These range from the presence of uncertainty and the lack of reliable information to questions of measurement and methods of aggregation over persons and time, to value judgments. Systematic reviews of methodologic issues in CEA and BCA in health have been presented by other authors (149,151).

Following descriptions of peptic ulcer disease and cimetidine in the next two parts of this case study, we present an analysis of the costs and benefits of cimetidine in peptic ulcer disease, using the general benefit-and-cost model described above. Later in the case study, we present a set of guidelines in the form of questions to be used in reviewing benefit-and-cost analyses in health care. These guidelines presume familiarity with the basic assumptions and approaches in BCA and CEA. We believe they are helpful for review of benefit-and-cost analyses of cimetidine such as that presented in the next to the last part of this case study.

PEPTIC ULCER DISEASE

Definition and Etiology

A peptic ulcer is a crater that extends through the full thickness of the mucosa (mucous membrane) of the stomach or duodenum (the first or proximal portion of the small intestine). The pathologic appearance of benign gastric (stomach) and duodenal ulcers is similar; both are believed to be related to too much stomach acid and pepsin for the level of mucosal resistance (82) .[3] Although the presence of stomach acid is necessary for ulcers to develop, the level of acid is often normal in patients with ulcer disease; these patients presumably have impaired tissue resistance. Sturdevant and Walsh (140) list 17 factors other than excessive gastric acidity that may predict increased likelihood of developing duodenal ulcer. These factors include sex, age, blood type, a few diseases, and habits such as smoking and drinking coffee. Despite the popular notion of the "high anxiety, ulcer-prone person, " psychological stress and personality factors have not been shown conclusively to be related to the development of ulcers,

The gastrointestinal tract is a continuous organ, and there is a continuum in the anatomic location of ulcers in the stomach and duodenum. For unknown reasons, peptic ulcers show a predilection for areas at or near rnucosal junctions (81). Since gastric and duodenal ulcers appear to differ in generic and other features, there are reasons to consider them separately in clinical and epidemiologic studies. Often, however, they are considered together, and the situation is further complicated by the frequent oc-

[3] Pepsins are digestive enzymes that are active only in the presence of acid Hence, it is difficult to separate the roles of acid and pepsin in the pathogenesis of ulcer.

currence of new duodenal ulcer in patients who previously had gastric ulcer (17).

Symptoms and Diagnosis

Both duodenal and gastric ulcers produce abdominal pain in the patient, typically in the epigastric region (upper middle abdomen). Less often, they produce nausea and vomiting. Usually, the pain is relieved by food, but in some patients, food may exacerbate pain. Most patients with epigastric pain do not have ulcers; a Danish study found that 68 percent of men and 83 percent of women with epigastric pain did not have ulcers (cited by 140). Some patients develop painless ulcers and have bleeding or perforation as the first manifestation of ulcer disease (119,140).

The specific diagnosis of peptic ulcer depends primarily on imaging examinations, with either barium X-rays or more direct fiberoptic endoscopy. Fully flexible fiberoptic gastroscopes were introduced in 1958 (77). Numerous technical improvements made since have enhanced the flexibility, ease of control, and clinical usefulness of these instruments (10). Endoscopists have formed their own professional society (the American Society for Gastrointestinal Endoscopy), and the endoscopic procedure is widely used. Radiographic examination of the stomach has been improved in recent years by the use of an air-barium, double-contrast technique involving high-density barium sulfate, effervescent tablets to distend the stomach and simethicone to break up small air bubbles (96).

Acid secretion and other tests play a secondary role in diagnosis, except in occasional patients, such as those whose ulcer is caused by gastrinoma (a gastrin-secreting tumor that produces the Zollinger-Ellison syndrome of severe ulcers, intractable pain, and diarrhea).

Treatment and Natural History

The treatment of peptic ulcer disease is intended to relieve symptoms, promote healing, and prevent recurrences and complications (140). Gastric acid is the focus of contemporary specific treatment for peptic ulcer—reducing acid secretion by pharmacologic or surgical means, neutralizing acid with antacids, or increasing tissue defenses against acid.[4] Some physicians begin treatment on the basis of clinical symptoms without pursuing a definitive **diagnosis** (140). A U.S. patient who is diagnosed as having a new peptic ulcer will typically be told to eat a regular, nutritious diet and to avoid aspirin, alcohol, cigarettes, and coffee. Specific medication might include antacids or cimetidine and possibly anticholinergic drugs (drugs that block the passage of impulses through the parasympathetic nerves).

Surgery is normally reserved for patients with recalcitrant symptoms, frequent relapse, or complications such as bleeding, perforation, or obstruction. A large variety of surgical procedures has been advanced over the past century, and there is considerable difference of opinion about the optimal timing and selection of an elective surgical procedure for patients with peptic ulcer disease (44,73,111,124). Highly selective vagotomy has been advocated recently (78). This procedure entails transection of only those nerve fibers that supply the lower esophagus and body of the stomach; the nerve supply to the remainder of the stomach and to other abdominal organs is left intact. Proponents of highly selective vagotomy believe that this procedure obviates some unpleasant side effects of standard vagotomy (cutting of the vagus nerve). The surgical procedure is technically demanding, however, and its comparative effectiveness in the hands of many different surgeons remains to be shown. Cochran, et al. (30) have described the complexity of evaluation and requirements for adequate assessment of any surgical treatment for ulcer disease.

