TIME RELEASE:
The Effect of Patent Expiration on U.S. Drug Prices, Marketing, and Utilization by the Public

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Which policies are most likely to provide as many people as possible with the best medical treatments? Pharmaceutical companies invest in the risky and time-consuming process of discovering and synthesizing new and more effective drugs because the patents protecting them offer the chance of large profits by restricting competition for a period of time. Critics of patent protection and its rationales, who are especially vocal in the information-technology realm, minimize patents' ability to add to the supply of novel, valuable products and instead focus on patents' suppression of demand. These advocates of file-sharing and open-source computer programs argue that the prices patent owners command for the duration of a patent restrict the number of people who can use the product in question, and thus who benefit from it. This critique is perhaps even more germane to the medical arena, where the high prices charged for drugs on patent could, in principle, deny some people crucial, even life-saving treatment.

The companies that own the patents to such medicines use the monopoly profits they collect not only to finance research and development but to pay for the marketing of these medicines once they have been approved. Marketing expands the number of doctors and patients who use the drug by informing them of its availability and benefits.

In this paper, we examine the role of marketing in generating demand for drugs by observing changes in market structure when patents expire and cheaper generic competitors enter the market. If the critics are right, what we call "utilization"—the number of prescriptions dispensed for the universe of drugs sold in the United States—should increase as prices drop.

While it is true that utilization of a drug is strongly affected by price, utilization is also affected by the marketing efforts of patent owners. So while lower prices of generic drugs stimulate demand, reduced investments in marketing, in response to generics' growing market share, may result in an offsetting decline in a drug's utilization. The latter effect may extend beyond the drug in question to other drugs in its category.

Using data on virtually all prescription drugs sold in the United States during the period 2000-2004, our study examines the effect of patent expiration on prescription drug prices, marketing, and utilization. We examine how prices, marketing, and utilization change over a typical drug's "life-cycle." The year a drug is first sold in the United States is considered year zero. During the first twelve years of a typical drug's life-cycle, it faces very little generic competition. Generic competitors tend to enter the market in years twelve to sixteen. In that period, both the prices of formerly patent-protected drugs and the marketing expenditures on their behalf fall by about sixty percent. However, we also find that the number of drugs dispensed doesn't change. Evidently, the increase in utilization that results from lower prices is offset by the reduction in utilization that results from less marketing.

The pharmaceutical industry is the most research-intensive industry in the world. Indeed, drug development remains an expensive and uncertain undertaking in which failure is far more common than success. To encourage investment, exceptionally high risks to companies and investors must be accompanied by the promise of limited monopoly profits.

While branded drugs are significantly more expensive than generics, this study does not find any evidence that patent protection reduces utilization of drugs. This may be because of high prescription drug insurance coverage that shields U.S. consumers from a large fraction of prescription drug costs. (In 2007, out-of-pocket payments by consumers accounted for only about 20 percent of total U.S. drug expenditure.) Declines in drug prices resulting from competition from generics may produce significant savings to insurers or pharmaceutical benefit managers that are not necessarily passed on to consumers.

Improvements in public health depend not only on access to existing health-care technologies but on the existence of financial incentives to develop new medicines. Our results indicate that weakening patent protection would not increase Americans' access to existing drugs. However, it would undoubtedly reduce the number of new drugs developed.

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TIME RELEASE: THE EFFECT OF PATENT EXPIRATION ON U.S. DRUG PRICES, MARKETING, AND UTILIZATION BY THE PUBLIC

Frank R. Lichtenberg & Gautier Duflos

BACKGROUND AND OBJECTIVES

U.S. patent law is based on Article I, Section 8, of the Constitution, which states that "the Congress shall have power to promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." The framers of the Constitution believed that, unless inventors were granted a monopoly on their discoveries, they would lack the incentive to pursue them. But this monopoly, the framers believed, should last for only a limited time, since inventions that enter the public domain are likely to be produced by more than one supplier, thereby benefiting the public by bringing down their price and increasing their availability.

The question of the socially optimal extent of intellectual-property protection has been hotly debated for over a century. In particular, with the extension of patents to biotechnology products came a powerful reaction against the sweep of intellectual-property rights, raising fears of the privatization of genetic inventions and the appropriation of the southern hemisphere's genetic resources by corporations based in rich countries. The reaction spread with the information-technology and Internet boom, which pitted supporters of freeware, file sharing, and open architecture against the owners and defenders of proprietary products.

As Gilbert and Shapiro (1990) observed, the primary purpose of the patent system is to reward innovators. Because these rewards are based on the creation of market power, which in turn may depend on restricting the extent of the public's utilization of an innovation, patents, for their duration, often necessitate some curtailment of the maximum possible gain in public welfare. Much of the debate about patent policy has focused on the trade-off between the dynamic benefits associated with innovation and the static costs of monopoly power that patents exact.

This study will examine the impact of the expiration of drug patents on three variables: U.S. drug prices; the amount of marketing that companies are willing to undertake;[1] and the quantity of drugs consumed. It does so by drawing on comprehensive data on virtually all drugs sold. Many studies have examined the effect of patent expiration and the ensuing entry of generics on drug prices, but we are aware of only two studies (Berndt et al. 2003; and Lakdawalla et al. 2006) that examined their effect on companies' marketing efforts and consumers' levels of utilization of previously patent-protected drugs. One of those studies examined data on just two drugs (cimetidine and ranitidine).

In general, increasing competition in a market, due to expiration of a patent or for other reasons, might be expected to reduce prices and thereby increase demand for, and thus production of, a good. However, this may not happen if demand for the good is not very sensitive to price, perhaps because insurers or other third parties usually pay for it, which is true of the U.S. prescription-drug market, where, in 2007, out-of-pocket payments by consumers accounted for only 20 percent of U.S. drug expenditure; or if demand is affected by factors other than price, such as marketing efforts on behalf of the product, which are extensive in the United States and which a patent's expiration would be expected to diminish.[2]

In this paper, we will provide evidence on the extent to which patent protection, the loss of it, and various ancillary consequences may restrict or enhance access to—and thus, use of—valuable, even lifesaving, drugs in the United States.

