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Methodology

Cost-Effectiveness Analysis of Branded Drugs With Market Demand and Insurance

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A B S T R A C T

Objectives: Cost-effectiveness analysis of branded pharmaceuticals presumes that both cost (or price) and marginal effectiveness levels are exogenous. This assumption underlies most judgments of the cost-effectiveness of specific drugs. In this study, we show the theoretical implications of letting both factors be endogenous by modeling pharmaceutical price setting with and without health insurance, along with patient response to the prices that depend on marginal effectiveness. We then explore the implications of these models for cost-effectiveness ratios.

Methods: We used simple textbook models of patient demand and pricing behavior of drug firms to predict market equilibria in the drug and insurance markets and to generate calculations of the cost-effectiveness ratios in those settings.

Results: We found that ratios in market settings can be much different from those calculated in cost-effectiveness studies based on exogenous prices and treatment of all patients at risk rather than those who would demand treatment in a market setting. We also found that there may be considerable similarity in these market cost-effectiveness ratios across different products because drug firms with market power set profit-maximizing prices.

Conclusions: We found that market cost-effectiveness ratios will always indicate an excess of benefits over cost. Insurance will lead to less favorable ratios than without insurance, but when insurers bargain with drug firms, rather than taking their prices as given, cost-effectiveness ratios will be more favorable.

Keywords: branded drugs, cost-effectiveness analysis, insurance.

Introduction

Cost-effectiveness analysis can determine whether branded pharmaceuticals are priced in accord with their therapeutic benefits and whether a drug represents good value for the price the drug firm sets. It is commonly carried out by estimating an incremental cost-effectiveness ratio (ICER), which is defined as the ratio of the estimated quality-adjusted life-years (QALYs) gained through a course of treatment relative to the price charged for the drug treatment plus or minus any cost offsets; unless stated otherwise, we follow the usual practice of using additional spending based on drug prices as the measure of cost in the cost-effectiveness ratio. When the resulting ICER value then meets a predetermined benchmark standard of value for a QALY, the drug's use for a particular indication is considered cost-effective.

There is an array of assumptions, often unstated, which underlie ICER computations. Our purpose here is to bring these assumptions to light, estimate their impact on the ICER values obtained, and analyze how ICERs in practice differ from the ICER values estimated in cost-effectiveness studies. We use conventional economic models of firm and consumer/patient behavior to explain what prices drug firms will set and what quantities patients will use. We then show that if a drug is not reported as cost-effective at its theoretical profit-maximizing price, there would generally be an error in that the firm has not correctly set the profit-maximizing price or a mistake is present in methods or assumptions. We also show that under reasonable assumptions about the demand curves, cost-effectiveness ratios at prices set by profit-maximizing firms lie within a small range, with lower values associated with low or no insurance coverage.

We also consider whether the ICER approach provides a useful normative criterion for decision making by those who purchase or regulate prices for new patent-protected pharmaceuticals. A well-known buyer that relies explicitly on ICER values is the British National Health Service, which purchases pharmaceuticals on behalf of most British consumers. Created by the Ministry of Health, the National Institute for Health and Care Excellence (NICE) determines whether new pharmaceuticals are cost-effective. New drugs where the cost per QALYs gained is less than the arbitrarily set figure of £30 000 (approximately US $37 000) are deemed cost-effective.[1] NICE determines whether the ICER for a new drug meets this standard. Only cost-effective drugs are recommended for purchase by the National Health Service, with the exception of some cancer drugs. Using a monetary value

for a QALY converts the analysis from cost-effectiveness to cost-benefit.

NICE officials state that they have no impact on prices and therefore take them as exogenously given. Nevertheless, this is unlikely to be correct because NICE's critical values are widely known. Indeed, one expects prices to be set at the highest level, which still meets the established cost-effectiveness criterion.[1,2] Profit-maximizing sellers will set prices such that the resulting ICER values fall just below the regulatory threshold. Although the US system is decentralized and informal, recent research shows that the relative prices of new branded pharmaceuticals in the United States track prices in the United Kingdom quite well.[1]

Our conclusions also suggest that almost all cost-effectiveness studies may provide misleading information for those seeking to design insurance plans. Such studies, based on average benefits in a clinical trial setting, do not reflect the fact that cost-effectiveness ratios in markets will typically vary with user prices.[3,4] Finally, this article indicates that in some cases, one can project the numerical value of cost-effectiveness or cost-benefit ratios in noncompetitive markets using information on the shape of patients' marginal benefit or demand curve, along with the presence and extent of insurance coverage. This is possible because the monopoly seller's profit-maximizing price is endogenous and is partly determined by cost-effectiveness.

