United States General Accounting Office

GAO

Report to the Chairman, Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives

September 1992

PRESCRIPTION DRUGS

Companies Typically Charge More in the United States Than in Canada

GAO/HRD-92-110

GAO

United States
General Accounting Office
Washington, D.C. 20548

Human Resources Division

B-249553

September 30, 1992

The Honorable Henry A. Waxman
Chairman, Subcommittee on Health
and the Environment
Committee on Energy and Commerce
House of Representatives

Dear Mr. Chairman:

The rapid rise in health care spending continues to be of concern to the U.S. public and the Congress. In particular, the escalation in prescription drug costs—borne by consumers, insurers, and other third-party payers—has stimulated congressional interest in the pricing practices of drug manufacturers.

Various studies have found that some prescription drug prices are substantially higher in the United States than in other countries.[1] For two reasons, however, these study findings do not support strong conclusions about the pricing practices of manufacturers. First, some studies measure pharmaceutical prices at the retail or wholesale—as opposed to the factory—level.[2] Consequently, they cannot distinguish the influence on price differentials of pharmacists and wholesalers from that of drug manufacturers. Second, some studies examine relatively small drug samples, which might give a misleading impression of the average price of a broad array of prescription drugs.

To supplement these studies, you requested that we compare the factory prices of identical prescription drug products sold by the same manufacturers in the United States and in other countries. You also asked that we identify, to the extent possible, the causes of any documented price differentials.

As agreed with your staff, this report compares U.S. factory prices with those in Canada; a subsequent report will present comparisons for the United States and various European countries. Our analysis compares the manufacturers' component of the prices paid by the typical retail consumer in both countries. We estimate that such consumers accounted for over half of prescription purchases in the United States in 1991. This

[1]A bibliography of selected studies follows appendix V.

[2]Pharmaceutical prices are measured at different points in the distribution chain. Retail prices are paid by the consumer to the pharmacist. Wholesale prices are paid by the pharmacist to the wholesaler. Factory prices (which account for approximately two-thirds of the average prescription charge) are paid by the wholesaler to the manufacturer.

initial report presents the results of our comparison of factory prices for 121 of the 200 most frequently dispensed prescription drugs in the United States with the prices of the identical drugs sold in Canada. Details of our scope, methodology, and results are described in appendix I. A brief description of the Canadian market for prescription drugs appears in appendix III.

Results in Brief

Manufacturers' prices to wholesalers for identical prescription drugs are typically higher in the United States than in Canada. The price differences are largely attributable to actions taken by Canada's federal and provincial governments to restrain drug prices, not to any differences in manufacturers' costs between the two countries. The implications of adopting Canadian regulations in the United States are in dispute. It is not clear how such regulations would affect manufacturers' ability to develop innovative drug products.

Manufacturers' Prices for Prescription Drugs Typically Higher in the United States

The same manufacturers charge wholesalers substantially more for identical prescription drugs sold in the United States than in Canada. An entire basket of the 121 frequently dispensed drugs we studied would cost 32 percent more in the United States than in Canada if a common U.S. prescription (such as 100 tablets) of each drug were purchased at factory prices in each country.[3] A large majority of the 121 drugs studied (81 percent) was more expensive in the United States. U.S.-Canadian drug price differentials for specific products vary widely. On a per package basis,[4] the U.S. price to wholesalers ranged from being 44 percent lower to 967 percent higher than the Canadian price (see pp. 12-14).

Major Causes of Drug Price Differentials

The major source of U.S.-Canadian differences in drug prices is not variations in manufacturers' costs. This holds true regardless of whether the cost differences relate to research and development, marketing, production, or distribution.

Instead, government regulations and reimbursement practices contribute to lower average drug prices in Canada. In setting prices, manufacturers of

[3]Price differentials are smaller, however, between Canada and some segments of the U.S. prescription drug market. In segments of the U.S. drug market that do not rely on wholesalers, institutional buyers sometimes are able to buy prescription drugs directly from manufacturers at prices substantially below the typical wholesale price. Such discounts do not apply, though, to the majority of U.S. drug sales, on which this study focuses.

[4]Package refers to the container from which a pharmacist dispenses drugs.

patented drugs must conform to Canadian federal regulations that review prices for newly released drugs and restrain price increases for existing drugs. Furthermore, drug benefit plans run by the provincial governments act to constrain manufacturers' discretion in price-setting. Through the plans' reimbursement of their enrollees' drug purchases, the provinces exercise concentrated buying power to obtain low prices. In addition, provincial officials can remove drugs from their list of reimbursable drugs if the manufacturers' proposed price increases are considered to be too high. (See pp. 14-21.)

Implications of Canadian Regulation for U.S. Market Are Unclear

After observing lower Canadian prices, some have proposed the adoption of a regulatory approach to limit U.S. drug prices. Proponents of this approach have debated with its critics over whether restraint of U.S. drug prices would have adverse effects on pharmaceutical research and development, and on the availability of new drug products. This issue cannot be resolved by referring to the Canadian experience with drug regulation, and lies beyond the scope of this report. (See pp. 21-22.)

The results of our analysis are restricted to the May 1, 1991, prices of the drugs that we analyzed and cannot be projected outside the scope of our study. In addition, our study is based on the prices for which drug manufacturers sell their products and does not measure the prices that a consumer pays for drugs at a retail pharmacy in the United States or Canada.[5] We conducted our review from June 1991 through May 1992 in accordance with generally accepted government auditing standards.

[5]Retail prices vary both inside and between the United States and Canada, making comparisons difficult. However, at the retail price level, U.S.-Canadian price differentials may be somewhat smaller than at the factory level; some evidence suggests that pharmacists may receive higher dispensing fees in Canada than in the United States.

As agreed with your office, unless you publicly announce its contents earlier, we plan no further distribution of this report until 30 days after its issue date. At that time, we will send copies to interested congressional committees and make copies available to others upon request. If you or your staff have any questions about this report, please contact me on (202) 512-7119. Major contributors to this report are listed in appendix V.

Sincerely yours,

Janet L. Shikles

Janet L. Shikles
Director, Health Financing and Policy Issues

Contents

Abbreviations

BAP	best available price
CPI	consumer price index
HHS	Department of Health and Human Services
ICI	Imperial Chemical Industries
IPPI	industrial products price index
MSD	Merck Sharp and Dohme
ODB	Ontario Drug Benefit Plan
PMPRB	Patented Medicine Prices Review Board
PPI	producer price index
PPP	purchasing power parity
R&D	research and development
SKF	Smith Kline and French Labs
WAC	wholesale acquisition cost

Analysis of U.S.-Canadian Drug Price Differentials

Reflecting congressional concern over prescription drug pricing, the Chairman of the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce, requested that we compare the factory prices of identical prescription drug products sold by the same manufacturers in the United States and other countries. He also asked that we identify, to the extent possible, the causes of any documented price differentials. This appendix summarizes the results of the first stage of our analysis, which is to compare U.S. prices with those in Canada. A subsequent report will present the results of our comparison of U.S. factory prices with those in other countries.

Background

Prescription drug prices in the United States rose sharply in the 1980s. From 1980 to 1990, both consumer prices (measured by the Consumer Price Index—CPI) and prices charged by producers (measured by the Producer Price Index—PPI) for prescription drugs rose on average 9.6 percent per year. This was roughly double the average rate of growth for the economywide CPI (4.7 percent per year), and over three-and-one-half times the average growth rate for the economywide PPI (2.6 percent per year).[1] The steep increase in drug prices in the 1980s is a marked change from the 1970s. In that decade, U.S. prescription drug prices rose about one-half as quickly as consumer prices in general (4.3 percent per year on average for prescription drugs, compared with 7.8 percent per year for general prices).

Increasing drug prices are reflected in growing expenditures. Between 1980 and 1990, real (inflation-adjusted) U.S. expenditures on prescription drugs and other medical nondurables grew an average 4.8 percent per year. Consequently, real spending on drugs and other medical nondurables increased by almost two-thirds—from $30.1 billion in 1980 to $48.4 billion in 1990.[2]

[1]Price indexes provide some indication of the rate of prescription drug price increases as compared with price inflation in the general economy. But some research indicates that prescription drug price indexes may over-sample medium-aged drugs that undergo above-average price increases, and under-sample younger products that experience less than average prices increases, thereby overstating average annual drug price inflation by up to 3 percentage points (see Ernst R. Berndt and others, "Auditing the Producer Price Index: Micro Evidence From Prescription Pharmaceutical Preparations," Working Paper No. 4009, National Bureau of Economic Research, Mar. 1992). Alternatively, indexes may understate annual changes in average drug prices because they generally do not measure the impact of new drugs, many of which enter the market at relatively high prices.

