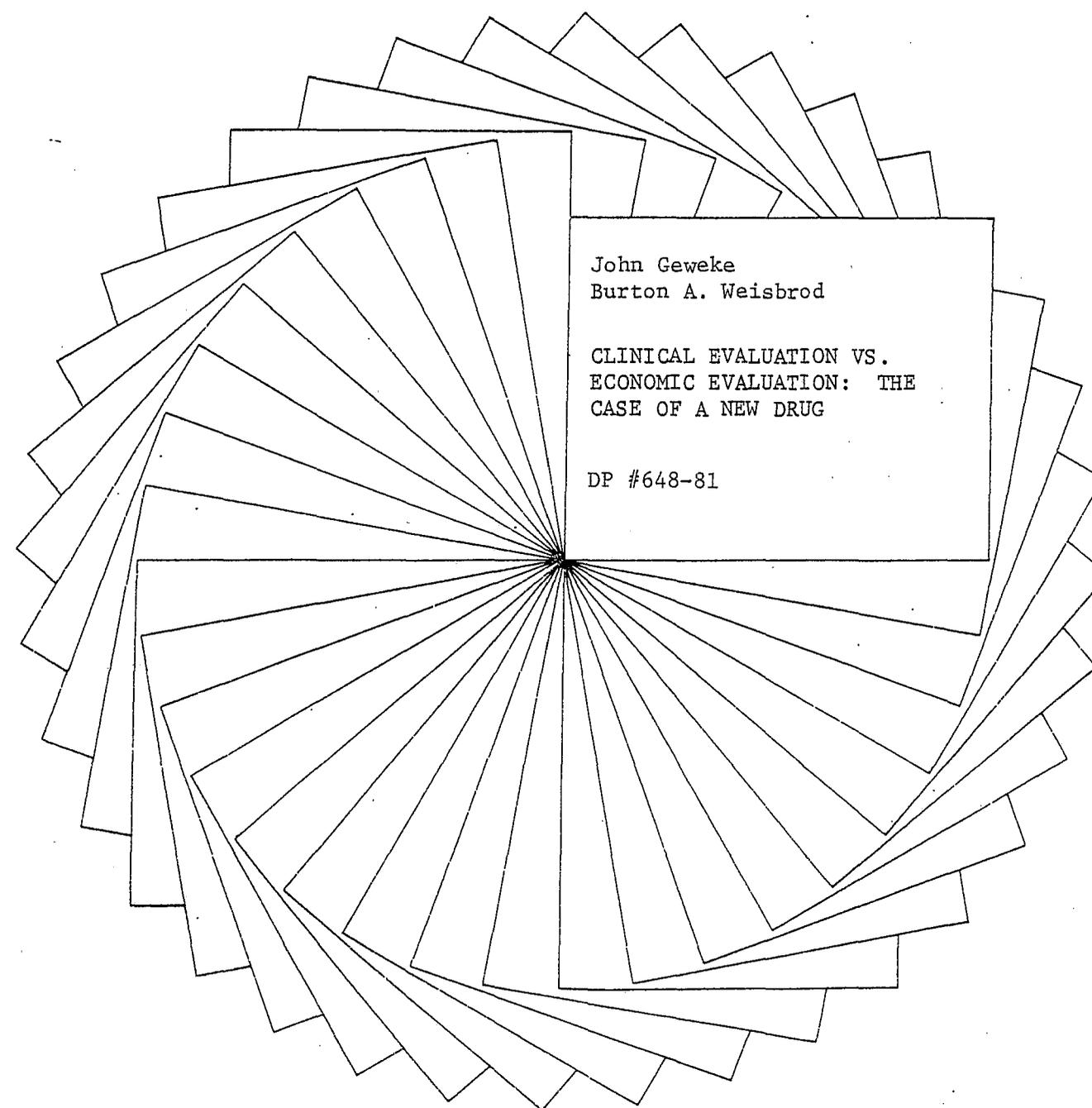




Institute for Research on Poverty

Discussion Papers



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CLINICAL EVALUATION VS.
ECONOMIC EVALUATION: THE
CASE OF A NEW DRUG

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Clinical Evaluation vs. Economic Evaluation