In what follows, we explore the cost-effectiveness ratios that arise from profit-maximizing behavior by drug manufacturers with monopoly power, a setting appropriate for the US context. That is, drug prices are endogenous and set by firms with market power at the profit-maximizing level. We then focus on the effect of insurance coverage and co-payments, exploring the well-known result that insurance coverage can cause the profit-maximizing price to rise.[5,6] We relate these results to those found in price-regulated settings, such as those used by NICE and other countries with full insurance and little or no cost sharing.

Important earlier work has tried to establish that very high cost-effectiveness ratios, greater than 1, imply that prices exceeding consumer valuations are possible.[7,8] These analyses correctly conclude that in such cases, the excessive incentives for innovation would arise, an outcome stressed by Garber et al.[7] This result, however, is based on treating insurance coverage and design as exogenous. Although that assumption may sometimes be justified by insurance mandates and targeted subsidies, it is not appropriate for private health insurance and perhaps not for public health insurance in the long run.

In the United States, there are 5 different actors in pharmaceutical payment and product streams: (1) drug manufacturers; (2) wholesalers and pharmacies, of which the big 3 chain drug stores are the most important; (3) private and public insurers and their agents, the pharmacy benefit managers; (4) plan sponsors who include employers, unions, government agencies, and others; and (5) consumers and their agents who are health professionals. Indeed, the multiplicity of actors in pharmaceutical markets often results in confusion and controversy.

Most analyses abstract from the roles played by one or more of these actors to explore more fully the motivations and effects of those remaining. For example, Einav et al[9] ignored the role played by drug manufacturers by assuming that insurers acquire the drugs at some predetermined fixed price per unit and, in effect, resell the drugs to their policy holders via a 2-part tariff (insurance premiums and policy holder co-payments).[9] As expected, insurance plans commonly take the form of a 2-part tariff with the premium and the level of cost sharing or coinsurance (which can be 0) designed to attract consumers.

Our objective was to determine the impact of anticipated monopoly pricing policies and drug insurance cost-sharing practices on ICERs in markets with and without insurance, so as to compare them with ratios found in cost-effectiveness research studies. On this account, we abstracted from plan sponsors and pharmacies. At first, we abstracted from the role played by insurers, subsequently analyzing their role. Thus, at the outset, we assumed that consumers purchase their pharmaceuticals directly from drug manufacturers without insurance.

Drug manufacturers respond to consumer demand conditions, whereas patients are advised by their physicians. This raises the question of whether imperfect principal-agent issues could affect demand conditions; nevertheless, we also abstracted from this problem. We assumed that physicians are expert agents for individual patients, advising the use of a drug only when the benefit to the patient exceeds the price faced by the patient. We assumed for simplicity that physicians provide, and patients believe, an unbiased estimate of the marginal health benefits expected to be obtained from a drug, given the patient's illness, illness severity, age, comorbid conditions, and other patient characteristics. Thus, drug-specific demand curves facing drug firms rest on both the distribution of health benefits from use of the drug and consumer monetary valuations of additional QALYs. We further assumed that all consumers value health by the same amount, so that heterogeneity in demand for the drug arises only from differing marginal health benefits.

The assumption of homogeneous monetary valuations of marginal health benefits makes the conversion of cost-effectiveness ratios to cost-benefit ratios a simple matter of multiplying the distribution of expected QALYs gained by the uniform value of a QALY. With this simple multiplication, the units of both costs and benefits (effectiveness times the value of a QALY) are expressed in dollars. This assumption allowed us to identify total value with total consumer surplus. At the outset, we assumed that buyers are as numerous as required to be price takers.

Drug Firm Monopoly, No Insurance

In our first set of models, consumers purchase a patent-protected pharmaceutical at a single market price with no insurance. There are no discounts, coupons, or rebates. Although nearly all consumers in developed countries have some measure of pharmaceutical insurance, this model sets an important benchmark for what follows. Consumers here are assumed to have a reservation price for the drugs and purchase those drugs when they are priced at or below their individual reservation prices but not those priced at higher levels. Manufacturers respond to consumer demand and set their profit-maximizing prices accordingly. For ease of exposition, we presumed that all drug company costs are fixed, so that the marginal cost of production and distribution is 0.

Homogeneous Consumer Demand

In the first demand structure, the consumers at risk are all assumed to be identical, with the same expected therapeutic benefits received from using the drug when ill and also the same valuation of the benefits obtained. In effect, these assumptions correspond to those implicit in most cost-effectiveness studies, which merely present average incremental effectiveness levels without concern for differences among patients. Hence, in this simple initial model, all consumers have the same willingness-to-pay (WTP) amounts. Finally, we also let each patient use, at most, 1 course of the drug treatment. Under these assumed conditions, the relevant demand curve facing the monopolistic seller is a horizontal line at the common value of benefit per treatment, which is also the average value across consumers. Facing this

demand structure, the monopolist sets its price equal to that value to maximize profit.

