

**ARE THERE BETTER WAYS TO SPELL RELIEF?:
A HEDONIC PRICING ANALYSIS OF ULCER DRUGS***

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Abstract

In an innovating industry product specifications are constantly changing as new technologies become available and as consumers express their preferences for particular product attributes. For many classes of drugs, a 1980 generation drug and its 1990 counterpart are only distant cousins. In this paper I take one specific market, the antispasmodic ("anti-ulcer") market between 1977 and 1989, and estimate a hedonic price function which attempts to account for quality changes in brand-name products over time. These results are used as a starting point for a discussion about the empirical importance of different non-price characteristics to physicians and patients. Using the hedonic price estimates I calculate a quality-adjusted price index for antispasmodic drugs. Comparing the quality-adjusted index with an unadjusted price index, I find a significant decrease in the rate of inflation in ulcer drug prices after accounting for non-price characteristics.

I. Introduction

It has become a fact of life for the pharmaceutical industry that prescription drug prices are closely watched by the public, private interest groups, and Congress. The most recent example is the release of a study by the General Accounting Office in August 1992 that reports an average increase over twenty-nine sampled prescription drugs of approximately 138 percent between 1985 and 1991.¹ These and other published prices indexes are increasingly being used in the public policy arena to focus the debate on the potential regulation of pharmaceutical prices and the determination and coverage of health insurance. How are we to interpret these price indexes?

There are numerous theoretical issues that have been researched concerning the construction and interpretation of price indexes.² In addition, there is an obvious issue of the changes in production costs over time that should be addressed. Unfortunately, cost data are difficult to obtain on a drug by drug basis. Rather than tackle the issue of appropriate price-cost margins in the pharmaceutical industry, this paper focuses on an equally important industry issue for the interpretation of price indexes--that of product quality measurement and quality change.

Following Rosen (1974), one can envision differentiated products as made up of various characteristics. These product characteristics are valued by both buyers and sellers. Each good in a differentiated products market is simply a different "bundle" of characteristics. Although

¹ General Accounting Office, "Prescription Drugs: Changes in Prices for Selected Drugs," August 1992. The average price increase figure reported above is a simple average of the price increases reported by the GAO in Table 1, p. 4 of the report. Similar averages were reported by the media after the release of the report, e.g. *CNN Moneyline*, August 25, 1992 (see Transcript #715).

² See, for example, Frank Fisher and Karl Shell [1983], *The Economic Theory of Price Indexes: Two Essays on the Effects of Taste, Quality and Technological Change*, Cambridge, Mass.: MIT Press.

individual characteristics are not priced explicitly in the market, the price of a given product represents the valuation of all the characteristics that are bundled in it. We can therefore speak of each characteristic as having an "implicit" price. The implicit marginal prices of these characteristics can be revealed by hedonic regressions.

Hedonic regressions have been widely applied in many markets, particularly the markets for housing and computers, to study the contributions of individual characteristics to the price of a differentiated good. In contrast, applied work on this issue to pharmaceuticals consists of qualitative surveys of physicians and consumers. In such surveys respondents are asked which drug characteristics they consider, e.g. price, side-effects, when prescribing or using a particular medication or class of medications. Econometric work on hedonic prices for pharmaceutical markets is scarce.³

In a constantly innovating industry, such as the pharmaceutical industry, product specifications are constantly changing as new technologies become available and as consumers express their preferences for particular product attributes. For many classes of drugs, a 1980 generation drug and its 1990 counterpart are only distant cousins. In this paper I take one specific market, the antispasmodic ("anti-ulcer") market between 1977 and 1989, and estimate a hedonic price function which attempts to account for the quality changes in brand-name products over time. Although there are drawbacks to any case study, this particular market is rich in examples of the type of product differentiation that characterizes many pharmaceutical markets.

³ Ernst Berndt of MIT and the NBER is currently working on a hedonic price model of cardiovascular drugs.

Using this approach I calculate a quality-adjusted price index for antispasmodic drugs. The results are used to compare quality-adjusted with unadjusted price indexes. I find a significant decrease in the rate of inflation in ulcer drug prices after accounting for non-price characteristics. The hedonic regressions can also be used as a starting point for discussions about the empirical importance of different non-price characteristics to physicians and patients. In particular, both the dosing regime and certain elements of the side-effect profile differ significantly across drugs in the sample; some of these characteristics are found to have a significant influence on the prices that manufacturers charge.

The analysis is conducted with publicly available data. This presents both costs and benefits. The highest cost is that the data set includes only information on shipments and sales of individual drugs. It does not include individual surveys of physicians and consumers or individual consumer demographics. Therefore, I do not identify characteristic demand functions, but concentrate solely on the broader price indexes. The benefit to confining the study to non-proprietary data is that the analysis can easily be repeated in other pharmaceutical markets.

Section II provides a brief history and description of the anti-spasmodic market. Section III describes the data. In Section IV, I discuss the hedonic analysis and presents the results. Section V presents concluding remarks.

II. Antispasmodic Market Background

Traditionally, non-surgical treatments of peptic ulcer disease have been directed at reducing acid secretion or neutralizing gastric acidity.⁴ Prior to 1977 the two major pharmaco-therapeutic

⁴ Bayless [1990], p.66.

approaches to reducing gastric acidity were antacids and anticholinergics. Antacids work by making acid less damaging to the stomach; they relieve the symptoms but do not heal the ulcer. Anticholinergics were first prescribed in the 1950's to reduce acid secretion. A leader in this class of drugs is Searle's Pro-Banthine, which was first marketed in 1953. Use of anticholinergics has been limited by the many side effects that occur when the necessary large doses are taken in order to significantly decrease gastric secretion. Therefore they are not recommended for use as the sole basis of therapy.

In 1977 a revolutionary class of ulcer treatments known as histamine H₂-receptor antagonists was introduced. These drugs act by blocking the action of histamine, a biochemical produced at an early stage of the process of acid secretion. A four- to six-week treatment period is associated with a healing rate of 70 to 80 percent in patients with duodenal ulcer. Best known of the H₂-antagonists are cimetidine (Tagamet), introduced by SmithKline Beecham in late 1977, and ranitidine (Zantac), a Glaxo, Inc. product which came on the market in 1983. Two other drugs in this class are famotidine (Pepcid), which arrived on the market in 1986, and nizatidine (Axid), introduced in 1988.