Over the years, an enormous variety of nonsurgical therapeutic regimens has been employed to treat peptic ulcers. An example is diet: Leube introduced a starvation regimen in 1876; Lenhartz recommended frequent small feedings in 1906; and Sippy proposed a bland diet in 1915, variations of which remained popular for-

[4]Improved resistance of cells lining the stomach and duodenum is the presumed mechanism of action of the drug carbenoxolone. Carbenoxolone is a licorice derivative, first used clinically more than 15 years ago. Although prescribed in more than 40 countries, it is not currently available in the United States (86).

many years (84, 119). Now dietary restrictions are believed to play no role in the management of peptic ulcers (119,140), Despite the demonstrated ineffectiveness of diet in the treatment of ulcers, special diets are still widely prescribed (153). The plethora of unsubstantiated, but traditional and trusted, treatments led one authority to exclaim in the late 1960's: "Few conditions provide such a splendid opportunity for practicing 19th century medicine in the second half of the 20th century as gastric ulcer" (37). The 1960's witnessed the introduction, spread, and decline of gastric freezing, a nonsurgical treatment intended to reduce stomach acid and promote healing. Such treatment was eventually proven to be ineffective and occasionally harmful. Some clinicians have also used X-ray therapy to treat ulcer disease in selected patients, and renal failure has been reported as one late complication of such therapy (143).

The reasons for such diverse treatments, and particularly, for the extended use of some ineffective approaches, rest partly in the expression and natural history of ulcer disease. First, as mentioned earlier, the cardinal symptom of ulcer disease is stomach pain; so subjective an expression of illness as stomach pain may respond to suggestion or placebo. Second, ulcers often heal spontaneously; thus, any apparent success with treatment should be compared to the natural rate of healing. Finally, ulcer disease tends to be chronic, with recurrences and remissions; effective short-term treatment may or may not alter the long-term outlook.

The subjective nature of ulcer disease and its variable course suggest that evaluations of treatment must be controlled carefully for bias, preferably with double-blind randomization, On this score, the state of clinical assessments of peptic ulcer disease appears to be improving. Chalmers, et al. (25) reviewed studies of peptic ulcer treatments published in a leading gastroenterology journal and found that more than so percent of the therapeutic trials published after 1976 had a randomized, controlled design, compared to 30 percent or fewer of those published between 1970 and 1974. In addition, improved endoscopic methods now permit a more definitive diagnosis to be established in patients included in clinical trials.

Assessment of long-term results of any intervention in ulcer disease requires comparison to the natural history of the disease. Ideally, the natural history of peptic ulcer disease would be defined through long-term followup of a representative sample of patients with ulcer disease. As discussed below, however, available information about the natural course of ulcer disease is fragmentary.

Fry (57) reported a 5- to 15-year followup of 212 patients with ulcer disease diagnosed between 1948 and 1957 in his general practice in London. He found that symptoms tended to recur and worsen for the first 5 to 10 years, and then usually diminished, irrespective of treatment. Sixteen percent of patients with duodenal ulcer and 18 percent with gastric ulcer required surgery. Complications of bleeding occurred in 14 percent and complications of perforation in 6 percent. Only one patient died from causes related to ulcer.

Krause (91) found similarly low mortality from ulcer in 371 Swedish patients with duodenal ulcer followed for 25 to 35 years. In a study based on a 50-percent random sample of all patients with duodenal ulcer diagnosed between 1963 and 1968 in the population of 500,000 persons living in Copenhagen County, Denmark, Bonnevie (20) found a significant additional mortality risk in the first year following diagnosis of ulcer, but not thereafter. Griebe, et al. (66) interviewed 154 patients living; in Copenhagen in 1976 who had developed duodenal ulcer disease in 1963. One hundred and twenty patients (78 percent) had been treated medically; nearly half of these patients were asymptomatic, and approximately 16 percent still had severe symptoms. Thirty-four patients had been treated surgically, but their clinical status is not described further.

A Veterans Administration (VA) study followed more than 600 patients with gastric ulcer diagnosed in 16 hospitals during a 7-year period (69). More than 75 percent of the patients experienced ulcer healing with medical treatment

within 12 weeks, but 42 percent of these patients had one or more recurrences in the following 2 years. Patients who failed to heal initially were assigned randomly to further medical or surgical treatment. Two years later, a higher proportion of patients in the the surgical group were alive and free of symptoms and recurrence, but the differences between the surgical and medical groups were not statistically significant. Expressed as a proportion of incidence per year among all patients, complications of hemorrhage occurred in 2.5 percent, obstruction in 1.2 percent, and perforation in 0.6 percent.

For several reasons, the available data on the natural history of ulcer disease are unsatisfying. The data come from different geographic 1ocations and cover different time periods and different mixes of patients with duodenal and gastric ulcer. Patients received various treatments (and differing proportions were offered surgery), and results reflect the history under varied treatments rather than a natural history of the disease. Rates of complication and death due to ulcer are low and difficult to assess in relatively small cohort studies; Bonnevie's analysis (20) is exceptional in specifying the attributable mortality risk from newly developed ulcer disease. Finally, such studies of the clinical course of disease are necessarily dated. If the course of ulcer disease is changing over time, data from previous patient cohorts may not apply today.

Epidemiologic Patterns

Ulcer disease is a common medical problem, but has apparently become less common over the past 20 years. Here we summarize estimates of the present incidence and prevalence of ulcer disease and describe the basis for the conclusion that ulcer disease is occurring less frequently. We conclude this section with comments directed specifically to the Health Interview Survey conducted by NCHS, since although its results are used in several estimates of the costs of ulcer disease and the benefits of intervention, we believe the Health Interview Survey overestimates the prevalence of ulcer disease.

Several aspects of the definition of disease and of data collection limit our ability to compare results from different studies of the occurrence of ulcer disease in the United States today. Any effort to assess the incidence and prevalence of ulcer disease is necessarily restricted to a particular place and time. Insofar as there are geographic variations and shifts in the disease over time, projections to other countries and to the present data are uncertain.

