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Incentives for R&D: Payment Options and Pricing Challenges

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1 Introduction

The issue of rising prescription drug prices is a concern in every country. Dozens of policy initiatives and hundreds of research projects over last the fifty years have attempted to find solutions to pricing that provide an appropriate balance between the cost to health care systems and incentives for R&D. To name but a few, these include reference pricing, managed entry agreements, price-volume agreements, rebates, and risk sharing. The ultimate solution, however, remains elusive.

2 Pricing, Innovation and Sustainability

Pricing challenges have not changed over time. Solving them must ensure that:

1. innovation "that matters" occurs (value)
2. patients have access to innovative treatments (access)
3. health systems remain financially sustainable (sustainability)

Balancing the need for innovation against other concerns requires a full understanding of the context, principles and constraints in the environment. No single payment method is likely to fit every situation, or every country, as experience has shown. But payment rules clearly have a powerful effect on incentives for R&D.

The link between pricing and innovation is what makes the challenge so difficult. If innovation were not a concern, then effective competition would allow prices to more closely reflect marginal costs. When innovation is a concern, however, incentives such as patents are important to encouraging continued innovation. The objective is to reward innovation, but at the same time achieve an optimal resource allocation, which raises both dynamic and static efficiency issues. At least as presently applied, patents cannot direct R&D efforts to a particular therapeutic area. Such "directed" innovation may be desirable because innovations vary in the value new treatments provide for both patients and the health care system. Pricing might spur innovation "that matters" by, for example, providing greater rewards for innovation in specific therapeutic areas that are more valued by society.

Perhaps what is needed, then, is competition among approaches to paying for innovation. Current incentives are based almost entirely on patents, a model that is appropriate for decentralised innovation where the market determines R&D choices. One approach to having more influence over R&D choices is through procurement, either through pricing and guaranteed markets or possibly by providing matching public-source funding for R&D in areas of interest. This introduces some elements of competition that are more directional than the approaches common today. One major flaw in this idea, however, is that firms make R&D choices with a global market in mind. Any system for rewarding innovation that is not a global system, as patents are, would require substantial agreement and co-ordination across countries. It is not clear how that might work. A problem would arise if larger markets such as the EU set a price and retain the property rights of the price. Countries whose need for innovative products is not the same as in the EU may object or even attempt to offer counterincentives. Such issues would need to be resolved given that R&D funding is finite and choices must be made. Such competition in approaches to guiding innovation, however, could produce some viable alternatives to the current patent system.

As an example of a new approach, suppose countries or payers were to buy a patent directly, before it expires, and immediately allow generic competition via licensing. Would this be cheaper in the long run? An example might be the cure for hepatitis C, a major recent innovation. Effective coordination across countries would be required, of course, but the idea is interesting. The ultimate effect on choices of R&D is not clear, however. If firms know that the end result may be outright purchase of the patent, this will affect incentives for R&D — in as yet uncertain ways. Innovations that affect large markets and are likely to be useful over a longer period of time might be discouraged if firms were aware that patent purchase would be likely.

Given that systems' change happens only slowly, the decentralised model of innovation will continue to dominate for some time. The challenges posed by pricing, then, will not change substantially in the near term. To understand the options for meeting the pricing challenge, we need to consider what factors drive pricing and how available resources can best be used.

With respect to pricing, an important aspect of the challenge that often is neglected is the role of institutional arrangements on pricing decisions. This includes, for example, economic evaluation and the use of ICER (incremental cost-effectiveness ratio) criteria, both of which are institutional arrangements that are specific to health care, and insurance, whether public or private. Whether and to what extent are institutional arrangements driving up prices, rather than containing them? Public discussions about drug pricing most often portray companies as the problem — with greed alone responsible. With a few spectacular exceptions, such as EpiPen pricing, this is a misreading of the situation. Instead, payers set the rules in a way that drives up prices of rational, profit-maximising, firms in their normal business strategies. Since such institutional mechanisms are under the control of policy makers, theoretically this could be remedied, or at least mitigated.

