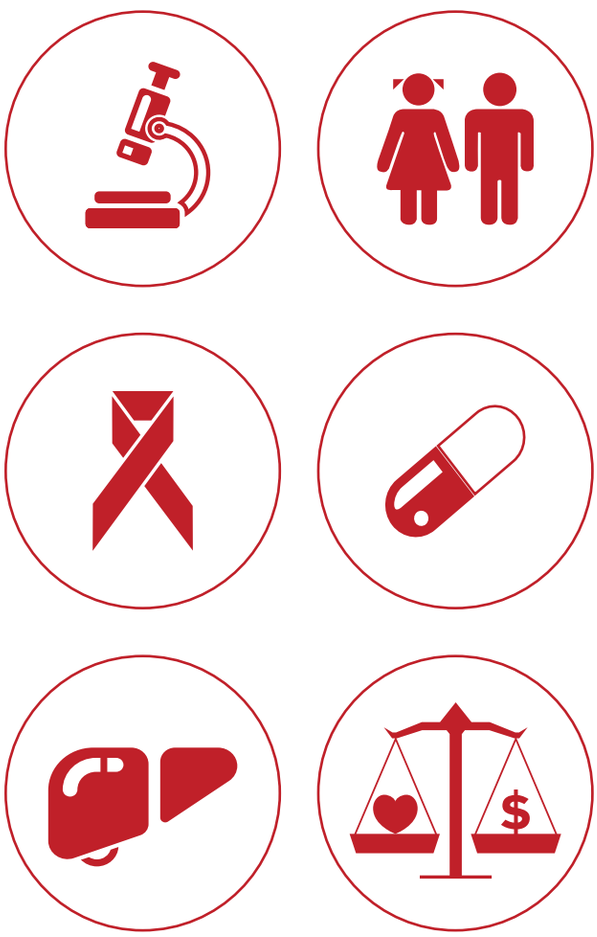
DISCUSSION PAPER

AN ECONOMIC PERSPECTIVE ON DELINKING THE COST OF R&D FROM THE PRICE OF MEDICINES



UNITAID

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Abbreviations

FDA	(United States) Food and Drug Administration
GNI	Gross national income
HER2	Human epidermal growth factor receptor 2
HIV	Human immunodeficiency virus
KEI	Knowledge Ecology International
MSF	Médecins Sans Frontières
NIH	(United States) National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
PhRMA	Pharmaceutical Research and Manufacturers of America
QALY	Quality-adjusted life year
R&D	Research and development
USA	United States of America
WHO	World Health Organization
WTO	World Trade Organization

Preface

In the context of debates on public health, innovation and intellectual property rights, suggestions have been made for a fundamentally different approach to financing innovation, by "delinking" the costs of research and development and the price of health products.

This paper explores, through economic modelling, the potential implications of delinkage. It was commissioned as a "think piece" to feed into UNITAID's own thinking. UNITAID believes, however, that the paper can also be a relevant contribution to a number of ongoing discussions at the international level.

This paper does not necessarily represent the views of the World Health Organization or UNITAID.

1. Introduction

1.1 Challenges regarding access and innovation

Medicines used to treat HIV infection and many other illnesses can be produced at relatively low cost. According to the Médecins Sans Frontières (MSF) periodic survey of antiretroviral prices [1] many HIV medicines can be acquired from generic manufacturers for prices under US$ 1 per gram of active pharmaceutical ingredient. Combination products from patent-holders that cost more than US$ 25 000 per patient per year in high-income markets can be available from quality-assured generic suppliers for less than US$ 200 per year in low-income markets.

According to some estimates, Gilead's new treatment for hepatitis C can probably be manufactured for US$ 2–4 per gram [2]. However, the treatment is priced at US$ 2500 per gram in some high-income countries and around US$ 30 per gram in Egypt [3]. Mark-ups are also very high for cancer medicines. For instance, trastuzumab (trade name: Herceptin) and T-DM1 (trade name: Kadcyla) are priced at US$ 7000–9000 per gram and US $26 000 per gram, respectively.

The reason society tolerates – and even encourages – high prices for new medicines is to stimulate research and development (R&D) for new products. Predictably, however, such high prices can lead to disparities in access, underutilization of medically important medicines, and financial hardships for consumers and reimbursement entities. The practice of rewarding medicine developers with time-limited marketing monopolies can also create other problems such as biases in R&D investments that favour products that match but do not improve medical outcomes, inadequate investment in early-stage science and product development, and perverse incentives to spend considerable resources on medically unimportant research and marketing efforts, as discussed in more detail in section 6.2 below.

In the context of debates on intellectual property, access to medicines and innovation, delinkage refers to separating the price of medicines, vaccines and diagnostics from the R&D costs associated with those products.

1.2 Objective and methodology

This paper assesses the implications for consumers, producers and third-party payers of a delinkage approach compared to the current situation, through stylized scenarios (economic modelling).

As in any analysis based on modelling, the scenarios are based on assumptions that may be more or less realistic. What matters most, therefore, are not the absolute numbers or outcomes but the changes therein which indicate who would stand to gain and who would stand to lose if certain policy measures were to be implemented.

This analysis was prepared by James Love. Helpful comments on an earlier draft were provided by Margo Bagley, Brook Baker, Michael Caroll, Carsten Fink, Sean Flynn, Aidan Hollis, Glynn Lunney, Alan Marco, Shilpa Modi Pandav, Manon Ress, Talha Syed, Robin Thompson, Karin Timmermans and participants at a workshop on price discrimination strategies for access to medicines held on 31 October 2014 at the Washington College of Law, American University.

2. Concepts and context

2.1 Price discrimination and tiered pricing

Medicines are sold by patent-holders at prices that are higher than competitive generic prices, with the mark-ups higher in markets (between countries and/or within countries) where incomes (and ability/willingness-to-pay) are greater. This practice is referred to as price discrimination.

Price discrimination is common, not only for medicines, and it could be argued that the absence of price discrimination is rare in many markets. The factors that facilitate or discourage price discrimination are several, including the availability of information and the existence of barriers to trade and marketing. Depending on the context and the jurisdiction, price discrimination may be allowed, mandated or prohibited [4-7].

Tiered pricing can be considered as a subset of price discrimination strategies. The term "tiered pricing" is used in some cases to describe a simplified structure for price discrimination – most often in policy debates where it is asserted that pricing tiers are related in a meaningful way to incomes.

Some debates on tiered pricing overstate the novelty of price discrimination, which is essentially standard practice in the marketing of pharmaceuticals. The implementation of price discrimination within and between countries is restrained only by practical and legal challenges.

Imperfect price discrimination

In the context of the debate on access to medicines, arguments about the benefits of price discrimination are based on the (implicit) notion that the seller would have sufficient information and incentives to avoid prices so high that they would block access. While a price-discriminating monopolist may set prices high and create financial hardship for consumers or reimbursement entities, the redeeming

feature would be that at least everyone receives treatment so long as the price discrimination is implemented with a high degree of precision that avoids outcomes that block access. However, such precision is difficult to achieve in practice, and perfect price discrimination is not feasible.[1] The question is, how imperfect is the price discrimination and what are the consequences?

Anyone implementing a tiered pricing scheme will face a number of challenges. For instance, there will be price differences between countries, but how many different prices are feasible? Will there be a different price for each country, or a set of prices for countries grouped by income bands? Data compiled by MSF demonstrate that AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Johnson & Johnson and Merck have special pricing policies for HIV medicines for two categories of countries [8]. Some companies have fixed prices for each of the two categories, while other companies have fixed prices for the lowest-income countries (category 1) and case-by-case pricing for countries in category 2. Countries are assigned to different categories by different companies. The factors used include such variables as HIV incidence, per capita gross national income (GNI), World Bank income categories, United Nations definitions for least-developed countries, and other criteria which can be fairly open-ended. There are also differences in prices within countries since some discount prices are offered only to public-sector buyers and are not available to persons who buy out of pocket or who have private insurance. While countless variables can be used to estimate ability- or willingness-to-pay, it is impractical to implement a highly-nuanced pricing policy, with the problem compounded by the use of reference pricing, partial mobility of products and other factors.

To the extent that the buyers/reimbursement entities always will have limited resources and prices are perceived to be high, consumers and reimbursement entities will have incentives to avoid higher-priced medicines, by excluding a patient from coverage altogether or by using less expensive alternatives even when they are inferior from a medical standpoint.

Tiered pricing

Tiered pricing can be seen as a form of price discrimination by a monopolist, a form of price regulation by buyers, or the outcome of a negotiation between buyers and sellers.

Tiered pricing has been criticized for a number of reasons, including the fact that industry influence and power in the negotiations are excessive, and unequal bargaining power will predictably lead to outcomes that reflect the interests of the seller more than those of the buyers.

Ramsey-Boiteux pricing

Economists Frank Ramsey and Marcel Boiteux separately examined the problem of pricing above marginal costs in the context of taxation and natural monopoly public utilities. Their well-known conclusion was that the optional departures from marginal costs were similar to monopoly pricing in that the mark-up over costs is high where there is a low elasticity of demand, and is low where there is a high elasticity of demand.[2] Medicines were considered an example of where Ramsey-Boiteux pricing was potentially inappropriate because it favours very high prices for goods that are essential for life or health. This concern is typically expressed in the context of a system that uses Ramsey-Boiteux pricing across different goods, not all of which would be considered essential.

When applied to medicines, as opposed to all goods, the Ramsey-Boiteux rule could have value if applied when allocating fixed costs for medicine development to different users, but only if policy-makers are willing to constrain mark-ups in order to recover only the required costs, consistent with the original proposal by Ramsey and Boiteux.

