INTERNATIONAL DIFFERENCES IN DRUG PRICES

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Abstract  This paper addresses how and why drug prices differ across countries. Studies of international variation in drug prices reach varied conclusions owing to methodological and data disparities. Price differences do exist across countries, with the United States footing the highest bill, but the differences are not nearly as large as they appear at first glance.

The higher prices in the United States are concentrated among a subset of brand-name drugs and among those without insurance covering drugs. Some U.S. health plans obtain price concessions from manufacturers similar to those obtained by national governments. Price concessions occur whenever purchasers are willing to let price be a consideration in decisions about access and utilization.

In low-income countries the vast majority are unwilling to pay for effective drugs simply because they are unable to pay. Low-income nations need more price discrimination—and vastly lower prices—if they are ever to afford the world’s most effective medicines.

INTRODUCTION

Different people pay very different prices for the very same prescription drug. Those price differentials exist across countries and across classes of consumers within specific countries. When consumers learn of such differences they are often perplexed and even angry. Those who pay higher prices feel cheated, especially when they are less affluent or more vulnerable medically than those who pay less. In other situations, policy makers argue that drug prices should vary more widely across countries by lowering prices in countries with the lowest incomes to provide better financial access to life-extending drugs.

Understanding the magnitude of drug price differences that exist today, the reasons for those differences, and the economic and political arguments for or against changing the present pricing structure is important for the current and future health of the world’s population. Because prices affect the revenues of drug companies, and the potential for future revenues is what induces investment in new medicines (35), public policies that alter the pricing structure for existing drugs can have important impacts on what gets developed and what does not.
This paper addresses three questions: (a) How do drug prices differ across countries?, (b) What accounts for those differences?, and (c) What are the arguments for changing the distribution of prices or keeping them intact? We conclude that findings about the extent of cross-country variation in drug prices differ widely, largely owing to methodological disparities and data problems. However, in general, the evidence suggests that although price differences do exist across countries, with the United States footing the highest bill, the differences are not nearly as large as they appear at first glance. And, the high prices paid in the United States may be concentrated among the small minority of individuals who lack health insurance covering drugs. The reasons for disparities among rich nations boil down to the willingness of purchasers to let price be a consideration in decisions about access and utilization. Low-income nations probably need even lower prices than currently prevail if they are ever to be able to afford the world’s most effective medicines.

To lay the groundwork for understanding the evidence on international drug price differences, this review begins with a discussion of some definitional and measurement issues associated with studies of international prices. Then, we describe the evidence available from several recent studies of drug price differences among high-income countries. Discussion of the meaning of those findings and their implications for public policy follows.

ISSUES IN EVALUATING THE EVIDENCE

The Impact of Study Objectives on Study Design

Knowing the motivation behind a given study does much to explain the differences in methods and results across studies. International drug price comparisons are undertaken for at least three different reasons.

First, governments that engage in drug price regulation often collect comparative pricing data to support program operations and evaluate the program’s effectiveness. Studies of this kind may be limited in scope to the kinds of drugs covered by the country’s regulatory program.

The second motivation for international comparisons is simply to demonstrate that manufacturers charge different prices to different buyers for the identical product—that they engage in price discrimination as defined in the economic literature (29). Implicit in those studies is the assumption that manufacturers found to price-discriminate across countries behave inappropriately in the interest of higher profits.

The third motivation is to determine whether, on the whole, purchasers of prescription drugs in one country must pay more or less for a representative market basket of drugs than do purchasers in other countries. Studies of this kind are designed to evaluate the overall effect of a nation’s political and market environment on the prices at which drugs are available compared with other countries.

If the goal of the study is to evaluate a country’s price control strategy or to demonstrate that manufacturers do engage in price discrimination, then the
definition of a drug must be narrowly crafted by each of the product characteristics that might affect prices apart from regulations or sellers’ pricing strategies. Defining characteristics include the active ingredient(s), formulation, route of administration (e.g., oral, intramuscular), dosage form (e.g., extended release capsule, liquid solution), strength (e.g., 10 mg, 100 cc), package size, and manufacturer or vendor. When products are defined so narrowly, the commonality across countries in marketed drug products is quite small. For example, it is frequently found that the strength or package size available in one country is not available in others. Therefore, to ensure comparison of identical items, the products subject to comparison must be restricted to a relatively small subset of those available in any particular country (17).

If the purpose of the analysis is to determine whether purchasers of a given market basket of drugs are better off in one country than another, products must be defined more broadly. In particular, when the active ingredient is available from more than one manufacturer in the same strength and dosage form, then treating the product of each manufacturer as distinct would not provide a good estimate of the effectiveness of the country’s health care system in controlling drug prices. For example, suppose that as a matter of policy one country allows high prices for as long as a drug is protected by patents but encourages rapid entry of generic competitors and very low generic prices once patent rights no longer apply. Rapid access to inexpensive generic versions of high-volume drugs can have a substantial impact on a country’s total drug bill. Any analysis of cross-national differences in vendor-specific prices would mask the important price-moderating impact of a progeneric policy. Therefore, the ideal definition of a drug would include only clinical characteristics, which leave out vendor-specific characteristics, such as manufacturer or package size. The appropriate price measure would be a weighted average of prices across all products with the same clinical characteristics.