Under these circumstances, there is no deadweight welfare loss at the monopoly price because all potential buyers who could benefit from the medication will receive it. Nevertheless, there is also no consumer surplus because the price paid is just equal to the uniform value of the marginal benefit. If we express the drug's effectiveness in dollar terms, the cost-effectiveness ratio equals 1. Expressed this way, the cost-benefit ratio and the cost-effectiveness ratio are interchangeable concepts.

In Figure 1, P' is the uniform valuation of the drug; the associated 100% quantity level indicates that all who could benefit from the drug are using it. Both costs and benefits are represented by the indicated rectangle, OP'AB. Taking the price charged as the drug's cost, the drug will then have a cost-effectiveness (cost-benefit) ratio of unity. In this model, drug company revenues are just equal to consumers' total valuation of the product. Furthermore, if there are many drugs with this distribution of health benefits, the price will vary across drugs depending on the amount of QALYs gained from their use, but the cost-effectiveness or cost-benefit ratio will be at unity for all drugs with uniform benefits.

Strikingly, this model corresponds to those used in countries that use a single threshold monetary value per QALY and thereby assume implicitly that all patients at risk receive the average increment in QALYs. In this case—and only in this case—results from clinical research–based cost-effectiveness studies are equal to those resulting from actual market behavior. That is because, in almost all research studies, subjects are provided the drug without regard to their individual characteristics or their WTP for the drug. They do not face a positive price that might deter them from use if they and their physicians anticipate few benefits from using the drug. Furthermore, should observed prices appear higher than those that yield a cost-effectiveness or cost-benefit ratio of unity, it could be because the firm has priced its product too high given its effectiveness, either the effectiveness estimate is too low, or too low a value of QALY has been assumed.

Heterogeneous Consumer Demand

We now introduce heterogeneity in consumer's WTP amounts after contracting an illness. We continue to assume that consumers know their expected health benefit from using the drug.

Heterogeneity of benefit among those who receive some health benefit from a drug generates a downward sloping schedule of monetary marginal benefits. A similar model of demand was shown in the study by Garber et al.[7] If we further let the distribution of these benefits be uniform over the proportion of patients at risk for the related ailment, the drug's demand schedule is linear and ranges from some high dollar amount to 0 as the percentage of those at risk using the drug increases from 0% to 100% of those with or at risk of the illness.

To compare this model with the previous one, suppose that the average value among heterogeneous consumers equals to the average value in the homogeneous case discussed earlier. In this case, the resulting price is the same as before; at P', however, the quantity is now only half as large. The linear demand curve D' in Figure 1 cuts the previous horizontal demand curve at precisely the 50% mark. Moreover, although the monopoly price is the same as before, only half of the drug's potential users now use the drug, which are those with demand prices above the market price, P'. Consumers with demand prices below P' do not use the drug.

Although the firm's profit-maximizing price is the same with heterogeneous as with homogeneous consumers, the cost-effectiveness ratio is now quite different. Although earlier the costs and benefits associated with the drug were equal for all

Figure 1. Demand and pricing: no insurance.
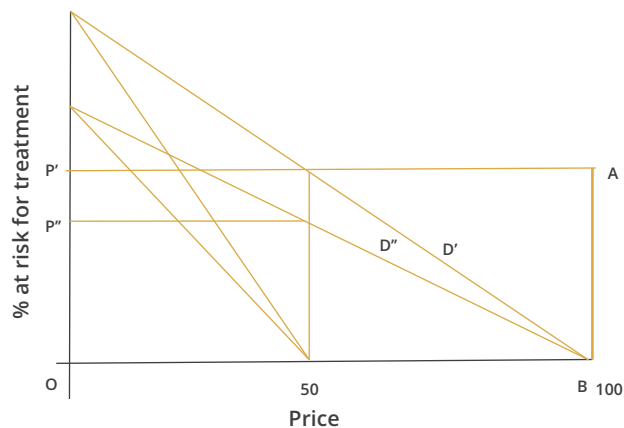
users so that the cost-effectiveness ratio equaled unity, there is now a positive surplus of benefit over cost, with the difference being the consumer surplus represented here by the triangle below the demand curve but above the price line. Therefore, the cost-effectiveness ratio now lies below 1. In the linear case, depicted in Figure 1, it is exactly two-thirds—given that the consumer surplus over price now equals one-third of the total surplus associated with the product's use. Garber et al[7] derive somewhat similar results from a different model.

Under consumer heterogeneity, the cost-effectiveness ratio is lower, with benefits exceeding costs, despite the substantial volume of health benefit which is lost because the consumers with lower benefits are excluded. This result demonstrates an important way in which research-based cost-effectiveness ratios do not track overall consumer welfare or economic efficiency very well.