In addition, different studies define the prevalence and incidence of this chronic and recurrent disease differently. Some (e.g., 35,36,57) define prevalence to mean the "period prevalence, " or the number of patients who suffer from ulcer disease during a given time period; others (e. g., 105) use prevalence to mean the "lifetime prevalence, " or the proportion of patients who have ever had an ulcer. Incidence may be taken to mean the proportion of a population at risk that first develops ulcers in a given time period (e.g., 18,19) or the percentage that develops either a new or recurrent active ulcer crater during a given time period (e. g., 147). The methods employed in different studies to detect disease also vary, ranging from the use of autopsy results, through review of clinical records, to the use of questionnaire surveys.

On the basis of a number of epidemiologic studies, some experts estimate that the current incidence of new cases of duodenal ulcer in the United States is about 200,000 per year and that the incidence of new cases of gastric ulcer is about one-fourth that (140).

Bonnevie (17, 18, 19) reported several comprehensive surveys of duodenal and gastric ulcer disease occurring between 1963 and 1968 in Copenhagen County, Denmark (an area with 500,000 inhabitants). Defining incidence as new ulcer disease and basing the diagnosis on review of hospital records, he estimated the annual incidence of duodenal ulcer per 1,000 persons age 15 and over to be about 1.8 for men, 0.8 for women, and 1.3 overall (18). The annual incidence of gastric ulcer alone per 1,000 inhabitants age 15 and over he estimated to be approximately 0.3 for both men and women (19). He also found that duodenal and gastric ulcers occur in the same patient much more often than would be expected by chance if the two types occurred independently (17). Bonnevie (18,19)

cites earlier population surveys conducted in England, Scotland, Norway, and Denmark that found incidence of duodenal ulcer ranging from 0.38 to 2.70 per 1,000 inhabitants age 15 and over and incidence of gastric ulcer ranging from 0.1 to 1.14 per 1,000 inhabitants age 15 and over.

A mail survey of Massachusetts physicians conducted in 1967 and 1968 found the incidence rates of reported duodenal ulcer of 1,000 persons age 25 and over to be approximately 2.9 per year for men and 1.5 per year for women (105). In the same study, physicians reported the incidence of gastric ulcer per 1,000 persons age 25 and over to be approximately 0.35 per year.

Different epidemiologic studies have found varying patterns of age-specific incidence of duodenal and gastric ulcer. In general, the incidence of duodenal ulcer appears to rise gradually with age or to remain essentially constant above age 35, and the incidence of gastric ulcer appears to rise more dramatically above age 40. Bonnevie (18) found the age-specific incidence rate of duodenal ulcer to increase gradually in both sexes to a maximum of 3 per 1,000 inhabitants between age 75 to 79. Gastric ulcer showed a more dramatic rise in incidence above age 40, peaking at a level of about 1 per 1,000 for men age 60 to 64 and for women above age 70 (19). Among Massachusetts physicians surveyed in the late 1960's, the incidence of duodenal ulcer in both sexes appeared to increase up to age 25 to 34, and then to remain fairly constant; gastric ulcer in male physicians continued rising to a peak at age 65 to 74 (105). Fry's review of his patient experience showed duodenal ulcers reaching their peak incidence in both sexes in the decade 1930-39 and gastric ulcers reaching their peak some 20 years later in the decade 1950-59 (57).

The aforementioned incidence figures are substantially lower than the rates found in recent household interview surveys conducted by NCHS (35,36). After we review evidence concerning the prevalence and changes in the occurrence of ulcer disease during the past 20 years, we will discuss NCHS's Health Interview Survey (which is based on household interviews) in more detail.

According to traditional medical lore, 1 U.S. male in 10 will develop a duodenal ulcer by age 55. As pointed out by Mendeloff (104), this easily remembered figure is based on projections made by Ivy in 1946 (84). A number of autopsy studies in Britain and elsewhere (cited by 104) confirmed this figure. It may be argued that insofar as the stress of illness can provoke ulceration, autopsy results may be misleading for the population at large. However, the previously cited survey of Massachusetts physicians (105) also found that approximately 10 percent of male physicians age 65 through 74 at some time had duodenal ulcer. The current level is a matter of conjecture, because the lifelong prevalence rate of ulcers ultimately depends on age-specific incidence rates, and these rates appear to be declining,

Ulcer disease appears to have been occurring less frequently or less severely, or both, over the past 20 years. This conclusion derives from several lines of clinical and epidemiologic evidence. These include overall declines in rates of mortality and hospitalization due to ulcer disease, and, especially, several age-cohort analyses of the incidence and mortality of ulcer disease.

Susser (141,142) deduced from age-specific mortality rates between 1900 and 1960 that there was a decrease in risk of ulcer disease in each successive age cohort, producing a rise in the mean age of patients. This decline was corroborated by a cohort analysis conducted by Monson and MacMahon in their survey of Massachusetts physicians (105). Monson and MacMahon found the age-specific risk of developing ulcer disease among physicians born between 1922 and 1932 to be much lower than the rate for those born in the preceding 20 years. A study of British physicians found a 40-percent decrease in the incidence of duodenal ulcer disease between 1947 and 1965 (103).

U.S. mortality from ulcer disease has declined steadily since the early 1960's (see table 2 and fig. 2). The age-adjusted mortality rate dropped by two-thirds in 1977 from its 1962 peak level

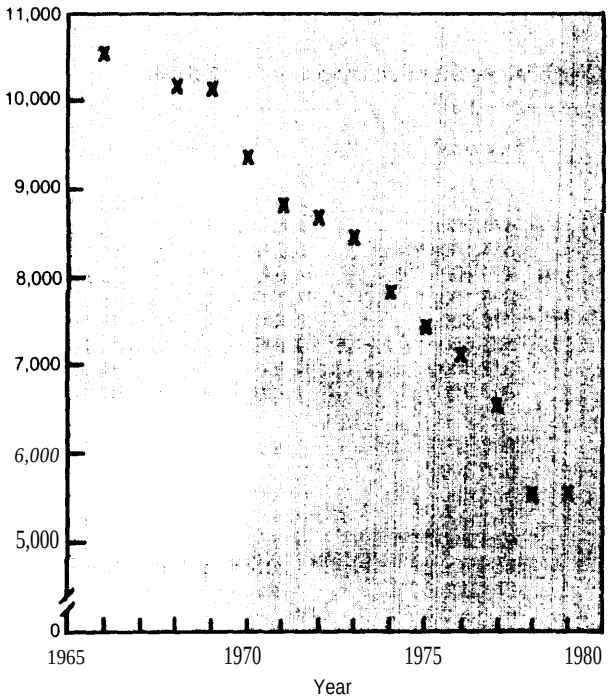
Table 2.–Number of Deaths in the United States With Ulcer Disease as the Primary Cause, 1960-79