The Case of a New Drug

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ABSTRACT

To make an economic evaluation of a new drug or other medical innovation one must assess the changes in both costs and benefits. Safety and efficacy matter, but so do resource costs and social benefits. This paper evaluates the effects on expenditures and social costs of the recent introduction of cimetidine, a drug used in the prevention and treatment of duodenal ulcers. This evaluation is of interest in its own right and also as a "template" for studying similar effects of other innovations.

State Medicaid records are utilized to test the effects on hospitalization and aggregate medical care expenditures of this new medical innovation. After controlling to the extent possible for potential selection bias, we find that: (1) usage of cimetidine is associated with a lower level of medical care expenditures and fewer days of hospitalization per patient for those duodenal ulcer patients whose health was "excellent" during the presample period (zero health care expenditures and zero days of hospitalization); an annual cost saving of some \$320 (20 percent) per patient is indicated. Further analysis disclosed, however, that this saving melted away and to some extent was reversed for the patients whose prior year's health status, as proxied by a high level of medical care expenditures and hospitalization, was lowest.

Clinical Evaluation vs. Economic Evaluation: The Case of a New Drug

1. INTRODUCTION

Approval of a new drug by the FDA is a form of consumer protection. The consumer of a prescription drug is told, in effect, that a professional judgment has been made attesting to the safety and, since 1962, the efficacy of that drug. As with consumer protection efforts generally, nothing is said about the economic value of one drug relative to another. Government is silent on whether differentials in drug prices and other economic dimensions are or are not related to differences in quality; the consumer knows only that each drug is not worthless medically.

For most consumer products the consumer is tolerably capable of judging the worth of alternatives, once certain technical characteristics are made known--e.g., the consumer can judge his or her preferences among the many varieties of children's pajamas, once their flammability is known. For prescription drugs, the consumer-patient would often not be well informed were it not for the advice of his or her agents--the physician--and, perhaps, government regulators.

The perspective changes somewhat when the consumers who make the purchase are not the same as the persons who pay for the purchase. With third-party payments so prominent in the medical care market, private insurers and public agencies are increasingly paying for the medical care "purchases" of others. Not surprisingly, they are asking, with growing

frequency and intensity, are new drugs (or other medical innovations) economically efficient as well as "safe" and "effective"? Does the new drug or other technology provide more per dollar spent than do the alternatives?

The current preoccupation of governmental officials with costs alone is understandable, given a national health care budget that has shot well past \$200 billion from \$75 billion as recently as 1970. When expenditures on a commodity rise at a faster rate than the entire gross national product (GNP) decade after decade, and when those expenditures are putting growing strains on governmental budgets, one can expect the cries for "expenditure control" to become even louder. Health care expenditures in the United States constituted 4.5 percent of GNP only 30 years ago, in 1950; they rose to 5.3 percent in 1960, to 7.6 percent in 1970, and to well over 9 percent today (Statistical Abstract, 1979, p. 325). At the same time the share being financed by government has also risen. Nonetheless, a new drug that is more costly than its substitutes may or may not be worth the added cost. To make an economic evaluation of a new drug or other medical innovation one must assess the changes in both costs and in benefits. Safety and efficacy matter, but so do economic issues--resource costs and social benefits.

2. METHODOLOGY

We turn now to an evaluation of the effects on expenditures and social costs of the recent introduction of cimetidine, a drug used in the prevention

and treatment of duodenal ulcers. This evaluation is of interest in its own right and also as a "template" for studying similar effects of other innovations. It shows the potential for such evaluations as well as some of the problems they may confront and the inevitable interpretational complexities.

Although a full evaluation would capture all real benefits, whether or not money flows were involved, our evaluation will focus on a more limited concept, expenditures. It should be noted, however, that changes in health care expenditures do reflect benefits of improved health, insofar as a person made healthier through medical innovation incurs lower medical care expenditures. Nonetheless, not all benefits from a medical innovation are captured by reduced expenditures--for example, the utility from feeling better or living longer.