In this model, total costs are P' times 50% in Figure 1, whereas total surplus is that rectangle plus the consumer surplus triangle, which lies above. The resulting cost-effectiveness ratio of two-thirds follows from assuming both linear demand curves and 0 marginal costs. It applies regardless of the slope of the demand curve because a higher value on the vertical axis leads to an off-setting increase in the profit-maximizing price. For example, if the demand curve had a less steep slope such as D" in Figure 1, the profit-maximizing price would be lower at P". Nevertheless, the smaller consumer surplus would again be half of the total expenditures on the drug, and therefore, the ratio of total benefit to total spending would remain at two-thirds. Regardless of the slope of any linear demand curve and the magnitude of the total benefit from a drug, in this set of models, the observed cost-effectiveness (cost-benefit) ratio is always two-thirds.

Further Implications From Models Without Insurance

If drug firms could observe variations in consumers' marginal valuations, perhaps related to their illness severity or what Bach[10] has called "indication," they would prefer to charge higher prices for patients who would benefit more from using the drug. This pricing structure in economics is termed "perfect price discrimination" and would lead all potential customers to have access to the product. Nevertheless, as Chandra and Garthwaite[11] have pointed out in a critique of Bach,[10] it would also lead to higher drug firm profits and higher use by those patients who receive the least benefit. Nevertheless, as we demonstrate below, this degree of price discrimination, if feasible, would also lead to improvements in efficiency defined as the sum of consumers' and

producers' surplus. In effect, price discrimination eliminates the loss in consumer surplus resulting from excluding potential patients whose reservation prices are below the simple monopoly price but above the zero marginal cost. It does so paradoxically by transferring consumers' surplus to gains for the producer. If the price paid is taken as the cost, as is common in cost-effectiveness studies, the cost-benefit ratio under perfect price discrimination will be unity because the monopoly seller captures all gains.

In the models explored earlier, we assumed a uniform distribution of QALYs gained over the range from 0 to maximum effectiveness. This assumption is associated with the linear demand curves depicted earlier. Nevertheless, a uniform distribution across patients in the marginal effectiveness of particular drugs may not describe actual circumstances very well. Instead, the distribution of therapeutic benefits from a pharmaceutical may be substantially skewed, such that most of those at risk get relatively small benefits from the drug, whereas a few get major benefits. Indeed, in many circumstances, a drug cures some patients but has little effect on others.[12]

This alternate structure of benefit distribution leads to the convex demand curve depicted in Figure 2. DC and its associated marginal revenue curve is shown in Figure 2. In this diagram, both marginal revenue schedules cross the zero cost axis at the same point, which is required for the case where quantities are the same with both linear and convex demands. The 2 demand curves coincide at the same equilibrium point, and therefore, firm revenues are equalized in the 2 cases.

What this diagram makes evident is that the resulting consumer surplus is greater with a convex than a linear demand curve, with the additional surplus gain depicted by the triangle above D' and below DC. Given the consumer valuations of therapeutic benefits associated with the drug, which are now greater than those with linearity, the cost-effectiveness ratio is smaller and necessarily lower than two-thirds.

To sum up, these findings have important implications for the interpretation of cost-effectiveness findings. Although the availability of substitutes to a specific pharmaceutical can lead to more elastic and less steeply sloped demand curves, along with lower prices, the associated cost-effectiveness ratios may not appreciably change. Although consumer welfare may be improved, it is not reflected in the related cost-effectiveness ratios. If there are several substitutes, the incremental value of any 1 drug, given the existence of the others, can be very small, yet the value of the whole class of drugs (or of the first drug) could be very large. This result provides further illustration that research-based cost-effectiveness ratios are poor proxies for consumer well-being or indeed for economic efficiency in a market setting, even in a static sense that ignores incentives for innovation.

Furthermore, the heterogeneity in health benefits from specific pharmaceuticals is more than an abstract concept underlying product demand curves. The advent of personalized medicine has potentially made heterogeneity more easily observable. This movement began with the observation that some members of apparently similar populations improved using a drug, whereas others did not or even had adverse effects. Sometimes a small fraction improved a lot, whereas most did not, as considered by the convex demand curve considered earlier, and other times almost everyone improved except a few outliers. This observation became useful with the development of companion diagnostics that can predict who will benefit or have a greater chance of benefiting. If only patients know the test values, the result is still a downward sloped demand curve; if insurers also know the values, they can tailor benefits to those cases where benefits are likely to be high enough to justify the drug's price.[13] If drug sellers know that some customers will benefit more than others, they will price

Figure 2. Convex demand curves and value (consumer surplus).
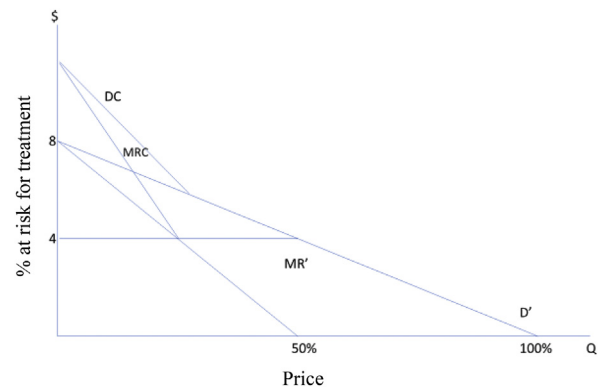
DC indicates demand curve, MRC, marginal revenue curve.

discriminate and raise the price to those who take this factor into account. In what follows, we abstract from the possibility of personalized medicine, but we suggest that its relationship to cost-effectiveness analysis deserves further investigation.