The original dosage of Tagamet was 300mg, 4 times daily. More potent than Tagamet, Zantac's dosage is 150mg twice daily.⁵ Physicians see this quality as an advantage for Zantac: "A twice-daily or once-at-bedtime regimen will increase patient compliance."⁶ Pepcid and Axid

⁵ These dosages are for treatment of an active ulcer. While short-term treatment often results in healing, discontinuance of therapy is frequently followed by recurrence of the ulcer. For patients in a high-risk group, maintenance therapy with a reduced nighttime dose may be instituted (see e.g. American Family Physician, April 1989, Vol. 39, no. 4, pp. 268-69).

⁶ American Family Physician, April 1989, vol. 39, no. 4, p. 266

are also long-acting drugs and can be given just once a day. A single daily dose form of Tagamet became available in 1987.

An alternative therapy is sucralfate (Carafate), which was introduced into the U.S. market in 1981 by Marion Labs. Carafate acts to form a protective coating over the ulcer that promotes healing. While it is relatively free from side effects, the dosage regime is inconvenient for many patients.⁷ Throughout the 1980's Carafate held roughly 6 percent of the anti-ulcer market.

Research into a new generation of ulcer drugs has continued. In 1989, Cytotec was approved for the prevention of gastric ulcers caused by nonsteroidal anti-inflammatory drugs. The active ingredient in Cytotec is a synthetic prostaglandin, which is believed to have a protective effect on the lining of the stomach.⁸ Other drugs, such as Losec, have come on the market since 1990, but are beyond the sample period of this study.

Zantac and Tagamet are the clear leaders in the market consisting of the "new" anti-ulcer drugs and a fierce battle between the two has been waged throughout the mid to late 1980's. Due to its different molecular structure, Zantac binds more efficiently to the H₂-antagonists than Tagamet, resulting in a greater inhibition of acid secretion and reportedly a decreased incidence of side effects. Glaxo made early claims about the better side-effect profile of Zantac when it launched a massive marketing campaign to introduce its product. This in turn sparked a heated debate over the side-effect profiles of Tagamet and Zantac.

⁷ Carafate does not seem to have presented any real competition to Tagamet. Although Carafate has been shown to be as effective in healing, it has a few disadvantages: (1) it does not relieve pain as quickly as the acid inhibitors (Chicago Tribune 6/4/86), (2) it has problems of convenience and compliance, given that it should be taken on an empty stomach one hour before meals (Drug Topics 1988). Its main advantage is its limited side effects, which makes it the ideal treatment for older patients and patients in intensive care.

⁸ Chemical Week, January 25, 1989, p. 9.

Following its U.S. introduction in 1983, Zantac generated the largest first-year sales for a new prescription drug in the history of the U.S. pharmaceutical industry.⁹ Zantac's sales did not initially come at the expense of Tagamet sales. Total H₂-antagonist sales grew from \$417 million to \$537 million from December 1983 through December 1984 (Zantac's first full year on the market). Over this twelve-month period Zantac sales shot up 290 percent (from \$41 million to \$159 million), while Tagamet sales increased by .2 percent (\$357.7 million to \$358.4 million). By 1989, Zantac's annual sales had grown to \$962 million, while Tagamet's sales had peaked in 1988 and declined to \$470 million by 1989.¹⁰

The market share battle was clearly won by Zantac. Tagamet's market share declined from a high of 86% in mid-1983 to a low of roughly 15% by the end of 1989. Zantac's share in December 1989 had grown to roughly 60%. This victory occurred even though Zantac was consistently priced roughly twenty to thirty percent higher than Tagamet on average. Some might argue that the market growth in ulcer treatments in general and Zantac's status as leader in particular was due to a successful advertising campaign by Zantac's promoters. I will argue that while this is likely to be true in part, it is also true that the bundle of product attributes that Zantac offered were of therapeutic value to both physicians and patients.

III. Data

A. Market Selection

The main data source for this paper is IMS America Ltd. Their database is organized by "therapeutic category" (e.g. "Psychotherapeutic Drugs" or "Antispasmodics"). These categories

⁹ Chemical Marketing Reporter, August 25, 1986, p. 18.

¹⁰ These figures are calculated from IMS data described in the next section.

are disaggregated further by IMS using their "Uniform System of Classification" or USC codes. Products are grouped into 5-digit USC classes within each therapeutic category.

The classification system developed by IMS is not always consistent with the grouping of products that would be chosen by an economist. As an example, consider the "Minor Tranquilizer" category, which is subdivided into four 5-digit USC classes. The product Valium falls within the 5-digit USC class "Minor Tranquilizers, Benzodiazepines," but it clearly competes with selected products in the other three 5-digit Minor Tranquilizer categories. In addition, Valium can be used as a muscle relaxant. The muscle relaxant drugs are in turn classified under a separate IMS therapeutic category. Thus, an economic study of pricing in the minor tranquilizer market would have to include data on products in each of these separate USC classifications.

Fortunately, the antispasmodic category as defined by IMS fits fairly closely with the definition of the economic market. Because antispasmodic drugs are used for little else, keeping a narrow focus is unlikely to cause major interpretation problems for the empirical results.¹¹ There are six 5-digit USC categories within the IMS therapeutic class 23000, Antispasmodic/Antisecretory Agents:

- 23100 Antispasmodic, Synthetic
- 23200 Antispasmodic, Belladonna
- 23300 Antispasmodic, with Tranquilizers
- 23400 Antispasmodic/Antisecretory, Other
- 23500 Urinary Tract Antispasmodics
- 23900 Other Gastrointestinal Agents

¹¹ Some of the anticholinergic drugs can be used as preanesthetic medication and appear to have a few other possible miscellaneous uses. (Drug Facts and Comparisons, 1990, p. 1374.)