As presented in the context of earlier debates on tiered pricing,[3] and championed by some, the challenge of constraining the mark-up so that it is limited to what is actually needed to pay for the fixed cost of medicine development is often ignored. When the issue of limiting the mark-up is ignored, what is left is simply the monopoly pricing rule, which is best for sellers, but not the best outcome for consumers or third-party reimbursement entities.

2.2 The current R&D financing model

In addition to high prices that restrict access, the current model of financing R&D through exclusive rights (monopoly rights) over the final product poses other challenges. In recent years, roughly 8% of global turnover on pharmaceuticals was reinvested into R&D by the private sector.[4] Much private-sector investment in R&D is spent on the development of medicines that offer few, if any, benefits over existing treatments, or to fund studies that have weak scientific merit but can be used to promote the use of a product facing competition within a therapeutic class [9-13].

There are also incentives in the current system to promote irrational use of products, where the net health benefits of use are negative or low compared to better alternatives [14-18].

The system of granting a monopoly for a new product also creates private incentives to restrict upstream access to research and/or patented inventions [19-21]. This undermines access to knowledge and contributes to wasteful and duplicative R&D expenditures.

While the private sector's role is important and significant in the development of medicines, so too is the role of the public sector. The budget of the United States National Institutes of Health (NIH) for HIV research is US$ 3 billion per year,[5] which is more than the annual budget of all HIV clinical trials funded by industry.[6] Not only is the public sector role in funding R&D significant in terms of the levels of funding but it also often focuses on the most risky aspects of R&D, including funding the basic and early applied research that contributes to breakthroughs in medicine development. Findings from publicly-funded research are generally shared openly, contributing to the advancement of science.

While a global framework of binding trade agreements underpins – and increases – the levels of protection for intellectual property, there is no similar global mechanism for public-sector R&D funding. The asymmetry of obligations leads to a bias against the most risky and potentially important stages of medicine development.

2.3 Delinkage

The term "delinkage" is used for a set of options that aspire to change fundamentally the paradigm for financing innovation. The term can best be understood as partly technical – the separation of R&D costs from product prices – and partly polemical – a demand that the R&D system be reformed to accommodate universal access to knowledge goods, to induce openness and sharing of knowledge in general, and to make investments in R&D more cost-effective and responsive to the needs of patients and society.

Because there is considerable freedom to design systems that delink the financing of R&D from the price of the product, it is a challenge to describe "the" delinkage approach. Ideally, delinkage would eliminate the monopoly to supply products and would provide a diverse set of alternative mechanisms to finance innovation. Products would be available at prices approaching marginal costs, while policy-makers would be free to spend as much or as little as they prefer on innovation and would have flexibility to design the funding mechanisms.

In delinkage approaches, it is still necessary to identify a source of money to pay for innovation. Sources may include budgets for medicines or health care, general tax revenue, a "Robin Hood tax" on financial transactions, or a Pigouvian tax on activities that impose social costs (such as use of a medicine that generates drug resistance).

If medicines are purchased or reimbursed by third parties, these entities could shift budget allocations from paying high prices for patented medicines to funding grants or rewards for innovation, typically at a lower cost. If medicine purchases are paid by consumers directly out-of-pocket, new financing mechanisms would be required.

The freedom for governments and buyers to determine the amount to spend and the nature of alternative mechanisms to fund innovation has created anxiety among medicine developers and companies that sell branded products. The two main reasons for their concern are: 1) a lack of confidence that buyers will allocate sufficient resources to R&D, and 2) a recognition that the comparative advantage for some companies lies in the marketing of products. Some experts and patients share concerns about the first issue.

Potential advantages of a delinkage approach include pricing closer to marginal costs, the inclusion of more patients in treatment, broader access to new medicines, including for uses that have differential benefits, more cost-effective and flexible targeting of R&D incentives and other subsidies, and lower total costs.

Mechanisms to implement delinkage

As mentioned above, delinkage can be implemented in different ways. One of the delinkage options is public funding of research, which should include all stages from discovery to late-stage and post-approval clinical testing. While public-sector R&D funding is typically managed at national level through institutions such as the USA's NIH, it could also be managed as a pooled resource at the plurilateral or multilateral level, or even through decentralized "competitive intermediaries".[7]

Delinkage options also include the use of prizes to induce innovation. Innovation-inducement prizes can be designed in different ways, as illustrated in Annex 1 and 2. As shown in Annex 1, there is significant flexibility in shaping prizes – and other delinkage approaches can be devised. For instance, developing countries could potentially eliminate monopolies on HIV/AIDS medicines in favour of a delinkage approach that includes the use of innovation-inducement prizes.

The HIV/AIDS market in developing countries is large in terms of utilization and in terms of patients who need treatment, but it is relatively small in terms of global sales compared to countries with incomes higher than US$ 20 000 per capita. In 2012, sales of HIV therapeutics were estimated at US$ 14.3 billion in just eight countries: Canada, France, Germany, Italy, Japan, Spain, the United Kingdom and the USA [22]. In the same year, UNITAID estimated antiretroviral sales in all low- and middle-income countries to be US$ 1.5 billion [23].

Given the substantial market for antiretrovirals in high-income countries, any proposal for delinkage regarding HIV medicines in developing-country markets can be seen largely as an access initiative, with innovation being a second benefit. For treatments for hepatitis C, the primary appeal of delinkage may also be to expand access, even in high-income countries. For cancer and other "Type I" diseases, delinkage can be implemented in order to expand access, but also to promote better and more cost-effective innovation, with somewhat different innovation objectives in high-income and low-income countries. For various Type III diseases,[8] delinkage could have a first order impact on innovation and the lower product prices are consistent with efforts to promote access in resource poor settings.

Chapter notes:

[1] "This evidence suggests that although price discrimination between MLICs countries [middle- and low-income countries] could in theory be a profit-maximizing (and welfare enhancing) strategy for originators, and generics are widely available, PCI [per capita income] related pricing is undermined if income distributions are skewed and/or competition focuses on brand, rather than price, due to asymmetric and uncertain quality of generics. Price discrimination within MLICs is unlikely to be feasible when drugs are sold to largely self-pay patients in retail pharmacy channels served by common distribution networks." [45]

[2] For a nuanced discussion of the dissimilarities, see reference [46].

[3] For example, during the Workshop on Differential Pricing & Financing of Essential Drugs, organized by WHO, WTO and the Global Health Council of the Norwegian Foreign Affairs Ministry, in Høsbjør, Norway, 8–11 April 2001.

[4] In 2012, PhRMA member R&D outlays (as reported by PhRMA), were 5.2% of global pharmaceutical sales (as reported by IMS). A Burrill & Co. analysis for PhRMA, published in the 2011 PhRMA Annual Membership Survey, estimated non-PhRMA drug company private-sector R&D outlays for the years 2004–2010. When combined for the seven-year period, the private-sector R&D outlays were equivalent to 8.2% of global pharmaceutical sales. For 2010, the last year of the Burrill analysis, global R&D of US$ 67.4 billion was 7.6% of global sales of US$ 891.3 billion.

[5] According to the NIH, spending on HIV/AIDS-related research averaged US$ 3.1 billion for fiscal years 2010–2013, and is estimated at US$ 3.005 billion for fiscal year 2015 [47]. This includes "both extramural and intramural research (including research management and support, Management Fund, and Service & Supply Fund), buildings and facilities, research training, and program evaluation, as well as research on the many HIV-associated co-infections and co-morbidities, including TB, hepatitis C, and HIV-associated cancers. It also includes all of the basic science underlying this research."

[6] For HIV trials registered in ClinicalTrials.Gov with a start date in 2012 or 2013, there are 132 industry-only funded trials with proposed enrolment of 39 815 patients, including both observational and interventional trials. During this same two-year period, the NIH budget for HIV research was US$ 5.972 billion, or roughly US$ 150 000 in NIH research funding for every patient enrolled in an industry-only funded trial.

[7] A similar competitive approach to rewarding upstream medical research is envisioned in S. 626, 113th Congress, Sec. 12, Competitive Intermediaries for Funding Interim Technologies. See also [48]. S. 626 provides a practical illustration how the decision making for innovation inducement prizes for upstream research can be decentralized in systems that have competitive tensions among the institutions making the awards. Competitive intermediaries can also manage grant programs, and indeed, the existence of several institutions that manage grant programs can already be described as one of competitive intermediaries.

[8] Type I diseases are defined as diseases that are "incident in both rich and poor countries, with large numbers of vulnerable are population in each". Examples include influenza and diabetes. Type II diseases "are incident in both rich and poor countries, but with a substantial proportion of the cases in the poor countries"; HIV/AIDS is an example. Type III diseases "are those that are overwhelmingly or exclusively incident in the developing countries, such as African sleeping sickness …" [49].

3. Models of delinkage in a single country

3.1 HIV, single price, differential benefits

To evaluate delinkage, it is worth considering first a stylized market of a single country where budgets to spend on medicines are fixed (an income elasticity of demand of -1), and there is an expectation that the country will spend US$ 1 million to support innovation out of a total medicines budget of US$ 10 million.

In this example, the US$ 1 million to support innovation is 10% of the medicines budget.[9] This is in line with global contributions to R&D; globally, private-sector investments in R&D in recent years have averaged roughly 8% of the total market for pharmaceuticals (including both patented and generic products).

In the first two scenarios (Table 3-1), there are three types of patients:

Group 1 (40% of patients) can be can be treated with older medicines, available off-patent, with a health benefit as measured by a quality-adjusted life year (QALY) of 1.

Group 2 (40% of patients) can also be treated with the older medicines, available off-patent, but with a lesser health benefit of 0.7. Group 2 patients would be better off (with a health benefit of 1) if they had access to newer medicines that are available only from patent-holders.

