

Incentivising research and development for the diseases of poverty



IPN WORKING PAPERS ON INTELLECTUAL PROPERTY, INNOVATION AND HEALTH

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International Policy Network
Third Floor, Bedford Chambers
The Piazza
London WC2E 8HA UK
t: +4420 7836 0750
f: +4420 7836 0756
e: info@policynetwork.net
w: www.policynetwork.net

Designed and typeset in Latin 725 by MacGuru Ltd
info@macguru.org.uk
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IPN aims to empower individuals and promote respect for people and property in order to eliminate poverty, improve human health and protect the environment. IPN promotes public awareness of the importance of this vision for all people.

IPN seeks to achieve its vision by promoting the role of market institutions in certain key international policy debates: sustainable development, health, and globalisation and trade. IPN works with academics, think tanks, journalists and policymakers on every continent.

Written by:

Julian Morris

Executive Director, International Policy Network

Philip Stevens

Director of Health Projects, International Policy Network

Alec van Gelder

Research Fellow, International Policy Network

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Introduction

Every year, millions of people die from diseases that could have been cured through the use of inexpensive existing treatments. Clearly, in terms of priorities improving access to these treatments must rank higher than the development of new drugs for those diseases. For what is the point of developing a new medicine if it will not reach those for whom it is intended?

However, this paper is not primarily about improving access to existing medicines. Rather, it addresses the related issue of the lack of commercial incentives to invest in the development of new drugs for many of the diseases endemic to poor countries, such as tuberculosis and malaria – the ‘diseases of poverty’. The question is what can be done, in the absence of a substantial market for such drugs, to incentivise research and development (R&D) into new cures?

In spite of the current poor distribution of existing drugs in many poor countries, which must be a top priority in fighting the diseases of poverty, this is not a merely prosaic question. The fact is that many of the existing drugs are beginning to lose their potency because of resistance. Meanwhile, some existing treatments are highly toxic, even frequently deadly. So it is clear that millions of people stand to benefit from the development of new and improved medicines for the diseases of poverty.

Nevertheless, any new medicines that are developed will face the same distribution hurdles as existing medicines, which will limit their effectiveness. Thus, the development of new medicines for the diseases of poverty must be as cost-effective as possible, so as not to divert funds away from enhancing crucial health infrastructure.

This paper provides an overview of proposals intended to improve the prospects of developing new drugs for the diseases of poverty. Part 1 considers the need for new medicines in the wider context of addressing the diseases of poverty. Part 2 examines barriers to innovation. Part 3 considers various mechanisms for funding R&D into new drugs. Finally, the various proposals are considered in perspective and conclusions drawn.

1

Assessing the need for new medicines

A large proportion of illness in low-income countries is entirely avoidable or treatable with existing medicines or interventions. Most of the disease burden in low-income countries finds its roots in the consequences of poverty, such as poor nutrition, indoor air pollution, and lack of access to clean water, proper sanitation and health education. The WHO estimates that diseases associated with poverty account for 45 per cent of the disease burden in the poorest countries.¹ However, a closer examination reveals that nearly all of these deaths are either treatable with existing medicines or preventable in the first place.

Tuberculosis, malaria and HIV

Tuberculosis, malaria and HIV/AIDS together account for nearly 18 per cent of the disease burden in the poorest countries,² but there are a range of preventative measures available.

Malaria can be prevented through a combination of removing insect breeding sites (such as stagnant pools of water), spraying dwellings with DDT and other long-lasting insecticides, using insecticide treated mosquito nets³ and taking prophylactic medicines, such as mefloquine, doxycycline and malorone. Malaria can also be treated, most effectively with artemisinin combination therapy.⁴

Tuberculosis can be prevented by improving nutrition, and can be treated with DOTS therapy, which is estimated to cure disease in up to 95 per cent of infectious patients, even in the poorest countries.⁵

Education is vital for the prevention of HIV/AIDS. Meanwhile, a combination of anti-retrovirals (ARVs) and good nutrition can help to control the viral load

(reducing subsequent transmission rates) and suppress the symptoms of HIV/AIDS.

Childhood diseases

Treatable childhood diseases such as polio, measles and pertussis, account for only 0.2 per cent of Disability Adjusted Life Years (DALYs) in high-income countries, while they account for 5.2 per cent of DALYs in high mortality low-income countries.⁶ Vaccines for these diseases have existed for at least 50 years, yet only 53 per cent of children in sub-Saharan Africa were immunised with the diphtheria-tetanus-pertussis (DTP) vaccine in 2000.⁷

Diarrhoeal diseases

Diarrhoeal diseases are caused by the poor sanitation inherent to the condition of poverty, yet are easily and cheaply treatable through oral rehydration therapy. However, diarrhoeal diseases still claim approximately 1.8 million lives each year.⁸

Respiratory infections

Acute lower respiratory infections (ALRI), such as pneumonia, represent the single most important cause of death in children under 5 years and account for at least two million deaths annually in this age group.⁹ Yet, many of these deaths could be prevented by reducing exposure to household smoke, which significantly increases the risk of ALRI.

