

ERNST R. BERNDT

*Massachusetts Institute of Technology and
National Bureau of Economic Research*

IAIN M. COCKBURN

*University of British Columbia and
National Bureau of Economic Research*

ZVI GRILICHES

*Harvard University and
National Bureau of Economic Research*

Pharmaceutical Innovations and Market Dynamics: Tracking Effects on Price Indexes for Antidepressant Drugs

THE CONSTRUCTION AND PUBLICATION of measures of price inflation are important tasks carried out by governmental statistical agencies. In the United States the Department of Labor's Bureau of Labor Statistics (BLS) publishes price indexes measured at the point of final consumer demand (the consumer price index, CPI) and at the initial transaction

We gratefully acknowledge the cooperation of officials from the U.S. Bureau of Labor Statistics, in particular Commissioner Katharine Abraham, as well as Assistant Commissioner John M. Galvin, Irwin Gerduk, and Douglas Kanoza in the Office of Industrial Prices and Dennis Fixler, Division of Price and Index Number Research. We have also benefited from the timely and able research assistance of Gillian Currie and Mark Moore. We thank Martin Baily, Stan Finkelstein, Richard Frank, Theodore Keeler, Peter Reiss, Jack Triplett, and Cliff Winston for comments. Research support from the National Science Foundation, the U.S. Bureau of Economic Analysis, the Alfred P. Sloan Foundation, and Eli Lilly Inc. is gratefully acknowledged, as is the considerable data support from Stephen Chappell and Robert Plefka at IMS International and from Rhea Mihalison, Phyllis Rausch, Ditas Riad, and Paul Snyderman at Merck & Co. The opinions and conclusions expressed in this paper are those of the authors and do not necessarily reflect views or positions of any of the organizations with which the authors are affiliated or those of any of the research sponsors.

point, that is, prices received by producers from whomever makes the first purchase (the producer price index, PPI). These price measurement tasks are difficult ones, particularly because new goods embody scientific discoveries and technological progress; inherent difficulties exist in measuring the output of services that themselves combine goods and time, and dynamic structural and compositional changes occur in the underlying markets for production, distribution, and sale.

The marketplace for health care contains all these features and presents particularly difficult challenges for price measurement. Health care expenditures represent a significant portion of gross domestic product (GDP) and are likely to become increasingly important as the U.S. population ages. The conceptual foundations for a health care–related CPI are clouded, not only because physicians typically act as agents for consumers, but also because insurance plans pay for many, but not all, health care products and services. Thus, for example, the CPI for prescription pharmaceutical products currently weights only cash payment transactions from drugstores and mail-order outlets; it excludes prescription drugs purchased by managed care plans, Medicaid, or other third parties on behalf of an individual.¹

Here we focus attention on the measurement of a health-care-related PPI, which, while arguably simpler than a CPI, nonetheless presents enormous measurement difficulties and obstacles.² A PPI measures changes in selling prices that domestic producers receive for their output. It is frequently used in deflating current dollar expenditures to obtain a measure of real output growth by industry. The reliability and accuracy of PPIs are therefore critical to understanding the substantial growth in health care expenditures during the last ten years. Growth rates in PPIs by industry are also used to assess inflationary pressures and pricing behavior in the health care sectors or to make international comparisons. While the PPI is an output price index for a specific industry, say, pharmaceuticals, it is also an input price index for wholesalers who in turn sell to retail drugstore chains, hospitals, mail-order

1. For further discussion, see Cleeton, Goepfrich, and Weisbrod (1992), and U. S. General Accounting Office (1996).

2. For a recent discussion on problems involved in interpreting various measures of wholesale prices such as the average wholesale price (AWP, also known as “Ain’t What’s Paid”), see Bill Alpert, “Hooked on Drugs: Why Do Insurers Pay such Outrageous Prices for Pharmaceuticals?” *Barron’s*, June 10, 1996, pp. 15–19.

firms, and managed care organizations.³ Because issues of pharmaceutical pricing and health care cost containment are currently of great importance to public policy analysts, government statisticians, consumers' groups, and industry officials, it is particularly timely to audit closely the accuracy and reliability of one of the BLS health care-related PPIs. That is our purpose in this paper. Although we focus on the PPI, many of the issues we address are also germane to concerns cited by the Advisory Commission To Study the Consumer Price Index in its final report, released in December 1996.

The market on which we focus our audit is that for antidepressant prescription pharmaceuticals sold between January 1980 and February 1996. We have chosen this market segment and time period for several reasons, all relating to the high likelihood of there being substantial challenges here in tracking price changes.⁴

First, several very successful new products have been introduced in the antidepressant drug class, with well-known brand names such as Prozac, Zoloft, and Paxil having combined annual sales of more than \$3 billion in the mid-1990s.⁵ Eight of the twenty-one currently marketed chemical entities (molecules) are new branded products launched since 1988. Thus, issues concerning the incorporation of new goods into price measurement, as well as adjustments for quality change, could be very important in this market class.

Second, not only has new product entry been substantial, but within the last ten years, seven branded antidepressants lost patent protection, and each has subsequently faced competition from lower-priced generic entrants. Those buyers who regard the branded and generic versions of a chemical entity as more or less perfect substitutes realize a substantial price decline after generic entry. Although the BLS has been making changes in its CPI procedures for several years, until mid-1996 its PPI methods did not adequately link generic products to their patented antecedents and instead generally treated generics as entirely new goods;

3. In the United States, the vast majority of pharmaceutical manufacturer sales are to wholesalers, not to hospitals, drugstore chains, or managed care organizations.

4. For related studies on issues in the economics of mental health, see Frank and Manning (1992), and Jonsson and Rosenbaum (1993). Keith and Berndt (1994) provide an overview of price measurement issues in the pharmaceutical industry.

5. Ellen Joan Pollock, "Side Effects: Managed Care's Focus on Psychiatric Drugs Alarms Many Doctors," *Wall Street Journal*, December 1, 1995, p. A1.

thus these older PPI methods failed to record price declines realized by some purchasers of generic drugs.

Recently the BLS announced that the May 1996 pharmaceutical PPIs would incorporate linking procedures for generic drugs that treat generics and their branded antecedents as perfect substitutes. The overall implications of this significant change are not yet clear. Our analysis of 1980–96 data in the antidepressant prescription drug marketplace provides important information on what BLS-measured price growth for antidepressants would have been had these changes been introduced earlier. We also assess the sensitivity of measured aggregate price growth to alternative linking and weighting assumptions that the BLS could have employed. Because we report findings for an entire therapeutic class, namely, antidepressants, this research extends that of Griliches and Cockburn, who provided illustrative empirical evidence concerning two systemic anti-infective drugs.⁶

A third reason for focusing on antidepressant drugs is that they are but one component in the treatment of depression, along with psychotherapy and medical management. To some extent, psychotherapy and antidepressant drugs are substitutes for each other; indeed, controversy surrounds the extent to which managed care organizations are substituting prescription drugs for talk therapy.⁷ The research findings reported here compose one element of a larger research effort in which we are creating a price index for the treatment of depression that incorporates both drug and talk therapy components.

In this paper we begin with a background discussion on the nature of the medical condition called depression and provide a historical overview on the evolving medical understanding of psychotherapeutic drugs used for the treatment of depression. We then outline data sources and describe the changing marketplace for antidepressant drugs from 1980 to 1996, particularly new product introductions and postpatent expiration entry by generic firms. We review BLS procedures for tracking producer prices in general and antidepressant drugs in particular. We next consider issues from economic theory and then present results

6. Griliches and Cockburn (1994).

7. See, for example, Carol Hymowitz and Ellen Joan Pollock, "Cost-Cutting Firms Monitor Couch Time as Therapists Fret," *Wall Street Journal*, July 13, 1995, p. A1; and Pollock, "Managed Care's Focus on Psychiatric Drugs Alarms Many Doctors," p. A1. For empirical evidence, see Berndt, Frank, and McGuire (forthcoming).

on alternative procedures for measuring price inflation, including those involving hedonic price adjustment. Finally we discuss implications of our results and offer suggestions for further research.

Depression: Diagnosis and Prevalence

Whether depressive disorders are discrete and distinguishable from “subclinical” depressive symptoms is a question clinicians and researchers have long debated; it still has no definitive answer. Almost everyone at some time or another has experienced melancholy or been depressed as a mood, affect, or emotion. To be human is to know about a variety of emotions, including sadness, disappointment, and despondency. Many such affective occurrences are within the normal range of human experience. It is only with greater degrees of severity or longer durations that such affective states come to be viewed clinically as symptomatic of depression.

The American Psychiatric Association has issued and updated clinical guidelines for diagnosing depression.⁸ The current guidelines, known as DSM-IV, list nine symptoms of depression: (1) a depressed mood; (2) diminished interest or pleasure in most activities; (3) significant unintentional weight loss or weight gain, or a decrease or increase in appetite; (4) insomnia or hypersomnia nearly every day; (5) psychomotor agitation or retardation nearly every day; (6) fatigue or loss of energy nearly every day; (7) feelings of worthlessness or excessive or inappropriate guilt; (8) diminished ability to think or concentrate, or indecisiveness; and (9) recurrent thoughts of death or suicide. To be diagnosed as having a major depressive episode, a person must show at least five of these symptoms (including either a depressed mood or diminished interest in most activities) for two or more weeks.⁹ These symptoms must also represent a change from the individual’s previous functioning.

A chronic but milder form of depression is known as dysthymia and is diagnosed when the patient has a depressed mood that persists for at

8. See American Psychiatric Association (1968, 1980, 1987, 1993).

9. It must also be the case that an organic factor cannot be established as initiating and maintaining the disturbance or that the disturbance is not a normal reaction to the death of a loved one.

least two years and has at least two other symptoms.¹⁰ Both forms of depression are serious. Even moderate levels of depression significantly impair functioning in work and school settings and in social situations.¹¹

Survey evidence suggests that in a given year, 9 percent of the employed labor force experiences a depressive episode and that 80 percent of these workers are below the age of 45.¹² Depression is widely believed to be an underdiagnosed condition; patients suffering from depression often present themselves to clinicians as having other medical symptoms such as lower back pain, gastrointestinal disorders, and headaches.¹³ Depression is a treatable condition; modern treatment success rates approach 80 to 90 percent.¹⁴ Episodes of illness come and go, last from several weeks to several months, and are followed by periods of relatively normal mood and behavior. Untreated, the average depressive episode lasts about four to six months. Between 50 and 85 percent of patients who seek treatment for depression will have at least one subsequent episode of depression in their lifetimes, usually within two or three years.¹⁵ The lifetime average for depressive episodes is five to seven, but as many as forty episodes have been reported.¹⁶ Although the reasons are still not fully understood, women are about twice as likely to suffer from depression as are men.¹⁷

Alternative Drug Treatments for Depression

Before discussing alternative drug treatments for depression, we briefly review several medical terms. A synapse is the point of contact between adjacent neurons, where nerve impulses are transmitted from one to the other. Neurotransmitters are the chemical “messengers” in

10. A tenth symptom associated with dysthymia is feelings of hopelessness.

11. See, for example, the studies and clinical trial findings referenced by Nolen-Hoeksema (1990, p. 5).

12. For further discussion and references, see Greenberg, Stiglin, and others (1993) and Greenberg, Kessler, and others (1996, p. 328).

13. See Eisenberg (1992) for discussion and references documenting the somatization phenomenon, and Katon and others (1992) for a discussion of the underdiagnosis of depression.

14. Regier and others (1988).

15. American Psychiatric Association (1993, p. 11).

16. Papolos and Papolos (1992, p. 7).

17. For an extended discussion, see Nolen-Hoeksema (1990).

the brain that transmit signals across synapses, setting in motion complex neural interactions that shape behaviors, feelings, and thoughts. Although there are many different neurotransmitters, the vast majority of them monoamines, three of particular importance are norepinephrine, serotonin, and dopamine. Today it is known that low levels of these monoamines are associated with depression. Moreover, after performing their messenger activities, these monoamines are eventually destroyed by monoamine oxidase (MAO), a liver and brain enzyme, through a bodily absorption process called reuptake. In this reuptake phase, however, MAO also destroys another amine called tyramine, a molecule that affects blood pressure.

Modern biological theories of depression apparently emerged from several chance discoveries. Clinicians testing the antituberculosis drug iproniazid in the early 1950s observed that subjects experienced relief from any depression, and some even experienced euphoria. Several years later, this drug was shown to inhibit the MAO enzyme.¹⁸ About the same time, clinicians prescribing reserpine, a drug commonly used to treat hypertension, noted that about 15 percent of patients taking this medication became seriously depressed. Subsequent research demonstrated that reserpine led to the depletion of all three of the important monoamine neurotransmitters.

In 1957 isoniazid was introduced; it was a more effective antituberculosis drug than iproniazid and did not inhibit MAO. Although the manufacturer had planned to cease production of the less effective iproniazid, the coincident publication of psychiatric research linking MAO inhibitors to the treatment of depression resulted in an unexpected surge in demand for it; in 1957 alone, unmet needs were so large that physicians prescribed iproniazid for more than 400,000 depressed patients.¹⁹ Because the MAO enzyme also inhibited tyramine, however, it was soon discovered that iproniazid, by inhibiting MAO, could indirectly increase the amount of tyramine present in the body, sometimes with lethal consequences. Excess tyramine can cause a sudden increase in blood pressure so severe it on occasion hemorrhages blood vessels in the brain and causes death. The potential frequency with which this fatal response could occur for patients taking MAO inhibitors was quite

18. Baldessarini (1990, pp. 414–18); Hyman, Arana, and Rosenbaum (1995, p. 82).

19. Turkington-Kaplan (1994, p. 49).

large, for tyramine is present in common foods such as chicken liver, aged cheese, broad-bean pods, soy sauce, and pickled herring. For this reason, MAO inhibitors (MAOIs) were taken off the U.S. market for a time. Eventually modified MAOIs were reintroduced, in large part because some depressed patients did not respond to any other medication. Today the MAOIs are used most often when other antidepressant drugs yield unsatisfactory results and when electroconvulsive treatment is inappropriate or refused.²⁰ Because of these complexities, psychiatric specialists currently write about 90 percent of MAOI prescriptions; general practitioners or internist physicians write only a small portion.²¹

During the 1950s much pharmaceutical research began to focus on various mental illnesses. Although initially analyzed by Swiss researchers for use as an antihistamine, a tricyclic drug called imipramine was tentatively hypothesized to be successful in treating schizophrenia. Researchers soon found that although imipramine was relatively ineffective in quieting agitated patients, it apparently bestowed remarkable benefits upon certain depressed individuals.²² Instead of stimulating the central nervous system (which amphetamines do) or inhibiting monoamine oxidase reuptake (a property of the MAOIs), imipramine increased the brain's supply of norepinephrine and serotonin; remarkably, about 70 percent of depressed patients responded to this drug. The introduction of imipramine (brand name Tofranil) in 1958 was soon followed by market introductions of numerous related tricyclic compounds. These compounds include amitriptyline (Elavil, 1961), nortriptyline (Aventyl, 1963), protriptyline (Vivactil, 1967), trimipramine (Surmontil, 1969), and doxepin (Sinequan, 1969).