The data used in this study consists of monthly observations for the 23100-23400 classes from January 1975 through December 1989. The products in the 23100-23300 classes are the anticholinergic drugs. All of the H₂-antagonist ulcer drugs fall within the 23400 category. In 1984, for example, there are fifty-three products in the 23000 category as a whole. Only three of those fifty-three products are classified in the 23400 category. Yet, these three drugs accounted for 79% of total 23000 market sales.

Class 23500 is excluded on the grounds that urinary tract drugs do not compete with the gastrointestinal anti-ulcer drugs. Class 23900 was first classified in June 1981. The brand-name drug in 23900 is Reglan (metoclopramide). This is an antiemetic drug that is used to help prevent or relieve nausea (during chemotherapy treatment, for example). It is a gastrointestinal stimulant, not an ulcer treatment, and is therefore excluded.

The units and sales data for specific ulcer drugs were obtained from the IMS U.S. Drugstores Audit. This audit is a monthly report on the volume, in dollars and in physical units, of ethical and proprietary pharmaceuticals purchased for resale by retail outlets in the continental United States. It represents the movement of drugs into drugstores and is gathered at the product pack level (e.g. 100mg tablets in bottles of 30, 60, or 100). The national estimates are based on the purchases of a panel of independent pharmacies, chain operations and wholesalers. Not estimated are purchases made by pharmacies in department stores and supermarkets.¹² Prices that are calculated from these data represent prices charged by manufacturers or wholesalers to the pharmacies, not prices charged to the ultimate consumer.

¹² Source for this description: IMS Pharmaceutical Database Manual.

B. Product Selection

The IMS audits present information at a highly disaggregate level. Sales and units data are given for each different "presentation" of the drug, be it in capsule form, tablet, or injection. Most empirical studies of pharmaceutical pricing use data only on the leading presentation of the leading products. Although I include *all* of the products in the 23400 category, I follow the normal practice and use only the leading presentations. In order to check the reasonableness of the underlying assumption, that prices for different presentations of the same product behave similarly, I first compared the raw price correlations for various presentations of the 23400 products over the sample period. As expected, the price correlations are extremely high (over .90) across presentations of a given product.

For the remaining three categories (23100, 23200, 23300) I use only the leading presentation of the leading product. The market share leaders over 1975-89 for the 23200 and 23300 classes were Sandoz's Bellergal-S and Roche's Librax, respectively. In contrast, there was no clear cut market share leader for 23100 over the 1975-89 time period. Two products were therefore chosen: Merrell-Dow's Bentyl and Searle's Pro-Banthine.

The result is a total of ten brand name products selected for the regressions (six in the 23400 class and four in 23100-23300). Of these ten leading products, there is only one company producing more than one antispasmodic drug: Searle manufactures both Pro-Banthine, introduced in 1953, and Cytotec, introduced in the U.S. in 1989.

There are generic equivalents to some of the older products on the market, although these generics account for a very small market share. Choosing representative generic products involved several steps. First, generic products within each 23100-23300 category were selected

that matched the chemical composition of the market leaders in the brand-name 23100-23300 data sets. For the market leader in the 23200 category, Bellergal-S, there appears to be no generic equivalent on the market. As a compromise I use a generic equivalent for the second ranked drug in that category, Donnatal. There is still no exact match, although generic products exist that contain some of the same active ingredients as Donnatal. Of these products chosen, Lilly is the only manufacturer that has both a generic in this class (an approximate match for Bellergal-S) and a brand name drug, Axid.

Table 1 presents the means of the IMS data for each of the drugs in the 23400 category and the market leaders in the 23100-23300 categories. The prices listed in Table 1 are daily dose prices (in 1982 dollars).¹³ For example, the recommended dosage for Zantac is 300mg per day. Therefore, to calculate the price that the patient would pay per day for Zantac 150mg tablets, the 150mg price is simply doubled. Table 1 shows that the average daily dose price of Zantac, whether presented as 150mg tablets or 300mg tablets, is approximately \$1.75 per day. Prices for different presentations of Tagamet range from \$1.27 to \$1.55. The older generation of drugs are priced significantly lower on average, as are the generic products.

The extent to which medical insurance programs cover expenditures for prescription drugs obviously affects the validity and interpretation of the price data. According to Dranove [1989, p. 143, fn. 1], over two-thirds of Medicaid programs cover prescription drugs. The problem for this study is not coverage of prescription drugs per se. If all drug treatments are covered equally, the price is simply reduced by a given percentage across the board. The problem arises if the

¹³ There are some compromises that had to be made in calculating the daily dosages. See the Data Appendix for details.

amount of coverage differs across anti-ulcer drugs or if it has changed over the 1975-89 sample period. In the aggregate, the percentage of all drug expenditures covered by private and public insurance has increased from roughly 16% in 1978 to almost 30% in 1989.¹⁴ Thus, the real insurance-adjusted price of drugs is below the price that IMS reports, and the bias has certainly increased over time. Unfortunately, systematic data on actual insurance coverage for specific anti-ulcer drugs over 1975-89 is unavailable.

IV. Hedonic Regression Results

A. Measuring Drug Characteristics

As with ordinary prices, an implicit price measures what the seller receives for a characteristic when it is sold as well as what the buyer pays for it. In general, the estimation of reduced form hedonic regressions reveals little information about the underlying demands and supplies of characteristics. The demand for a characteristic j can be written as

$$q_j = f(P_j^*, X),$$

where P^* is the marginal price and X denotes exogenous shift variables.

There are several methods that have been suggested for identifying the characteristic demand functions.¹⁵ However, the data set used for this analysis does not lend itself to solving the identification problem. In one method suggested for identification, the researcher makes use of

¹⁴ Various issues of the Sourcebook of Health Insurance Data. The percentage of coverage is calculated by taking "National Health Expenditures on Drugs, Paid for by Private Insurance and Government" as a percentage of "Total National Health Expenditure on Drugs."