Cimetidine was granted a conditional use permit by the FDA in September 1977. It is fundamentally different from antacids, the most commonly used medical treatment for duodenal ulcer (DU), and from an older group of drugs, anticholinergics. Since the FDA approval process does not utilize controlled experiments to evaluate economic and social effects as well as clinical effects, inferences about socioeconomic effects must presently be drawn in nonexperimental settings (see, however, Ricardo-Campbell et al., 1980).

Many of the difficulties in assessing socioeconomic effects of new medical technologies in nonexperimental settings result from potential selection bias. It is normally the case in the introduction of any new technology, including cimetidine, that systematic differences between the

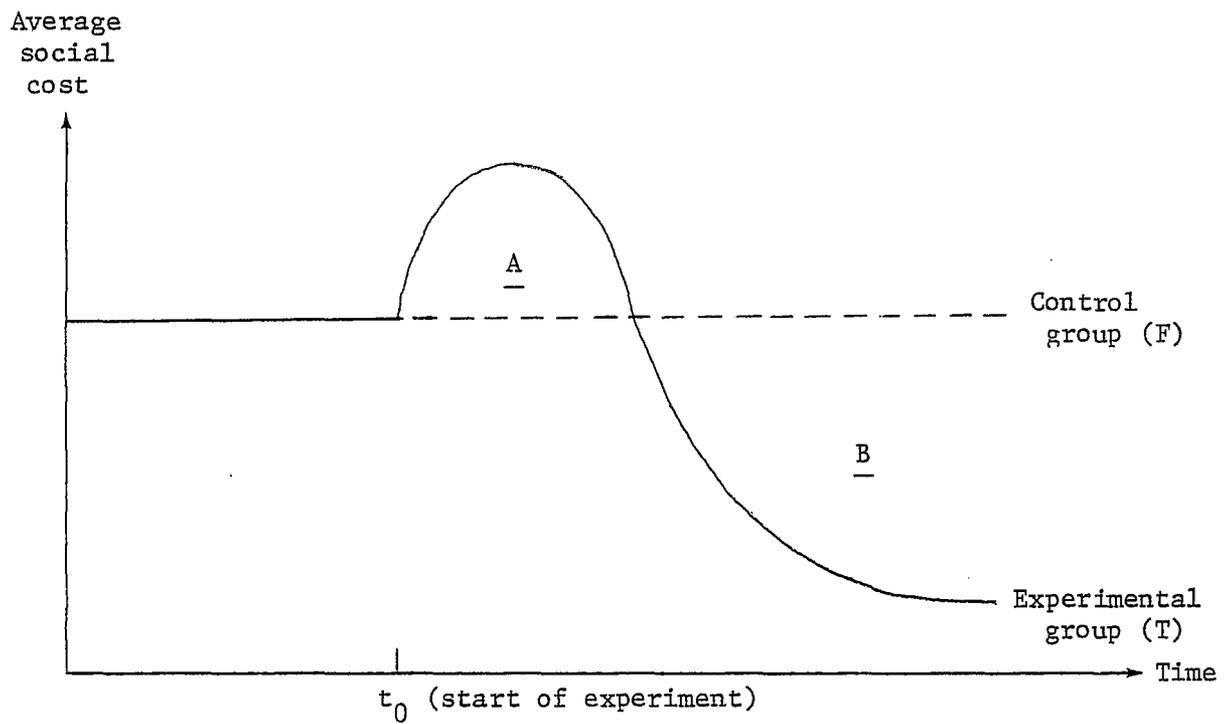
"experimental" group--users of the new approach--and the "control" group--nonusers--exist. In the actual introduction of any new drug, assignment to treatment and nontreatment groups is made by the actors themselves--primarily providers but, to varying degrees, the patients as well. We have no practical way of knowing whether these providers and patients who use the new technology differ in important ways from those who do not use it. Unlike the FDA clinical trials methodology, the "fairness" of the assignment process is not assured by random assignment of patients and providers. Selection bias--which physicians recommend cimetidine therapy for which patients--can produce serious interpretational difficulties. It could be that as soon as the new drug is approved for conditional use by the FDA, all providers have access to the drug and are fully aware of how it should be used in conjunction with other treatments, but this is rather implausible. It might also be that in the new technology all patients receive the drug just introduced; but this is also unlikely. If neither of these polar cases prevails, systematic differences between the experimental and control groups are likely to exist. In particular, patients whose social costs are higher may well be proportionately more important in one group rather than the other.