The tricyclic antidepressant class of drugs has been enormously successful in treating depression, and experience with these drugs has been extensive. Today it is known that the various members of this class of drugs differ in the extent to which they affect the three monoamines. Although on average there is no statistically significant difference in efficacy rates among the various tricyclics, often patients who do not respond to one tricyclic do respond to another. About two-thirds of people find relief with the first tricyclic they are prescribed.²³

20. Baldessarini (1990, p. 414); American Psychiatric Association (1993, p. 2).

21. IMS America (1993).

22. Baldessarini (1990, p. 405).

23. Turkington and Kaplan (1994, p. 91).

Not all patients can tolerate these drugs, however. Because they affect several neurotransmitters other than serotonin, dopamine, and norepinephrine, as well as receptors, the tricyclic drugs are often associated with side effects. Although the side-effect profiles of the individual tricyclic drugs differ slightly, common side effects include anticholinergic effects (dry mouth, constipation, urinary hesitance, blurred vision), weight gain, increased heart rate, drowsiness (which may be a beneficial side effect initially for those depressed patients experiencing insomnia), increased heart rate, decreased blood pressure, dizziness when standing up, and sexual dysfunction; side-effect profiles are given in table 1. The tricyclics also differ in their half-lives and in daily dosing frequency. Patient compliance in taking medications is of course negatively affected by adverse side effects and more frequent required daily dosing. A significant unattractive characteristic of the tricyclic drugs is that overdoses are potentially lethal, a factor quite important for depressed patients with suicidal tendencies.²⁴

The most recent major therapeutic development is the 1988 launch of fluoxetine (brand name Prozac), the first of the selective serotonin reuptake inhibitors (SSRIs); subsequent SSRI introductions include sertraline (Zoloft, 1992), paroxetine (Paxil, 1993), and fluvoxamine (Luvox, 1994). In contrast to the MAOIs and tricyclics that affect several neurotransmitters, the SSRIs are selective and specific in that they inhibit the reuptake only of serotonin. Thus, side effects associated with the reuptake of norepinephrine or dopamine are reduced with the SSRIs, and serotonin levels are increased. The 70 percent efficacy rates of the SSRIs are not statistically significantly different from the MAOIs and tricyclics, but adverse interactions with other drugs occur less frequently, and the consequences of overdoses are much less severe.²⁵ With the SSRIs, anticholinergic effects, drowsiness, dizziness when standing up, interaction with the cardiovascular system, and weight gain side effects are very rare. Nausea is still a common side effect of the SSRIs, as are headaches, nervousness, anxiety, and various forms

24. American Psychiatric Association (1993, p. 9); as the same article notes, however, "the vast majority of studies suggest that all available antidepressants decrease, rather than increase, suicidal thoughts and indicate no predilection on the part of a particular agent to either ameliorate or aggravate suicidal tendencies." Also see Potter, Rudorfer, and Manji (1991, p. 636).

25. American Psychiatric Association (1993, pp. 7–10). Also see Potter, Rudorfer, and Manji (1991).

Table 1. Characteristics of Drugs Prescribed for the Treatment of Depression

Chemical entity	Typical daily dose (milligrams)	Half-life (hours)	Daily frequency	FDA OCD	AC	DR	IA	OH	CA	GI	WTG	Index of side effects (0 = rare, 4 = common)			
												DR	IA	OH	CA
<i>MAOIs</i>															
isocarboxazid	20	2	1	0	1	1	2	2	0	1	2				
phenelzine	45	2	1	0	1	1	2	2	0	1	2				
tranylcypromine	50	2	3	0	1	1	2	2	0	1	2				
<i>TCAs</i>															
amitriptyline	75	24	1	0	4	4	0	4	3	0	4				
amoxapine	200	10	1	0	2	2	2	2	3	0	1				
clomipramine	100	24	1	1	3	4	1	2	2	0	3				
desipramine	150	18	1	0	1	1	1	2	2	0	1				
doxepin	100	17	1	0	3	4	0	2	2	0	3				
imipramine	100	22	1	0	3	3	1	4	3	1	3				
maprotiline	100	43	1	0	2	4	0	0	1	0	2				
nortriptyline	100	26	1	0	1	1	0	2	2	0	1				
protriptyline	30	76	3.5	0	2	1	1	2	2	0	0				
trimipramine	100	12	1	0	1	4	0	2	2	0	3				

SSRIs, related drugs

fluoxetine	20	168	1	1	0	0	2	0	0	3	0
paroxetine	30	24	1	0	0	0	2	0	0	3	0
sertraline	50	24	1	0	0	0	2	0	0	3	0
fluvoxamine	100	15	1	1	1	3	3	1	0	3	0
nefazodone	300	18	2	0	3	4	1	1	0	3	0

Others

bupropion	225	14	3	0	0	0	2	0	1	1	0
trazodone	300	8	3	0	0	4	0	1	1	1	1
venlafaxine	112.5	5	3	0	2	3	2	1	1	3	0

Sources: Depression Guideline Panel (1993, tables 7, 8, pp. 56, 59); for clomipramine, fluvoxamine, nefazodone, and venlafaxine, Physicians' Desk Reference Generics (1996, pp. 735–39, 1383–1683, 2246–50, 3071–76).

Notes: See text for discussion of typical daily dosages in milligrams. Half-life is average of elimination half-lives in hours. Daily frequency is that recommended for maintenance therapy after titration has determined daily dosages. FDA OCD = 1 if FDA has approved obsessive-compulsive disorder indication. For side effects, AC = anticholinergic (dry mouth, blurred vision, urinary hesitancy, constipation); DR = drowsiness; IA = insomnia-agitation; OH = orthostatic hypotension (abnormally low blood pressure); CA = cardiac arrhythmia; GI = gastrointestinal disease; and WFG = weight gain (more than 6 kg).

of sexual dysfunction; some patients encounter insomnia, while a small portion experience drowsiness.

In addition to their use as antidepressants, two of the SSRIs—Prozac and Luvox, along with a tricyclic, Anafranil—have received Food and Drug Administration (FDA) approval for use in treating obsessive-compulsive disorders (OCD). Within the class of SSRIs, Prozac has the longest half-life (see table 1); this has disadvantages for those who experience negative side effects but can be beneficial for those who occasionally might forget to take their medication.

Three related drugs have recently been introduced into the antidepressant market: nefazodone (brand name Serzone), a serotonin-related compound that may cause less sexual dysfunction; venlafaxine (Effexor), a compound that inhibits reuptake of norepinephrine and serotonin, but not dopamine, and thus exhibits some of the features of both the tricyclics and SSRIs; and bupropion (Wellbutrin), a compound whose mechanisms of action are still not well understood. More generally, researchers of the central nervous system still do not understand precisely how the SSRIs affect depressive moods and the role of serotonin in this process. Although serotonin levels increase within several days of taking SSRI (and other antidepressant) medications, typically a change in depressive moods manifests itself much later, after two, four, or perhaps even six weeks. It is possible that serotonin causes slight effects in other neurotransmitter systems, which in turn relieve depression. Apparently the serotonin neurotransmitter system is very complex.

Although much progress has been made in developing psychotherapeutic drugs for treating depression, the causes and optimal treatments of depression remain unresolved. This has led the American Psychiatric Association to issue the following current medical practice guidelines:

No one medication can be recommended as optimal for all patients because of the substantial heterogeneity among patients in their likelihood of beneficial response to these medications and the nature, likelihood, and severity of side effects. Furthermore, patients vary in the degree to which particular side effects and other inconveniences of taking medications (e.g., cost and dietary restrictions) affect their preferences.²⁶

26. American Psychiatric Association (1993, p. 7).

Finally, it is widely believed that psychotherapy, drug therapy, or their combination is an effective treatment for cases of mild to moderate depression. Although this consensus is based on extensive clinical experience, and on clinical trial data for drugs, evidence concerning the efficacy of psychotherapy based on controlled experiments is not as extensive, in part because controlled experiments involving uniform and consistent forms of psychotherapy have proved difficult to design and conduct.²⁷ For the more severe forms of depression, both drug treatment and electroconvulsive treatments appear to be more efficacious than psychotherapy alone.²⁸

The Changing Marketplace for Antidepressant Drugs

Our description of the changing marketplace for antidepressant drugs is based on the following data sources. Monthly price and quantity data for drugstore purchases of antidepressant drugs are from IMS America, a Pennsylvania firm that collects and sells data on the sales and marketing of pharmaceutical products. The transactions monitored by this data are from wholesalers and manufacturers to drugstores (or their purchasing agents) and are based on actual invoices; IMS tracks more than 99 percent of manufacturer and wholesaler transactions and thus provides a near-census universe of drugstore purchases.²⁹ These invoices reflect slightly imperfectly the prices manufacturers receive. The invoice data provide a dollar sales amount and quantity number for each type of transaction; they include chargebacks (credits to wholesalers for any special price agreements negotiated among drug stores, manufacturers, and wholesalers), but rebates (direct payments from manufacturers to health care providers and others, such as health maintenance organizations and pharmaceutical benefit management firms) are not always included, nor do the dollar purchase amounts on the invoices reflect prompt payment cash discounts (usually 2 percent off).³⁰ Further

27. See, however, the seminal study by Elkin, Parloff, and others (1985) and Elkin, Shea, and others (1989).

28. See Depression Guideline Panel (1993).

29. IMS America (1996b, p. 39–6).

30. Rebates occur in part because health maintenance organizations and pharmaceutical benefit management companies can affect market shares, but often these organizations do not actually take possession of drug products.

discussion of the IMS price data is given in Berndt, Griliches, and Rosett, who report that from 1986 through 1991, the period covered in their study, the IMS data and price data provided them by four manufacturers had very similar growth rates.³¹

In the paragraphs that follow, we report sales data, measured in both dollars and daily dosage units.³² Frequently a drug is available in various strengths; considerable differences also occur in the total daily dosage taken by individuals. To develop a quantity measure providing some comparability across diverse chemical entities and dosage strengths, we first take the midpoint of the normal recommended daily milligram dosage range during the maintenance phase, as specified for each chemical entity in the 1996 *Physicians' Desk Reference* and then assess what integer number of equal-strength tablets at recommended daily frequencies could feasibly make up the total daily dosage closest to this midpoint.³³ In cases of ambiguity, we consulted IMS data on volume sales by tablet strength. The resulting "typical daily dosages" are listed in table 1 for each chemical entity. To express quantities in total number of daily dosages, we divide the total number of milligrams of active ingredient sold over the various presentations of the drug by this typical daily dosage. The typical daily dosage price is then computed as sales in dollars divided by total typical daily dosages.

The Overall Market for Antidepressant Drugs

Growth in the overall market for antidepressant drugs since 1980 has been sustained and substantial. In 1980 about 452 million daily dosage units of antidepressant drugs were sold; by 1995 this number had increased to about 2.44 billion, a factor of more than five; the implied average annual growth rate (AAGR) is 11.9 percent. Growth of dollar revenues has been even stronger, from a \$128 million market in 1980 to \$3 billion in 1995, for an AAGR of 23.5 percent; using the GDP deflator to convert into constant 1980 dollars, the 1995 sales are \$1.65 billion, implying an AAGR of 18.6 percent. Growth has accelerated

31. Berndt, Griliches, and Rosett (1993, p. 255).

32. Because their uses are often for very different purposes and because their volumes are relatively small, all liquid forms, such as oral solutions and injections, are excluded.

33. The midpoint dosage was often an infeasible number, unless patients broke up tablets into smaller units. Thus we sought an integer value.

dramatically since 1988, the year in which the first SSRI was introduced. From 1980 to 1987, for example, the AAGR in daily dosage quantities was about 5.3 percent, but from 1987 to 1995 this AAGR more than tripled to 18.3 percent; in real dollars, these AAGRs are 9.5 percent and 26.9 percent.

Entry and Exit

There has been much entry and some exit in the market for antidepressant drugs. Two types of entry occurred, one involving introductions of patented products and products newly approved by the FDA, and the other involving generic introductions after patent protection expired. In some cases branded products left the market, while both entry and exit occurred for generic products. This entry and exit behavior is summarized in table 2. Of the twenty-one antidepressant chemical entities on the market in February 1996, fifteen were either new branded products or generic versions introduced within the past ten years.

All three MAOI products were introduced in the 1959–61 time period, and although patent protection has expired, the market for these products is apparently so small and unattractive that generic entry has not been induced.

Among the ten tricyclics and related tetracyclic (hereafter, TCA) chemical entities, the two oldest are imipramine and amitriptyline. The branded pioneers, Elavil and Tofranil, not only faced competition from generic entry beginning in the 1970s, but from 1975 on they also experienced branded competition from other major pharmaceutical manufacturers (Endep for Elavil, and Janimine for Tofranil).³⁴ The competition these secondary brands encountered from the primary branded products and the generics must have been considerable, for Janimine exited in 1985, and Endep in 1988.³⁵

The TCA class of drugs attracted considerable branded entry, especially in the 1960s, but in the 1980s generic entry was predominant, reflecting in part the reduced costs of generic entry made possible by

34. Although the distinction is not completely clear, we distinguish branded products from those generics sold primarily by their chemical entity name, often under a private label; thus Endep is distinguished from, say, Walgreen imipramine.

35. It is possible that these brands exited only from the IMS data base, not from the market, in that their sales may have fallen below a minimum reporting threshold imposed by IMS.

Table 2. Entry and Exit in the Antidepressant Drug Market

Generic name	Originator brand		Secondary brand			Generic distributors		
	Name	Year	Name	Entry	Exit	Entry	1988	1996
<i>MAOIs</i>								
isocarboxazid	Marplan	1959				None	0	0
phenelzine	Nardil	1959				None	0	0
tranylcypromine	Parnate	1961				None	0	0
<i>TCA's</i>								
amitriptyline	Elavil	1961	Endep	1975	1988	1977	13	24
amoxapine	Asendin	1980				1989	0	14
clomipramine	Anafranil	1990				None	0	0
desipramine	Pertofrane	1971	Norpramin	1975	1989	1987	9	20
doxepin	Sinequan	1969	Adapin	1973	1991	1986	12	22
imipramine	Tofranil	1958	Janimine	1975	1985	1975	12	16
maprotiline	Ludiomil	1981				1988	7	11
nortriptyline	Aventyl	1963	Pamelor	1977		1992	0	17
propriptyline	Vivactil	1967				None	0	0
trimipramine	Surmontil	1969				1988	5	0
<i>SSRIs, related drugs</i>								
fluoxetine	Prozac	1988				None	0	0
fluvoxamine	Luvox	1994				None	0	0
nefazodone	Serzone	1995				None	0	0
paroxetine	Paxil	1993				None	0	0
sertraline	Zoloft	1992				None	0	0
<i>Others</i>								
bupropion	Wellbutrin	1989				None	0	0
trazodone	Desyrel	1981				1986	22	22
venlafaxine	Effexor	1994				None	0	0

Sources: IMS America, Inc., and Food and Drug Administration (annual).

passage of the 1984 Waxman-Hatch Act.³⁶ By 1996 eighteen or so distributors were offering generic products for each of the TCA drugs facing generic competition, up sharply from about ten in 1988. Not all generic entry has been sustained; although Surmontil faced generic entry in 1988, in 1992 the generic competition exited, and none has emerged since then.

The introduction of Prozac in 1988 marked the entry of an entire new class of antidepressants, the highly successful SSRIs. Other SSRI branded drugs were Zoloft, introduced in 1992, Paxil in 1993, Luvox in 1994, and Serzone in 1995; Effexor, a related product, was also introduced in 1994.

Prices and Market Shares

Next we look at market share and price movements, first among the four classes of antidepressant drugs listed in table 2. During 1980–88 the MAOIs had only a very minor unit and revenue market share, between 1.4 percent and 2.4 percent, and after 1988 this share dropped even further; the 1996 share was but 0.3 percent.

In 1980 the TCAs accounted for about 98 percent of both the daily dosage quantities sold and total antidepressant revenues. By 1987 the TCA unit share fell slightly, to 90 percent, as trazodone (from a different class of drugs) increased its unit market share to about 8 percent; the corresponding TCA revenue shares were 77 percent and 21 percent. Among the TCAs, three dominated in 1980: amitriptyline had a 50 percent unit share, doxepin 22 percent, and imipramine 18 percent, for a combined share of 90 percent. By 1987 this combined share fell to 80 percent, as sales of products such as desipramine, amoxapine, and nortriptyline (having fewer and less severe side effects—see table 1) increased to a combined 14 percent unit share. The three largest TCAs accounted for about 82 percent of total TCA dollar sales in 1980, but only 49 percent in 1987, in large part because all three products faced increased generic competition in the 1980s.

The launching of Prozac was a huge success. Not only did this first SSRI take market share away from the TCAs, but it also expanded enormously the size of the overall antidepressant drug marketplace.