A drug’s price can be measured at different points in the supply chain, which starts with the manufacturer and ultimately ends with the patient. The price charged by manufacturers is generally lower than the amount paid by ultimate purchasers, with the difference flowing to wholesale and retail organizations. In the United States, wholesalers and retail pharmacies keep about 25% of payments for prescription drugs; the remaining 75% goes to manufacturers (22a). Because drug distribution systems vary across countries, price differences found at one point in the supply chain may not reflect differences that exist at another. Virtually all international comparisons of drug prices have focused on the prices charged by manufacturers at the factory.\footnote{Recently interest in the United States has focused on the prices that individuals covered by health plans or pharmacy benefit managers pay for drugs at the pharmacy, compared with individuals who have no drug coverage (27, 40). There are no studies of how different national systems for distributing and dispensing prescription drugs affect the final price paid by purchasers.} The emphasis on manufacturers’ prices is understandable not only because manufacturers receive most of the dollars spent on
drugs, but also because drug wholesale and retail industries generally do not operate across international boundaries. Therefore, the issue of international price discrimination at the wholesale or retail level is irrelevant. For the purpose of determining whether a given market basket of drugs is available more cheaply in one country than in another, prices to the final purchaser are most relevant, and manufacturer prices may be misleading in that regard.

To the patient, the most important price is the one that he or she will have to pay out of pocket at the time of purchase. Differences both across and within countries are much greater for out-of-pocket prices than they are for any other measure, but such differences are due in much greater part to the design of insurance benefits than to different prices charged by the manufacturers or dispensers of drugs. For example, in the United States, most individuals with drug coverage through group health plans pay a fixed amount—roughly $10 to $25—for a prescription, depending on whether it is a generic, a brand with preferred status with the health plan, or a brand that has no preferred status (17a). A prescription available at the pharmacy for a price of $100 would cost an insured individual $25, but would cost an uninsured consumer the full $100. If the health plan was able to negotiate a 20% discount, the final purchaser, comprising both the patient and the plan, would pay $80. However, the patient enrolled in the health plan would still pay $25, and the differences in out-of-pocket expenses would not change. Insured patients would benefit from the discount by paying lower premiums, but the savings would be spread across the pool of all insured individuals, regardless of their drug purchases. Thus, differences in out-of-pocket prices are stark and may raise questions of social justice, but they are mostly due to the underlying structure of drug coverage and not to differences in the full price paid, although those may also exist. This paper focuses on differences in the full price paid by the final purchaser, consisting of the patient and the insurer, not on the out-of-pocket prices paid by different kinds of patients.

Problems in Measuring Prices

Manufacturers' prices are difficult to measure accurately, especially in countries without publicly funded universal drug coverage. Estimates of manufacturer prices in some countries, notably in the United States and Canada, are generally based on list prices published by the manufacturer rather than on actual selling, or transaction, prices. This is because manufacturers carefully guard as trade secrets the average and lowest price they charge for their products. List prices are unlikely to be good proxies for transaction prices for a number of reasons. Discounts for volume purchases are not reflected in list prices.

Employers may also gain in the first instance because employer premium subsidies would decline as well as employee contributions. Economists generally assume that wages, which are determined in the labor market, are paid out by employers in a variety of forms, including benefits such as subsidy of insurance premiums (14). Thus, employees, in the end, reap the full savings from any price discounts obtained by health plans.
Volume discounts are particularly important for generic manufacturers of multi-
source drugs. (Multisource drugs are those available from more than one generic
or brand-name supplier.) Manufacturers of generic drugs usually must offer large
discounts to pharmacy chains and other high-volume dispensers to win a sole-
source supply contract. Therefore, list prices associated with generic drugs, to
a large degree, are upwardly biased when used as estimates of transaction
prices.

The upward bias is particularly acute in the United States, where reimburse-
ment systems employed by the public Medicaid program and other payers create
incentives for generic manufacturers to establish high list prices but to offer large
discounts to pharmacies. Table 1 shows the weighted average list price and the
weighted average manufacturer’s price for drugs dispensed in pill form to U.S.
Medicare beneficiaries in 1995. Multisource drugs were available from generic
manufacturers at prices that were, on average, 78% below their list prices, whereas
the manufacturers’ prices for single-source drugs (those with intellectual property
protection precluding generic competition) were only 22% below their respective
list prices.

Single-source drugs are less likely to be sold to pharmacists with big discounts
because pharmacies must stock brand-name drugs for the convenience of their
customers. They cannot negotiate with multiple suppliers for low prices because
there is only one supplier. The prices paid by pharmacies for single-source drugs
clustered tightly around 83% of the list price in 1999 (36). However, single-source
drugs are sometimes vulnerable to price competition from other products with
similar therapeutic effects. This kind of competition does not manifest itself in
discounts to pharmacists, who may dispense only the prescribed molecule without
consent of the prescribing physician. Rather, manufacturers, who have always vied
for the physician’s loyalty by using advertising and promotion, now compete for

| TABLE 1 | Weighted average price of drugs used by Medicare beneficiaries, 1995 (oral
solid dosage forms; per-pill price)  |
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Single-source drugs</strong></td>
<td><strong>Multisource drugs</strong></td>
</tr>
<tr>
<td>($ per pill)</td>
<td>($ per pill)</td>
</tr>
<tr>
<td>Brand-name list price</td>
<td>1.29</td>
</tr>
<tr>
<td>Brand-name manufacturer price</td>
<td>1.00</td>
</tr>
<tr>
<td>Generic list price</td>
<td>0.36</td>
</tr>
<tr>
<td>Generic manufacturer price</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Source: Reference 41a. Methods: Weighted average prices are based on relative frequency of use of different
Each drug is defined by active ingredient(s), dosage form, and strength(s) reported in the survey. List price is
the average wholesale price published in the Drug Topics Redbook (21a). Manufacturer’s price is the Average
Manufacturer’s Price reported by manufacturers to the U.S. Health Care Financing Administration as part of the
Medicaid rebate program (U.S. Health Care Financing Administration, unpublished data). For any drug available
from multiple sources, price was computed as the average price across all suppliers participating in the U.S. Medicaid
program, weighted by the quantity of the drug dispensed by each supplier to Medicaid recipients.
the business of the health plan, which in turn uses a variety of tools to influence patients and physicians to be more sensitive to drug prices (34).