Our data, from Medicaid records, are nonexperimental and so they do not reflect the controlled, randomized assignments that would be preferred. We know only that some providers prescribed cimetidine to some patients. We identify all DU patients who received cimetidine

between September 1, 1977, and June 30, 1979, as the T group, all other patients who received treatment (but not with cimetidine) for DU during that period as the F group, and we control for selectivity bias to the extent we can do so with the available data.¹

A patient is assumed to have an active ulcer problem if any treatment is provided for duodenal ulcer (DU) or if he or she is treated with an antiulcer drug² and has a primary or secondary diagnosis of DU within the past year. The time of incidence of any indicator of socioeconomic cost for each patient is measured with reference to the first indication of an active ulcer problem within the sample period for those in group F, and with reference to the prescription of cimetidine for those in group T. The "point of reference" is the analogue of the start of the experiment in a controlled environment and corresponds to the point t_0 in Figure 1. (The upward bulge in the cost for the T group reflects one possible scenario, in which the new technology leads to increased costs early in the treatment period, but reduces them subsequently.) For group F, the point of reference is chosen to be the first indication of ulcer rather than September 1, because the latter choice could cause to be included in F some patients with no active ulcer problem at the reference point, whereas all patients in T do have an active ulcer problem at the time cimetidine is prescribed; presumably there would then be a downward bias in the measurement of social costs for group F relative to group T, and a resulting upward bias in the estimated cost-reducing effects of cimetidine.

Figure 1
One Possible Relationship of Costs per Patient,
Experimental and Control Groups



Samples F and T are then subdivided to control for all measured factors that might affect real treatment costs. The divisions are made conditional on two groups of variables.

The variables in the first group are demographic: the sex, race, and age of each patient are known, and our subsample could be further divided, conditional on these variables. There is an obvious and large potential for selectivity bias if demographic factors are ignored. (As we shall see, even if all demographic groups were identical with respect to the relevant medical factors, and were proportioned in the same way between F and T, there could still be reason to separate these groups for the purposes of assessing social costs of medical care.)

The variables in the second group are associated with the "severity" of a given disease. We can never measure adequately all those factors that would be controlled implicitly in a randomized experiment. Physicians may (even subconsciously) take into account unmeasured or unmeasurable dimensions of a patient's health in deciding whether or not to prescribe cimetidine. There is no way to account for those nonrandom factors that affect "assignment" to groups F and T but which are uncorrelated with measured variables. The best that one can do is to account adequately for the variables that are measured.

In the case of the present study, there are available four specific variables, which, it is reasonable to assume, are associated with potentially nonrandom assignment factors and which, in turn, are related to social costs: first, the number of Medicaid claims in a prespecified period before the reference point, which we call the "presample period";

second, expenditures on health care in that same period; third, days hospitalized in that period; and fourth, the number of different diagnoses other than DU during that period. Each is important because it may be positively correlated with medical care costs over the sample period, subsequent to t_0 in Figure 1, whether cimetidine was prescribed or not. Failure to account for these variables could thus introduce a potentially large source of selectivity bias: one has only to conjecture polar situations in which providers prescribe cimetidine only to patients at death's door or, alternatively, those in which cimetidine is given only to those who are relatively healthy or are on no other medication and consequently unlikely to suffer complications.