THEORY

The theoretical framework is summarized by the following diagram:
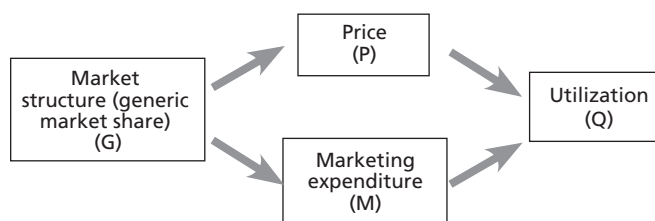
As shown on the right side of the diagram, we hypothesize that utilization of a drug (the total number of prescriptions dispensed) depends on two variables: the average price of the drug and marketing expenditure.[3] In particular, we hypothesize that utilization is inversely related to price and directly related to marketing expenditure.

As shown at the top left of the diagram, we hypothesize that mean price is inversely related to generics' market share (generic prescriptions/total prescriptions). Also, as shown at the bottom left of the diagram, we hypothesize that marketing expenditure is inversely related to generics' market share.

The hypothesis of a negative effect of generics' market share on marketing expenditure is based on the following reasoning. Suppose that marketing expenditure has a positive effect on utilization but that marketing is subject to diminishing marginal returns. We also assume that there are marketing spillovers, whereby the promotion of a branded pharmaceutical by its manufacturer affects the total number of prescriptions written for a range of products containing the underlying molecule and not just the number of prescriptions written for the marketer's own proprietary product.[4] The branded firm will increase marketing up to the point where the marginal private return is equal to the marginal cost of marketing. This tendency implies that an increase in generics' market share will reduce marketing expenditure.

This conceptual framework has interesting implications. First, while conventional analysis implies that

market structure affects utilization only via its effect on price, this framework implies that market structure affects utilization, *conditional on price*. Holding price constant, an increase in generics' market share will reduce utilization. Second, since increases in generics' market share are hypothesized to reduce both price and marketing expenditure, and these variables are hypothesized to have opposite effects on utilization, the net effect of an increase in generics' market share on utilization is an empirical question.

ECONOMETRIC APPROACH

We will use longitudinal, molecule-level data on virtually all prescription drugs sold in the United States to investigate the effect of market structure on price and marketing activity and then the effects of these variables on utilization. We will conduct two types of analyses.

First, we will compute the age profiles of four variables: the fraction of prescriptions for a given drug molecule that were written for generic products; the average price of these prescriptions; marketing expenditure on behalf of the drug; and the number of prescriptions dispensed, where age is defined as the number of years since the drug was first marketed.

Second, we will estimate a prescription-drug demand equation, in which the quantity of drugs sold is a function of both price and marketing expenditure, using longitudinal molecule-level data. We will also estimate relationships between each of these variables (drug quantity, price, and marketing expenditure) and generics' market share, also using longitudinal molecule-level data.

DATA

We obtained monthly data for 2000–2004 from IMS Health on virtually all prescription drugs sold in the United States. Our data set contained the number of prescriptions, manufacturer-wholesaler revenue, and marketing expenditure (cost of professional promotion), by product and month, for more than 19,000 products. In addition, the data set revealed the following fixed product attributes: product name and manufacturer, active ingredient(s), date the product was first marketed, and product status (branded, generic, branded generic, other). We aggregated the product-level data to the molecule (or combination of molecules) level. We also computed average price (manufacturer-wholesaler revenue per prescription), generics' market share, and molecule age, by molecule and month.

The data set contains information on about 1,560 molecules or combinations of molecules. A relatively small number of prescription drugs are also available over the counter (OTC), that is, without a doctor's prescription.[5] We determined from the FDA's Orange Book that 3.2 percent (fifty out of 1,560) of the molecules or combinations were available as OTC products; and 7.3 percent of prescriptions issued from 2000 to 2004 were for drugs that were available over the counter. We do not have any information about utilization of OTC products, so we will exclude molecules that were available over the counter.[6]

Table 1 shows aggregate annual data on the number of prescriptions, manufacturer-wholesaler revenue, average revenue per prescription, generics' market share, and marketing expenditure. The top twenty-five molecules, ranked by total number of prescriptions issued in

Table I: Summary Statistics					
Year	Total number of prescriptions*	Manufacturer-wholesaler revenue*	Manufacturer-wholesaler revenue per prescription	Generics' market share	Professional promotion expenditure*
2000	2,813,203	$129,565,642	$46.06	37%	$12,583,737
2001	2,981,866	$154,087,916	$51.67	37%	$15,085,286
2002	3,146,565	$176,087,414	$55.96	39%	$17,412,398
2003	3,288,211	$202,513,267	$61.59	41%	$20,211,506
2004	3,380,304	$221,994,992	$65.67	44%	$22,955,232
* in thousands					

Table 2: Top 25 Molecules, Ranked by Total Number of Prescriptions (2000-2004)

Molecule	Number of prescriptions (2000-2004)*	Year first marketed
ACETAMINOPHEN/HYDROCODONE	433,947	1978
LEVOTHYROXINE	396,930	1963
ATORVASTATIN	316,240	1997
AMOXICILLIN	293,264	1974
ALBUTEROL	238,338	1981
METOPROLOL	226,809	1978
ATENOLOL	220,880	1981
FUROSEMIDE	215,518	1966
LISINOPRIL	210,945	1987
ESTROGENIC SUB, CONJUGATED	186,319	1942
AZITHROMYCIN	180,271	1992
AMLODIPINE	175,413	1992
HYDROCHLOROTHIAZIDE	169,460	1959
METFORMIN	161,739	1995
ALPRAZOLAM	161,066	1981
SERTRALINE	150,556	1992
ACETAMINOPHEN/PROPOXYPHENE	139,941	1975
PAROXETINE	137,818	1993
WARFARIN	137,579	1954
SIMVASTATIN	135,362	1992
LANSOPRAZOLE	135,349	1995
HYDROCHLOROTHIAZIDE/TRIAMTERENE	134,846	1968
FLUOXETINE	127,738	1988
CELECOXIB	125,514	1999
CEPHALEXIN	122,546	1975

* in thousands

2000–2004, are shown in Table 2. Monthly data on the respective market shares of six major generic drugs with the largest increases in market share in 2000–2004 are shown in Figure 1.

