Setting Cost-Effectiveness Thresholds As A Means To Achieve Appropriate Drug Prices In Rich And Poor Countries

ABSTRACT Finding better mechanisms to enable differential pricing that reflects different degrees of willingness to pay across countries with different income levels is an important challenge for drug manufacturers and policy makers. Drug prices must be high enough to meet manufacturers’ needs—covering costs and ensuring adequate investment in research and development, as well as producing a profit—but low enough to allow consumers access to medicines that they need. Examining drug pricing, we found that in rich countries, insurance coverage can make consumers insensitive to price, which means that manufacturers’ prices are largely unrestrained unless payers intervene. In middle- and low-income countries, where most consumers pay for drugs out of pocket, we found that the poorest countries face the highest prices, relative to their mean per capita income. We recommend that countries and payers set their own cost-effectiveness thresholds to reflect how much they are willing to pay for “health gain”—in other words, for a measured improvement in the health of a person or a population. Adopting this approach broadly should lead to appropriate price differences across and within countries, benefiting consumers and manufacturers alike.

Pricing and use of pharmaceuticals is a contentious issue for policy makers in both industrialized and developing countries. From an economic perspective, efficiency requires two potentially conflicting conditions: first, that existing drugs be available to patients whose expected benefit exceeds the drugs’ marginal production cost; and second, that manufacturers have incentives to develop new drugs for which expected benefits exceed costs. Patents are an imperfect but practical way to balance these concerns, enabling companies to price drugs above their marginal cost and thereby recoup expenditures on research and development, although at the cost of potentially excluding some consumers because of the drugs’ prices. All high-income countries have comprehensive public or private health insurance systems, which ensure to varying degrees the affordability of medicines, despite high prices because of patents. However, insurance makes patients insensitive to cost, which encourages manufacturers to charge even higher prices than would result from the patent process alone. Excessive prices resulting from consumers’ price insensitivity potentially distort incentives for research and development and lead to excessive taxes or premiums to fund the insurance. Thus, the key pricing question in countries with comprehensive insurance is how to constrain this insurance-induced effect on drug prices, while providing appropriate incentives for manufacturers to invest in research and development.
Because innovative pharmaceuticals are global products, prices should differ across countries to reflect each country’s valuation of each product’s health benefit, which will reflect local preferences and income levels. Most people agree that high-income countries should pay more than very poor countries. Yet there is no consensus on how much more, or on the appropriate prices for middle- and low-income countries. The key pricing question in countries without comprehensive insurance systems, where most patients pay out of pocket for drugs, is how to ensure that competition in cash-paying markets operates efficiently, to achieve a balance between affordability and making some contribution toward research and development.

This paper summarizes our analysis of these two major pricing policy challenges. Specifically, it asks the following questions: First, in countries with comprehensive insurance coverage, how might third-party payers achieve optimal pharmaceutical prices and use for drugs that have patent protection? In particular, how might these be achieved, given the dual objectives of appropriate use of existing drugs and appropriate incentives for research and development, and reflecting the willingness and ability to pay for medical care of citizens in those countries? Second, in middle- and low-income countries lacking comprehensive insurance, where patients pay out of pocket, do markets work well enough to keep at reasonable levels the prices of both generic drugs and “originator” drugs—those that are based on research and that might be patented? And third, if markets do not produce reasonable prices, why are they failing to do so?

We first outline how payers can address the issue of optimal pricing in comprehensive insurance systems. We then summarize the results of our study of pharmaceutical markets in middle- and low-income countries, focusing on the prices of drugs to treat HIV/AIDS, TB, and malaria. We compare the prices for originator and generic drugs that manufacturers charge to the retail pharmacy sector and the prices that manufacturers charge to nongovernmental organizations that procure these drugs on behalf of low-income countries. We conclude by summarizing policy implications for pharmaceutical pricing in both insurance-based systems and cash markets, with a view to increasing efficiency in the use of existing drugs and in levels of global research and development.