If high prices are unavoidable, and they may be, then the second half of the challenge is intertemporal in nature: how best to fund expenditures that are sustainable today and that sufficiently encourage R&D to produce innovation for tomorrow. This is a particularly thorny issue for cures for infectious

diseases such as hepatitis C, which may be particularly expensive now but will substantially reduce the burden of disease in the future. An obvious approach to controlling prices, is to make such drugs generic as soon as possible to move the pricing to marginal cost, but this then reduces R&D capacity in the private sector. If the higher price is paid today, however, current generations bear the cost burden and ensuing generations enjoy a free ride. Spreading the cost burden across generations is a new challenge for policy makers.

The reasons for high prices of drugs, then, include market power, the existing mechanisms for approving new drugs and influencing prices, and the consequence of attempts to direct innovation to therapeutic areas where benefits are expected to be greater. Managed entry agreements (MEAs) are one of the more recent approaches intended to ensure maximum benefit from newer, costlier drugs. Under MEA, volume of use is controlled and benefit is maximized by limiting use to specific populations. In theory, tailoring use makes sense, but this will not ensure lower prices.

Part of the problem is defining what price is "excessive". Competition authorities shy away from such discussions generally, for all industries, not just prescription drugs. Theoretically, however, it should be possible to develop criteria for identifying excessive prices. This would not take the place of important existing approaches — ICER, for example — but would supplement them and affect pricing decisions more directly. Of course, this also has implications for the profitability of companies and changes incentives for R&D which, in turn, may affect health care for ensuing generations of patients. These important effects need to be kept in mind.

3 Developing a Model

To summarise, attempts to manage the impact of prices on health care system spending must consider three factors:

1. balance between innovation and "excessive" market prices

2. the role of current institutional arrangements and how companies adjust to them

3. the role of intertemporal effects.

A starting point for developing a viable approach to the challenges is Nordhaus's model for innovation, published in 1969 (Nordhaus, 1969). It is simple: the probability of the innovation occurring times the value of that innovation minus the cost of the innovation. I have coupled this idea with work by Jena and Philipson (2008) that incorporates the effects of institutional arrangements through insurance and cost-effectiveness analysis. Of particular interest is the idea that the moral hazard created by insurance may provide too much private incentive for innovation.

Including the intergenerational intertemporal effect may be somewhat less complicated. The idea here is that innovative products may benefit more than one generation of patients, but the current generation pays for most of the reward for innovation through prices set under patents. Cures for infectious diseases are an obvious example. New payment models should recognise this implicit intergenerational transfer; such assessments are not done today and no instruments have been developed to measure such effects. The optimal time profile of prices is difficult to identify.

The challenge is shaped also by the characteristics that make pharmaceutical markets different from other markets. Two are particularly important. The first is that the choice of therapy is not made by the patients, who directly benefits, but by the doctor whose incentives may not be the same. This is far too complicated to dissect, at least initially, so we must assume perfect agency, that is, what the doctor suggests is what the patient would prefer. The second feature is that neither the doctor, who

decides, nor the patient, who benefits, pays directly for the product — insurance does so. Patients do not pay out of pocket, or not enough out of pocket to influence choice.

Step 1 in developing a model is insurance. As Pauly noted in 1968, insurance has a moral hazard impact that reduces the price sensitivity of consumers and increases the demand for new drugs. This makes higher prices possible (Pauly, 1968). Patents allow monopoly pricing, which may produce unrealistically high incentives for innovation (Jena and Philipson, 2008; Garber, Jones and Romer 2006).

The model below helps illustrate the situation today, providing a starting point for exploring how a benchmark for excessive prices might be set and incorporating the influence of institutional arrangements. This draws on Jena and Philipson (2008) and Garber, Jones and Romer (2006). The basic demand structure is linear:

$$B = a - p$$

In the case of pharmaceuticals, marginal benefit is linked to effectiveness and effectiveness declines as use expands, that is, the marginal patient typically benefits less than the inframarginal patient. A core of patients for whom the drug is particularly effective will benefit a great deal, about equally. Effectiveness will decline, however, as the pool of patients expands beyond this core and will decline toward zero as use widens. Marginal benefits, then, decrease as usage expands.