EMPIRICAL ANALYSIS

Estimation of age profiles of generics' market share, average price, advertising expenditure, and number of prescriptions

Estimates of the age profile of generics' market share are shown in Figure 2. Mean generic-market share is essentially zero in years 0 (the year the drug was first launched) to 6 of a molecule's life cycle. A modest number of generics enter the market in the next six years; after twelve years, mean generic market share is 10 percent. Generics' market share increases sharply and suddenly after year 12. By year 16, mean generic market share is 54 percent. This finding is quite consistent with the Congressional Budget Office's finding that the average period of marketing under patent protection since enactment of the Hatch-Waxman Act and the Uruguay Round Agreements Act of 1994 is about 11.5 years.[7]

Estimates of the age profile of average price (manufacturer-wholesaler revenue per pre-

Figure I: Generic Market Shares of the Six Drugs with the Largest Increases in Generic Market Share (2000-2004)

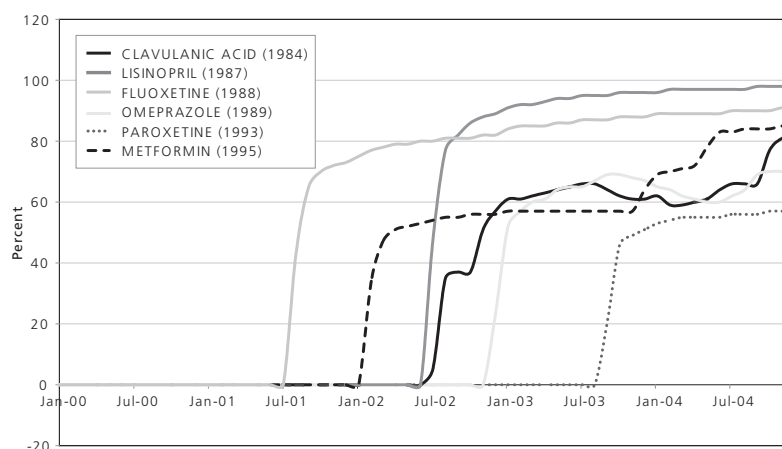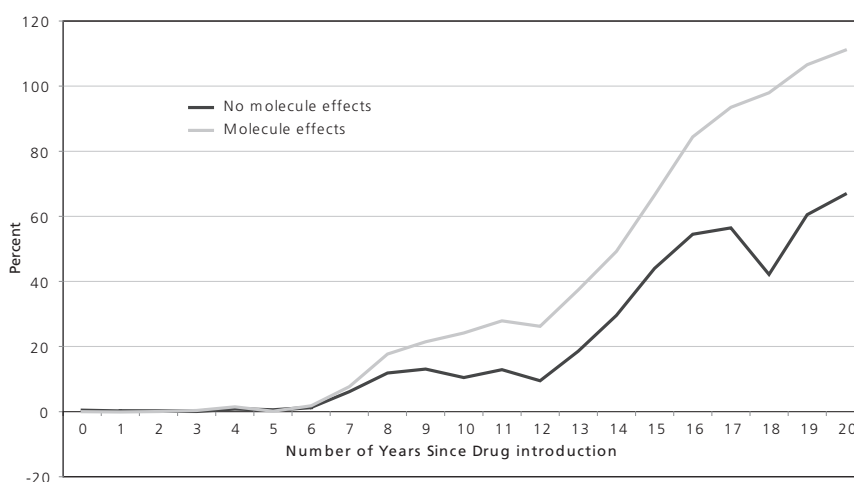## Figure 2: Mean Generic Market Share, by Age of Drug

Figure 2: Mean Generic Market Share, by Age of Drug

scription dispensed) are shown in Figure 3. The average price increases about 44 percent (averaging about 3.5 percent per year) from year 0 to year 12. Between year 12 and year 17, the price declines by 61 percent.

Estimates of the age profile of total cost of advertising directed to the professional audience are shown in Figure 4. Advertising expenditure rises fairly steadily during years 0–12 and is 2.3 times as high in year 12, when it reaches its peak, as it was in year 1. It declines sharply after year 12. It is 20 percent lower

one year after the peak and 60 percent lower four years after the peak. Berndt et al. (2003) found that marketing efforts on four H2-antagonist prescription drugs declined prior to patent expiration. However, these age profiles suggest that the decline in marketing coincides with an increase in generics' market share.

Estimates of the age profile of the prescriptions dispensed by pharmacies are shown in Figure 5. The number of prescriptions increases rapidly during the first several years: it is about twice as great five years after launch as it was one year after

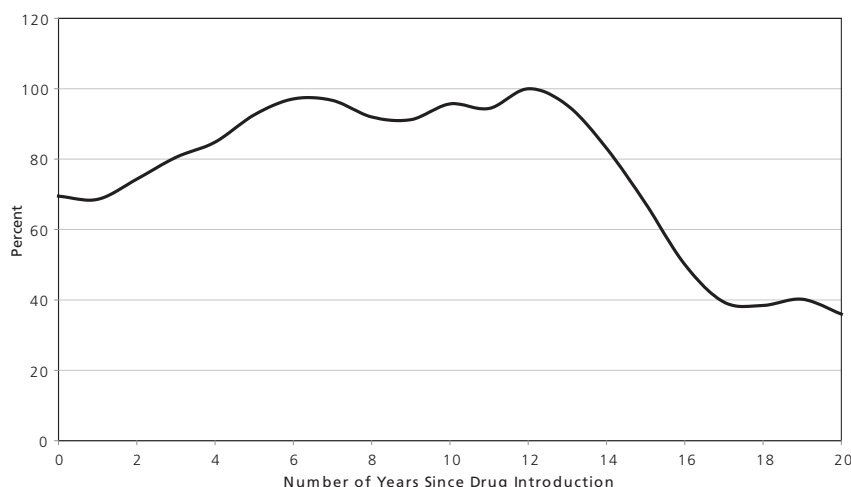## Figure 3: Mean Drug Price Relative to Price in Year I2