In principle, selectivity bias would be minimized by evaluating treatment costs conditional on each of these factors, but the number of observations may preclude such a detailed treatment. We tested for the existence of selectivity bias for each of seven dimensions (sex, race, age, number of Medicaid claims, expenditures on health care, days of hospitalization, and number of other diagnoses) by testing the hypothesis that the proportion receiving cimetidine is unaffected by variations in that dimension in the presample period. We include as controls in our analysis only those variables that significantly affect the probability of receiving cimetidine.

For each individual, we monitor indicators of social cost in the fashion anticipated in Figure 1. We compare these indicators over various time intervals beyond t_0 for patients who did, and did not, receive cimetidine, controlling for selectivity bias through regression. In each

regression equation, the dependent variable is a measure of social cost during a portion of the period following t_0 , and the independent variables are some of the control dimensions, selected as just described. The regression equations are estimated separately for the groups that did and did not receive cimetidine. The proposition that social costs for the two groups are the same is equivalent to the statistical hypothesis that the two regression equations are the same, and this hypothesis may be tested formally. In addition, using the coefficient estimates for the two equations we can compare expected social costs for the two groups, given any conjectured values of the independent variables, and test the hypothesis that costs were greater for one group than for another.

3. DATA BASE

All the data used in this study are taken from Medicaid claims in the state of Texas for the period September 1976 through December 1979. The data were collected originally for accounting purposes and were made available to us by Pracon, Inc., of Fairfax, Virginia, an independent consulting firm. Pracon, working closely with Texas Medicaid officials, assured patient and provider confidentiality and converted the data from its original form to a format more suitable for studying the health care experience of individual patients.

The basic organizational unit from which our files were constructed is the claim. A claim is a bill submitted to the state of Texas for a medical service or drug. In some cases, claims are amended after their original submission, in which case the claim as amended was used.

Associated with each claim is a patient identification number; an identification number for the provider (for example, a physician or pharmacy); a primary and, in some cases, a secondary diagnosis if the claim is for hospital, physician, or nursing home services; the date of the claim; the date on which the service was rendered; the nature of the service performed by the physician (for example, surgery or consultation); the length of stay for hospital and nursing home claims; the amount filled, in the case of drug claims; and the dollar amount of the claim. The sex, race, and age of each patient are also provided.

From the original file of about 12 million claims, the samples described in the previous section were constructed. These samples were restricted to those individuals who were eligible for the Medicaid program during the entire period September 1976 through August 1979. The sample was further restricted to those who had not reached their 65th birthday by August 1979, since for individuals over 65 most medical care expenditures are paid by Medicare, and Medicaid claim amounts consequently reflect only a fraction of the expenditures involved. Sample T comprises the 308 individuals with a DU diagnosis on some claim during the period September 1976 through August 1978, who also had a claim for cimetidine in the period September 1977 through August 1978. Sample F is composed of the 386 individuals with a DU diagnosis on some claim during the period September 1976 through August 1978, who had either a claim with a DU diagnosis or a claim for prescription of an antiulcer drug (but not cimetidine) during that period. Once the base date for each individual was established, claims were organized by month of service relative to the base date. The

presample period for each individual (the analogue of time before t_0 in Figure 1) consists of the 12 months prior to the base date, and the sample period (the analogue of time after t_0 in Figure 1) consists of the 12 months following the base date.

4. FINDINGS

Tests for selectivity bias indicated that of the seven dimensions considered, only total health care expenditures and days of hospitalization in the presample period were significantly associated with the probability that a patient would receive cimetidine during the sample period. Propensity to receive cimetidine was independent of demographic factors, and was found unrelated to the number of claims or the number of other diagnoses in the presample period. The control variables used were total health care expenditures in the 12 months preceding t_0 (HCE), the square of this variable (HCE^2), days hospitalized in the 12 months preceding t_0 (DH), and a dummy variable (DH^*) which was set to zero when $DH=0$ and was 1 otherwise. The term HCE^2 and the dummy variable were included to allow plausible nonlinearities in the relationship of health care expenditures and days of hospitalization in the presample period to social cost variables in the sample period.