With health insurance, the patient directly pays only a fraction of the price. Demand then becomes

$$q = a - sp$$

Here, *q* captures the idea that the quantity of patients who are treated is determined by suitability for treatment — the benefit for the patient — minus the price and the payment by the insurer. Price sensitivity changes with insurance.

As Jena and Philipson (2008) pointed out, societal and individual perspectives on value are likely to vary as follows.

Value of innovation from a societal perspective, where c = the marginal cost of production:

$$SW = \frac{(a-c)^2}{2}$$

Value of innovation from private (individual patient's) perspective:

$$V^m = \frac{(a-sc)^2}{4s} \qquad \frac{\partial V^m}{\partial s} = -\frac{a-sc}{s^2}(a+sc) < 0$$

The situation may be even more complicated when, for example, payers determine both price and quantity. When insurance decreases price sensitivity, prices may be higher than optimal and encourage innovation that delivers lower value — "too much" innovation. Even if insurance rates rise to pay for higher prices, a general equilibrium effect, this will not be enough to substantially change the desensitising effect of insurance.

Step 2 Introduces the effects of institutional arrangements and requirements, which attempt to formalise demand. Cost-effectiveness evaluations are a common approach. As Equation 1 shows, price will be equal to the monetised value of average effectiveness.

Benefits (effectiveness) are represented by $B(q)$, which is the monetised value of health gain provided by a new drug for each patient. Costs, expenditures incurred, are given by $qp(q)$. The expected benefit for patient if use is limited to those patients who will benefit. Average effectiveness is

$$\bar{B} = \int_0^{\hat{q}} B(q')dq'/\hat{q} \qquad (1)$$

When ICER is a component, the differential benefits or differential costs produce a threshold of cost-effectiveness that assigns a monetary value to a unit of effectiveness. Price may increase as long as it remains below the threshold. Obviously, including ICER in the equation would require more terms, but the point here is that price is equal to average effectiveness.

Measuring average effectiveness is crucial. For a new drug, this is affected by the number and characteristics of patients included in the clinical trials. Companies can manipulate this, to some extent, by choosing which indication to study, knowing that a higher price will be agreed for a drug that most effectively treats a patient population which can be rather easily defined. Payers will accept the price that a firm proposes for a new drug as long as it does not exceed the cost effectiveness threshold. Subsequent indications for the same drug may be developed and marketed, with a lower average effectiveness. Strategic decisions about which indications to target first are driven to a varying, but important, degree by the institutional framework that determines pricing.

$$p = p(\hat{q}) = \int_0^{\hat{q}} B(q')dq'/\hat{q}$$

In effect, this process allows firms to set monopoly pricing indirectly by controlling quantity. The value function (profit) is given by the margin (price minus cost) times the quantity. The first-order condition for the choice of the critical *q*, how trials are design, i.e. which indication is chosen, then leads to the same price that a monopolist acting directly on price would follow.

$$V = (p(\hat{q}) - c)q(sp(\hat{q}))$$

$$\partial V/\partial \hat{q} = \partial V/\partial p \times \partial p/\partial \hat{q} = 0$$

Over the past few decades, ICER has been important in determining the value of therapeutic interventions. Few would dispute this. Its usefulness in establishing price is more questionable; monopoly pricing still will be the end result as long as companies choose the indications and the range of patients for clinical trials. Institutionalizing cost-effectiveness, then, provides the same incentives for R&D as does monopoly pricing and also may result in excessive investment in innovation. This approach cannot solve the problem of high prices, then, although it does virtually eliminate payment for innovation of low value.

Step 3 in the modelling exercise considers how pricing might be moderated, given the current institutional framework. Patent systems have been in operation for more than a century; the objective is to spur innovation by allowing a period of market exclusivity long enough to allow firms to recoup

R&D costs. This encourages innovation in all areas — consumer goods and industrial equipment, health care and software, mobile phones and computers. Concern about the effect of patents on the price of such items as cell phones is almost entirely absent for one simple reason: the consumer makes the value calculation, deciding whether the value of the product justifies the price. Price sensitivity in health care, however, is dampened by insurance. The societal reasons for health insurance are not at question, but the unintended consequence is a disconnect between demand and price.