Countries With Comprehensive Insurance Coverage
The starting point for any economic analysis is the assumption that consumers’ preferences, as reflected in their willingness to pay, should drive resource allocation between different goods and services. Given the characteristics of health care—including its uncertainties and possible high costs—most people want to buy insurance. Most industrialized countries have committed to providing coverage for all citizens that ensures their access to basic health care—including drugs—regardless of ability to pay and with only modest patient cost sharing. But as noted above, by protecting consumers from health care costs, insurance creates incentives for manufacturers to charge higher prices. Insurers and all other third-party payers struggle with the challenge of how to constrain drug prices while still encouraging research and development.

One possible response to that challenge is to control drug prices directly. However, all current systems of price controls are ad hoc and poorly designed to achieve the goals of reconciling appropriate access to drugs with appropriate research and development incentives. We elaborate below on the problems with the two main approaches to controlling prices: internal and external referencing.

Cost sharing is the preferred approach in the United States to constraining drug prices, but it is either ineffective or inappropriate for high-price medications and for even modest-price medications for chronic conditions. This is because most people’s insurance coverage appropriately includes a limit on overall cost sharing, keeping the total below “catastrophic” levels. Patients who take high-price drugs or even several modest-price drugs soon exceed this catastrophic limit, after which they face no more than nominal cost sharing. Patients who lack such catastrophic protection may simply decide not to take medication unless they are eligible for manufacturers’ assistance programs, in which case they, too, face at most nominal cost sharing.

A Cost-Effectiveness Framework We propose instead that each public and private payer should set a maximum for a measured improvement in the health of a person or a population—in other words, a price per unit of “health gain”—that it is willing to pay. That price would reflect its budget and ultimately its beneficiaries’ willingness to pay taxes or premiums to buy medical care rather than other goods and services. The price per unit of health gain can be expressed as an incremental cost-effectiveness ratio threshold. In this scenario, a manufacturer could freely decide what to charge for a drug but would effectively be constrained to choose a price in proportion to the drug’s incremental benefit. Patients would face modest cost sharing, and the payer would pay a reimbursement to “top up” to the manufacturer’s price. The payer would limit
eligibility for such reimbursement to patients for whom the drug is cost-effective at the manufacturer’s price. We now flesh out the details of this proposal.

One widely used measure of health gain is the quality-adjusted life-year. For example, the independent National Institute for Health and Clinical Excellence in the United Kingdom estimates the additional life-years and quality of life that the use of a new product would provide, as well as the product’s cost as an additional treatment. The ratio of extra cost to extra benefit can then be expressed as a cost per quality-adjusted life-year gained. If this ratio is below the institute’s threshold of $33,000–$50,000, it recommends the product for use. In the case of the cost-effectiveness of Herceptin for treatment of breast cancer, a study found a gain of 1.7 quality-adjusted life-years for additional costs of $45,000, giving a cost of $26,400 per quality-adjusted life-year gained. The institute’s analysis used lower costs but fewer quality-adjusted life-years, for a ratio of $30,000 per quality-adjusted life-year. This was below its threshold, and the treatment was approved for use in the English National Health Service.

By setting a threshold price per unit of health gain or cost-effectiveness ratio as a condition of reimbursement for drugs and other products, the payer indirectly controls the price—at least in proportion to the drug’s incremental value. A new drug that offers meaningful benefits beyond those provided by existing drugs can charge a commensurately higher price than the older drugs’ prices and still meet a cost-effectiveness threshold.

This approach resembles value-based pricing, but it leaves the manufacturer free to choose its own price or prices, given the effectiveness of its product and each payer’s willingness to pay for health. Constraining prices by means of a cost-effectiveness threshold aligns prices with the degree of therapeutic value provided, which provides optimal incentives for innovation.

In our proposal, patients would face modest cost sharing to deter overuse and to provide partial financing for the insurance program, but payers would decide what use they would reimburse based on cost-effectiveness at the manufacturers’ prices. These assumptions roughly describe the current practice in most national or social insurance systems. And even in the United States, private and public insurers use step therapy and prior authorization requirements to limit access to expensive drugs or procedures to those patients expected to derive the greatest benefit from them.