Malnutrition

Malnutrition particularly affects people in poor countries. For example, vitamin A deficiency results in 500,000 children going blind each year,¹⁰ despite the fact that such outcomes can be avoided by cheap, easy-to-administer food supplements.¹¹ Vitamin deficiency also weakens the human body's defences and leads to hundreds of thousands of deaths every year from a variety of preventable diseases.

Lives needlessly lost

Poverty-related diseases cause far higher levels of mortality in low-income than in high-income countries (Table 1). Most of these diseases and deaths can be prevented with existing treatments and prevention programmes. Diseases for which there is no treatment currently available, such as dengue fever, contribute a far smaller proportion of low-income country mortality than diseases which are easily preventable or treatable. It is estimated that over 80 per cent of child diarrhoeas, child malaria and other childhood illness, such as measles and tetanus, could be prevented using existing treatments.¹² In other words, three million child lives could be saved each year if these existing medicines could be distributed effectively to all those who would benefit from them.

Access to the essential medicines that could alleviate the suffering and death caused by curable diseases remains patchy, with an estimated 30 per cent of the world population lacking regular access to existing drugs.¹⁴ The WHO further estimates that this figure rises to over

50 per cent in the poorest parts of Africa and Asia¹⁵ (Figure 1.1).

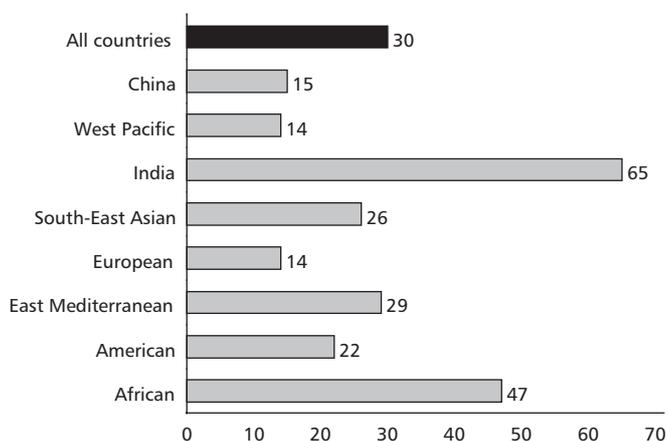
Many factors conspire to bring about this dismal state of affairs. At the most basic level, the majority of low-income countries lack the basic infrastructure required to successfully distribute medicine. Road networks are often unreliable or non-existent, making it difficult to ensure a constant supply of medicines to remote areas. Electricity is often unavailable and where it is available, power cuts are frequent, making it impossible to run efficient refrigeration in clinics and hospitals. As a result, vaccines are often not maintained at sufficiently low temperatures to ensure product stability. Protease inhibitors (used in second-line ARV treatments) are one example of a drug that needs to be refrigerated,¹⁶ yet it is impossible to ensure this in the world's poorest countries.

Because most low income countries also have incomplete and fragmented public health systems, the distribution of effective health education and treatment is nearly impossible. In this situation, it is also extremely difficult to ensure the distribution of the safe and effective medicines that have already been developed to tackle the diseases of poverty. For example, the administration of DOTS to tuberculosis patients requires a treatment course of between 6 to 8 months with close patient monitoring to ensure compliance.¹⁷ ARV treatment for AIDS sufferers also requires close supervision. Even in the relatively efficient health care systems of high-income countries, maintaining adherence to HAART (Highly Active Anti-Retroviral Therapy) treatment during clinical trials is fraught with

Table 1 **Deaths caused by poverty-related diseases**¹³

<i>% of deaths caused by/in</i>	<i>High mortality low-income countries</i>	<i>Low mortality low-income countries</i>	<i>High-income countries</i>
Infectious and parasitic diseases	34.1	24.8	2.1
Respiratory infections	9.9	8.0	3.7
Perinatal and maternal conditions	8.4	6.8	0.4
Nutritional deficiencies	1.3	1.1	0.0
Tropical diseases	0.5	0.3	0.0
Total 'poverty-related' diseases	54.1	40.7	6.2

Figure 1.1 **Percentage of WHO regions lacking access to essential medicines**²⁹



Source: WHO, *State of the world's vaccines and immunisation, 2002*

complexity.¹⁸ Achieving such adherence in poor countries with weak health care systems is practically impossible.

Intervention by global public health authorities and the provision of public funds is not a guarantee that existing medicines will be effectively distributed. A recent example is malaria, where despite the establishment of the Roll Back Malaria initiative and the injection of specific funds, the most modern and potent anti-malarial drugs were still not being properly used six years after the initiative began.¹⁹ The failure to distribute simple childhood disease vaccines and medicines results in the unnecessary deaths of three million children each year.²⁰

The issue of access also has ramifications for the development of new drugs: if cheap, off-patent medicines are not currently reaching those people who need them, what chance do new medicines have? So it is clear that the development of new medicines should be a lower priority than facilitating access to existing medicines.