Introducing Insurance

In this section, we account for the fact that risk-averse consumers may demand insurance to cover the unpredictable risk of spending on pharmaceuticals. This risk arises in the first instance because the chance of contracting a disease is uncertain, and so also is the severity of the disease. For example, as depicted in Figure 1, if the price for a particular pharmaceutical was set at P' and having the related indication along with its severity was highly uncertain, then risk-averse consumers might want protection against the financial risks of getting sick and having to pay P' compared with the more likely alternative of not getting sick at all (and not being affected by whatever price is set).

Both in theory and practice, pharmaceutical insurance can take various forms. The insurer can be a passive payer who simply reimburses consumers for any pharmaceutical spending incurred, with some form of cost sharing to limit use and claims. Alternatively, or in combination with cost sharing, an insurer can control use through managed care tools, with the resulting lower premium serving as the incentive for consumers to accept such limits on quantity and purchase the insurance. Finally, an insurer can negotiate directly with the drug company based on its ability, in varying degrees, to restrain the quantities of the drug bought.

Pharmaceutical insurance cost sharing can also take various forms: from proportional coinsurance to fixed dollar co-payments to fixed prices per treatment, which can be reference based. Consumers who purchase private market insurance can select from among plans with premiums sufficient to cover benefits and administrative costs and also different menus of managed care and cost sharing with their associated effects on premiums. For private insurance plans, we assume that competition for both individual insured and group insurance purchasers limits insurer profit margins, which therefore forces premiums down to the competitive, zero-economic-profit levels for any pattern of coverage and cost sharing. We assume in what follows that cost sharing takes the form of proportional (ad valorem) coinsurance and that income effects are absent, so that the area under relevant demand curves serve to measure the associated consumer surplus.

Passive Insurers

The potential impact of insurance coverage on the profit-maximizing drug price and the quantity patients will demand will vary depending of the form of the insurance and cost sharing.[6] Suppose initially the insurer covers all drugs that are both approved by the Food and Drug Administration and ordered by a physician at a predetermined coinsurance rate that must be uniform across all drugs, as modeled by Garber et al[7] and Besanko et al.[8] In these circumstances, insurance coverage creates moral hazard problems. If coinsurance is low, patients who receive little marginal benefit relative to the price of the drug will nonetheless purchase it because the insurance will pay most of that price. Empirically, there is evidence that more complete insurance coverage has long been associated with a higher use of and spending on prescription drugs.[14-16]

Nevertheless, what coinsurance rate will insurance firms offer to buyers for different drugs at the prices drug manufacturers have set? To answer the question, consider first how different levels of coinsurance affect the monopolist's demand curve. At coinsurance rates less than 1, this demand curve rotates upward relative to the no-insurance demand curve (its elasticity is lower at every price.) In addition, with a rotated market demand curve, the monopolist seller's optimal price will increase[5] compared with less or no insurance. Indeed, in the basic model of a linear demand, zero-marginal-cost case, for any positive proportion of costs paid by insurers, the equilibrium gross price always rises to such an extent that the user price after insurance coverage (the coinsurance dollar amount) equals the gross price without insurance coverage. The equilibrium quantity remains the same as without insurance, and the amount and distribution of out-of-pocket payments return to the level before insurance was obtained—again as long as consumers continue with the same insurance plan after the price increase.[6]

Figure 3 shows a simple numerical example. With the no-insurance demand curve as drawn, the simple monopoly price is at P = 4. Now let insurance cover two-thirds of each person's cost. The demand curve pivots out to the right. With this new demand curve, the new equilibrium price is 12, but the equilibrium out-of-pocket payment remains at 4 (and the quantity at 50%).

If marginal cost were positive, coinsurance coverage leads to somewhat lower user prices net of insurance, lower prices to drug firms, and higher quantities, all relative to the zero-marginal-cost case. Results differ somewhat in detail for alternative forms of co-payment.[5] Nevertheless, the spirit of the result remains. Exogenous passive simple health insurance in which all drugs are covered with a given and uniform coinsurance level leads to higher prices than with no insurance and can even lead to gross prices exceeding consumer valuations[7,8] for some drugs. The cost-effectiveness ratio will be more adverse with more generous insurance payout.