36. For discussion of this legislation and its consequences, see Grabowski and Vernon (1992).

General practitioners and internists, not just psychiatrists, were now able to prescribe antidepressants comfortably, for concerns about side effects and adverse interactions with Prozac were much less intense than with the TCAs. Moreover, because the daily dosage for Prozac was the same for almost everyone, specialist knowledge and experience concerning optimal patient-specific dosages, typically required for many of the TCA drugs, were no longer necessary. At the end of its first year on the market (1988), the Prozac daily dosage share among all antidepressants was 11 percent, and given its higher price, its dollar market share was 21 percent; by 1991 these shares had increased to 29 percent and 51 percent, respectively.

The SSRI market continued to grow rapidly following entry by additional SSRIs, and by 1996 the SSRI market share among all antidepressants was 63 percent in daily dosage units and a remarkable 84 percent in dollars; unit market shares for the TCAs fell from 90 percent in 1987 to 27 percent in 1996, while revenue shares dropped even more dramatically, from 77 percent to 7 percent. Clearly, for many physicians and patients dealing with the treatment of depression, the SSRIs were enormously successful in fulfilling unmet needs.

Within the SSRI subclass of drugs, unit sales of Prozac continued to grow, from 340 million daily units in 1991 to 645 million in 1995. But the great success of Zoloft and Paxil in expanding the overall SSRI market has implied a loss in Prozac's market share; in 1996 SSRI daily dosage market shares for Prozac, Zoloft, and Paxil were 41.6 percent, 41.5 percent, and 12.6 percent, respectively, while corresponding dollar market shares were 48.0 percent, 29.8 percent, and 17.8 percent. Moreover, the unit shares of Prozac, Zoloft, and Paxil prescriptions written by nonpsychiatrists were 39 percent, 51 percent, and 49 percent, respectively, indicating proportionally more nonspecialist prescriptions written for Zoloft and Paxil than for Prozac.³⁷

Prozac and other SSRI entrants have been tremendously successful despite their higher daily dosage prices. When Prozac was launched in 1988, for example, its daily price was about \$1.18, almost double the \$0.60 daily price of the branded version of the leading selling tricyclic, amitriptyline, and more than twenty times the \$0.05 daily price for generic versions of that chemical entity; doxepin, the second best-

37. IMS (1996a).

selling tricyclic, was also much cheaper than Prozac—\$0.70 a day in its branded version and \$0.21 in generic form. When Zoloft, the second SSRI entrant, was launched in 1992, its daily price was set at about 25 percent lower than that of Prozac—\$1.26 compared with \$1.69. Serzone, the most recent SSRI, is priced in between Prozac and Zoloft.

In constructing a price index, what happens following entry of generic competition is very important.³⁸ In table 3 we summarize price and market share developments at twelve, twenty-four, and thirty-six months following initial generic entry for the seven chemical entities experiencing initial generic competition since 1980. The top panel shows that although considerable variability is present, unweighted average generic prices are about 57 percent, 43 percent, and 35 percent of brand prices after one, two, and three years.³⁹ Substantial differences in market share penetration are also present. Measured in daily units, generic market shares vary from 5 percent to 68 percent of brand shares after one year and average about 27 percent, while they average about 44 percent and 54 percent after two and three years, respectively.

There does not appear to be any dominant time trend to generic penetration rates, although the market share of the most recent generic entrant, nortriptyline, is the largest after one, two, and three years. Because generic prices are lower than brand prices, dollar shares are smaller than unit shares; even so, after just one year the nortriptyline dollar share is 56 percent.

The generic price can fall relative to the brand price if the generic price decreases, the brand price increases, or both. As the second panel of table 3 shows, manufacturers have tended to increase the price of branded products following generic entry, apparently focusing on the price inelastic market segment and letting generics gain market share from the elastic segment; after one, two, and three years, the average

38. For discussion of generic pricing and responses by incumbents, see Caves, Whinston, and Hurwitz (1991); Frank and Salkever (1992); Grabowski and Vernon (1992); Griliches and Cockburn (1994); Hurwitz and Caves (1988); and Masson and Steiner (1985).

39. These trends in prices of generic drugs for treatment of a relatively chronic condition such as depression differ considerably from those reported by Griliches and Cockburn (1994) for systemic infectives, which tend to be used in the treatment of more acute conditions. For generic antidepressants (except nortriptyline), the initial price discount is larger, but after that the relative price is flatter than that of generic systemic anti-infectives.

Table 3. Relative Prices and Market Share Penetration of Generic Antidepressant Drugs Introduced since 1986 Twelve, Twenty-four, and Thirty-six Months after Introduction
Percentage

Chemical entry	Entry year	Relative price generic to brand			Generic market share in units			Generic market share in dollars		
		12	24	36	12	24	36	12	24	36
doxepin	1986	38	30	25	39	54	67	20	26	34
trazodone	1986	62	42	18	23	44	70	16	25	29
desipramine	1987	61	37	31	29	61	58	20	37	30
maprotiline	1988	61	54	42	10	22	33	6	13	17
trimipramine	1988	60	53	58	5	11	11	3	6	7
amoxapine	1989	58	51	50	14	37	51	9	23	35
nortriptyline	1992	61	36	22	68	80	85	56	58	56

	Pioneer brand price after generic entry (Generic: entry date = 1.00)			Real GDP-deflated price		
	Nominal price per day			Real GDP-deflated price		
	12	24	36	12	24	36
doxepin	1.11	1.35	1.50	1.08	1.27	1.35
trazodone	1.01	1.22	1.58	0.98	1.14	1.42
desipramine	1.13	1.35	1.60	1.09	1.25	1.42
maprotiline	1.14	1.21	1.28	1.08	1.11	1.12
trimipramine	1.14	1.23	1.43	1.09	1.12	1.25
amoxapine	0.97	1.39	1.45	0.94	1.33	1.29
nortriptyline	1.04	1.06	1.11	1.01	1.01	1.05

Source: IMS America, Inc.

nominal price increases for the branded products are about 11 percent, 26 percent, and 42 percent (average real price increases are about 7 percent, 18 percent, and 27 percent, respectively).

With this data as background, we now summarize procedures the BLS has used to track and measure price indexes in this rapidly changing antidepressant drug marketplace.

BLS Procedures and Samples for Tracking the Antidepressant Drug Market

Currently the PPI program at the BLS encompasses the construction of monthly aggregate price indexes for almost five hundred mining and manufacturing industries, including approximately ten thousand indexes for specific product categories, based on reports from approximately twenty-five thousand companies that respond voluntarily. For the specific product category called prescription pharmaceutical preparations, the BLS has been publishing a PPI since January 1961. In June 1981 the BLS began publishing a price index for a category of drugs called psychotherapeutics. The specific products the BLS sampled for this price index were drawn in 1980 and are known as "Cycle A" items. Although the psychotherapeutic category consisted of subcategories for tranquilizers and antidepressants, separate price indexes for these distinct and more disaggregated subcategories were not officially published. Unfortunately, the BLS has not kept files on which particular psychotherapeutic drugs and presentations made up the Cycle A sample and what their index weights were.

About six years later, in December 1987, the BLS drew up a new sample, implementing where possible a sampling procedure in which items were chosen in such a way that the probability of selection was proportional to a product's value of shipments.⁴⁰ A separate antidepressant drug subcategory was created, and specific items were chosen for that subcategory in what the BLS calls its "Cycle B" sample. For six years beginning in December 1987, the BLS computed and published a PPI for antidepressant drugs based on this Cycle B sample. In

40. For a discussion, see the appendix in Berndt, Griliches, and Rosett (1993).

December 1993 the BLS again updated its sample; the items making up this new sample of antidepressant drugs are called “Cycle C” products.

Under strict confidentiality agreements, BLS officials have made available to us information concerning the set of antidepressant drugs, and their item weights, that make up the Cycle B and Cycle C samples. As best we can determine, six items were originally in Cycle B, and one additional item was linked in around May 1990. Two of the seven items may be misclassified, because the FDA has not approved them for treatment of depression, nor does the American Medical Association list them as antidepressant treatments.⁴¹ All seven Cycle B items apparently were branded products; when the Cycle B item sample was implemented, three of the six brands faced generic competition. Generics as a group accounted for 11 percent of total antidepressant revenues and 44 percent of total daily dosage units sold. Prozac, the pioneer SSRI, did not enter the market until January 1988, and thus none of the new generation of SSRIs was included in the Cycle B sample. During the six-year Cycle B period (1987–93), an additional two of the seven branded drugs in the sample lost patent protection and faced competition from generic entrants. Thus at the end of the Cycle B era (December 1993), while five of the Cycle B items faced generic competition, all seven sample items were branded products.

Details concerning procedures used to construct the Cycle B sample are no longer available. BLS officials have, however, informally described how the Cycle C sample was drawn and how its item weights were determined. In early 1993 the BLS contacted a private data source to provide 1991 and 1992 annual sales data by drug, separately for several market segments such as drugstores and hospitals. Based on this and related FDA data, the BLS chose a preliminary set of therapeutic classifications and, using a sampling procedure designed to ensure that a manufacturer’s probability of being selected was proportional to its sales, selected about 120 manufacturers for sampling, of which approximately 75 percent cooperated voluntarily. Item weights were then constructed based on information these manufacturers provided to the BLS. The resulting Cycle C sample of products used to

41. American Medical Association (1991). Both of these products are known to be prescribed “off-label” infrequently by some physicians for treatments occasionally associated with depression. BLS officials have suggested that these products may have been selected as antidepressants by the responding firms, rather than by the BLS.

construct PPIs for prescription pharmaceuticals numbered between 500 and 520.⁴²

Within this Cycle C sample, first used in December 1993, the BLS retained five of the seven Cycle B chemical entities (each with different weights, and one switched from brand to generic, with a changed milligram strength), including one drug not normally considered an antidepressant. Two Cycle B items were dropped, and five new items were added. Of the ten Cycle C items, three are generic and seven are branded. Among the latter, three faced competition from generic entry at the time the Cycle C item sample was drawn.⁴³

Because Prozac is manufactured in Puerto Rico (along with many other drugs, in part because of provisions in the federal tax code) and because Puerto Rico is not considered part of the United States for purposes of PPI calculations, Prozac could not be part of the Cycle C sample even though it is the largest-selling SSRI. More generally, unlike the CPI, which includes drugs manufactured in Puerto Rico for use in the fifty states and the District of Columbia, the PPI excludes all Puerto Rican production. Government statistical agencies do not all deal with Puerto Rican economic accounts in the same way. For example, the national income and product accounts from the Bureau of Economic Analysis exclude Puerto Rican production and that of other dependencies, but in the balance of payments accounts, Puerto Rico is treated as domestic.⁴⁴ The Census Bureau defines the United States as the U.S. customs territory, which consists of the fifty states, the District of Columbia, and Puerto Rico, plus U.S. foreign trade zones and the U.S. Virgin Islands.⁴⁵ There appears to be some ambiguity, however, in determining what constitutes Puerto Rican production from the viewpoint of the BLS. One of the products in the current Cycle C sample, for example, is produced both on the mainland (45 percent of domestic consumption) and in Puerto Rico (55 percent of domestic consumption).

42. In December 1995 the BLS supplemented the original Cycle C sample by introducing fifty-one additional products, based in part on data from new drug products introduced after 1992, as published in the FDA's "Orange Book." None of these products is in the antidepressant drug class (but see footnote 47). Kanoza (1996) provides further details.

43. In December 1993 generics accounted for about 8 percent of total antidepressant market revenues, and 37 percent of daily dosage units.

44. Bureau of Economic Analysis (1985a, p. 2; 1985b, p. 10).

45. Bureau of Economic Analysis (1987).

The BLS includes this product in its sample, even though most of its domestic consumption emanates from Puerto Rico.⁴⁶ This issue of how one treats Puerto Rican production is important, for Puerto Rican pharmaceutical production is about 20 to 25 percent of mainland U.S. production.⁴⁷

The current Cycle C sample incorporates items from several of the subclasses of antidepressant drugs displayed in tables 1 and 2, but the weight given the SSRI subclass item(s) is (are) considerably less than IMS data would indicate appropriate (ignoring Puerto Rico production complications). Moreover, the older antidepressants appear to be over-weighted. Specifically, when one assigns each antidepressant chemical entity in the IMS data base the date of its initial market introduction, calculates its age as of 1993:12 (the beginning of the Cycle C sample), and then sales-weights each entity's age using IMS sales of daily units as weights, one obtains a sales-weighted average age for each entity. In 1993:12 the sales-weighted average age of the IMS universe of antidepressant drugs was 15.18 years, while that of the new BLS Cycle C sample was an older 18.50 years; if one excludes Prozac from the IMS universe, however, the sales-weighted average age jumps to 18.53 years, virtually identical to that of the BLS Cycle C sample. In February 1996, the last month in our data series, the sales-weighted average ages for the IMS universe, BLS Cycle C sample, and IMS universe excluding Prozac were 12.97, 16.58, and 14.78 years, respectively.⁴⁸

Based on the information it collects, the BLS calculates the PPI according to a modified Laspeyres formula, in which the value of base-

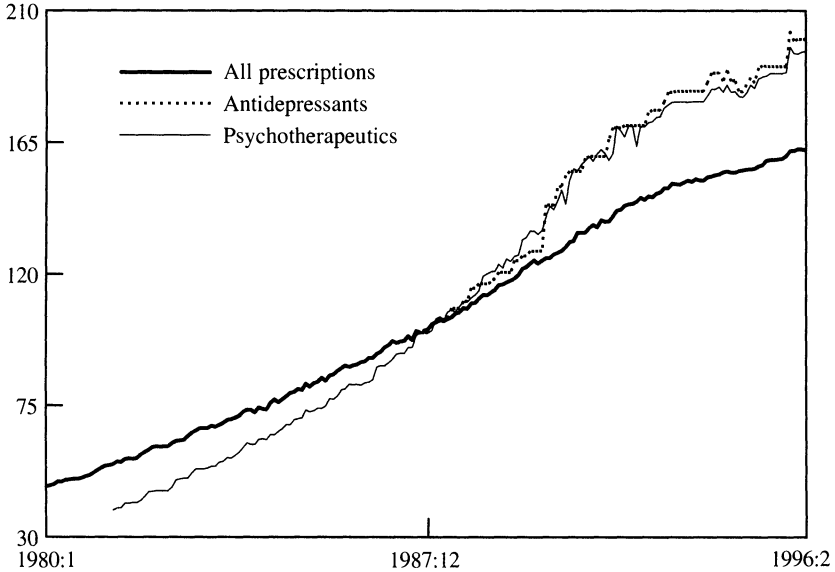
46. This information was provided to us by the manufacturer of the product. Note that the weight employed by the BLS for this product could reflect only the mainland production.

47. When the BLS supplemented its Cycle C sample in December 1995 (see footnote 42 above), it chose four additional antidepressant drugs. All four of these were found to be manufactured in Puerto Rico, and thus they were not included in the supplemental sample. Regarding relative importance, it is not clear how best to measure the Puerto Rican production proportion of U. S. pharmaceutical consumption. If one simply employs value of shipments (VOS) data from the 1994 *Economic Census of Outlying Areas* (table 4, p. 32) and from the 1992 *Census of Manufacturers, Industry Series Drugs* (table 5b, p. 28C-14), both published by the Bureau of the Census, one finds that Puerto Rican VOS is 22 percent of "domestic" VOS—\$11.1 billion, compared with \$50.4 billion.

48. The IMS universe and BLS Cycle B sales-weighted average ages at the beginning of Cycle B were 21.82 and 20.42 years, respectively; six years later, at the end of Cycle B, the respective average ages were 15.18 and 28.17.

Figure 1. BLS Pharmaceutical Price Indexes, 1980-96

Index (1987:12 = 100)



Source: BLS producer price indexes.

period quantities at current-period prices is divided by the value of base-period quantities at (perhaps temporally different) base-period prices, that is,

$$(1) \quad I_t = \left[\frac{\sum Q_a P_t}{\sum Q_a P_o} \right] \cdot 100 = \left[\frac{\sum Q_a P_o (P_t/P_o)}{\sum Q_a P_o} \right] \cdot 100,$$

where Q_a represents the quantity shipped during the weight-base period, P_t is the current price of the commodity, and P_o is the price of the commodity in the comparison period; the summation is over i goods, but i subscripts are omitted. Note that this index can be written as a weighted average of price relatives P_t/P_o , where the weights are fixed within each cycle.