[2]Although drug prices and expenditures increased over this period, drugs and other medical nondurables as a percentage of national health expenditures decreased slightly, from 8.6 percent in 1980 to 8.2 percent in 1990.

Some policymakers and analysts point to the level of drug industry profits as evidence that prescription drug prices are too high. By most estimates, U.S. drug manufacturers are more profitable than other U.S. manufacturers.[3] Pharmaceutical manufacturers' representatives contend, however, that high prices—and high profits—are justified. They point to the large investment in research and development (R&D) that must be made to bring a product to market, as well as the high risk associated with that investment.

Those who claim that drug prices are too high in the United States cite evidence suggesting that prices for the same products are lower in Canada than in the United States. Among the most recent of these studies is a 1990 report from the Department of Health and Human Services (HHS), which found that wholesale prices for a selected sample of drugs were significantly higher in the United States than in Canada.[4] The data in the HHS report do not, however, permit the identification of wholesale margin and factory price contributions to price differentials. The Congress has recently considered a number of proposals to limit prescription drug costs. In enacting the Ommibus Budget Reconciliation Act of 1990, it required drug manufacturers to give rebates to state Medicaid programs, basing them on the discounts offered to large purchasers. A current legislative proposal calls for a study to review the impact of regulating prescription drug prices.[5] Other proposals seek to lower prescription drug prices paid by federally funded health programs (such as those of the Department of Veterans Affairs and Community and Migrant Health Centers).[6]

Approach

We compared factory prices of drugs bought in retail pharmacies in the United States to the factory prices of similarly purchased drugs in Canada. This measure captures the manufacturers' component of the price paid by the typical consumer. Our measure excludes manufacturers' discounts to

[3]For example, the median Fortune 500 industry in the United States received profits in 1990 that represented 13 percent of equity. This is substantially less than the median profits for pharmaceutical companies, which were 26 percent of equity. Estimates of the degree to which profits (relative to assets) in the pharmaceutical industry exceed those in other industries vary, depending on how research and development is accounted for. (See citations in William S. Comanor, "The Political Economy of the Pharmaceutical Industry," Journal of Economic Literature, XXIV, No. 3, Sept. 1986, pp. 1183-1186.)

[4]HHS, Office of the Inspector General, Strategies to Reduce Medicaid Drug Expenditures, 1990. The study compared prices for 48 of the top 100 prescription drugs dispensed in the United States.

[5]S. 2000, 102d Congress.

[6]S. 1729 and H.R. 2890, 102d Congress.

some buyers in the United States—such as Medicaid, many managed care programs, and mail-order pharmacies.

To determine if these prices differ at the factory level between the United States and Canada, we selected the 200 drugs most frequently dispensed by U.S. drugstores, which represent 54 percent of all prescriptions dispensed in U.S. drugstores during 1990.[7] These drugs often come in multiple dosage forms, dosage strengths, and package sizes, each with its own price. To compare unit prices in the United States and Canada, we selected a single, commonly used U.S. dosage form, dosage strength, and package size for each of the drugs in our sample.[8] We then obtained U.S. and Canadian prices for each specific drug product. (We developed this methodology in consultation with Professor Stephen W. Schondelmeyer, Endowed Chair in Pharmaceutical Management and Economics and Director of the PRIME Institute at the University of Minnesota.)

Of the 200 drugs in our study, we were able to match 121 by brand name, manufacturer, dosage strength, and dosage form in both the United States and Canada.[9] (See app. II.) The 121 matched drugs included 39 of the 50 most commonly prescribed drugs (the top 50 ranked drugs represent 31 percent of all prescriptions dispensed in U.S. drugstores in 1990). We excluded 79 of the 200 drugs from our analysis for one or more of the following reasons:

- The manufacturer did not sell the drug in Canada in the same dosage strength or dosage form as in the United States.
- The drug was sold by prescription in one country and over the counter in the other.
- The drug sold in the United States was a generic product that was manufactured by a company that had no affiliate marketing it in Canada.
- The manufacturer selling the drug in the United States did not sell the drug in Canada.

[7]The top 200 drugs are listed in American Druggist, Feb. 1991.

[8]We determined the common prescription for each drug and manufacturer by consulting each product's labeling along with the following references: Facts and Comparison, American Hospital Formulary Service, and USP Dispensing Information. Generally, a 100-unit package size was used unless there was a frequently used patient package, such as 60 units for a drug used twice a day.

[9]For purposes of this study, drugs with different brand names in the United States and Canada were considered equivalent if they had the same generic name and were sold by the same manufacturer. Additionally, drugs with different manufacturers were considered equivalent if the drugs were sold by a different firm in Canada that was operating with a marketing or licensing agreement from, or as a subsidiary of, the company selling the product in the United States.

We obtained U.S. factory prices from the Wholesale Acquisition Cost (WAC) listed as of May 1, 1991, in the Medi-Span Master Drug Data Base-Select.[10] For 101 of the 121 matched drugs, we obtained Canadian factory prices from the Best Available Price (BAP) listed in the February 1991 Ontario Drug Benefit (ODB) Formulary. These Canadian prices were in effect from February 1991 through July 1991. According to government officials and pharmaceutical experts in Canada, the ODB formulary is generally representative of factory prices throughout Canada. For the 20 drugs not listed on the ODB formulary, we obtained Canadian factory prices directly from the manufacturers of the drugs or from a major Canadian wholesaler. All prices used in our study represent what wholesalers and retailers would pay for drugs if purchased directly from manufacturers on May 1, 1991.

Although U.S. drug prices were obtained for specific package sizes, most of the Canadian prices listed in the ODB formulary were unit prices (for example, per tablet or capsule). In these instances, we converted the Canadian unit price to a price per package by multiplying by the number of units in the U.S. package.[11] We used the May 1, 1991 exchange rate to convert Canadian prices to U.S. dollars.[12]

In addition to comparing each drug's U.S. and Canadian factory price per package, we compared the aggregate cost of purchasing a common prescription of all 121 drug products in both the United States and Canada. This comparison more accurately measures the difference in U.S. and Canadian prescription drug prices because prices are weighted by the typical U.S. prescription size. We were unable to weight individual drug price differences by relative sales volume because we were unable to obtain U.S. sales information for each of the drugs in our study.

[10]Medi-Span is a private firm that gathers pharmaceutical information.

[11]The per unit ODB formulary BAP almost always is based on the largest package size of a given drug product sold in Canada. Our study's Canadian factory price per package (derived from per unit BAPs) might, therefore, understate Canadian versus U.S. package prices where the U.S. price is based on smaller (relatively more expensive on a per dose basis) package sizes. However, when we compared drugs in our study using the largest U.S. package sizes, the median U.S.-Canadian price differential decreased somewhat (from 43 to 35 percent).

[12]The May 1, 1991, U.S.-Canadian exchange rate is close in magnitude to the average exchange rates for the month of May, the second quarter of 1991, and the entire year of 1991. When we used the purchasing power parity (PPP) to compare U.S. and Canadian drug prices, the median U.S.-Canadian price differential increased from a 43 percent price differential (using the May 1, 1991, U.S.-Canadian exchange rate) to a 54-percent differential (using the 1991 PPP). The PPP measure is sometimes used in international comparisons to better capture longer run influences on the exchange rate (such as, in this case, differences in U.S. and Canadian incomes and general price levels).

To identify the possible causes of price differentials, we interviewed government officials, industry representatives, academic researchers, and pharmaceutical industry experts in both the United States and Canada. Included in these interviews were officials from six drug manufacturers that sold 29 percent (35) of the drugs in our study. In addition, we performed statistical analyses to determine if the size of the U.S.-Canadian price differential varied with a drug's therapeutic category, manufacturer's headquarters location, year of U.S. drug approval, listing on the ODB formulary, presence or absence of federal price review, or competition with generic substitutes in either the United States, Canada, or in both countries (see app. IV).