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Figure 4: Mean Professional Promotion Expenditure, Relative to Expenditure in Year 12

Number of Years Since Drug Introduction
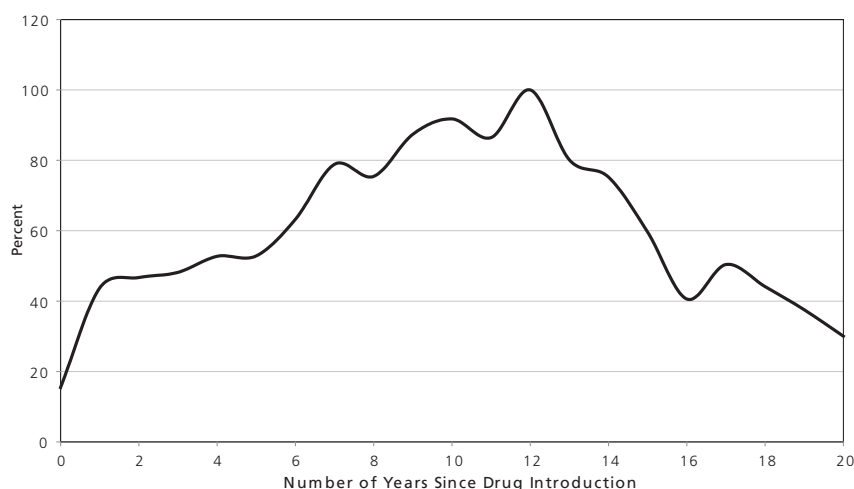
Figure 5: Mean Number of Prescriptions, Relative to Number of Prescriptions in Year 12

Number of Years Since Drug Introduction
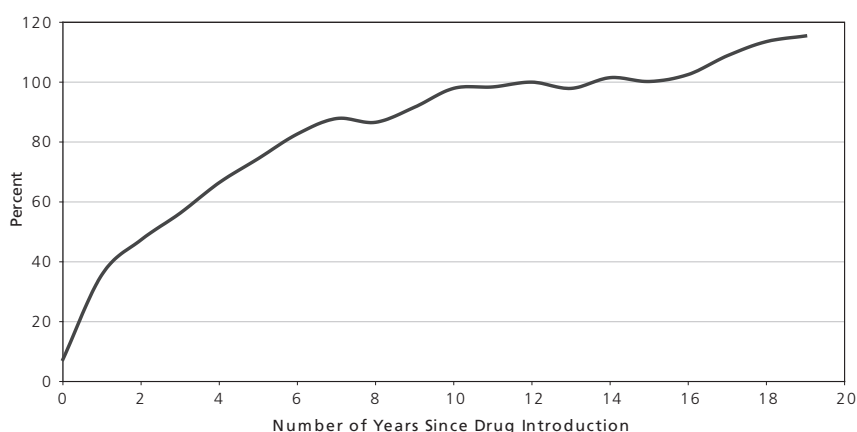
launch. The number of prescriptions increases by 15 percent between year 8 and year 12 but remains constant between years 12 and 16, despite the sharp decline in average price shown in Figure 3. Both average price and the number of prescriptions during years 8–16—the four years preceding and the four years experiencing the sharpest increase in competition from generics—are shown in Figure 6. These data indicate that increased utilization of prescriptions for generics after patent expiration is almost perfectly offset by reduced utilization of branded prescriptions.

The lack of a change in utilization in response to the sharp decline in price contrasts sharply with Lichtenberg and Sun's (2007) findings about the impact of Medicare Part D on prescription-drug use by the elderly. As shown in Figure 7 (reproduced from their paper), they identified a sharp and immediate increase in prescription-drug use by the elderly when Medicare Part D reduced the cost of medications to them. The absence of any increase in the number of prescriptions during the period of rapidly increasing competition from generics may be due to the sharp decline in advertising shown in Figure 4.[8]