Keeping the pipeline full

Nevertheless, there remains a need for new, innovative treatments. Bacterial and viral resistance to existing medicines is a major problem in treatments for diseases such as malaria and tuberculosis.²¹ Constant efforts must be made to ensure the development of new treatments for these diseases. In addition, specific subpopulations such as pregnant women and children are most at risk from diseases such as malaria, and require medicines with specific formulations.²² Furthermore, some diseases lack any effective and safe treatments; in particular this applies to African Trypanosomiasis, leishmaniasis, Chagas disease and Dengue fever.²³

Incentivising R&D for dysfunctional markets

The lack of effective distribution of existing medicines in many poor countries, combined with the low purchasing power of potential consumers, means that the market for new medicines for the diseases of poverty is currently weak. If the problems of distribution were overcome, the size of the market would increase, even if purchasing power remained low. In principle this should stimulate innovation, as companies seek to fulfil unmet wants.

However, the small size of the market is not the only barrier to the creation of new treatments for the diseases of poverty. Governments in poor countries exacerbate the weaknesses of the existing market through a host of short-sighted public policies. These include, but are not limited to, the imposition of taxes and price controls on essential medicines, weak intellectual property laws and generally poor law enforcement. These are discussed at greater length in the next section.

Win-win solutions

The question is how to create incentives for the development of new drugs to treat and prevent the diseases of poverty in a way that does not divert scarce resources from distribution. This paper assumes that it would be possible to save many more lives if scarce public resources were utilised to improve healthcare

delivery systems in lower-income countries, rather than if those same resources were utilised to develop new drugs. However, there is certainly a need for new treatments and drugs that address diseases and challenges which are unique to these countries.

In order to square this circle, we need to create win-win solutions that will incentivise the development of new medicines, while at the same time not drawing limited funds away from the distribution of medicines and other healthcare priorities.

Barriers to innovation

Most new medicines – including over 90 per cent of those presently on the WHO's list of 'Essential Medicines' – were developed by the private sector.²⁴ So it is important to understand what motivates the private sector to develop a new drug, and how this is affected by various political and economic factors.

In many respects, the market for medicines looks much the same as that for any other good or service. Producers respond to the perceived demands of consumers, whether those consumers are individuals, health agencies, insurance companies or governments.

One problem with the market for medicines in poor countries is that most people are unable to pay high prices. This limits the potential to profit from developing a new medicine. But the weak buying power of consumers in lower-income countries is only one of a raft of factors that constrain the market for drugs for the diseases of poverty. As this section hopes to demonstrate, poor public policy often does more to stymie both the demand for and supply of new drugs than the lack of wealthy consumers. (The following arguments are elaborated more fully in our companion paper, *'Barriers to Access and Innovation'*, available for download at www.policynetwork.net.)

Demand-side barriers

Taxes and tariffs

Many governments of lower-income countries distort the market for medicines by imposing a range of taxes on medicines, including port charges, central, regional and local taxation, as well as import tariffs. Taken together, these add significantly to the retail price of a drug, with negative consequences for the amount of drugs sold and on access to medicines, especially for the poorest.

According to a survey undertaken by the European Commission in 2003, the global average of these combined taxes was 18 per cent of the total price, with Malaysia having the lowest rate at 0.01 per cent and India the highest at 55 per cent.²⁵

By driving up the cost of medicines, these taxes and tariffs price the poorest people out of the market for life-saving treatments and add significant burdens to the budgets of cash-strapped public health systems. In this way, taxes on medicines reduce demand, and therefore act as a disincentive to would-be suppliers of the market.

Inadequate health insurance

If a population is adequately covered by health insurance, the demand for medicines remains steady and predictable, because fewer people will have to make a choice between paying out of pocket for treatment and other paying for other goods and services. Several studies have shown the link (in the United States) between higher medicine use among poor and vulnerable populations, and the availability of health insurance.²⁶

However, most low-income countries have poorly functioning health insurance schemes, with total coverage (public and private) standing at a mere 10.3 per cent in sub-Saharan Africa and 27.3 per cent in Asia (excluding China and India).²⁷ The majority of people in these regions therefore pay for treatment out of their own pockets, which means the demand for medicines will remain low.

Many governments of low income countries have failed to foster the kind of environment in which health insurance systems can thrive. Chief amongst these

failings must rank the frequent absence of the rule of law, which makes the enforcement of legal agreements and contracts difficult. Governments also erect bureaucratic obstacles to entrepreneurship, meaning that many people are forced into the informal sector for employment. It is extremely difficult to foster functional insurance systems if the majority of the population has no formal status in the economy.

