3.10 *Financing innovation for neglected diseases*

MARISA MIRALDO, MUJAHEED SHAIKH, MOHAMED GAD

Key messages

Chapter 3.10 evaluates innovative financing for neglected diseases. Neglected diseases account for about a fifth of the global burden of disease and affect over 1 billion people. They are neglected because the pharmaceutical sector does not consider it profitable to develop treatments for them. This reflects the fact that neglected diseases are most prevalent in low- and middle-income countries (LMICs) with relatively low purchasing potential. Key learning includes that:

- Global pharmaceutical R&D invests a disproportionate share of innovation and activity in diseases that affect high income countries, something which fosters significant inequities.
- A range of push and pull incentive mechanisms have been developed to delink the cost of research from market profitability and promote innovation in areas of need. These include measures to:
  - reduce the upfront costs by subsidizing R&D pre-discovery (push incentives); and
  - offer a reward post-discovery (pull incentives).
- The evidence on the effectiveness and reach of incentive schemes is scant and more needs to be done to understand the relative cost–effectiveness of the different incentive mechanisms and the extent to which they mitigate inequalities in innovation and access to new medicines.
- A global, unified governance framework for needs assessment and resource allocation could usefully:
  - carry out systematic comparisons of the relative needs associated with neglected diseases globally;
  - assess the costs and benefits of addressing these;

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

- set priorities for the coordinated global allocation of funding and targeted incentive mechanisms; and
- consider payment mechanisms that will translate research into market launches.

Introduction

Neglected diseases (NDs) comprise a diverse set of around 20 diseases and disease groups, depending on the classification used. Typically considered to offer little scope for profitability to the pharmaceutical industry, these diseases are known as neglected diseases either because their prevalence is proportionally small (rare diseases) or because they are endemic in LMICs that cannot afford to buy either treatment or prevention therapies at market prices. As a result, market incentives for R&D to develop therapies for these conditions are weak (Maurer, 2005).

Neglected diseases include several parasitic, viral and bacterial diseases that cause substantial illness globally (Table 3.10.1). Neglected disease products were only 4% of all therapeutic products registered between 2000 and 2011 (Belen et al., 2013). Despite these diseases affecting more than 1 billion people, causing around 19% of global burden of disease, with devastating health, social and economic consequences (Fitzpatrick et al., 2017; IHME, 2019), there is substantial inertia in the development of treatments and prevention targeting these diseases. Fig. 3.10.1 illustrates the wide geographical distribution of disability-adjusted life years (DALYs) from neglected diseases between 1990 and 2010 for both sexes and all ages.

Table 3.10.1 *Neglected diseases affect more than 1 billion people globally*

Disease categories
1. HIV/AIDS
2. TB
3. Malaria
4. Diarrhoeal disease (rotavirus, cholera, shigella, cryptosporidiosis, enterotoxigenic *Escherichia coli*, enteroaggregative *E. coli* and giardiasis)
5. Kinetoplastid disease (sleeping sickness or HAT, Leishmaniasis, Chagas disease (American trypanosomiasis))

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.1 (*cont.*)

6. Bacterial pneumonia and meningitis (*Streptococcus pneumoniae*, *Neisseria meningitidis*)
7. Salmonella infections (typhoid and paratyphoid, non-typhoidal *Salmonella enterica*)
8. Helminths infections (schistosomiasis, onchocerciasis, lymphatic filariasis, tapeworm, hookworm, whipworm, roundworm, strongloidiasis)
9. Dengue
10. Hepatitis B
11. Hepatitis C
12. Leprosy
13. Cryptococcal meningitis
14. Snakebite envenoming
15. Buruli ulcer
16. Trachoma
17. Leptospirosis
18. Rheumatic fever
19. Mycetoma
20. Other diseases (rare diseases, chikungunya, dracunculiasis, rabies, scabies, yaws)

HAT: human African trypanosomiasis; TB: tuberculosis.
Note: Definitions of neglected diseases vary widely; this table combines definitions in G-Finder in addition to other diseases from the World Health Organization's neglected disease list.

Sources: WHO (2010); 2023; Policy Cures Research (2021b).

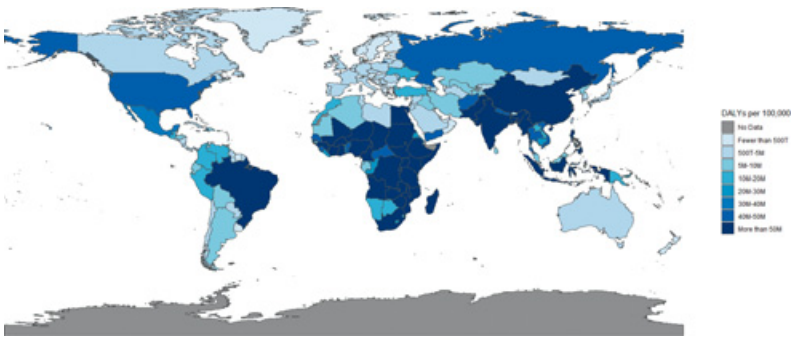


Fig. 3.10.1 Neglected diseases disproportionately affect LMICs
DALYs: disability-adjusted life-years.

Source: IHME (2019).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

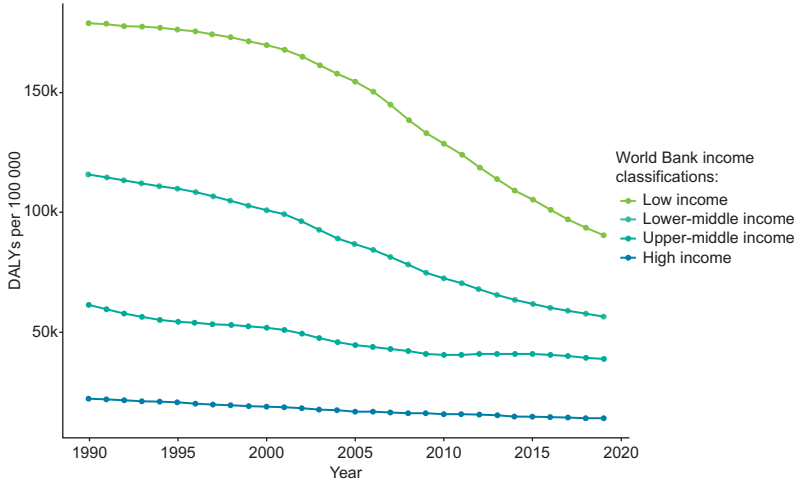


Fig. 3.10.2 Neglected diseases have declined in richer countries but remain constant in LMICs

B: billion; DALYs: disability-adjusted life-years; M: million.

Source: IHME (2019).

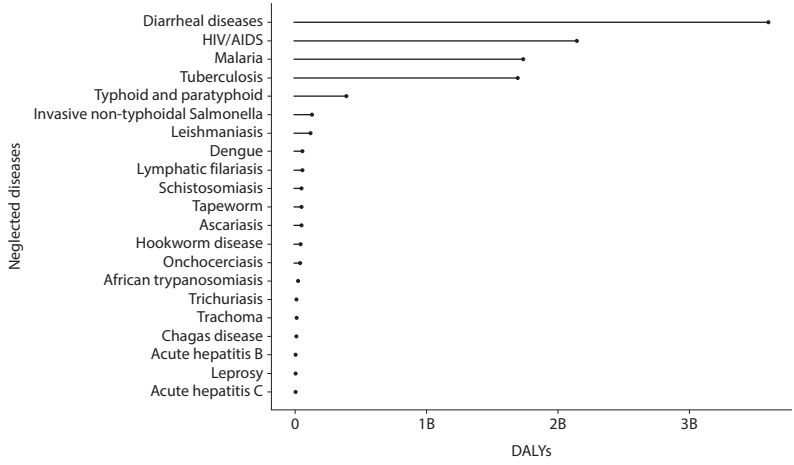


Fig. 3.10.3 Top five neglected diseases: diarrhoeal diseases, HIV/AIDS, malaria, TB, and typhoid and paratyphoid

B: billion; DALYs: disability-adjusted life-years.

Source: IHME (2019).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

While over time there has been a decline in the global burden of disease associated with neglected diseases, they still disproportionately affect LMICs (Fig. 3.10.2).

Diarrhoeal diseases, HIV/AIDS, malaria, tuberculosis (TB) and typhoid and paratyphoid are the top five diseases that contribute the highest burden of DALYs (Fig. 3.10.3). The bottom five diseases that contribute the lowest burden of DALYs are trachoma, Chagas disease, acute hepatitis B, leprosy and acute hepatitis C (Fig. 3.10.3).

World Health Organization's (WHO's) neglected diseases roadmap, 2021–2030

The WHO Road Map for Neglected Tropical Diseases 2021–2030 sets out global targets and milestones for 2030, including 90% reduction in cases requiring interventions, 75% reduction in DALYs lost to neglected diseases, working to eliminate at least one neglected disease in 100 countries, and eradicating two neglected diseases globally. The roadmap highlights research, development and innovation as "fundamental enablers of programmatic progress for all neglected diseases" (WHO, 2021a). To achieve this endeavour, the WHO Council highlights the need for a systematic approach to innovation and the elimination of unacceptable inequities in access to treatment and prevention (WHO, 2021b).

Delinking the costs of R&D from the cost of new therapies: financing incentive mechanisms

The eradication of neglected diseases or the mitigation of their impacts requires greater pharmaceutical innovation. The report on financing and coordination by WHO's consultative expert working group on R&D (WHO, 2012) highlights that novel financing incentive mechanisms are required to address these challenges. The World Health Assembly passed a resolution in 2006 that highlighted the importance of "incentive mechanisms . . . addressing the linkage between the cost of R&D and the price of medicines, vaccines, diagnostic kits and other health care products" in addressing unmet needs for neglected diseases (WHO, 2007). The design of financing incentive mechanisms is

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

important to ensure not only sustained investment in R&D but also an efficient targeting of effort and resources towards key areas of need.

In this chapter, we quantify some of the systemic gaps with regards to the distribution of pharmaceutical R&D activity and funding across neglected diseases, and describe some of the underlying reasons for these gaps. We then discuss the financial incentive mechanisms in use since 2007 in terms of pre-discovery push (public–private partnerships, in particular product development partnerships, R&D grants and subsidies, fiscal measures) and post-discovery pull (transferable patent extensions, patent buyouts, priority review vouchers (PRVs), advance market commitments (AMCs), prizes). We examine the evidence for their effectiveness levels, noting their relative advantages and disadvantages. We conclude with insights into the overall state of R&D funding for neglected diseases.[1]

Trends in funding, 2007–2019

Fig. 3.10.4 illustrates total spending in US dollars by source of spending on R&D for new products and technologies to address challenges in public health caused by neglected diseases between 2007 and 2019. Total spending is around US$ 3.25 billion per year and was highest in 2009, 2017, 2018 and 2019 and lowest in 2007 and 2015. Between 2015 and 2018 spending on R&D for neglected diseases amounted to US$ 17.9 billion, 2.7% of global pharmaceutical R&D spending (US $ 660 billion) (Statista, 2021), signalling underinvestment in neglected disease R&D, considering that neglected diseases account for 19% of the total global burden of disease (IHME, 2019).

Between 2007 and 2019, on average, the three areas that accounted for the highest proportion of spending, in descending order, were vaccines, drugs and basic research (Fig. 3.10.5). The year 2014 saw the highest spending, with vaccines, drugs and basic research accounting for about 37.5%, 22.5% and 20% of total spending, respectively, when compared to other products such as diagnostics and core funding and other R&D products. Cumulatively, between 2015 and 2019, there was a gradual decline in total spending across all the different types of products.

[1] Please note that this chapter focuses on the financing of medicines and vaccines in relation to neglected diseases rather than access; while access issues are important, we do not assess them here. We also do not comprehensively cover preventive technology such as diagnostics or medical devices.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

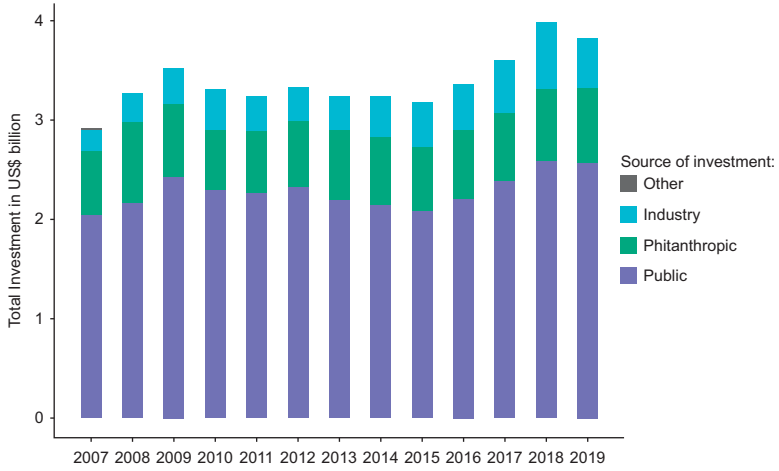


Fig. 3.10.4 Global pharmaceutical companies are underinvesting in neglected disease R&D, 2019
B: billion.