Year	Gastric	Duodenal	Peptic, site unspecified	Gastrojejunal	Total
1960	5,707	5,653	—	322	11,682
1963	6,330	5,831	—	244	12,405
1966	5,599	4,722	—	197	10,518
1968	3,829	4,413	1,218	721	10,181
1969	3,719	4,381	1,212	798	10,110
1970	3,502	3,916	1,189	739	9,346
1971	3,385	3,680	1,055	700	8,820
1972	3,274	3,510	1,132	756	8,672
1973	3,289	3,385	1,014	765	8,453
1974	3,050	3,048	971	751	7,820
1975	2,900	2,920	923	710	7,453
1976	2,834	2,686	908	698	7,126
1977	2,669	2,452	779	662	6,562
1978	—	—	—	—	5,550[a]
1979	—	—	—	—	5,560[b]

[a]Preliminary figures, extrapolated from a 10-percent sample
[b]Preliminary figures extrapolated from a IO percent sample over the first 6 months of 1979

SOURCE National Center for Health Statistics, Division of Vital Statistics, Hyattsville, Md

Figure 2.— Deaths in the United States With Ulcer Disease as the Primary Cause, 1966-79



Note: 1978 and 1979 figures are preliminary.

SOURCE Based on data from the National Center for Health Stat{ stics, Division of Vital Statistics Hyatt sville Md

(see table 3), Hospitalizations for ulcer disease have also declined steadily in both the United States (see table 4 and fig. 3) and Great Britain (21). The drop in U.S. hospitalizations appears mainly due to a fall in admissions for duodenal ulcer, whereas the drop in Great Britain is due more to declining admissions for gastric ulcer. Mendeloff (104) reported a sO- percent decline in the number of diagnoses of duodenal ulcer between 1960 and 1972 among an apparently constant population in the U.S. armed forces. Data from a large U.S. manufacturing company showed a 56-percent drop in episodes of disability due to duodenal ulcer and a 68-percent drop in episodes of disability due to gastric ulcer between 1960 and 1970 among male employees (3).

Some of these trends might be explained by the advent of a dramatic and continuing improvement in the prevention and care for ulcer disease during the past 20 years, but no likely candidate representing this can be found (21). The data are consistent with a shift in the spectrum of ulcer disease toward less severe forms, a possibility posited by Mendeloff (104). Such a shift may accompany what appears to be the simplest explanation: Ulcers are occurring less frequently than they did previously. The rea-

Table 3.—Mortality Rates in the United States for Deaths Due to Ulcer Disease 1953-78

Year	Age-ad lusted rate per 100,000 populatation[b]	Crude rate
1953	5.1	
1958	5.3	—
1960	5.2	—
1961	5.2	—
1962	5.4	—
1963	5.2	—
1964	4.6	—
1965	4.3	—
1966	4.2	—
1967	3.9	—
1968	3.7	—
1969	3.6	—
1970	3.2	—
1971	3.0	—
1972	2.9	—
1973	2.7	—
1974	2.4	—
1975	2.2	3.2
1976	2.1	2.7
1977	1.8	2.7
1978	—	2.6

[a]Rates shown include gastric, duodenal, and peptic ulcer (site unspecified)
[b]Adjusted to 1940 population, the standard population used by the National Center for Health Statistics

SOURCE National Center for Health Statistics, Division of Vital Statistics, Hyattsville, Md

sons for the apparently declining incidence and severity of ulcers are matters for speculation,

The data on ulcer disease from the Health Interview Survey of NCHS warrant separate consideration for three reasons. First, the Health lnterview Survey data are gathered in a unique manner; they are based on self-reported conditions in household interviews. Second, estimates of disease incidence and consequences obtained from Health Interview Survey data are substantially greater than those obtained from other sources, including other NCHS sources and epidemiologic studies such as those described above; also, estimates from the Health Interview Survey show little change between the years 1968 and 1975. Finally, the survey data deserve special attention, because they are used to estimate some of the costs and benefits of treatment for ulcer disease that we review later in this case study.

Household surveys of chronic digestive diseases in the United States were conducted in

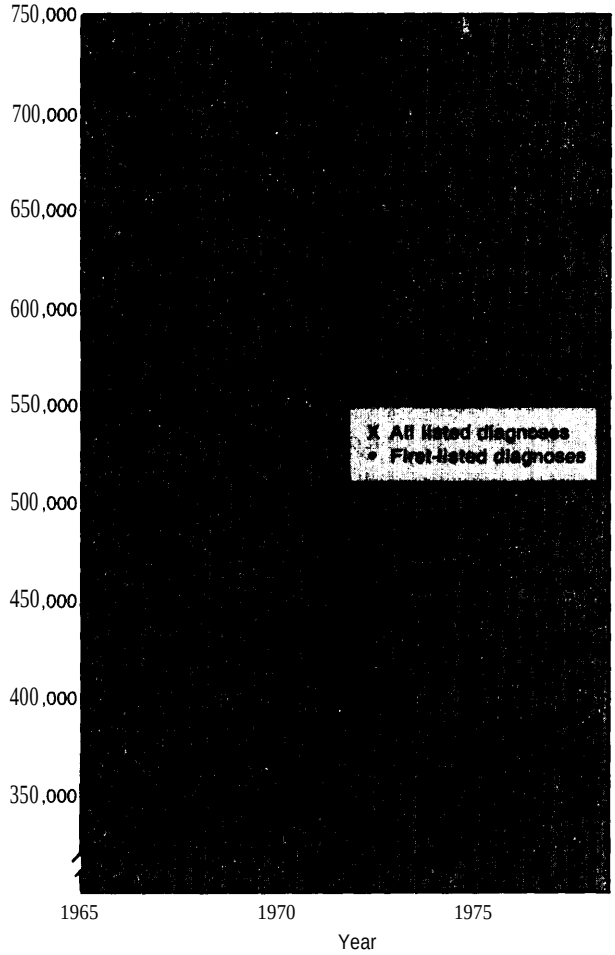
Table 4.—Number of U.S. Hospital Discharges With Ulcer Disease Diagnoses, 1966-78