Group 3 (20% of patients) cannot be treated at all with the older medicines but do respond to the new ones, with a health benefit of 1.

In this market, there are more patients needing treatment than can be treated within the US$ 10 million budget for medicines.

Delinkage outcomes are compared to the more conventional method of enforcing patent monopolies to reward drug developers, using assumptions very favourable to the conventional method. Two initial scenarios are considered. In the first, suppliers are allowed to charge a single price that will return a US$ 1 million mark-up over costs and the government optimizes health outcomes, given the constraints of the budget. In the second scenario, both the treatment budget and the R&D contribution are the same, but the contribution to R&D costs a separate portion of the budget and both new and old medicines are available at the same generic price of US$ 200.

TABLE 3-1

HIV, R&D costs built into price, or via a separate portion of budget.

Scenario 1: R&D costs built into price of new medicine	Group 1 patients	Group 2 patients	Group 3 patients	Total
Proportion of patients	40%	40%	20%	
QALY per patient	1	0.7	1	
Number of patients	18 000	18 000	9000	45 000
Cost (US$)	3 600 000	3 600 000	2 800 000	10 000 000
Price per patient (US$)	200	200	311	
QALY (total)	18 000	12 600	9000	39 600

Scenario 2: Delinkage, R&D costs are a separate budget item	Group 1 patients	Group 2 patients	Group 3 patients	Total
Proportion of patients	40%	40%	20%	
QALY per patient	1	1	1	
Number of patients	18 000	18 000	9000	45 000
Cost (US$)	3 600 000	3 600 000	1 800 000	10 000 000
R&D contribution		1 000 000		
Price per patient (US$)	200	200	200	
QALY (total)	18 000	18 000	9000	45 000

In this simple scenario, the budget and the number of patients treated are the same, but the health outcomes are better in case of the delinkage approach because both Group 2 and Group 3 have access to the newer medicine.

Delinkage as a Pareto improvement

Among the key concepts of modern neoclassical welfare economics is the concept of a "Pareto improvement" in social welfare, defined as an improvement in economic outcomes where no party is worse off. In the example in Table 3-1, patients are better off in the delinkage scenario, and the developers of medicines are no worse off, receiving US$1 million to offset R&D costs in both cases. In this sense, the delinkage alternative is "Pareto efficient", which is an attractive situation in both economics and politics.

No contributions to R&D costs

A third option could be a situation where there is no contribution to R&D costs and no access to the newer medicines (Table 3-2). When all of the US$ 10 000 000 is spent on older medicines, and no contribution is made to R&D, the overall number of patients treated is larger (50 000 instead of 45 000), but no one in Group 3 receives treatment (clearly a bad outcome for the Group 3 patients), and the Group 2 patients receive the older (and for them inferior) medicine.

Given the 0.7 QALY for Group 2 using the older medicines, the total QALY benefit in this third scenario is inferior to the Scenario 2 delinkage alternative, even though the total number of patients treated is higher. Even without introducing assumptions about the QALY benefits to the Group 2 patients, this scenario is problematic in that many of the Group 2 and Group 3 patients begin as Group 1 patients, and the lack of treatment options for Group 3 can be seen as an eventual treatment failure if resistance or side effectives become an issue making the older medicine ineffective or undesirable.

TABLE 3-2

HIV, No contribution to R&D, no access to new medicines

Scenario 3: No access to new medicines	Group 1 patients	Group 2 patients	Group 3 patients	Total
Proportion of patients	40%	40%	20%	
Proportion of patients treated	50%	50%	0%	
QALY per patient	1	0.7	0	
Number of patients	25 000	25 000	0	50 000
Cost (US$)	5 000 000	5 000 000	-	10 000 000
Price per patient (US$)	200	200	-	
QALY (total)	25 000	17 500	-	37 500

If a country can obtain both old and new medicines for $200 per patient without making any R&D contribution, it will be even better off, and for some markets this may be realistic. However, as evidenced by the growing web of trade agreements with TRIPS+ provisions on medicines, there will be markets where some contribution to R&D costs is expected and in the absence of an accepted delinkage approach, higher prices will be hard to avoid.

For the scenarios above, delinkage dominates for the simple reason that it allows access to the newer medicines at marginal cost. This is true even though, in the other scenarios, the assumed price for the new medicine was only 55% higher than the generic alternative.

The parameters can of course be changed but, for many realistic scenarios, the alternatives that tie R&D costs to prices on patented medicines will appear worse and not better, judging from the actual prices observed for medicines available from patent-holders. Some of these latter prices are more than an order of magnitude higher than generic prices, even for medicines to treat HIV/AIDS in developing countries where some pricing discounts are expected.

3.2 Hepatitis C, single market with insurance

A further case for consideration is a stylized market for a hepatitis C medicine in a single market where patients have insurance. Among those who are infected with hepatitis C, some will overcome the infection without treatment. Among those who have chronic infections, some will eventually have chronic illnesses and, among those, some will have acute and severe outcomes such as cancer and, eventually, death.

In this example, the reimbursement authority would perceive value in treating patients in each of the four groups, but would be less willing to pay for treating those who may never become sick than for those who are sick and/or face severe outcomes.

In Tables 3-3 and 3-4, the value of treatment is highest for patients with acute illnesses facing severe outcomes and relatively less for other patients, depending on their condition and diagnosis at the time.

TABLE 3-3
Hepatitis C, single market with insurance, value of treatment

Patient groups	Proportion of infected population	Relative value of treatment to reimbursement entity[a]
Infected, not chronic	20.0%	0.013
Chronic, minimal impact on health	60.0%	0.018
Chronic illness (not most severe)	18.0%	0.09
Acute, severe outcomes	2.0%	1

[a] Compared to the value for patients with severe outcomes.

TABLE 3-4
Hepatitis C, single market with insurance, possible revenue to supplier

Least severe diagnosis to be included	Number of patients	Cumulative number of patients buying the medicine, given the price	Price for the medicine (US$)	Feasible revenue (US$)
Acute, severe illness	2000	2000	80 000	160 000 000
Chronic illness (not most severe)	18 000	20 000	7200	144 000 000
Chronic, minimal impact on health	60 000	80 000	1440	115 200 000
Patents Infected, but not chronic	20 000	100 000	1040	104 000 000

TABLE 3-5
Hepatitis C, single market with insurance, delinkage outcome

Patient groups	Value of treatment per patient (US$)	Number of patients in group	Value of treatment for group (US$)
Infected, not chronic	1040	20 000	20 800 000
Chronic, minimal impact on health	1440	60 000	86 400 000
Chronic illness (not most severe)	7200	18 000	129 600 000
Acute, severe illness	80 000	2000	160 000 000
Total		100 000	396 800 000

The parameters in Table 3-3 and the prices in Table 3-4 were selected to be consistent with the estimates of medical conditions among persons infected with hepatitis C virus (in terms of the proportions) and with a pricing structure that limits access to the most acute and severe cases. A pricing strategy that results in the product being sold exclusively to a small number of persons who have acute illness makes sense to the manufacturer only if the reimbursement authority perceives a much higher relative value of treatment for the patients with severe health issues. The stylized parameters in Tables 3-3 and 3-4 are designed to capture that dynamic, for purposes of illustrating the consequences of linking and delinking R&D costs.

Table 3-4 reviews the market from the point of view of the drug developer, for a hypothetical country with 100 000 infected persons and with a willingness-to-pay twice its US$ 40 000 per capita income to treat a patient with acute and severe illness and relatively less for other groups. The table shows the possible market outcomes if the costs of manufacturing the medicine are trivial and the supplier can offer only a single price for the market.

In this example, the supplier is best off when the price is US$ 80 000 and only 2% of the market is served. But this outcome is inefficient. Society has a positive value for each of the three excluded groups, yet none of them are served.

If delinkage would be implemented in this market by purchasing the patent rights for US$ 160 000 000, the supplier would earn the same amount and everyone could be treated. The net benefits to society would be significant, as illustrated in Table 3-5.

Chapter notes:

[9] Financing considerations are discussed in more detail below, but note that for HIV the payment for drugs is already largely financed by third parties, making the implementation of delinkage alternatives less challenging in terms of identifying the sources of funding. For HIV, the sources of funding for innovation can be same entities as those faced with purchasing patented drugs at high prices, and delinkage can be implemented at the same or lower cost than the current approach.

4. Concepts and context – Part 2

4.1 Consumer surplus, producer surplus and deadweight loss

Although they have some limitations, the concepts of producer surplus, consumer surplus and deadweight loss are sometimes used by economists to quantify the benefits and costs of various policy options and market outcomes.

Consumer surplus is the difference between what a consumer is willing to pay, and what is actually paid. In the examples discussed here, the term "consumer" can be used to describe the patient or the third party reimbursing the treatment – such as a government, employer or insurance company. If the value to society of a treatment for a patient with a severe illness is US$ 80 000 and the price is US$ 7200, the "consumer surplus" is US$ 72 800 for that patient.

Producer surplus is the difference between the revenue to the supplier and the cost of goods. If production costs are negligible, or even zero, as in the case of some information goods, all revenues are considered net benefits to suppliers.