¹⁵ See, for example, R. Palmquist, "Estimating the Demand for the Characteristics of Housing," *Review of Economics and Statistics*, Vol. 3, 1984, pp. 394-404; R. Mendelsohn, "Identifying Structural Equations with Single Market Data," *Review of Economics and Statistics*, Vol. 67, 1985, pp. 525-529; D. Clark and J. Cosgrove, "Hedonic Prices, Identification, and the Demand for Public Safety," *Journal of Regional Science*, Vol. 30, 1990, pp. 105-121.

data from markets separated either by time, or in the case of cross-section studies, by geography. While my sample of temporally distinct markets could theoretically be used for identification, the number of observations in any given year are too few. There are only five drugs at the beginning of the sample in 1977 (Tagamet plus four older drugs) and the number of products grows over time only to a total of ten in 1989. For this reason I pool the data into one panel data set and focus on estimating a quality-adjusted price index, rather than on estimating the underlying characteristic demand functions.

In order to estimate a hedonic price function, one first must decide what list of attributes should be included. There have been numerous surveys conducted to throw light upon which factors are important in drug selection or prescription. One study which specifically focused on ulcer treatments was funded by SmithKline Beecham in 1988.¹⁶ In a telephone survey, 800 heads-of-household were asked "what they look for in a drug to treat ulcer-related symptoms." Those surveyed rated four attributes on a 6-point scale, where 6 is "very important" and 1 is "not very important." The highest rated attribute according to these potential patients was that the drug "Be safe." This was followed by "Make you feel better quickly," "Be convenient to take," and "Be affordable in cost," respectively.

These same broadly defined attributes were found to be important in a more general survey of price sensitivity of European physicians by Dajda and Owen [1987]. The physicians sampled listed the following characteristics in order of importance for prescription decisions:

¹⁶ "Consumer Concerns with Ulcer Symptoms and Experience with Antacid Usage," March 1, 1988, prepared by Yankelovich, Skelly and White/Clancy, Shulman.

effectiveness, freedom from side-effects, reliability, convenient dosage, ease of use, and price.¹⁷

McCann [1987] chose the asthma market to investigate price awareness on the part of physicians. The five factors ranked by doctors were: dose regime, side effects, price, efficacy, and speed of action.¹⁸

The above studies indicate that there are several standard attributes, in addition to price, that physicians and potential patients consider important in choosing which brand of drug to use for treatment. With this in mind, the attributes that I have measured for the ulcer market are: dose regime, number of drug interactions, side-effect profile, and average efficacy. Two pharmacological actions are also included. The first is the absorption rate, which measures the speed of action. The absorption rate is an indicator of how quickly the drug enters the bloodstream measured as the fraction of a dose reaching the plasma site of measurement. The second is the half-life, an indicator of how long the drug remains in the body, measured as the time required for the blood drug concentration to decrease by half. The half-life of a drug is an important characteristic in that it helps to establish a drug's dosing interval.

The supply-side variables are few. Cost data is unavailable, but I have included the approximate patent expiration date for each brand-name drug. All of the H₂-antagonist drugs in this sample will be going off patent by the year 2000.

The variable acronyms and definitions are given in Table 2. The range of each variable is reported, rather than the mean, because I feel it is more informative in this case. The characteristics were measured over time for each of the ten brand-name drugs in the sample.

¹⁷ Dajda and Owen [1987], Table 1, p. 105. Unfortunately, neither this study, nor the McCann study cited next define how the non-price attributes are measured.

¹⁸ McCann [1987], p. 140.

Unfortunately, the generic products could not be included in the hedonic model, due to a lack of information on their attributes.

The drug attribute information was compiled primarily from the 1980-90 volumes of the U.S. Pharmacopeial Convention, Dispensing Information, or USP DI. There are two USP DI volumes: one is for the "health care provider" which was used for the attribute data, and the other is "advice for the patient." It is stated in the preface to each volume that prescribing information is "full disclosure" information. In contrast, "dispensing information is written under the assumption that the decision to prescribe has already been made. USP DI is not intended to be 'full disclosure' information... [instead, the] USP DI contains selected information. Selection is based on what is considered practical, clinically significant information needed to assist in the monitoring of drug use and to help assure that a drug is being safely and effectively used" [1983 edition, p. viii].

Time series information on attributes from the USP DI was available for the 1980-89 period only. The hedonic regressions are run over 1977-89 by using the 1980 characteristics for 1977-79 for those few drugs which existed before 1980. Details on the methodology, definitions, and assumptions for the attributes data are given in the Data Appendix to this paper.

Tables 3A and 3B give selected information on the characteristics for individual drugs in this sample as compiled from the USP DI. Table 3A shows a cross-section for 1989. The first column in Table 3A lists the typical dosage of each drug (for example, in 1989 Tagamet was administered as a 400mg tablet, twice daily). Columns 2 through 7 give the side-effect profile of each drug. The USP DI has two categories of side effects, (1) those indicating need for medical attention, and (2) those indicating need for medical attention only if they continue or are

bothersome. In Tables 3A and 3B, these are labeled SE1 and SE2, respectively. Within each category, the side-effects are grouped according to reported incidence: more frequent (M), less frequent (L), and rare (R). In the SE2 category the USP DI often groups the L and R categories together, and this is reflected in the heading of column 7 (SE2-L&R). Notice the difference in the most serious side effects (SE1M) between the older and newer drugs. Also noteworthy is the significantly higher average healing rates of the newer generation of drugs.

Table 3A shows only the 1989 values for the product attributes. The absorption rate, half-life, average healing rate and patent expiration data are, in fact, constants over time.¹⁹ The dosing interval, number of drug interactions, and side-effects are not. Of the drugs listed in Table 3A, Tagamet had the most recorded changes in its attributes over the 1980-89 period. Table 3B therefore shows Tagamet's entire time series of attributes.

Looking at the first column of Table 3B one can see how the dosage frequency declined over time. This change was a direct response to Zantac's lower daily dosage. On the other hand, the number of drug interactions and less frequent or rare side effects have increased over time. These changes reflect the normal increase in information over the lifetime of a drug as it is prescribed to thousands of patients over the years. Although not reported in the tables, the values of SE1R and SE2-L&R for Zantac also increased from 3 to 6 and from 5 to 7, respectively, between 1984 and 1989.²⁰

¹⁹ Note that not all of these attributes just referred to are literally constants. For some it has been difficult to find a consistent data source which would show time-series variations in these variables.

²⁰ An interesting issue for further research, beyond the scope of this paper, is the rate at which this kind of information on changes in the side-effect profile is disseminated to physicians.