The combination of taxes and other government barriers, including restrictions on the provision of insurance, act as a disincentive to pharmaceutical innovation because they constrain demand for medicines. If these demand side barriers were lifted, the market for medicines would expand, incentivising would-be drug developers to manufacturer products specifically designed for poor countries.

Supply-side barriers

The absence of a functioning market economy in low-income countries not only keeps people poor and undermines demand for medicines and other goods; it also directly affects the supply of medicines. Because markets work effectively only in the context of certain institutions, including property rights, contracts and effective legal systems, companies are discouraged from supplying medicines when the rule of law is absent. Slow, expensive court systems make it difficult to enforce contracts, which then discourages potential suppliers from entering into supply contracts. Many of the world's poorest countries suffer from these institutional weaknesses.

These general institutional failures undermine incentives to develop new medicines, especially for the diseases of poverty. In addition, there are several specific institutional failures in many poor countries that discourage the development of new medicines.

Weak intellectual property legislation

When it comes to incentivising the development of new medicines for the diseases of poverty, protection of intellectual property can play a crucially important role. The high cost of developing a new pharmaceutical product (estimated at upwards of \$800 million in the

US²⁸), combined with the relatively low cost of copying the pharmaceutical (typically a few million dollars), means that developers must be assured that they 'own' the product before they will commit substantial sums to innovation. Robust intellectual property legislation provides that guarantee, and is one way of encouraging developers to enter a market. Furthermore, stronger intellectual property protection in poor countries may stimulate innovation by multinationals to serve local needs (e.g. developing drugs to combat tropical diseases).²⁹ By contrast, countries that continue to have weak intellectual property regimes actually reduce the incentives for companies to engage in research and development.³⁰

Pre-market regulations

The large and rising number of regulations with which companies are required to comply before they can launch a pharmaceutical product onto the market also drives up the costs of supply. It is estimated that some \$300–450 million of the \$800 million it takes to develop a drug is spent on the clinical development required by regulatory agencies.³¹ There is therefore a risk that manufacturers will concentrate their resources on developing 'blockbuster' drugs that will provide a return on that significant investment. Thus, the increasing cost of R&D could discourage investment not only in drugs for less common conditions in the wealthier world (such as psychiatric disorders), but also for more common diseases in lower-income countries. Regulatory authorities, therefore, must examine their own requirements to determine if they can reduce the costs of drug development by streamlining regulatory approvals.

Price controls, price differentiation and compulsory licenses

Market segmentation and price differentiation are methods used by companies to ensure that the widest variety of consumers can afford to buy their products.

Unfortunately, governments often restrict the ability of companies to implement differential pricing strategies. For example, governments frequently impose price controls, capping the price of drugs and forbidding any

other retail price – so the price ceiling becomes a price floor.³² Not only does this restrict the ability of companies to sell their products to certain groups of consumers, it also eliminates the possibility for the firm to implement any price differentiation strategy. As a result, fewer drugs are supplied, at a price higher than would be paid by the poorest consumer. The firm's profits are lower, and the incentive to invest in new products for development in these markets is suppressed.

Compulsory licenses – or the threat of issuing a compulsory license – can have a similar effect to price controls. In the interest of improving public health, compulsory licenses can be a way for extremely poor countries to procure inexpensive medicines, when all attempts to secure such products voluntarily have been exhausted. In practise, however, middle-income countries that enjoy relatively high standards of living (such as Brazil) have used the threat of compulsory licensing as a negotiating tool to secure cheaper prices.³³ This can be a politically popular move in the short-term but in the medium- and long-term it undermines the ability of innovator companies to sell at different prices in different markets. It also strains existing pricing strategies, under which medicines are offered at the lowest prices to patients in extremely poor countries, and acts as a further disincentive for firms to develop new and improved medicines for the diseases of poverty.³⁴

Mechanisms for funding R&D

In the short term, it is unlikely that policymakers in low income countries will improve the institutional environment sufficiently to rectify the glaring gaps in both the demand for and supply of new medicines to treat the diseases of poverty. In the absence of a properly functioning market, other ways the development of new medicines must be found.

Any mechanism to encourage the development of new medicines for the diseases of poverty must – to a greater or lesser degree – overcome the various regulatory and cost barriers previously discussed, as well as ensuring that a useful product will eventually be produced.

Generally, such mechanisms can be split into two categories: “push” and “pull”. Push mechanisms enhance the funds available to research and development, in the hope that a useful drug will be produced; pull mechanisms provide enhanced incentives for investments in R&D by increasing the value of the end product to the innovator. Reducing the burden of taxation on R&D investments made by private corporations is one example of a “push” mechanism for targeted research projects.³⁵ An example of a pull mechanism is the offer of a reward to the inventor of a drug that treats a specified disease. We discuss specific push and pull mechanisms in more detail below.