Year	Gastric	Duodenal	Peptic, site unspecified	Subtotal[a]	Gastrojejunal	Total[b]
Ulcer as first-listed diagnosis						
1966	166,100	345,200	—	511,300	14,700	526,000
1970	89,200	273,500	68,300	431,000	7,400	438,400
1971	94,100	251,400	68,600	414,100	6,600	420,700
1972	99,300	241,400	81,200	421,900	7,400	429,300
1973	102,900	227,100	68,100	398,100	7,200	405,300
1974	101,500	239,800	75,300	416,600	8,700	425,300
1975	101,500	224,100	77,000	402,600	9,100	411,700
1976	103,400	194,000	81,100	378,500	6,900	385,400
1978	105,100	166,300	81,900	353,300	7,200	360,500
Ulcer as a listed diagnosis						
1966	223,800	464,300	—	688,100	17,500	705,600
1970	127,200	384,200	108,900	620,300	9,100	629,400
1971	137,200	358,600	110,800	606,600	9,100	615,700
1972	147,300	362,300	131,800	631,400	9,500	640,900
1973	149,800	339,900	123,700	613,400	9,600	623,000
1974	156,400	360,200	136,100	652,700	11,200	663,900
1975	158,400	336,200	150,300	644,900	12,400	657,300
1976	160,700	302,300	158,300	621,300	10,700	632,000
1977	173,000	285,900	159,300	618,200	8,700	626,900
1978	165,400	279,400	184,600	629,400	10,800	640,200

[a]Includes gastric, duodenal, and peptic ulcer (Site unspecified)
[b]Includes gastric, duodenal, peptic (site unspecified), and gastrojejunal ulcer

SOURCE. National Center for Health Statistics, National Hospital Discharge Survey, Hyattsville. Md

Figure 3.—U.S. Hospital Discharges With Ulcer Disease Diagnoses, All Sites, 1966.78



SOURCE Based on data from the National *Center* for Health Statistics, National Hospital Discharge Survey Hyattsville Md

Table 5.—Ulcer Disease in the United States According to the Health Interview Survey, NCHS[a]

Measure	1968	1975	1978
Number of conditions (in 000's)	3,360	3,955	3,778
Prevalence per 1,000 persons[b]	17.2	18.9	17.7
Incidence per 1,000 persons[c]	3.0	2.9	–
Ever hospitalized for ulcer disease	40.60/0	38.30/0	—
Ever had surgery for ulcer disease	6.90/o	8.1%	–
Currently under M.D. care	61.1 0/0	65.40/o	—
M.D. visits in past 12 months:			
0	32.4%	36.1%	–
1	17.1%	17.8%	—
2 to 4	23.70/o	26.30/0	—
5 or more	18.20/o	15.80/o	—
Unknown	4.60/0	4.00/0	—
Number of bed-disability days[d]:			
0	74.5	74.5	—
1 to 3	—	7.4	–
4 to 7	—	5.2	–
8 to 14	4.9	4.4	—
15 to 30	3.6	3.6	–
31 or more	3.4	2.2	–

[a] Includes gastric, duodenal, peptic (site unspecified), and gastrojejunal ulcer
[b] Condition reported as having been present at some time during the Year Prior to Interview
con set reported as within year prior to interview
[d] A bed-disability day is a day in which a person stays in bed for all or most of the day because of ulcer

SOURCE National Center for Health Statistics, Division of Health Interview Statistics, Hyattsville, Md

by NCHS 1968 and 1975 (35,36). The surveys consisted of questions asked at a sample of households designed to represent the civilian, noninstitutionalized U.S. population. Selected Health Interview Survey results pertaining to ulcer disease are summarized in table 5. The projected incidence of new ulcers based on the Health Interview Survey, approximately 600,000 cases per year, is more than double that based on other epidemiologic evidence described earlier. People interviewed at home reported approximately 7 million physician visits for ulcers in 1975, nearly triple the 2.5 million physician visits for ulcer disease that year reported in the NCHS National Ambulatory Medical Care Survey (34). In contrast to other epidemiologic evidence for the declining incidence of ulcers, the Health Interview Survey results show little change, with even a slightly increased prevalence between 1968 and 1975.

These discrepancies may derive from several sources. Most likely, more people report having ulcers in the Health Interview Survey than actually have them. Some individuals without medical training may think of any stomach trouble as "ulcers" and use the specific medical term more broadly than is clinically correct. In 1975, more than 36 percent of the people who reported having ulcers in the previous year did not see a doctor for that reason. (The proportion with newly reported ulcers who were self-diagnosed is not given.) Many of those who did see a doctor may have been treated on the basis of symptoms without a definite diagnosis. The Health Interview Survey may be an accurate summary of what the noninstitutionalized public reports, but that is not the same as an ac-

curate epidemiologic assessment of a disease problem.