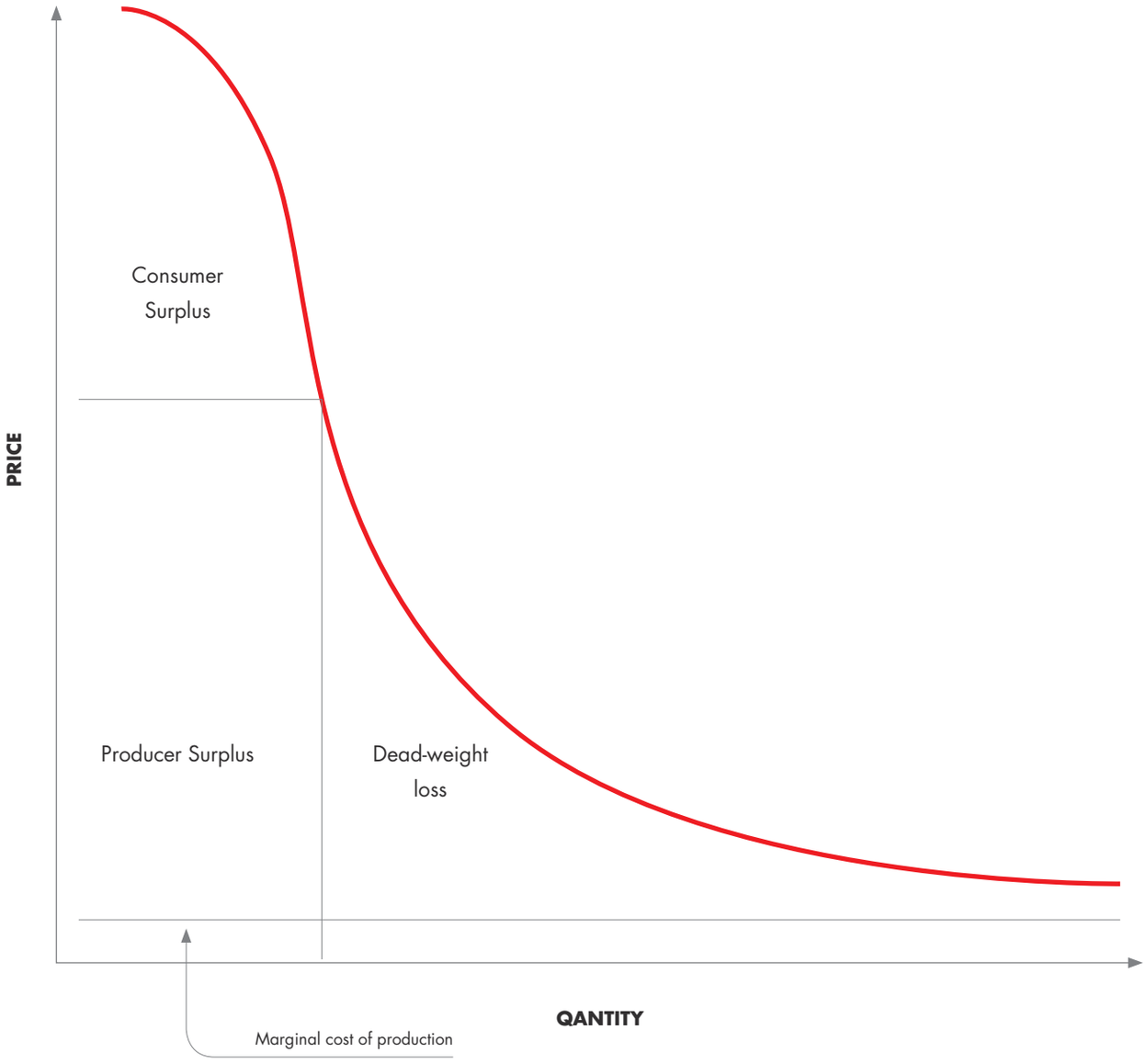
In neoclassical economic analysis, deadweight loss is a term used to describe the value from transactions that do not take place but which would have provided net benefits.

These concepts are illustrated in the context of a simple demand curve in Figure 4-1.

The concepts and theory behind consumer and producer surpluses and deadweight loss are not value-free constructs, particularly when applied to markets where the differences in willingness-to-pay reflect different incomes and where deadweight loss is equivalent to human suffering, serious disease and death. They do, however, provide an additional illustration of the consequences of relying on the product's price to contribute to R&D costs when the value of a product is different for different users.

FIGURE 4-1

Consumer surplus, producer surplus, and deadweight loss



As the names suggest, consumer surplus is a good thing from the point of view of consumers and/or reimbursement authorities, and deadweight loss is a bad thing.

In Table 4-1, the two business models discussed in section 3.2 are compared in a scenario where the outcomes are revenue-neutral for both the government and the supplier. The supplier is no worse off but the government and the hepatitis C patients are far better off. There is no consumer surplus in the single-price business model, and significant deadweight loss. The reverse is true for the delinkage scenario which has significant consumer surplus and no deadweight loss.

TABLE 4-1

Hepatitis C, single market with insurance, single price and delinkage outcomes compared, revenue-neutral for supplier

		Single price scenario (a)	Delinkage scenario, revenue-neutral for supplier (b)
1.	Patients receiving treatment	2000	100 000
2.	Value of treatment to government (US$)	160 000 000	396 800 000
3.	Revenue to supplier (US$)	160 000 000	160 000 000
4.	Consumer surplus [line 2 minus line 3] (US$)	0	236 800 000
5.	Producer surplus [same as line 3] (US$)	160 000 000	160 000 000
6.	Deadweight loss [2(b) minus line 4 minus line 5] (US$)	236 800 000	0

4.2 Additional benefits of delinkage

The delinkage model has several additional benefits. For instance, while the examples above assume that every dollar in the mark-up over costs in the tiered-pricing scenario is a contribution to R&D, this overstates the efficiency of the tiered-pricing model. Some (and perhaps a significant) amount of the higher prices will be spent on marketing costs by companies that have legal monopolies to sell products.

At present, developing countries represent only a small fraction of the global market for most medicines. For patent-holders, the small increase in returns from sales in developing countries is unlikely to drive R&D priorities. In a delinkage scenario, there is more flexibility to direct and shape the outlays on R&D in order to focus on the most important unmet needs of developing countries – such as medicines (and diagnostics) that work best in resource-limited settings – and to induce greater participation by suppliers of R&D in developing countries.[10]

Chapter notes:

[10] Both grants and innovation-inducement prizes can be, and often are, designed to favour domestic suppliers of innovation. For example, the recent European Union innovation prize for heat-stable vaccine technologies was limited to innovators from the European Union. See reference [50].

5. Scenarios with multiple countries

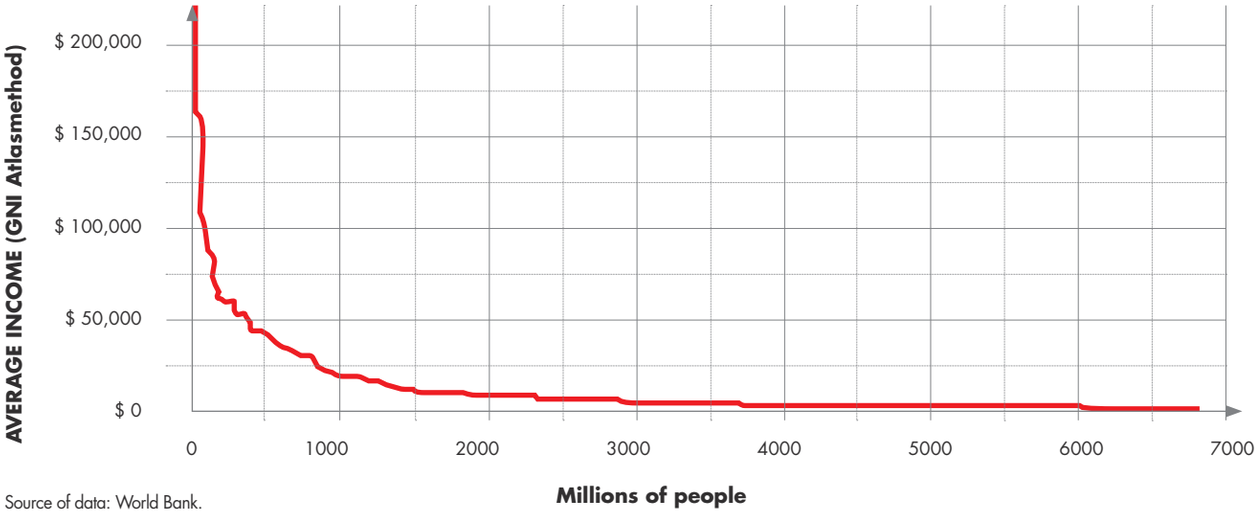
5.1 Model and assumptions

While the examples above consider pricing models and a delinkage approach in the context of a single market, the world is of course a patchwork of markets with very unequal incomes.

The World Bank has estimates of the distribution of income for 150 countries, broken down by the top two and last two deciles and the middle three quintiles. This covers 97% of the population and 98% of the income for all countries in the World Bank database.

In Figure 5-1, the average income by country decile or quintile (whichever is available from the World Bank) is plotted against the population for the 150 countries for which such data are available. For any good with a constant income elasticity of demand, this is effectively a global demand curve and it illustrates just how unequal incomes are.

FIGURE 5-1
Average incomes, 2012, by country decile/quintile



Source of data: World Bank.

For the persons living in these 150 countries, the top 10% have 58% of all income. The top 20% of people have 77% of the income. The bottom 20% have just 1.2%, and the bottom 10% have about 0.3%. The total population of the entire 150-country market consists of 6.824 billion persons, and the average income is US$ 10 219.

When companies choose prices for goods, these income differences have consequences. To illustrate these consequences, several stylized markets for innovative products are considered in the following sections.

Assumptions

The discussion in the subsequent sections groups countries by World Bank income groups, since this is a well-known way of grouping countries. This classification however has limitations, which are summarized in Box 5-1.

World Bank data for the 150 countries in 2012 were used to model the population, incomes and distribution of incomes within countries. Moreover, the following assumptions underpin the stylized markets in sections 5.2 and 5.3.