B. Model Specification

I specify the hedonic price function for product i in year t as:

$$(3) \quad p_{it} = p(z_{it}) + r_{it},$$

where the z_i are product attributes, $p(z_i)$ is the systematic component and r is the residual price (an independently and identically distributed error term).

As Trajtenberg writes, there are "virtually no theoretical guidelines to follow" for choosing a functional form for the hedonic equation.²¹ It is common to compare the fit of four functional forms: linear, semi-logarithmic, log-linear, and inverse semi-logarithmic. However, most of the drug attribute variables I use have zero as a meaningful value (e.g., zero recorded side effects). Therefore, I have restricted my consideration of functional form to linear and log-linear. The log-linear form emerged as the clear choice:

$$\log p_i = \beta_0 + \sum_j \beta_j z_{ij} + e_i, \text{ for } i=1, \dots, 10,$$

where i indexes products and j indexes attributes (with the t subscript suppressed). There are a total of 130 possible observations for the regression--13 years, from 1977-89, and 10 products. However, since not all of the products were on the market for all years, the actual number of observations for this panel is 88.

I expect a positive sign for the coefficients on healing rate, absorption level, half-life, and patent expiration. A negative correlation is expected between price and drug interactions, side effects and frequency of medication. The expected sign on tablet strength (in milligrams) is

²¹ Trajtenberg [1990], p. 109.

ambiguous: it is not clear that "mg" independent of frequency is valued by physicians or patients. It may be a crude proxy for incremental costs.

A series of annual time dummies are added to capture inflationary effects. A hedonic price index can then be constructed directly from the regression coefficients. This estimated quality-adjusted price index will isolate pure price changes, unrelated to quality variations.

Most hedonic regressions would include a list of individual consumer characteristics as shift variables. In this instance there are only a few demographic variables that have been statistically linked to ulcer occurrence. Duodenal ulcers are rare in children and less frequently observed in adults after the age of 50 or 60. Men have more ulcers than women, but the gap has been narrowing over the last two decades. As reported in a *U.S News and World Report* article (Nov. 30, 1981), the only two factors that researchers on this issue are certain of as predictors of ulcers are a genetic predisposition and smoking.

Even if individual patient data were available on age, genetic history, and smoking patterns, they would not be appropriate for the dependent variable used here. The drug prices in the hedonic regression are annual averages for the United States. (Although the price data are available on a monthly basis the attribute data are only available annually.) Therefore, I have included two broad shift variables, POP2054 and DPI (defined in Table 2), to capture adult population and income trends in the United States.

C. Empirical Results

The results of the basic hedonic regression are given in Table 4. In column 1 are the results using grouped time dummies. In the remaining columns the full set of individual time dummies

is used, but selected characteristics are dropped to cope with singularity problems.²²

Almost all of the coefficients have the expected sign. For example, an increase in the frequency of dosage decreases the price. This results fits well with the statements of consumers and physicians who purport to value "convenience" in a drug. An increase in the number of most serious side effects, SE1M, also is associated with a lower price and therefore carries a negative value to users. The coefficient on patent expiration is positive, implying that the longer a product has left on patent, the higher the price.

Those variables not having the expected sign are the "less dangerous" side-effect variables (SE2M and SE2LR). The positive coefficients imply that the higher the number of these side-effects the higher the price, contrary to intuition.²³

There is a high degree of multicollinearity amongst the five side-effects variables, and between the side-effects variables, the measure of drug interactions, and the average healing rate. Column 2 of Table 4 shows the results of dropping SE1L and HEAL in order to cope with the multicollinearity problem. A full set of individual time dummies can then be included in the regression.²⁴

²² Due to a lack of variation in some of the attributes over time, there were singularity problems when using the full set of attributes *and* the full set of time dummies.

²³ In an earlier draft of this paper the side-effects measure was a single variable derived as a simple sum of the number of side effects reported. The sign on this variable was positive. It was suggested that this might be due to measurement error. Although the problem has not disappeared with the addition of the disaggregate side-effects variables, it is somewhat comforting that the expected negative sign now appears for the more important side-effects variables.

²⁴ The two broad demographic variables POP2054 and DPI are not included in the remaining regressions. They are statistically insignificant and their exclusion does not change the results.

In terms of coefficient signs, the results are almost identical. The economic significance of the coefficients is easy to interpret given the log-linear functional form. The mean value of $NOMP=.373$ over the sample of both old and new anti-ulcer drugs. This implies, for example, that the $FREQ$ coefficient can be interpreted by adjusting by the mean price:

$$\frac{\partial \log P}{\partial FREQ} = -.189 \Rightarrow \frac{\partial P}{\partial FREQ} = -.189 (.373) \cong -.07$$

An increase by one in the number of times per day one must take the drug means a decrease in the price per tablet of seven cents. Similarly, an increase of one year in patent length implies a 2.5¢ increase in price.

One hypothesis to test is that quality does not matter in the pricing of ulcer drugs. An F-test of the joint hypothesis that the estimated coefficients on the attributes are zero is rejected at the 1% level (F-statistic = 58.37). Similarly, we can reject the joint null hypothesis that, once adjusted for quality change, there has been no inflation in ulcer drug prices (F-statistic = 17.62).

Using the estimates in column 2 a quality-adjusted (quality held fixed) price index can be computed. The quality-adjusted price index for ulcer drugs over the 1977-89 period is given in Table 5, where the 1977 index level is normalized to 100. The rate of increase was fairly flat at the beginning of the sample, but then begins to increase in 1981. In fact, the highest rate of price increase occurred in 1981, although prices continued on an upward trend. The next column of Table 5 gives the unadjusted raw data price index over both old and new drugs. This raw data index shows twice the percentage price increase over the 1977-89 period.

The largest price increases come in 1981, 1985, and 1989. Coincidentally, these increases lead the entry of Zantac, Pepcid, and Losec (which entered the market in 1990). This pattern

may be due to a segmenting of the market as new products enter to serve different market niches or different consumer profiles. This result requires further investigation into firm behavior and pricing patterns before any definitive conclusions can be drawn.