In the United States, pharmacy benefit managers (PBMs)—companies that process drug payments for insured individuals on behalf of their health plans—receive rebates from manufacturers in exchange for steering their enrolled patients and prescribing physicians to specific drugs (11, 34). PBMs use economic incentives and educational tools directed at both the patient and physician to influence prescribing behavior. Rebates obtained through such efforts are not reflected in manufacturers’ list prices and may vary widely across drug products, depending on the amount of competition a drug faces from similar medicines (11, 34).

Measuring prices paid by the ultimate purchaser (the patient and his or her insurer) is also difficult. In countries with universal government-administered drug coverage, those prices are generally published by the agencies in charge of negotiating or regulating them. However, in the United States, where PBMs negotiate discounts with pharmacies and rebates with manufacturers, neither PBMs nor manufacturers disclose the effective price paid by the final purchaser. The same is true for public payers in the United States. For example, the U.S. Medicaid program, which paid for about 17% of all drugs dispensed on an outpatient basis in 2001 (32), makes public detailed information on amounts paid to pharmacies but does not make public the rebate that Medicaid obtains through a side payment from the manufacturer. Thus, in the United States the price that the final purchaser pays for any drug generally cannot be obtained from sources available to the public. Only prices paid for drugs purchased directly at retail pharmacies by patients without any third-party coverage can be estimated accurately through pharmacy surveys. Those prices are effectively the highest paid by any consumers in the United States (11).

Other Methodological Issues

Several additional technical and statistical issues complicate international price comparisons, particularly when the goal is to construct summary indexes of price levels across countries (3, 7). Foremost among them is the sample of drugs chosen for analysis. As discussed above, some studies examine only a small number of brand-name products, narrowly defined. A sample comprising the “leading” drugs—those with the highest sales revenue—is sure to be biased toward inclusion of single-source drugs.

Another source of difference among studies is the method used to weight the drugs in the sample. In some studies the summary price index is the simple average of prices across sampled drugs; however, weighting by the quantity of each drug dispensed is a sounder method for developing a comparative index of price levels. That said, the quantity of drug dispensed typically varies by country. Therefore, the country whose quantity weights are selected as the basis for comparison can influence the resulting index of relative prices. Studies evaluating national price regulatory systems tend to use their own country’s weights because the question
at hand is how costly the market basket of drugs actually dispensed in the home country would be if purchased elsewhere. However, the comparator country does not purchase the same market basket of drugs, so for policy makers in the second country, the relative price index so constructed is not indicative of the savings that would be achieved if drugs consumed in the second country could be purchased at the prices of the first country. To answer that question on behalf of the comparator country, its own weights should be used, and studies show the resulting differences are not trivial (6).

EVIDENCE OF INTERNATIONAL DIFFERENCES IN MANUFACTURER PRICES

A recent study by the Australian Commission on Productivity (26) is a carefully executed evaluation of a national drug price regulation system. Australia subsidizes prescription drug purchases for all residents and actively monitors and regulates the prices it will pay for single-source drugs. The Australian Pharmaceutical Benefits Scheme (PBS) relies on a detailed review of the clinical effectiveness and costs of new medicines in relation to products already on the market to establish a price at which it will subsidize consumers’ purchases. It also regularly reviews the prices of existing drugs that have close therapeutic competitors. In 2001, the Australian Productivity Commission, an agency unrelated to the ministry that manages the scheme, was requested by the Treasury to compare drug prices in Australia with those in other countries. To accomplish this, the study’s authors selected the top 150 molecules ranked by expenditures and weighted by the number of prescriptions filled for each specific product by the PBS (e.g., strength, package size, etc.) in 2000. Table 2 shows the pair-wise ratios of list prices between Australia and each of the selected countries for all drug products and for three subgroups of drugs, categorized as new innovative molecules (i.e., single-source molecules with no close competitors), me-too molecules (single-source molecules with similar therapeutic alternatives available in Australia), or multisource molecules. In all three categories, prices appear to be substantially higher in the United States versus Australia for the market basket of products that are common between the two countries. Australia tended to do better on the whole than most other countries as well.