Push mechanisms

Push mechanisms aim to encourage the development of treatments for specific diseases by providing upfront financial support for research into those diseases.

There are, however, significant drawbacks to upfront funding. Subsidies to R&D do not necessarily lead to the development of useful medicines. Estimates suggest that of every 5,000 new chemical entities (NCEs) screened,

on average only five go through to clinical trials, and only one of those yields an approved medicine for patient use.³⁶ Publicly-funded projects that focus on the development of only a few selected chemical compounds are therefore extremely likely to fail, resulting in the waste of significant sums of public money.

There are two main types of ‘push’ mechanism: direct funding and public-private partnerships.

Direct funding

Direct public funding might take the form either of public funding for research and clinical trials carried out by private firms, or of increased funds to public, non-profit research organisations.³⁷

Advocates of direct funding argue that subsidised or even wholly nationalised research and development is the best way to produce safe and effective medicines for the diseases of poverty.³⁸

Notwithstanding the issues related to marketing and distribution, the problem with direct funding is determining exactly what level of financial resources are required to develop a successful treatment, and how best to deploy those resources to create an incentive-compatible system.

First, it is extremely difficult to determine at the outset the exact amount of funding that will be required. Second, there is also a risk of overspend as the project may encounter previously unknown obstacles or avenues of research. Third, project leaders may be tempted to exaggerate the likely cost of research in order to secure as much funding as possible. Finally, the involvement of public stakeholders may skew research objectives, as their demands may reflect political rather than clinical preferences.

In addition to inefficiency and waste, there is no guarantee that a government subsidy will produce any of the specified outcomes. A neat illustration of the drawbacks to public procurement of R&D was a US Agency for International Development (USAID) initiative in the 1980s to fund development of a vaccine for malaria. This initiative absorbed \$60 million but failed to achieve any of its goals.

The problem with the USAID malaria vaccine initiative was that the researchers were operating to the demands of a public sector employer rather than the market. As a result, they produced wildly optimistic statements about the progress of their work in order to ensure a continued supply of funds. Government-funded project directors also have an incentive to fund unpromising work – illustrated by the US AID project leader's demand for further funds, despite the unpromising nature of its early work. Because the recipients of government subsidies are paid before delivery, they lack appropriate incentives to conclude the research.

Public Private Partnerships (PPPs)

In wealthier markets, the supply of new drug targets has been enhanced by special relationships between small entrepreneurial firms that specialise in scientific research and large pharmaceutical companies. Despite these agreements, rapidly advancing science and technology and especially the rapid rate of new biological and chemical discoveries means that even large firms may be unable to follow all of the new developments in research.

In the field of genomics, for example, the number of biological targets has increased to between 3,000 and 10,000, from only 500 before the results of the Human Genome project were compiled.³⁹ The sheer cost of keeping up with such developments would be beyond the means of most individual firms.

For this reason, public private partnerships (PPP) have emerged as a complement to pure private drug development for specifically targeted diseases. PPPs can incorporate several facets of the discovery, development and delivery process, but one particular model highlights the role the public sector can play in coordinating basic research for the diseases of poverty.⁴⁰

The National Institutes of Health (NIH), which operates in the United States⁴¹ is one of the best examples of a PPP. In 2003, the NIH provided more than \$27 billion to fund and coordinate health research, making it the largest public health research body in the world. The NIH national research centre supports research in many different fields and also coordinates activities by many researchers, including small scale biotechnology firms. These research projects provide inventories of promising chemical compounds which can be utilised by private sector research-based companies to develop medicines.

Several public-private partnerships exist that specifically focus on diseases of poverty. In particular, the Medicines for Malaria Venture (MMV)⁴², the Global TB Vaccine Foundation (Aeras)⁴³, the International Aids Vaccine Initiative (IAVI)⁴⁴, and the Infectious Disease Research Institute (IDRI)⁴⁵ coordinate publicly funded R&D projects with private companies. Due in part to these arrangements, there are at least 86 drugs in the R&D pipeline targeting HIV/AIDS, including 15 vaccines.⁴⁶ There are at least 30 more drugs in the R&D pipeline for malaria, and 22 for tuberculosis.⁴⁷

In addition, there are now PPPs that focus on developing drugs for African Trypanosomiasis, Chagas Disease, Leishmaniasis, and Dengue Fever, which have bolstered the number of potential treatments in the R&D pipeline for these diseases. There are currently at least eight potential treatments in varying stages of clinical trials, and a further 16 in preclinical development.⁴⁸

Pull mechanisms

While push mechanisms require upfront funding for research activities in the hope that they will develop a useful drug, pull mechanisms act at the other end, providing funding or other pecuniary incentives only when a specific, predetermined outcome has been achieved.

Pull mechanisms have the singular advantage for the funding entity that they withhold payment until a demonstrably effective and tested product has been manufactured. This means that drug developers can get on with the business of developing the drug without interference from the funder, while the funder is freed from the responsibility of having to manage the R&D

process. Furthermore, because the funder only pays for the drug when it has been fully developed, the possibility of being left with a costly white elephant is dramatically reduced.