Turning back to the hedonic equations, one might wonder whether there is a different relationship between price and characteristics over the restricted sample of post-1977 ulcer drugs. Column 3 of Table 4 shows regression results restricting the sample to only the class 23400 drugs. SE1M had to be dropped due to collinearity problems. The same F-tests as above can be performed and the null hypotheses rejected: an F-statistic of 461 for the null hypothesis that "quality does not matter" and an F-statistic of 23.7 for the null hypothesis of "zero inflation."

While the FREQ coefficient is robust to the change in sample, the other coefficients are not. The magnitude of the side-effects variables and drug interaction variable declines markedly. The exception is the SE2M variable, which is now large and correct in sign. The patent coefficient increases as well when the sample is restricted to the newer class of drugs. Note, however, that the mean value of the dependent variable increases from .373 to .647 when the hedonic regression is run over the class 23400 drugs. This slightly mitigates, but does not completely account for, the decrease in the magnitude of the coefficients.

Two explanations for these changes in the magnitude of the coefficients are possible. First, there is less variation in some of the SE and DI variables over the new drug sample, suggesting a closer clustering of products in their therapeutic profiles. For example, the variance of DI falls from 9 to 5.3 when the sample is restricted to class 23400 drugs, and the variance of SE2M falls from 7.1 to 0.27. Second, the firms producing the new drugs may be exerting their market power by setting prices more independently of the product characteristics. Because the hedonic equation

reflects both demand and supply forces, it is possible that while the general direction of the correlation is the same between attributes and price, the magnitude of the effect is being dampened by supply-side forces.

The implied quality-adjusted price index for new drugs along with the associated raw-data price index (for new drugs only) are presented in columns 3 and 4 of Table 5. The quality-adjusted new price index shows the same pattern as in column 1, but with even less inflation. The quality-adjusted price increase in 1983 is decidedly less than the raw data price increase shown in column 4. The difference is, of course, that the estimated index number in 1983 in column 3 accounts for the value of the characteristic bundle that Zantac brought to the market. As before, there is a significant difference overall between the adjusted and unadjusted price indexes towards the end of the sample.

Many would argue that promotional expenditures should be included as a product "attribute." Table 6 gives the annual promotional expenditures for drugs in the 23400 category over 1977-89.²⁵ These data are IMS's "Combined Media" data, which are aggregated from separate audits covering promotions by mail, advertising in magazines and professional journals, and "detailing" or direct sales calls by company representatives to physicians and hospitals. According to a pharmaceutical company representative, the IMS estimates of detailing expenditures are an underestimate of actual promotional expenditures.²⁶ For example, IMS does not capture expenditures on promotional displays put on by drug companies at medical conventions. The bias in the data is reportedly thought to occur across the board and is not

²⁵ I do not have promotional data for the 23100-23300 categories due to budgetary constraints.

²⁶ Telephone conversation with a Glaxo, Inc. representative.

particular to any product or manufacturer. Compared to SmithKline's initial promotional expenditures on Tagamet, the data in Table 6 show that Glaxo has heavily promoted Zantac since its introduction in 1983. Cytotec's promotional campaign was also aggressive in its introductory year on the market. When added to the hedonic regressions, the coefficient on PROMO is positive, as expected, but insignificantly different from zero and is not reported in Table 4.

V. Concluding Remarks

Measuring the characteristics important in drug demand is a difficult task. Even something as apparently straightforward as the dosing interval is dependent upon the particular therapy, the patient profile, and the physician's discretion. This paper takes an initial step towards quantifying the important characteristics for pharmaceutical products in order to estimate a hedonic price function. Although many of the finer details recognized by those in medicine or the pharmaceutical industry had to be left out, certain results are clear. First, increases in the dosage frequency, number of drug interactions, and the more serious elements of the side-effect profile all are correlated with a lower selling price. Second, there is a positive relationship between the patent expiration date and the price. This naturally brings up the question of pricing patterns in response to generic entry. For the antispasmodic market, the data to study this question will not exist for a few more years. The results of this paper, however, show that there is additional empirical work needed in the area of brand-name pricing in differentiated products markets. Future research is called for both in the refinement of hedonic regressions such as those in this paper and in the development of models of competition in pharmaceutical markets incorporating the hedonic price function as an integral part of the model.

Data Appendix for Drug Attributes

The drug attribute information was compiled primarily from the 1980-90 volumes of the U.S. Pharmacopeial Convention, Dispensing Information, or USP DI.²⁷

The dosage information is for the "usual adult oral dosage" (tablet form) for an active duodenal or benign gastric ulcer. Various complications arose in using the dosage information. As one example, Table 3B shows the usual dosage for Tagamet changing from 300 mg, 4 times daily (4x) to 400 mg, 2x. The USP DI does not actually state which is the preferred dosing regime. They merely show that as of 1986 Tagamet was available in a 400 mg strength, along with the recommended dosage for 400mg tablets. In 1987, Tagamet could also be taken as an 800 mg tablet once per day. I have used the 400mg, 2x figure as an average. Other drugs cause different problems. Pro-banthine, for example has a usual dosage of 15 mg, 3x *and* 30 mg, 1x. I do not try to distinguish between different strengths of a drug taken at different times during the day. Still other dosages may be listed as "1 or 2 tablets, 3 or 4 times daily." In such cases a simple average is used for calculating daily prices.

Drug interactions are selected on the basis of their potential clinical significance. Those considered by the USP DI to have greater significance are identified at the margin with a chevron (»). Only these more significant drug interactions were counted.

Selected side effects are also listed in the USP DI. Selection is based on seriousness, frequency of occurrence, the effect on life style and/or the likelihood that a nonthreatening side

²⁷ Note that the 1982 volume of the USP DI was not published, due to a format change. 1981 data are used for 1982.

effect might cause concern in the patient if he or she were not aware that the effect might occur [1983, p. ix].

The average healing rate is measured as the average rate at which the ulcer is expected to be healed over a 4 week period. Information was obtained from the medical sources listed in the references to this paper. Earlier editions of these sources were used for the 23100-23300 drugs. Documentation on the 23400 drugs is much more detailed, both because these drugs are newer and because they are used much more frequently than the drugs in 23100-23300.