Experts in the United States and Canada, officials from Canada's Patented Medicine Prices Review Board (PMPRB), and officials from the ODB reviewed a draft of this report. We incorporated their comments as appropriate.

Principal Findings

Drug Manufacturers' Prices Higher in the United States Than in Canada

For the prescription drugs we examined, drug manufacturers charge wholesalers significantly more in the United States than the same manufacturers do in Canada. If a common U.S. prescription of each drug included in our study was purchased at factory price in both countries, the entire basket of 121 prescriptions would cost 32 percent more in the United States than in Canada. Alternatively, when price differentials are computed drug by drug, the median price differential per package between the United States and Canada was 43 percent.[13]

U.S.-Canadian price differentials at the factory level vary widely for particular drugs. Price differences ranged from the U.S. price being 44 percent lower to 967 percent higher than the Canadian price (see app. II). Despite this wide range, most drugs we studied were more expensive in the United States (see fig. I.1). Of the drugs we compared, 98 were priced higher in the United States than in Canada while 23 were priced lower in the United States than in Canada. Almost half the 121 drugs studied were priced over 50 percent more in the United States than in Canada (see fig. I.2).

[13]When the price differentials are ranked from highest to lowest, the middle value in that ranking is termed the median.

Figure I.1: Range of U.S.-Canadian Drug Price Differentials

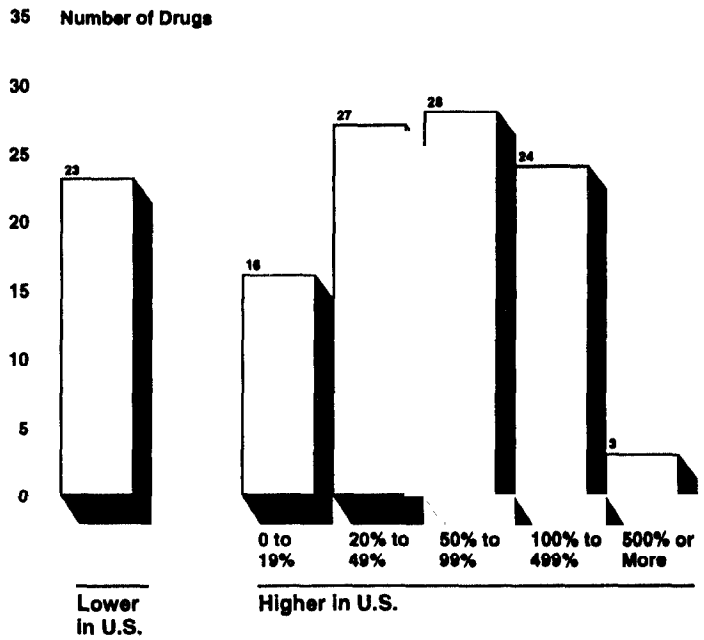
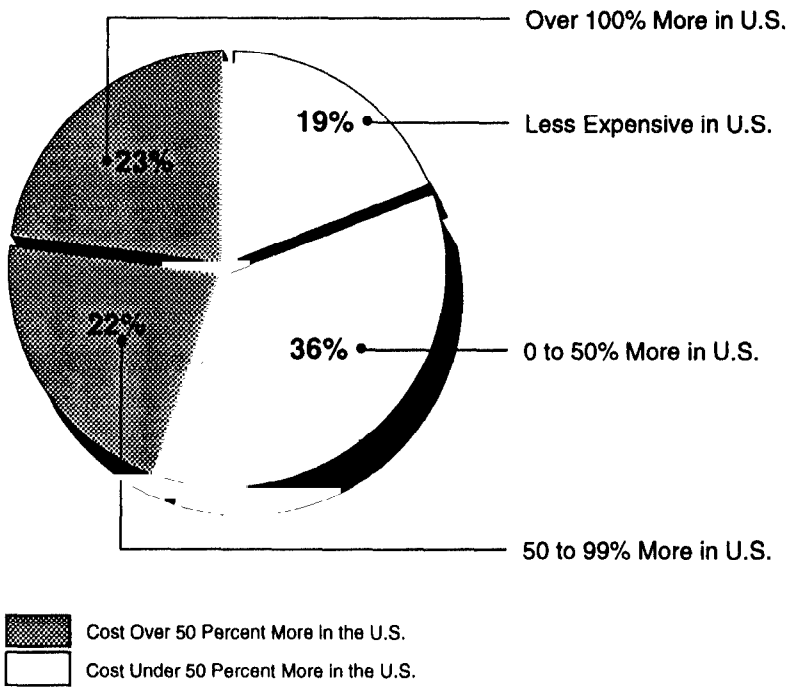


Figure I.2: Many Drugs Cost Over 50 Percent More In the United States Than in Canada



The five most commonly dispensed products exemplify U.S.-Canadian price differentials. Amoxil, the most commonly dispensed product in the United States in 1990, cost only 5 percent more per package in the United States than in Canada. Lanoxin, Zantac, Premarin, and Xanax—the second, third, fourth, and fifth most commonly dispensed products in the United States—cost 16, 30, 162, and 183 percent more per package in the United States than in Canada, respectively (see app. II).

Costs Unlikely to Cause Price Differentials for Prescription Drugs

Pharmaceutical industry experts and some manufacturers do not attribute U.S.-Canadian differences in drug prices to U.S.-Canadian differences in research, production, or distribution costs. They cite three reasons why drug manufacturers' costs are not important sources of U.S.-Canadian price differentials:

1. A substantial proportion of drug costs is not allocated to specific products in specific countries. For example, the R&D costs associated with a specific product are not allocated differently to that drug product when sold in the United States and in Canada. Consequently, R&D costs would

not result in differences in the cost or price of a given product between the two markets.

2. Although some other costs, such as those linked to marketing and sales or to regulatory compliance, are allocated to individual drug products, the experts with whom we spoke said that these costs do not differ materially between the United States and Canada.

3. The costs of production and distribution also are allocated to specific drug products but make up only a small share of the total cost of any drug. Even if these costs were to differ greatly between the United States and Canada, they would not affect the total cost of a drug—or its price—substantially. Consequently, production and distribution costs cannot be a major source of price differentials.

Regulatory and Other Factors Linked to Lower Drug Prices in Canada

Price differentials appear to be driven by factors that influence how much manufacturers can charge for drug products in the U.S. and Canadian markets. Specifically, manufacturers selling drugs in Canada face two constraints that do not exist in the United States: (1) federal regulations that are designed to restrain introductory prices for new patented drugs as well as price increases for existing patented drugs; and (2) provincial drug benefit plans. The latter can exercise concentrated buying power, refuse to list new products as program benefits if provincial officials believe that the price is not commensurate with the perceived therapeutic benefits, remove drugs from their formulary list of reimbursable drugs if they consider proposed price increases too great, and provide information on products and prices to other drug purchasers and to prescribers.[14]

Federal Regulation of Patented Drug Prices

In a 1987 revision of the Patent Act, the Canadian federal government made a number of changes pertaining to pharmaceutical products. These changes included extending the time period during which generic competitors are prohibited from entering the market and competing with patented medicines. In conjunction with this change, the government established a quasijudicial price monitoring body, the Patented Medicine Prices Review Board. The PMPRB's mandate is to review the prices of patented medicines and ensure that they are not excessive. It examines both the introductory prices and subsequent price increases of drugs patented in Canada after 1987 and price increases for patented drug products that were on the market in Canada in 1987. The PMPRB reviews a

[14]These constraints are in addition to factors that affect prices in both the United States and Canada; for example, the medical condition or indication for which a drug is approved and the prices of drugs with similar therapeutic properties.

manufacturer's price in reference to PMPRB price guidelines. If the price of a drug product appears to be outside the guidelines, the PMPRB staff follow procedures designed to induce the manufacturer to lower the price voluntarily. After a public hearing, the PMPRB can order a price reduction to a level that is not excessive or remove market exclusivity to the manufacturer of the drug in question or of another drug product marketed by the same company.

The PMPRB appears to restrain Canadian drug prices. Our statistical analysis shows that price differentials are higher for drugs under PMPRB's jurisdiction. This analysis controls for other factors that may affect the drug price differentials, such as the drug's therapeutic category and availability of generic substitutes (see app. IV).