Total health care expenditures and days of hospitalization during the sample period provide our measures of social cost. The former in fact constitutes only those monetary expenditures that were reimbursed by the state of Texas Medicaid program; a more inclusive measure is not available. Days of hospitalization is closely associated with total health

care expenditures, but is also associated with indicators of social cost like morbidity, which we could not measure.

Values of these variables were constructed for each patient in each month. All patients had some health care expenditures in the first month of their sample period, and many had some days of hospitalization. In subsequent months, the fraction of patients having some health care expenditures or days of hospitalization in any month was very small. Hence we considered separately the value of each measure in the first month of the sample period--HCE(+1) and DH(+1)--its value in the following 11 months--HCE(+2/+12) and DH(+2/+12)--and its values over the entire twelve months--HCE(+1/+12) and DH(+1/+12).

The estimated regression equations are shown in Table 1. These estimates are difficult to interpret without further computations, but may, in fact, be used to compare expected health care expenditures and days of hospitalization for patients who did, and did not, receive cimetidine. To answer the question of whether the two groups had different health care expenditure and hospitalization experiences, we tested the hypotheses that the two corresponding equations in each of the six pairs shown in Table 1--e.g., the pair of equations 1 and 7--were the same. The "F" test statistics for these hypotheses are shown in Table 2. We cannot reject the hypothesis that total health care expenditures and days of hospitalization were the same for the two groups in the first month of the sample period, but the equations clearly differ for the entire 12-month postsample period and for months 2 through 12 of that period.

Table 1
Regression Estimates
(Standard Errors in parentheses)

With cimetidine (n = 308):

- (1) HCE(+1) = 401 + .111 HCE - .281 HCE² - 10.5 DH - 94.7 DH*
(62.4) (.057) (.321) (7.59) (132)
- (2) DH(+1) = 2.05 + .000517 HCE - .00228 HCE² - .0546 DH + .108 DH*
(.376)(.000395) (.00193) (.0457) (.794)
- (3) HCE(+2/+12) = 1078 + .677 HCE - 1.63 HCE² + 4.58 DH - 22.3 DH*
(150) (.138) (.770) (18.2) (316)
- (4) DH(+2/+12) = 3.89 + .00140 HCE - .00971 HCE² + .348 DH - 1.68 DH*
(.850)(.000780) (.00437) (.103) (1.80)
- (5) HCE(+1/+12) = 1480 + .788 HCE - 1.91 HCE² - 5.92 DH - 117 DH*
(172) (.158) (.882) (20.9) (363)
- (6) DH(+1/+12) = 5.94 + .00191 HCE - .0120 HCE² + .293 DH + 1.789 DH*
(.948)(.000870) (.00487) (.115) (2.00)

Without cimetidine (n = 386):

- (7) HCE(+1) = 645 - .00942 HCE + .122 HCE² + .327 DH - 208.06 DH*
(85.5) (.0950) (.784) (11.9) (173.84)
- (8) DH(+1) = 3.68 - .000336 HCE + .000212 HCE² + .0506 DH - 1.05 DH*
(.438)(.000487) (.00402) (.0607) (.891)
- (9) HCE(+2/+12) = 1158 + .432 HCE + 3.77 HCE² - 31.7 DH - 1.12 DH*
(135) (.150) (.124) (18.8) (2.75)
- (10) DH(+2/+12) = 5.03 - .00166 HCE + .0190 HCE² + .355 DH + 1.23 DH*
(.710)(.000789) (.0065) (.098) (1.44)
- (11) HCE(+1/+12) = 1803 + .422 HCE + 3.89 HCE² - 31.4 DH - 209 DH*
(164) (.182) (1.50) (22.7) (333)
- (12) DH(+1/+12) = 8.71 - .00199 HCE + .0192 HCE² + .405 DH + .182 DH*
(.861)(.00096) (.00790) (.120) (1.75)

Source: Data from Texas state Medicaid records, 1976-78.