Equilibrium Allowing for Reactive Changes in Insurance Coverage

To our knowledge, existing models of market equilibrium with insurance and seller monopoly end with this step, in which sellers react to the insurance coverage that consumers first obtain, but that response is not an equilibrium. An increase in price and premium for the initial level of coinsurance will prompt buyers to change insurance coverage. If buyers select a new higher coinsurance rate in response to an increase in seller price, the demand curve will rotate downward, and the profit-maximizing price will fall. This independent adjustment process will continue until an equilibrium is reached.

Figure 3. Pricing with simple coinsurance.
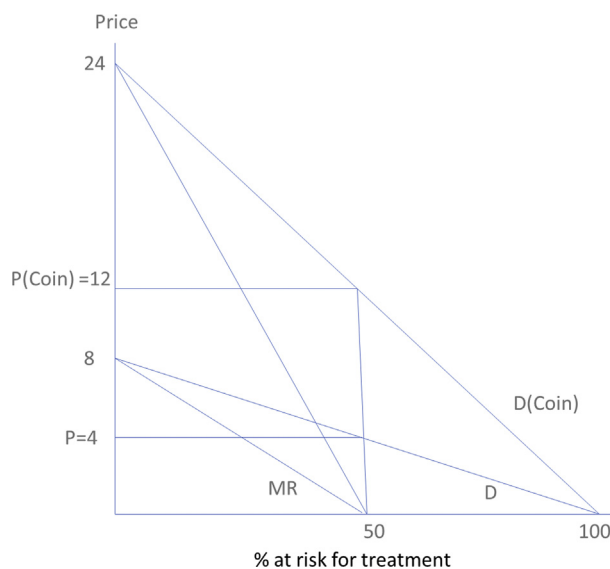
MR indicates marginal revenue.

An important special case exists if coinsurance is exogenously set so low that consumer surplus for some drugs is eliminated or even made negative by substantial drug firm price increases—but where coinsurance is required to be uniform across all approved drugs. This case is also explored by Garber et al[7] and Besanko et al.[8] Under these circumstances, the prices charged for some drugs may actually exceed consumer benefit.

This result disappears, however, when insurance decisions are considered endogenous and variable across drugs. A consumer who can make a choice between insurance coverage leading to negative consumer's surplus will of course choose not to purchase insurance unless the risk reduction benefits from the insurance offset the negative consumer surplus.[17] In effect, the optimal coinsurance rate jumps from whatever level trades off risk reduction benefits against moral hazard, given that the drug is used, to 100% coinsurance (no coverage) because of the high price. This possibility is an important constraint on pharmaceutical pricing and prevents the outcomes with incentives to over-investment in developing and marketing drugs that are not cost-effective from the societal perspective, one that takes account of the real resource costs of research and development investment.

To be sure, imposing the requirement that coinsurance be uniform precludes this reaction. A version of this important constraint exists in Medicare Part D drug insurance or in various Medicare Advantage plans because certain drugs are required by regulation to be covered and premiums are heavily subsidized, but it does not exist in unsubsidized private insurance where insurance buyers can choose lower premium policies with restrictions on coverage of some high-priced drugs. When consumers may voluntarily purchase plans, they might still buy coverage under a requirement of uniform coinsurance if consumers' surplus remains positive for most other drugs. Nevertheless, a cost-effectiveness ratio greater than 1 for some drugs results from the requirement that they be included in the bundle of covered drugs, not from market processes.

How will any action-reaction process end? First, consider a simple Nash noncooperative equilibrium. A Nash equilibrium occurs if, given some overall price, consumers choose the level of coinsurance that leads to a demand curve at which that price is

profit maximizing. In other words, the drug price is the manufacturer's best response to the coinsurance rate, and the coinsurance rate is the insurer's (consumers') best response to the drug price. Precisely whether and where the equilibrium values are reached depends on the demand for insurance. The less risk averse the insurance buyer, the higher the optimal coinsurance rate in equilibrium as long as there is an equilibrium value.

Does Practice Match Theory?

The simple passive-insurance model predicts high prices with low consumer surplus (which industry critics think is the case) but quite incomplete insurance, with high coinsurance rates (which is not the case). Actual market performance seems not to fit this benchmark model. The literature finds average branded pharmaceutical prices set to yield cost-effectiveness ratios well below our reference point of 0.67.[2,18,19] Furthermore, we observe low consumer coinsurance and co-payments. A Kaiser Family Foundation survey of US employee health benefits found that 39% of employees had coinsurance coverage for drugs and that conditional on having coinsurance, the rate varied between 19% and 31%, depending on tier. Co-payment amounts were slightly more common at 53% of employees, varying between US $11 and US $105 per prescription, depending on tier.[20] These coverage rates will be affected by the tax subsidy to employment-based health insurance, so they may not correspond to the theoretical equilibrium discussed in previous paragraphs.