Provincial Purchasing of Drug Products

By virtue of their role as large third-party payers of prescription drug bills, provincial governments in Canada can exert pressure on manufacturers to lower their prices. Each of the 12 Canadian provinces or territories has its own drug benefit program, which results in that government wielding concentrated buying power. In nine of the provinces or territories (including the most populous provinces of Ontario and Quebec), the drug programs pay only for drugs used by the elderly and low-income persons. In the remaining three (British Columbia, Manitoba, and Saskatchewan), the drug programs pay for drugs used by all residents.[15]

Ontario's Drug Benefit Plan provides an example of how provincial plans affect factory prices for prescription drugs in Canada. Ontario is the most populous province (accounting for about 36 percent of Canada's population in 1988), and its plan pays for approximately 40 percent of the drugs sold in Ontario. The number of recipients using the ODB plan is larger than the entire population of many other Canadian provinces. Additionally, the reimbursement prices paid by the Ontario plan for specific drug products are considered to be generally representative of factory prices in other provinces.

In Ontario, the ODB plan establishes a formulary—a list of drug products it will reimburse. Each product in the formulary is listed with its own maximum price at which the pharmacist is reimbursed—the best available price. The BAP generally represents the lowest amount for which a listed originator (nongeneric) drug product (in each dosage form and strength)

[15]Several provinces require some cost-sharing by patients.

can be purchased in Canada for wholesale or retail sale in Ontario.[16] To have a drug listed on the formulary, a manufacturer must submit efficacy, safety, price, and supply information to provincial authorities. Using these measures, the authorities recommend a product for listing.

The ODB formulary is updated periodically (during the time of this study, the ODB shifted from a semiannual to an annual update), at which time manufacturers must submit updated BAPs for their products. If a submitted drug price is deemed too high, the Ontario Drug Program Branch may negotiate a lower price with the manufacturer or refuse to list the drug on the new formulary. In July 1991, 200 of 2,437 prices submitted by manufacturers reflected price increases that were considered excessive. In October 1991, 42 of these products were dropped from the formulary.

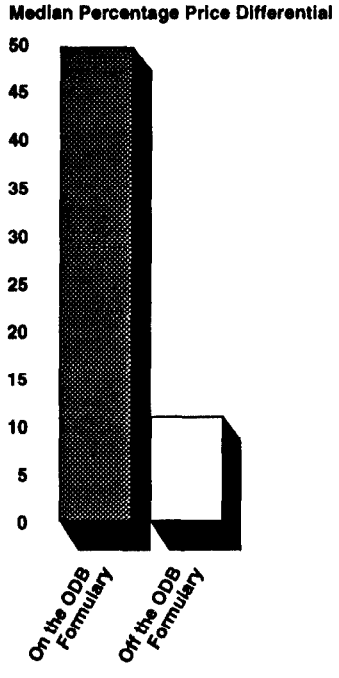
Use of the formulary indirectly exerts downward pressure on prices in Ontario. That is, the formulary affects the drug price by (1) specifying that the province will reimburse only the lowest price offered in Canada and (2) using price as a criterion for listing on the formulary. To gain—and retain—access to 40 percent of Ontario's prescription drug market, manufacturers must both submit prices that are acceptable to provincial authorities and supply the market at the BAP.[17] In addition, manufacturers' prices in Ontario are restrained indirectly by the formulary's dissemination of pricing information. The formulary listing, which includes drug product specifications and prices, is publicly available. Physicians can use the formulary as they prescribe drug products to patients and often view the formulary listing as a "seal of approval" for the drug. Private third-party payers also use it to establish drug reimbursement rates.

We found that a drug's listing on the ODB formulary was associated with higher prices in the United States relative to Canada—after controlling for other factors (see app. IV). The median differential between U.S. and Canadian drug prices falls from 49 percent, for drugs listed on the ODB formulary, to 10 percent, for drugs not listed on the formulary (see fig. I.3). Consistent with this finding, drugs are more likely to have lower Canadian prices (relative to U.S. prices) when they are covered by the ODB plan (see fig. I.4).

[16]In general, when generic substitutes are available, the ODB plan limits its payment to the BAP for the lowest priced product in an interchangeable category. However, the ODB plan pays product-specific BAPs for single-source products, noninterchangeable drugs, or cases where the prescribing physician designates "no substitution" for the brand name drug. For drugs with generic substitutes, the product-specific BAPs may be higher than the BAPs for generic substitutes.

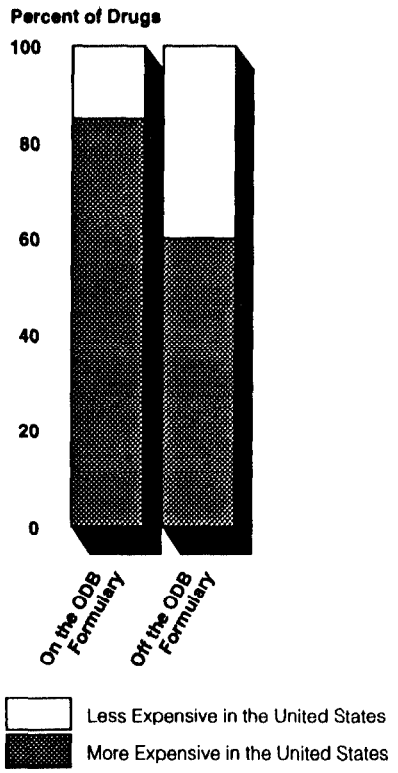
[17]Some drugs, such as those used predominately by the elderly, are even more heavily dependent on the formulary for sales because the ODB covers a high proportion of their sales.

Figure I.3: Drugs on the Ontario Drug Benefit Formulary Have Larger U.S.-Canadian Price Differentials



Note: Of the 121 drugs studied, 101 are on the ODB formulary.

Figure I.4: Drugs on the Ontario Drug Benefit Formulary Are More Likely to Be More Expensive in the United States Than in Canada



Note: Of the 121 drugs studied, 101 are on the ODB Formulary.

Use of Generic Drugs in Canada

In addition to regulations and provincial drug purchasing, the more rapid availability of generic substitutes probably contributes to lower prices of drugs in Canada. Canadian patent law traditionally promoted the sale of relatively low-cost generic alternatives. This reduces the average Canadian price paid for a given type of drug, relative to the average price paid in the United States for the same drug if a low-cost generic alternative is not yet on the market in the United States.

In examining price differentials only for originator (nongeneric) drugs, we did not estimate the direct effect of wider availability of generic substitutes on the average price paid for all drugs. However, we did estimate the indirect effect that generic substitutes have on the prices of originator drugs. In particular, our statistical analysis suggests that manufacturers of originator products respond to generic competition in a counterintuitive manner—by increasing price (see app. IV). This finding is consistent with findings from other studies, which contend that

manufacturers do not react to generic competition by lowering prices. Rather, they try to differentiate their product on the basis of perceived quality, brand loyalty, and line extensions (such as a sustained release form of a drug).[18] Because the market niche they are able to retain is likely to be less responsive to high prices than the niche of generic purchasers, producers can raise prices.

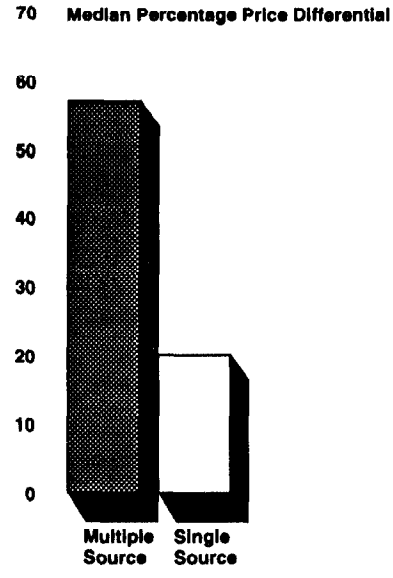
But our data suggest that in the Canadian market, manufacturers' ability to raise prices after encountering generic competition is limited by the combined effects of the PMPRB and the provincial drug purchasing plans. If manufacturers reacted to generic competition the same way in both countries, the price differentials would be similar for both single-source[19] and multiple-source[20] products. However, drugs that are single-source in both the United States and Canada display the smallest disparity in price, while drugs that are multiple-source in both countries have a larger disparity in price (see fig. I.5 and app. IV).