Cost of Illness

Studies of the cost of peptic ulcer disease are among the earliest efforts by economists to assess the costs of individual diseases (14). Beginning with the very first studies, a basic distinction was drawn between direct costs (health system expenditures to prevent, diagnose, and treat the disease) and indirect costs (economic losses due to morbidity and mortality). Most economic studies measure the indirect costs of illness in terms of loss of productivity due to disability from disease and loss of future productivity due to premature death.

The same basic categories of direct and indirect costs continue to be used in contemporary economic analyses of the cost of illness (31,114). Most researchers take an aggregate approach to measuring direct costs of disease, using data from third-party payers, NCHS, and other hospital and physician surveys, and estimating total expenditures for a given disease population in a given time period, usually 1 year; we will return to these methods shortly. First, however, we will mention patient-specific alternatives to measuring direct costs of illness.

One alternative is to trace over time expenditures for a cohort of patients with a particular disease. As far as we know, no such studies of ulcer disease have been published, but at least one study now under way at the University of Wisconsin may produce useful information of this sort (58). We comment on this study by Weisbrod and Geweke in our discussion of cimetidine. Such cohort studies have the advantage of being patient-specific and may show relationships between interventions and expenditures at one point in time and subsequent clinical courses and health expenditures. Cohort cost studies thus could complement other research, possibly as a part of longitudinal studies of the clinical course of disease.

A second patient-specific approach is to study the cost of treating episodes of illness. Duodenal ulcer disease was one of eight medical conditions studied in this way by Scitovsky and McCall (128), These investigators defined an episode of duodenal ulcer illness as a 6-month period beginning with the date of diagnosis of duodenal ulcer. They assessed the cost of treating episodes of duodenal ulcer disease for nonhospitalized patients treated at the Palo Alto Medical Clinic in 1964 (35 patients) and in 1971 (27 patients). In constant dollar terms, the overall cost of treating ambulatory patients with duodenal ulcer declined slightly (but not significantly) between 1964 and 1971. The average number of physician visits per patient during the defined 6-month episode of illness fell from 4.7 in 1964 to 3.8 in 1971. The average number of X-rays also declined slightly. These decreases were nearly offset by increased expenditures for drugs.

Patient-specific studies are very useful for many purposes, but they are not intended to provide a cross-sectional view of all costs for all patients with ulcer disease in a given time period. Providing such a view is the aim of studies that take an aggregate approach to estimating direct costs of disease.

In two recent studies of the cost of ulcer disease discussed below, the indirect costs of ulcer disease were measured by using the "human capital" approach of estimating losses in productivity attributable to the disease. A number of philosophical objections have been raised to the "human capital/lost productivity" approach to valuing lives, e.g., productivity measures omit consideration of pain and suffering. Alternative methods for valuing life, such as a "willingness-to-pay" approach, have been used (1), but not as often as the human capital approach. Over the past 20 years, the sophistication of lost productivity estimates has increased considerably, and now may include the discounting of future earnings, the adjustment of future earnings for productivity gains, adjustments for labor force participating rates, and calculation of productivity loss for people performing unpaid housework (31), In addition to the sophistication of analysis, a second major difference between recent studies of the cost of ulcer disease and the earliest studies 20 years ago is the greater amount of information now available about the prevalence, distribution,

and health consequences of the disease. As discussed in the previous section of this case study, however, uncertainty about the evolving epidemiology of ulcer disease is a major source of discrepancies in contemporary estimates of the cost of the disease.

One of the two recent analyses of the cost of ulcer disease that we will now discuss was undertaken as part of the NCDD assessment of the socioeconomic impact of digestive diseases (4). The other analysis was prepared at SRI under contract with Smith Kline & French Laboratories by Von Haunalter and Chandler (146). Both the NCDD and SRI studies estimated the cost of ulcer disease in 1975, and we focus primarily on those figures. In addition, the SRI study projected estimates for 1977; these served as the basis for a major cost-effectiveness study of cimetidine (the study by Robinson Associates (121)) that is reviewed in another part of this case study.

The costs of peptic ulcer disease in 1975, as estimated by NCDD and SRI, are summarized in table 6. The total cost (direct and indirect) estimated by NCDD is approximately $1.3 billion; the estimate by SRI is approximately $2.6 billion.[6] Table 6 also shows a "midpoint estimate" of approximately $2 billion. We believe $2 billion to be a defensible overall cost estimate, for reasons we shall explain. Peptic ulcers accounted for less than 1 percent of total costs of all illness in 1975 (114), and, according to NCDD figures, health system expenditures for ulcer were approximately 9 percent of health expenditures for all digestive diseases in 1975. Of the total $2 billion costs for ulcer disease, just under half are attributed to health system costs (direct costs); the rest are attributed to lost productivity due to premature mortality and to morbidity (indirect costs).

A comparison of the NCDD and SRI estimates by cost category reveals that the discrepancy between them is largely due to differences in the indirect costs attributed to morbidity (see table 6). In addition, SRI's estimates of direct costs for hospital and physician services are notably higher than NCDD's (see table 6). Closer examination of the sources of these discrepanices in direct cost estimates reveals variation in the two studies' analytic methods, as well as shortcomings in data needed for such cost estimates.