- For the sake of simplicity, it is assumed that the markets are for a pure knowledge good with a zero cost of reproduction.

- Demand/willingness-to-pay are correlated and normalized to average incomes, either within a country or within a country income decile or quintile, depending on the model. In other words, the figures for willingness-to-pay and income are considered to be the same.

For several pricing and business models, prices, access, the distribution of benefits between consumers and producers, and measures of deadweight loss are calculated and compared in the next two sections.

BOX 5-1

Limitations of the World Bank income group definitions

The World Bank income groups are not ideal in terms of market segmentation. They were created in the 1980s, as a measure of relative well-being, based on what was considered a relevant standard of living at that time. According to the World Bank, "An explicit benchmark between the middle-income and high-income countries was established in 1989 at $6,000 per capita in 1987 prices." After the original per capita income thresholds were established, they have been "updated every year to incorporate the effect of international inflation, which is now measured by the average inflation of Japan, the United Kingdom, the United States and the Euro Zone" [24].

By 2012, the four groups were defined by annual per capita GNI, using the Atlas Method. Thus:

- low income = US$ 1035 or less;
- lower middle income = US$ 1036–4085;
- upper middle income = US$ 4086–12 615; and
- high income = US$ 12 616 or more.

In 1987, the World Bank high-income threshold was 49% of the average for all countries defined by the World Bank as high-income, and 42% of the average for OECD high-income countries. By 2000, this had fallen to 41% and 35%. In 2012, the World Bank threshold for a high-income country had fallen to below 34% of the average for all countries defined as high-income, and below 30% for the countries defined as OECD high-income.

For OECD high-income countries, real per capita incomes increased by 34% from 1987 to 2000. By 2012, real per capita incomes were 49% higher compared to 1987. In contrast, the inflation-adjusted increase in the World Bank definition for high-income countries was zero over this period.

The standards for qualifying as high-income have clearly slipped in relative terms, and the same can be said of the middle-income thresholds. Few people in developed countries realize that, in 2012, a country with an average per capita income of US$ 87 per month qualifies as a middle-income country, or that a country with an average per capita income of US$ 341 per month is defined as an upper-middle income country [25,26].

5.2 Markets with incomes segmented within countries

Several scenarios can be envisaged for the stylized 150-country market for which the demand curve is illustrated in Figure 5-1.

The data underlying any given demand curve can be used to calculate the revenue maximizing price, as well as other conventional cost benefit parameters, such as consumer surplus, producer surplus and deadweight loss.

5.2.1 Single global price

The first scenario is a case where the supplier offers a single price to everyone. At a high price, fewer persons will have access. At a lower price, more people will have access.

From the point of view of the supplier of the knowledge good, the optimal price is the one that maximizes revenues. In general, the flatter (i.e. more equal) the distribution of income, the more equal the access will be. However, as noted above, incomes globally and within countries are in fact quite unequal, and a single global price results in fairly extreme disparities in access [27].

If a seller is allowed to charge only a single price (and the costs of manufacturing, marketing and distributing products are zero, to simplify the illustration) a seller would calculate the price that maximizes revenue globally. The price that maximizes global revenues for the demand curve in Fig 5-1 is US$ 28 722. At this price, there would be access for 776.8 million persons – just 11.4% of the global population.

Among those 776.8 million persons, 92% live in high-income countries and 8% live in upper-middle-income countries. There would be no access in lower-middle- and low-income countries.

When the knowledge good is an important medicine or vaccine, the exclusion of more than 88% of the population is the most significant measure of the inefficiency of the outcome.

In terms of conventional economics measures, the deadweight loss associated with the single global price is equal to 38% of total willingness-to-pay, including 100% of the willingness-to-pay in lower-middle-income and low-income markets.

The persons included (and excluded), the distribution of benefits between consumers and producers, and the deadweight loss for the single global price scenario are presented in Table 5-1, using in this illustration the country GNI as a proxy for the ability/willingness-to-pay.

TABLE 5-1
Single global price

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Willingness-to-pay (as represented by GNI) (US$)	47 859 225 618 952	16 526 688 498 155	4 891 761 675 954	457 533 792 507
Population	1 217 905 568	2 363 438 430	2 487 412 206	755 481 932
Single price (US$)	28 722	28 722	28 722	28 722
Population with access	714 922 194	61 880 829	0	0
Population with access (%)	58.7%	2.6%	0.0%	0.0%
Maximum revenue (US$)	20 534 323 656 773	1 777 369 591 734	0	0
Consumer surplus (US$)	20 191 274 193 599	705 418 378 642	0	0
Deadweight loss (US$)	7 133 627 768 580	14 043 900 527 779	4 891 761 675 954	457 533 792 507
Producer surplus	42.9%	10.8%	0.0%	0.0%
Consumer surplus	42.2%	4.3%	0.0%	0.0%
Deadweight loss	14.9%	85.0%	100.0%	100.0%
% with access	11.4% (of the population of all countries combined)			

5.2.2 Single price for each of the four World Bank income groups

Despite limitations to the use of World Bank income groups in the context of price discrimination and market segmentation (Box 5-1), this way of segmenting the market is sometimes used in practice. Thus, in the next scenario, the supplier is setting a different price for each of the four World Bank income groups.

If a supplier is able to offer only a single price within each of the four World Bank income groups, the revenue-maximizing price for the high-income countries would remain at US$ 28 722. However, the supplier would further increase revenues by offering significantly lower prices for each of the other three income groups, thereby expanding access overall from 11.4% to 53.9% of the population, including 61% of the population of countries in the two lowest income groups. The average price would fall to US$ 7903, and the supplier's total revenue would increase from US$ 22.3 billion for the single global price scenario to US$ 29 billion for the four pricing tiers scenario. Consumers in each of the three lowest income groups would unambiguously be better off, as measured by average prices paid, persons with access, and consumer surplus (Table 5-2).

5.2.3 Country-by-country pricing

Given the advantages of moving from a single global market to a segmented market of four income groups, would it make sense to have even more market segmentation? What would be the effect if the supplier would charge a different price in each of the 150 countries?

For the supplier, this would result in a better outcome. Revenues for all four groups combined would amount to US$ 34 billion, a 17% increase over the scenario with a single price for each of the four World Bank income groups.

For consumers, the outcomes are mixed (Table 5-3). Overall, access would expand from 53.9% to 56.7%. The largest increase in access (6.6%) is in the high-income group. There is a small decrease in access in the upper-middle-income group, and a 3.5% increase in access for the two lowest groups. For some countries, prices fall, and for others, prices increase. However, on average, prices increase for each of the four income groups. For the upper-middle-income group, prices increase by 181% from US$ 2732 to US$ 7703.

In terms of the distribution of benefits, the producer revenue/surplus increases from 42% to 49% of the total willingness-to-pay. Consumer surplus decreases from 41% to 31%, and the deadweight loss increases from 18% to 20% of the total willingness-to-pay.

Overall, the greater freedom to engage in price discrimination (comparing the four income-based market groups to the 150 separate national markets) is better for suppliers than for consumers.

TABLE 5-2
Single price for each World Bank income group

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Willingness-to-pay (US$)	47 859 225 618 952	16 526 688 498 155	4 891 761 675 954	457 533 792 507
Population	1 217 905 568	2 363 438 430	2 487 412 206	755 481 932
Single price (US$)	28 722	2732	1238	411
Population with access	714 922 194	980 983 650	1 556 160 173	429 573 305
Population with access (%)	58.7%	41.5%	62.6%	56.9%
Maximum revenue (US$)	20 534 323 656 773	6 457 355 238 873	1 925 922 401 080	176 634 378 250
Consumer surplus (US$)	20 191 274 193 599	5 702 216 810 114	2 209 800 474 109	203 838 328 686
Deadweight loss (US$)	7 133 627 768 580	4 367 116 449 168	756 038 800 766	77 061 085 572
Producer surplus	42.9%	39.1%	39.4%	38.6%
Consumer surplus	42.2%	34.5%	45.2%	44.6%
Deadweight loss	14.9%	26.4%	15.5%	16.8%
% with access	53.9% (of the population of all countries combined)			

TABLE 5-3
Single price for each country

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Willingness-to-pay (US$)	47 859 225 618 952	16 526 688 498 155	4 891 761 675 954	457 533 792 507
Population	1 217 905 568	2 363 438 430	2 487 412 206	755 481 932
Single price (US$)	30 307	7703	1391	468
Population with access	794 718 057	978 178 566	1 644 544 044	454 497 203
Population with access (%)	65.3%	41.4%	66.1%	60.2%
Maximum revenue (US$)	24 085 175 427 521	7 534 743 244 875	2 287 864 781 952	212 726 363 581
Consumer surplus (US$)	16 263 558 622 520	3 881 655 310 707	1 626 331 700 808	144 646 512 286
Deadweight loss (US$)	7 510 491 568 911	5 110 289 942 573	977 565 193 194	100 160 916 640
Producer surplus	50.3%	45.6%	46.8%	46.5%
Consumer surplus	34.0%	23.5%	33.2%	31.6%
Deadweight loss	15.7%	30.9%	20.0%	21.9%
% with access	56.7% (of the population of all countries combined)			

5.2.4 Effect of delinkage

When implementing delinkage in a revenue-neutral manner for each of the three scenarios described in section 5.2: i) the producer surplus would remain the same (otherwise the implementation would not be revenue-neutral); ii) the deadweight loss would become zero; and iii) the consumer surplus would become equal to the sum of the (earlier) consumer surplus plus the (earlier) deadweight loss (e.g. in the case of the scenario with a single price for each country, as in Table 5-3, the consumer surplus for low-income countries under delinkage would be 31.6% + 21.9% = 53.5%).