Figure 6: Mean Price and Number of Prescriptions Relative to Price and Number in Year 12
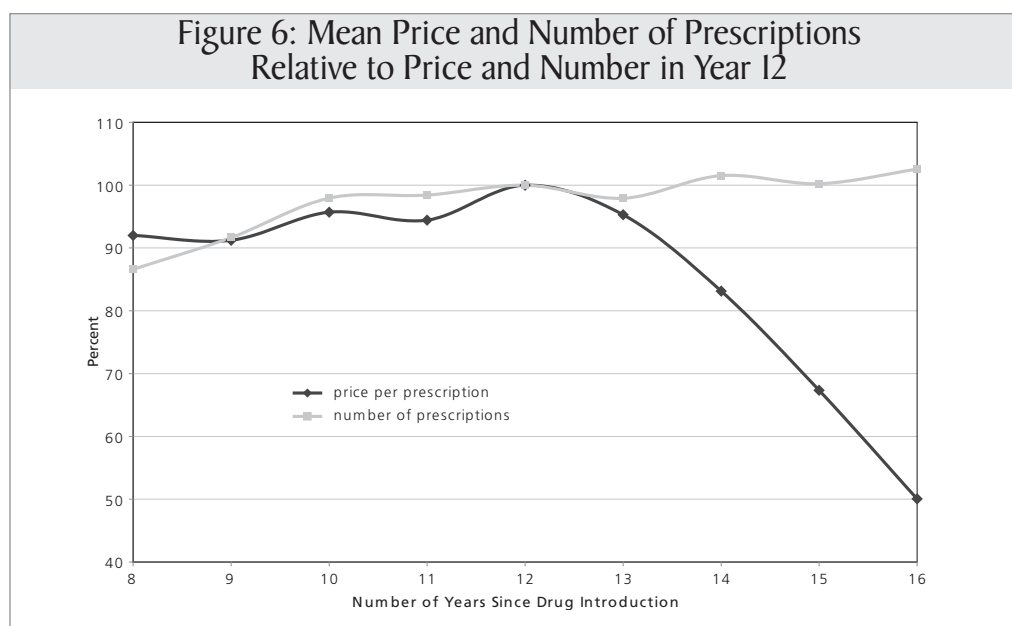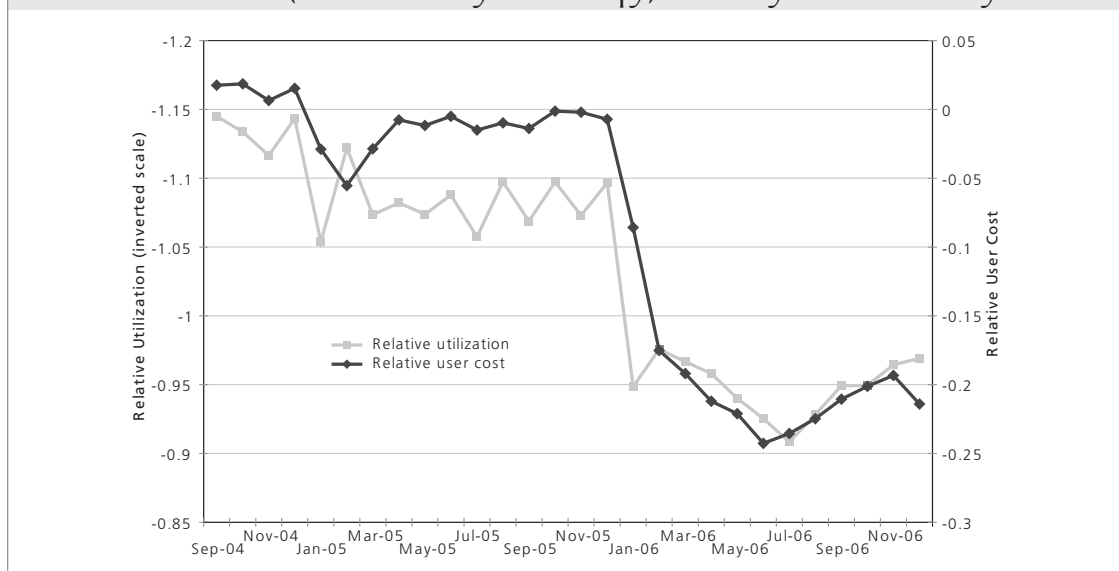

Figure 7: Relative User Cost (Mean Amount Paid by the Patient per Day of Therapy) and Relative Utilization (Number of Days of Therapy) of Elderly and Non-elderly Patients

Estimation of prescription-drug demand function and other relationships

Now we will estimate a prescription-drug demand function and analyze the impact of changes in competition due to the introduction of generics (which appears to be primarily attributable to patent expiration) on drug prices, marketing, and utilization, using longitudinal molecule-level data. As shown above in Figure 2, the largest increases in competition from generics usually occur twelve to sixteen years after a drug is first introduced.[9] Therefore, drugs introduced between 1984 and 1992 were likely to experience the largest increases in competition from generics during the period covered by our IMS Health data, which was 2000–2004.

We estimated four regression equations. The first is a standard demand model, according to which quantity

demanded depends on both the price of the good and marketing expenditure. We expect the effect of price on utilization to be negative and the effect of marketing expenditure on utilization to be positive. The model controls for any time-invariant, molecule-specific determinants of demand and for time-varying factors that influence demand and do not vary across molecules. If the coefficient on price is negative, the drugs whose prices increased faster than average during the period in question had slower than average growth in utilization, conditional on growth in marketing.

The second equation allows us to estimate the effect of changes in competition from generics on the average price (manufacturer-wholesaler revenue per prescription). The third equation allows us to estimate the effect of changes in competition from generics on marketing expenditure. The fourth equation allows us to estimate the effect of changes in such competition on utilization. We hypothesize that this form of competition affects utilization primarily via its effects on price and marketing.

Estimates of the effects of price and marketing on utilization were consistent with our expectations: the price effect is negative and highly significant, and the advertising effect is positive and highly significant.[10] There was also a strong inverse correlation between changes in generics' market share and changes in average manufacturer-wholesaler revenue. The magnitude of this estimate is quite consistent with the age profiles of generics' market share and the manufacturer price, as shown in Figures 2 and 3, respectively. Between years 12 and 16, generics' mean market share increases from 8 percent to 65 percent. The regression coefficient implies that this should result in a 49 percent price decline. The actual mean price decline between year 12 and year 16 is 44 percent.

There was also a strong inverse correlation between changes in generics' market share and changes in marketing expenditure. The regression coefficient estimate implies that the increase in generics' mean market share that occurs between years 12 and 16 should result in a 78 percent decline in marketing expenditure. The actual mean decline in marketing

expenditure between year 12 and year 16 is somewhat smaller: 57 percent.

The estimates indicated that changes in generics' market share have no effect on the total number of prescriptions. This is consistent with the age profile of utilization shown in Figures 5 and 6. It is also consistent with the hypothesis that competition from generics does not have any effect on utilization independent of its effects on price and marketing.

FREE SAMPLES AND SPILLOVER EFFECTS ON OTHER DRUGS WITHIN THE SAME CLASS

So far, we have examined the effect of expiration of a drug's patent(s) on the number of prescriptions for that drug dispensed by pharmacies. But for two reasons, this number may not reflect the overall effect of patent expiration on drug utilization. First, some medicines utilized by patients are not obtained from pharmacies: they are free samples obtained from physicians. Second, expiration of a drug's patent may have spillover effects, that is, it may cause the amount of utilization of other drugs in the same therapeutic class to change ("therapeutic substitution"). We will attempt to assess how these two phenomena—free samples and therapeutic substitution—might cause the effect of patent expiration on utilization of other similar drugs to differ from its effect on the number of prescriptions for that drug dispensed by pharmacies.