The challenge for pricing in the health care sector is to devise methods for screening for excessive prices, that is, prices that are higher than would be the case without health insurance. If patients pay only a fraction of the price, the demand curve will rotate. With full insurance where the patient pays nothing at all, no co-pays, demand will increase up to the point of zero marginal benefits.

$$V = (p - c)D(sp)$$

With $s < 1$, the monopoly price follows $p^m(s), \qquad p_s^{m'} < 0$

So $p^m(1) < p^m(s)$ and $\dfrac{\partial V}{\partial p} > 0$

For $V^1 = (p^m(1) - c)D(p^m) = (p^* - c)D(sp*)$, (2)

To obtain the same profit as with without insurance protection, the price should be lower. Thus, to provide firms the same profits they would retain under a private market without health insurance, the price allowed would be smaller than what firms would charge in such a private market, which in turn is smaller that the price a monopolist charges in a private market with health insurance protection to patients.

Determining an appropriate level of profits is difficult. A price is excessive if it provides more profit with insurance than would be possible without insurance. A benchmark such as that suggested in Equation 2 still is generous because price-demand elasticity is low for pharmaceutical products even in the absence of insurance. The challenge is to use information available to approximate the free market price without insurance. Although the monopoly price may not be known, the slope of demand may be indicated by the relationship between the effectiveness of treatment and the range of patients.

An advantage of this approach is that it does not rely on the usual arguments: that price transparency must increase or that more should be revealed about the costs of R&D. Such viewpoints rely implicitly on a cost-plus pricing approach, which provides poor incentives for innovation. Knowing more about R&D costs may be desirable for other reasons, but not from the perspective of the economics of disparity.

4 The role of MEAs

MEAs that are conditional on outcomes have been presented as a way forward and are an important approach for dealing with uncertainty about how well a drug may perform in the future. Paying according to value means a different price for high- and low-value drugs. Although MEAs can help shape R&D incentives, however, they cannot address prices per se.

To understand the effect of MEAs, assume two drugs — one with higher value and one with lower value. With all new drugs, some uncertainty exists about effectiveness in actual use. In some cases, this information may be asymmetric, that is, the company knows more about the new drug than the payer. An MEA can work as a signalling model in such cases, as follows. Requests for a higher price must be backed by proof of greater effectiveness than the alternative treatment. If the product likely represents only modest improvement, then showing enough effectiveness to justify a higher price will require clinical trials either in a smaller number of well-defined patients or for narrow conditions of use. The expense to the company of such research will be greater for a low-improvement product than a high-improvement one. Because of the need to prove effectiveness, the company with a lower-improvement product cannot request both a high price and widespread use, so the need to show effectiveness restricts quantity or volume of use. This entails costs for the company, both in clinical trials and in the restricted range of patients treated, volume of use.

Although MEA agreements can help distinguish among potential value and costs, this approach still allows firms to set a monopoly price by defining the range of patients, and indications, included in the cost effectiveness studies that will determine the price. It is important to point out that the institutional setting is driving this situation and that even though signalling works, the result still is monopoly pricing. The MEA approach, then, does not solve the pricing problem.

When information is symmetric, uncertainty exists for both payer and company. Agreements about effectiveness in use and possible price adjustments or rebates can deal with such uncertainty. An interesting point in this case is the effect on R&D. The investment in R&D can be lower with an MEA where the payment is conditional on effectiveness than when it is based solely on expected value. MEAs, then, do not necessarily lead to greater investment in R&D. It is not difficult to show that if the MEA produces ex-post different prices (after the value of the drug becomes known), with ex-ante uncertainty about it, then incentive for investment can be higher or smaller under the MEA, depending on probability of having a high value product. Without the MEA, investment is based on profit valued at the price based on expected value of demand, while with the MEA, the relevant reference is the expected value of profits based on each ex-post price. If the probability of finding a high-value product is sufficiently low, then incentive to invest in R&D under the MEA will smaller than without the MEA.