5.3 Markets with national insurance

When a national market has a unitary system of insurance or other third-party reimbursement system, there is effectively no in-country market segmentation but only a single national market and a willingness-to-pay that is based on the average income.

5.3.1 Single global price, with insurance

If all countries would have national health insurance and there is a single global price, the overall level of access is roughly the same as in the example with in-country market segmentation (11.7% compared to 11.4%). However, several other outcomes are significantly different (Table 5-4).

Only in the 19 wealthiest countries in the high-income category would people have access. Additionally, with national health insurance in every country, the market clearing price is now US$ 38 495, an increase of 34% over the cases where there is in-country market segmentation (Table 5-4 compared to Table 5-1). The total revenue increases from US$ 22.3 billion for the case with in-country market segmentation to US$ 30.4 billion for the case with insurance, as persons with higher incomes subsidize purchases by those with lower incomes in those 19 countries.

Overall, the supplier revenue/surplus increases from 32% to 44% of the overall willingness-to-pay, while globally consumer surplus drops from 30% to 12%. The combined data for the 150 countries (all income groups taken together) are presented in Table 5-5.

TABLE 5-4
Single global price, national insurance

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Willingness-to-pay (US$)	47 780 323 956 110	16 510 613 390 691	4 878 273 355 049	459 056 833 346
Population	1 217 905 568	2 363 438 430	2 487 412 206	755 481 932
Price (US$)	38 495	38 495	38 495	38 495
Population included	788 970 875	2 170 308 565	2 178 908 246	659 830 352
Included %	64.8%	0%	0%	0%
Maximum revenue (US$)	30 371 443 425 153	0	0	0
Producer surplus (US$)	30 371 443 425 153	0	0	0
Consumer surplus (US$)	8 590 551 670 280	0	0	0
Deadweight loss (US$)	8 818 328 860 677	16 510 613 390 691	4 878 273 355 049	459 056 833 346
Producer surplus	63.6%	0%	0%	0%
Consumer surplus	18.0%	0%	0%	0%
Deadweight loss	18.5%	100%	100%	100%
% with access	11.7% (of the population of all countries combined)			

TABLE 5-5
Single global price, in-country market segmentation and national insurance compared

	In-country market segmentation (all four income groups)	National insurance (all four income groups)
Population	6 824 238 136	6 824 238 136
Population with access	776 803 023	788 970 875
Willingness-to-pay (US$)	69 735 209 585 568	69 628 267 535 196
Maximum revenue (US$)	22 311 693 248 506	30 371 443 425 153
Population with access (%)	11.4%	11.7%
Price (US$)	28 722	38 495
Producer surplus (US$)	22 311 693 248 506	30 371 443 425 153
Consumer surplus (US$)	20 896 692 572 241	8 590 551 670 280
Deadweight loss (US$)	26 526 823 764 821	30 666 272 439 763
Producer surplus	32.0%	43.6%
Consumer surplus	30.0%	12.3%
Deadweight loss	38.0%	44.0%

5.3.2 Single price for each of the four World Bank income groups, with insurance

If the supplier can charge four different prices – one for each of the four World Bank income groups (Table 5-6) – prices and access are unchanged for the high-income countries, but prices are lower and access is expanded considerably in all three of the lower-income groups (when compared to the single global price scenario). Overall, the producer surplus/revenue increases to US$ 46 billion, or 66.7% of global willingness-to-pay. Access expands to 85% of the population but the consumer surplus is only 18.7%.

TABLE 5-6
Single price for each of the four World Bank Income groups, national insurance

	High-income countries	Upper-middle-income countries	Lower-middle-income countries	Low-income countries
Willingness-to-pay (US$)	47 780 323 956 110	16 510 613 390 691	4 878 273 355 049	459 056 833 346
Population	1 217 905 568	2 363 438 430	2 487 412 206	755 481 932
Price (US$)	38 495	5724	1547	384
Population included	788 970 875	2 170 308 565	2 178 908 246	659 830 352
Included %	64.8%	91.8%	87.6%	87.3%
Maximum revenue (US$)	30 371 443 425 153	12 422 715 915 693	3 370 803 560 654	253 371 324 596
Producer surplus (US$)	30 371 443 425 153	12 422 715 915 693	3 370 803 560 654	253 371 324 596
Consumer surplus (US$)	8 590 551 670 280	3 116 599 853 563	1 111 451 391 687	181 286 561 606
Deadweight loss (US$)	8 818 328 860 677	971 297 621 435	396 018 402 708	24 398 947 144
Producer surplus	63.6%	75.2%	69.1%	55.2%
Consumer surplus	18.0%	18.9%	22.8%	39.5%
Deadweight loss	18.5%	5.9%	8.1%	5.3%
% with access	85% (of the population of all countries combined)			

5.3.3 Country-by-country pricing, with insurance

If the seller sets prices country by country and everyone has insurance, everyone receives access but at a very high price. In the stylized market described here, the entire income of each country would go to the seller.

Both deadweight loss and consumer surplus would vanish, and the seller would capture the entire global willingness-to-pay. This is a very good outcome for the seller, but it is not the best outcome for the buyers.

5.3.4 Effect of delinkage

When implementing delinkage in a revenue-neutral manner for each of the three scenarios described in section 5.3: i) the producer surplus would remain the same; ii) the deadweight loss would become zero; and iii) the consumer surplus would become equal to the sum of the (earlier) consumer surplus plus the (earlier) deadweight loss (e.g. in the case of the scenario with a single global price and national health insurance in all countries, as in Table 5-5, the consumer surplus under delinkage for all countries combined would be 12.3% + 44.0% = 56.3%).

6. Discussion

6.1 Traditional efforts to control prices

Individuals have limited, if any, power to influence prices. Governments, insurance companies, initiatives such as the Global Fund to Fight AIDS, Tuberculosis and Malaria or the U.S. President's Emergency Plan for AIDS Relief, and even large employers, have some actual and potential power to influence prices of medicines. This power can be exercised in a variety of ways, including, for instance, the ability of governments simply to dictate prices, or to revoke, regulate or otherwise overcome patent and test data monopolies, or to refuse to buy or reimburse products. In practice, these measures and others are used with varying degrees of effectiveness. Nevertheless, high prices of a number of new medicines strain budgets and reduce access. High prices exist even for several products for which government was the primary or leading source of R&D funding or for which outlays on R&D were demonstratively small.[11]

The failure to deal more effectively with excessive pricing of products can be attributed to several factors, including asymmetries of information regarding both the economic and the medical aspects of new products [28-31], the lobbying and political power exercised by large pharmaceutical companies [32-36], the weakness of buyers or reimbursement entities threatening to withhold access to a medically important medicine [37-39], and the impaired analysis and paralysis of action that often seems to accompany arguments that high medicine prices are necessary to stimulate innovation [40-42].

To the extent that countervailing power by buyers is used to control or moderate medicine prices, the outcomes described above can be improved from the point of view of the buyers.

On a global scale, if price regulations were effective, nuanced as to differential benefits from the same medicine for different patient groups and optimized to maximize social welfare, one could imagine in theory a Ramsey optimal outcome of distribution of the cost of R&D across a set of patented medicines. However, even in the best circumstances, price mark-ups on new medicines are an inferior outcome compared to reasonably well-designed delinkage approaches.

The reasons for the inferiority of the price regulation approach include the practical challenges and high costs of effectively regulating prices and preventing arbitrage in medicine pricing between and within countries, the inability to price knowledge goods at a marginal costs of production, the narrow base for collecting revenue, and the excessive reliance on rewards for successful end-products, when public and private investments in upstream research are also important.

6.2 Rent dissipation

The current system of financing the development of pharmaceuticals through high prices for medicines (based on patents or other intellectual property and regulatory-enforced monopolies) tends to overvalue products that match health outcomes of existing products, at the expense of products that improve health outcomes. This is an inherent feature; it cannot be repaired without delinking R&D rewards from product prices. To illustrate this point, one could consider two products – one a completely new therapy that dramatically improves health outcomes, and the second a "me-too" product that essentially replicates the outcomes of the first product or offers small improvements for some patients without technically infringing on the patent.

If the second product is actually better, even by a small amount, a reimbursement entity setting prices on the basis of outcomes would probably provide at least as high a price for the second product as for the first product, and physicians would likely recommend use of the second product.

If the second product improved outcomes by, for example, 2%, society would have gained an improvement in health outcomes of 2%. But the reward for the developer of the second product would be 100% -- 50 times the incremental improvement. The second product could also significantly reduce or wipe out the sales (and rewards) of the first product. This is problematic since society would pay too much for the follow-on innovation and would pay too little reward for the first breakthrough product. Not only is there an incentive to invest in products that offer few if any benefits over the first product, but often the competing products can be distinguished only by marketing efforts which can be costly and wasteful, and which ultimately reduce profits for all suppliers. This cycle of wasteful spending on the development and marketing of medically unimportant or less important products can be considered as "rent dissipation" – a term used by economists to describe activities designed to extract profits without making contributions to productivity.

6.3 Distributional Aspects

A significant component of the cost of new medicines, vaccines and diagnostic tests is the acquisition of knowledge and know-how. In principle, knowledge is non-rival in consumption and in some cases can be available at zero or near-zero marginal cost. This creates the technical feasibility of vastly expanding access to the knowledge good. In the examples provided above, if the knowledge good was available at a price of zero, access would be universal – the best outcome in terms of access.

The distributional aspects of delinkage would also depend on how the R&D is financed,[12] and how large the rewards to product developers would be. One possible approach would be to provide rewards equal to the amount of revenue the supplier would have obtained with the monopoly, as in a voluntary patent buy-out. This would be an expensive approach in some scenarios but would provide for the possibility of Pareto improvements (no party is worse off, and some parties are better off) over approaches involving negotiations over prices charged by the holder of a monopoly.