[18]See Health Care Financing Administration, Manufacturers' Prices and Pharmacists' Charges for Prescription Drugs Used by the Elderly, June 1990; Richard G. Frank and David S. Salkever, Pricing, Patent Loss and the Market for Pharmaceuticals, A Report to the Office of Technology Assessment, Dec. 1990; Paul K. Gorecki, Containing Drug Expenditures in Canada: The Ontario Experience, Economic Council of Canada and the Ontario Ministry of Health, 1992, pp. 83-106.

[19]Drug products for which there is only one manufacturer or supplier or for which there is a cross-licensing/marketing agreement between two manufacturers.

[20]Drug products for which there are generic versions from one or more suppliers or manufacturers.

Figure I.5: Drugs With Multiple Sources in the United States and Canada Have Larger U.S.-Canadian Price Differentials



Do Price Differentials Widen Over Time?

Statistical analysis offers support for another factor—the length of time that a drug has been on the market—as a cause of drug price differentials. One explanation for this phenomenon, suggested by some representatives of pharmaceutical manufacturers, is the potential for exchange rate changes over time to exaggerate true price differentials between countries. In particular, they contend that the identical drug product, introduced in two countries in the same year and at the same price, could display a large price differential 5 or 10 years later, solely because the exchange rate between the two countries had changed. Alternatively, our analysis could be capturing a compounding over time of the effect of Canada's drug price regulations. That is, if these regulations constrain the Canadian price relative to the U.S. price by, for example, 1 percent each year, the price differential would be greater for older drugs than for newer drugs. We were not able to determine the extent to which either of these two factors is responsible for greater price differentials among older drugs. (See app. IV.)

Implications of Canadian Regulation for U.S. Market in Dispute

That drug prices are lower in Canada than in the United States and that Canada regulates its drug prices have led some to propose restricting U.S. prices through regulation. The burden of prescription drug costs on public and private payers and on individuals would be lessened, to the extent that lowering the average level of U.S. drug prices to the Canadian level would

reduce U.S. drug expenditures. Critics and advocates of price regulation debate whether achieving an average U.S. drug price level similar to Canada's would have adverse effects.

A major focus of this debate is pharmaceutical innovation and its relationship to drug prices. Critics of U.S. drug price regulation claim that it would reduce research and development, thereby limiting the availability of innovative, new drugs in the future and denying their significant medical benefits to patients. An alternative possibility, however, is that price regulation may have little effect on the development of innovative products, but would instead simply reduce drug company profits and marketing outlays.

The debate over the linkage of drug prices to innovation in the United States cannot be resolved solely by referring to the Canadian experience with drug price regulation. First, the influence on R&D of Canadian price regulation cannot be disentangled from other factors that changed at the same time. The introduction of federal review of drug prices in Canada coincided with a commitment (to the government) by the drug companies to increase their R&D outlays in Canada. Subsequently, these outlays have increased. Second, Canada represents a small share of the world market. With the United States representing 31.5 percent of pharmaceutical sales in countries belonging to the Organization for Economic Cooperation and Development[21] (13 times more than the Canadian market), regulations that reduced drug prices in the United States would have a much more adverse effect on manufacturers' revenues than would similar regulation in Canada. We cannot predict the extent to which these reduced revenues would result in reduced R&D expenditures, nor the extent to which reduced expenditures would lead to less innovation or merely would encourage companies to adopt more efficient R&D activities.

In any case, the larger issue of the relationships between drug prices, drug company profits, and research and development lies beyond the scope of this study.

[21]An international organization of 24 industrialized countries in Europe, North America, and the Pacific.

Differences in Manufacturers' U.S. and Canadian Prescription Drug Prices (May 1, 1991)

Rank[a]	Product/ unit	Manufacturer or vendor	Package size	U.S. price[b]	Canadian price[b]	Price differential	Percent differential[c]
1	Amoxil, 250mg cap	Beecham	100	$17.27	$16.46	$ 0.81	5%
2	Lanoxin, .25mg tab	Burroughs Wellcome	100	7.83	6.75	1.08	16
3	Zantac, 150mg tab	Glaxo	60	70.19	53.82	16.37	30
4	Premarin, .625mg tab	Ayerst	100	26.47	10.10	16.38	162
5	Xanax, .5mg tab	Upjohn	100	47.81	16.92	30.89	183
7	Cardizem, 60mg capcr	Marion	100	49.00	57.51	-8.51	-15
8	Synthroid, .05mg tab	Boots	100	11.80	3.13	8.68	278
9	Ceclor, 250mg cap	Lilly	100	134.18	84.14	50.04	59
11	Vasotec, 10mg tab	MSD[d]	100	66.90	78.75	-11.85	-15
12	Tenormin, 50mg tab	ICI[e]	100	61.68	47.34	14.34	30
13	Procardia, 10mg cap	Pfizer	100	39.46	42.14	-2.68	-6
14	Ortho-novum 7/7/7, tab	Ortho	28	16.00	8.75	7.25	83
15	Capoten, 25mg tab	Squibb	100	41.73	43.36	-1.63	-4
16	Naprosyn, 375mg tab	Syntex	100	72.36	42.64	29.72	70
17	Tagamet, 300mg tab	SKF[f]	100	57.16	34.27	22.89	67
18	Calan, 240mg tabsr	Searle	100	85.74	115.80[g]	-30.06	-26
19	Prozac, 20mg cap	Dista	100	139.85	129.12	10.73	8
20	Ortho-novum 1/35, tab	Ortho	28	15.79	9.05	6.75	75
21	Tylenol w/codeine, 3 300/30mg tab	McNeil	100	19.38	3.32	16.06	484
23	Lopressor, 50mg tab	Geigy	100	35.71	15.80	19.91	126
24	Augmentin, 250mg tab	Beecham	30	36.60	22.29	14.31	64
25	Lasix, 40mg tabpp	Hoechst	100	14.20	9.55	4.65	49
26	Voltaren, 50mg tab	Geigy	100	64.70	52.04	12.66	24
28	Dilantin, 100mg capex	Parke-Davis	100	15.03	4.67	10.36	222
29	Theo-Dur, 300mg tabcr	Schering	100	18.70	22.33	-3.63	-16
30	Inderal, 40mg tab	Ayerst	100	35.79	10.21	25.58	251
31	Ventolin, 90mcg aero	Allen & Hanburys	17	15.53	10.24	5.29	52
32	Mevacor, 20mg tab	MSD[d]	60	88.49	85.19	3.30	4
33	Halcion, .25mg tab	Upjohn	100	47.69	16.09	31.61	196
35	Cipro, 500mg tab	Miles	100	213.24	205.30	7.95	4
36	Monistat, 2% cream	Ortho	45	13.30	10.56	2.74	26
37	Provera, 5mg tab	Upjohn	100	36.30	20.79	15.51	75
39	Triphasil, tab	Wyeth	28	15.60	9.46	6.14	65
40	Micro-K, 8meq capcr	Robins	100	9.49	6.35	3.15	50
41	Feldene, 20mg cap	Pfizer	100	167.54	123.61	43.93	36
46	Valium, 5mg tab	Roche	100	40.41	7.57	32.84	434

(continued)