The monthly time series for the BLS PPI for all prescription pharmaceutical products, for the aggregate class of psychotherapeutics, and for the antidepressant subcategory of drugs are displayed in figure 1; selected AAGRs are given in table 4. For the period covered by Cycles

Table 4. Average Annual Growth Rates of Alternative Price Indexes

Price index	Percentage		
	Entire period 1980:1-1996:2	Cycle A* 1981:12-1987:12	Cycle B 1987:12-1993:12
<i>BLS series</i>			
All Rx	7.94	9.82	7.13
Psychotherapeutics	NA	15.64	10.04
Antidepressants	NA	NA	10.40
<i>Antidepressants</i>			
<i>BLS and IMS data</i>			
<i>BLS sample items</i>			
BLS fixed weights	NA	NA	8.69
IMS fixed weights	NA	NA	8.57
Divisia	NA	NA	10.89
<i>IMS data only</i>			
<i>Laspeyres—fixed</i>			
All	5.04	9.35	4.17
Brands	9.26	12.37	10.34
Generics	-6.09	-4.71	-6.79
<i>Divisia—chained</i>			
All	7.51	10.35	7.90
Brands	8.83	11.43	9.62
Generics	-8.88	-5.13	-8.99
			1993:12-1996:2
			3.06
			4.23
			4.27
			4.61
			3.64
			3.46
			0.42
			3.65
			-5.66
			2.34
			3.63
			-18.93

Paasche—all	7.11	9.87	7.45	2.29
Divisia brands				
SSRIs	NA	NA	NA	3.94
TCAs	9.22	11.02	10.82	4.31
MAOIs	9.63	10.96	11.72	5.63
Others	10.89	12.77	15.29	4.11
Laspeyres brands				
SSRIs	NA	NA	NA	3.62
TCAs	9.02	12.41	9.40	4.28
MAOIs	9.07	10.69	12.53	1.07
Others	NA	NA	16.11	3.13
Divisia generics				
TCAs	-9.96	-4.88	-10.72	-22.30
Others	NA	NA	-6.40	-6.88
Laspeyres generics				
TCAs	-6.08	-4.71	-6.81	-5.57
Others	NA	NA	-6.40	-6.88

Source: Authors' calculations; see text for explanation.

NA: Not available.

*Cycle A is defined here as 1981:12–1987:12.

B and C (1987:12 through 1996:2), the PPI for all prescriptions increased by about 63 percent (an AAGR of 6.08 percent), much less than the PPIs for psychotherapeutics (96 percent, AAGR of 8.53 percent) and for antidepressants (101 percent, AAGR of 8.80 percent). This faster growth of psychotherapeutics compared with all prescription drug prices continues a trend going back at least to the beginning of Cycle A; from 1981:12 through 1987:12, the price index of psychotherapeutics increased 139 percent (AAGR of 15.64 percent), compared with a PPI for all prescription products of 75 percent (AAGR of 9.82 percent).⁴⁹ Finally, annual average growth rates for all three price indexes (all prescription drugs, psychotherapeutics, and antidepressants) are greater during the Cycle B era (7.13 percent, 10.04 percent, and 10.40 percent, respectively) than during the Cycle C time span to date (3.06 percent, 4.23 percent, and 4.27 percent).

Given its fixed weights in the context of a rapidly changing market, the reliability with which the BLS PPI for antidepressants could be expected to track actual marketplace developments is ambiguous at best, but whether the BLS sampling procedures impart a systematic bias to the index is unclear. The undersampling of generics would likely impart an upward bias, given the substantial price reductions they have experienced, but the revenue shares of generics in total are small and falling (11 percent in December 1987, 8 percent in December 1993, and 3 percent in February 1996).⁵⁰ The BLS lags marketplace developments in the choice of its sample, and the net effect of this lag on an aggregate price index is therefore an empirical issue. But a different consideration unrelated to sampling issues—namely, the absence, until recently, of a link between generics and their patented antecedents—can more clearly be expected to result in an upward bias to the BLS index.

Alternative Price Indexes: Theory and Evidence

The price of a good before its market introduction cannot be observed. After a new good enters the market, it may take quite some

49. Of the twenty-five seven-digit products in SIC 2834-1, only two have a greater rate of price increase than psychotherapeutics—central nervous system stimulants and antiobesity preparations, and sedatives. See Bureau of Labor Statistics (1996, p. 61).

50. The corresponding daily unit dosage shares are 44 percent, 38 percent, and 27 percent, while daily dosage levels of generics are 32 million, 56 million, and 58 million.

time for statistical agencies to track its price. As Early and Sinclair have discussed, the BLS periodically revises the sample items and “links in” new commodities.⁵¹ For example, in December 1995 the BLS supplemented its Cycle C prescription pharmaceutical sample with fifty-one items, thereby incorporating selected market developments since the original sample (based on 1991–92 data) was drawn for implementation in December 1993. Once items are selected for an updated sample, the BLS includes their price changes in its price index computations. Because this procedure makes no comparisons between new and incumbent goods, however, changes in the aggregate price index reflect only changes in the prices of the products and ignore any absolute price differentials between the new and comparable incumbent products. Although such a procedure may perhaps be appropriate for truly new goods, it surely is not appropriate for many goods such as pharmaceuticals for which some forms of substitute goods or services are available.

Considerations from Economic Theory

The theoretical solution to this “new goods problem” has long been known: for the time period just before the introduction of the new good, find that price at which quantity demanded is just equal to zero and put this “reservation price” into the price index calculation for the time period just before the new product is launched.⁵² This theoretical insight is informative, but it is also challenging to implement empirically, for it requires estimation of demand models that may have burdensome data requirements, it may entail making strong assumptions, the estimated reservation prices might be sensitive to the choice of functional form, and the issue of proper item weights is left open.

The special characteristics of generic drugs provide an opportunity to modify price index computations in a relatively simple way, thereby taking into account the implicit price declines experienced by those consumers who switch from brand to generic versions of a chemical entity. Specifically, generic drugs can be envisaged as a particularly simple case of the new goods problem, because a generic is a variety of an existing product identical in almost all respects to the “old”

51. Early and Sinclair (1983).

52. Hicks (1940), Rothbarth (1940–41), and Fisher and Shell (1971, 1972).

version. In the United States, the FDA publishes an “Orange Book,” *Approved Drug Products with Therapeutic Equivalence Evaluations*, that certifies therapeutic equivalence. Although the generic versions differ from the branded product in packaging (including the inert matter enclosing the active ingredients), labeling, and provenance, the FDA certifies that the generics are equivalent to the branded product in two senses: pharmaceutical equivalence, that is, the active ingredient is chemically identical, has the same strength, dosage form, and route of administration, and is manufactured in compliance with Current Good Manufacturing Practice regulations; and the generic version is “bio-equivalent” in that it is statistically indistinguishable from the branded product in key pharmacological aspects of therapeutic use, such as blood concentration profiles.

The extent to which generics and branded products are in fact “almost perfectly substitutable” is a hotly debated topic. Therapeutically equivalent products may still vary in characteristics such as inert material, shape, color, flavor, scoring, packaging, labeling, shelf life, and stability under adverse storage conditions. Insofar as any of these characteristics affects patients’ ability to distinguish between different tablets and dosages, their readiness to take the medicine at the time and in the amounts prescribed, or their possible reactions to coloring or preservative ingredients, these apparently trivial factors may in fact influence the realized effectiveness of the generic drug relative to the branded product. Moreover, variations in the inert matter encasing the active ingredient can affect the speed of absorption of a medication.

If one takes the FDA at its word—“a pill is a pill is a pill”—the reservation price is the branded price just before the generic enters the market, and in this case the appropriate price index for a particular chemical entity is straightforward, being the weighted average price of a tablet across all generic and branded manufacturers. If, however, one takes the opposite extreme position—that taken until recently by the BLS for its PPI—then one implicitly treats generic versions of a drug as entirely distinct, nonsubstitutable commodities. In that case, the generic launch price is also its reservation price. As we noted earlier, the BLS has recently changed its policy and is now introducing a linking procedure consistent with perfect substitutability: “...the predecessor brand-name drug price and successor generic drug price will *always* be directly compared *without* quality adjustment. The direct comparison

is predicated on the assumption that the two products are of equal quality, because the FDA has determined them to be therapeutically equivalent.’’⁵³

Generic prices tend to be considerably lower than that of the branded version, and the spread between them tends to increase over time. Given the magnitude of the price differential, it is striking that not all consumers switch to the cheaper variety. Apparently consumers, or rather physicians who prescribe for them, differ in their perceptions concerning the efficacy and quality of generics, despite FDA certification, and some consumers, prescribers, and insurers prefer the much higher-priced branded versions. Some consumers, prescribers, and insurers, however, do switch to the cheaper generic version, either perceiving no difference between brand and generic varieties or taking the price differential as more than sufficient compensation for any difference in quality. Clearly, there are considerable differences in information and knowledge and in tastes and preferences among consumers, prescribers, and insurers concerning brand-generic differences.

Alternative Procedures for Incorporating Generics

We now consider alternatives to these two extreme positions, variants we believe more accurately reflect the price declines realized by intermediate purchasers of prescription drugs such as pharmacies. These alternatives vary in how diverse ultimate consumer, physician, and insurer choices are taken into account when reservation prices are being computed. Fisher and Griliches have shown that even when consumers are heterogeneous, aggregate Paasche and Laspeyres price index computations provide bounds for a hypothetical social planner’s ideal index, giving the minimum amount needed to keep all individuals on their base utility level when prices change.⁵⁴ Griliches and Cockburn present formulas for such aggregate indexes in a world in which either the branded or the generic version of a particular chemical entity is purchased.⁵⁵

Let p_b be the unit price of a branded drug, and let p_g be the generic price. In a simple linear random utility framework, purchaser h chooses

53. Kanoza (1996, p. 9). The italics are in the original.

54. Fisher and Griliches (1995).

55. Griliches and Cockburn (1994).

the generic version if $p_b > p_g + b_h$, where b_h is the subjective premium required by purchaser h when buying the generic to compensate for the putative loss in security or quality associated with the switch. If one knows the reservation price p'_h for each purchaser, then Griliches and Cockburn show that the aggregate Paasche price index between periods 0 and 1 is appropriately calculated as

$$(2) \quad p_a^1 = \frac{Q_b^1 p_b^1 + Q_g^1 p_g^1}{Q_b^0 p_b^0 + Q_g^0 \bar{p}_r}, \quad \text{where } \bar{p}_r \equiv \frac{\sum_{h=1}^H q_{gh} p'_h}{Q_g^1},$$

where the 0 and 1 superscripts refer to time periods, Q denotes aggregate quantities over all H consumers, and q_{gh} is the number of units of the generic version bought on behalf of consumer h .

Although elegant, this theoretical framework requires estimation of reservation prices, a nontrivial task. One feasible approach involves making an assumption concerning the distribution of preferences for brandedness. In the linear random utility framework, the probability of any purchaser switching from brand to generic depends on $p_b - p_g > b_h$, and thus the share of generic users in the total is $s_g = F(b_h)$, where $F(b_h)$ is the cumulative distribution of reservation prices, given a fixed p_b . If no buyer is willing to pay more for a generic version than for a branded one when the branded one is available, then $b_h \geq 0$, and in this case the average reservation price for switchers must be bounded between p_b and p_g , with the precise location depending on the shape of $F(b_h)$. Following Griliches and Cockburn, one can assume that unobserved tastes for brandedness among purchasers are uniformly distributed, in which case the average reservation price is half way between p_b and p_g , thus "splitting the difference" between the two extremes of the old BLS approach, which assigns *all* of the brand-generic price differential to quality differences (p_g being the reservation price), and the FDA approach, which assigns *none* of it (p_b being the reservation price).

One notable feature of these markets is that a new generic product typically takes several months to achieve significant sales. The product may take time to move through distribution channels, and it may take time for physicians and purchasers to become aware of its availability or to acquire other information germane to prescribing and buying decisions. Regardless of its causes, the lagged response of demand to

price changes has important implications for price index computations, particularly at monthly frequency, since weights of new generic products are typically initially low.

This “diffusion problem” can be approached in several ways. One way is to link in the new generic good after sufficient time has passed (say, six months to a year), thereby allowing much of the early diffusion of generics to be completed before evaluating their direct contribution. We discuss the BLS variant on this approach below. Alternatively, as Griliches and Cockburn have proposed and implemented, the Paasche index formula can be adjusted to reflect the assumption that those shifting later on to generics do so from the branded good, with an average reservation price that is half way between the prices of the branded and generic good. In such a case, the Paasche equation 2 becomes

$$(3) \quad p_a^1 = \frac{Q_b^1 p_b^1 + Q_g^1 p_g^1}{Q_b^1 p_b^0 + Q_g^1 p_g^0 + (Q_b^1 - Q_g^0) \cdot \bar{p}_r}, \quad \bar{p}_r' \equiv (p_g^1 + p_b^0)/2.$$

Thus shifters from the branded to the generic version are assumed to have experienced a price decline equal to half of the branded-generic price differential also in periods subsequent to the initial appearance of generics.⁵⁶

The new BLS approach to this diffusion issue, given its fixed-weight Laspeyres index, is considerably more parsimonious in its data requirements than are the above alternatives and addresses the choice of reservation price and item weights simultaneously. Based on a review of published research materials, data from the FDA “Orange Book,” and consultations with various industry experts, the BLS has determined that in the month when initial generic entry occurs for a chemical entity in its sample, the previous fixed branded quantity weight, say, x_o , will be split into two components, with a $0.642 \cdot x_o$ quantity weight assigned to the generic, and a $0.358 \cdot x_o$ weight given the branded version. These weights are then fixed until a new or supplemental sample is drawn and are the same for all generic entities. The 64.2 percent generic weight turns out to be quite close to the generic quantity share of the seven antidepressants experiencing initial generic entry after 1980 (see table 3); specifically, the 64.2 percent share falls in between the daily dosage-

56. Ibid. The procedure used here is referred to in Griliches and Cockburn (1994) as “Paasche-UD.”

weighted average generic quantity share of 57.0 percent after twenty-four months and 68.9 percent after thirty-six months.

Finally, yet another alternative approach to deriving reservation prices, one that we plan to pursue in subsequent research, is to estimate demand curves from data on prices and quantities and then to project the estimated demand function to find the brand-generic price differential that would choke off demand for the generics to zero. A related research project involves using similar data to estimate the shape of $F(b_n)$ consistent with observed relationships between prices and market shares.

New Products and Hedonic Regressions

As noted earlier, generics are a special case of the new goods problem, for with generics the FDA has certified equivalence. In general, however, new goods differ in significant ways from older products, reservation prices are more difficult to quantify, and thus incorporating new goods into price indexes is more complex. One way in which the effects of new goods could be incorporated into a price index is simply first to regress for each branded product-month, say, the logarithm of daily dosage price on time dummies, and a dummy variable for each distinct brand. One could then use the predicted price for the month prior to a good's introduction as an approximation of the reservation price, thereby linking in the price of the new good.

The hedonic price approach employs instead quality attributes as regressors, in effect making parameters on the brand dummy variables functions of quality attributes.⁵⁷ The hedonic approach is particularly relevant for branded products, because their prices are set by firms having some market power. For generic products, the hedonic approach might be less useful, particularly if competition drives prices down to marginal production-distribution costs, and when such marginal costs are not dependent on quality attributes.