Free samples

About 75 percent of professional promotional expenditure goes toward providing free samples (Narayanan and Manchanda 2006). As shown above, professional promotion expenditure, on average, declines by 60 percent between years 12 and 16—when competition from generics rises rapidly—and there is a strong negative correlation across molecules between changes in generics' market share and changes in professional promotion expenditure. This strongly suggests that patent expiration sharply reduces utilization of free samples obtained from physicians.

More direct evidence about the effect of patent expiration and competition from generics on utilization of free samples can be obtained from the 1996–2006 Medical Expenditure Panel Survey (MEPS) prescribed medicines files. MEPS household respondents were asked in each round whether they received any free samples of each reported prescribed medicine during the round. A MEPS variable indicates whether a respondent reported having received a free sample of the prescription medicine in the round.[11] We used these data to obtain estimates of the number of people who received free samples of each molecule in each year.

Estimates of the number of people receiving free samples in years 0–20 relative to the number of people receiving free samples in year 12 are graphed in Figure 8. The figure also shows the molecule-age profile of professional promotion expenditure, reproduced from Figure 4.

The MEPS data indicate that the number of people receiving free samples of a drug increases fairly steadily from year 0 to year 10, when it reaches a peak. Between years 10 and 15, the number of people receiving free samples declines by 50 percent. The number of people receiving free samples appears to peak about two years before professional promotion

expenditure does. However, the age profiles of the two variables are broadly consistent. Both decline sharply during the period in which generics' market share rapidly increases. The effect of patent expiration on the total number of prescriptions for a drug (prescriptions dispensed by pharmacies plus free samples) is therefore lower (more negative) than its effect on the number of prescriptions dispensed by pharmacies. We estimate that, overall, the ratio of the market value of free samples to the sum of the market values of free samples and pharmacy prescriptions in 2003 was 7 percent. If patent expiration had no effect on the number of pharmacy prescriptions (as suggested by Figures 5 and 6 and Table 1) and reduced the number of people receiving free samples by 50 percent, it would reduce the total number of prescriptions by 3.5 percent (= 7% * 50%).

Between-drug spillover effects

Expiration of a drug's patent may have spillover effects: it may cause the extent of utilization of other drugs in the same therapeutic class to change. The estimates described above do not account for these potential spillovers. In this section, we will first argue that these spillover effects can go in both directions. Therefore, failure to account for spillovers could result in either understatement or overstatement of the

Figure 8: Number of People Receiving Free Samples as a Percentage of Number of People Receiving Free Samples in Year 12
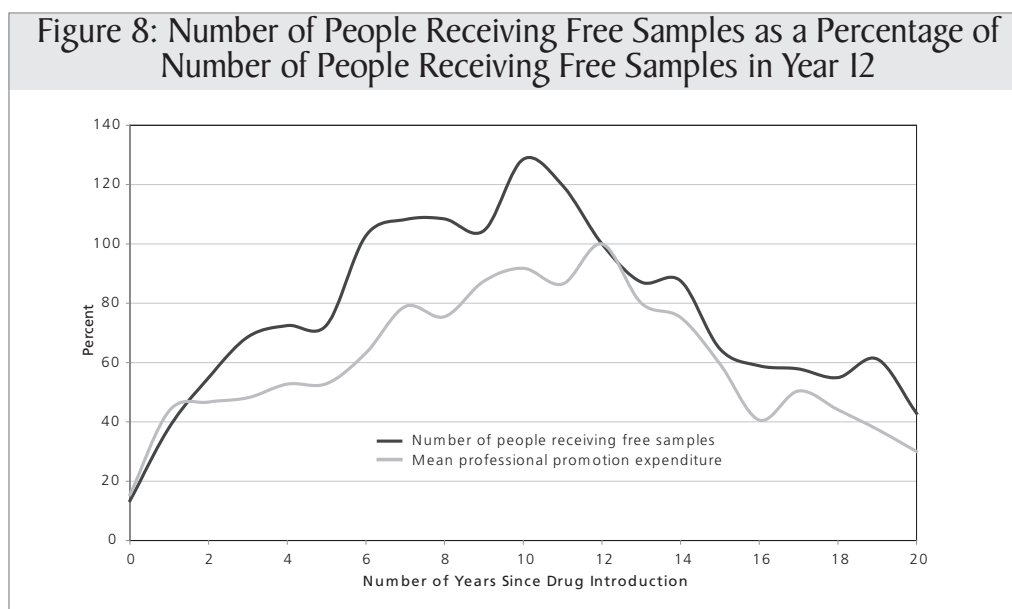
effect of patent expiration on drug utilization. Then we will present estimates of a model that accounts for potential spillovers.

Positive spillovers. Monopolists may have little incentive to research and develop new products that will compete directly with their currently marketed products. Consequently, "generic entry can … have a small positive effect on the incentive to innovate."[12] Graham and Higgins (2006) find that "pharmaceutical firms act strategically, targeting the three-year window around the loss of exclusivity to introduce new products." Schering-Plough launched the antihistamine Clarinex shortly before the patent on its older drug Claritin (loratadine) expired (Rubin 2002). The change in total utilization of antihistamines is presumably much larger than the change in loratadine sales.

Negative spillovers. Merck's cholesterol-lowering drug Zocor (simvastatin) lost its U.S. patent protection in June 2006, becoming the largest-selling drug yet to be opened to competition from cheap generics. That change cost Merck billions of dollars a year. But it may have been nearly as damaging to Pfizer, whose rival cholesterol drug, Lipitor, was the world's most popular, with global sales last year of $12 billion. After the patent expired, insurers hoped to convince patients and doctors that cheap clones of Zocor made full-priced Lipitor an unnecessary luxury (Berenson 2006). The change in total utilization of cholesterol-lowering drugs is presumably much smaller than the change in generic simvastatin sales.