For many reasons, it is difficult to map these survey results to an estimate of the average coinsurance rate. An alternative approach is based on aggregate data. The percentage of prescriptions paid in cash is estimated to be 8%.[16,21] The percentage of dollars spent out of pocket for pharmaceuticals is estimated at 14%. Making the slightly heroic assumption that the average prices of drugs is about the same for cash versus insurance, we can calculate the average percent paid by consumers for insured drug purchases as 6.5%. Therefore, if we treat all insurance as if it used coinsurance, the estimated coinsurance rate is 6.5%.

Overall, it is clear that empirically observed coinsurance rates for drugs are far lower than is consistent with the passive-insurer model and that at those rates drug firm prices are well below the profit-maximizing level. We conclude that, even after allowing for endogenous insurance choices, the passive-insurer model does not appear to fit the stylized data well unless the response to the tax subsidy is implausibly large.

Active Insurers

The most plausible explanation for the observation of lower coinsurance and lower prices than those suggested by the theoretical models considered so far is one in which insurers play more aggressive roles. Even the most passive unregulated private insurer has the authority to refuse to cover new drugs whose effectiveness is unproven or is low relative to its launch price. This is equivalent to consumers choosing the option of no insurance when the price and related premiums are too high. At the other extreme, insurers also have managed care tools to channel the drug to their beneficiaries who will get the most benefit from it. Indeed, insurers use various tools to influence quantity levels.[16,20,22,23]

Furthermore, on the seller side, it seems likely that sellers would anticipate changes in coverage because they vary their price and take that into account in setting their price. Among the possible insurance equilibria with anticipation, the one with coinsurance closest to two-thirds will yield the highest price (1.5 times the uninsured price) at the quantity of 0.5. Note that this type of equilibrium is not Nash equilibrium. It is an equilibrium of an asymmetric model, with the pharmaceutical manufacturer as the leader. This type of pricing generates the maximum possible cost-effectiveness ratio of 1.0. The outcome is still inefficient because 50% of consumers who would get a benefit from the drug are inefficiently excluded.

Two-Part Pricing Models With Bargaining

The models described earlier are largely concerned with single-price outcomes in which sellers set the price for the drug in question and buyers react accordingly. This might be a plausible model for a passive insurer. Nevertheless, as noted earlier, all insurance policies take the qualitative form of a 2-part tariff, where consumers pay both a fixed price or "entrance fee" to use a market and then a positive price for each additional unit they buy. This is a concept well known in economics. Lakdawalla and Sood[24] have suggested that this structure, one that combines lump sum premiums with positive marginal user prices, implies that markets with branded drugs and low marginal costs are more efficient than meets the eye. In this section, the measure of cost used to make efficiency judgments is the incremental real resource costs of producing and distributing the drug.

Although few insurance companies would describe what they do in this fashion, we believe the 2-part pricing model to be preferable. In its classic presentation, a monopolist charges a fixed fee to consumers for the ability to purchase even a single unit of the product but then also charges a per-unit price. It sets the per-unit charge equal to the marginal cost of production and distribution to maximize the amount of consumer surplus available, thus the maximum possible fixed fee. This charge ensures that efficient quantities of the drug are sold and eliminates any deadweight loss associated with inefficient exclusion from the purchase of the drug. Applying that model to the conditions depicted in Figure 1, the optimal per-unit cost-sharing amount is 0 because marginal costs there are assumed to be 0. The resulting quantity used of the drug is thereby 100%, and the aggregate premium equals the total consumer surplus gained. Note that except for distributional differences among consumers, this outcome is identical to the one in which the drug firm practices perfect price discrimination, as discussed earlier. The monopoly drug firm's revenues equal the aggregate consumer surplus obtained by consumers for the relevant pharmaceutical.

Consider how the fixed fee per insured person is to be established. Although there may be very high costs of discovery, these have already been incurred and thereby represent fixed costs. Moreover, in this model, marginal costs are assumed to be 0. In these circumstances, the drug firm seeks maximum revenues to be received from the insurer.

One possibility is for the drug firm to demand the same revenue as would be received under simple monopoly pricing and thereby set the same monopoly price indicated in Figure 1. In that case, the drug firm makes the same profit from the fixed fee arrangement as if it had sold to only a portion of insureds: those with high ex post valuations of the drug's health benefits. In addition, it would require only a token additional payment from the insurer to induce the drug firm to make enough of the drug available to treat all other insureds who could benefit from the drug. Note that this arrangement between the drug firm and an insurer is an all-or-nothing deal—the insurer must pay for all its insureds and not deny the drug to the subset of its insureds with marginal benefits lower than either the simple monopoly price or the average price.

In this case, the insurance premium will be higher than that under a simple monopoly because of the need to make the

additional payment to the drug firm. Nevertheless, the insurance company will make more profits, and the drug will now become available to all those who would get any benefit from it. Nevertheless, contrary to Chandra and Garthwaite,[11] this outcome would represent a more efficient policy and also one that consumers would prefer ex ante, before they know if and how much benefit they would receive from the drug. Consumers receive more valuable drugs, which offset higher payments to and profits for the insurer.