It is important to note that price indexes linking in new products using predicted prices from hedonic price equations can grow at rates less than, the same as, or greater than those that entirely ignore the link and instead incorporate only the price changes after new product launch, that is, those indexes that treat the reservation price as equal to the new

57. See Griliches (1971, 1990) for a discussion of this methodology.

product's launch price. The relationship between the two growth rates depends critically on whether the actual price of the new product at the time of its launch is above or below that predicted by the hedonic price equation, given the new product's quality characteristics. Any difference between the linked and nonlinked series will emerge only if there is positive or negative nonpriced quality at launch.⁵⁸ If the new product has a launch price that just compensates for its hedonic-estimated quality, then the launch date hedonic residual would be zero, and AAGRs of price indexes based on the nonlinked and the hedonic quality-adjusted linked procedures would coincide. If the launch price of the new product were set above (below) its estimated hedonic quality, however, then hedonic residuals would be positive (negative), and the hedonic quality-adjusted linked price index would grow at a greater (lesser) rate than the nonlinked index. The magnitude of any difference would also depend of course on how quickly the quantity weights become substantial, that is, the speed of diffusion.

Launch date residuals from an estimated hedonic price equation are therefore quite important, for they purport to measure deviations from reservation prices. Whether these residuals in fact reflect price discounts or premiums relative to "true" quality is unknown, however, for hedonic residuals could instead be manifestations of important quality aspects that have been omitted or other specification or measurement errors. Evidence on unmeasured quality as a possible specification error could be obtained by examining relationships between hedonic equation residuals and realized market quantity shares; a negative relationship between them would be consistent with the notion that residuals instead reflect unobserved quality differentials.

Later we present findings based on hedonic price equations for branded products.⁵⁹ First, however, we focus on alternative price indexes where issues of sample selection and item weighting are central.

Empirical Evidence: Sampling and Weighting Issues

In table 4 we report AAGRs for several alternative price index calculations. In the top panel we list official BLS growth rates, which for

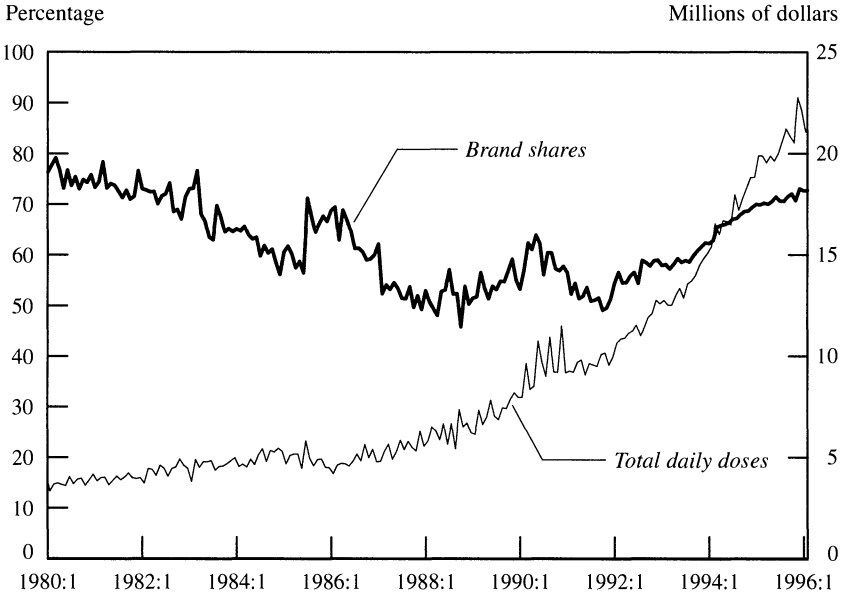
58. For examples and further discussion, see Berndt and Griliches (1993) and Berndt, Griliches, and Rappaport (1995).

59. For earlier attempts to estimate hedonic price equations for branded prescription pharmaceuticals, see Berndt and Finkelstein (1992) and Suslow (1996).

the antidepressant class of drugs is 10.40 percent (Cycle B) and 4.27 percent (Cycle C). Based on the BLS sample information provided us, we employ the IMS price data but the BLS item weights to construct an aggregate index, mimicking BLS fixed-weight Laspeyres procedures, with weights updated at 1987:12 and 1993:12. It is not possible to obtain an exact correspondence, because two of the seven items in the BLS Cycle B are not generally considered antidepressants, nor is one of the ten in Cycle C, whereas the IMS data are confined to antidepressants. If these items are removed, we obtain AAGRs for the partial BLS item sample that are lower than those reported by the BLS during Cycle B (8.69 percent, compared with 10.40 percent), and close but slightly larger during Cycle C (4.61 percent, compared with 4.27 percent). The relatively close correspondence during Cycle C is reassuring, particularly because the one omitted item has a relatively low item weight, whereas the two omitted items during Cycle B have a larger combined relative weight.

If one retains the BLS sample items but uses instead of the BLS weights those based on IMS data, the resulting difference in AAGRs is small during Cycle B (8.57 percent, compared with 8.69 percent), but larger during Cycle C (3.64 percent using the December 1993 IMS weights, compared with 4.61 percent using the necessarily older 1992 or 1993 BLS weights). Finally, if one uses the partial BLS item sample and allows weights to change monthly with the Divisia index, one obtains rather different results, suggesting that weights do matter. Specifically, as seen in the bottom row of the second panel of table 4, during Cycle B the AAGR of the Divisia index is 10.89 percent.

It is useful to distinguish between the choice and accuracy of fixed weights and the effects of changing weights. We begin by comparing AAGRs of the BLS official PPI for antidepressants with those based on the IMS universe, using comparable fixed-weight Laspeyres index procedures. As the row marked Laspeyres-All shows, during Cycle B the Laspeyres index based on the universe of antidepressants grows much less rapidly than does the BLS index, 4.17 percent a year (compared with 10.40 percent). In Cycle C the IMS universe data have an AAGR of only 0.42 percent, while the BLS grew at ten times this rate, 4.27 percent. This large disparity is surprising, given that the only underlying difference is one of weights drawn from a sample rather than the universe, and not the Laspeyres index.

Figure 2. Daily Doses of Antidepressants

Source: IMS America, Inc.

Recall that the BLS Laspeyres fixed-weight procedure entails a change of weights only at six-year intervals. If the sizes of the weights selected at 1981:12, 1987:12, and 1993:12 do not accurately portray actual data trends during the subsequent six years, the resulting indexes can yield very misleading AAGRs, with the sign of the bias being generally indeterminate. Apparently, that is what has happened.

To see this, notice in figure 2 that the time trend of the brand share of daily dosages over the sixteen-year period is approximately U-shaped, starting at 77 percent in 1980:1, falling to 47 percent in 1988:8, and then increasing to 73 percent by 1996:2. When the BLS drew its Cycle B sample in 1987, the generic share was near its peak at 47 percent, but by the end of Cycle B in late 1993, it had fallen to about 37 percent, and by 1996, to 27 percent; the corresponding brand shares increased with time, 53 percent in 1987, 63 percent in 1993, and 73 percent in 1996. Thus, if the BLS fixed-weight procedure had been applied to the *universe* of antidepressant drugs, over the entire Cycle B and in Cycle C to date, generic products would have been overweighted

(their unit share fell as brand dosages grew more rapidly, led by new SSRIs such as Prozac), and brands would have been underweighted. Recall from our earlier discussion that prices of (overweighted) generics have been falling, while (underweighted) brand prices have generally been increasing. Together these trends imply that had the six-year fixed-weight procedure been applied to the universe of drugs, the resulting AAGRs would have severely understated price growth in both Cycles B and C. The much higher AAGR for the BLS published PPI based on its *sample* than for the Laspeyres based on the universe reflects the fact that the BLS sample was in fact nonrepresentative, fortuitously weighting generics less and brands more than the then-current market conditions warranted. (Recall that none of the seven items in the Cycle B sample was a generic.) Clearly, using six-year fixed weights in a rapidly changing environment can lead to highly unreliable results.

One way to assess the role of changing weights is to compute a Divisia index, which weights percentage price changes by the average share in the current and previous month, in contrast to the fixed-weight BLS procedure in which the weights are changed only every six years. Alternatively, one can employ a Paasche index that sequentially updates the weights monthly. As seen in the row marked Divisia-All, based on the IMS universe, the Divisia grew more rapidly than the Laspeyres during all three cycles—10.35 percent compared with 9.35 percent in Cycle A, 7.90 percent compared with 4.17 percent in Cycle B, and 2.34 percent compared with 0.42 percent in Cycle C; for the entire sixteen-year period, the Divisia has an AAGR of 7.51 percent, compared with 5.04 percent for the Laspeyres index. Finally, as the row marked Paasche-All shows, the AAGR of the chained Paasche index over the sixteen years is, at 7.11 percent, slightly smaller than the Divisia index, but two percentage points larger than the fixed-weight Laspeyres.

Differences between the Laspeyres and Divisia also persist when antidepressants are disaggregated into brands and generics. Although Laspeyres-Divisia differences are modest for brands (9.26 percent compared with 8.83 percent over the sixteen-year time frame), for generics the disparity is larger in Cycle B (–6.79 percent compared with –8.99 percent), and in Cycle C it is dramatic (–5.66 percent compared with –18.93 percent). Note that the Divisia index incorporates new generics, unlike the fixed-weight Laspeyres.

If one disaggregates even further to within brands and within generics, for the branded SSRIs, TCAs, and others, Laspeyres-Divisia differences are modest, but for the generic TCAs, these differences are larger in Cycle B (-6.81 percent compared with -10.72 percent) and enormous in Cycle C (-5.57 percent compared with -22.30 percent).

It is also interesting to note that during Cycles B and C, the oldest branded products, the MAOIs, generally have larger Divisia price increases than the younger TCAs, which in turn have larger price increases than the most recent SSRIs. This age-price pattern is consistent with the product life cycle pricing results reported by Berndt, Griliches, and Rosett for all branded prescription products.⁶⁰

Finally, no matter what index procedure is employed, the prices of generic products clearly have been declining throughout the sixteen years and, as measured by Divisia indexes, the rate of decline has sharply accelerated over time.⁶¹

Empirical Evidence: Effect of Linking Generics to Brands

We now consider effects of linking generic prices to their branded versions, rather than following the old BLS procedure of not linking them at all. There are at least three ways to introduce a link between generics and their patented antecedents. In what we call the “FDA Average Price Procedure,” generics and branded versions of the same chemical entity are treated as perfect substitutes, and the average price of the entity is simply a current-month weighted average of generic and branded versions. An alternative is to assume that preferences for brandedness are uniformly distributed and then to adjust for diffusion using equation 3. We call this the Griliches-Cockburn adjusted “Paasche Diffusion” method (GCPD). Finally, we mimic the new procedure recently adopted by the BLS, in which the Laspeyres fixed branded weight is split into a 64.2 percent generic component and a 35.8 percent branded component upon initial generic entry and is fixed thereafter; we call this the “New BLS Procedure with Fixed Split

60. Berndt, Griliches, and Rosett (1993).

61. An implication is that private sector price indexes based only on brand prices, such as the PRIME index published by the National Association of Chain Drug Stores (1995), are likely to overstate price inflation significantly.

Table 5. Average Annual Growth Rates of Price Indexes that Link Generics to Their Patented Antecedents

Percentage				
	<i>Entire Period</i>	<i>Cycle A</i>	<i>Cycle B</i>	<i>Cycle C</i>
<i>Procedure</i>	<i>1980:1– 1996:2</i>	<i>1981:12– 1987:12</i>	<i>1987:12– 1993:12</i>	<i>1993:12– 1996:2</i>
All drugs, no link:				
Paasche	7.11	9.87	7.45	2.29
Divisia	7.51	10.35	7.90	2.34
Laspeyres	5.04	9.35	4.17	0.42
FDA Average Price Procedure				
All with generics	–2.98	5.33	–6.49	–17.22
All drugs linked	2.95	5.71	1.33	1.10
Griliches-Cockburn Adjusted Paasche Diffusion Procedure				
All with generics	0.96	6.97	0.42	–12.68
All drugs linked	4.73	7.08	4.44	1.69
New BLS procedure with fixed split generic/brand weights				
All with generics	2.69	7.18	1.97	–4.15
All drugs linked	3.71	7.41	2.49	0.42

Source: Authors' calculations; see text for explanation.

Generic-Brand Weights.⁶² AAGRs based on these three linking procedures are given in table 5. In each panel we report AAGRs of price indexes where generics have been linked to their patented antecedents, first for the subset of drugs that experienced generic entry and then for all the drugs in the IMS antidepressant universe with generic versions. For purposes of comparison, at the top of table 5, we give AAGRs for Paasche, Divisia, and Laspeyres indexes with generics not linked in at all.

Of particular interest is the effect that linking in generics has on growth of the overall antidepressant drug price index, and how this effect varies among the three alternative methods. When generics are linked in using the FDA Average Price Procedure, AAGRs are affected

62. New generics are introduced within cycles with split weights, with the brand portion retaining the base price of the brand and with the generic portion having as its base price the price of the brand in the time period prior to entry date.

dramatically, and the overall price index grows less than half as fast as it does when no attempts are made to link in generics. In particular, during the entire sixteen-year period, the generic-linked AAGR grows at only 2.95 percent, compared with 7.11 percent for the unlinked Paasche index or 7.51 percent for the unlinked Divisia index. This difference is particularly large during Cycle B when considerable generic entry occurs, with the linked AAGR being 1.33 percent, dramatically lower than the unlinked Paasche (7.45 percent) or unlinked Divisia (7.90 percent); during Cycle C they are somewhat closer at 1.10 percent, compared with 2.29 percent and 2.34 percent.

Even under the more conservative GCPD “split-the-difference” assumptions, the impact on aggregate growth rates of linking in the generic drugs is very substantial. As seen in table 5, AAGRs are about a third lower than they are in the unlinked indexes. Specifically, for the sixteen years, the generic linked price index grows at 4.73 percent, compared with 7.11 percent for the unlinked Paasche index and 7.51 percent for the unlinked Divisia index; again the difference is largest during Cycle B, still large in Cycle A, and smallest in Cycle C.

Finally, when we mimic the new BLS procedure of splitting the Laspeyres fixed weight into 64.2 percent generic and 35.8 percent brand components following generic entry, we obtain results that generally yield an impact in between the FDA and GCPD procedures; the all-drug linked index has an AAGR over the sixteen years of 3.71 percent. Had the BLS implemented the procedures it will now employ, the fixed-weight Laspeyres AAGR would have been only 2.49 percent for the IMS universe of antidepressant drugs during Cycle B, substantially lower than the published 10.40 percent based on the BLS sample (which entirely neglected generics).

These results dramatically illustrate that the old BLS policy of not linking prices of newly introduced generic goods to the prices of their branded predecessors exerted a very substantial upward bias on the overall price index for antidepressant drugs. The effects of the new BLS procedure, beginning in January 1996, might well be expected to result in lower measured rates of price inflation, all else being equal, although the magnitude of this effect will depend on which products will lose their patent protection and how important they are. It is worth noting that in the antidepressant market, no drugs are currently scheduled to lose U.S. patent protection before the year 2000.

Empirical Evidence: Hedonic Regressions

As we noted earlier, differences in the efficacy rates among the various antidepressant drugs are statistically insignificant, but the side-effect and adverse interaction profiles vary considerably, with the newer generations of drugs generally having superior characteristics; these side-effect profiles were summarized in table 1. To capture and quantify these quality improvements over time, we have undertaken a hedonic price analysis. The results we report here represent ongoing research.

As the dependent variable in the hedonic regression, we compute for each of the branded drugs in our sample the monthly price per daily dose equivalent for the period 1980:1 to 1996:2; this price is not the same as a Laspeyres, Paasche, or Divisia index, for those indexes do not provide absolute comparisons across drugs. Because their characteristics are so different from other antidepressant drugs and their market shares are so small (less than 1.5 percent), the MAOIs are excluded from the sample of branded drugs. That leaves up to nineteen branded drugs in any one month and a total of 2,478 observations.