**Changing Prices for Drugs:** Some drugs are highly effective for one indication but less effective for others. For example, many drugs work well on one type of cancer but less well on other types. In these cases, drug prices could vary, with lower prices for indications with lower effectiveness, and still meet the cost-effectiveness threshold. This would ensure optimal use of drugs and optimal incentives for research and development. In practice, unfortunately, it may be too difficult to administer reimbursements for more than one price per drug.

The problem of appropriate pricing for a drug with different levels of effectiveness applies not just to our proposal but to any value-based pricing scheme. Similarly, all such schemes need to determine how prices should be updated over time, as evidence on effectiveness or other factors change.

**Patients’ Copayments:** Other economists have proposed setting patients’ copayments at the marginal cost of a drug and letting patients determine use in response to financial incentives. The payer would give the manufacturer a top-up payment, based on the demand for the drug by its beneficiaries, as an incentive for research and development. Our approach also includes a two-part payment, consisting of the patient’s copayment and the payer’s top-up payment. However, for several reasons we reject the proposal to set copayments equal to marginal cost and let patients determine use.

First, the marginal cost for a drug is ambiguous because there are many margins. If the copayment were set at the marginal production cost of one more pill, for example, which is just a few cents for many drugs, overuse would be likely and top-up payments would have to be very high, which could lead manufacturers to develop new drugs of low marginal benefit and require excessive funding costs for the insurance. Conversely, if the copayment were set at the marginal cost of selling the drug in a particular country—including country-specific expenses for overhead, production, and promotion—this could be too expensive for many patients, especially for costly drugs such as biologics.

Second, as explained above, most private and public insurance plans, including Medicare Part D, have a catastrophic limit on a patient’s out-of-pocket expenses, including copayments. Many patients who take drugs for chronic conditions or costly medications exceed this limit, which makes cost sharing an ineffective way to constrain prices for costly drugs.

Third, defining the appropriate top-up payment based on patients’ demand once they have insurance and face only cost sharing would lead to excessive payments. Instead, use and the top-up payment should reflect consumers’ demand and willingness to pay for health before insur-
Global Pharmaceutical Pricing

The challenges in this case include determining which costs should be included and how long-term benefits should be estimated. Given patients’ differences in income, preferences for various treatments, and other factors, any common cost-effectiveness threshold for all patients and all diseases is likely to underestimate or overstate what some people are willing to pay for medical care. But this is true for any reimbursement or eligibility rules that apply uniformly to everyone in a health plan.

Single-payer and social insurance systems can vary cost-effectiveness thresholds by condition to address social preferences. For example, the National Institute for Health and Clinical Excellence introduced an “end of life” adjustment that permits a higher cost-effectiveness threshold for certain terminal conditions. Individual differences can be partially accommodated by permitting individuals to pay out of pocket for services that are not covered. In pluralist health systems such as that of the United States, health plans could compete by offering different threshold ratios, which would imply different levels of patient access, drug prices, and premium costs. In practice, however, medical malpractice standards and other legal requirements—such as mandatory coverage of some services—limit how much difference there can be between health plan offerings.

Appropriate Price Differentials Across Countries

If each country with comprehensive insurance chooses its own cost-effectiveness threshold based on its citizens’ willingness to pay for medical care, countries with higher per capita incomes are likely to choose higher thresholds, which means that manufacturers can charge higher prices in these countries.

We do not assume that our proposal would make prices exactly proportional to per capita income, because willingness to pay for medical care may also reflect factors such as income and preferences for various treatments, as noted above. However, provided that each country’s cost-effectiveness threshold reflects its citizens’ willingness to pay, these prices should differ appropriately across countries and in the aggregate should provide appropriate incentives for manufacturers to invest in research and development.