Sources of R&D funding

In any approach that includes a contribution or reward for R&D costs, a source of funding has to be identified, and each source presents its own challenges and distortions of economic activity. This applies to delinkage as well as to other approaches. In the context of delinkage, various funding sources have been proposed (see Box A-1 in Annex 1).

The patent system can be thought of as a privately imposed tax that is high on new products and zero on older ones. The percentage increase in prices (the tax) on new medicines can be very high, leading to economic distortions and a potentially significant deadweight loss.[13]

In the context of discussions about delinking funding for medical R&D from the price of medicines, there have been proposals to fund R&D from a share of the overall budget for medicines procurement, while buying all medicines – including new medicines – at generic prices. This can be considered as a quasi-delinkage approach, because the products do have a premium on the price that is used to fund R&D.

Using a share of national outlays on health insurance or, more generally, of the health budget would have certain advantages over targeting only the budget for medicines procurement. The base for revenue collection would be broader and, by incorporating the cost of innovation into the general health-care budget, the allocation of resources between medicines, and between medicines and other treatment outlays, would result in fewer distortions in matching the marginal benefits to the marginal costs of health inputs. As the method of collecting revenue would be shifted to a broader set of outlays, the economic distortions are also likely to be smaller.

In the case of HIV, hepatitis C or cancer, where prices of new medicines that are under patent can be very high, the availability of these medicines at competitive generic prices would increase the benefits of investment in treatment and could expand political support for more robust treatment budgets. To the extent that the R&D outlays are targeted more efficiently to address actual health needs, funding innovation could also be a potential cost-saving measure in some areas.

The delinkage scenarios appear strongest when one considers more explicitly the costs of managing a system of price discrimination and the inefficiency of the product price mechanism when the benefits of a particular product differ for different patients, as was illustrated in the hepatitis C and HIV examples above, or when there are budget constraints.

Ultimately, the challenge for delinkage approaches lies not so much in ensuring access, which – due to the fact that delinkage enables supply of medicines at cost price – is optimal. Rather, the challenge lies in demonstrating the feasibility of actually funding R&D (in the absence of a monopoly).

Chapter notes:

[11] Gleevec, Fabrazyme and Xtandi are examples of high priced drugs for which the United States' NIH funded early research and which were approved based upon relatively small clinical trials.

[12] The term delinkage, in the current policy debate, does not prescribe how to finance R&D; rather, it establishes how not to finance R&D.

[13] In public finance theory, it is generally recognized that a modest tax on a broad base of economic activity creates fewer economic distortions than a higher tax rate on a narrower base. An important finding in economics is that the deadweight loss from taxation increases in proportion to the square of the tax rate.

7. Outcomes

The summary in Table 7-1 compares the distribution of benefits between producers and consumers, and reports deadweight loss and the outcomes regarding the percentage of persons with access for each of the four income groups. The delinkage comparisons are for revenue-neutral cases for various pricing options, including a single price for each of the four income groups, a single price for each country, or a single price for the whole world.

The most important and compelling outcome of delinkage approaches is the vast expansion of access as the cost of the knowledge component of the product falls to zero. Deadweight loss for a pure knowledge good falls to zero in these calculations, and access is universal.

As shown in Table 7.2, a world with a single payer insurance system in every country, and seller price discrimination by income group or by country, results in high access, including universal access for the country-by-country price discrimination case, but at a high cost and loss of consumer surplus -- the seller gets all of everyone's money.

It bears mentioning that the assumptions for universal access through a unitary national insurance system are extreme; they are not feasible in the foreseeable future, and indeed, unrealistic where insurance is currently available. Note, for example, the limited access to expensive medicines for cancer such as D-DM1 or enzalutamide, where bargaining over prices of the medicines has led to withholding reimbursement even in high income countries. Even when reimbursements are available, the coverage can be limited, or subject to restrictions that are designed to limit access and control costs [43,44].

The delinkage alternative always provides for universal access in our simulations, it can do so more reliably, and without breaking the bank, which makes it a more robust and reliable mechanism to expand access.

TABLE 7-1

Overview: delinkage compared to rewards linked to prices (without unitary national insurance)

Income group	Percentage with access	Deadweight loss	Consumer surplus	Producer surplus
1.a Single price for world				
High-income	58.7%	14.9%	42.2%	42.9%
Upper-middle-income	2.6%	85%	4.3%	10.8%
Lower-middle-income	0%	100%	0%	0%
Low-income	0%	100%	0%	0%
1.b Delinkage: comparison is revenue neutral for a single price for world (see section 1.a above)				
High-income	100% (▲ 41.3%)	0%	57.1% (▲ 14.9%)	42.9%
Upper-middle-income	100% (▲ 97.4%)	0%	89.3% (▲ 85%)	10.8%
Lower-middle-income	100% (▲ 100%)	0%	100% (▲ 100%)	0%
Low-income	100% (▲ 100%)	0%	100% (▲ 100%)	0%
2.a Single price for each of four income groups				
High-income	58.7%	14.9%	42.2%	42.9%
Upper-middle-income	41.5%	26.4%	34.5%	39.1%
Lower-middle-income	62.6%	15.5%	45.2%	39.4%
Low-income	56.9%	16.8%	44.6%	38.6%
2.b Delinkage: comparison is revenue-neutral for a single price within the four income groups (see section 2.a above)				
High-income	100% (▲ 41.3%)	0%	57.1% (▲ 14.9%)	42.9%
Upper-middle-income	100% (▲ 58.5%)	0%	60.9% (▲ 26.4%)	39.1%
Lower-middle-income	100% (▲ 37.4%)	0%	60.7% (▲ 15.5%)	39.4%
Low-income	100% (▲ 43.1%)	0%	61.4% (▲ 16.8%)	38.6%
3.a Single price for each country				
High-income	65.3%	15.7%	34.0%	50.3%
Upper-middle-income	41.4%	30.9%	23.5%	45.6%
Lower-middle-income	66.1%	20.0%	33.2%	46.8%
Low-income	60.2%	21.9%	31.6%	46.5%
3.b Delinkage: comparison is revenue-neutral for a single price for each country (see section 3.a above)				
High-income	100% (▲ 34.7%)	0%	49.7% (▲ 15.7%)	50.3%
Upper-middle-income	100% (▲ 58.6%)	0%	54.4% (▲ 30.9%)	45.6%
Lower-middle-income	100% (▲33.9%)	0%	53.2% (▲ 20.0%)	46.8%
Low-income	100% (▲ 39.8%)	0%	53.5% (▲ 21.9%)	46.5%

TABLE 7-2

Overview: delinkage compared to rewards linked to prices (with unitary national insurance)

Income group	Percentage with access	Deadweight loss	Consumer surplus	Producer surplus
1.Single price for world, with unitary national insurance				
High-income	64.8%	18.5%	18.0%	63.6%
Upper-middle-income	0%	100%	0%	0%
Lower-middle-income	0%	100%	0%	0%
Low-income	0%	100%	0%	0%
2. Single price for each four income groups, with unitary national insurance				
High-income	64.8%	18.5%	18.0%	63.6%
Upper-middle-income	91.8%	5.9%	18.9%	75.2%
Lower-middle-income	87.6%	8.1%	22.8%	69.1%
Low-income	87.3%	5.3%	39.5%	55.2%
3. Single price for each country, with unitary national insurance				
High-income	100%	0%	0%	100%
Upper-middle-income	100%	0%	0%	100%
Lower-middle-income	100%	0%	0%	100%
Low-income	100%	0%	0%	100%
4. Delinkage[a]				
High-income	100%	0%	49.7 - 57.1%[a]	42.9 – 50.3%[a]
Upper-middle-income	100%	0%	54.4 – 89.3%[a]	10.8 – 45.6%[a]
Lower-middle-income	100%	0%	53.2 - 100%[a]	0 – 46.8%[a]
Low-income	100%	0%	53.5 - 100%[a]	0 – 46.5%[a]

[a] Revenue neutral compared to the scenarios without unitary national insurance (see Table 7.1).

Delinkage approaches are expected to significantly change the distribution of benefits between suppliers and consumers – to the benefit of consumers. At present, following product development, the seller has enormous power in negotiations because of the legal ability to withhold access to an important medicine, and this power can lead to aggressive pricing for the products even when development costs are believed to be quite modest. For a number of important medicines – such as sofosbuvir, trastuzumab and imatinib – the risk-adjusted development costs for the first registration of the lead indication are believed to have been recovered in a relatively short time.[14]

Under a delinkage approach, governments can better:

- optimize the allocation of R&D funding between direct funding of research and providing incentives for successful development,
- fund/reward upstream R&D, target R&D outlays on innovations that improve rather than match outcomes, and
- eliminate the waste of resources associated with marketing of patented medicines.

With delinkage, governments can also choose the level of funding for innovation without delaying or reducing access to newer products. There are concerns that this freedom could reduce overall levels of funding for innovation, but there is also counter-evidence, such as the considerable national expenditures on health-care research and the political support for tough global norms for patents and other intellectual property, which in the case of medicines and vaccines are justified only as instruments to promote innovation. Delinkage is an innovation for the innovation system – a way to fund innovation without restricting access to the resulting innovative products.