The specification of attributes or characteristics in hedonic price equations is always somewhat problematic, and that is the case here as well. Considerable collinearity frequently occurs among possible attributes, which is to be expected in this case because of the biological and chemical relationships. Another specification issue is that knowledge about the attributes of drugs diffuses at different rates even though these attributes are relatively constant (indeed, here we have them fixed over time). Further, how one scales attributes such as drug side-effect profiles is not without ambiguity, because frequency and severity are not necessarily related.⁶³

Given these difficulties, we have chosen to pursue a relatively simple and parsimonious specification, in which we regress the logarithm of the price of the i^{th} antidepressant drug in month t on a constant, on 193 monthly time dummies (that for 1980:1 is omitted), and on several attribute measures that proxy for quality. We consider six quality attributes, whose values are given in table 1: *HALF* (mean half-life of elimination, measured in hours), *DR* (a drowsiness side effect, scaled zero for rare and four if frequent), *AC* (anticholinergic side effects,

63. For an extended discussion of related issues in the specification of hedonic equations for antihypertensive drugs, see Berndt and Finkelstein (1992).

zero to four), *GI* (gastrointestinal side effects, zero to four), and *WTG* (weight gain greater than six kilograms, zero to four). When greater frequency of occurrence of an attribute such as anticholinergic side effects is usually considered as being undesirable, we expect the corresponding hedonic price coefficient to be negative. Our specification also includes dummy variables *GEN* for whether the brand faced competition from generics, and *OCD* if the FDA had also approved the antidepressant drug for treatment of obsessive-compulsive disorders.

Estimation by ordinary least squares (OLS) yielded the following equation, with heteroskedasticity-robust standard errors in parentheses:

$$\begin{aligned} \ln P_{it} = & -0.217 + \text{time dummies} + 0.245 \cdot \textit{GEN} - 0.005 \cdot \textit{HALF} \\ & (0.089) \qquad\qquad\qquad (0.014) \qquad\qquad\qquad (0.0002) \\ & + 0.577 \cdot \textit{OCD} + 0.056 \cdot \textit{DR} - 0.056 \cdot \textit{AC} - 0.069 \cdot \textit{GI} \\ & (0.027) \qquad\qquad (0.006) \qquad\qquad (0.006) \qquad\qquad (0.007) \\ & - 0.277 \cdot \textit{WTG}, R^2 = 0.8489. \\ & (0.008) \end{aligned}$$

Estimation with a random effects variance components specification yielded same-signed coefficient estimates, but generally larger standard errors:⁶⁴

$$\begin{aligned} \ln P_{it} = & -0.391 + \text{time dummies} + 0.125 \cdot \textit{GEN} - 0.002 \cdot \textit{HALF} \\ & (0.155) \qquad\qquad\qquad (0.010) \qquad\qquad\qquad (0.002) \\ & + 0.312 \cdot \textit{OCD} + 0.064 \cdot \textit{DR} - 0.012 \cdot \textit{AC} - 0.130 \cdot \textit{GI} \\ & (0.169) \qquad\qquad (0.050) \qquad\qquad (0.081) \qquad\qquad (0.053) \\ & - 0.191 \cdot \textit{WTG}. \\ & (0.060) \end{aligned}$$

Several results are worth noting. Consistent with previous findings, all else being equal, branded products have higher prices after facing generic competition; here this effect is estimated at between 12 percent and 24 percent. The *a priori* expectation on the sign of *HALF* is ambiguous, for short half-life is beneficial to those experiencing serious side effects or adverse interactions, but longer half-life may be preferable for those who might forget to take medication, such as the elderly.

64. Note that fixed-effect estimation is not feasible, because the quality attributes are fixed over time for each drug.

In this market, the estimated impact is negative, but it has statistical significance only with the OLS estimates. The estimated parameter on *OCD* is positive and substantial but of marginal statistical significance in the random effects estimation. The *a priori* expectation on the sign of drowsiness is ambiguous, for a considerable number of depressed patients with an acute episode initially experience insomnia, and thus for them the *DR* side effect is beneficial; for others, however, it may be unwanted. The 0.06 positive estimates here suggest that *DR* is, on balance, valued as beneficial in the marketplace.

The *a priori* sign expectation on the remaining three attributes is clearer, and in each case both OLS and random effects parameter estimates are negative as expected. Specifically, more frequent anticholinergic side effects (such as dry mouth, constipation, urinary hesitance, and blurred vision), gastrointestinal impacts, and substantial weight gain are each perceived as negative attributes in the antidepressant marketplace. The estimated impact of *WTG* is particularly large and significant.

With these estimated hedonic price equations relating prices of antidepressant drugs to their quality attributes and time, we have the building blocks necessary to construct a price index that links in quality change.

Changing Weights, Hedonic Adjustments for Nonpriced Quality Change, and Linking Generic Products: Results from a Merged Analysis

As noted earlier, one way to link nonpriced quality improvements into a price index is to use as an approximation to the reservation price the predicted price of a product just before its market introduction, based on the estimated hedonic price equation. This predicted price is then linked to the actual launch price of the new product.

When the new product is priced above (below) its estimated hedonic quality at launch, then the hedonic residual in that month will be positive (negative), and the hedonic quality-adjusted linked price index will grow at a greater (lesser) rate than the unlinked index. This implies that residuals from estimated hedonic price equations have an important impact, for they are a measure of unpriced quality change. In our sample of ten new products, the launch period OLS hedonic residuals of six

Table 6. Effects of Simultaneously Linking Generics and New Products—Average Annual Growth Rates of Price Indexes

Percentage				
<i>Index number procedure</i>	<i>Entire period 1980:1–1996:2</i>	<i>Cycle A 1981:12–1987:12</i>	<i>Cycle B 1987:12–1993:12</i>	<i>Cycle C 1993:12–1996:2</i>
Paasche—all (no link)	7.11	9.87	7.45	2.29
Paasche—all (GCPD link, no hedonics)	4.73	7.08	4.44	1.69
Paasche—all (GCPD link and hedonics)	4.33	7.08	3.99	0.52

Source: Authors' calculations; see text for explanation.

antidepressants turned out to be negative: -0.22 for Asendin, -0.63 for Luvox, -0.62 for Wellbutrin, -0.31 for Effexor, -0.45 for Zoloft, and -0.07 for Serzone. With four new products, however, the launch period residuals were positive: 0.03 for Ludiomil, 0.05 for Prozac, 0.21 for Paxil, and 0.08 for Anafranil.⁶⁵ Interestingly, while signs of residuals were equally mixed for products introduced during Cycle B, in Cycle C all three of the new products had negative residuals (that is, positive nonpriced quality improvements).

Using these predicted prices and residuals, we have computed a Paasche aggregate price index over all drugs, simultaneously linking in the generics using the GCPD method and accounting for nonpriced quality differentials at launch month for the new products; as quantity weights for new goods in this merged index, for the first three months in the market, we employ the average over those three months. Results are summarized in table 6.

The net effect of our estimated nonzero residuals on the growth of the aggregate Paasche price index depends, of course, on the quantity and price growth paths of all ten new products; note that six new products had negative residuals while four had positive ones at launch date, and that all three of the new products introduced during Cycle C had negative residuals. As seen in table 6, for the entire 1980:1–1996:2 time period, the hedonic-adjusted AAGR is four-tenths of a percentage

65. These residuals are based on the random effects model. Similar findings resulted from OLS estimates, as well as from other specifications involving alternative quality attribute measures.

point less than one not incorporating hedonic quality adjustments (4.33 percent, compared with 4.73 percent). Because no new products were introduced during Cycle A, the hedonic-adjusted and unadjusted AAGRs are identical at 7.08 percent. Although the AAGR of the hedonic-adjusted price index is about half a percentage point smaller during Cycle B (3.99 percent, compared with 4.44 percent), during Cycle C the AAGR of the hedonic-adjusted price index lags more than a percentage point behind the index not adjusted for quality (0.52 percent, compared with 1.69 percent). Thus, somewhat surprisingly, linking in generics has a much more substantial effect on AAGRs of price indexes during Cycle B, when generic entry was substantial, than does accounting for estimated nonpriced quality differentials. In Cycle C, however, the hedonic adjustment results in a larger price decline than does the linking in of generics.

Discussion

This detailed audit of the IMS universe of antidepressant drug prices reveals substantial differences between the AAGRs of the published BLS price indexes and those computed in a variety of alternative ways. We now define our “audited” price index with generics linked in using the GCPD procedure, hedonic nonpriced quality changes included, chained Paasche weights, and the IMS universe of antidepressants as the data base. As the bottom line of table 7 shows, during Cycle B this audited price index grows at an AAGR of 3.99 percent, whereas the published BLS PPI has an AAGR of 10.40 percent. For Cycle C, the audited price index has an AAGR of 0.52 percent, much smaller than the 4.27 percent AAGR of the published BLS index. In both periods, the BLS index overstates price inflation by a very substantial amount. It is useful to summarize the sources of these differences in growth rates, which we do in tabular form in table 7.

The first source of differences concerns sample representativeness of the fixed weights. If we employ the BLS Laspeyres fixed-weight procedures, but instead of utilizing the BLS item sample, we use the IMS universe of drugs, we obtain results given in the second row of table 7. The difference is very large during both Cycles B and C and, as noted earlier, reflects the fact that universe item weights set at 1987:12 and

Table 7. Explaining Differences in Average Annual Growth Rates of Prices for Antidepressant Drugs

<i>Procedure</i>	<i>Entire period 1980:1–1996:2</i>	<i>Cycle A 1981:12–1987:12</i>	<i>Cycle B 1987:12–1993:12</i>	<i>Cycle C 1993:12–1996:2</i>
BLS index	NA	NA	10.40	4.27
Sampling procedures				
Sample vs. universe weights	5.04	9.35	4.17	0.42
Weights				
Divisia—chained	7.51	10.35	7.90	2.34
Paasche—chained	7.11	9.87	7.45	2.29
Laspeyres—fixed	5.04	9.35	4.17	0.42
Laspeyres—chained	7.88	10.83	8.24	2.38
Linking generics				
FDA average price	2.95	5.71	1.33	1.10
GCPD	4.73	7.08	4.44	1.69
New BLS	3.71	7.41	2.49	0.42
Linking generics and hedonics				
GCPD	4.33	7.08	3.99	0.52

Source: Authors' calculations; see text for explanation.

1993:12 would subsequently overweight generics whose prices were falling, and underweight brands whose prices were increasing. More frequent supplemental sampling could help to reduce this discrepancy, although issues concerning Puerto Rican production would still remain.⁶⁶

The second source of differences involves whether fixed or changing weights are used. As shown in the third panel in table 7, if one uses the Divisia or Paasche index, based on monthly updates instead of the relatively fixed-weight Laspeyres (changed only every six years), over the IMS universe of drugs, the AAGR rises from 3.3 to 3.7 percentage points during Cycle B, and about 1.9 percentage points during Cycle C. Weights are very important.

Obtaining data necessary to update weights more frequently is of course possible, but not without costs. To obtain some evidence on the possible benefits of updating weights more frequently, we have calculated AAGRs of Laspeyres price indexes over the IMS universe of products when, like that for the chained Divisia and Paasche, the weights are updated monthly. As seen in the bottom row of the middle panel in table 7, when Laspeyres weights are chained on a monthly basis, AAGRs are very close but slightly larger than those of the Divisia—7.88 percent, compared with 7.51 percent over the entire period. Thus what is empirically significant is failure to update weights more frequently, rather than choice of index number formula.⁶⁷

A third source of differences concerns the linking of generics to their patented antecedents. As shown in the fourth panel of table 7, the effects of linking are substantial. Over the last sixteen years, the AAGR using the FDA procedure is more than four percentage points less than that of a comparable Paasche index that does not link in generics (2.95 percent, compared with 7.11 percent). During the same period, the effect of the new BLS procedure is only slightly smaller (3.71 percent, compared with 7.11 percent). During Cycle B the new linked procedure would have generated a price series that grew at 2.49 percent a year, almost eight percentage points slower than its published fixed-weight Laspeyres (10.40 percent). Because patents on SSRI drugs in the United

66. See footnote 47.

67. IMS America and the PRIME Institute construct aggregate price indexes that they distribute to clients; these indexes use Laspeyres index number procedures with weights updated each year, but generic products are not linked to predecessor brands.

States all expire after the year 2000, the new BLS policy that links in generics will not have any measurable impact in this therapeutic class for some time, but in other therapeutic classes where patent expiration and generic entry is more extensive, the effects could be considerable.

The fourth and final source of differences involves nonpriced quality differentials embodied in new goods. As shown in the bottom panel of table 7, during Cycle B nonpriced quality results in a modest difference (less than half a percentage point for the GCPD), but during Cycle C the effect of accounting for nonpriced quality becomes quite substantial (the AAGR is 1.2 percentage points less than the GCPD index). Although accounting for nonpriced quality change plays a significant moderating role in the growth of prices in the market for antidepressant drugs, the impact is smaller than that in other high-tech markets. For example, in the personal computer market the price of a typical model has been about \$2,500 for more than a decade, but that \$2,500 now buys much more performance in an ever smaller footprint. As has been shown elsewhere, quality-adjusted personal computer prices decline at almost 30 percent a year, more than double that for price indexes not adjusted for quality change.⁶⁸

Conclusions and Issues for Further Research

The market for antidepressant drugs is dynamic. Of the twenty-one entities on the market in 1996, eight are entirely new, having been introduced to the market within the last decade, and an additional seven brands have experienced new generic competition following patent expiration.

Tracking prices and then constructing aggregate price indexes for such a rapidly changing marketplace are challenging tasks, particularly for statistical agencies such as the BLS whose resources are tightening. In this paper we have audited the reliability of the BLS producer price index in an admittedly dynamic market that presents enormous measurement challenges. We find major differences between the published BLS numbers and the results we obtain from our audit; in both Cycles

68. For further discussion, see Berndt and Griliches (1993) and Berndt, Griliches, and Rappaport (1995).

B and C, audited growth rates are less than half those published by the BLS.

Of the four sources of difference that we have examined in detail, one—nonpriced quality changes embodied in new goods—plays a modest to significant role depending on the time period, and another—the linking of new generic products to their patented antecedents—is one on which the BLS has just recently announced a major policy change. The other two sources of differences (nonrepresentative sampling, and use of fixed-weight formulas) could be addressed by the BLS obtaining more frequent (and more costly) information, and using this data to update its weights more often.

Concerning sample representativeness, one issue that merits greater attention is the treatment of production from Puerto Rico. In some of the national accounts, national production includes Puerto Rico; in others such production is excluded. For pharmaceuticals, this issue is significant because Puerto Rican pharmaceutical production is roughly a fifth to a quarter of that from the U.S. mainland. If Puerto Rico is to be excluded, as is now the case for the antidepressant PPI, then to the extent public policy analysts and others seek to track the price growth emanating from U.S. producers (many of whom choose to produce significantly in Puerto Rico), it will be necessary to collect and publish “import” price series from Puerto Rico, and then to combine those data with the more narrowly defined “domestic” mainland price series.⁶⁹

In this paper we have examined alternative measures of price growth, but we have not addressed the reasons underlying this price growth, nor have we attempted to model quantities sold by manufacturer and the remarkable growth of the entire therapeutic class. It is worth emphasizing that the measures of price growth presented here are not purported to be closely related to measures of economic welfare and consumers’ surplus. There is reason to believe that measures of price growth employing predicted prices from estimated hedonic price equations could differ considerably from exact price indexes that employ

69. One incentive for Puerto Rican production has been Section 936 of the Internal Revenue Code, which has provided tax benefits to firms producing in Puerto Rico. It is worth noting that under the 1996 federal minimum wage bill, these tax incentives will be phased out over the next decade.

reservation prices based on estimated structural demand models.⁷⁰ Pakes has argued that under a plausible set of conditions, the hedonic-based prices provide an upper bound to growth of an exact price index.⁷¹ It is worth noting that innovations providing new varieties of a product such as antidepressant drugs have an unambiguous beneficial welfare implication in that consumers are given the choice of another product, one that may “work” for them, while others have not.

Although our analysis here has been confined to the market for antidepressant drugs, our results on the importance of linking generics to their patented antecedents may have implications for nonpharmaceutical markets. For example, in the consumer electronics industries, new products from branded manufacturers typically embody quality improvements; these manufacturers subsequently often sell a virtually identical product under a private label or “knock-off” brand at a much lower price.⁷² To the extent that such lower-priced versions are not linked to branded antecedents, the price indexes will fail to incorporate these implicit price declines realized by some consumers.