Disadvantages of Current Approaches to Price Controls

All third-party payers use multiple approaches to managing drug prices and spending. Many countries increasingly use cost-effectiveness and value-based pricing concepts, consistent with our proposal. However, such approaches are often embedded in other cost-control strategies that are not well designed to reward manufacturers for producing effective drugs and to provide appropriate incentives for research and development. Many payers use internal referencing, which compares the price of a new drug to prices of existing drugs in a class, sometimes with ad hoc markups for innovation but sometimes with none. Even worse is the trend toward increased use of what is called “external referencing,” whereby one country sets its price for a drug based on the average or lowest price of the same drug in a basket of referenced countries. External referencing enables countries to avoid defining their own willingness to pay by simply adopting other countries’ limits. This approach also undermines appropriate price differences across countries. Manufacturers respond in a rational way, seeking the same prices across countries that are linked by referencing (for example, one European Union country might reference the lowest price in other European Union countries)—and not selling drugs in countries that will not pay these prices or delaying drugs’ launch in those countries. This results in relatively high prices and limited access to new drugs in lower-income countries, especially those whose markets are small.

Similarly, “parallel trade”—in which wholesalers and other intermediaries import drugs from a country where prices are lower, often due to lower income, to a higher-price, higher-income country to make a profit—undermines price differences between countries. This practice is legal in the European Union.

Middle- And Low-Income Countries

Characteristics Tending to Reduce or Increase Prices

Most middle- and low-income countries lack comprehensive insurance systems. Consumers pay out of pocket for health care, including drugs, which naturally gives them incentives to keep costs down. Patients directly express their willingness or ability to pay in competitive markets. In such contexts, manufacturers of originator drugs may have incentives to set prices reflecting each country’s ability to pay, and competition should keep generic prices relatively low. However, several factors may increase prices.

First, most middle- and low-income countries have highly skewed income distributions. Although the majority of their populations are themselves middle- and low-income, the countries have growing high-income subpopulations.
Charging different prices to high- and low-income groups within a country could increase a manufacturer’s profit, but different prices are often not an option. In most of these countries, single distribution networks serve pharmacies; in some countries, regulation requires uniform prices. And if a manufacturer can charge one price to a group of consumers with diverse incomes, the price is likely to be what high-income consumers can pay, even though that makes the products unaffordable for most low-income consumers.\textsuperscript{11}

Second, competition is ineffective at reducing prices. Originator drugs in middle- and low-income countries generally have competition from other originator drugs in the same therapeutic class as well as generic copies. Unlike generics in developed countries, these products are not required to meet bioequivalence standards, and consumers therefore cannot be certain of the generics’ quality. Generics are marketed under their own generic brand and compete based on brand as an indicator of quality, instead of competing based on price. Because a low price implies low quality to many consumers in these countries, it may be rational for manufacturers of originator drugs to charge higher prices, targeting consumers who want high quality and are not sensitive to price.\textsuperscript{12,13}

**Comparing Prices and Incomes Across Countries** To analyze whether the overall effect of conditions in middle- and low-income countries would tend to raise or lower prices, we examined how prices compared to average per capita incomes across the countries. We analyzed drug prices charged in these countries by manufacturers of originator and generic drugs. Specifically, we examined how far manufacturers’ prices were constrained by consumers’ ability to pay (average per capita income) and by competition from other originator and generic products, and whether prices were higher in countries with greater income dispersion—that is, where income varied more.

We focused on drugs for HIV/AIDS, TB, and malaria, which enabled us to compare manufacturers’ prices to the retail pharmacy sector with their prices to large nongovernmental organizations such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the William J. Clinton Foundation, established by donors to procure drugs for these diseases on behalf of the governments of middle- and low-income countries. The organizations are able to negotiate low prices because they use competitive tendering—that is, purchasers take bids and buy from the lowest bidders—and because they buy drugs in large quantities and only from manufacturers that have met the quality standards of the World Health Organization. The organizations’ high demand has stimulated the growth of suppliers of generic drugs in countries such as India, which operate on a large scale and with low production costs. However, the organizations have bought originator drugs as well as generics.