Chapter notes:

[14] Sofosbuvir generated more than US$ 5 billion in the two first full quarters of sales. The registration was based on relatively brief trials involving roughly 2500 patients. Trastuzumab generated more than US$ 0.5 billion per month in sales for Roche in 2014, and was approved for sale on the basis of trials involving 1206 patients – just 23% of the average number of patients in the widely quoted DiMasi study of drug development costs. Imatinib generated more than US$ 390 million per month for Novartis in 2013. The 2001 approval for imatinib was the fastest FDA approval of a cancer drug. Novartis is estimated to have spent less than US$ 25 million for the three phase III trials used to support the approval, and a combination of non-profit organizations and the NIH paid for an estimated 90% of preclinical research.

8. Outstanding questions

While the modelling undertaken for this paper indicates that delinking funding for medical R&D from the price of the final product has the potential to improve outcomes significantly, notably with regard to access, many questions remain. These include, but are not limited to, the following:

1. What are the scenarios for implementation of delinkage in markets for HIV/AIDS medicines? For example, could donors, private-sector insurers and governments who pay for HIV medicines create innovation prize funds that are sufficiently large to induce the development of new HIV/AIDS medicines?

2. What would be the possible incentives for middle-income countries to contribute to innovation-inducement prize funds? For example, could licensed territories for generic medicines be related to the participation by a government in funding the innovation-inducement prize?

3. How much prize money would be needed to induce expanded licensing, and how would the costs compare to the benefits in terms of access to generic medicines?

4. How could delinkage be implemented in the context of open source diagnostic technologies? Would it make sense to begin with narrowly defined innovation objectives, or to create funds that reward innovations in diagnostics for a wider set of objectives?

5. What would be the alternative financing models for innovation prizes for medicines, vaccines or diagnostics? Would the financing models be different for medicines than for vaccines or for diagnostics?

6. Would there be a role for the open source dividend with or without

end-product prizes?

7. Should prize funds have centralized or decentralized management and governance?

8. What licensing terms should be tied to innovation-inducement prizes?

9. What are the trade-related issues for delinkage models? Are the benefits local or global? Would innovation-inducement prizes be considered an R&D subsidy under trade rules? Would they contravene the "national treatment" principle?

ANNEX 1

OPTIONS FOR IMPLEMENTING INNOVATION INDUCEMENT PRIZES

Delinkage can be implemented in a variety of ways, including through direct grants and research contracts, research subsidies or incentives. Important tools for reforming the current monopoly incentive are innovation inducement prizes, which can be thought of as the substitution of money for monopolies, as the reward for successful performance.

Innovation-inducement prizes can be designed in different ways. Among the more important design options are prizes relating to end-products, prizes for achieving interim results (including but not limited to so-called "milestone" prizes), and open-source dividend prizes.

End-product prizes can have difficult-to-meet requirements such as a highly accurate and low-cost diagnostic test or a vaccine with a very high degree of efficacy, or they can have lower minimum requirements, including prize fund systems that share prize fund rewards between competitors, based upon relative performance toward a competitive criteria.

An important innovation for the end-product prize design for drug development was first proposed in the context of a series of bills in the USA sponsored by Senator Bernie Sanders. In the Sanders prize fund approach, designed in 2003–2004, any medicine qualifying for Food and Drug Administration (FDA) marketing approval would qualify to participate in the annual distribution of innovation prizes from a prize fund for a period of 10 years. The amount of money given to a particular drug developer would be based on the health benefits of the product when benchmarked against the benefits of existing treatments, in a competition that would pit each developer against the others as suppliers of health benefits.

Developers that supply more benefits would receive a greater share of money from the prize fund, although the legislative proposal allowed for flexibility to consider a variety of factors. These include, for instance, the public interest in the development of treatments for rare or neglected diseases. A drug developer also could be rewarded for finding new uses for older medicines, or reducing the adverse and harmful effects of medicines.

Open-source dividend prizes were proposed in 2007 in connection with an MSF proposal for a prize for new diagnostic devices for tuberculosis. Because access to knowledge is important for innovation in diagnostics and since end-product prizes and other pull incentives may encourage secrecy and restrict access to research data, the open-source dividend prize was designed to create a countervailing incentive to share upstream research. In various proposals, the dividend would be a share of 3–10% of the end-product prize (or revenue, if implemented without end-product prizes). To qualify for a share of the end-product prize, researchers would have to share openly, on a nondiscriminatory and royalty-free basis, knowledge, data, materials and technologies relevant to the development of the new products.

Interim research prizes are the third major category: Interim prizes can be implemented in a variety of ways. Notable examples would be the prize for identifying a biomarker for amyotrophic lateral sclerosis (ALS) disease, or the European Commission's 2-million euro prize for the "best" technologies for making vaccines heat-stable for use in resource-poor settings. Interim prizes can be designed as large or small rewards, and with almost any licensing terms, including, if desired, requirements that the innovations be available to third-parties.

BOX A-1

Examples of innovation-inducement prize proposals

There has been a proliferation of proposals for innovation-inducement prizes. In the area of medicines, vaccines and diagnostic devices, several such proposals were made in the context of the negotiations of the 2008–2009 WHO Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) and, more recently, in the context of the call for demonstration projects by the WHO Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG). This includes proposals by Bangladesh, Barbados, Bolivia and Suriname that addressed both medicine development and diagnostics. Other examples are proposals from MSF, the Drugs for Neglected Diseases Initiative (DNDi), Knowledge Ecology International (KEI), Incentives for Global Health, Bioventures for Global Health, the government of Colombia and Senator Sanders of the USA.

These proposals vary with regard to their objectives and the proposed source of funding. For instance, in Sanders' proposals for medical innovation prize funds, the entities currently providing reimbursements for medicines would be the source of funds; the amount would be in proportion to the number of patients they insure. The funding level would be fixed at a proportion of gross domestic product. In the proposals by Bangladesh, Barbados, Bolivia and Suriname for cancer or HIV innovation prize funds, the source of funding would be a percentage either of overall medicine purchases or of the overall treatment budget (which would be a broader base). The KEI proposal on funding R&D for new antibiotics includes an excise tax on antibiotic sales (proposed earlier by the Infectious Diseases Society of America and others). The antibiotics excise tax proposal is in part based on the notion that some level of taxation on consumption is appropriate as a Pigouvian tax on a use that can contribute to the negative externality of antibiotic resistance. The excise tax proposal is also a means of broadening the existing base for mark-up over costs, which is currently focused only on new patented medicines.

ANNEX 2

THIS ANNEX BRIEFLY REVIEWS TWO "SPECIAL CASES" OF DELINKAGE.

A. Financing patent buy-outs, where benefits occur over time

One interesting delinkage approach involves buy-outs of medicine patents. The advantage of a patent buy-out is that the product would be available at marginal cost, and would be available to patients who have different incomes and differential health benefits from the treatment. The challenge is to finance a patent buy-out in a situation where the benefits of the treatment take place over time. Hepatitis C treatments are a case in point. For some patients, a treatment will meet an immediate treatment need but for others a treatment today will have a possible positive impact after several years or even several decades.

Regardless of how the price of the buy-out is determined, and regardless of whether the buy-out is voluntary or not, someone will be faced with the task of finding the money today to pay for health benefits that impact on future budgets.

For society, it may make sense to treat today in order to avoid costs later. However, private insurance companies or employers will not want to pay now if they think the patient will be someone else's reimbursement problem later. In theory, governments could take the longer view but, in practice, today's leaders may not want to raise taxes or cut expenditures on other programmes just to lower future costs.

Where the cost of the patent buy-out is significant, it may be possible to devise a long-term financing scheme for the buy-out, in the way that governments consider selling bonds to pay for investments in transportation infrastructure, sewers, dams or the building of new schools.

The structure of the buy-out scheme can also be sophisticated enough to accommodate issues such as the risks that products may be withdrawn from the market, or that future medicines may be better than existing medicines. The patent buy-out could be a fixed amount of money or an amount based on a fraction of health budgets, funded over time and allocated to products over time on the basis of relative benefits in treatment -- allowing even for continued innovation in the treatment class.

For a product with significant possibilities for cross-border diversion, it may be useful to consider patent buy-outs in the context of plurilateral actions by governments. It has been suggested that a World Trade Organization agreement on the supply of public goods may be useful in creating more confidence that multi-year patent buy-out costs will be fairly and reliably shared by participating governments. [15]

B. Diagnostics

Diagnostics are another interesting area for innovation and the implementation of delinkage. For many diseases, the costs of diagnosis are high because of patent monopolies and the opportunities that patents create to charge high prices. For drug manufacturers and health authorities, inexpensive diagnostics are quite important since they drive demand for products and allow more targeted and effective interventions as well as earlier treatment.

For society to have the benefits of better diagnostics, there have to be incentives to invest in R&D to develop products that are cheap and easy to use. The incentive from a patent monopoly is the ability to charge high prices, but this is the opposite of what is needed. Innovation-inducement prizes, implemented in a variety of ways, can provide strong financial incentives to develop inexpensive diagnostic technologies.

The challenge for implementing innovation-inducement prizes is to create a sustainable system of finance. If pharmaceutical manufacturers use traditional approaches of price discrimination, it may be useful to consider taxing medicine sales in order to pay for innovation prizes to improve diagnostics. The incidence of the tax would largely be on the patent-holders but they would also often benefit from the better diagnostics, particularly when the diagnostics are necessary for identifying persons who would benefit from the medicine – such as genotyping for hepatitis C virus or identifying HER2+ breast cancer.

If the medicines market would operate with R&D costs delinked from medicine prices, other financing options for diagnostic innovation prizes would potentially be more appropriate. For example, reimbursement authorities as a group would benefit from improvements in diagnostics, particularly if the new technologies were open source and cheap. Creating a budget item for innovation prizes for open source diagnostics would make most sense if there is widespread participation in the financing.

Annex notes:

[15] See: http://keionline.org/wtoandpublicgoods, accessed 16 January 2015.

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