Table 2
Overall Comparison of Regression Equations

H_0 : Regression Equations the Same

<u>Equations</u>	<u>F(5, 684)</u>
HCE(+1)	1.09
DH(+1)	1.79
HCE(+2/+12)	4.99***
DH(+2/+12)	4.19***
HCE(+1/+12)	3.61***
DH(+1/+12)	3.93***

* rejection of H_0 at the 10% level; ** at the 5% level; *** at the 1% level.

Source: Data from Texas state Medicaid records.

Given the estimates presented in Table 1, we may prepare estimates of expected health care expenditures and days hospitalized for an individual with certain presample characteristics, under the assumption that he or she was treated with cimetidine, and under the assumption that he or she was not. Comparisons for three hypothetical sets of characteristics are provided in Table 3. In each case, point estimates of health care expenditures or days hospitalized are provided by replacing the independent variables in the equations of Table 1 by each of three sets of values for HCE and DH shown in Table 3. Standard errors are constructed from the variance matrix of the coefficient estimates of Table 1, and a "t" statistic for the hypothesis that an individual with the specified characteristics would be expected to have the same health care expenditures or days of hospitalization whether treated with cimetidine or not is computed accordingly.

The estimates for individuals with zero health care expenditures or days of hospitalization in the presample period -- the top panel of Table 3, for persons in "excellent health" -- are simply the intercept coefficients in Table 1. These individuals are not typical of our sample, but neither are they rare, comprising 12% of the sample. Similarly, the "poor health" example (bottom panel) is extreme: it characterizes less than 5 percent of the sample, but to public policymakers concerned with program costs, this example may be very important.

The results in Table 3 show a systematic pattern. The better an individual's health in the presample period, as measured by our control variables, the more likely he or she is to have lower health care

Table 3

Specific Comparisons (based on Table 1)

	<u>Without cimetidine</u>	<u>With cimetidine</u>	<u>"t"</u>
Excellent Health (HCE = 0, DH = 0)			
$\hat{HCE}(+1)$	645 (86)	401 (62)	2.31**
$\hat{HCE}(+2/+12)$	1158 (135)	1078 (150)	0.39
$\hat{HCE}(+1/+12)$	1803 (164)	1480 (172)	1.36
$\hat{DH}(+1)$	3.68 (.44)	2.05 (.38)	2.84***
$\hat{DH}(+2/+12)$	5.03 (.71)	3.89 (.85)	1.03
$\hat{DH}(+1/+12)$	8.71 (.86)	5.94 (.95)	2.17**
Median Health (HCE = 400, DH = 1)			
$\hat{HCE}(+1)$	434 (143)	340 (115)	0.51
$\hat{HCE}(+2/+12)$	1304 (226)	1329 (276)	-0.07
$\hat{HCE}(+1/+12)$	1669 (316)	1738 (274)	-0.02
$\hat{DH}(+1)$	2.55 (.73)	2.30 (.69)	0.25
$\hat{DH}(+2/+12)$	5.98 (1.19)	6.46 (1.56)	-0.25
$\hat{DH}(+1/+12)$	8.53 (1.44)	8.76 (1.75)	-0.10
Poor Health (HCE = 2000, DH = 8)			
$\hat{HCE}(+1)$	425 (98)	433 (80)	-0.06
$\hat{HCE}(+2/+12)$	1917 (154)	2381 (192)	-1.89*
$\hat{HCE}(+1/+12)$	2343 (187)	2815 (220)	-1.64
$\hat{DH}(+1)$	2.37 (.50)	2.66 (.48)	-0.41
$\hat{DH}(+2/+12)$	6.54 (.81)	10.76 (1.09)	-3.11***
$\hat{DH}(+1/+12)$	8.92 (.98)	13.41 (1.21)	-3.02***

HCE = Total health care expenditures, presample period, in dollars.

HCE^2 = Square of $HCE \times 10^{-5}$.

DH = Days hospitalized, presample.