A more careful look at the table reveals the importance of the price measure in creating a seemingly high difference between the United States and Australian prices. As discussed earlier, list prices are poor indicators of the true transaction

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3 For other examples, see studies sponsored by the government of Canada (5, 23).
5 The analysis also used dollar sales to weight products in constructing the relative price ratios. Differences between the two approaches were small.
TABLE 2  Price ratios in selected OECD countries compared with Australia, June 2000, weighted by number of prescriptions filled under the Australian PBS list prices. Source: Reference 26, Tables E4–E7

<table>
<thead>
<tr>
<th></th>
<th>Australia</th>
<th>United States</th>
<th>Canada</th>
<th>United Kingdom</th>
<th>Sweden</th>
<th>France</th>
<th>Spain</th>
<th>New Zealand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of products</td>
<td>All Drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>273</td>
<td>242</td>
<td>326</td>
<td>187</td>
<td>176</td>
<td>204</td>
<td>266</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High**</td>
<td>3.44</td>
<td>1.82</td>
<td>1.64</td>
<td>1.56</td>
<td>1.17</td>
<td>1.04</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>Low**</td>
<td>2.61</td>
<td>1.54</td>
<td>1.50</td>
<td>1.47</td>
<td>1.12</td>
<td>0.98</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>Me-too</td>
<td>High</td>
<td>2.30</td>
<td>1.66</td>
<td>1.30</td>
<td>1.18</td>
<td>0.96</td>
<td>1.13</td>
<td>1.14</td>
</tr>
<tr>
<td>Low</td>
<td>2.20</td>
<td>1.57</td>
<td>1.25</td>
<td>1.13</td>
<td>0.96</td>
<td>1.07</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>New innovative</td>
<td>High</td>
<td>1.69</td>
<td>1.06</td>
<td>0.99</td>
<td>0.82</td>
<td>0.75</td>
<td>0.89</td>
<td>1.13</td>
</tr>
<tr>
<td>Low</td>
<td>1.61</td>
<td>1.05</td>
<td>0.99</td>
<td>0.78</td>
<td>0.75</td>
<td>0.89</td>
<td>1.13</td>
<td></td>
</tr>
<tr>
<td>Multisource</td>
<td>High</td>
<td>3.65</td>
<td>2.19</td>
<td>1.41</td>
<td>1.17</td>
<td>1.04</td>
<td>1.04</td>
<td>1.00</td>
</tr>
<tr>
<td>Low</td>
<td>1.99</td>
<td>1.54</td>
<td>1.13</td>
<td>1.06</td>
<td>0.89</td>
<td>0.96</td>
<td>0.90</td>
<td></td>
</tr>
</tbody>
</table>

High estimate is based on the highest price listed by producers of multisource drugs, or the price for a larger but similar package size available in the comparator country when the Australian package size was not available.

Low estimate is based on the lowest price listed by producers of multisource drugs, or the price for a smaller but similar package size available in the comparator country when the Australian package size was not available.
prices for multisource drugs in the United States. List prices may also overstate manufacturer prices for me-too drugs, as those are the molecules most likely to generate rebates from manufacturers to PBMs or health plans. The price ratio for new innovative drugs is less subject to measurement error because the mechanisms available in the United States to exact price concessions for the other kinds of drugs are not available for new innovative medicines.

It is impossible to know how the aggregate ratio would be affected if actual transaction prices in the United States were made available for multisource and me-too drugs, especially since the weights used for drugs were not provided. Still, the price ratio is likely to be greater than 1. It is also worth noting that the ratio would likely be lower if prescription patterns in the United States had been used as weights (6).

Several studies, undertaken for the purpose of asking whether pharmaceutical manufacturers engage in price discrimination across countries, have found unequivocally that they do. A series of studies in the early 1990s by the U.S. General Accounting Office (GAO) (37, 38) focused on differences in factory prices between the United States and Canada as well as the prices between the United States and the United Kingdom for samples of frequently dispensed brand-name drugs. The methods underlying these pair-wise comparisons of prices in the United States with other developed countries differed in important ways, but for the specific set of brand-name drugs examined in each study, prices in the United States were higher than in the comparator country. In Canada (as exemplified by the Province of Ontario) the unweighted mean price of a market basket comprising 121 frequently prescribed brand-name drugs sold in both countries was 32% lower than in the United States. In its comparison of the United States and the United Kingdom, GAO found that the 1993 factory price of a market basket of 77 leading brand-name drugs, weighted by their volume of use in the United States, was about 60% higher in the United States than in the United Kingdom (38). The U.K. study is sounder in design, but it is limited to a relatively small and biased sample of 77 leading brand-name drugs. For those drugs, the GAO evidence is strong that

6 The authors attempted to correct for the list price bias by using prices published under the U.S. Federal Supply Schedule (FSS) for purchases by the Department of Veterans Affairs (DVA) and other Federal health providers. The resulting ratio for multi-source drugs declined slightly to 1.88–3.93, but FSS prices for generics are unlikely to reflect the actual prices available to wholesalers and retailers in the United States. This is because the DVA’s buying strategy for multisource drugs involves high-volume contracts through competitive bids. Therefore, generic manufacturers have no incentive to offer a low FSS price, which does not govern purchases.

7 GAO studied price differentials between the United States and Sweden, but they reported such differences only for a small number (i.e., 20) of products and did not develop a summary measure (17). A separate study comparing drug prices in the United States with those in France was restricted to a review of other older studies (2). For a summary of spending controls in the four countries, see Gross et al. (13).
manufacturers’ transaction prices were higher in the United States compared with the United Kingdom.

Danzon & Chao (6) provide the best example of a study that addresses the question of whether purchasers in one country are able to obtain a representative market basket of drugs at lower or higher cost than they could if they were able to purchase at the prices extant in another country (6). They compared manufacturers’ list prices in the United States with prices in 6 other OECD (Organization for Economic Cooperation and Development) countries using a large representative sample of drugs. They reported pair-wise price ratios for each country in comparison to the United States, using first U.S. prescriptions and then comparator country prescriptions as weights. Table 3 shows the results. U.S. weights universally resulted in higher price ratios for each country than did the comparator country’s weights, and in two cases—Canada and Germany—the prices in the comparator countries were higher overall than U.S. prices.