**Study Data And Methods**

Our data on prices in the retail pharmacy sector are from IMS Health—the leading global source of data on pharmaceutical sales through retail pharmacies.\textsuperscript{14} For the HIV/AIDS, TB, and malaria drugs purchased by nongovernmental organizations for middle- and low-income countries, we obtained prices from the World Health Organization’s Global Price Reporting Mechanism database for January 2004 through June 2008.\textsuperscript{15} Our main analysis is based on these HIV/AIDS, TB, and malaria drugs, for which we can compare the prices charged to the procurement process involving nongovernmental organizations to the prices charged to the retail pharmacy sector. To validate our results for effects of income and competition on prices, we used a broader set of drugs from the full anti-infective and cardiovascular therapeutic classes, which are available only for the retail pharmacy sector. Our unit of analysis is average annual treatment price per molecule-country-year, with separate data for generic and originator drugs, and for prices manufacturers charged the pharmacy retail sector and prices paid by nongovernmental organizations.

We estimated regressions for three groups of countries: all countries for which we had data, including high-income countries; the eleven middle- and low-income countries for which both the retail and nongovernmental organization databases have information, hereafter referred to as the “matched countries”;\textsuperscript{16} and all middle- and low-income countries in the same income range as the matched countries, hereafter the “matched income sample.” This matched income sample includes seventy-three additional countries and hence provides more robust evidence, with no material differences in demographic characteristics compared to the eleven matched countries. The annual per capita income in these seventy-three countries ranges from $1,000 to $10,500, with a mean of around $4,000.

We first combined our four price samples—originator and generic drugs, sold in the retail and procurement sectors—in a regression model, using the prices charged by originator manufacturers to retailers as the baseline. We tested for the impact on prices of per capita in-
come, income dispersion within a country, HIV prevalence, and the number of originator and generic competitors for each drug. We also performed separate regressions for each of the four price samples individually, obtaining results similar to those from the combined regression.

**Study Results**

**Effects of Income and Disease Burden** For our full sample of countries, the elasticity of prices with respect to per capita income is only 0.4. (An elasticity of prices with respect to income of 1.0 would imply that prices increase exactly proportionally to average per capita income across countries.) For middle- and low-income countries, the corresponding figure is only 0.15. This difference implies that prices are highest, relative to average per capita income, for the poorest countries.

We obtained similar or lower figures for the elasticity of prices with respect to income for drugs in the entire anti-infective and cardiovascular therapeutic classes for these middle- and low-income countries. Income dispersion contributed to higher prices for both originator and generic drugs in the retail pharmacy sector in middle- and low-income countries, which implies that in fact, as suggested by theory, manufacturers target the highest-income subgroups in countries with highly unequal incomes. Income dispersion had no effect on prices of drugs bought by nongovernmental organizations.

Prices of originator drugs in both the retail pharmacy and procurement sectors are lower in countries with a high prevalence of HIV—an effect that is small but statistically significant. This suggests that the manufacturers of originator drugs set their prices according to disease prevalence as well as to a country’s ability and willingness to pay.

**Effects of Competition and the Procurement Process** In these middle- and low-income countries in the matched income sample, nongovernmental organizations were able to negotiate significantly lower prices for both originator and generic drugs than the retail pharmacy sector paid (Exhibit 1). In general, generics in the retail sector were cheaper than originators, presumably because of perceptions of their lower quality. However, some generics had very low prices, while others’ prices were the same as or even higher than originators’ prices, possibly reflecting consumers’ confidence in the quality of the different brands.

Also noteworthy is the fact that retail pharmacies paid about the same prices for generic drugs as nongovernmental organizations paid for originator drugs. The 42.0 percent average discount that manufacturers of originators gave to the organizations (Exhibit 1) presumably reflected not only the pressures of competitive tendering but also the fact that the organizations were buying and distributing products to low-income consumers and reducing the risk of parallel trade and external referencing.