Some countries now are considering abandoning the practice of basing price on cost effectiveness and just negotiating explicitly on price, with cost effectiveness being one point in the negotiation. Other approaches to date have not been successful in exerting downward pressure on prices. Competition clearly has an impact, but some expensive treatments, such as the cure for hepatitis C, are patent protected so generic competition is some years off. Competition from other patented drugs does have an effect, albeit a lesser one.

Step 4 considers intertemporal effects and cost sharing across generations. The issue here is how best to pay for a one-time treatment that has an impact over time, across generations. Currently, the approach to paying for such higher priced cures spreads risk and payment over time but does nothing to address price levels. Innovation may be paid for by one generation — for both patented and generic versions — but the next generation reaps even greater benefits because the prevalence of the disease lessens dramatically. The issue is greatest for diseases that are chronic; patients treated in the first generation will continue to need treatment at the same time that the second generation initiates treatment.

Ramsey pricing is one way to discuss how to fund R&D across different markets. In this case, the markets are two time periods — the first generation and the second generation. The general rule of higher prices as the result of lower demand elasticity holds; but particularly in the case of cures, intertemporal effects disrupt the situation. Demand is not the same in the two periods because treating patients now lowers the incidence of disease and so demand for treatment later. Also, given

the time lag, some products will be generic by the time the second period arrives. The net effect of Ramsey pricing can be either p1 > p2 > p3 (equal to marginal cost, due to generics competition) or p2 > p1 > p3 (equal to marginal cost). The second-period benefit for those treated in the first period depends only on the price when they were treated, that is, in the first period. Second-period demand arises from new patients and, for incurable diseases, existing patients. These can be modelled as general demands in each period, with demand in the second period being a function of the price in the first period.

$$\int_{p_1}^{\infty} D_1(p_1)dp_1 + \int_{p_2}^{\infty} D_2(p_2;p_1)dp_2 + (1+\lambda)[(p_1-c_1)D_1(p_1) + (p_2-c_2)D_2(p_2;p_1) - F]$$

$$\frac{\partial D_2}{\partial p_1} > 0$$

Increasing the price today, in the first period, may reduce use today pushing use, and cost, to the future. The question of delaying some consumption benefits the firm in terms of recovering R&D cost. The solution to the Ramsey problem of optimal prices is given by:

$$\frac{p_1 - c_1}{p_1} = \frac{\lambda}{1+\lambda}\frac{1}{\varepsilon_1} + \frac{\partial D_2}{\partial p_1}(p_2 - c_2)\frac{1}{\varepsilon_1} + \frac{1}{\varepsilon_1}\int_{p_2}^{\infty}\frac{\partial D_2}{\partial p_1}dp_2\frac{1}{1+\lambda}$$

$$\frac{p_2 - c_2}{p_2} = \frac{\lambda}{1+\lambda}\frac{1}{\varepsilon_2}$$

$$(p_1 - c_1)D_1(p_1) + (p_2 - c_2)D_2(p_2;p_1) - F = 0$$

The time profile of prices is not clearly determined. If some consumption is delayed to the future, the firm will recover some of the margin in the future. It may not be, then, that the best option is a lower price and greater volume today because this will lower volume in the future. If not treating patients today means that their condition will worsen, then treatment costs will increase in the future. Ramsey pricing, then, does not solve the issue of how to find a clear price pattern.

5 Conclusions

Pricing of pharmaceuticals is a complex challenge that seems to require different approaches based on the situation. Different tools will be needed to address different situations, but common challenges include the following.

1. Uncertainly about product quality
2. The effect of market power and institutional settings
3. Differences in benefit across generations (with time progression liming the scope for ex-post redistribution)

4. New methods for evaluating upfront costs and benefits over time

Practical steps to resolving pricing issues are not obvious. The effect of current institutional arrangements is to provide indirect incentives that produce higher prices. One approach to mitigating this effect may be to create a benchmark price that subtracts out the effect of moral hazard. MEAs cannot sufficiently address pricing issues, although they may be effective in dealing with the uncertainty created by asymmetry in information. The time profile of regulated prices currently is a period of profit-maximization with varying degrees of competition, followed by strong competition from generics. This is unlikely to be optimal, but defining the optimum seems not only complex, but also difficult to translate into simple policy action.

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