However pull mechanisms have several potential drawbacks.⁴⁹ First, the donor must specify the outputs before research commences, which may be difficult. Second, if outcomes are not well defined, it may not be clear what basic research is necessary, so the whole project could stall – indeed there could be serious consequences for the whole stratum of basic research, especially if the model were applied widely. Third, developers may – legitimately, given the fickle nature of political commitments – be concerned that the funder might renege on his commitment. Finally, because pull mechanisms often result in a ‘winner takes all’ situation, they run the risk of stifling the kind of incremental innovation that results from ‘inventing around’ the original drug, which could have negative implications for future drug-resistance and effectiveness in subpopulations.

Nevertheless, pull mechanisms offer considerable promise for the development of treatments for certain diseases. Some of the more notable proposals are discussed below, with a brief evaluation of their strengths and weaknesses.

Transferable patent extensions

One suggestion has been for pharmaceutical R&D companies based in wealthy markets such as Europe, the USA and Japan to receive a patent extension for one of their existing products in those markets, in return for inventing a vaccine or treatment for a disease of poverty on a pre-determined list. This mechanism would be attractive to larger, established R&D companies, and it would certainly result in an additional flow of private sector resources into the quest for drugs for the diseases of poverty.

The effect of such a mechanism, however, would be to transfer the financial burden of developing new medicines onto consumers of specific drugs in rich markets. Where similar competitor drugs exist, consumers may simply switch to products that do not have their price inflated by a transferable patent. This

would negate the financial compensation potentially to be gained by the investor from diverting resources into the research into the diseases of poverty in the first place. Conversely, if no such competitor product existed, the price inflation caused by the transferable patent could prove politically difficult for governments that wish to control spiralling healthcare costs.

An alternative would be to allow companies to extend the patent life on a range of their drugs for a short period. This would disperse the cost over a wider range of consumers and is less likely to be self-defeating.

Advance purchase commitments

A potentially useful way to stimulate R&D into the diseases of poverty is for donor agencies or governments to guarantee in advance the bulk purchase of a drug that meets a set of pre-established criteria. The funder would make a legally binding commitment to pay for a new drug if and when one is developed, which would be set at a price sufficient to cover the cost of R&D.

According to the Center for Global Development, a prominent supporter of such schemes, this would create a win-win solution for both donors and the private sector. For donors, such a commitment would have no impact on their existing budgets, and would not mean that funds are diverted to research projects which run a high risk of failure.⁵⁰ For drug developers, the main advantage lies in the fact that new markets would be opened in previously unattractive areas, while at the same time the risk of compulsory licensing would be removed. It would also lessen the chances of industry being compelled by Government to conduct research into unprofitable areas.

The main objection to such schemes lies in the problems associated with the valuation of the end products. The donor will not be able to assess the financial value of the final innovation in the same way consumers would, which may lead to under- or over-reward. Advanced purchase commitments also suffer from the so-called ‘hold up problem’. Since the innovator’s costs are already sunk, the prize-awarding body may be tempted to award prizes which are much lower than the true value of the innovation. Both of these factors will erode incentives for future innovation. Conversely, there is also

the risk that R&D companies may be tempted to exaggerate costs in order to secure a greater reward from the funder.

Advance purchase commitments may also stifle incremental innovation. Because they create a ‘winner takes all’ solution, it would be difficult for incremental, follow-on competitors to emerge, thus dulling the benefits of competition on cost and improvements. The innovation that wins will crowd out competing inventions because it is being given away free by the public sector. This ‘crowding out’ effect means that no improvements will be made to the winning formulation, and this may have negative consequences for resistance and effectiveness in subpopulations.

As with all prize mechanisms, the potential for political rent-seeking is great, as the prize-awarding authority may be tempted to favour political or commercial allies. Senior individuals within the authority might even accept bribes. Furthermore, the donor’s view of what constitutes a socially useful innovation will reflect their own priorities, and could result in areas being neglected or over-prioritised. Project choice, for example, might reflect the preferences of bureaucrats rather than those on the ground. Priority setting by outside agencies might result in R&D being directed only at one type of country, one region of the world, or one disease – with other equally needy causes missing out on the additional investment.

It is also worth considering the historical record of prizes – of which advance purchase commitments are a special type – as a stimulus to investment. In individual instances, these have clearly worked in the past. For example, a prize from the British government led to the creation of the Harrison clock. More recently, the \$10 million “X Prize” most likely contributed to the development of the first major private sector spaceflight.

Yet it is doubtful that prizes can in general be relied upon to deliver new developments. The experience of the Soviet Union is apposite: innovators in the USSR were rewarded for less than the value of their innovations and unsurprisingly the USSR’s record of industrial and scientific innovation was not impressive.