The absorption and half-life data comes from a variety of sources: USP DI, Medex and Genmed files on Lexis, and clinical pharmacology books listed in the references to this paper. Time-series data on the pharmacological properties of the drugs in the sample was not available, but it is unlikely that there would be much variation.

Approximate patent expiration dates were obtained from the Official Patent Gazette, when available. More precise dates were available for the newer drugs with the cooperation of Joe DiMassi, at the Center for Study of Drug Development, Tufts University. The patent dates that he provided were for chemical compounds. For Pepcid (famotidine) the patent expiration date provided by DiMassi was for a process patent.

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USP DI, various years.

TABLE 1
MEANS: UNITS, SALES, and PRICE

	#OBS ¹	MEAN	STD DEV	MIN	MAX
<u>UNITS (1000s tablets)</u>					
<u>23400</u>					
TAGAMET-300mg	149	64995.34	24893.72	4010	116060
ZANTAC-150mg	78	39009.26	18055.30	6498	70088
PEPCID-40mg	38	4006.05	1453.20	67	6265
CARAFATE	98	13998.73	8986.07	2140	32045
AXID	20	1287.90	552.03	331	2045
CYTOTEC	11	5330.91	873.84	4066	7022
<u>23100</u>					
BENTYL	180	3133.69	570.30	1788	4570
PRO-BANTHINE	180	1934.72	841.38	610	3930
<u>23200</u>					
BELLERGAL	159	3407.88	706.95	2043	5320
<u>23300</u>					
LIBRAX	180	14454.77	9988.65	1507	34700
<u>SALES (\$1000s)</u>					
<u>23400</u>					
TAGAMET-300mg	149	20294.01	7764.13	928	34046
ZANTAC-150mg	78	36495.62	21067.59	4498	75735
PEPCID-40mg	38	6729.34	2801.33	107	11415
CARAFATE	98	5046.03	3930.03	516	13010
AXID	20	2193.05	988.31	535	3564
CYTOTEC	11	2386.73	386.44	1729	3040
<u>23100</u>					
BENTYL	180	315.98	61.15	192	467
PRO-BANTHINE	180	263.08	59.85	127	422
<u>23200</u>					
BELLERGAL	159	731.82	226.27	326	1276
<u>23300</u>					
LIBRAX	180	1628.93	524.24	611	2529
23100 TOTAL	180	2324.47	268.18	1670	2978
23200 TOTAL	159	2501.27	377.96	1866	3582
23300 TOTAL	180	3566.34	814.40	1728	5056
23400 TOTAL	149	55219.52	47994.19	928	174274

TABLE 1, cont'd.

<u>PRICES</u> (1982 \$/DAY)	#OBS	MEAN	STD DEV	MIN	MAX
<u>23400</u>					
TAGAMET-300mg	149	1.27	0.36	0.88	2.00
TAGAMET-400mg	72	1.43	0.24	0.93	1.76
TAGAMET-800mg	44	1.55	0.08	1.40	1.71
ZANTAC-150mg	78	1.75	0.27	1.36	2.18
ZANTAC-300mg	47	1.76	0.12	1.58	1.93
PEPCID-40mg	38	1.65	0.13	1.48	1.89
PEPCID-20mg	38	1.70	0.15	1.51	1.96
CARAFATE	98	1.29	0.26	0.89	1.88
AXID	20	1.69	0.07	1.55	1.81
CYTOTEC	11	1.79	0.04	1.70	1.82
<u>23100</u>					
BENTYL	180	0.32	0.12	0.17	0.64
PRO-BANTHINE	180	0.87	0.50	0.24	1.89
<u>23200</u>					
BELLERGAL	159	0.93	0.45	0.44	2.03
<u>23300</u>					
LIBRAX	180	1.06	0.63	0.37	2.72
<u>GENERIC²</u>					
RUGBY LABS(a)	72	0.05	0.01	0.03	0.06
BARR LABS(a)	58	0.11	0.01	0.06	0.12
GOLDLINE	25	0.50	0.26	0.08	0.71
ROXANE	56	0.27	0.05	0.20	0.35
LILLY1	80	0.02	0.01	0.01	0.04
BARR LABS(b)	74	0.24	0.08	0.11	0.42
RUGBY LABS(b)	31	0.17	0.01	0.13	0.19

Notes:

1. Although the sample period is 1975-89, the number of observations varies by the date of entry of the product.
2. Bentlyl generics = Rugby Labs(a) and Barr Labs(a)
 Pro-Banthine generics = Goldline and Roxane
 Bellergal generic = Lilly (not a direct match)
 Librax generics = Barr Labs(b) and Rugby Labs(b)

TABLE 2 -- VARIABLE DEFINITIONS IN HEDONIC REGRESSIONS

Name	Description	Range
NOMP	Nominal price per tablet	.07 - 1.80
MG	Milligrams of tablet	0.2 - 1000
FREQ	Frequency of dosage per day	1 - 5
DI	Number of drug interactions	0 - 9
SEIM	Number of more frequently occurring side effects requiring immediate attention	0 - 7
SEIL	Number of less frequently occurring side effects requiring immediate attention	0 - 4
SEIR	Number of rarely occurring side effects requiring immediate attention	0 - 9
SE2M	Number of more frequently occurring side effects needing attention if they continue or are bothersome	0 - 6
SE2LR	Number of less frequently or rarely occurring side effects needing attention if they continue or are bothersome	2 - 17
ABS	Absorption rate (%)	5 - 94
HL	Half-life (hours)	0 - 3
HEAL	Average healing rate for 6-week treatment (%)	40 - 84
PAT	Patent expiration date	1967 - 2000
PROMO	Promotional expenditure (\$1000s)	19 - 2983
D78,...D89	Dummy variables, 1 if YEAR=78,...89	0-1
POP2054	U.S. population, ages 20-54 (millions)	101.4 - 124.4
DPI	U.S. disposable personal income (\$1982)	2067 - 2869