Rank[a]	Product/ unit	Manufacturer or vendor	Package size	U.S. price[b]	Canadian price[b]	Price differential	Percent differential[c]
48	Coumadin, 5mg tab	Dupont	100	36.70	19.59	17.11	87
49	Motrin, 400mg tab	Upjohn	100	13.85	15.93	-2.08	-13
50	Diabeta, 2.5mg tab	Hoechst	100	20.42	9.70	10.72	111
52	E-mycin, 250mg tab	Boots	100	6.42	10.91	-4.49	-41
53	Timoptic, .5% ophth	MSD[d]	15	34.99	37.20	-2.21	-6
54	Retin-A, .05% cream	Ortho	45	34.30	13.54[g]	20.76	153
56	Nitrostat, .3mg tabsl	Parke-Davis	100	3.77	2.17	1.60	74
57	Pepcid, 20mg tab	MSD[d]	100	103.74	76.72	27.02	35
58	Estraderm, .05mg patch	Ciba	8	11.72	15.96[g]	-4.23	-27
60	Carafate, 1g tab	Marion	120	58.50	45.94	12.56	27
61	Lotrisone, 1% cream	Schering	15	10.90	7.39[g]	3.51	48
64	Eryc, 250mg cap	Parke-Davis	100	26.55	24.64	1.91	8
66	E.E.S.400, 400/5ml, liquid	Abbott	100	6.47	11.62	-5.15	-44
67	PCE, 333mg tab	Abbott	500	304.32	211.98	92.34	44
68	Slow-K, 8meq tabcr	Summit	100	11.58	5.65	5.93	105
69	Zestril, 10mg tab	Stuart	100	58.81	70.24[g]	-11.43	-16
70	Ativan, 1mg tab	Wyeth	100	49.43	6.16	43.27	702
72	Trental, 400mg tab	Hoechst	100	34.03	51.84	-17.81	-34
73	Macrodantin, 50mg cap	Norwich	100	46.71	27.14	19.58	72
74	Corgard, 40mg tab	Bristol	100	61.19	37.37	23.82	64
76	Nicorette, 2mg gumtab	Lakeside	96	26.00	20.83[g]	5.17	25
77	Tegretol, 200mg tab	Geigy	100	24.38	20.10	4.28	21
79	Terazol, .4% vag cr	Ortho	45	15.92	14.36[g]	1.56	11
81	Zovirax, 200mg cap	Burroughs Wellcome	100	62.50	92.88[g]	-30.38	-33
82	Clinoril, 150mg tab	MSD[d]	100	68.89	46.61	22.28	48
83	Ceftin, 250mg tab	Allen & Hanburys	60	120.74	69.01[g]	51.73	75
84	Transderm- Nitro, 5mg patch	Summit	30	31.69	30.35[g]	1.34	4
88	Slo-bid, 300mg capcr	Rorer	100	27.00	22.35	4.65	21
91	Anaprox DS, 550mg tab	Syntex	100	87.35	87.78[g]	-0.43	0
93	Flexeril, 10mg tab	MSD[d]	100	69.68	45.74	23.94	52
94	Isoptin, 80mg tab	Knoll	100	32.95	46.67	-13.72	-29
95	Prinivil, 10mg tab	MSD[d]	100	58.81	70.24[g]	-11.43	-16
97	Persantine, 50mg tab	Boehringer Ingelheim	100	33.90	30.03[g]	3.87	13
98	Buspar, 10mg tab	Mead Johnson	100	68.79	77.91[g]	-9.12	-12
102	Wymox, 250mg cap	Wyeth	100	16.84	16.46	0.38	2
103	Ansaid, 50mg tab	Upjohn	100	54.20	37.87	16.33	43

(continued)

Rank[a]	Product/ unit	Manufacturer or vendor	Package size	U.S. price[b]	Canadian price[b]	Price differential	Percent differential[c]
104	Percocet, 5/325mg tab	Dupont	100	43.70	30.35	13.35	44
106	K-Dur, 20meq tabcr	Key	100	22.60	21.55	1.05	5
108	Duricef, 500mg cap	Mead Johnson	100	203.69	100.39	103.30	103
112	Orudis, 50mg cap	Wyeth	100	69.99	28.14	41.85	149
113	Atrovent, 20mcg aero	Boehringer Ingelheim	14	17.87	13.13	4.75	36
114	Erythromycin Base, 250mg tab	Abbott	100	11.16	4.69	6.47	138
117	Hytrin, 2mg tab	Abbott	100	71.93	55.17	16.76	30
118	Sinemet, 25/100mg tab	Dupont	100	45.25	44.17	1.08	2
120	Isordil, 10mg tab	Wyeth	100	17.41	1.63	15.78	967
122	Intal, 20mg cap	Fisons	120	55.10	46.01	9.09	20
124	Vancenase AQ, 42mcg/ml nasal	Schering	25	22.82	8.71	14.11	162
129	Restoril, 30mg cap	Sandoz	100	45.25	18.06	27.19	151
130	Beconase AQ, 42mcg/ml nasal	Allen & Hanburys	25	22.82	14.60	8.22	56
131	Catapres, .1mg tab	Boehringer Ingelheim	100	35.51	22.62	12.89	57
133	Klonopin, .5mg tab	Roche	100	42.16	15.51	26.65	172
134	Dolobid, 250mg tab	MSD[d]	60	39.84	27.79	12.05	43
137	Ventolin Syrup, 2mg/5ml syrup	Allen & Hanburys	480	22.23	26.21	-3.98	-15
140	Erythrocin Staerat, 250mg tab	Abbott	100	11.00	9.90	1.10	11
141	Tri-Norinyl, var., tab	Syntex	28	15.54	8.39[g]	7.15	85
142	Nolvadex, 10mg tab	ICI[e]	60	63.82	61.33	2.49	4
143	Moduretic, 5/50mg tab	MSD[d]	100	35.40	28.52	6.88	24
146	Reglan, 10mg tab	Robins	100	34.46	5.34	29.12	545
149	Rogaine, 2% topsol	Upjohn	60	42.50	52.69[g]	-10.19	-19
152	Noroxin, 400 tab	MSD[d]	20	35.09	35.74	-0.65	-2
153	Cleocin T, 1% topsol	Upjohn	30	7.74	7.08[g]	0.67	9
154	Tenoretic, 50/25mg tab	ICI[e]	100	70.41	52.02	18.39	35
158	Norinyl, 1/50 tab	Syntex	28	16.17	8.81	7.36	84
159	Bactroban, 2% oint	Beecham	15	10.16	6.22	3.95	63
160	Axid, 300mg cap	Lilly	30	59.53	35.21	24.32	69
161	Achromycin V, 250mg cap	Lederle	100	5.46	4.02	1.44	36
163	Elavil, 25mg tab	Stuart	100	27.61	10.85	16.76	154
164	Phenergan, 25mg tab	Wyeth	100	18.43	9.14	9.29	102
167	Questran, 4g powder	Bristol	378	23.27	26.43	-3.16	-12

(continued)

Rank[a]	Product/ unit	Manufacturer or vendor	Package size	U.S. price[b]	Canadian price[b]	Price differential	Percent differential[c]
172	Deltasone, 5mg tab	Upjohn	100	2.35	1.29	1.06	82
174	Suprax, 400mg tab	Lederle	50	191.31	126.34[g]	64.97	51
180	Aldomet, 250mg tab	MSD[d]	100	24.61	13.52	11.09	82
181	Indocin, 25mg cap	MSD[d]	100	38.78	25.84	12.94	50
182	Pediazole, 200/600m susp	Ross	150	16.63	12.62	4.01	32
183	Tobrex, .3% ophth	Alcon	5	11.25	7.09	4.16	59
185	Premarin vaginal, 625mg/g vagcr	Ayerst	42.5	20.70	12.20	8.50	70
186	Dalmane, 30mg cap	Roche	100	40.80	12.13	28.67	236
187	Propine, .1% ophth	Allergan	15	24.72	20.99	3.73	18
190	Betoptic, .5% ophth	Alcon	10	22.50	18.72	3.79	20
191	Anaprox, 275mg tab	Syntex	100	56.11	46.67[g]	9.44	20
193	Bactrim DS, 800/160m tab	Roche	100	77.36	22.62	54.74	242
194	Vanceril, 42mcg inhale	Schering	16.8	21.14	8.71	12.43	143
196	Tussi- Organidin, 30/10 soln.	Wallace	480	35.06	14.92[g]	20.14	135
198	Topicort, .25% cream	Hoechst	15	9.66	7.68	1.98	26
200	Zovirax ointment, 5% oint	Burroughs Wellcome	15	24.29	29.51	-5.22	-18

[a]Product's rank among American Druggist's 200 most commonly prescribed drugs in the United States in 1990.

[b]U.S. prices are the May 1, 1991, Wholesale Acquistion Cost, as listed in the Medi-Span Master Drug Data Base-Select. Unless otherwise noted, Canadian prices are the Best Available Price listed in the February 1991 ODB formulary. All prices expressed in 1991 U.S. dollars, using May 1, 1991, exchange rate of C$1.1520 = US$1.00.

[c]The percent differential is rounded to the nearest 1 percent.

[d]Merck Sharp and Dohme

[e]Imperial Chemical Industries

[f]Smith Kline and French Labs

[g]Prices were obtained from the manufacturer or from a wholesaler in Ontario, Canada.