As with the studies reviewed above, the price measure used by Danzon & Chao (6) was restricted to list prices in the United States. Therefore, the reported ratios are likely to be inflated, largely because list prices substantially overstate true generic manufacturer prices in the United States. The authors also found that for a subset of drugs that are available globally (i.e., in all seven countries), the ratio of list prices in each country to those in the United States was closer to 1 than the equivalent ratio for all drugs. This finding implies that prices for drugs that are clinically important enough to be sold across all developed countries do not vary much, at least among the seven OECD countries studied.

Taken together, the literature on international price differences suggests that price discrimination does indeed exist at the manufacturer level. Some countries appear to get better prices than others for certain kinds of drugs. However, as demonstrated above, the true differences are likely to be less than what is found in these studies because of the variability of the list prices used, particularly for older

### TABLE 3

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of molecules</th>
<th>Price in country/price*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>420</td>
<td>0.447–1.021</td>
</tr>
<tr>
<td>Germany</td>
<td>438</td>
<td>0.403–1.247</td>
</tr>
<tr>
<td>France</td>
<td>373</td>
<td>0.330–0.678</td>
</tr>
<tr>
<td>Italy</td>
<td>386</td>
<td>0.485–0.871</td>
</tr>
<tr>
<td>Japan</td>
<td>365</td>
<td>0.457–0.884</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>377</td>
<td>0.560–0.834</td>
</tr>
</tbody>
</table>

*Lower ratio based on country’s quantity weights; higher ratio based on U.S. quantity weights.
multisource drugs and for drugs in crowded therapeutic categories. Furthermore, for drugs available generically, list prices are especially misleading as a basis of comparison, particularly when the United States is one of the comparators. In the case of new innovative drugs, where list prices are likely to be less subject to deep discounts and rebates, prices are higher in the United States than in some other countries, which does confirm the existence of price discrimination. Australia, as an example of a country that stringently regulates the entry price of new drugs, appears to be able to exact sizable price concessions on those drugs compared with purchasers in the United States.

WHY DO DRUG PRICES DIFFER ACROSS COUNTRIES?

Economic theory posits that a seller can engage in price discrimination only if three conditions hold: (a) the seller has monopoly power over production of the product; (b) different buyers are willing to pay different prices for the product; and (c) buyers cannot trade already purchased items among themselves (29).

Single-source prescription drugs meet all three conditions for price discrimination. By definition, they are protected by patents or other exclusive marketing rights that are enforced by national governments. Secondly, buyers find it difficult to resell prescription drugs to others. Wholesalers and retailers must generally be licensed in the country in which they want to sell, and cross-national licenses are a rarity. Finally, different buyers are willing to pay different prices for access to the same drug. The gradation of patients’ willingness to pay higher prices, especially for drugs with important clinical benefits, depends mainly on their financial resources. In low-income countries, few people have the financial resources to afford the high costs both of life-saving drugs and of other necessities such as food and shelter, and often times, individuals in these countries are forced to choose between the two.

The makers of single-source drugs typically engage in a particular form of price discrimination referred to as third-degree discrimination (29). In that form the seller has the power to charge a different price to two or more separate classes of buyers but must charge a single price to all members within each respective class. Each country, with its separate regulations governing the rights to market, prescribe, and dispense drugs, represents a separate buyer class. Separate buyer classes also exist within some countries, notably the United States and Canada;

8Although there are instances of cross-national trade in pharmaceuticals between pharmacies or wholesalers in low-price countries and those in high-price countries, especially in the European Union, for the most part manufacturers of single-source drugs can depend on maintaining different prices across countries. Recent outrage in the United States over high prices for Medicare patients who lack drug insurance has led to legislative proposals to allow reimportation of prescription drugs from countries with lower prices, particularly Canada (24, 28). Should such proposals be codified in law, price discrimination between the United States and Canada would be difficult to maintain.
in these countries, manufacturers can negotiate different price concessions in the form of rebates to members of different health plans (11).

It is in the interest of sellers to engage in price discrimination whenever possible. By doing so, the monopolist can extract a higher proportion of the amounts the buyers from each class are willing to pay. The monopolist could not generate these higher amounts if he or she was restricted to selling at the same price across all classes. Thus, price discrimination transfers much or all of the value inherent in the product from the buyers to the seller. That redistribution of value from the buyer to the monopolistic seller is what has given price discrimination in prescription drugs a bad name.

Despite its negative associations, price discrimination can improve the well-being of the world community, especially if it increases the amount of product sold overall (20, 41). The benefits of price discrimination are obvious for life-saving drugs such as those for HIV/AIDS. If a manufacturer was forced to sell these drugs at a single price to all nations, it would mean that the residents of some low-income countries would not be able to afford the drugs. A profit-seeking manufacturer would be unwilling to sacrifice the revenues available in high-income nations for the small gain in revenues achievable from selling at a low price to purchasers in low-income countries (5a).

The widespread availability of insurance coverage for drugs in virtually all developed countries has a profound effect on how price discrimination operates across international boundaries. All of the 15 member states of the European Union mandate universal coverage of prescription drugs, and except for the Netherlands, all administer their drug coverage through public programs (18). Most other OECD countries have public insurance for prescription drugs. However, in the United States and Canada the majority of residents are insured for prescription drugs through private insurance programs (10). Insurance for prescription drugs reduces out-of-pocket costs at the point of purchase and, therefore, increases demand for a drug at any price. The better the coverage is—that is, the lower the out-of-pocket price—the greater the stimulus is to demand. Because of this correlation, one would find little reason for drug companies to charge substantially different prices for highly effective single-source drugs across countries with generous drug coverage. Patients in all such countries would be able to afford equally high prices. Of course, governments that sponsor drug coverage (or, in the case of the United States, employer-based health plans) virtually always attempt to constrain the cost of their programs by managing consumer demand, moderating drug prices, or both. It is these cost-containment efforts—not deliberate strategy on the part of manufacturers—that have created price differentials among developed nations with universal or near-universal prescription drug coverage. Nations that are particularly effective in pressuring manufacturers to reduce their prices are the ones that will pay the lowest prices.