For generics, the difference between retail and nongovernmental organizations’ prices (Exhibit 1) reflects the fact that such organizations require that generics meet minimum quality standards; focus competition on price—rather than brand—through competitive bidding; and also attract the participation of multinational manufacturers of generic drugs, whose large-scale operations probably lead to lower operating costs than those of the small, local manufacturers of generics that dominate the retail pharmacy sector.

Having at least one generic competitor in a drug therapeutic class or a country is associated with higher prices for originator drugs (roughly 26 percent; data not shown). Although at first that seems counterintuitive, it is to be expected if originators’ manufacturers follow a strategy of charging what the most inelastic market segment is willing to pay, when competing drugs are perceived to be of lower quality. Generics’ prices are also higher if the originator is being sold in the same market, consistent with shadow pricing strategies—pricing a generic just below the price of an originator—by generics’ manufacturers. The presence of additional generic competitors tends to lower prices, but the effect is significantly greater (a reduction of 3.1 percent in price) on prices charged by a manufacturer to a nongovernmental organization than on prices charged to retail pharmacies (a reduction of 0.8 percent).

Of course, these average effects across all of the middle- and low-income countries and drug classes in our sample may mask differences between countries. For example, adding another generic competitor may have a minimal effect in India—where, on average, each drug class contains twenty-six generics sold in the retail sector—but have a greater effect in countries with fewer generic competitors. Overall, however, the presence of generic competitors has only a small effect on prices. Why so few manufacturers of generics sold to nongovernmental organizations also sell those drugs in the retail pharmacy sector (as shown in Exhibit 2), and whether their presence might increase price competition in the retail sector, are important topics for future research.

Prices in our study were positively associated with the number of originator competitors in a drug class or a country. Although this estimate
may be a biased measure of the effect of more competitors on prices, it seems safe to conclude that competition between originator drugs is not effective at reducing prices in these markets. We also found significant differences in the prices paid by various nongovernmental organizations. Contrary to the common assertion that size increases leverage, two of the larger purchasers in our study—the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the IDA Foundation—paid prices for generic drugs that were 22 percent and 19 percent higher, respectively, than prices paid by smaller purchasers. UNICEF, another large purchaser, paid 6 percent less than the small purchasers in our study for generics (this was not statistically significant), but 24 percent more for originator drugs, which was statistically significant.

Our results controlled for which drugs were purchased, so the price differences we found cannot be explained by possible differences in the drug mix purchased by different organizations. Rather, the differences in the case of UNICEF, and possibly the other large purchasers, may reflect intentional policies to pay prices high enough to ensure that multiple manufacturers, including multinational producers of originator drugs, continue to bid in this market.

**Policy Implications**

Finding better mechanisms to enable differential pricing that reflects different degrees of willingness to pay across countries with different income levels is an important challenge for drug manufacturers and policy makers. In addressing the global challenge of optimal pharmaceutical pricing, we have argued that although the goals are similar, countries with comprehensive insurance systems, which are mostly high-income countries, should adopt different policies than countries where most patients pay out of pocket for drugs—a group that includes many middle- and low-income countries.

Comprehensive insurance protects patients from financial risk but thereby makes them insensitive to prices. This reality encourages man-

---

**Exhibit 1**

Prices For HIV, TB, And Malaria Drugs Relative To Prices For Retail Originator Drugs, 2004-08

<table>
<thead>
<tr>
<th>Drug type, region</th>
<th>Retail only</th>
<th>Retail and nongovernmental organization</th>
<th>Nongovernmental organization only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORIGINATOR DRUGS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>5</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Americas</td>
<td>6</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Asia/Pacific</td>
<td>6</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Europe</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td><strong>GENERIC DRUGS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>58</td>
<td>3</td>
<td>47</td>
</tr>
<tr>
<td>Americas</td>
<td>35</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>Asia/Pacific</td>
<td>199</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>Europe</td>
<td>88</td>
<td>0</td>
<td>27</td>
</tr>
</tbody>
</table>

**Source**: Authors’ analysis of IMS Health and World Health Organization data [see Notes 14 and 15 in text].

**Notes**: Originators are research-based drugs that would be patented in most countries, although generic copies may exist because of late or weak patent protection.