Note: Authors' analyses
Data source: Policy Cures Research (2021b).

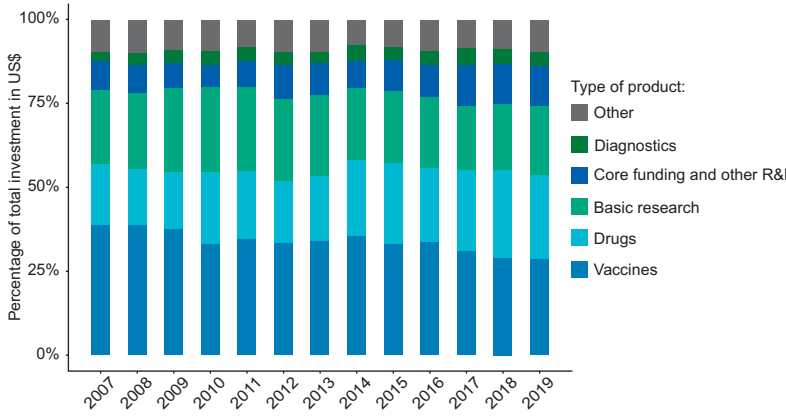


Fig. 3.10.5 Most money is spent on vaccines, drugs and basic research
R&D: research and development.

Note: Authors' analyses
Data source: Policy Cures Research (2021b).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

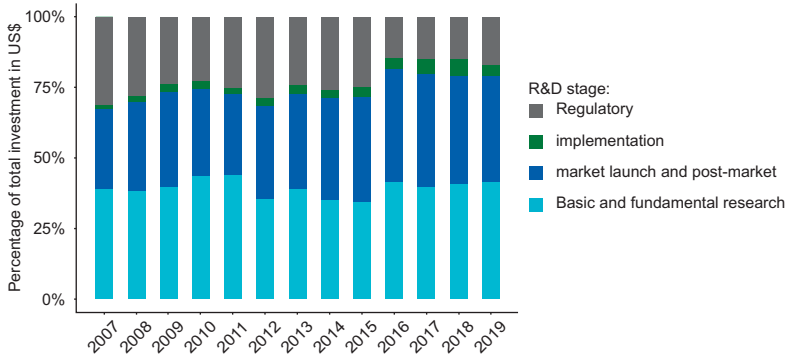


Fig. 3.10.6 Most R&D spending to address neglected disease challenges goes on just two stages

R&D: research and development.

Note: Authors' analyses
Data source: Policy Cures Research (2021b).

Between 2007 and 2019, although around 30% of total spending was unspecified, the majority (approximately 70%) of spending was shared between two stages, namely the clinical and the basic and fundamental research stages (Fig. 3.10.6). The regulatory, implementation, market launch and post-market stages received the smallest proportions of the total funding. Even though the proportion of total funding invested in clinical research has remained constant at around 35% during the period 2015 to 2019 (Fig. 3.10.6), the increased funding in clinical and preclinical R&D over the years could be translated into further innovation for neglected diseases in the years to come.

Sources of funding

The three most common sources of funding were industry, philanthropic and public sources. Between 2007 and 2019, public and philanthropic sources accounted for more than 70% and 20% of total expenditure, respectively, while industry sources accounted for about 10%.

The United States of America (USA) consistently ranks as the top funder, funding on average 65% of total spending between 2007 and 2019. Apart from the EU, which funds on average 3% of the total

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

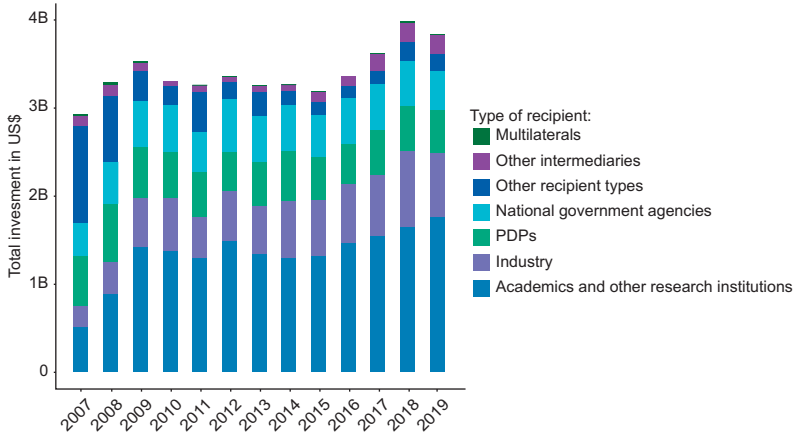


Fig. 3.10.7 Academics and research institutions receive the biggest proportion of investment

PDP: product development partnership.

Note: Authors' analyses
Data source: Policy Cures Research (2021b).

expenditure, other top funding countries include the United Kingdom and France, which fund on average 6% and 2%, respectively. However, it is important to note that over the same period, about 13% of the total spending came from countries that were not specified.

Fig. 3.10.7 shows total neglected disease R&D spending by type of recipient. On average academics and other research institutions receive the highest amount of investment followed by industry, whereas "other intermediaries"[2] receive the lowest amount of funding.

Inequities and inequalities in R&D activity and funding

When we compare the distributions of pharmaceutical R&D activity and global DALYs across neglected diseases (Fig. 3.10.8), for the

[2] Intermediaries are organizations that receive funding for R&D and allocate it as onward funding to product developers. There are two types of intermediaries: product development partnerships (PDPs) and "other intermediaries". The latter are coordinating entities where money flows to them as well as from them. The former, beyond coordination, engagement and advocacy activities, also conduct their own R&D. Further information can be found at: https://gfinderdata.policycuresresearch.org/assets/media/pdf/Glossary.pdf.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

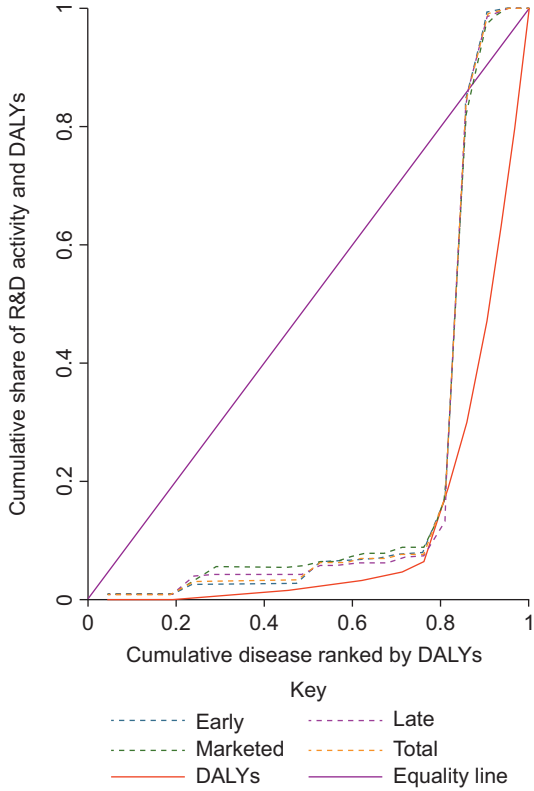


Fig. 3.10.8 Low-burden diseases receive more than their fair share of R&D
DALYs: disability-adjusted life-years; R&D: research and development.
Note: Authors' analyses.

Sources: DALYs data from IHME (2019); R&D data from IQVIA (2019).

diseases at the top of the distribution of DALYs there is a disproportionate concentration of innovation in low-burden diseases, meaning that low-burden diseases receive more than the fair share of R&D activity when we consider their need relative to other diseases (inequity pro-low burden). This inequity is even more pronounced once we consider market launches in LMICs where we see low-burden diseases experience more market launches than their relative need would warrant when compared to high burden diseases (Fig. 3.10.9).

These inequities can be attributed to inequalities in the distribution of R&D funding across neglected diseases and/or the fact that most

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

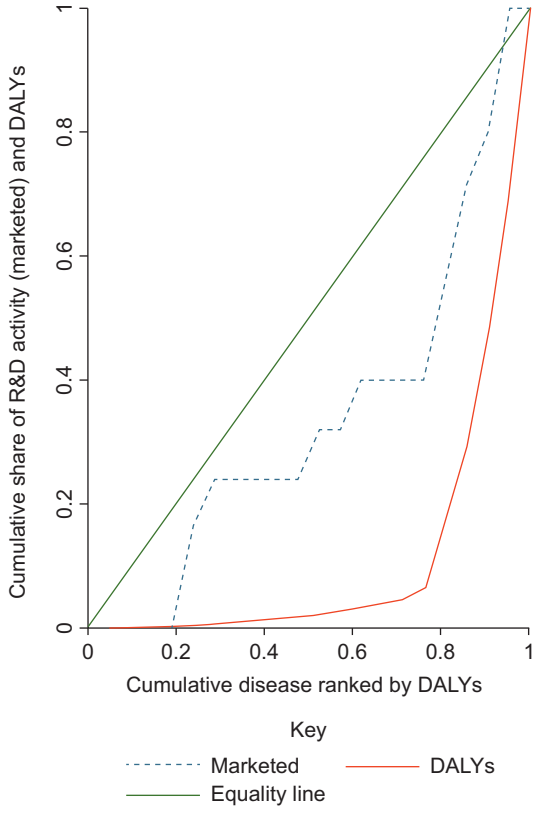


Fig. 3.10.9 LMICs receive few market launches for new pharmaceutical products

DALYs: disability-adjusted life-years; R&D: research and development.

Note: Authors' analyses.

Sources: DALYs data from IHME (2019); R&D data from IQVIA (2019).

LMICs lack the resources and research infrastructure to develop their own medicines (Mrazek & Mossialos, 2003).

The 10 neglected diseases that received the highest R&D investment in US dollars between 2007 and 2019 for new products and technologies to address challenges in public health are shown in Fig. 3.10.10. HIV/AIDS received the highest investment by about US$ 16.9 billion, followed by malaria and TB, with US$ 7.9 billion and US$ 7.8 billion, respectively. Mycetoma, leptospirosis and hepatitis B received the

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

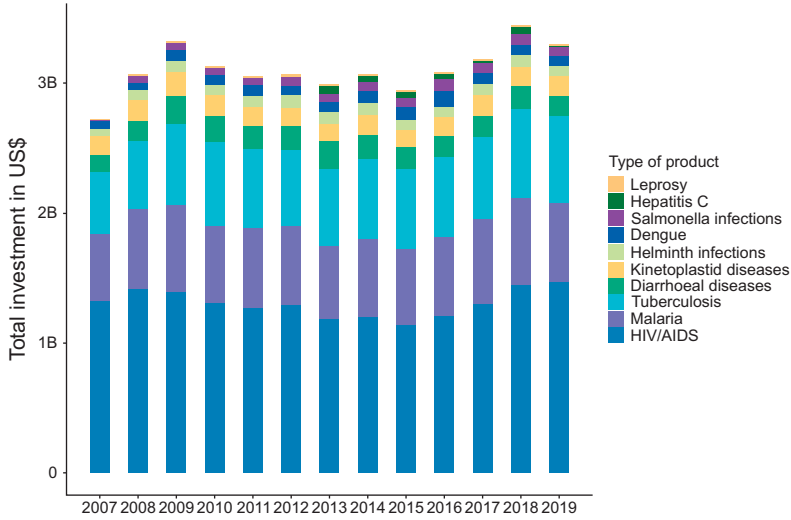


Fig. 3.10.10 HIV/AIDS, malaria and TB receive most investment
B: billion.

Note: Authors' analyses
Data source: Policy Cures Research (2021b).

lowest investment, which cumulatively in the last five years (2015 to 2019), was around US$ 1.5 million, US$ 9.3 million and US$ 16.5 million, respectively (Policy Cures Research, 2021a).

Between 2015 and 2018 the cumulative spending has seen a steady increase, albeit remaining concentrated on HIV/AIDS, malaria and TB. Looking at global spending for R&D activity for neglected diseases, we observe a disproportionate concentration on low-burden neglected diseases.