If advance purchase commitments are to work successfully, they must be clearly targeted and

appropriately establish the conditions of the prize – including both the conditions for success and the size of the award.

Orphan drug type legislation

While not related specifically to the diseases of poverty, orphan diseases share similar characteristics to those suffered predominantly in low-income countries. The numbers of people who suffer from orphan diseases make them “uneconomical” for private sector companies to justify the investments needed to develop specific drugs that treat or cure each condition. In the United States, these include Huntington’s disease, myoclonus, ALS (Lou Gehrig’s disease), Tourette syndrome, and muscular dystrophy.⁵¹

In reaction to this, the US orphan drug legislation combines several interesting aspects of individual push and pull programmes to stimulate private sector R&D activities for the development of treatments for rare diseases. These include offering market exclusivity for ‘orphan’⁵² products receiving FDA approval, tax credits for R&D investments⁵³, and an orphan drug development grant program to provide funding for eligible researchers⁵⁴. Most importantly, orphan drug applications are eligible for fast-track regulatory approval⁵⁵, which makes the drug development process easier and more cost-efficient for firms. These legal interpretations only make the option of pursuing R&D projects more interesting for private researchers, and therefore enhance the chances that new and improved medicines will be developed.

Since the original Orphan Drug Act⁵⁶ was passed in 1983, more than 900 drugs and biological treatments have been designated as orphan products, and over 200 have been given FDA approval.⁵⁷ Reducing regulatory barriers for drug developers can stimulate more research on rare diseases, and these legislative efforts have proven to yield some beneficial innovations that otherwise might not have been introduced.

Open source

In addition to the ‘push’ and ‘pull’ mechanisms described above, it is worth discussing a recent proposal

that drug development should take place at least in part in an 'open source' environment.⁵⁸ The concept of 'open source' is common in software development, and refers to a situation where developers share intellectual property with one another and develop new technologies collaboratively. In the context of software, several applications, including the Linux operating system, Apache server software, and the Firefox web browser⁵⁹ have emerged as moderately successful products, competing against more widely-known brands.

Open source has been suggested as a way of limiting the costs incurred by any one individual or research agency during the lengthy process of drug development. It typically relies on an electronic network of scientific researchers from a host of different corporations, organisations and universities who then work together for a common cause, in this case to research and select the most promising chemical compounds for a specific disease, and then eventually develop treatments.

Many people point to the success of the open source model in the software industry and envision that the same results would occur in drug discovery and development. Advocates believe that the model would give scientific researchers more freedom to explore more options for diseases which are suffered predominantly in poorer countries.

The major advantage of open source is that any decentralised research project can draw on scientific expertise from various participants without worrying about intellectual property issues. Given the currently low cost and remarkable ease of communicating over the internet, the possibilities for collaboration have expanded dramatically. Having a team of scientists working together instead of in direct competition may also reduce the chances of duplicative research, and limit the errors made during isolated research efforts.

In the context of drug development, open source could apply at various different levels in the development chain. Most plausibly it would apply at the lowest level, where researchers would share knowledge about the theoretical uses of specific chemicals with one another and test these using computer models.

Once a set of potentially useful chemicals has been

identified for the treatment of a disease, it would then be necessary to carry out more rigorous testing, which at some stage would entail conducting 'wet' clinical trials. Such trials require substantial resources (including lab animals and expensive and complex equipment), so the question would then arise as to how these trials would be funded, which brings the discussion back to intellectual property rights.

In the context of open source software, there are several competing IP models. The most popular of which are the Gnu General Public Licence (GPL) and the Berkeley Software Distribution (BSD) model. Under a GPL, innovators who alter GPL software must apply an identical GPL to the software they create, which means they cannot benefit from mass marketing the software – rather, they benefit financially (if at all) from developing bespoke software or selling support services associated with the software.

Under a BSD licence, however, downstream innovators are permitted to protect any software they develop using intellectual property. Given the objective of developing new drugs for the disease of poverty, it seems clear that the appropriate licence type would be a BSD, since this would give companies a mechanism to benefit from the investments they make in drug development.

Conclusion

Many push and pull mechanisms have some merit in stimulating research into diseases endemic to poorer countries. However, all of these solutions must only be considered as short-term expedients, because they do little to alter the fundamental problems associated with developing and delivering drugs for the diseases of poverty.

In the longer term, governments must create environments that are conducive to the fragile process of innovation. This is the only way to bolster the pipeline of new drugs in a sustainable manner.

If health distribution and communications channels are ineffective, new medicines may not reach new patients at all,⁶⁰ dampening the overall potential of a new drug.⁶¹ Furthermore, the lack of proper healthcare systems in poor countries makes it difficult to glean data about the

disease profile of a country, and this undermines the ability of companies and governments to determine what new medicines are required. This in turn makes effective research prioritisation next to impossible.