**Exhibit 2**

Number Of Manufacturers Selling Drugs In Different Market Sectors And Regions, 2004-08

<table>
<thead>
<tr>
<th>Drug type, region</th>
<th>Market sector</th>
<th>Originator drugs</th>
<th>Generic drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Africa</td>
<td>Americas</td>
</tr>
<tr>
<td><strong>ORGANIZER</strong></td>
<td></td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td><strong>GENERIC</strong></td>
<td></td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td><strong>ORGANIZER</strong></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>GENERIC</strong></td>
<td></td>
<td>47</td>
<td>40</td>
</tr>
</tbody>
</table>

**Source**: Authors’ analysis of IMS Health and World Health Organization data [see Notes 14 and 15 in text].

**Note**: Originators are research-based drugs that would be patented in most countries, although generic copies may exist because of late or weak patent protection.
The poorest countries face the highest prices for drugs, relative to their mean per capita incomes.

Manufacturers of patented drugs to raise prices unless insurers add constraints on prices. Designing such constraints to provide appropriate incentives for manufacturers to invest in research and development is a critical policy issue.

We have argued that in countries with comprehensive insurance, each country or payer should use a cost-effectiveness threshold that reflects how much it is willing to pay for health gain. This approach would permit manufacturers to set prices freely, but it would make reimbursement conditional on meeting the cost-effectiveness threshold. Such an indirect constraint on prices would reward value and offer incentives for innovation. And if payers reimbursed all uses of a drug in which the patients’ expected health gain meets the cost-effectiveness threshold at a particular price, the approach we propose would also ensure that existing drugs were used appropriately.

If countries set their cost-effectiveness thresholds unilaterally and did not practice external referencing or parallel trade, manufacturers would set different prices across countries in response to the countries’ differing willingness to pay. These price levels and differentials would be socially appropriate and would provide the optimal incentives for research and development. Prices would be likely to vary directly with income, but the precise relationship would depend on social preferences and other factors.

Richer countries should shift the focus of health care debates from whether or not to use cost-effectiveness criteria to which cost-effectiveness threshold each country should adopt, and how possible heterogeneity in citizens’ preferences could be reflected in both universal and pluralistic health care systems. Implementation of cost-effectiveness thresholds would certainly be imperfect, but so are all of the alternatives. Doing nothing—which includes relying on ineffective cost sharing—would lead to prices that are excessive, because of insurance. At the other extreme, imposing arbitrary price controls that do not reflect citizens’ preferences would distort both innovation and access to health care.

Equally important is avoiding external referencing to lower-income countries, which would undermine appropriate differentials in drug prices and contribute to inappropriately high prices in certain countries and delays in introducing drugs to the market in other countries. Poorer countries that lack comprehensive insurance would be at a disadvantage relative to the rest of the world. The poorest countries face the highest prices for drugs, relative to their mean per capita incomes. In these countries, the key policy challenge, in the absence of insurance, is to create incentives that will lead manufacturers of both originator and generic drugs to charge prices that will cover the producers’ marginal cost but also be affordable for lower-income people.

Being able to charge different prices for patented drugs within a country would allow manufacturers to receive market prices from high-income groups in poor countries, while expanding the market to poorer groups by charging less—for example, to public hospitals. It would be important to prevent products from “leaking” from the low-price market into the high-price one. For drugs not under patent protection, regulatory requirements that generic versions be of equivalent quality, and economic incentives for pharmacies and patients to prefer generics, could help reduce prices.

Our evidence supports the prediction of economic theorists that if firms can charge only one price, this price will be what higher-income consumers can pay, and the product will be unaffordable to many lower-income consumers. This effect applies to both originator and generic drugs. Although there are multiple originator and generic competitors in most drug classes and middle- and low-income countries, this competition is not effective at reducing prices in the retail pharmacy sector.