Fig. 3.10.11 (the concentration curve of global R&D activity (1980–2019) and DALYs in LMICs (2018–2019)) and Fig. 3.10.12 (the concentration curve of market launches in LMICs (1980–2019) and DALYs (2018–2019) in LMICs (2018–2019)) show that low-burden diseases receive more than their fair share of funding given their relative disease burden. With the exception of spending on regulatory, implementation, market and post-market launch activities, this inequity is more pronounced when one considers funding allocated only to LMICs.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

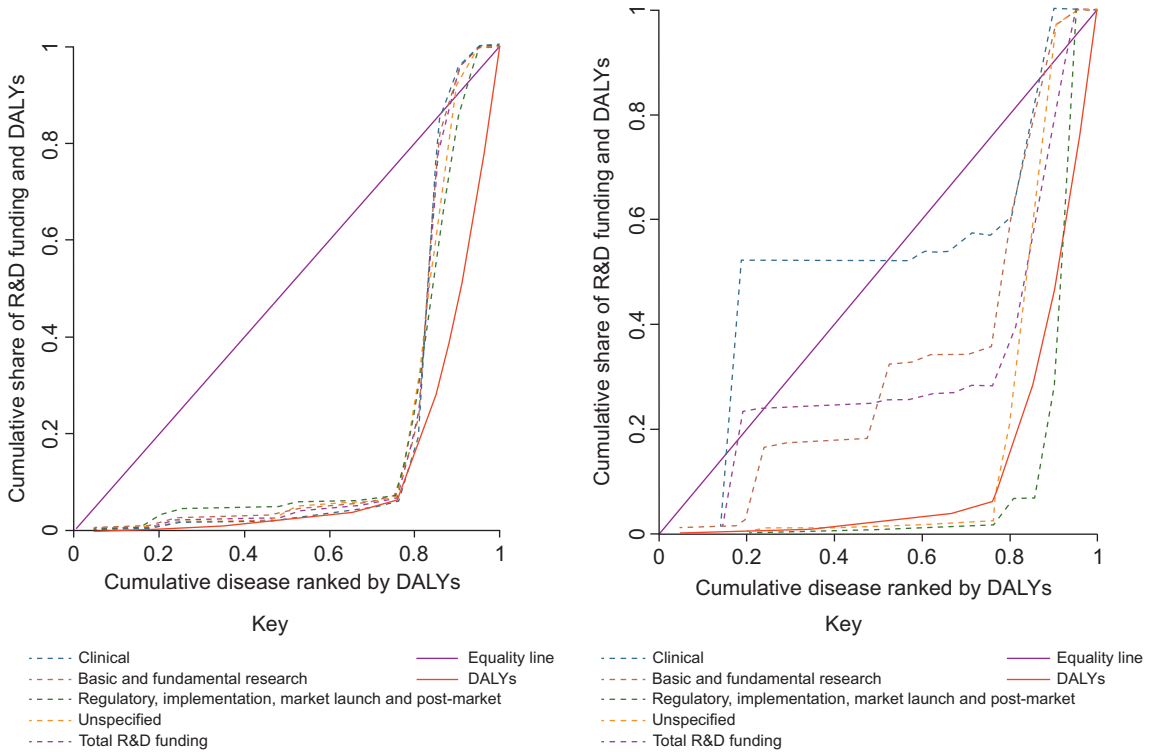


Fig. 3.10.11 and 3.10.12 Low-burden diseases received more than their fair share of funding
DALYs: disability-adjusted life-years R&D; research and development.
Note: Authors' analyses.

Sources: DALYs data from IHME (2019); R&D data from IQVIA (2019).

Reasons for inequities and inequalities

Several mechanisms may explain these inequities in innovation that impact differential access to treatment for neglected diseases to the detriment of health and well-being in LMICs. Concerns around pricing, affordability and the low potential for profit of those treatments in LMICs implies that firms have little incentive to develop innovations for these populations. This is aggravated by HICs giving priority to fund R&D for diseases that impact their own populations and the lack of international coordination in pooling and allocating resources to innovation taking account of health needs across all disease areas and geographies, as well as affordability.

These inequities are also intrinsically related to market failures and the effectiveness of mitigating strategies, including financing and incentive mechanisms.

Market failures in R&D: misalignment between private incentives and health need

There are several features of the R&D sector in the context of pharmaceutical innovation that are associated with market failures as a result of which the resource allocation for R&D efforts is not socially optimal (Arrow, 1962), thus justifying government intervention. Most notably there is imperfect appropriability, with significant knowledge spillovers implying that firms will not fully recoup the benefits of their investment in R&D (Henderson & Cockburn, 1996; Bloom, Schankerman & Van Reenen, 2013). Research shows social rates of return to R&D (i.e. returns to the innovator, benefits to other firms and to society) to be up to five times higher than private rates of return (Salter et al., 2000). These may lead to underinvestment (Romer, 1990), in particular in risky areas where prospects of profitability are uncertain, such as neglected diseases.

There is also information asymmetry between pharmaceutical firms and funders because several aspects of innovation and its processes are difficult to describe contractually and there are often no incentives for private firms to disclose them. Asymmetry of information between firms and funders typically leads funders to underinvest in R&D in the light of risk and uncertainty (Czarnitzki & Toole, 2007). This underinvestment may be more accentuated in markets with high levels of uncertainty such as those for neglected diseases. It also

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

disproportionately impacts firms that may lack the financial resources to self-fund their activities; thus, decreasing prospects of breakthrough innovation by smaller but innovation-agile firms that play a crucial role in neglected disease markets (BVGH & BIO, 2012). Small and medium-sized enterprises (SMEs) play an important role in the development of innovation for neglected diseases being engaged in 41% of drug and vaccine R&D activity (BVGH & BIO, 2012), but they face severe funding constraints and often bear the risks and uncertainty associated with therapy development.

Infectious diseases do not have borders, thus eradication and to some extent herd immunity is a public good, which implies that some countries will free-ride on others' efforts to invest in control and prevention measures. At an individual level there are externalities, implying that the social marginal benefits of infection control are higher than the marginal private benefits, leading to under provision of preventive and infectious control measures.

These factors, combined with the fact that pharmaceutical innovation is costly, lengthy and risky, result in firms focusing on markets that maximize the return on investment and therefore the level of innovation for neglected diseases is suboptimal.

These issues are often used as the rationale for intellectual property rights. Beyond the standard drawbacks of patent systems (e.g. costly patent races, incentives for incremental rather than breakthrough innovation, barriers to entry, pre-emptive patenting, etc.; see Gallini and Scotchmer (2002) for a review), patent systems bring additional challenges in the context of neglected diseases. Patents are associated with lack of affordability in low-income settings where neglected diseases are endemic. And importantly, since markets for neglected diseases are therefore small, the incentives inherent in patent systems are reduced in the context of these diseases.

As a result, market incentives reinforced through a patent system alone are insufficient to stimulate innovation for neglected diseases and should, therefore, be coupled with other incentive mechanisms. In particular, policies related to public and donor financing have an important role to play. These financing policies can aim to build research capacity through the direct funding of innovation, or they can be designed to steer R&D and ensure equity and affordability through the implementation of a set of incentive mechanisms that directly or indirectly affect investment in R&D.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Using incentive mechanisms to stimulate innovation for neglected diseases: an overview

The underlying principle behind these mechanisms is the "delinkage" of the cost of research from market profitability so that the incentive to enter the market is not (or is less) contingent on the ability to charge high prices and recover costs through sales. Push mechanisms reduce upfront costs inherent to R&D activities by subsidizing R&D activities prior to product discoveries (i.e. ex ante). Pull mechanisms, on the contrary, offer a reward contingent on successful product discoveries (i.e. ex post). Hybrid mechanisms combine pull and push incentives.

Push mechanisms work better in settings where developers are capital constrained and risk averse. By subsidizing R&D costs push mechanisms also stimulate competition in innovation by enabling small companies and start-ups that lack capital to develop R&D activities. However, when effort is difficult to monitor and contracts are incomplete with research outcomes not contractable, push incentives lead to moral hazard, resulting in suboptimal levels and scope of innovation (Kremer, 2002).

Adverse selection may also arise. Payers have little insight into the relative chances of success of different R&D targets and the effort exerted in each project. Therefore, push mechanisms may incentivize projects with small chances of success (Kremer, 2002).

Under pull incentives, on the other hand, the risk lies with the innovator, with incentives accruing only when innovation occurs and targets key public health priorities. Innovators are better informed about the risk of investment but also, bearing the risk of development, have a strong incentive to prioritize projects with a higher chance of success and better prospects of social and financial impact. If public health needs are well defined, these pull mechanisms enable the funder to direct incentives to key priority areas as the reward is attributed after the innovation has occurred.

However, these mechanisms benefit larger companies that can leverage capital for R&D. Smaller firms (e.g. biotech companies) that are capital constrained and more risk averse are less likely to benefit from pull incentives. This is particularly relevant in markets where the prospects of profitability are weak or uncertain such as in the case of neglected diseases.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

The extent to which push and pull incentives are effective also depends on the stage of the R&D process they target, given that the costs and risk vary considerably during the R&D process.

Pull incentives require the desired innovation to be specified in advance, so are less likely to encourage basic and fundamental research (Moran et al., 2005; Grace & Kyle, 2009). Push mechanisms, on the contrary, incentivize R&D by decreasing the marginal cost of development and/or by ensuring access to key research inputs through collaboration with key stakeholders, thus favouring the invention phase of the R&D process when compared to pull. The facilitated collaboration with other stakeholders that is inherent to some forms of push mechanism (e.g. public–private partnerships) implies that they are also useful in supporting advanced stages of the R&D process, including regulatory hurdles and market launch.

The effectiveness of pull and push incentives is also likely to vary depending on the type of technology. Drug therapies that target treatment or management of chronic conditions offer a broader prospect for recouping R&D investments than prevention therapies or vaccines. Therapies and vaccines that target larger markets with high willingness and ability to pay for therapies (e.g. HIV) are less risky than smaller markets (e.g. schistosomiasis). Therapeutic areas also differ on scientific challenges and development times and costs. One could expect incentive mechanisms that enable collaboration among different stakeholders with different expertise and inputs to therefore perform better in areas where it is scientifically more challenging to innovate than those mechanisms that bring only R&D subsidization.

In what follows we present an overview of the main types of push and pull incentives. A full discussion of the advantages and disadvantages can be found in Table 3.10.2. Note that, in addition to push and pull mechanisms, pool mechanisms can be seen as indirect mechanisms to incentivize R&D. In pool mechanisms intellectual property and knowledge is "pooled" to enable collaboration in research, technology and knowledge sharing to fast-track R&D (Gold et al., 2007). While these mechanisms relate to intellectual property and knowledge sharing rather than financing mechanisms, they have the potential to substantially decrease the costs and thus incentivize innovation. AMCs, one of the pull mechanisms discussed below, also involves pooling, but in terms of purchasing, rather than intellectual property and knowledge.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.2 *Advantages and disadvantages of incentive mechanisms for innovation and access to innovation*

Type	Mechanism	Commitment timing	Payment timing	Mechanism focus	Monitoring challenges	Intellectual property appropriability	Incentives for access	Disease focus (general versus targeted)/scope for steering social desirable innovation	Time inconsistency	Risk sharing (borne mostly by funder, by developer, shared)	Knowledge sharing/pooling of expertise
Push	Research grants	Pre- and during innovation	Pre-innovation	Advance lump sum funding (depends on the grant where some may cover initial R&D costs while others may not)	Funders are unable to perfectly monitor research activity and effort or use of funds. Moral hazard and misdirection of resources towards other activities is possible	Retained by: Originator unless donor sets IP or price conditions	Pricing or access conditions are not usually specified, hence may neither enable nor hinder access	Can be general but can also target investment towards priority areas with large social benefits, if funder prespecifies conditions of award around breakthrough innovation, otherwise firms can apply for grants with any project so long as private marginal cost is close to zero	Not an issue since grant is not contingent on successful innovation	Mostly borne by funders since grants are awarded ex ante on the premise of a potential product, not on an actual delivery	Both possible if multiple partners involved in innovation are set as precondition for award
	PPPs (PDPs)	Pre- and during innovation	Pre-innovation since funding is provided to alleviate capital constraints	Funding from public or philanthropic donors (covers upfront R&D costs)	Significant monitoring challenges due to large information asymmetries between funders and developers	Varies; IP and pricing conditions may be set	High (variable IP arrangements but most set price or accessibility conditions)	Both possible: funding by government tends to have unrestrictive use while private funding tends to be restricted, although better prioritization of neglected diseases since collaborative agreements are normally independent of market size	Not an issue since funding is not contingent on successful innovation	Borne by funder, i.e. public sector bears most of the financial risk	High between collaborating partners, reduces duplication of efforts and increases scale and scope of activities
	Fiscal incentives	All stages of innovation	All stages of innovation	Tax credits, tax exemptions, tax deductions, tax allowances, e.g. depreciation allowances once inputs are realized (covers R&D costs)	Vary across mechanisms. When inputs are rewarded monitoring is difficult if firms use creative accounting to increase claims. If incentives are pre-innovation, monitoring may be difficult	Retained by: Originator but IP and price conditions may be set for selected markets	Ultimately depends on whether there is passthrough of tax credits onto consumers. Do not generally accommodate provisions ensuring accessibility or affordability but in some cases may require companies to donate licenses to foreign government or non-profit entity (e.g. ND tax credit HR 3156)	Can target specific disease area or groups of diseases/R&D targets normally at the discretion of private developers and may be misaligned with social priorities	Limited scope for time-inconsistency issue since incentives applicable for inputs and not actual product development	Shared between developer and funder. The extent to which risk is shared varies by specific fiscal incentive, the timing of its application in the R&D process and the financial value of the incentive. Fiscal incentives on NTDs tend to reduce expenses on early R&D activities and therefore risk sharing is subject to degree of costs sharing	Some mechanism (e.g. tax credits) require donating licenses to not-for-profit entities enabling knowledge sharing/target different types of innovators allowing pooling from diversified sources of knowledge and expertise, including small firms for whom financial incentives may be crucial for survival in the market
Pull	Transferable Patent Extensions	Pre-innovation	Post-innovation	Reward (ring fences revenues)	Generally irrelevant but rent-seeking behaviour may occur if qualification criteria for an extension are incomplete and nonspecific	Retained by: Originator	Hinders access if innovator applies extension to another blockbuster drug, can limit generic entry of that drug and limit its access and affordability	Targeted towards innovation in critically needed but less profitable areas/High	Not an issue since there is no commitment of extension pre-innovation	Borne by the developer since no upfront funding is involved	Does not enable knowledge sharing/Low since collaboration between different firms is unlikely