To examine the effect of changes in a drug's market structure on utilization of all drugs in the same therapeutic class (i.e., accounting for potential spillovers), we estimated the relationship between utilization and generics' market share at the level of the therapeutic class as opposed to the molecule level.

We used the Anatomical Therapeutic Chemical (ATC) Classification System[13] to aggregate molecules into therapeutic classes. The ATC system is controlled by the World Health Organization Collaborating Centre for Drug Statistics Methodology and was first published in 1976. The system divides drugs into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics. In this system, drugs are classified into groups at five different levels. There are fourteen main groups. The first level of the code indicates the anatomical main group and consists of one letter (Example: C Cardiovascular system). The second level of the code indicates the therapeutic main group and consists of two digits (Example: C03 Diuretics). The third level of the code indicates the therapeutic/pharmacological subgroup and consists of one letter. (Example: C03C High-ceiling diuretics). The fourth level of the code indicates the chemical/therapeutic/pharmacological subgroup and consists of one letter (Example: C03CA Sulfonamides). The fifth level of the code indicates the chemical substance and consists of two digits (Example: C03CA01 Furosemide).

We estimated the relationship between utilization and generic market share at the fourth and third ATC levels. Molecules in the same fourth-level class are likely to be better substitutes than molecules that are in the same third-level class but not the fourth.

There was not a significant relationship between changes in utilization and changes in generics' market share at the fourth ATC level or the third level. This finding indicates that the increases in generics' market penetration do not affect drug utilization, whether or not potential spillovers to other drugs in the same therapeutic class are taken into account.

SUMMARY

In general, increasing competition in a market, due to expiration of a patent or for other reasons, might be expected to reduce price and thereby increase demand for a good and thus its total production and consumption. However, this need not be the case if the demand for the good is sensitive to factors other than price (e.g., marketing) and if patent expiration has an important impact on these other factors. This study examined the impact on U.S. drug prices, marketing, and utilization of changes in market structure (changes in generic drugs' market share) primarily resulting from patent expiration, using comprehensive data on virtually all prescription

drugs sold between 2000 and 2004. We excluded a small number of molecules that were available over the counter because we do not have any information about utilization of such products.

We hypothesized that utilization is inversely related to price and directly related to marketing expenditure. Due to marketing spillovers, whereby the promotion of a drug by a manufacturer increases the total number of prescriptions for that drug and not just those of the marketer, the advent of price competition from generics following patent expiration reduces the incentive to maintain marketing expenditures at their former levels. Because a decline in marketing expenditure produces a decline in demand, just as a decline in price increases demand, the net effect of increased competition from generics on utilization is indeterminate, a priori.

We conducted two types of analysis. First, we computed the age profiles of generics' market share, average price, marketing expenditure, and number of prescriptions, where age was defined as the number of years since the drug was first marketed. We found that there is little competition from generics in the first twelve years of the product life cycle but that generics' market share increases sharply and suddenly in the next four years. This is quite consistent with previous evidence that the average period of marketing under patent protection after enactment of the Hatch-Waxman Act and the Uruguay Round Agreements Act of 1994 is about 11.5 years. Price and marketing expenditure both decline by about 50–60 percent during years 12–16, but the number of prescriptions remains essentially constant during those years. This finding implies that the effect on utilization of declining price is approximately offset by the effect of declining marketing and that increased utilization of generic prescriptions after patent expiration is approximately offset by reduced utilization of branded prescriptions.

Second, we obtained estimates of a prescription-drug demand function—the relationship between changes in utilization and changes in average price and marketing—and of models of the effect of generics' market share on price, marketing, and utilization, using longitudinal molecule-level data. Consistent with our expectations, the effect of price on demand was negative and highly significant, and the effect of advertising on demand was positive and highly significant. The estimated effect of price appeared low; this may be due, to an important extent, to "mismeasurement" of the price of drugs. Patients' demand for drugs presumably depends on the average price that they pay, not on average revenue received by manufacturers and wholesalers. Using data from the Medical Expenditure Panel Survey, we showed that the change in the average price paid by patients is correlated across drugs with the change in the average proceeds received by manufacturers, but it is not perfectly correlated.

We found a strong inverse relationship between changes in generics' market share and changes in average manufacturer-wholesaler revenue. The slope of the estimated relationship was quite consistent with the age profiles of generics' market share and manufacturer price. There is also a strong inverse correlation between changes in generics' market share and changes in marketing expenditure.

We found no evidence of a relationship across molecules between changes in the total number of prescriptions and changes in generics' market share. The two hypothesized effects of increased competition from generics—increased utilization due to falling prices, and decreased utilization due to reduced marketing—appear approximately to offset each other. Competition from generics does not appear to have any effect on utilization independent of its effects on price and marketing.

Even if expiration of a drug's patent(s) does not affect the number of (branded plus generic) prescriptions for that drug dispensed by pharmacies, it could still affect drug utilization, for two reasons. First, it could affect the number of free drug samples that patients obtain from physicians. We found that the number of free samples declined sharply after patent expiration and therefore that the effect of patent expiration on the total number of prescriptions for a drug (prescriptions dispensed by pharmacies plus free samples) is lower (more negative) than its effect on the number of prescriptions dispensed by pharmacies. We estimated

that if patent expiration had no effect on the number of pharmacy prescriptions, it would reduce the total number of prescriptions by 3.5 percent.

Second, expiration of a drug's patent may have spillover effects: it may cause utilization levels of other drugs in the same therapeutic class to change. These spillover effects can go in both directions. We attempted to account for potential spillovers by estimating the relationship between changes in utilization and changes in generics' market share at the level of the therapeutic class rather than the molecule level. We did not find a statistically significant relationship. Increases in generics' market penetration do not appear to affect levels of drug utilization, whether or not potential spillovers to other drugs in the same therapeutic class are taken into account.