Our research could be extended in a number of ways. First, our data is from the IMS, and it would be useful to compare the IMS price data with actual transactions data from the pharmaceutical manufacturers, although our earlier research on this issue did not reveal any systematic differences.⁷³ Second, as implied earlier, it would be informative to model much more completely the diffusion process of antidepressant drugs, both over time and among different market segments, such as drugstores and managed care organizations. It would also be useful to assess how the various price indexes change when the frequency of the data is reduced from monthly to quarterly. Third, we have examined here only the drug component for the treatment of depression, entirely ignoring “substitutable” inputs such as talk therapy. Assessing the effects of the new generation of SSRIs, along with increased pressures of cost containment, on the changing mix of drug and talk therapy in the overall treatment of depression is a most interesting avenue for future research.

70. For discussion, see Triplett (1983).

71. Pakes (1996).

72. Several other examples of this brand-generic phenomenon are discussed in De-neckere-McAfee (1996).

73. Berndt, Griliches, and Rosett (1993), and Berndt and Greenberg (1996).

References

- Advisory Commission To Study the Consumer Price Index. 1996. *Toward a More Accurate Measure of the Cost of Living*. Final report to the Senate Finance Committee. Washington, D.C. December 4.
- American Medical Association. 1991. "Drugs Used in Mood Disorders." *Drug Evaluations*, 7th ed.
- American Psychiatric Association, Committee on Nomenclature and Statistics. 1968. *Diagnostic and Statistical Manual of Mental Disorders*, 2d ed. Washington, D.C.
- American Psychiatric Association, Task Force on Nomenclature and Statistics. 1980. *Diagnostic and Statistical Manual of Mental Disorders*, 3d ed. Washington, D.C.
- American Psychiatric Association. 1987. *Diagnostic and Statistical Manual of Mental Disorders: DSM-III-R*, 3d ed. rev. Washington, D.C.
- . 1993. "Practice Guidelines for Major Depressive Disorder in Adults." *American Journal of Psychiatry* 150 (4, April, Supplement): 1–26.
- Baldessarini, Ross J. 1990. "Drugs and the Treatment of Psychiatric Disorders." In *The Pharmacological Basis of Therapeutics*, edited by Alfred Goodman Gilman and others, 383–435. 8th ed. New York: Pergamon Press.
- Berndt, Ernst R., and Paul E. Greenberg. 1996. "An Updated and Extended Study of the Price Growth of Prescription Pharmaceutical Preparations." In *Competitive Strategies in the Pharmaceutical Industry*, edited by Robert B. Helms, 35–48. Washington, D.C.: American Enterprise Institute.
- Berndt, Ernst R., Richard G. Frank, and Thomas G. McGuire. forthcoming. "Alternative Insurance Arrangements and the Treatment of Depression." *American Journal of Managed Care*.
- Berndt, Ernst R., and Stan N. Finkelstein. 1992. "Price Indexes for Anti-Hypertensive Drugs that Incorporate Quality Change: A Progress Report on a Feasibility Study." Unpublished working paper 6-92. MIT Program on the Pharmaceutical Industry, Cambridge, Mass. December.
- Berndt, Ernst R., and Zvi Griliches. 1993. "Price Indexes for Microcomputers: An Exploratory Study." In *Price Measurements and Their Uses*, edited by Murray F. Foss, Marilyn E. Manser, and Allan H. Young, 63–93. University of Chicago Press for the National Bureau of Economic Research.
- Berndt, Ernst R., Zvi Griliches, and Joshua G. Rosett. 1993. "Auditing the Producer Price Index: Micro Evidence from Prescription Pharmaceutical Preparations." *Journal of Business and Economic Statistics* 11 (3, July): 251–64.
- Berndt, Ernst R., Zvi Griliches, and Neal J. Rappaport. 1995. "Econometric Estimates of Price Indexes for Personal Computers in the 1990's." *Journal of Econometrics* 68 (1, July): 243–68.

- Bureau of the Census, U. S. Department of Commerce. 1992. *1992 Census of Manufactures, Industry Series Drugs*. MC92-I-28C. Washington, D.C.
- . 1994. *1992 Economic Census of Outlying Areas, Industry Statistics—Puerto Rico*. Washington, D.C.
- Bureau of Economic Analysis, U.S. Department of Commerce. 1985a. “Business Situation.” *Survey of Current Business* 65 (10, October): 1–7.
- . 1985b. “Revised Estimates of the National Income and Product Accounts of the United States, 1929–85: An Introduction.” *Survey of Current Business* 65 (12, December): 1–19.
- . 1987. “Foreign Transactions.” In *Methodology Papers: U.S. National Income and Product Accounts*. Washington, D.C. May.
- Bureau of Labor Statistics, U.S. Department of Labor. 1996. *Producer Price Indexes: Data for January 1996*. Washington, D.C. June.
- Caves, Richard E., Michael D. Whinston, and Mark A. Hurwitz. 1991. “Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry.” *Brookings Papers on Economic Activity, Microeconomics:1*. 1–48.
- Cleaton, David L., Valy T. Goepfrich, and Burton A. Weisbrod. 1992. “What Does the Consumer Price Index for Prescription Drugs Really Measure?” *Health Care Financing Review* 13 (3, Spring): 45–51.
- Deneckere, Raymond J., and R. Preston McAfee. 1996. “Damaged Goods.” *Journal of Economics and Management Strategy* 5 (2, Summer): 149–74.
- Depression Guideline Panel. 1993. *Depression in Primary Care. Vol. 2: Treatment of Major Depression*. Clinical Practice Guideline, No. 5, Rockville, Md.: U. S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication 93-0551.
- Early, John F., and James H. Sinclair. 1983. “Quality Adjustment in the Producer Price Increases.” In *The U.S. National Income and Product Accounts: Selected Topics*, edited by Murray F. Foss. Studies in Income and Wealth, vol. 47. University of Chicago Press for the National Bureau of Economic Research.
- Eisenberg, Leon. 1992. “Treating Depression and Anxiety in Primary Care: Closing the Gap Between Knowledge and Practice.” *New England Journal of Medicine* 326 (April 16): 1080–84.
- Elkin, Irene, Morris B. Parloff, and others. 1985. “NIMH Treatment of Depression Collaborative Research Program.” *Archives of General Psychiatry* 42 (March): 305–16.
- Elkin, Irene, Tracie Shea, and others. 1989. “National Institute of Mental Health Treatment of Depression Collaborative Research Program: General Effectiveness of Treatments.” *Archives of General Psychiatry* 46 (November): 971–83.
- Fisher, Franklin M., and Karl Shell. 1971. “Taste and Quality Change in the

- Pure Theory of the True-Cost-of-Living Index.” In *Price Indexes and Quality Change: Studies in New Methods of Measurement*, edited by Zvi Griliches, 16–54. Harvard University Press.
- . 1972. *The Economic Theory of Price Indices: Two Essays on the Effects of Taste Quality and Technological Change*. New York: Academic Press.
- Fisher, Franklin M., and Zvi Griliches. 1995. “Aggregate Price Indices, New Goods, and Generics.” *Quarterly Journal of Economics* 110 (1, February): 229–44.
- Food and Drug Administration. annual. *Approved Drug Products with Therapeutic Equivalence Evaluations* (“The Orange Book”). Washington, D.C.: U.S. Department of Health and Human Services, Public Health Service, Center for Drug Evaluation and Research, Office of Management.
- Frank, Richard G., and David S. Salkever. 1992. “Pricing, Patent Loss, and the Market for Pharmaceuticals.” *Southern Economic Journal* 59 (2, October): 165–79.
- Frank, Richard G., and Willard G. Manning, Jr. 1992. *Economics and Mental Health*. Johns Hopkins University Press.
- Grabowski, Henry G., and John M. Vernon. 1992. “Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act.” *Journal of Law and Economics* 35 (2, October): 331–50.
- Greenberg, Paul E., Laura E. Stiglin, and others. 1993. “The Economic Burden of Depression in 1990.” *Journal of Clinical Psychiatry* 54 (11, November): 405–18.
- Greenberg, Paul E., Ronald C. Kessler, and others. 1996. “Depression in the Workplace: An Economic Perspective.” In *Selective Serotonin Reuptake Inhibitors: Advances in Basic Research and Clinical Practice*, edited by J. P. Feighner and W. F. Boyers, 321–58. 2d ed. Chichester, U.K.: John Wiley and Sons.
- Griliches, Zvi, ed. 1971. *Price Indexes and Quality Change: Studies in New Methods of Measurement*. Harvard University Press.
- . 1990. “Hedonic Price Indexes and the Measurement of Capital and Productivity: Some Historical Reflections.” In *Fifty Years of Economic Measurement: The Jubilee of the Conference on Research in Income and Wealth*, edited by Ernst R. Berndt and Jack E. Triplett. NBER Studies in Income and Wealth, vol. 54. University of Chicago Press for the National Bureau of Economic Research.
- Griliches, Zvi, and Iain Cockburn. 1994. “Generics and New Goods in Pharmaceutical Price Indexes.” *American Economic Review* 84 (5, December): 1213–32.
- Hicks, John R. 1940. “The Valuation of Social Income.” *Economica* 7 (26, May): 105–24.

- Hurwitz, Mark A., and Richard E. Caves. 1988. "Persuasion or Information: Promotion and the Shares of Brand Name and Generic Pharmaceuticals." *Journal of Law and Economics* 31 (October): 299–320.
- Hyman, Steven E., George W. Arana, and Jerrold F. Rosenbaum. 1995. *Handbook of Psychiatric Drug Therapy*, 3d ed. Little, Brown and Company.
- IMS America. 1993. *National Disease and Therapeutic Index—Drugs, July 1993–June 1994*. Plymouth Meeting, Pa.
- . 1996a. *National Disease and Therapeutic Index—Disease, July 1995–June 1996*. Plymouth Meeting, Pa.
- . 1996b. *Information Services Manual*. Plymouth Meeting, Pa.
- Jonsson, B., and J. Rosenbaum. 1993. *Health Economics of Depression*. Vol. 4: *Perspectives in Psychiatry*. Chichester, U.K.: John Wiley & Sons.
- Kanoza, Douglas. 1996. "Supplemental Sampling in the PPI Pharmaceuticals Index." *Producer Price Indexes Detailed Price Report* (January): 8–10.
- Katon, Wayne, and others. 1992. "Adequacy and Duration of Antidepressant Treatment in Primary Care." *Medical Care* 30 (January): 67–76.
- Keith, Alison M., and Ernst R. Berndt. 1994. "A Primer on Issues in the Measurement of Price Change and Price Impact: An Application to Pharmaceuticals." Working Paper 25-94. MIT Program on the Pharmaceutical Industry, Cambridge, Mass. September.
- Masson, Alison, and Robert L. Steiner. 1985. *Generic Substitution and Prescription Prices: Economic Effects of State Drug Product Selection Laws*. Washington, D.C.: Federal Trade Commission, Bureau of Economics.
- National Association of Chain Drug Stores. 1995. "NACDS PRIME Index Reports Increases in Prices for Top 500 Prescriptions Dispensed in Community Pharmacies." News release, Alexandria, Va., December 7.
- Nolen-Hoeksema, Susan. 1990. *Sex Differences in Depression*. Stanford University Press.
- Pakes, Ariel. 1996. "Hedonic Bounds to Exact Price Indexes." Unpublished draft manuscript. Yale University, Department of Economics. May.
- Papoulos, Demetri F., and Janic Papoulos. 1992. *Overcoming Depression*, rev. ed. Harper Collins Publishers.
- Physicians' Desk Reference Generics*. 1996. 2d ed. Montvale, N.J.: Medical Economics Company.
- Potter, William Z., Matthew V. Rudorfer, and Husseini Manji. 1991. "Drug Therapy: The Pharmacologic Treatment of Depression." *New England Journal of Medicine* 325 (9, August 29): 633–42.
- Regier, Darrel A., and others. 1988. "The NIMH Depression Awareness, Recognition, and Treatment Program: Structure, Aims, and Scientific Basis." *American Journal of Psychiatry* 145 (November): 1351–57.
- Rothbarth, Erwin. 1940–41. "The Measurement of Change in Real Income under Conditions of Rationing." *Review of Economic Studies* 8 (2): 100–7.

- Suslow, Valerie Y. 1996. "Measuring Quality Change in the Market for Anti-Ulcer Drugs." In *Competitive Strategies in the Pharmaceutical Industry*, edited by Robert B. Helms. Washington, D.C.: American Enterprise Institute.
- Triplett, Jack E. 1983. "Concepts of Quality in Input and Output Price Measures: A Resolution of the User-Value Resource-Cost Debate." In *The U.S. National Income and Product Accounts: Selected Topics*, edited by Murray F. Foss. University of Chicago Press for the National Bureau of Economic Research.
- Turkington, Carol Ann, and Eliot F. Kaplan. 1994. *Making the Prozac Decision: Your Guide To Antidepressants*. Los Angeles: Lowell House.
- U. S. General Accounting Office. 1996. *Consumer Price Index: Cost-of-Living Concepts and the Housing and Medical Care Components*. Report to the Ranking Minority Member, Committee on Banking and Financial Services, House of Representatives, GAO/GGD-96-166. Washington, D.C. August.

Comments

Comment by Theodore E. Keeler: This is an interesting paper with important and worthwhile contributions. Many complain about rapidly rising costs in the health care sector, yet because of the complexity of the product and changes in technology and product quality, it is especially difficult to determine whether these rapid cost increases stem from higher prices, higher quantities, or quality improvements. The present paper adds valuable insight into this area.

The results are of special interest in that they indicate the importance of understanding the value of improved products and of reduced costs from generic products. The results show also the importance of quality change and represent innovative use of hedonic price indexes, and they represent a clear improvement over conventional BLS price indexes. Overall, then, I find much to agree with in this paper.

Nevertheless, I do have an area of concern: specifically, all the index number theory employed by the authors of this paper assumes that prices of each drug represent a consumer's marginal willingness to pay for those drugs. For many people, however, prescription drugs are paid for through health insurance, and the existence of moral hazard combined with reasonably generous health insurance policies can call into strong question the validity of the simple proposition that prices represent consumers' marginal willingness to pay for the relevant products. It is easy to see why a study such as this would abstract from the matter of moral hazard with insurance, because the likely effects are complicated, and the present study innovates in other directions.

Nevertheless, I believe it is worthwhile to try to understand something about these effects, because they are potentially important. Any-

thing near a complete or rigorous discussion of these effects are well beyond the scope of these comments and would be a paper in itself; my goal, instead, is to sketch very crudely and intuitively some likely effects of moral hazard for this analysis, suggesting, I hope, both the importance of the issue and the need for further research.

Moral Hazard and Pharmaceutical Price Indexes

Health insurance will likely exaggerate a consumer's apparent marginal willingness to pay for newer or more expensive drugs. Take the case that the authors make of the introduction of a generic substitute for an existing branded drug. Because the two drugs are therapeutically the same, one would expect patients to move in large numbers to the generic if the branded drug costs much more. In fact, that does not always happen. The authors of this paper and Griliches and Cockburn in an earlier (1994) article are puzzled slightly by the fact that even if the price of a branded drug is much more than that of the generic, the branded drug maintains much more market share than one might expect. I strongly believe that health insurance should explain at least some of that: if the patient pays only 10–20 percent of the difference in prices (or even less), then the patient might well prefer the branded product, if it is thought to be even modestly superior. A study that ignores this fact may tend to overstate consumers' true willingness to pay for more expensive products of any type.

To see this point from a slightly different perspective, consider the following grossly simplified case. Recall from the paper that one relatively accurate way to incorporate a new product into a price index is to include the reservation price of a "typical" consumer for the product just before it is introduced. BLS indexes are asserted to overstate increases in these prices in part because they fail to incorporate these relatively high reservation prices at the earliest time of introduction of the product.

Moral hazard may cause this estimated reservation price to be overstated, however. To see this, consider the effects of the introduction of a new (expensive) drug with the simplest (but most expensive) likely form of health insurance, that which simply reimburses the provider (doctor, drug store, hospital, and so on) a fixed percentage (often 75 to

80 percent) of total expenses (with no overall limitation on them), so that the patient makes a copayment of, say, 20 percent and the insurance company pays the rest. If, in fact, the consumer's willingness to pay per dose is \$1, then, with the introduction of insurance, the *observed* reservation price (including that observed in econometric studies such as are included in this paper) will be $\$1.00/0.2 = \5 —much higher than the real reservation price.