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

	Priority review vouchers	Pre-innovation	Post-innovation	Reward (ring fences revenues)	Irrelevant since voucher is granted conditional on the innovation of ND-specific drugs	Retained by: Originator	Early market entry enables faster access in high-income countries. Market based nature of the scheme, however, means that access depends on firms pricing strategies, and therefore does not ensure access to deprived populations where neglected disease may be endemic	Targeted at key areas of need/High since PRV will be used for drugs with highest expected return for firms and valued highly by society	Limited scope for time inconsistency since PRVs are rewarded post-innovation	Borne by the developer since voucher is conditional on innovation for a specific neglected disease being delivered	Low
	Advanced market commitments	Pre-innovation	Post-innovation	Reward (ring fences revenues)	Irrelevant since buyer commits to purchase only upon successful innovation	Retained by: Originator	High (award conditional on negotiated low prices) – attempts to provide short and long-term access for low-income countries but depends on complexity of intervention and facility to scale up production	Targeted/reward output rather than input so less prone to moral hazard allowing effort allocation to socially desired outcome	Time-inconsistency problems can occur in that the government commits ex ante but may not comply with commitment ex post	Developer bears risk entirely during development phase. Post development though there is purchasing commitments by payers mitigating risk for developers	Low since scheme fosters more competition – several companies compete simultaneously to develop the product fastest
	Prizes	Pre-innovation	Post-innovation	Reward (prize)	Irrelevant if prize awarded for finished product. However, if prize is awarded to encourage early-stage research, then monitoring of effort may be difficult	Variable; patent expropriation in some cases, in others IP is retained by originator	Low unless IP is expropriated	Targeting specific diseases/High	Time-inconsistency problem with uncertainty on whether sponsor commits to agreed size of reward post-innovation	Borne by the developer since prize award is fixed and awarded only upon successful innovation	Low scope of collaboration due to the "winner takes it all" nature of the scheme
	Patent buyouts (proposal)	During and post-innovation	Post-innovation	Reward in the form of a prize or premium paid by the government	Generally irrelevant since reward is contingent on successful innovation	Government can acquire patent directly from the innovator and place it in the public domain in exchange for a payment	If patent is bought, it is proposed to be made available publically so it enables lower prices and better access to innovation once rights have been bought out	Targeted/encourages sequential and complementary innovation if the government buys the patent and places in the public domain eliminating need for contracting or licensing	Limited scope for time inconsistency since there is no commitment pre-innovation	Developer bears complete risk of innovation in the development phase	High since the patent is placed in the public domain

IP: intellectual property; ND: neglected disease; NTD: neglected tropical disease; PPP: public–public partnership; PRV: priority review voucher; R&D: research and development.

Source: Authors.

Push mechanisms

Product development partnerships (PDPs)

PDPs are the most common type of public–private partnerships for neglected diseases (Aerts et al., 2017; Widdus, 2005). PDPs may exist as voluntary collaborations between private companies and public funders, but may also involve contract-based stakeholders such as academic centres that provide scientific expertise in drug development (Moran, 2005; Moran et al., 2005; Widdus, 2005). More recently, along with public and private partners (e.g. academia, public funding organizations and pharmaceutical companies) PDPs, and public–private partnerships more broadly, include diverse stakeholders such as regulators, insurers and patient organizations (de Vruehm, de Vlieger & Crommelin, 2019).

In 2017, there were around two dozen PDPs for neglected diseases, most created around 2000 (Borrás, 2017), with most focusing on malaria, HIV/AIDS and tuberculosis (TB). Notable examples are shown in Table 3.10.3 (Munoz et al., 2015; Borrás, 2017).

While focusing on all R&D stages, PDPs are particularly relevant in incentivizing early-stage innovation when firms may not have easy access to capital (Grace & Kyle, 2009) by financing the large upfront R&D cost through public or private funding, or a combination of both (Chapman et al., 2020; Sloan & Hsieh, 2017).

External financing (mainly through the public sector and multiple philanthropic organizations) and amounting to 16% of total "external" R&D funding for neglected diseases (Chapman et al., 2020) reduces the cost of failure for collaborating partners by sharing the risk of failure early on between them, thus incentivizing private R&D (Moran et al., 2005; WHO, 2013). In exchange for funding and research inputs, the developer commits to invest in less profitable products at early R&D stages of basic research and to a reduction in eventual profits. The public sector contributes to the development and/or clinical trial stages that require most of the investment (Moran, 2005). In most cases, PDPs channel funding through pharma partners, who own the rights to the product. In return for those rights, the partner commits to ensuring global access to the product at a reasonable price for those in developing countries (NBR, 2014). Notably in some product development schemes intellectual property rights (IPR) are owned by the partnership, so enabling some pricing control once the innovation is developed and thus promoting affordability and access (Buse

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.3 *PDPs have increased overall investment in R&D and innovation for neglected diseases*

Name of PDP	About/purpose of PDP	Funding amount	Stakeholders involved	Disease focus	Type of technology	Targeted R&D stage	Intellectual property rights implications
Drugs for Neglected Disease Initiative (DNDi)	Collaborative PDP Non-profit R&D organization established in 2003 to fund and manage R&D development for medicines across over 200 partners. DNDi has already delivered eight field adapted and affordable treatments for five deadly diseases, and aims to have delivered 25 new treatments by 2028	€615.5 million (raised by end of 2019). Funding source: 57% public 43% private	**Founding partners:** WHO TDR, MSF, Malaysian Ministry of Health, Kenya Medical Research Institute, Indian Council of Medical Research, Oswaldo Cruz Foundation and Institute Pasteur. **Donors:** 1.Public: Australian Trade and Investment Commission, United Kingdom Department of Health and Social Care, Dutch Ministry of Foreign Affairs, French Development Agency, GIZ, European Commission, etc. 2.Private: BMGF, MSF, Takeda pharmaceuticals, Wellcome Trust, etc.	Visceral Leishmaniasis, Human African trypanosomiasis (sleeping sickness), Chagas, paediatric HIV, filarial infections, mycetoma and hepatitis C	Treatment (drugs)	Drug discovery, translational research, clinical trials and registration and access	Variable per drug DNDi adheres to basic principles stated in its intellectual property rights policy. The overarching theme is that it will ensure that the results of the work carried out under its auspices are disseminated as widely as possible and its products made readily available and affordable in developing countries

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.3 (*cont.*)

Name of PDP	About/purpose of PDP	Funding amount	Stakeholders involved	Disease focus	Type of technology	Targeted R&D stage	Intellectual property rights implications
Medicines for Malaria Venture (MMV)	Collaborative PDP Non-profit product development partnership established in 1999 to fund and manage R&D development and access to antimalarial medicines across around 400 partners in 50 countries (donors and clinical centres in endemic countries)	US$ 350 million (raised by the end of 2018) Funding source: More than 60% private	**Founding partners:** Launched with initial seed finance of US$ 4 million from Government of Switzerland, United Kingdom Department for International Development, the Government of the Netherlands, the World Bank and The Rockefeller Foundation. **Clinical centre partners:** 50 clinical trial sites in sub-Saharan Africa, South-East Asia and South America. **Donors:**	Malaria	Treatment (drugs)	Drug discovery, translational research, clinical trials and registration and access	MMV retains rights to any Intellectual property rights that is essential in allowing them to develop and launch drugs for the benefit of MMV target group. Principles include: exclusivity, royalty-free, transferable Intellectual property rights

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

	MMV has validated more than 19 new malaria drug targets since 1999		1.Public: United States government (USAID, NIH), Australian Government Development of Foreign Affairs and Trade, United Kingdom Government (DFID and DoH), Netherlands Ministry for Development Cooperation, etc. 2.Private: BMGF, Wellcome Trust, GSK, Sanofi, etc.				
TB Alliance	Collaborative PDP Non-profit product development partnership of around 38 partners established in 2000 to fund and manage R&D development and access to TB medicines.	Around US $ 184 million (raised by end of 2019)	**Founding partners:** Launched with issuance of Cape Town Declaration by around 28 partners including BMGF, European Commission, MSF, WHO, World Bank, Wellcome Trust, etc. **Donors:** 1.Public: Australian Aid, United Kingdom FCDO & MRC, USAID,	Tuberculosis	Treatment (drugs)	Drug discovery, translational research, clinical trials and registration and access	TB Alliance's mission includes an explicit commitment to "AAA Mandate" – that all new products will be adopted, available and affordable to those with TB.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.3 (*cont.*)

Name of PDP	About/purpose of PDP	Funding amount	Stakeholders involved	Disease focus	Type of technology	Targeted R&D stage	Intellectual property rights implications
	TB Alliance has more than 30 projects of medical products in the pipeline		Germany Federal Ministry of Education and Research, Netherlands Ministry of Foreign Affairs, Ministry of Foreign Affairs (Republic of Korea), etc. 2.Private: BMGF, The Rockefeller Foundation, EDCTP, Global Health Innovative Technology Fund (Japan), UNITAID, etc.				No further information on Intellectual property rights implications

BMGF: Bill & Melinda Gates Foundation; DFID: Department for International Development; DNDi: Drugs for Neglected Disease Initiative; DoH: Department of Health; EDCTP: European and Developing Countries Clinical Trials Partnership; FCDO: Foreign, Commonwealth and Development Office; GIZ: German International Cooperation Society; MMV: Medicines for Malaria Venture; MRC: Medical Research Council; MSF: Médecins sans Frontières; NIH: US National Institute of Health; PDP: product development partnership; TB: tuberculosis; TDR: Special Programme for Research and Training in Tropical Diseases; WHO: World Health Organization.

Sources: DNDi (2004; 2019a; 2019b; 2023); MMV (2018; 2023a; 2023b; 2023c; 2023d); TB Alliance (2019; 2020; 2023).

& Walt, 2000). Box 3.10.1 provides a case study of a PDP and Table 3.10.3 provides selected examples to show PDPs' common features and differences with regard to IPR.

Box 3.10.1 PDP case study: Medicines for Malaria Venture and Coartem

Who are Medicines for Malaria Venture (MMV)?

A collaborative non-profit product development partnership established in 1999 to fund and manage R&D and access to antimalarial medicines for 400 partners in 50 countries. This includes clinical centres in endemic countries across sub-Saharan Africa, South-East Asia and South America. The mission of MMV is to support specific, targeted interventions to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating the delivery of new, effective and affordable antimalarial drugs.

Funding

US$ 350 million, funding source more than 60% private.

How does the PDP model work?

With financial support from donors including government agencies, private foundations, international organizations, corporations, corporate foundations and private individuals, MMV operates a virtual R&D model bringing together partners from academia and the public and private sectors and uses funds to establish a portfolio of R&D projects for developing antimalarial medicines.

The PDP does not itself have the capacity or infrastructure to undertake early-stage development projects in-house; instead, it relies on its partners for financing and other in-kind contributions (i.e. laboratories and expertise) and then allocates resources to the most promising projects, coordinates partner activities for various stages of the R&D process and manages the project portfolio. The PDP acts as a facilitator, bringing dedicated sources of funding and know-how to committed researchers so they can collaborate on the right projects to fulfil the objectives of the PDP's mission.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Box 3.10.1 (cont.)

IPR and access

When MMV enters into contractual relationships with partners, they encourage partners to work with them to guarantee that malaria drugs that they develop and launch will be accessible to those most in need in malaria endemic countries. This means ensuring first and foremost that agreements made within the PDP meet this public health mission. MMV negotiates for new medicines to be made available at an affordable price – typically with no profit and no loss – through public sector channels.

To achieve this, MMV must retain the rights to any intellectual property arising from the R&D undertaken by their partners. This is essential in allowing them to develop and launch drugs for the benefit of target patient groups. The following principles are applicable to all MMV contracts.