Consider now the cost-effectiveness ratio based on real resources costs (not prices) as the measure of cost that is likely to arise in these circumstances, in particular how it is likely to compare with that found under simple monopoly. What is apparent is that when compared with any version of the single-price monopoly model, moving to this version of the 2-part tariff model implies a more favorable ICER. This is because the additional benefit associated with the drug now includes the health benefits for all those who had not received the drug under the single-price regime, whereas the additional cost is merely the small additional payment needed to ensure the drug is supplied to those whose benefits lie below the single-price monopoly level.

Another way of thinking about the relationship uses the Nash bargaining model. In this model, the entire gain in surplus from the use of the drug is split between the insurer and the drug manufacturer. Making the simplifying assumption that their bargaining skills and patience are equal, the split of the surplus is 50-50. This gives rise to a cost-effectiveness ratio of 0.5 for our zero-marginal-cost model, regardless of the shape of the demand curve.

Competition Among Pharmaceutical Firms

Even if there are no substitutes, insurers have ways to affect quantity that gives them the ability to bargain for lower prices with the drug firms. Where there are potential substitutes for a firm's drug, insurers have greater ability to bargain for lower prices. The possibility of interproduct substitution enhances payers' ability to negotiate lower prices in return for it being treated as a preferred (lower coinsurance) product. Alternatively, an insurer may set reimbursement amounts at a fixed reference amount and require consumers to pay the full cost of choosing a higher priced treatment. The tools to influence quantity discussed earlier are more powerful when there are substitute drugs available. They enable insurers to negotiate lower prices.

There is direct evidence of the presence of competitive effects among branded drugs on the list prices set for new entrants. Holding therapeutic benefits constant, adding a single alternative pharmaceutical in the limited therapeutic class led to a 38% decline in average launch prices, and increasing the number of substitutes from 2 to 3 led to a further 19% decline.[25] Because of the substitutes, the incremental value of any single drug declines, but so does its price. Moreover, drug firms can set prices based on expected competitive entry in the future. This could lead to low and extremely favorable cost-effectiveness ratios if firms price low in anticipation of new competition.

Conclusion and a Paradox

One general conclusion from this analysis is that with or without insurance, there may be considerable similarity in market cost-effectiveness ratios (given a level of insurance coverage) for different drugs as drug firms with market power choose to set prices. These market cost-effectiveness ratios also will differ, possibly substantially, from the research ratios reported in the typical cost-effectiveness literature—depending on what smaller proportion of the population uses the drug in the market, how much higher their benefit is than the average over all with the illness, and where and how the market price is set. This conclusion follows with either passive insurers or active bargaining insurers. To the extent that there are limits to bargaining, the market equilibria will be somewhat influenced by the completeness of insurance, as in the case of simple passive insurance. Therefore, more generous insurance coverage will lead to higher price and a less favorable cost-effectiveness ratio but still one below unity. Unless the 2-part pricing model is in place, consumer welfare is not approximated well by cost-effectiveness ratios, which assume that all at risk will use the drug at the current price (as in clinical cost-effectiveness studies). Further work to offer analysis and guidance about launch prices of new drugs should present market cost-effectiveness ratios in addition to research ratios and should also specify the extent and form of insurance coverage that will determine the market ratios.

The benchmark model of passive insurers leads to an empirical paradox. The benchmark simple monopoly model predicts relatively high coinsurance, and yet the data show that average consumer out-of-pocket payments have risen only from US $10.34 per prescription in 2015 to US $10.67 in 2019.[26] Moreover, with passive insurers, drug-seller revenues (paid as insurance benefits and out-of-pocket prices) should extract a high proportion of the consumers' surplus from patent-protected drugs. We have shown that treating insurance choice as endogenous rules out the Garber et al[7] and Besanko et al[8] case of cost-effectiveness ratios over 1 on theoretical grounds. Empirically, as discussed earlier, it seems that the proportion of surplus actually captured, even in the years of patent exclusivity, is much less than the full amount.[2] The data reject high cost-effectiveness ratios even more decisively than the theory. Overall, drugs are a bargain, which may mean that incentives for efficient investment in new drugs are suboptimal, perhaps extremely so.

So what is propping insurance coverage up and yet holding price down? We believe that the insurer's use of active bargaining is an import factor. As indicated earlier, the coinsurance rate under a 2-part pricing model would be set so the marginal user price equals the marginal cost. Of course, right now few drug firms or insurers have fully or perfectly implemented the 2-part pricing model—an explicit version is being tested for the first time in some state Medicaid programs. Nevertheless, we believe that some implicit elements of 2-part, all-or-nothing deals are naturally present and therefore affect the list price at launch used in research studies. This may be the solution to the paradox.

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