Our analysis of HIV/AIDS, TB, and malaria drugs shows that nongovernmental organizations can negotiate significantly lower prices for originator and generic drugs. For manufacturers of originators, these differences may reflect not only the organizations’ requirement of lower prices but also greater willingness on the part of manufacturers to discount prices in return for increased certainty that the drugs will not be resold elsewhere at a higher price. For manufacturers of generics, the organizations’ minimum quality requirements and use of competitive tendering may be most important.
The equivalent of a nongovernmental organization within a country—with informed buyers who insisted on high-quality products, encouraged price competition among generic drugs, and purchased drugs for low-income groups—oretically could achieve differential pricing within that country, and thereby provide drugs at lower prices to poor subgroups than would be possible in the retail sector. Whether public hospitals, insurance programs designed for low-income groups, or other intermediaries might serve as such a mechanism for providing a broad range of drugs in at least some middle- and low-income countries is an important question for future research. ■

This research was supported by the Eli Lilly Inc. Project on Fair Prices for Pharmaceuticals. The research was based in part on data obtained under license from the IMS Health MIDAS database. The conclusions and views expressed herein are not necessarily those of Eli Lilly or IMS Health. The authors thank these sponsors for making the research possible.

NOTES

12 For a discussion of originator price increases following generic drugs’ entry into the US market, see Frank RG, Salkever DS. Pricing, patent loss, and the market for pharmaceuticals. Southern Econ J. 1992; 59(2):165–79.
16 The eleven countries were Algeria, Brazil, China, Egypt, India, Indonesia, Morocco, the Philippines, South Africa, and Thailand, plus French West Africa—an aggregation constructed by IMS Health comprising ten countries in sub-Saharan Africa (Benin, Burkina Faso, Cameroon, Côte d’Ivoire, Gabon, Guinea, Mali, Republic of the Congo, Senegal, and Togo).
In their article in this issue of Health Affairs, Patricia Danzon and coauthors argue that the pricing of drugs in both rich countries and poor countries is seriously flawed, although for different reasons, and they make proposals for changes. They recommend that in rich countries, where insurance shields patients from the impact of high drug costs, pricing be tied to a measure of the health gain provided by each drug. In poor countries, where most people pay for drugs out of pocket, the authors recommend that drug prices be set at two levels: a higher one for higher-income consumers, and a lower one for those who are poorer.

“Ultimately, the common theme is how to get to appropriate drug prices both in an individual country and across countries,” Danzon says. “Pharmaceuticals are global; the same drugs are for the entire global community. What is an appropriate difference in price between poor and rich countries and within each country?”

Danzon, an internationally recognized expert in the fields of health economics, pharmaceuticals and biotechnology, and insurance, is the Celia Moh Professor of Health Care Management at the Wharton School, University of Pennsylvania. She has held faculty positions at Duke University and the University of Chicago. She is a member of the Institute of Medicine and the National Academy of Social Insurance.

Danzon has served as a consultant to the World Bank, GAVI (formerly the Global Alliance for Vaccines and Immunization), the European Commission, the New Zealand Treasury, the Asian Development Bank, the US Agency for International Development, and other organizations. She received her doctorate in economics from the University of Chicago.

Adrian Towse is director of the UK Office of Health Economics in London. He is also a visiting professor at the University of York and a visiting senior researcher at the Department of Public Health and Primary Care at the University of Oxford. He served for ten years as the nonexecutive director of the Oxford Radcliffe Hospitals NHS Trust.

Towse’s current research includes the use of coverage with evidence development and risk-sharing arrangements between health care payers and pharmaceutical companies. He has a master’s degree in politics, philosophy, and economics, and an M.Phil. in management studies from Oxford.

Andrew Mulcahy is an associate policy researcher at the RAND Corporation. His current research focuses on the determinants and welfare implications of patent challenges in the pharmaceutical industry. He earned a doctorate in health care management and economics from the Wharton School and a master’s degree in public policy from the Johns Hopkins University.