Exclusivity: If MMV does not own the necessary IPR outright, it insists on being granted an exclusive licence to use the "programme intellectual property rights" and any necessary "background intellectual property rights" to develop a drug for malaria and bring it to market. That licence must be worldwide, to ensure maximum flexibility for later-stage activities such as manufacturing and distribution.

Royalty-free: Any such licenses are preferably royalty-free, at least in malaria endemic countries, to help keep costs to a minimum and ensure that the drug will be sold at the lowest price possible in these countries.

Transferable: MMV does not conduct any R&D in-house or any manufacturing and, therefore, requires IPR that can be transferred to other partners – especially manufacturing partners – if necessary.

Portfolio

MMV and partners manage a portfolio of over 65 projects, the largest portfolio of antimalarial R&D and access projects ever assembled. The 2021 portfolio includes 11 compounds in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria and drugs that could support the elimination/eradication agenda.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Box 3.10.1 (cont.)

Notable successful products – Coartem Dispersible

Coartem is an antimalarial paediatric formulation that was developed by Novartis and gained approval by securing a United States Food & Drug Administration (FDA) priority review voucher ("fast-track voucher") in 2009. It is approved in over 80 countries and by several regulatory agencies in Africa, Swissmedic and the EMA, and it is the only artemisinin-based combination therapy which has been approved by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use regulatory authorities. The Coartem combination of artemether and lumefantrine reduces the risk of resistance developing to either agent, and is therefore useful for the treatment of chloroquine-resistant *Plasmodium falciparum* cases.

Despite the wide proliferation of public–private partnerships in recent years, in particular those focused on product development, a systematic review by Aerts et al. (2017) did not find a single impact evaluation related to them, barring one analysis that compared the cost–effectiveness of the PDP model against AMCs and a hybrid scheme (PDP until phase II trials, followed by AMCs later) in the context of immunizations for malaria. While costs were lowest for the PDP scheme, DALYs averted were also the lowest, rendering PDPs a non-cost-effective approach. Most descriptive evidence, however, suggests that PDPs have led to a substantial increase in investment in R&D and innovation for neglected diseases. Between 2009 and 2013, 57% of new approvals in WHO's list of essential medicines were developed through PDPs. PDPs have been particularly successful in vaccine development, with more than 400 PDP-led vaccines under development (Breitstein & Spigelman, 2013); and over half of the vaccines for neglected diseases during the period 2009 to 2013 resulting from PDPs (Cohen, Sturgeon & Cohen, 2014). Despite these promising results, impact evaluations are seriously lacking and consistent data collection and availability of data to analyse cost–effectiveness of PDPs are necessary.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

R&D grants and subsidies

Grants and subsidies are normally in-advance lump sums awarded to fund R&D. They tend to focus on key priority areas identified by funders and cover the initiation of discovery or early stage research. Grants and subsidies constitute the main means to fund R&D adopted by public funders and third parties, contributing to 77% of total R&D funding for neglected diseases (Chapman et al., 2020). They specifically focus on early basic research, preclinical and clinical development stages, but tend to cover a wide range of neglected diseases (WIPO, 2014) and are primarily provided by public and philanthropic sources. This includes, for example, governments that allocate a proportion of their gross domestic product (GDP) such as the USA through the United States National Institute of Health and USAID, or the United Kingdom through the Department for International Development (DFID)[3] and Medical Research Council (MRC), as well as philanthropic organizations such as the Bill & Melinda Gates Foundation (BMGF) and the Wellcome Trust (Chapman et al., 2016). Grant funds are channelled either directly to researchers and developers or through a conduit (20% of research grants) such as public–private partnerships/PDPs with some private sector participation (Pugatch Consilium, 2017), or through non-PDP intermediaries such as the Global Health Innovative Technology Fund (GHIT) and the European and Developing Countries Clinical Trial Partnership. Non-PDP intermediaries generally have a broader funding base than PDPs, supported by science and technology organizations, aid agencies and philanthropic foundations, making them less vulnerable to changes from one donor funding stream (Table 3.10.4).

Evidence of the impact of grants and subsidies on neglected disease-specific R&D is lacking. However, general pharmaceutical industry research suggests that grants and subsidies have a positive effect on R&D investment, and the innovation of new molecules and patent applications (Toole, 2012; Azoulay et al., 2019; Kourouklis, 2021). These effects vary across different stages of drug development – in the case of orphan drugs, they are most pronounced in phase I and phase II of the drug development process (Kourouklis, 2021).

[3] Following a merger in 2020, DFID is now the Foreign, Commonwealth & Development Office (FCDO) in the UK.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.4 *Selected examples of grants intermediaries*

Name of intermediary	About/purpose of intermediary	Funding amount	Stakeholders involved	Disease focus	Type of technology	Targeted R&D stage	Intellectual property rights approach
Global Health Innovative Technology Fund (GHIT)	GHIT fund is a general incorporated association in Japan (PPP), founded in 2012 to facilitate and invest in global partnerships (including PDPs) for the discovery and development of new health technology for infectious diseases prevalent in developing countries	More than US $ 260 million invested at the time of writing	Japanese Government, BMGF and 6 Japanese pharmaceutical companies, and foundations such as the BMGF and Wellcome Trust	Malaria, TB and the 17 WHO defined NTDs	Drugs, vaccines and diagnostics	Discovery, preclinical and clinical stages and registration	Supports open access innovations through its access policy. When product development partners and/or participants are successfully granted a patent deriving from projects invested by the GHIT Fund, product development partners and/or participants will grant royalty-free licenses to users operating in least developed countries as categorized by the United Nations classification and low-income countries categorized by the World Bank classification

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.4 (*cont.*)

Name of intermediary	About/purpose of intermediary	Funding amount	Stakeholders involved	Disease focus	Type of technology	Targeted R&D stage	Intellectual property rights approach
European and Developing Countries Clinical Trials Partnership (EDCTP 1 &2)	EDCTP is an EU funded PPP established in 2014 between countries in Europe and sub-Saharan Africa to enhance research capacity, collaboration and accelerate the development of new or improved medical interventions for the identification, treatment and prevention of poverty-related infectious diseases. EDCTP 1 (2003–2015). EDCTP 2 (2014–2024)	Total fund around € 752.7 million at the time of writing	14 European and 16 sub-Saharan African countries, supported by the European Union, third parties and participating states	TB, HIV, malaria, diarrhoeal diseases, lower respiratory tract infections, other neglected infectious diseases, including emerging and re-emerging infections of particular relevance in sub-Saharan Africa	Drugs, vaccines and diagnostics	Phase I to IV clinical trials, with an emphasis on phase II and III trials and access (product focused implementation research). EDCTP also funds capacity development and international networking	No specific information on Intellectual property rights implications was detected

BMGF: Bill & Melinda Gates Foundation; EDCTP: European and Developing Countries Clinical Trials Partnership; EU: European Union; GHIT: Global Health Innovative Technology Fund; NTDs: neglected tropical disease; PDPs: product development partnership; PPP: public–public partnership; TB: tuberculosis; WHO: World Health Organization.

Sources: GHIT (2013; 2022; 2023a; 2023b), EDCTP (2020; 2022a; 2022b; 2022c).

Fiscal incentives

Fiscal incentives focus on reducing the cost of R&D, raising the long-term rate of return on R&D investments, and include: tax exemptions, tax deferrals, tax allowances and tax credits (OECD, 2016).[4] Some apply to current expenditures, others to capital or revenues. Tax allowance, exemption and deduction consist of reducing the taxable amount by reducing the tax base before the tax liability is computed. With tax credits, in contrast, the tax liability is reduced by subtracting the credit after the liability has been determined. Tax deferrals do not reduce tax liability but defer tax payment. These incentives can be used to target single firms or foster collaboration across firms, with some schemes designed to support SMEs, and they can also be used to target a specific disease area or groups of diseases.

In practice, fiscal incentives for neglected diseases are mostly in the form of tax credits, exemptions and reliefs. Although the R&D phases targeted by fiscal incentives may vary across initiatives, tax incentives for neglected disease R&D have often been considered for encouraging basic and non-clinical research for vaccines or medicinal products (Rao, 2011). By reducing the R&D cost, these incentives encourage innovation in areas of high risk and smaller returns on investment – such as neglected diseases. These particularly benefit SMEs that, while financially constrained, are often agile and innovative in neglected disease innovation (BVGH & BIO, 2012), thus increasing the prospects of breakthrough innovation.

There are two main tax incentive initiatives highlighted in literature (Monroe, Greenberg & Basey, 2015; Pugatch Consilium, 2017). These are the United States Neglected Disease Tax Credit Proposal (HR3156) which mandates a transfer of IPR, and the United Kingdom Vaccine Research Relief which is not necessarily limited to a neglected disease focus, but rather extends to orphan drugs and humanitarian driven innovations (Monroe, Greenberg & Basey, 2015; UK Government, 2016; US Congress, 2009a) (Table 3.10.5).

Given the reduced number of fiscal incentives for neglected diseases, their effectiveness in spurring research for neglected diseases is difficult to ascertain. Rao (2011) argues that tax credits in the United Kingdom did not attract new firms to invest in R&D for neglected diseases and alone

[4] Most fiscal incentives implemented to date subsidize R&D costs and are therefore categorized as "push"incentives. However, fiscal incentives can also be used as "pull"incentive by applying to sales (Webber & Kremer, 2001).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.5 *Fiscal incentives' effectiveness in stimulating neglected disease research is unclear*

Fiscal incentive	About the scheme/incentive nature	Eligibility criteria/ disease focus	Targeted companies	Benefits claimed	Intellectual property rights implications
United Kingdom Vaccine Research Relief (VRR)	Proposed and introduced in 2003, implemented and expired in 2017. In the United Kingdom R&D tax credits were introduced for SMEs in 2000 and extended to large companies from 2002. This is normally done through SME scheme and Research and Development Expenditure Credits (RDEC) (non-neglected disease specific). VRR was introduced as an additional "top-up" relief for vaccines research. All companies may deduct a standard 100% of their R&D expenditure from their taxable income under SME scheme and RDEC. While VRR allows 50% deduction on top for eligible R&D expenditure	HIV/AIDS, TB and Malaria. Expenditures on activities ranging from identification of a chemical entity, or a potential vaccine through completion of Phase III clinical trials	All companies. Large companies claiming VRR can only use the deduction option; they cannot claim payable credits for VRR	Number of claims under the VRR scheme remained at about 10 a year with support claimed of less than £5 million each year between 2003–2004 and on average around £20 million each year in the period up to 2012–2013	No information detected on intellectual property rights implications

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

United States neglected disease tax credit proposal (HR 3156)	Proposed in 2009, no information detected on introduction or implementation. This proposal was put forward by the biotechnology company ("biotech") Genzyme with the sponsorship of Representative Donald Payne and others". 50% tax credit for non- clinical expenses for research on neglected disease treatments	All NTDs (see Table 3.10.1) and any infectious disease with unmet need or disproportionately affecting the poor. Qualified research: Only preclinical or basic research. Companies could not use the credit for expenses incurred from clinical trials or regulatory review. This includes expenses for in-house or contracted research activities undertaken for the purpose of non-clinical basic research only. With this specific criteria of discovering information – which is (i) technological in	All companies. In-house or contracted research services	No information detected on implementation	Mandates a transfer of intellectual property rights and could only apply for the credit if they have donated a royalty-free licence to a foreign government or a non-profit research organization for the claimed research in that year

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.5 (*cont.*)

Fiscal incentive	About the scheme/incentive nature	Eligibility criteria/ disease focus	Targeted companies	Benefits claimed	Intellectual property rights implications
		nature, and (ii) the application of which is intended to be useful in the development of a new or improved business component of the taxpayer			

NTD: neglected tropical disease; SME: small and medium-sized enterprise; TB: tuberculosis; VRR: Vaccine Research Relief.

Sources: US Congress (2009a; 2009b), UK Government (2016; 2020) and European Commission (2008).

are insufficient to increase R&D spending in global health. In contrast, the tax credits created in the Orphan Drug Act (P.L. 97–414) in 1983 have had a significant impact on orphan drug development, leading to 201 new orphan drugs in the market and this trend has been particularly strong in recent years; for example, 18 new drugs gained approval in 2014 (EY, 2015). Yin (2008) shows that the Orphan Drug Act-led income tax credit (equal to 50% of clinical trial expenses) increased the annual flow of clinical trials for drugs for rare diseases by 69%.