How do the managers of drug insurance programs go about demanding lower prices? Two basic strategies have been used throughout the developed world, and many cost-containment approaches involve a combination of the two.
Concentrate buying decisions. The national authority (or, in the case of the United States, a health plan) can decide whether a particular drug will be included on the list of covered products (referred to as the formulary). This decision may be a function of the price at which the product is offered for sale in the country. Price concessions can be quite large when more than one similar medication is available to treat the same condition. The authority can pit one manufacturer against another in the race to gain listing on the formulary. On the other hand, the maker of a truly unique and life-saving drug may not need to offer a substantial price concession to gain access to the formulary because the authority would have to consider the clinical implications of denying its enrollees financial access to such a product.

Some nations, such as Canada and the United Kingdom, offer the manufacturer an all-or-nothing deal: access to the national market at a “reasonable price,” as determined by the regulatory scheme, or no access at all. In the United Kingdom, the reasonable price is determined through a complex cost-accounting and rate-of-return system. In Canada, when a new drug is introduced, the reasonable price is the median price at which the product sells in a set of comparator countries, and the price cannot increase faster than inflation.9

Make enrollees more sensitive to price. By making patients more price sensitive, the authority can sometimes bring about reductions in the price at which a drug is offered in its country. Adding or raising deductibles (the spending threshold below which the patient must bear the full cost of a purchase) and raising the patient’s portion of the payment for each purchase are examples of approaches that many public programs have used to manage demand (18). This strategy has proven to lower prices in some countries.

When several similar therapeutic alternatives are available for the same condition, the authority can use the patient’s price sensitivity to inject more price competition in the market. Fixed out-of-pocket payments can be set at lower levels for drugs with lower prices than for similar drugs with higher prices. For example, a 30-day prescription for the lowest price drug among those in a therapeutic category might be assigned an out-of-pocket payment of $5, whereas a prescription for any other drug in the category would cost the patient $30. Another strategy would be to require the patient to pay, say, 20% of the cost of the lowest price drug, plus the full difference in the price between the lowest price and the price at which the purchased drug is offered.

The ability of an authority to induce or force manufacturers to reduce prices of single-source drugs is determined in large measure by the clinical importance of the drug and the extent to which it alone can deliver the clinical benefits to the patient.

9In Canada, the provincial governments run public drug subsidies for eligible groups. Those programs have attempted to extract additional price concessions through the use of the strategies discussed here (1, 16, 22).
Unique life-saving drugs are least likely to be amenable to price concessions. Drugs in crowded therapeutic classes, with many me-too alternatives available, are most vulnerable to price concessions. The evidence on international price differentials, imperfect though it is, supports these conclusions (6, 26). When a therapeutic class contains both single-source and multisource molecules, the potential for obtaining price concessions is very high because generic drugs can substitute for at least one of the brand-name drugs in the class.

Why are certain high-income countries able to obtain lower prices for certain kinds of drugs than are other countries? The politics and economics of each nation determine the answer. First and foremost, the smaller the role of government is in subsidizing drug purchases, the lower the probability is that the state will assume responsibility for controlling prices. In the United States, strategies to control drug costs must be implemented by a large number of private and public health plans, including employers, unions, private insurance companies, state governments, and federal agencies. Although actual prices in the United States do not appear to be much higher than in some other countries, the effectiveness of many different private insurers is likely to vary. None of the insurers has the power to keep a drug off the entire market if its maker refuses to sell at a favorable price, as does a national government providing universal drug coverage for all its residents.

Permissive pricing policies may also be a response to political pressures applied by a large domestic industry intent on protecting its interests. The United States and Switzerland are two countries with substantial employment in research and development (R&D) and manufacture of brand-name pharmaceuticals as well as little or no direct regulation of drug prices. Australia and New Zealand, on the other hand, have almost no research-intensive pharmaceutical industry, and both have experimented with tough strategies for controlling prices (26, 42). Pricing policies can also be part of a national industrial policy intended to encourage the development of a research-based pharmaceutical industry. Granting higher prices on drugs developed or produced in the home country is an indirect subsidy to the domestic industry. For example, the U.K. price-regulation scheme, which allows companies to set prices within a proscribed profit band, favors domestic companies with high levels of invested capital in the United Kingdom (21, 22b).

One policy undertaken by the U.S. federal government to control prices paid by the Medicaid program has had a perverse effect on the ability of private health plans to obtain large price concessions. The Medicaid program operates under a “best price” provision, which requires that manufacturers of brand-name drugs offer to Medicaid the lowest price they give any private health plan or provider. Because Medicaid represents a large portion (17%) of the outpatient prescription drug market, any price concession to a small health plan that bargained aggressively would carry a large penalty in the form of lower prices to Medicaid. The available evidence suggests that the best prices offered to the private sector by makers of brand-name drugs rose after the “best price” provision was enacted (33). Although Medicaid obtains lower-than-average prices from manufacturers as a result of the
law, it may be uniquely responsible for keeping average prices higher across all payers than they are in other countries.