Table 6.—Costs of Ulcer Disease in 1975 as Estimated by NCDD and SRI (millions of dollars)

	NCDD estimates	SRI estimates	Approximate midpoint estimates
Direct costs			
Hospitalization	$501	$ 803	$652
Physician visits	123	240	182
Drugs		100	
Nursing home care	102[a]	11	108a
Other professional	1	3	}
Subtotal	$726	$1,157	$942
Indirect costs[b]			
Mortality	$369	$ 357	$ 369c
Morbidity	179d	1,116	648
Subtotal	548	1,473	1,017
Total	$1,274	$2,630	$1,959

[a]This sum represents the total for drugs, nursing homes, and other professional costs Figures were not broken down further
[b]Future earnings discounted at 25 Percent
[c]The higher NCDD figure is adopted for reasons explained in the text
[d]This figure is imputed from Information supplied in the NCDD report

SOURCES **NCDD estimates:** T P Almy, et al , "Report of the Workgroup on the Socioeconomic Impact of Digestive Diseases of the Subcommittee on Epidemiology and Impact. " in *Report to the Congress of the United States of the National Commission on Digestive Diseases,* 1979 (4)
SRI estimates: G Von Haunalter and V V Chandler, Cost *of Ulcer Disease in the United States,* 1977 (146)

Medical care costs attributable to a particular disease may be estimated in two ways: 1) by a "top-down" approach that begins with total expenses for all disease and imputes to a particular disease the proportion of costs equal to the proportion of total units of service used by patients who have the disease; or 2) by a "bottom-up" approach that prices and sums the units of service consumed by patients who have a particular disease. Each approach has its strong points, and ideally, the two would corroborate each other. In general, the top-down approach is simpler; by definition, the sum of all top-down estimates for each disease equals the total expenditures for all disease. Theoretically, the same would be true for bottom-up calculations, but such calculations are typically undertaken

'Smith Kline & French markets cimetidine.
*Peptic ulcer disease was only one 01 n umerous digestive diseases for which NCDD developed cost estimates. The authors of the NCDD report (4) state clea r] v that they consi der thei r esti ma tes to be conserva t ive.

for a single disease only, and potential inconsistencies between known total expenditures for all disease and the sum of disease-by-disease expenditures bottom-up calculations remain untested in typical bottom-up calculations.

NCDD and SRI both used a bottom-up approach to estimate hospital costs due to ulcer disease, but differed in the detailed assumptions they employed. NCDD began with the number of hospital days for each ulcer diagnosis obtained by the Hospital Discharge Survey of NCHS, and multiplied that number by the average charge per hospital day, The average was obtained from Blue Cross/Blue Shield figures for Federal workers and from medicare data for patients over 65 years of age. SRI also began with NCHS figures on numbers of discharges, but it used a more complicated calculation that involved an estimated proportion of surgical and nonsurgical cases from the Commission on Professional and Hospital Activities (CPHA), an allocation to hospitals of different sizes based in part on American Hospital Association data, and estimated daily costs based on information from disparate sources combined in an unspecified manner. The end result of SRI'S calculation was an estimate of hospital costs ($803 million) that is approximately 60 percent larger than NCDD's estimate ($501 million). Further exploration of the discrepancy between the two figures would require more details about the calculation:; than was provided in either report. Interestingly, and usefully, SRI also applied a top-down cross-check using estimated hospital expenditures for 1975 and the proportion of ulcer hospital days to total hospital days, and came up with an estimated cost of $738 million, reasonably close to our $652 mill ion midpoint estimate for this cost component.

To estimate the cost of physician services, NCDD used a top-down approach, multiplying the cost of all physician services for fiscal year 1975 by the proportion of total visits attributable to ulcer. SRI used a bottom-up approach, multiplying units of service (computed separately for initial and followup visits) by unit costs, estimated on the basis of multiple sources. SRI's estimate for physician visits for ulcer disease ($240 million) is approximately double that obtained by NCDD ($123 million) and, if correct, would imply that a physician visit for ulcer disease is twice as expensive as a typical physician visit. Although this seems unlikely, it is impossible to judge the difference in the cost of physician visits without a more comprehensive analysis. We settled on a $182 million midpoint estimate of the cost of physicians' services as a reasonable compromise.

Estimates for remaining direct costs are comparable in the NCDD and SRI studies. We have imputed the NCDD figure of $102 million from a more global estimate for selected digestive diseases that included ulcer disease and was adopted by NCDD (113). Summing the above components for each report, we find that the estimated direct costs presented in the two reports differ by more than $400 million: NCDD, $726 million; SRI, $1,157 million. Our final midpoint estimate is $942 million.

Indirect cost estimates for ulcer mortality loss are straightforward. NCDD and SRI used identical methods to estimate lost future earnings from death due to ulcer. The small difference in the two studies' figures for mortality loss (NCDD, $369 million; SRI, $357 million) is presumably due to the fact that SRI used smaller, preliminary mortality figures (6,840 deaths) rather than the final NCHS figures (7,245 deaths) that NCDD used. We have adopted NCDD's $369 million estimate.

The very large difference in the NCDD and SRI studies' estimated ulcer morbidity costs (NCDD, $179 million; SRI, $1,116 million) stems from several sources. Most important, SRI attributed to ulcer disease morbidity as estimated in the Health Interview Survey conducted by NCHS in 1975. As discussed earlier, the Health Interview Survey estimates are based on the responses of people interviewed at home who say they have had an ulcer at some time during the past year. These estimates are inconsistent with other evidence for the declining prevalence of ulcer disease, and they almost surely overestimate morbidity due to the disease. Furthermore, SRI assumed that the economic effects of work loss are distributed by age

in the same way the disease is distributed. Since older patients tend to lose more days of work and earn less per day, the assumption of uniform effects inflates the actual productivity loss. This flaw is acknowledged in SRI's report, but no correction or sensitivity analysis is offered. Ulcer patients who continue to work might have lower productivity, and this effect, also omitted from SRI's calculations, would increase the actual loss of productivity due to ulcer disease and tend to offset the effect of the assumption about age distribution.