The Canadian Market for Prescription Drugs

Prescription drugs compose a significant and increasing share of health care spending in Canada. In 1989, Canadians spent 3.9 billion Canadian dollars, or 6.9 percent of total health care expenditures, on prescription drugs. Expenditures on drugs have increased rapidly, growing at an inflation-adjusted annual rate of 10.6 percent between 1980 and 1989. Also, as in the United States, drug prices have been increasing in Canada. Between 1981 and 1990, consumer and wholesale prices for pharmaceutical products (measured by Canada's Consumer Price Index and Industrial Products Price Index) grew at average annual rates of 8.7 and 7.7 percent respectively. For the same period, the average annual Canadian growth rate for the CPI (for all products) was 5.2 percent and for the IPPI (for all products) was 3.1 percent.

In contrast to the United States, which has a large innovative drug industry, most of the innovative prescription drugs sold in Canada are supplied by foreign manufacturers. These manufacturers do little research and development in Canada. Canadian-owned drug manufacturers generally produce generic products that require little investment in research.[1] As a result, Canada's R&D activities on prescription drugs, as a percentage of sales, are about half as high as in the United States: in 1990, 8.8 percent of pharmaceutical sales were spent on R&D in Canada, while approximately 17 percent of sales was spent in the United States.[2,3] Canadian patent law provides 20 years of patent protection for innovative pharmaceutical products. But Canadian periods of patent protection do not reflect the effective periods of monopoly power enjoyed by patented drug products. Specifically, Canadian periods of monopoly power are limited by a practice called compulsory licensing, which allows generic manufacturers to sell generic copies of products that are still on patent in Canada.[4] Patent law also provides for the review by a federal body, the Patented Medicine Prices Review Board, of factory prices of all patented drugs sold in Canada.

[1]Generic products account for about 10 percent of the Canadian prescription drug market.

[2]Patented Medicine Prices Review Board, Third Annual Report, June 10, 1991, p. 19; Pharmaceutical Manufacturers Association, Statistical Fact Book, Sept. 1991, p. 3.

[3]A future GAO report will examine drug prices in European countries that, like the United States, have domestic R&D-oriented pharmaceutical manufacturers.

[4]The 1987 amendments to the patent act (Bill C-22) established minimum periods of 7 or 10 years to be the sole seller of a product. Canada has recently announced its endorsement of proposals in the Uruguay Round of the General Agreement on Tariffs and Trade, which would require the elimination of compulsory licensing, thereby extending the period of market exclusivity for drug manufacturers.

Although the Canadian federal and provincial governments provide universal health insurance for their residents, many Canadian citizens obtain drug coverage through employee benefit plans or third-party payers or pay out-of pocket. The federal government does not require provinces to cover prescription drugs, leaving each province or territory to develop its own drug benefit program. Provincial drug plans pay about half of all prescription drug expenditures in Canada.[5]

[5]In the United States, public payers such as Medicaid cover a smaller share of drug spending—roughly 19 percent.

Multivariate Analysis of Factors Associated With Prescription Drug Price Differentials Between the United States and Canada

Through the use of a multiple regression model to analyze the data we collected, we identified factors that are associated with the differentials in prescription drug prices between the United States and Canada. These factors included Canadian price regulation, centralized purchasing by the provinces, the effects of generic substitutes on the market, and differences among certain therapeutic categories.

The statistical approach allowed us to estimate the effect of each factor on price differentials while controlling for the other factors. Our regression model explained 21 percent of the variation in price differentials.

Factors in U.S.-Canadian Drug Price Differences

Our data show a wide variation in the differences between factory prices for prescription drugs in the United States and Canada. Among the most commonly prescribed drugs in the United States, 1991 prices ranged from over 40 percent below to over 900 percent above the corresponding Canadian price. We tested whether the following factors are associated with variations in U.S.-Canadian drug price differentials for the drugs studied:[1]

- Whether the drug is subject to price regulation in Canada. If the PMPRB is effective at restraining the prices or price increases of introductory drugs (relative to what they would have been without regulation), there should be a greater difference between U.S. and Canadian prices for these drugs than for drugs not under PMPRB jurisdiction.
- Whether the drug is listed on the Ontario price formulary. Not only do the ODB's prices apply to about 40 percent of Ontario's prescription drug sales, but the prices—which are publicly available—are used by other third-party payers to set their reimbursement rates.[2] (Lower prices for drugs on the ODB formulary may be due to the ODB policy, but may also be affected by other provinces' price restraint efforts). These two effects may lead to a higher differential between U.S. and Canadian prices.
- Whether generic substitutes for the drug are available. The presence of generic substitutes in the United States, or in both countries, may increase prices in the United States relative to prices in Canada. Counter to conventional expectations of how firms react to competition, prices of

[1]Supply factors—such as those associated with R&D, marketing and sales, production and distribution, or regulatory compliance—are not included in our regression analysis. The exclusion of these factors is not likely to bias our results. Drug manufacturers and outside experts generally agree that these factors do not contribute substantially to drug price differentials between the United States and Canada.

[2]In addition, physicians—who often view the formulary listing as a "seal of approval"—may be reluctant to prescribe a drug not on the formulary.

nongeneric prescription drugs often rise in response to market entry by lower priced generic products.[3] While these price increases are not subject to regulatory control in the United States, in Canada the combined power of the PMPRB and the provincial drug benefit plans may reduce the amount by which manufacturers can raise their prices.

- Whether the drug manufacturer is U.S.-based. Although the pharmaceutical industry is multinational, manufacturers may be more knowledgeable about conditions in their home markets and thus able to obtain higher prices.[4] If so, the U.S.-Canadian price differential should be higher for drugs produced by U.S.-based manufacturers. In addition, U.S.-based manufacturers may charge higher prices, seeking to recoup higher marketing and R&D costs than are faced by their foreign competitors.
- Whether the differentials vary because of characteristics associated with major therapeutic categories. Manufacturers may be able to sustain higher prices for some types of drugs than for others; price differentials for these drugs will be higher to the extent that high prices for these drugs are restrained in Canada (either by the PMPRB or by provincial purchasing practices). For example, price differentials for central nervous system drugs may be higher than those for anti-inflammatory medications. As central nervous system drugs are less substitutable for each other than are anti-inflammatory drugs, demand for those drugs is likely to be less sensitive to price increases. Similarly, the price differential for central nervous system drugs should be higher than that for cardiovascular drugs. This is because proportionately more central nervous system drugs are off-patent than cardiovascular drugs—and likely have captured the part of the market that is least sensitive to price.
- The date of introduction. Drug price differentials may vary with how long the drug has been on the market. Some pharmaceutical manufacturers have suggested that price differentials between the United States and Canada would be smaller for drugs introduced more recently. In particular, changes in currency exchange rates could exaggerate price

[3]According to some industry experts, manufacturers of originator drug products do not compete with generic drugs on the basis of price. These experts suggest that manufacturers instead adopt other strategies to maintain revenues. One of these strategies is to try to establish a market niche based on brand loyalty. Once they establish this niche, which is likely to be less responsive to price increases than the generic drug purchasers, they can raise prices. A second strategy is to issue line extensions of existing products, such as a sustained release product, that are not subject to generic competition and, therefore, can garner higher prices.

[4]For example, they may be more aware of other drugs against which the product is competing or of the market's responsiveness to different price levels. Drug prices also may differ with the degree to which drugs in the therapeutic category are off-patent.

differences that are caused by internal market forces.[5] Alternatively, the compounding effect of Canadian price regulations may affect drug price differentials. If these regulations kept Canadian prices from growing less rapidly than U.S. prices, price differentials would have grown over time.

Multiple Regression Model

The dependent variable in our model (LFRAC) is the natural logarithm of the ratio between the U.S. and Canadian price per package. The independent variables (see table IV.1) are all dummy variables designed to capture the effects described in the previous section.