TABLE 3A
Drug Attributes: 1989 Cross-Section

<u>Drug</u>	<u>DOSE</u>	<u>DI</u>	<u>SE1</u>			<u>SE2</u>		<u>HEAL</u>	<u>PAT</u>	<u>ABS</u>	<u>HALF</u>
			<u>M</u>	<u>L</u>	<u>R</u>	<u>M</u>	<u>L&R</u>				
Tagamet	400;2	7	0	0	6	0	7	72	1993	70	2.0
Zantac	150;2	7	0	0	6	0	7	70	1995	50	2.5
Pepcid	40 ;1	1	0	0	6	0	4	72	2000	45	3.0
Axid	300;1	1	0	0	1	0	2	77	2000	5	0.0
Cytotec	0.2 ;4	0	0	0	0	2	6	77	1995	94	1.5
Carafate	1000;4	0	0	0	0	1	9	84	1986	88	0.5
Bentyl	20 ;3	6	1	1	1	3	9	40	1967	67	1.8
Pro-Banthine	15 ;5	7	1	1	2	6	10	40	1970	50	1.6
Bellergal	n.a.;3	3	7	--	4 --	6	8	40	1983	50	2.7
Librax	n.a.;2	7	0	--	9 --	6	5	40	1976	10	2.4

TABLE 3B
Drug Attributes: Tagamet, 1980-89

<u>Year</u>	<u>DOSE</u>	<u>DI</u>	<u>SE1</u>			<u>SE2</u>	
			<u>M</u>	<u>L</u>	<u>R</u>	<u>M</u>	<u>L&R</u>
1980	300;4	1	0	0	1	0	5
1981	300;4	1	0	0	4	0	5
1982	300;4	1	0	0	4	0	5
1983	300;4	2	0	0	5	0	8
1984	300;4	2	0	0	5	0	6
1985	300;4	2	0	0	5	0	6
1986	400;2	7	0	0	5	0	6
1987	400;2	7	0	0	5	0	6
1988	400;2	7	0	0	5	0	6
1989	400;2	7	0	0	5	0	7

Key: DOSE = mg;frequency per day

DI = # drug interactions

SE1 = # side effects requiring immediate attention (More frequent, Less frequent, Rare)

SE2 = # side effects needing attention if they continue or are bothersome (M,L&R)

HEAL = average healing rate (%)

PAT = patent expiration date

ABS = absorption rate (%)

HALF = half-life (hours)

TABLE 4: Hedonic Price Function -- Log Nominal Price

VARIABLE	(1)	(2)	(3)
MG	.75E-03 (.33E-03)	.664E-03 (.231E-03)	-.003 (.20E-03)
FREQ	-.213 (.041)	-.189 (.028)	-.186 (.021)
DI	-.410 (.020)	-.025 (.011)	-.002 (.007)
SE1M	-.233 (.031)	-.232 (.022)	
SE1L	.035 (.046)		
SE1R	-.117 (.026)	-.138 (.020)	-.006 (.015)
SE2M	.349 (.100)	.286 (.030)	-1.32 (.081)
SE2LR	.008 (.010)	.011 (.006)	.003 (.003)
HEAL	.017 (.036)		
PAT	.051 (.036)	.068 (.004)	.099 (.009)
ABS	.681E-04 (.003)	-.003 (.001)	-.023 (.002)
HL	.704 (.259)	.598 (.102)	-1.26 (.101)
POP2054	.022 (.012)		
DPI	.648E-03 (.343E-03)		
D78		.042*	-.011*
D79		.094	-.016
D80		.182	.016
D81		.437	.133
D82		.549	.147
D83		.660	.230
D84		.702	.291
D85		.863	.403
D86		.917	.506
D87		.996	.542
D88		1.13	.637
D89		1.27	.727
D7780	-.253 (.145)		
D8185	-.064 (.103)		
D8687	-.052 (.063)		
CONST	-107.62 (68.27)	-137.65 (7.49)	-193.85 (18.02)
N	88	88	36
R ²	.98	.98	.99

Notes to table on next page

Notes

* Standard error for all time dummies is approximately .09 for column 2; for column 3 the standard errors range from .04 for D78-80 to .07 for D81-89.

Column 1 includes grouped time dummy variables; Column 2 includes full series of time dummies, but eliminates collinear characteristics variables; Column 3 is run over only class 23400 drugs.

TABLE 5
Price Index for Ulcer Drugs 1978-89*

Year	(1)		(2)		(3)		(4)	
	Index	Ann. % Chg	Index	Ann. % Chg	Index	Ann. % Chg	Index	Ann. % Chg
1977	100	--	100	--	100	--	100	--
1978	104*	4.3%	103	2.6%	98.9	-1.1%	99	-1.1%
1979	110	5.1	107	3.8	98.4	-0.5	98	-0.5
1980	120	8.4	115	7.6	102	3.0	102	3.1
1981	155	22.5	142	19.0	114	11.0	108	5.7
1982	173	10.6	156	8.8	116	1.4	109	1.5
1983	193	10.5	233	33.0	126	8.0	179	39.0
1984	202	4.1	250	6.9	134	5.9	188	4.6
1985	237	14.9	283	11.6	150	10.6	209	10.3
1986	250	5.2	449	36.9	166	9.7	348	39.9
1987	271	7.6	464	3.2	172	3.6	350	0.5
1988	309	12.5	615	24.6	189	9.0	450	22.2
1989	357	13.2	647	4.9	207	8.6	436	-3.2

* Note that price index column has been rounded, but % chg column has not.

Col. 1 corresponds to Table 4, col. 2; Col. 2 is a raw data price index;

Col. 3 corresponds to Table 4, col. 3; Col. 4 is a raw data price index for class 23400 drugs.

TABLE 6
Annual Promotional Expenditures--23400 Category (\$1000s)

Year	Tagamet	Carafate	Zantac	Pepcid	Cytotec	Axid
1975
1976
1977	362
1978	650
1979	461
1980	663
1981	817	19
1982	959	1059
1983	1436	440	1324	.	.	.
1984	1275	604	1699	.	.	.
1985	1384	605	1250	.	.	.
1986	1416	692	2050	223	.	.
1987	1608	784	1959	1238	.	.
1988	2689	850	2653	1226	.	1263
1989	1891	912	2983	1825	2337	1606