NCDD considered and expressly rejected using data from the Health Interview Survey, because "there were also serious questions raised by experts in digestive diseases about the validity of the self-reported diagnosis-specific morbidity information" (4). Instead, NCDD accepted a more global estimate of morbidity loss due to 15 different digestive diseases, including liver disease, gallbladder disease, and hernia (113). The NCDD figure for morbidity loss due to ulcer disease shown in table 6 is approximately 6 percent of that total, a percentage equal to the ratio of the mortality cost for ulcer compared to that for all 15 diseases.[7] The NCDD report also refers to data collected for an earlier review of the medical and socioeconomic importance of digestive disease, published by Almy and his coworkers (3). That earlier publication included data on absenteeism due to digestive disease at a large northeastern U.S. manufacturing company during the 13-year period from 1959 to 1972. In persons who missed 3 or more days of work during that period due to 1 of the 15 digestive diseases covered by the NCDD morbidity estimate, more than 20 percent of days lost were attributed to ulcer. We do not propose translating such figures, obtained over a 13-year period from one large firm, to a national estimate of days of work lost in a later year. However, if ulcer disease does account for 20 percent of the total morbidity costs assigned to the 15 digestive diseases in the NCDD report, the NCDD morbidity figure would be very close to our midpoint estimate of $648 million.

The magnitude of indirect cost estimates is very sensitive to the rate at which future costs are discounted. Both NCDD and SRI discounted future earnings at 2.5 percent, although NCDD also presents some alternative calculations at a 10-percent discount rate. Economists agree more on the appropriateness of discounting than on the appropriate rate to employ, but 2.5 percent is at the very low, end of the spectrum. The smaller the discount rate, the higher the present value of future earnings and the higher the apparent indirect cost of illness. For example, the "present" value of lifetime earnings for a 32-year-old man in 1975 was $148,195 at a 2.5-percent discount rate and $176,882 at a IO-percent discount rate (4). This is not a differential point between the NCDD and SRI analyses, since they both used the same low discount rate, but the reader should be aware of the large difference a change in the discount rate can make and be wary of unadjusted comparisons between these and other cost-of-illness studies that may use different discount rates. In addition, "present" values are usually expressed in terms of dollars in the base year. Estimates discounted to different base years will differ in part because of inflation and are directly comparable in resource cost terms only if adjusted into constant dollars.

In the SRI analysis, Von Haunalter and Chandler extrapolated their estimated costs to 1977 (expressed in 1977 dollars) by assuming variably inflated rates for different unit costs of medical care and a 2-percent annual increase in the number of persons with ulcer disease (see table 7). The presumed 2-percent annual increase, based on responses to the Health Interview Survey in 1968 and 1975, is contrary to all other indicators of the changing epidemiology of ulcer disease; it is also contradicted by subsequent preliminary data obtained in the 1978 Health Interview Survey (see table 5, p. 17). The presumed growing population with ulcers is also treated by Von Haunalter and Chandler as having the identical age distribution and spectrum of disease severity as assumed for the population in 1975. Their assumptions about

[7] This imputation brings the total costs NCDD would assign to peptic ulcer to $1.3 billion, which is consistent with their stated overall economic loss due to peptic ulcer of $1 billion to $1.6 billion (4).

Table 7.—Costs of Ulcer Disease in 1975 and 1977 as Estimated by SRI (millions of dollars)[a]

	1975		1977	
Direct **costs**				
Hospital care	$ 803	—	$1,072	—
Physicians	240	—	283	–
Drugs	"loo	—	113	—
Nursing home care	11	—	15	—
Other professional	3	—	3	–
Subtotal	$1,157	440/o	$1,486	460/0
Indirect costs[b]				
Mortality	357	—	408	—
Morbidity	1,116	—	1,330	—
Subtotal	1,473	56%	1,738	54%
Total	$2,630	**1000/0**	$3,224	1000/0

[a]Figures for 1975 and 1977 are expressed in terms of dollars in the respective base years, not in constant dollars

SOURCE Adapted from G VonHaunalter and V V Chandler, *Cost of Ulcer Disease in the United Stales*, 1977(1 46)

these characteristics of the presumed growing ulcer population are questionable for reasons discussed in the section of this case study above on epidemiologic patterns of peptic ulcer disease. Von Haunalter and Chandler's projection of the population with ulcers to 1977 thus compounds the problem of overestimation of the costs of ulcer disease, particularly indirect costs. Some specific estimates that feed into direct costs are also Inappropriately projected upward. For example, the percentage of hospitalized patients undergoing surgery for ulcer disease is presumed in the analysis to increase between 1975 and 1977. According to data from both NCHS and CPHA (42), however, the percentage actually decreased (see table 8).

Summary

We may summarize the salient clinical and epidemiologic features of peptic ulcer disease as follows,

Ulcers probably have multiple causes, but gastric acid and pepsin appear to be necessary ingredients. Epigastric pain 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 treatment of ulcer disease is directed at reducing the presence or effects of gastric acid.

Ulcer disease is a chronic condition with spontaneous remissions and recurrences. Rates of complication 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 gastic ulcers. Some studies have found that the incidence of duodenal ulcer rises gradually with age, others have found that it remains fairly constant after age 35. After age 40,

Table 8.—NCHS and CPHA Data on Number of Selected Surgical Procedures (partial Gastrectomy, Vagotomy) **in the United States, 1966-78**

	Partial gastrectomy		Vagotomy		Total	
Year	NCHS	CPHA	NCHS	CPHA	NCHS	C P H A
1966	74,500	—	61,200	—	135,500	—
1970	55,800	59,000	62,800	30,000	118,600	89,000
1971	—	57,000	—	28,000	—	85,000
1972	63,300	52,000	59,300	24,000	122,600	76,000
1973	—	52,000	—	27,000	—	79,000
1975	53,300	45,000	52,800	23,000	106,100	68,000
1976	54,200	45,000	48,300	16,000	102,500	71,000
1977	51,100	37,000	45,500	19,000	96,600	56,000
1978	39,700	29,200	29,200	17,000	68,900	46,000

SOURCES ***NCHS data:*** National Center for Health Statistics, National Hospital Discharge Survey, Hyattsville, Md
CPHA data: Commission 01 Professional and Hospital Activities data compiled by J D Elashoff and M I Grossman, 1960 (42)