Table IV.1: Definitions of Variables Used in Multiple Regression Model

Variable	Definition	Mean[a]
LFRAC	Natural logarithm of the ratio between the price per package (in U.S. dollars) of a prescription drug in the U.S. and Canada	0.406[b]
PRE-C22	Dummy variable for patented drugs subject to PMPRB regulations on price increases but not subject to PMPRB review on introductory prices. These drugs were patented prior to passage of the C-22 legislation that established the PMPRB. Equal to 1 for patented drugs introduced before 1988; otherwise equal to 0	0.333
D88/89	Dummy variable equal to 1 for patented drugs introduced in 1988 or 1989; otherwise equal to 0	0.066
POST89	Dummy variable equal to 1 for patented drugs introduced after 1989; otherwise equal to 0	0.058
ODB	Dummy variable equal to 1 if drug is listed on the ODB formulary; otherwise equal to 0	0.835
GENERIC-US	Dummy variable equal to 1 if generic substitutes for the drug are available in the U.S. but not in Canada; otherwise equal to 0	0.107
GENERIC-CAN	Dummy variable equal to 1 if generic substitutes for the drug are available in Canada but not in the U.S; otherwise equal to 0	0.190
GENERIC-BOTH	Dummy variable equal to 1 if generic substitutes for the drug are available in both countries; otherwise equal to 0	0.372
ANTI-INFLAM	Dummy variable equal to 1 for anti-inflammatory drugs; otherwise equal to 0	0.174

(continued)

[5]Fredrik Andersson, "The U.S. Pharmaceutical Expenditures in an International and National Perspective," Batelle Medical Technology Assessment and Policy Research Center, Feb. 1992, pp. 11-13.

Variable	Definition	Mean[a]
CARDIO	Dummy variable equal to 1 for cardiovascular drugs; otherwise equal to 0	0.190
NERVSYS	Dummy variable equal to 1 for central nervous system drugs; otherwise equal to 0	0.207
HORMONES	Dummy variable equal to 1 for hormones and synthetic substitutes; otherwise equal to 0	0.107
USMFTR	Dummy variable equal to 1 if drug is produced by a U.S.-based manufacturer; otherwise equal to 0	0.603
POST84	Dummy variable equal to 1 if drug was first approved in the U.S. after 1984; otherwise equal to 0	0.333

[a]With the exception of LFRAC, all mean values denote the percent of total observations in each category. For instance, 33.3 percent of the observations are PRE-C22 drugs, 6.6 percent are D88/89, and 5.8 percent are POST89 drugs.

[b]The standard deviation for LFRAC is 0.52.

Three independent variables—PRE-C22, D88/89, and POST89—denote whether a drug's price falls under PMPRB jurisdiction. PRE-C22 refers to drugs that were patented and sold before the effective date of the 1987 legislation (known as C-22) that established the PMPRB and therefore have been subject only to regulations that affect price increases. D88/89 refers to drugs that were patented and introduced in 1988 and 1989. These drugs were subject to PMPRB regulation on both introductory prices and price increases. However, the introductory prices may have been set before the 1990 publication of the PMPRB guidelines on setting introductory prices (these guidelines were applied retroactively). POST89 refers to drugs that were issued after 1989; we assume that the introductory prices of these drugs were set with knowledge of the PMPRB guidelines. In addition, many of these drugs many not have been on the market long enough to have been subject to PMPRB regulations on price increases at the time we collected our data.

ODB reflects whether the drug is listed on the Ontario price formulary. The presence of generic substitutes is measured by GENERIC-US, GENERIC-CAN, and GENERIC-BOTH. Four therapeutic category dummies—ANTI-INFLAM, CARDIO, HORMONES, and NERVSYS—are proxies for characteristics that are unique to certain classes of drugs (such as differences in consumers' responsiveness to price changes, as well as for the degree to which there are therapeutic substitutes for a drug).

USMFTR measures whether the manufacturer is based in the United States, and POST84 represents drugs approved in the United States since 1985.[6]

Results of Estimating the Regression Model

The results of our regressions are listed in table IV.2. The high F-statistic suggests that the regression model as a whole is statistically significant, but the adjusted R-squared value of 0.21 shows that its explanatory power is modest. The low R-squared reflects the importance of factors for which data are lacking (such as aspects of the demand for particular drugs). The size and statistical significance of the coefficients are not sensitive to the specification of the model. Some of the coefficients did change in magnitude when we excluded apparent outliers—observations where the U.S.-Canadian price differential was far greater than those of the rest of the sample.[7] But generally there was little change in the confidence level of the estimates (exceptions are discussed below). There was also little change in the model's explanatory power when the outliers were excluded; the adjusted R-squared rose from 0.2147 to 0.2186.

[6]We chose 1985 as a cut-off point because it corresponds to the first year subsequent to the passage of the Waxman-Hatch Act (formally known as the 1984 Patent Term Restoration and Drug Pricing Competition Act). This law eased the entry of generic substitutes in the United States, and therefore may have represented a major structural change in the U.S. market.

[7]The outliers that were excluded in alternative specifications were observations in which the U.S.-Canadian price differential ranged from 434 percent to 967 percent of the Canadian price. The next highest price differential was about 278 percent of the Canadian price.

Table IV.2: Estimate of the Regression Equation

Dependent variable: LFRAC

Variable	Coefficient	Standard error
Intercept	-0.188	0.18
PRE-C22	0.288[a]	0.10
D88/89	0.206	0.19
POST89	0.420[a]	0.24
ODB	0.265[a]	0.15
GENERIC-US	0.247	0.16
GENERIC-CAN	0.123	0.13
GENERIC-BOTH	0.389[b]	0.12
USMFTR	0.092	0.09
ANTI-INFLAM	-0.110	0.13
CARDIO	-0.039	0.13
NERVSYS	0.294[b]	0.12
HORMONES	0.278[c]	0.16
POST84	-0.182[c]	0.10

[a]Significant at the .05 level (one-tailed test)

[b]Significant at the .05 level (two-tailed test)

[c]Significant at the .10 level (two-tailed test)

R-squared	0.3005
Adjusted R-squared	0.2147
Observations	120
F-statistic	3.5020

In brief, the results suggest the following:

- Higher price differentials are associated with patented drugs whose price increases were reviewed using the PMPRB's CPI guidelines only (PRE-C22), those drugs released after 1989 with knowledge of the PMPRB's guidelines on introductory prices (POST89), and drugs listed on the Ontario Drug Benefit Formulary. This is consistent with the effectiveness of PMPRB price

regulations and ODB leverage in restraining prices in Canada, relative to prices in the United States.[8]

- Higher price differentials are associated with drugs that have generic substitutes in both the United States and Canada (GENERIC-BOTH).[9] This finding supports the hypothesis that in the United States, manufacturers react to generic competition by raising their prices on their product, while in Canada, manufacturers are constrained from raising prices—either by the influences of the PMPRB or the provincial drug benefit plans.
- Some of the price differential may be explained by factors associated with particular therapeutic categories. Differentials are higher for both central nervous system drugs (NERVSYS) and for hormones and synthetic substitutes (HORMONES).[10] But there are no significant differences associated with anti-inflammatory drugs (ANTI-INFLAM) or cardiovascular drugs (CARDIO).
- When we control for other factors, there is no evidence that price differentials are higher for drugs produced by U.S. manufacturers than for drugs produced by foreign firms (USMFTR).
- There is some evidence that price differentials are lower for drugs introduced in the United States after 1984. The coefficient on POST84 is less than zero, with a 10-percent significance level.[11] We could not determine the extent to which this coefficient measures the effect of changes in exchange rates or the compounding effects of Canadian price regulations. The confidence level on coefficients associated with time on the market fell with alternative specifications of the variable.[12]

[8]When outliers are excluded from the model, the coefficients on PRE-C22 and POST 89 fall but are still positive and significantly different from zero. However, the confidence interval for PRE-C22 falls to 90 percent. The coefficient on the other variable relating to the PMPRB—D88/89 (denoting drugs that were introduced during a period in which there was uncertainty about how the PMPRB guidelines would work for introductory prices) is not significantly different from zero in any specifications of the model.

[9]When outliers are excluded, the coefficient on GENERIC-US becomes significant at a 90-percent confidence level, and the coefficient on GENERIC-BOTH falls by half but is still significantly different from zero at a 95-percent confidence level.

[10]When outliers are excluded, the coefficients on NERVSYS and HORMONES change, but are still positive and significantly different from zero. The confidence interval for HORMONES rises to 95 percent.

[11]The significance level on POST84 rises to 95 percent when the outliers are excluded from the equation.

[12]As an alternative way of capturing the effect on the price differential of the time at which a drug entered the market, we defined a variable equal to the number of years since approval. (The variable's value was truncated at 15; that is, all drugs approved more than 15 years before 1991 were given a value of 15 for the number of years since approval.) When our regression used the number of years since drug approval, the square of the number of years since approval, or both terms, the coefficient estimates on time were not significantly different from zero.

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