**IMPLICATIONS OF PRICE DIFFERENTIALS AMONG HIGH-INCOME NATIONS**

Several observers have questioned the inherent fairness of national pricing regimes that leave some high-income nations with high prices and others with lower prices (12, 39). Consumer advocates in the United States claim that manufacturers of single-source drugs reap high profits from U.S. sales, while giving substantial discounts to residents of other high-income countries. Implicit in these arguments is the suggestion that prices in the United States should be reduced to levels obtained by other countries. Aside from the question of how great the differences in transaction prices are across high-income countries (discussed above), it is worth asking whether prices are too high in the United States or too low in other countries. What would be gained or lost from a one-price policy that either reduced the high prices or raised the low prices?

In the short run, consumers across the developed world would be better off with a one-price policy that settled at the lowest prices paid among industrialized countries. The gains to consumers would come largely at the cost of lost revenue to pharmaceutical companies that make single-source drugs. Although lower prices might stimulate demand somewhat in the previously high-price countries, the extra demand would not replace the revenue lost from the price reduction. If it could, manufacturers would already have lowered their prices in the rich countries.

Lower revenues would not keep pharmaceutical companies from producing drugs already on the market because manufacturer prices of most single-source drugs far exceed the marginal costs of producing them. This is true even in countries that obtain relatively low prices for single-source drugs. Table 1 gives a rough estimate of the premium that single-source drugs command over the cost of production in the United States. Average manufacturer prices of generic drugs were only 20% as high as the equivalent price of brand-name multisource drugs purchased by Medicare beneficiaries in 1995, and only 8% as high as the equivalent price of brand-name single-source drugs. For the most part, generic manufacturers face vigorous price competition; therefore, generic prices can be considered reasonable proxies for the cost of production. If the GAO finding is correct that U.K. prices are just 60% as high as U.S. prices (38), a reduction in U.S. prices to the level prevailing in the United Kingdom would still leave substantial net revenues available to the sellers of such drugs.

The main loss from reducing prices to those currently obtained by low-price countries would come though reductions in investments in R&D that would
inevitably result. R&D decisions depend on investors’ evaluation of the potential returns from each project (35). If prices were systematically reduced, investors would expect lower revenues from any future drugs that might reach the market. Projects with lower chances of success or those with higher expected R&D costs would no longer find investors. Conversely, raising prices in all countries to those of the high-price country would induce investment in higher-cost or more risky R&D projects. To the extent that the burden of price reduction fell differentially on certain kinds of drugs, R&D for those projects would decline disproportionately.

For example, if price differences were relatively greater for unique innovative drugs than for me-too molecules, a one-price policy at the lowest price would reduce future R&D for the most innovative products. The evidence reviewed in this paper suggests that the opposite is true: Price differences are smaller for unique drugs than for those with many similar competitors. Thus, eliminating price disparities across all products would have less of an effect on unique drugs than on drugs with similar competitors.

In the end, a one-price policy would probably settle at a price somewhere between the high and low ends of the existing price spectrum (5a). Consumers in some countries would gain from lower prices, while those in other countries would lose, but the gains and losses would be smaller than under extreme scenarios. R&D effects also would be less dramatic.

Critics of international price differences often contend that nations engaging in stringent price controls gradually see R&D move to countries with more favorable price strategies (4, 5b). According to Calfee (4, p. 46), “as other advanced nations have implemented pharmaceutical price controls, the locus of research has moved steadily to the United States, where firms produced all ten of the worldwide best-selling drugs.” However, correlation does not imply causation. The United States is not only the largest single market, comprising approximately 40% of the world pharmaceutical market (25), but also it has a well-developed academic research establishment, robust and growing public investment in biomedical research, and favorable laws regarding transfer to the private sector of technology developed under government-funded research. The locus of drug development is also influenced by regulations of the U.S. Food and Drug Administration (FDA) and equivalent agencies in other nations that limit the acceptability of clinical research conducted in foreign countries. Thus, although the United States may have an effective industrial policy that stimulates R&D, there is no evidence to

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11 In the past, the regulations of the U.S. FDA and equivalent drug registration agencies in Europe and Japan governing clinical research to support new drug approvals differed in important respects that created barriers to the acceptance of data produced in foreign clinical trials. In 1990, an International Conference on Harmonization (ICH) was formed to address artificial impediments to more efficient drug development. The ICH began as a single meeting but has emerged as an intergovernmental process for the development of common guidelines across countries. As national agencies implement the guidelines governing all aspects of the drug approval process, the location of clinical research becomes less closely tied to specific markets. More information about the ICH is available at http://www.ich.org/ich2.html.
suggest that relative price levels are responsible for the predominance of U.S. pharmaceutical R&D.

A simple thought experiment illustrates how price controls might affect R&D. Suppose, first, that Australia were to abandon, unconditionally, all price regulation of prescription drugs. Would such a move spur drug companies to close research facilities in the United States and set up research facilities in Australia? Probably not in the absence of other incentives, such as subsidies for construction of R&D facilities or policies that condition access to Australia’s market on increasing R&D in Australia. Australia’s move might stimulate worldwide R&D slightly because that country’s willingness to pay for new drugs would have increased, but the R&D would not need to be located in Australia. Then, suppose that the United States were to adopt a universal drug insurance program with the government in charge of setting prices. Suppose, also, that those prices were set at much lower levels than exist at present. Would that strategy spur drug companies to move their research facilities from the United States to another country? Probably not, though a decline in the willingness to pay for new drugs in a market comprising 40% of world pharmaceutical sales would undoubtedly have important negative impacts on worldwide R&D.