Pull mechanisms

Transferable patent extensions

Transferable patent extensions (TPEs) or wildcard patent extensions are a form of supply-side production response intended to encourage R&D for critically needed drugs in less attractive disease areas (Sonderholm, 2009). A successful innovator of a new drug is granted a one-time patent extension (ranging from six months to two years in the USA and five years in Europe) that can be applied to one of the innovator's other drugs or sold to another firm. Such an extension is worthwhile for companies with a drug in their portfolio whose patent is near to expiry, and provide a source of return on investment (Moran, 2005; Sonderholm, 2009; Seabury & Sood, 2017). These incentives can be particularly important for attracting companies to undertake R&D for neglected diseases because the return on investment in neglected disease markets remains insufficient due to limited market size and affordability (Seabury & Sood, 2017). Our review did not yield notable examples of TPEs granted for neglected diseases, but they have been proposed as a potential incentive in the context of developing new antimicrobials to tackle the problem of antimicrobial resistance (AMR) (Spellberg et al., 2007; Spellberg et al., 2008; Outterson, Samora & Keller-Cuda, 2007). Within this context, Outterson and McDonnell (2016) calculate the potential costs of a 12-month extension and conclude that such an extension would cost the USA's health system more than US$ 4.8 billion, making such an extension extremely inefficient.

Patent buyouts

A patent buyout is an outcome-based pull mechanism aimed at delinking returns from price and volume-based sales by acquiring the patent

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

directly from the innovator in exchange for a payment (Batista et al., 2019). The government offers to buy the rights to the patent to encourage innovation and subsequently places the patent in the public domain for unrestricted access. The scheme may specify criteria ex ante to run a prize-like competition or may engage in ex post identification of a suitable patent candidate (Robinson, Ritchie & Kenny, 2020). Patent buyouts add a markup to private market valuations and internalize the social returns to innovation, which in the context of limited market size for neglected diseases, assures innovators a satisfactory return on investment. By abolishing private patent rights, it also fosters access to innovation through lower prices.

Despite the theoretical applicability of buyouts, there is a lack of real-world application and empirical evidence on its effectiveness in the context of neglected diseases. In the context of neglected diseases, patent buyouts have only been proposed within the Medical Innovation Prize Fund (S.2210) as an end-product prize (US Congress, 2007). Theoretical evidence on welfare effects concludes that buyouts rewarding innovators based on observed market outcomes are an effective tool to improve social welfare (Galasso, Mitchell & Virag, 2016; Radhakrishnan, 2016). Outterson (2006) argues that by recovering lost R&D costs, buyouts are a cost-effective method to improve access and health outcomes in LMICs. For example, the lost R&D cost recovery for GlaxoSmithKline's Cervarix human papillomavirus vaccine is as little as US$ 29.2 million. Therefore, for a patent buyout that would cost as little as US$ 30 million, the medicine could be immediately available for millions in LMICs in its generic form.

Priority review vouchers (PRVs)

The PRV scheme enables firms with drugs approved for certain tropical diseases to apply for a voucher that can be used to obtain priority review for an unrelated drug application, so shortening the regulatory agency review time from a standard average of 10 months to a maximum of 6 months (Ridley, Grabowski & Moe, 2006; Gaffney, Mezher & Brennan, 2019; Aerts et al., 2022). Alternatively, the firm can sell the voucher to another firm.

The innovator retains IPR and prices may be unaffordable if this mechanism is not complemented by differential (tier) pricing, donation or a drug access programme.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

At the time of writing, PRV initiatives are primarily offered through the United States FDA's scheme (FDA, 2020). To be eligible, products need to satisfy certain criteria including: approval by the FDA or the EMA; recognition as a product for serious conditions where there is unmet medical need; adequate and well-controlled trials have established that the drug influences a surrogate end-point and there is clinical superiority to other existing therapies. PRVs mostly focus on late-stage clinical development, registration and post-marketing and delivery stages of the R&D model and are commonly awarded to drugs. For a potential blockbuster drug, the value of PRV has been estimated by some experts to be worth anywhere between US$ 50 million to US$ 500 million (Robertson et al., 2012). As of late 2018, seven PRVs had been awarded for neglected/tropical diseases – in malaria, tuberculosis, leishmaniasis, cholera, onchocerciasis (river blindness) and Chagas disease (US FDA, 2017; Cohen, 2018). Since then, the PRV programmes have expanded substantially, with many more vouchers issued across tropical disease, rare paediatric disease and medical countermeasure indications).

Notable examples include: Coartem, which is now a first-line treatment for malaria across Africa and South-East Asia; benznidazole indicated for Chagas disease (in use as early as the 1970s, approved by FDA in 2017); Krintafel, the first new antimalarial in over 18 years (approved in 2018); and Moxidectin, a treatment for onchocerciasis (approved in 2018) (MDGH, 2018; Cohen, 2018) (Table 3.10.6).

Evidence on the impact of PRVs on R&D is hampered by a lack of data; sample sizes are small due to the low number of vouchers issued. PRVs have been found to not significantly impact clinical trial activity for neglected tropical disease (Aerts et al., 2022; Jain et al., 2017) nor for rare paediatric conditions (Hwang et al., 2019) but have been found to increase the likelihood of initiation of large patient trials for paediatric rare disease (Hwang et al., 2019).

Advance market commitments (AMCs)

In AMCs the funder/donor commits to (fully or partially) subsidize the initial purchases of innovative medicines at an agreed price, for an established maximum threshold, to be provided to a specified set of countries. The subsidy is normally only triggered when countries purchase the innovation. The binding agreement is signed before the medicine is developed and contains a full specification of the desired product and use. They also often involve a commitment by the firm to

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.6 *PRVs' impact on R&D is unclear because of a lack of data*

Drug name	Supplier(s)	Year PRV granted	Disease focus	How was the voucher redeemed/traded?	Approach to IPR transfer
Coartem (artemether/ lumefantrine)	Novartis	2008	Malaria	First PRV so market value of PRV was unknown. In 2011, Novartis redeemed the voucher on a BLA for Ilaris (canakimumb) to treat gouty arthritis. FDA declined the application	Innovator retains IPR
Benznidazole	Chemo Research	2017	Chagas	No information found or anonymously redeemed	Innovator retains IPR
Krintafel	GSK	*2018*	*P. vivax* malaria		Innovator retains IPR
Moxidectin	Medicines Development for Global health	2018	Onchocerciasis (river blindness)		Innovator retains IPR

BLA: biologics licence application; FDA: Food & Drug Administration; IPR: intellectual property rights; PRV: priority review voucher.

Sources: FDA (2008; 2017; 2018; 2020) and Wang (2018).

sell at an affordable price (close to marginal cost and below the AMC price) all quantities beyond the agreed subsidization threshold in the agreed countries (Levine, Kremer & Albright, 2005).

By "pooling" purchase commitments across many countries the scheme creates a profitable and less risky market for the developer by establishing volume guarantees. By pooling funding from several donors and negotiating a low price it enables LMICs to access the medicine. The risk is shared by the developer and the funder: while in the development phase costs are born entirely by the developer who still bears fully the risks associated with the scientific challenges of R&D, when innovation occurs the funder commits to a level of demand in participating countries, thus minimizing for the developer the risk associated with low demand and reduced affordability in LMICs (including international advocacy for low prices of novel treatments) (Berndt et al., 2007). For the funder/sponsor the scheme is beneficial as the financial commitment only occurs if a medicine with social value targeting key areas of need is developed and launched in the market.

AMC is intended to focus on clinical development, registration and post-marketing and delivery stages of the R&D model (Pugatch Consilium, 2017). At the time of writing, only two AMCs have been implemented. In 2007, BMGF initiated the first AMC pilot programme targeting the development of pneumococcal conjugate vaccine (PCV) (Gavi-run pilot Pneumococcal AMC) and in June 2020, Gavi launched the second AMC, COVID-19 Vaccines AMC (COVAX AMC) to accelerate access to 1.8 billion COVID-19 vaccine doses for 92 lower-income countries (Gavi, 2022). Price details of the most recent Gavi supply agreement are provided in Table 3.10.7.

With only two AMCs fully implemented, evidence is either descriptive due to a lack of appropriate counterfactuals or based on simulations. For the PCV AMC, Médecins sans Frontières (MSF) indicated that for over 12 years donors have granted more than US$ 1 billion in subsidies to two vaccine producers, GSK and Pfizer (main producers of the vaccine in the market) (MSF, 2020). Although in principle both manufacturers were obliged to cut the price after a predetermined level of doses was sold, or to license their technology to other manufacturers, prices were only marginally reduced and the transfer of technological know-how was not adequate to expand the manufacturer base into LMICs (MSF, 2020). COVAX AMC has also gathered more than US $ 6 billion in funds from governments, foundations and the private sector (WHO, 2021c). Further evidence suggests that the AMC for

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.7 *Selected example of advanced market commitments*

Name	About/purpose of AMC	Funding amount	Stakeholders involved	Eligibility criteria and disease focus	How is AMC awarded?	Type of technology	Targeted R&D stage	IPR implications
PneumoAMC 2009	It was launched by donors in 2009 to accelerate the development of vaccines that meet country needs, scale production and accelerate vaccine uptake, while testing the AMC concept for future applications.	US$ 1.5 billion to the Pneumococcal AMC (as of January 2021).	**AMC donors:** BMGF, Governments of Canada, Italy, Norway, the Russian Federation and United Kingdom. Vaccines rolled out in 45 countries across 3 continents by 2015. **Manufacturers:** GSK, Pfizer and SII	Pneumococcal disease Target product profile required to be prequalified by WHO.	The AMC is delivered through supply agreements with manufacturers where donors make a financial commitment through Gavi alliance to fully or partially finance the purchase of treatments meeting pre-established criteria at a specified price to be distributed on Gavi countries. Specific supply agreements are available on the Gavi Pneumo AMC.[a] Latest AMC was awarded in June 2020 by UNICEF in its capacity as Gavi's procurement agency to SII for its recently WHO prequalified PCV10 product.	Vaccines	Focused mainly on late-stage R&D and launch	Innovator retains IPR

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

					SII received an award of 10 million doses annually (Annual Supply Commitment) from 2020 for a period of 10 years, for a cumulative total of 100 million doses.
					5% of the AMC funds are allocated to SII according to the AMC terms and conditions, representing US$ 75 million. The Tail Price for this agreement is US$ 2.00 per dose (for the 5-dose vial presentation) from 2020 onwards, a reduction of over 30% from the previous lowest Tail Price of US $ 2.90 per dose

[a] Gavi: Supply agreements, https://www.gavi.org/investing-gavi/innovative-financing/pneumococcal-amc/manufacturers/supply-agreementsAMC: advance market commitment; BMGF: Bill & Melinda Gates Foundation; IPR: intellectual property rights; R&D: research and development; SII: Serum Institute of India. WHO: World Health Organization

Sources: Gavi (2020a; 2020b; 2021).

PCV has increased vaccination coverage across 60 countries immunizing over 49 million children and saving 14 to 17 million DALYs through to 2015 (Kremer, Levin & Snyder, 2020; BCG, 2015). Both the PCV AMC as well as a vaccine AMC for malaria, TB and HIV/AIDS have been shown to be cost-effective in modelling studies (Berndt et al., 2007; Tasslimi et al., 2011).

Prizes

Prizes are rewards for innovations that may focus either on the technical specifications of a product or on the desired outcomes it delivers. Prizes may adopt different models but essentially are a pay for performance scheme where the developer receives a lump sum amount if a certain innovation with social impact is achieved (Hollis, 2005a; 2005b; Love & Hubbard, 2007), with the risk borne by the developer. Prizes thus incentivize innovations where social marginal benefits outweigh (or are equal to) marginal costs of development, thus promoting an efficient allocation of innovation effort. Some propose that this mechanism be voluntary, and complement the patent system by imposing structure on market rewards defined on the basis of incremental benefits (Hollis, 2005a; Pogge, 2005); for example, the Health Impact Fund prize scheme proposed by Hollis and Pogge (2008). Others recommend that such schemes be compulsory, with companies forgoing IPR so the developed drug could be made available globally, i.e. also in economically deprived populations (Love & Hubbard, 2009; Syed, 2009; Shavell & Van Ypersele, 1999).

In the context of neglected diseases, prize schemes have mostly been used to reward innovation in relation to a specific disease; however, there have been some schemes that encompass any innovation for neglected diseases (Pugatch Consilium, 2017).

To date, only five of the 11 prize schemes in health targeted neglected diseases (Monroe, Greenberg & Basey, 2015; Pugatch Consilium, 2017), including the Qualcomm Tricorder XPRIZE (run by the XPRIZE Foundation and sponsored by the Qualcomm Foundation), the Health Impact Fund, the EU vaccine prize led by the European Research Council, the Longitude Prize led by Nesta (a United Kingdom innovation foundation) and a combined initiative proposed by Bangladesh, Barbados, Bolivia and Suriname. With a combined funding purse of roughly US$ 130 million, these prizes mostly focus on basic

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

R&D research, preclinical development and post-marketing and delivery stages of the R&D model. Disease fields included treatments for TB, AMR and vaccine cold chain development, with some prizes allowing companies to maintain IPR and others replacing IPR rights with respective prize awards (Table 3.10.8).