Policymakers in poor countries must, as a priority, remove barriers to the provision of healthcare, especially the tax and regulatory barriers that currently prevent the poor from obtaining essential medicines. In addition, the governments of these countries should improve the institutional environment more generally, so that people can generate wealth and thereby ensure that healthcare systems become self-sustaining – and provide a strong demand driver for the development of new drugs.

Finally, weak intellectual property legislation in countries with incipient or extant knowledge-based industries also acts as a serious disincentive on R&D into the diseases of poverty, not least because it jeopardises the ability to generate enough sales to cover the extremely high cost of innovation.

This is particularly true of highly politicised diseases such as HIV/AIDS; with countries such as Brazil threatening to implement compulsory licenses for ARVs, it becomes more difficult for R&D companies to devote resources to searching for new medicines.

Strong intellectual property legislation can also go some way to encouraging the development of an indigenous R&D industry in countries where it currently does not exist. As India comes to terms with its recently enacted patent legislation, for example, it is likely that more companies will turn to value-added R&D work, rather than merely producing copies. It is also likely these companies could find commercial benefit in developing drugs for diseases prevalent among local populations, which, due to their lower cost base, could likely also be developed at prices far lower than equivalent development in wealthy countries.

The development of new medicines, however, must be viewed in the context of the wider health issues facing low income countries. A large proportion of the disease burden in such countries is unnecessary, since it could be reduced by the effective distribution of medicines that are currently available and inexpensive.

If we focus simply on the development of new

medicines, there is a risk that we will overlook the real reasons why low income countries continue to suffer from diseases that were eradicated in wealthier countries many years ago. Namely, this is poverty – which leads to poor nutrition and generally unhealthy living conditions, as well as an inability to afford better medicines.

The link between increased wealth and increased health has been long established.⁶² When poverty is reduced, health outcomes improve. People in rich countries can expect to live longer and have better access to medical care. With greater wealth, scientists and innovators, both private and public, have better opportunities to conduct research into health and disease. Greater availability of financial resources means that more can be spent on education and to improve literacy, which in turn can promote the adoption of new technologies and ensure that these technologies are more widely diffused.

The world's wealthiest countries also have the resources to run coherent AIDS control and containment programmes, and have few problems with tuberculosis. By the end of the 1970s, European nations were able to banish malaria from the continent⁶³ through a combination of new building technologies for dwellings (including mosquito-proof windows and roofs), drainage, land reclamation, new cattle rearing practices, and greater access to medical care.⁶⁴ This was the by-product of increasing wealth. Unfortunately for many impoverished nations that suffer from malaria and other diseases of poverty today, such conditions (which result from prosperity) are far off.

It is unlikely that good health will ever be sustained without long-term wealth creation that can pay for the ongoing improvements in water, sanitation, nutrition, living conditions, health education and hospitals which are vital for the control of diseases such as malaria, tuberculosis and AIDS. Unfortunately, the governments of poor countries continue to hinder the creation of wealth, imposing obstacles in the way of owning and transferring property, imposing unnecessary regulatory barriers on entrepreneurs and businesses, and restricting trade through extortionate tariffs. If these things were addressed, many diseases of poverty would be relegated to history, as they have been in the world's wealthiest countries.

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53. Some numbers put the tax break on Orphan disease research investments as high as 50%.

<http://rarediseases.about.com/library/weekly/aa053000a.htm>

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Incentivising research and development for the diseases of poverty

The proportion of people who have access to medicines remains deplorably low in most poor countries. This problem, which is largely the result of inadequate healthcare infrastructure and government interventions of various kinds, is clearly one that must be addressed as a matter of priority. Nevertheless, even as this problem is tackled, there is a continuing need for new medicines for the diseases of poverty. Drug resistance is a problem for most of these diseases (in part because of poor oversight of treatment) and especially for tuberculosis, malaria and AIDS. Meanwhile, a small cluster of tropical diseases lack any medicines at all.

The comparative lack of research and development (R&D) activity in this area is not evidence of market failure, as is often claimed by activists. In fact, it would be more accurate to describe it as government failure. Taxation, price controls, a lack of respect for intellectual property and other more general institutional failures constrain both the demand for and supply of new drugs, making R&D into the diseases of poverty commercially nonviable in most cases.

In the short term, it is necessary to examine alternative ways to incentivise R&D for the diseases of poverty. This paper critically surveys the most interesting proposals so far generated by this debate, ranging from 'push' mechanisms such as public private partnerships, to 'pull' mechanisms such as advance purchase commitments.

While many of the ideas on the table have some merit, policymakers should not lose sight of the fact that the best way to improve health is to create wealth. Governments of lower-income countries will therefore need to address their institutional failings if they hope to create self-sustaining healthcare systems that effectively drive demand for new drugs. Unfortunately, many governments place needless barriers in front of this process, thereby condemning their people to a future of continued ill-health and a reliance on philanthropy from the West.



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