To the extent that U.S. transaction prices for single-source drugs are indeed higher than prices paid in other countries, other equally high-income countries get to ride free on the R&D that those higher prices induce (20). All people gain from the availability of new drugs on the world market. But, there is no way of knowing whether the existing array of prices paid across countries induces an aggregate level of R&D that is efficient in an economic sense.\textsuperscript{12} More R&D is not always better for the world as a whole, given the lost opportunities for other uses of the funds, and, conversely, less R&D is not always worse. Less R&D is likely to result in fewer new drugs, but that absolute loss must be considered in light of the alternative uses to which the freed resources can be put. Thus, the argument frequently made by those opposing stringent price regulations in the United States that R&D would suffer, while true, does not invalidate arguments for lower prices. Conversely, calls for lower prices in the United States could have worldwide long-term effects that might be far from benign.

\section*{IMPLICATIONS OF PRICE DIFFERENTIALS BETWEEN HIGH-INCOME AND LOW-INCOME NATIONS}

As discussed above, manufacturers of single-source drugs should be willing to charge lower prices in low-income countries. Although some single-source drugs have been made available for free or at nominal charge to developing countries with high endemic rates of diseases such as HIV/AIDS and tuberculosis (15),

\textsuperscript{12}Economic efficiency requires, first, that an extra dollar devoted to drug R&D would not yield greater benefits to society than would any alternative uses to which the dollar could be put, and, second, that one less dollar devoted to drug R&D could find no alternative use that would provide as much benefit to society.
manufacturers of single-source drugs are reluctant to offer vastly lower prices across the wider spectrum of drugs. For countries with extreme rates of poverty, anything but very low prices would render single-source drugs unavailable to all but the few wealthy residents. The principal impediments to low prices are the fears of the drug companies that a resale market would develop across national borders from low-income countries to high-income countries or that political pressures would develop in high-income countries to demand the lower prices given to the low-income countries (20). These fears may be justified given the history in the United States of consumer groups and policy makers questioning the need for high markups on production costs (27) and calling for relaxation of rules governing cross-border trade in pharmaceuticals (24, 28).

As the impact of HIV/AIDS, malaria, tuberculosis, and other diseases on the lowest-income countries has become impossible to ignore, governments, international agencies, nongovernmental organizations, and industry have begun to address how to make highly effective drugs available at an acceptable cost.\(^\text{13}\) There are other hurdles in getting such drugs to those who need them most, such as the lack of social infrastructure, including adequate health delivery systems. These hurdles are becoming increasingly important because for certain highly visible diseases the cost of the drug itself is unlikely to remain the principal impediment to treatment for much longer, as drug companies negotiate with international organizations to provide their drugs at low cost while protecting their pricing structures in high-income countries.

Some diseases endemic to low-income countries are rare in high-income nations. The potential market for future therapies is therefore small, and private R&D is simply not pursued for many such diseases (31). Offering low prices to low-income countries cannot solve the problem because there are no products available on the market. Rather, the problem is one of inadequate incentives for the private sector to engage in R&D for such drugs. A recently announced initiative of Medicins Sans Frontier, the World Health Organization, foundations, and drug companies, called Drugs for Neglected Diseases, will fund investments in R&D for such drugs (19).\(^\text{14}\) The success of such an effort will depend on the ability to find sources of R&D subsidy in the governments and institutions of high-income countries.

**CONCLUSIONS**

Although drug manufacturers do indeed charge different prices for the same drug in different countries, the reasons for such differences have more to do with the political and health insurance environments of individual nations than with innate

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\(^{13}\)See, for example, the ongoing efforts of the Global Fund to Fight AIDS, Tuberculosis, and Malaria, established in 2002, to bring resources to bear on the three major diseases of low-income countries (30). Information on the Global Fund may be found at http://www.globalfundatm.org/.

\(^{14}\)For information on the Drugs for Neglected Diseases initiative, see http://www.msf.org.
differences in willingness to pay, at least among the world’s high-income countries. Patent protection and other intellectual property rights combine with rigid regulation of prescribing and dispensing practices to give makers of single-source drugs substantial market power by precluding competition from generics. Universal or near-universal drug insurance in high-income countries artificially creates low price sensitivity on the part of patients. Only by harnessing demand either by regulatory fiat or through mechanisms to reduce insured individuals’ willingness to pay can individual nations or health plans obtain price concessions from makers. Even then, it appears that such differential price concessions are lower for drugs with unique clinical benefits than for those with close competitors.

The weight of the evidence suggests that residents of the United States may pay more of the manufacturer’s share of the cost of single-source drugs than do residents of certain other high-income countries, but the differences are not as large as commonly claimed by critics of differential pricing and may be concentrated in buyers who have no insurance. Health plans in the United States have used mechanisms similar to those applied by national governments to obtain price concessions from manufacturers. U.S. health plans may be hindered by the Medicaid “best price” law, however, which effectively limits their ability to bargain with drug makers for rebates on drugs with close therapeutic competitors.

Low-income countries are in a special position. The vast majority of their residents are unwilling to pay for effective drugs that are widely available in high-income countries simply because they are unable to pay for them. For those countries, active price discrimination by manufacturers, buttressed by political acceptance of such pricing strategies by rich countries and rigid enforcement of separate markets, is a potential solution to the problem of access to the most effective single-source drugs in low-income countries.

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