DH^* = 0 if $DH = 0$, 1 otherwise.

Arguments of dependent variables denote months of sample to which HCE or DH pertains.

Standard errors are in parentheses.

* Significance at 10% level; ** at 5%; *** at 1% level.

Source: Data from Texas state Medicaid records.

expenditures and fewer days of hospitalization in the sample period if he or she was treated with cimetidine than if not. Within the sample period, reductions are more likely in the first month than in the later months. That is, in the top panel of Table 3, HCE and DH are significantly lower for the cimetidine users during the first month of the sample period, and are lower, but not significantly so, during the remainder of the sample year.

For the "median health" group, expected health care expenditures and days of hospitalization are negligibly different for cimetidine and non-cimetidine users, both for the first sample month and for the remainder of the year. For persons in the "poor health" group (lower panel of Table 3) the difference in both HCE and DH for cimetidine and noncimetidine users during the first sample month was also negligible; however, the lower levels for noncimetidine users grew and became statistically significant during months 2-12 of the sample period.

These results must be interpreted carefully. In the case of individuals with very low health care expenditures in the presample period, it is plausible to assume that the only health care problem of consequence is the duodenal ulcer. Individuals with higher presample health care expenditures almost always show one or more other diagnoses. In many instances, duodenal ulcer is the result of stress caused by treatment of other diseases, and cimetidine is often used to treat such "stress ulcers." Such complications within the sample period could lead to the association of cimetidine use with higher health care expenditures and more days of hospitalization, as shown in Table 3. A more detailed study of

individuals with complicated health care histories is required for a reliable interpretation of the experiences of such individuals with cimetidine.³

5. CONCLUSION

A rich body of data, state Medicaid records, has been utilized to test the effects on hospitalization and aggregate medical care expenditures of a new medical innovation. While our data were for one state, Texas, and the innovation was for a new drug, cimetidine, used in the treatment of duodenal ulcers, both the approach and the data have wide potential use.

Since the data are not derived from an experimental research design, we are cautious in our interpretations, for we cannot be confident that our efforts to deal with potential selectivity bias have been successful. What we have found, however, after controlling to the extent possible for such potential bias, is the following: (1) usage of cimetidine is associated with a lower level of medical care expenditures and fewer days of hospitalization per patient over a 12-month sample period for those duodenal ulcer patients whose health was "excellent" during the presample period (zero health care expenditures and zero days of hospitalization); a cost saving of some \$320 (20 percent) for each patient with duodenal ulcer is indicated. Further analysis disclosed, however, that this saving melted away and to some extent was reversed for the patients whose prior year's health status, as proxied by a high level of medical care expenditures and hospitalization, was lowest.

Any new medical technology is likely to have substitutes; cimetidine has substitutes in the forms of both surgery and conventional antacids. From a narrow viewpoint of minimizing government expenditure, the question is, which alternative or combination involves the lowest level of expenditure?

In general, a change in expenditures on a commodity is of dubious worth as an index of its net benefits. Reduced expenditures on medical care and specifically on duodenal ulcer therapy, however, do reflect both savings in resource costs and increases in social benefits resulting from improved health and the decreased demand for medical attention.

While our quantitative findings about cimetidine are of interest, we wish to emphasize the applicability of the methodology to a broad range of health care innovations that includes, but is not limited to drugs. As improved data become available--for example, the Medicaid data for Michigan which we plan to utilize and which contain far more complete diagnostic information--it becomes more feasible to supplement conventional analyses of an innovation's efficacy and safety with assessment of its expenditure consequences.

Notes

¹For further description of the research methodology and data limitations, see Geweke and Weisbrod, 1981.

²Any one of the antispasmodics, anticholinergics, or antacids used in treating digestive disorders, as defined in the National Drug Commission codes.

³In the Texas data diagnosis is omitted on about 20% of hospital and physician claims, and only amounts reimbursed (rather than bill amounts) are available. A study using State of Michigan data, in which diagnosis is always included on hospital and physician claims and bill amounts are available, is now under way.

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