Improving public health depends on both the creation and use of new medical goods and services, such as new drugs. As we discussed earlier, there is a continuing debate over the optimal length and breadth of patents, including whether patents—particularly in the health-care context—limit utilization of important medical products. Our findings suggest that, at least in the United States, patent expiration (and the consequent large declines in price) does not significantly increase utilization. Although patent expiration causes a large decline in price, high levels of prescription-drug insurance coverage prevent this price decline from stimulating consumer demand as much as a price decline by itself would otherwise. Moreover, patent expiration causes a sharp reduction in marketing activity, which reduces demand.

Concerns have been expressed regarding the role of industry marketing to physicians (physician detailing) and direct-to-consumer advertising. While this study does not address any claims as to the medical appropriateness of such activity (which is, at a minimum, regulated by the U.S. Food and Drug Administration), we do note that marketing has a significant impact on utilization. Insofar as increasing the utilization of medical innovations improves public health, limitations on advertising may unduly diminish it and therefore should not be undertaken without inquiring into their ancillary effects.

Questions surrounding patents, marketing, and access are at the forefront of policy debates at both the state and federal level. In the past decade, the U.S. Supreme Court has issued several decisions that have weakened patent protection. In 1999, the Court granted states immunity from claims of patent infringement (Chartrand 1999). In 2007, the Court, in its most important patent ruling in years, raised the bar for obtaining patents on new products that combine elements of preexisting inventions (Greenhouse 2007). As a result, judges now have more leeway to dismiss lawsuits for patent infringement without requiring a jury trial, and patent examiners, who generally grant patent applications unless they find prior references to the same invention, now are freer to deny them. These decisions have not reduced patent length, but they have reduced the scope of patent protection. In the long run, weaker patent protection, like shorter patent protection, is likely to reduce the amount of medical innovation—the rate at which novel medical goods are created.

In principle, the adverse effect of less innovation on public health could be offset by greater access to existing products. However, our findings imply that, in practice, weaker (or shorter) patent protection would not increase Americans' access to prescription drugs, all of which have been synthesized and marketed under a regime affording greater patent protection than some are now proposing. Due to broad prescription-drug insurance coverage and the role of marketing in increasing awareness of both the efficacy and availability of pharmaceuticals, weaker patent protection would not increase utilization of prescription drugs.

1. Due to data limitations, marketing expenditure will be defined as "cost of professional promotion": the total cost of promotion that is directed to the professional audience. It is the sum of three items: the cost of contacts (physician office or hospital calls, service visits, or telephone contacts); dollars spent in medical journals; and the retail value of samples. Direct-to-consumer (DTC) advertising is not included. However, DTC advertising accounts for a very small share of total pharmaceutical marketing expenditure.

2. Centers for Medicare and Medicaid and Services (CMS).

3. Pindyck and Rubinfeld (2009, p. 424) hypothesize that the quantity of a firm's output demanded "depends on both its price and its advertising expenditure in dollars."

4. Marketing has been found to have spillover effects in a variety of industries. Vardanyan and Tremblay (2006) found significant marketing spillovers in the U.S. brewing industry, and Verbeek and Huij (2007) found that mutual funds with high marketing expenses enhance cash inflows to funds in other fund families with low marketing expenses.

5. In Canada, "the share of non-prescribed drugs in total drug expenditure is expected to have reached 16.7 percent in 2006 and 16.4 percent in 2007" (Canadian Institute for Health Information 2008).

6. A provision of the Waxman-Hatch Act of 1984 granted pioneer manufacturers an additional three years of limited market exclusivity if they obtained FDA approval for a new presentation and indication for the chemical entity. By timing the OTC launch to coincide approximately with the pioneer Rx patent expiration date, a company could potentially benefit from an additional three years of market exclusivity on the OTC version of a drug, thereby offsetting somewhat its loss of Rx sales after the patent has expired. In theory, "the impact of a brand's OTC introduction on its own Rx sales … could be either positive or negative" (Berndt et al. 2003, p. 251).

7. Congressional Budget Office 1998. The figure for the post–Hatch-Waxman period is based on the average effective patent term for the fifty-one drugs approved between 1992 and 1995 that received a Hatch-Waxman extension. The post–Hatch-Waxman figure is based in part on Grabowski and Vernon 1996.

8. In Figures 3 and 6, price is defined as manufacturer-wholesaler revenue per prescription, whereas Lichtenberg and Sun (2007) defined price as the average cost of a prescription to the patient. While the latter is the theoretically preferred measure, as discussed below, there is a strong positive correlation across drugs between changes in prices charged by manufacturers and changes in prices paid by patients.

9. The difference between the patent life (usually twenty years) and the effective duration of a drug's market exclusivity is due to the time it takes to complete the clinical trials needed to obtain FDA approval.

10. Although these parameters have the expected signs, the (absolute and relative) magnitudes of these coefficients are surprising in certain respects. In particular, the magnitude of the price coefficient is smaller than expected. This may be due, to an important extent, to "mismeasurement" of the price of drugs. Patients' demand for drugs

presumably depends on the average price that they pay, not on average revenue received by manufacturers and wholesalers. Using data from the Medical Expenditure Panel Survey, we examined the correlation between the average cost of a prescription to patients and the total amount paid for a prescription. We found that there is a strong link between prices paid by patients and revenues per prescription received by manufacturers-wholesalers: drugs with above-average reductions in revenues per prescription received by manufacturers (i.e., due to patent expiration) tended to experience above-average reductions in prices paid by patients.

11. However, respondents were not asked to report the number of free samples received, nor was it made clear that free samples were included in the count of the number of times that the respondent reported purchasing or otherwise obtaining the prescribed medicine during the round. Therefore, SAMPLE is not a count variable of free samples; SAMPLE =1 for all acquisitions of a prescribed medicine that a respondent reported getting a free sample of during the round (http://www.meps.ahrq.gov/mepsweb/data_stats/download_data/pufs/h102a/h102adoc.shtml#2725TheSample).

12. Tirole (1988, p. 392), quoting Kenneth J. Arrow; and Congressional Budget Office (1998, Appendix D).

13. See http://en.wikipedia.org/wiki/Anatomical_Therapeutic_Chemical_Classification_System.

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