Different prize schemes focusing on specific disease areas and sometimes on unmet needs have spurred innovative activity in early stages of R&D. For instance, the Gotham Prize for Cancer research has led to the development of novel approaches to treat cancer (Bernstein, 2008). Similarly, the Dr Paul Janssen Award, aimed at solving unmet medical needs and rewarding scientists for basic or clinical research, has advanced innovation in the treatment of rare diseases such as mosaicism (Johnson & Johnson, 2020). The Prize4Life organization has accelerated discovery of treatment of amyotrophic lateral sclerosis (ALS) through its ALS Prediction Prize scheme (Leone, 2012). While such awards have increased early-stage discovery in critical areas as described above, systematic evidence on the impact of prizes on stimulating R&D for neglected diseases is virtually non-existent.

Policy relevance and conclusions

Since the early 2000s there has been a considerable amount of effort to tackle the global burden associated with neglected diseases by fostering innovation in safe, effective and affordable medicines and prevention. To stimulate R&D investment a complex range of innovative financing mechanisms have been proposed, with most of the funding provided by public, philanthropic and private industry sources. Over the course of the last decade total R&D funding grew by 14%, rising from US$ 3 410 billion in 2010 to US$ 3 876 billion in 2019 (Chapman et al., 2020). And although progress has been made, control of neglected diseases is still largely inadequate and extremely difficult to monitor or evaluate. There is little evidence on the effectiveness of the current mix of innovative financing mechanisms, either at the individual or the collective level.

At the disagregated level the prospect for effective delinkage of R&D from market considerations varies across schemes and specificities of initiatives (in particular, schemes that only partly fund R&D costs only enable partial delinkage; for example, in the case of prizes it can be difficult to measure the expected effects of a registered health product in order to estimate a suitable prize amount). The heterogeneity and lack

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.8 *Selected examples of prizes*

Name	About/purpose of prize	Prize amount	Stakeholders involved	Eligibility criteria and disease focus	How is prize awarded?	Who was awarded?	Type of technology	Targeted R&D stage	IPR implications
XPRIZE Foundation	Milestone inducement prize. Non-profit organization that designs and hosts public competitions intended to encourage technological development to benefit humanity. Many of the prize competitions are not global health or neglected disease specific. In 2008, the Foundation has recently partnered with the Bill & Melinda Gates Foundation to develop a prize for a better TB diagnostic tool	US$ 10 million	Prize partners: BMGF Qualcomm Foundation, ANA, American, Telemedicine Association, Arthur Clarke Center for Human Imagination, Continua Health Alliance, Health 2.0, HIMSS, IEEE, Mems Industry Group, Point Clear Solutions, Open Photonics Inc., Quest, Shimmer, US San Diego Clinical and Translational Research Institute, Wireless Life Sciences Alliance and Xamarin	TB The winning team was required to develop a tricorder device that: (i) accurately diagnose 13 health conditions; (ii) capture five real-time health vital signs; (iii) provide a compelling consumer experience	Any company can enter a competition style prize, with awards to 1st and 2nd place among competing teams from various companies	Pennsylvania-based team, Final Frontier Medical Devices (1st place). Taiwan-based finalist, Dynamical Biomarkers Group (2nd place)	Diagnostics	Clinical testing and registration. The foundation conducts consumer testing at the Altman Clinical and Translational Research Institute. This testing included the same rigour and protocols as a clinical trial but focused on the objectives of the XPRIZE competition	No information found

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

EU Vaccine Prize	Inducement prize competition launched in 2012 by European Commission with more prizes to be offered via the Horizon 2020 Research Funding programme. The prizes intend to accelerate development of vaccines and solve common issues of vaccine access	€2 million	Donors: EU Research Council	Cold chain development for vaccines. Competition criteria, includes alternative ways of formulating, preserving or transporting vaccines	Competition cash prize with a jury appraising submissions and deciding on winner. No particular approach was prescribed and competitors were invited to convince the jury that their solution could respond best to the competition criteria, including alternative ways of formulating, preserving or transporting vaccines	CureVac GmbH (2014)	Vaccines	Discovery, preclinical and clinical stages, and registration	Owner maintains IPR
Health Impact Fund (proposal)	A new proposal by Incentives for Global Health to provide a complementary or alternative to the patent system for development of	A reasonable minimum required is US$ 6 billion per year	Founding partner: Incentives for Global Health. Potential funding partners: Governments, charitable	Pharmaceutical innovations intended for poor patients	The product is supplied at a generic price with a potential mark up for increment health gains, and the developer is	–	Drugs	Discovery, preclinical and clinical stages, and registration	Developer making IPR available for competing manufacturers

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.8 (*cont.*)

Name	About/purpose of prize	Prize amount	Stakeholders involved	Eligibility criteria and disease focus	How is prize awarded?	Who was awarded?	Type of technology	Targeted R&D stage	IPR implications
	pharmaceutical innovations intended for poor patients		foundations or international taxes		not rewarded for the R&D element until it can demonstrate that the resulting product has health value for the intended patients. A 10-year fixed payment contingent on developer making IPR available for competing manufacturers, and calculated according to health impact of developed product				
Longitude Prize	An ex ante inducement prize launched in 2014 awarded to the submission considered most impactful and feasible, currently for a competitive AMR innovation	£10 million prize fund	Lead by: Nesta (United Kingdom). Funding partners: Innovate United Kingdom and Biotechnology Industry	AMR. Any team of innovators from anywhere in the world that can invent an affordable, accurate, fast	Competition style prize, with £8 million pay-out to winner, judged by a Prize Advisory Panel	The first challenge is ongoing with around 50 registered teams	Diagnostics	n/a Testing will take place over the six months following the Prize Advisory	Developer maintains IPR

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

			Research Assistance Council (BIRAC). Supported by: Amazon, BBC, Science Museum, and Marks & Clerk IP services	and easy-to-use point-of-care diagnostic test for bacterial infections that will allow health professionals worldwide to administer the right antibiotics at the right time (prize rules)				Panel's decision. If the Panel judges that the testing confirms that the entry meets the criteria, they will recommend the entry as a potential winner	
BBBS open-source dividend	Proposal by Bangladesh, Barbados, Bolivia and Suriname. Introduced in 2009 and 2015, of an open-source dividend and milestone prizes fund to reward R&D open innovation and access for donor supported markets. Some of the Bangladesh, Barbados, Bolivia and Suriname proposals include the obligation to grant	US$ 100 million for TB. US$ 250 million for Chagas. 10% of donor assistance for health (DAH) to enhance access	BBBS, WHO, and Knowledge Ecology International	Chagas disease, TB, HIV/AIDS, and malaria. Information on technical specification information not found	BBBS developed a prize fund that is endowed through a committee placed in WHO which then allocates prizes to neglected diseases in separate disease-specific proposals each drafted separately. The main objective is to share a percentage of end-product prize money	No information found	Drugs, diagnostics and vaccines	Clinical trials	IPR to be transferred to patent pool

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Table 3.10.8 (*cont.*)

Name	About/purpose of prize	Prize amount	Stakeholders involved	Eligibility criteria and disease focus	How is prize awarded?	Who was awarded?	Type of technology	Targeted R&D stage	IPR implications
	open, reasonable and non-discriminatory licenses to patent pools (such as the UNITAID patent pool)				with those who openly, freely share knowledge materials and technology. Example: The 2015 Development of Low-Cost Rapid Diagnostic Test for Tuberculosis Proposal suggests endowing a $100 million for an entrant TB diagnostic that satisfies criteria set by WHO committee.				

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

	A licensing pool would manage the intellectual property and guarantee that the diagnostic would be made available at an accessible price

AMR: antimicrobial resistance; ANA: All Nippon Airways; BBBS: Bangladesh, Barbados, Bolivia and Suriname; BBC: British Broadcasting Corporation; BMGF: Bill & Melinda Gates Foundation; EU: European Union; HIMSS: Healthcare Information and Management Systems Society; IEEE: Institute of Electrical and Electronics Engineers; IP: intellectual property; IPR: intellectual property rights; TB: tuberculosis; WHO: World Health Organization.

Sources: For XPRIZE: XPRIZE Foundation (2020; 2023), Philanthropy News Digest (2008); for EU Vaccine Prize: European Commission (2014); Health impact fund (Incentives for Global Health (2021)); Longitude prize (Longitude Prize, n.d. a; n.d. b; n.d. c); BBBS: WHO (2011; 2015a; 2015b).

of widespread implementation of these schemes means there is little evidence on whether they succeed in stimulating innovation in key areas of need and the extent to which they may lead to crowding-out of private investment.

From a policy perspective, it is important to assess the extent to which these different funding incentive mechanisms work, as well as their relative cost–effectiveness. This can be achieved by international collaboration in devising and implementing pilot schemes designed to allow an assessment of the factors that hinder or enable a particular mechanism's effectiveness. Yet, to date, the rolling out of these schemes seems to be linked to political will and the strength of their proponents' advocacy rather than the need to gather and examine evidence. For example, tax credits have been considered to have a low uptake as an incentivizing mechanism for R&D in the United Kingdom. The tax credit-based vaccine research relief initiative came to an end in 2017, with United Kingdom assessors having found evidence for minimal or negligible impact on incentivizing R&D uptake (UK Government, 2016). Meanwhile, in the USA, pharmaceutical companies can receive a 20% R&D tax credit (that can be increased to 50% if the neglected disease is low burden), reflecting a contrasting view of the potential effectiveness of this approach (Mueller-Langer, 2013).

Another issue that can be observed among innovative financing mechanisms is their primary focus on "innovation" as an objective rather than "access and affordability". The ultimate desirability of each of these mechanisms relies on the extent to which they either embed or are complemented by provisions to ensure innovation is affordable and supplied in LMICs. Such provisions include knowledge and technology transfer, pricing and financing policies. In their absence, some of the incentives may further widen existing health inequalities, for example by enabling high prices through extending the effects of IPR arrangements. Schemes that combine incentives to foster innovation coupled with specific provisions with regard to weakening IPR and/or pricing arrangements (e.g. AMCs and the Health Impact Fund) are therefore more likely to contribute effectively to tackling neglected diseases in LMICs.

On the collective level, the current push and pull mechanisms remain fragmented and consistently lack a governing overarching framework. Most schemes implemented to date target one or few disease areas, with allocation of resources across neglected diseases

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

largely depending on donors' views of need or particular remit of action. There is no needs assessment that systematically compares the relative needs associated with neglected diseases globally, assesses the costs and benefits of addressing them, and defines guidance on priority-setting for the coordinated global allocation of funding and targeted incentive mechanisms. This state of affairs risks a suboptimal allocation of funding as well as negative spillover effects across initiatives. The relationship between push mechanisms (such as R&D tax credits or PDPs) and pull mechanisms (such as the prizes, patent system, patent pools, AMCs or wildcard extension) is a good example. The Medical Innovation Prize Act (US Congress, 2007) was proposed as a replacement for the patent system, while others such as the earlier United States Orphan Drug act (US Congress, 1983) aim to complement or augment existing patency jurisdictions.

A governance and resource allocation framework that embeds incentive schemes would need to assess their relative ability to generate valuable innovations across the different disease areas, how they interplay with intellectual property regulations, and consequently their implications for affordability. Given that the R&D landscape is not comprehensively mapped or supranationally governed, it is challenging to produce such a framework, hindering the ability to make informed decisions to allocate resources efficiently across key priority areas. As a result, considerable systemic gaps in funding exist across different R&D stages and disease areas. The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property drawn up by WHO's consultative expert working group (WHO, 2012) highlights the key elements desirable in such a framework as being: needs assessment and prioritization; promoting R&D and R&D capacity; transfer of technology; application and management of intellectual property to contribute to innovation and promote public health; improving delivery and access; promoting sustainable financing mechanisms; and establishing and monitoring reporting systems.

Finally, WHO recognizes that the way research is currently funded is integral to the perceived need for better coordination. There are many funders in both public and private sectors, as well as many research organizations in public and private sectors and in partnership between them. Coordination among these actors is strongly needed to identify

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

and manage research priorities. Not only will coordination provide opportunities for pooling resources for donors to fund a multiplicity of research institutions in developing country neglected diseases, but it will also enable the strategic governance of initiatives and inputs made in priority-setting, monitoring and evaluation, coordination and advocacy, and impact assessment (WHO, 2012).[5]

Additional resources

Drugs for Neglected Diseases Initiative [website]. DNDi; 2024 (https://dndi.org).

Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030. Geneva: World Health Organization; 2021 (www.who.int/teams/control-of-neglected-tropical-diseases/ending-ntds-together-towards-2030).

Global Policy and Incentive Mechanism Mapping for Pharmaceutical Innovation [database]; 2025 (https://flourish-user-preview.com/25911008/b6flEFZm-ENW1rXrqSjixB7SqTRyJNmHwtLk-H9hl0cmCDLa-QMJAR3i_-tj4HYf/).

Kremer M, Glennerster R (2004). Strong medicine: creating incentives for pharmaceutical research on neglected diseases. Princeton, NJ: Princeton University Press.

Mueller-Langer F (2009). Creating R&D incentives for medicines for neglected diseases. an economic analysis of parallel imports, patents and alternative mechanisms to stimulate pharmaceutical research. Wiesbaden: Gabler.