Any discussion of biases in an estimated index would have to deal with relative changes in prices over time, and real-world insurance is also more complicated—involving issues that go beyond my comments here. But it would seem quite possible that moral hazard could easily bias upward the estimate of a person's reservation price for a new drug, which could clearly affect calculations of price indexes.

To make our analysis more realistic, consider the case of two substitute drugs, a branded one and a new generic. Assume also that reservation price differentials are distributed among patients, so that some will switch to the generic at a low price differential, but others require a higher differential. This realistic situation is the one on which the authors have built up a new Paasche index of pharmaceutical prices. Once again, however, moral hazard could easily render the use of direct comparison of market prices inaccurate. Suppose that one particular consumer is observed to be willing to switch from the brand to the generic at a price difference of \$1 per daily dose (that is, if the brand costs \$2, the consumer will buy the generic only if its price falls to \$1 a dose). In reality, though, if insurance is covering 80 percent of the difference, the real reservation price differential is only 20 cents: observed market data will exaggerate the apparent willingness of the consumer to pay for the more expensive drug.

If this simplified view of reality is correct, it has clear implications: consumer preferences could easily be closer to the FDA approach of considering branded and generic drugs equivalent than the observed data would suggest. This view also implies that the coefficients in the hedonic price equations might well also overestimate the consumer's marginal willingness to pay to obtain the positive aspects of a drug, or to avoid the negative effects, relative to the consumer's true preferences. Why not buy expensive drugs with fewer side effects if insurance is paying for it?

*Theoretical and Empirical Validity of Moral Hazard in
Pharmaceuticals Consumption*

Most health economists are convinced that moral hazard is rampant in the fee-for-service part of the U.S. health care sector, but not everyone might agree. After all, people seem to want to buy health insurance—in some meaningful sense, maybe what their insurance pays is a measure of the value they attach to medical care. Where is the market failure? There are strong reasons to question that. First, the tax benefits accorded to employer-provided health care have historically tended to cause overprovision of it; second, during the 1960s and 1970s, Blue Cross and Blue Shield had a largely artificial monopoly on U.S. health insurance, and they represented the interests of the providers (doctors and hospitals) who controlled them.¹ For various reasons they endeavored to continue the existence of this type of fee-for-service indemnity insurance. The growth of managed care in the 1980s and 1990s is a sign that over the very long pull, the marketplace will not support this moral hazard (more about that below), and it is likely to be less important today than it was in 1980, the first year of the study.

In health care as a whole, there is ample evidence that American patients are indeed prone to moral hazard in a fee-for-service setting. This evidence is based not only on econometric studies, but also on a large, expensive, controlled experiment conducted by the RAND Corporation, in which a carefully selected sample of the population was given varying amounts of insurance, and the amount of health care then consumed was observed.²

There is, however, less evidence as to whether expenditures on pharmaceuticals (typically covered by insurance) are prone to moral hazard. One study, that of Sean Sullivan (1992), based on the elderly with and without pharmaceutical supplemental insurance to Medicare, provides strong evidence that patients are indeed responsive to pharmaceutical prices, and that moral hazard does exist in this area.³ Specifically, the

1. For a discussion of these forces in health insurance, see, for example, Feldstein (1993, pp. 149–69).

2. For a survey of the effects of moral hazard in health insurance on the demand for health care in general, see any good textbook in health economics, such as Feldstein (1993, pp. 74–105). For results of the RAND experiment, see Manning and others (1987).

3. Sullivan (1992).

study found that controlling for many other variables, patients with drug insurance spend 12.5 percent a year more on drugs than do patients without such insurance. Another recent study, however, found that insurance status of patients does not significantly affect whether the patient is prescribed a generic or brand drug, except that HMO patients are more likely to be prescribed generic drugs (see below).⁴ The data set, however, did not include basic variables such as drug prices. Rika Mortimer, a Ph.D. student at Berkeley, is currently investigating this very issue but has no results as yet.

Managed Care

Given the costs of moral hazard, it is reasonable to expect that the market would provide forms of insurance that avoid it. Health maintenance organizations (HMOs) clearly do have an incentive to use less expensive drugs and to avoid moral hazard. That is because they collect a fixed (capitation) fee per patient per unit of time, and the less they spend on health care, the more money they make. Empirical evidence indeed shows that patients in HMOs do indeed use generic drugs more than do patients using more conventional indemnity insurance with fee-for-service reimbursement.

This fact has implications for the authors' empirical work. Specifically, it implies that in years in which HMOs had a greater market penetration, the effects of moral hazard on their hedonic coefficients are likely to be weaker. The market share of HMOs has indeed grown from 1980 to the present.⁵ That means that the observed willingness to pay for various attributes (and hence the coefficients) may well have shifted substantially over time. It would seem to make sense to test for that possibility, but to keep in mind that this change may represent not changes in consumer preferences, but changes in insurance reimbursement.

4. Hellerstein (1994).

5. According to Oberlander (forthcoming), as of 1995, 58 percent of insured employees of firms with more than ten employees belonged to indemnity or PPO plans, whereas fully 42 percent belonged to HMOs or point-of-service plans. In 1994, 62 percent belonged to indemnity plans or PPOs. In contrast, in 1990 HMO penetration rates were only 15 percent or so. HMO penetration of Medicare is currently still minimal—only 10 percent of Medicare enrollees are enrolled in any form of managed care.

An Opposite Bias with Fee-for-Service Insurance

In the specific case of antidepressants, it is possible to find an example with fee-for-service reimbursement in which the techniques used by the authors might possibly *underestimate* the marginal willingness of consumers to pay for drugs. To see this, recall that talk therapy is often viewed as a substitute for drugs. Furthermore, talk therapy is quite expensive relative to many drugs (a once-a-week visit to a psychiatrist can average out to \$15 to \$20 a day—more than the cost of the daily dose of many drugs). If talk therapy were covered by insurance, patients might prefer a talk-intensive, drug-free (or drug-extensive) treatment. Conversely, consumers who have to pay out of their own pockets might instead prefer a drug-intensive treatment, with little talk therapy, even at relatively high drug prices. So elimination of moral hazard in mental health treatment could actually raise the willingness to pay for drugs relative to what is happening with insurance today. This might seem probable, given that, as the authors point out, HMOs often prefer to substitute drugs for talk therapy if they can, and HMOs may in some ways mimic health care consumers would choose in the absence of moral hazard. Even ten years ago, however, most indemnity and PPO (preferred provider option) insurance companies, even if they would reimburse most things on a fee-for-service basis, nevertheless tended to put tight restrictions on reimbursement for psychotherapy, because it was known to be especially prone to moral hazard. This means that the amount of moral hazard connected to talk therapy is likely to be limited in most standard insurance policies.

Obviously these comments only sketch a rough outline of some of the effects of health insurance on the authors' results. Nevertheless, I hope it is clear now why I believe that if we are to understand and interpret those results accurately, we need to better understand the implications of health insurance on pharmaceutical consumption and why further research in this direction is justified.

Comment by Martin Neil Baily: The general discussion of depression and its treatments in a historical setting I found very interesting. It is unusual to see such a section in an economics paper, but as a sometime macroeconomist, I found it refreshing to see human beings described with normal frailties and not just as maximizing robots.

Moving to the meat of the paper, I had trouble at the outset because the interpretation of a producer price index (PPI) for the ethical drug industry is problematic. The issue surfaces almost immediately when it is discovered that Prozac, a principal innovation in recent years, is not included in the sample because it is not manufactured in the United States. The true value added in the actual manufacture of drugs is small for most drugs, and the final price is determined by research and development costs, marketing, and profit. The ex-factory price of the drug is set by the company based in part on taxes and does not accurately reflect the contribution to value by the manufacturing process. Prozac and other drugs may be manufactured in Puerto Rico, but their value was created by research and development and marketing carried out in the United States or, possibly, overseas.

PPIs are often used in the calculation of real manufacturing output and hence productivity, which can create significant distortions. In the case of “foreign” manufacture, the value may be incorrectly attributed by country, but even when all of the value-added is created within the United States, there is misattribution by industry. This paper does not use the PPIs for that purpose, so I am not criticizing what they have done. But thinking about this problem made me realize how difficult it is to use PPIs for real output computations in a world where the non-manufacturing input to production is growing. Ethical drugs are at one end of a spectrum, but the same problem arises elsewhere. The value-added created by an auto or a machine tool plant depends heavily on the design and process engineering that is done elsewhere.

In this paper, the authors are essentially treating the PPI for antidepressants as an input into the consumer price index. The discussion of generics and the use of hedonic regressions all go in this direction, so I will simply accept that framework without further comment. The interesting issue then is how the BLS deals with generics and new products and how the results of what they do compare with approaches suggested by index number theory.

The authors deserve a lot of credit, as indeed they do for their previous work in this area, for pointing out some of the problems that exist in BLS procedures—in particular, the fixed market basket that delays the introduction of major new products and that delays recognition of changes in market shares. The authors also point to some odd quirks of the BLS sample, which apparently includes drugs that are not

antidepressants. They make some important points and add significantly to their earlier work.

Previous research, including work by Caves, Whinston, and Hurwitz reported in this journal, has shown that the prices of branded drugs increase when generics are introduced.⁶ Together with the fact that traditionally the BLS has handled generics by making them distinct new products, that implies that rapid entry of generics will result in an increase in drug prices. The Berndt, Cockburn, and Griliches paper is valuable in showing the inflation implications of the pattern of market behavior and index number methodology. The fact that the BLS has now changed its approach and is treating generics as identical products to the branded drugs makes the Berndt, Cockburn, and Griliches story less dramatic but is very welcome in terms of the accuracy of price indexes going forward. The authors' results showing how much difference the alternative approach would have made in the past are dramatic enough.

The results for new drugs led me to think about an argument that is made concerning the extent to which existing index number methods may capture innovation and new products. The argument holds that existing products have to compete with the new products and that in a perfectly competitive market, therefore, the price of the old products has to go down to reflect the entrance of the new products. In practice there are differentiated products in imperfect competition, and the entry of new products may change the elasticity of demand and cause the price of the existing products to rise. For example, CDs and CD players have largely driven out LPs and turntables. But there is still a niche market of buyers who believe in the old products. Perhaps the prices of these products have gone up and not down. Discount clothing stores sell copies of the latest fashions—perhaps that drives up the price of the high fashion items. In general, if the pricing behavior that is seen in drugs also applies to other products, then existing price indexes will miss much of the impact of new products and quality change. We desperately need more data on these issues.

The issue of how to value the generics raises interesting questions of consumer sovereignty. The traditional BLS method did assume a full

6. Caves, Whinston, and Hurwitz (1991).

consumer sovereignty notion. The BLS assumed that a branded antidepressant was twice as valuable as the generic that is next to it.

A counterargument is that the price differentials reflect inefficiency in the market. People do not realize that a generic drug is chemically identical to an existing branded drug. In this case, as the share of generic drugs increases, we should count that legitimately as a price decrease. This is the new BLS approach.

My own reaction is that the new BLS approach is correct. I would count fully the generic as a reduction in price. But, nevertheless, one of the procedures that is suggested in this paper, the procedure of splitting the difference, is a reasonable, practical alternative. It is a reasonable compromise between the two alternatives of saying that people feel better because they are buying a branded drug rather than a generic one or, conversely, saying that people are foolish or lack information when they buy a branded, rather than a generic, product.

A reason that I prefer the new BLS method of counting the full price decline associated with the introduction of a generic is that there is a private market incentive for companies to disseminate what is, according to the FDA, false information, namely that the branded drug is superior to the generic. If the FDA is correct that the two are equivalent, then it is still in the interest of the manufacturers of the branded product to persuade customers and doctors that is not the case.

Turning to the hedonic approach that is used in this paper, I had trouble understanding what the coefficients on the different drug characteristics in their regressions actually represent. The right model for antidepressants may be a matching model, a model such as those used in job search.

A standard view of hedonics is that consumers trade off price against some side-effect characteristics. To put it bluntly, you would pay a little bit more for a drug in order to have a little bit less constipation or a little bit less of some other side effect.

My understanding of the treatment for depression is that a doctor will suggest a particular antidepressant based on the patient's history and the nature of the depression and other information. There is then, essentially, a trial for some period of time to see if that drug works. The information about the effect of a given drug on a patient is costly to acquire. Doctor and patient may not know for some period of months

whether a drug is going to be effective or the nature of the side effects. If the drug works, then the patient stays on it. If it does not, then the doctor gives the patient a prescription for a different antidepressant. Some people have to cycle through various drugs for as long as a couple of years, trying to find an appropriate match between a drug and their particular problems.

Such a matching model helps explain in part why the demands are relatively inelastic, because a patient who has finally found a drug that works will develop a great allegiance to it. There is resistance to changing the drug just because a new one comes on the market or just because there is a price change.

How are price differentials among drugs established? Perhaps the simple reduced form hedonic regression works fine, but that is not obvious beforehand. Presumably, all else being equal, the doctor and patient will start out with a cheaper drug first. (All else being equal presumably means where drugs have the same initial probability of creating a successful match.) There would be some price elasticity in that process. A further complication is created by third-party payment, however. Many patients have part or all of their drug cost covered by insurance. This point is stressed extensively in Ted Keeler's comments.

Limits set by insurance providers mean that many people are on drug plans that specify a certain list of antidepressants, and so they have to choose one of those or face a sharp increase in the incremental cost to move off that list.

HMOs, which account for an increasing share of medical care, if they are providing drugs as part of their package, would have an incentive to have their doctors start with the cheaper drugs—assuming equivalent probability of success.

In general this is not a market that resembles a simple textbook utility tradeoff. There are third-party payments. Decisions are made when patients do not have full information. And the particular market equilibrium may look more like a matching model. It would have been helpful if the authors had discussed how we should actually interpret their coefficients and whether they would be the right ones for use in a price index given these market characteristics.

My concerns about the hedonics would have been more muted except for the fact that the results seem surprising to me. It may be the method used, or the data, or the time period, but somehow the impact on welfare

of the introduction of the new classes of antidepressants may not be fully captured.

The results reported in the paper are that when you adjust for quality, the impact is not all that great. I would like more explanation of how much of the quality improvement is being captured. There is the shift from the old class of drugs to the new class of drugs. And then there are new entrants with slightly different profiles. The impact of the first should be huge. And the impact of the second should also be fairly large because the class of drugs becomes usable for a broader group of patients—more drugs, even when they look similar in average performance, allow for more successful matches.

In conclusion, this is a paper that is in progress, and I want to applaud the work these authors have done in this paper and in previous ones on price indexes. It is just terrific as a set of work, and I congratulate them on it and look forward to further progress ahead.

Commentators' References

- Caves, Richard E., Michael D. Whinston, and Mark A. Hurwitz. 1991. "Patent Expiration, Entry, and Competition in the U.S. Pharmaceutical Industry." *Brookings Papers on Economic Activity, Microeconomics: 1*: 1–48.
- Feldstein, Paul. 1993. *Health Care Economics*, 4th ed. Albany: Delmar Publishers.
- Griliches, Zvi, and Ian Cockburn. 1994. "Generics and New Goods in Pharmaceutical Price Indexes." *American Economic Review* 84 (December): 1213–32.
- Hellerstein, Judith K. 1994. "The Demand for Post-patent Prescription Pharmaceuticals." NBER Working Paper 4981. National Bureau of Economic Research, Cambridge, Mass. December.
- Manning, Willard G., and others. 1987. "Health Insurance and the Demand for Medical Care: Evidence from a Randomized Experiment." *American Economic Review* 77 (June): 251–78.
- Oberlander, Jonathan. forthcoming. "Managed Care and Medicare Reform." *Journal of Health Politics, Policy, and Law*.
- Sullivan, Sean. 1992. "The Demand for Prescription Drugs among Elderly Americans." Ph.D. dissertation, University of California.