Neglected diseases data visualisation [database]. Surry Hills, NSW: Policy Cures Research; 2023 (https://gfinderdata.policycuresresearch.org/pages/data-visualisations/allNeglectedDiseases).

UCL Institute for Innovation and Public Purpose (2018). The people's prescription: re-imagining health innovation to deliver public value. IIPP Policy Report, 2018–10. London: IIPP, Global Justice Now, Just Treatment, STOPAIDS (www.ucl.ac.uk/bartlett/public-purpose/wp2018-10).

Acknowledgements

We are grateful to Nick Jayanth and Daniela Uribe Mateu for their support in data analyses and literature search. Marisa Miraldo acknowledges funding from UKRI as part of the EU's HORIZON-HLTH-2022-IND-13 research

[5] Unless noted otherwise in the chapter text, the book covers developments up until the end of 2023.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

and innovation programme HI-PRIX (Health Innovation Next Generation Payment & Pricing Models), grant agreement #101095593. Views and opinions expressed are, however, those of the author(s) only and do not necessarily reflect those of the EU, nor the granting authority can be held responsible for them.

References

Aerts C et al. (2017). Are public-private partnerships the solution to tackle neglected tropical diseases? A systematic review of the literature. Health Policy.121(7):745–754.

Aerts C et al. (2022). The impact of the priority review voucher on research and development for tropical diseases. Pharmaceut Med.36(3):189–197 (https://doi.org/10.1007/s40290-022-00427-x). Erratum in: Pharmaceut Med.36(6):405.

Arrow K (1962). Economic welfare and the allocation of resources for invention. In: Universities-National Bureau Committee for Economic Research, Committee on Economic Growth of the Social Science Research Council, editors. The rate and direction of inventive activity: economic and social factors. Princeton: Princeton University Press: 609–626 (www.nber.org/chapters/c2144).

Azoulay P et al. (2019). Public R&D investments and private-sector patenting: evidence from NIH funding rules. Rev Econ Stud.86(1):117–152.

Batista PHD et al. (2019). IP-based incentives against antimicrobial crisis: a European perspective. IIC Int Rev Intellect Prop Compet Law.50:30–76 (https://doi.org/10.1007/s40319-018-00782-w).

BCG (2015). The advance market commitment pilot for pneumococcal vaccines: outcomes and impact evaluation. Boston, MA: Boston Consulting Group (www.gavi.org/sites/default/files/document/pneumococcal-amc-outcomes-and-impact-evaluationpdf.pdf).

Belen P et al. (2013). The drug and vaccine landscape for neglected diseases (2000–11): a systematic assessment. Lancet Glob Health.1(6):e371–379.

Berndt ER et al. (2007). Advance market commitments for vaccines against neglected diseases: estimating costs and effectiveness. Health Econ.16:491–511 (https://doi.org/10.1002/hec.1176).

Bernstein E (2008). Gotham Prize honors new cancer research. The Wall Street Journal. 1 April (www.wsj.com/articles/SB120701217876278991).

Bloom N, Schankerman M, Van Reenen, J (2013). Identifying technology spillovers and product market rivalry. Econometrica.81:1347–1393 (https://doi.org/10.3982/ECTA9466).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Borrás S (2017). Instruments of transformative governance. Product development partnerships for neglected diseases. In: 3rd International Conference on Public Policy, Lee Kuay Yew School of Public Policy (NUS), Singapore, 28–29 June (www.ippapublicpolicy.org/file/paper/5942546bae177.pdf).

Breitstein J, Spigelman M (2013). The role of product development partnerships in advancing the development of drugs for unmet needs. Clin Pharmacol Ther.93(6):468–470.

Buse K, Walt G (2000). Global public-private partnerships: part II – What are the health issues for global governance? Bull World Health Organ.78(5):699–709.

BVGH, BIO (2012). Bringing innovation to neglected disease research and development. A joint report by BIO Ventures for Global Health (BVGH) and the Biotechnology Industry Organization (BIO). San Francisco, CA: BIO Ventures for Global Health (https://archive.bio.org/sites/default/files/FINAL%20Biotech%20report.pdf).

Chapman N et al. (2016). Neglected disease research and development: a pivotal moment for global health. Surry Hills, NSW: Policy Cures Research (https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/01/09162330/2016-G-FINDER-report.pdf).

Chapman N et al. (2020). Neglected disease research and development. Where to now? Surry Hills, NSW: Policy Cures Research (https://policy-cures-website-assets.s3.ap-southeast-2.amazonaws.com/wp-content/uploads/2021/04/15055816/G-FINDER-2020_Final-Report.pdf).

Cohen J (2018). Priority review vouchers revitalizing neglected disease drug development. Jersey City, NJ: Forbes (www.forbes.com/sites/joshuacohen/2018/11/05/priority-review-vouchers-revitalizing-neglected-disease-drug-development/#62fbad1665ed).

Cohen JP, Sturgeon G, Cohen A (2014). Measuring progress in neglected disease drug development. Clin Ther.36(7):1037–1042.

Czarnitzki D, Toole AA (2007). Business R&D and the interplay of R&D subsidies and product market uncertainty. Rev Ind Organ.31(3):169–181.

de Vrueh RLA, de Vlieger JSB, Crommelin DJA (2019). Editorial: public–private partnerships as drivers of innovation in healthcare. Front Med (Lausanne).6:114 (https://doi.org/10.3389/fmed.2019.00114).

DNDi (2004). Intellectual property policy. Geneva: Drugs for Neglected Diseases Initiative (https://dndi.org/wp-content/uploads/2018/03/DNDi_Intellectual_Property_Policy.pdf, accessed 23 May 2023).

DNDi (2019a). Annual report 2019. Geneva: Drugs for Neglected Diseases Initiative (https://dndi.org/wp-content/uploads/2020/07/DNDi-AnnualReport-2019.pdf).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

DNDi (2019b). 2019 Financial and performance report. Geneva: Drugs for Neglected Diseases Initiative (https://dndi.org/wp-content/uploads/2020/06/DNDi-FinancialPerformanceReport-2019.pdf).

DNDi (2023). About us – our donors [website]. Geneva: Drugs for Neglected Diseases Initiative (https://dndi.org/about/donors/).

EDCTP (2020). EDCTP2 work plan 2020. The Hague: Europe and Developing Countries Clinical Trials Partnership (www.edctp.org/web/app/uploads/2020/05/EDCTP2-Work-plan-2020-web.pdf).

EDCTP (2022a). The establishment of EDCTP. Cape Town: Europe and Developing Countries Clinical Trials Partnership (www.edctp.org/about-us/the-establishment-of-edctp/).

EDCTP (2022b). EDCTP's investment in research & development. Cape Town, The Hague: Europe and Developing Countries Clinical Trials Partnership (https://edctp.maglr.com/international-partnerships-against-infectious-diseases/edctp-s-investment-in-r-d).

EDCTP (2022c). Public portal of the EDCTP grants system. Cape Town, The Hague: Europe and Developing Countries Clinical Trials Partnership (www.edctp.org/edctp2-project-portal/).

European Commission (2008). State aid N 816/2006 – UK – R&D tax credits for SMEs. Brussels: European Commission (https://ec.europa.eu/competition/state_aid/cases/217831/217831_826025_56_2.pdf).

European Commission (2014). German company wins EU's €2 million inducement prize for innovative vaccine technology. Press release, 10 March. Brussels: European Commission (https://ec.europa.eu/commission/presscorner/detail/en/IP_14_229).

EY (2015). Impact of the Orphan Drug Tax Credit on treatments for rare diseases. London: Ernst & Young.

FDA (2008). Coartem NDA approval letter. Silver Spring, MD: US Federal Drug Authority (www.accessdata.fda.gov/drugsatfda_docs/appletter/2009/022268s000ltr.pdf).

FDA (2017). FDA approves first US treatment for Chagas disease. News release. Silver Spring, MD: US Federal Drug Authority (www.fda.gov/news-events/press-announcements/fda-approves-first-us-treatment-chagas-disease).

FDA (2018). Krintafel NDA approval letter. Silver Spring, MD: US Federal Drug Authority (www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/210795Orig1s000Ltr.pdf).

FDA (2020). Tropical disease priority review voucher program. Silver Spring, MD: US Federal Drug Authority (www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/tropical-disease-priority-review-voucher-program).

Fitzpatrick C et al. (2017). Chapter 17 – An investment case for ending neglected tropical diseases. In: Holmes KK et al., editors. Major

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

infectious diseases, 3rd edition. Washington, DC: International Bank for Reconstruction and Development, World Bank.

Gaffney A, Mezher M, Brennan Z (2019). Regulatory explainer: everything you need to know about FDA's Priority Review Vouchers. Rockville, MD, Regulatory Affairs Professionals Society (www.kidsvcancer.org/wp-content/uploads/2017/09/Everything-You-Need-to-Know-About-FDA%E2%80%99s-Priority-Review-Vouchers.pdf).

Galasso A, Mitchell M, Virag G (2016). Market outcomes and dynamic patent buyouts. Int J Ind Organ.48:207–243.

Gallini N, Scotchmer S (2002). Intellectual property: when is it the best incentive system? In: Maurer S, editor. On the shoulders of giants: colleagues remember Suzanne Scotchmer's contributions to economics. Cambridge: Cambridge University Press, pp. 50–54 (https://doi.org/10.1017/9781316443057.019).

Gavi (2020a). Supply agreements. Geneva: Gavi – The Vaccine Alliance (www.gavi.org/investing-gavi/innovative-financing/pneumococcal-amc/manufacturers/supply-agreements, accessed on 23 May 2023).

Gavi (2020b). Advanced market commitment for pneumococcal vaccines – annual report 2020. Geneva: Gavi – The Vaccine Alliance (www.gavi.org/sites/default/files/document/2021/2020-PCV-AMC-Annual-Report.pdf).

Gavi (2021). Pneumococcal AMC. Geneva: Gavi – The Vaccine Alliance (-www.gavi.org/investing-gavi/innovative-financing/pneumococcal-amc).

Gavi (2022). Covax AMC. Ensuring access to COVID-19 vaccines for low- and middle-income economies. Geneva: Gavi – The Vaccine Alliance (www.gavi.org/gavi-covax-amc).

GHIT (2013). Access policy. Tokyo: Global Health Innovative Technology Fund (www.ghitfund.org/applyforfunding/accesspolicy).

GHIT (2022). Portfolio. Tokyo: Global Health Innovative Technology Fund (www.ghitfund.org/assets/othermedia/GHIT_Fund_Portfolio.pdf, accessed on 23 May 2023).

GHIT (2023a). Investment Overview. Tokyo: Global Health Innovative Technology Fund (www.ghitfund.org/investment/overview/en, accessed on 23 May 2023).

GHIT (2023b). Funding Partners and Sponsors. Tokyo: Global Health Innovative Technology Fund (www.ghitfund.org/overview/partners/en, accessed on 23 May 2023).

Gold ER et al. (2007). A preliminary legal review of proposed medicines patent pool. Montreal: The Innovation Partnership.

Grace C, Kyle M (2009). Comparative advantages of push and pull incentives for technology development: lessons for neglected disease technology development. Glob Forum Update Res Health.6:147–151.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Henderson R, Cockburn I (1996). Scale, scope, and spillovers: the determinants of research productivity in drug discovery. RAND J Econ.27(1):32–59.

Hollis A (2005a). An efficient reward system for pharmaceutical innovation. Working paper. Washington, DC: Knowledge Ecology International (www.keionline.org/misc-docs/drugprizes.pdf).

Hollis A (2005b). An optional reward system for neglected disease drugs. Rio de Janeiro: Working Group on Intellectual Property (GTPI) (https://deolhonaspatentes.org/media/file/Publicacoes/optionalrewards.pdf).

Hollis A, Pogge T (2008). The Health Impact Fund: making new medicines accessible for all. New Haven, CT: Incentives for Global Health.

Hwang TJ et al. (2019). Impact of the priority review voucher program on drug development for rare pediatric diseases. Health Aff.38(2):313–319.

IHME (2019). Global Burden of Disease by DALYs – GBD Compare Viz Hub. Seattle: Institute of Health Metrics and Evaluation (https://vizhub.healthdata.org/gbd-compare).

Incentives for Global Health (2021). Health Impact Fund pilot proposal. New Haven, CT: Incentives for Global Health (https://healthimpactfund.org/pdf/HIF_pilot_proposal_2021_04.pdf).

IQVIA (2019). Pipeline intelligence – providing key decision-makers with comprehensive pipeline data. Durham, NC: IQVIA (www.marketingweb.iqvia.com/iqvia-pipeline-intelligence-social-media/, accessed on 23 May 2023).

Jain N et al. (2017). Association of the priority review voucher with neglected tropical disease drug and vaccine development. JAMA.318(4):388–389 (https://doi.org/10.1001/jama.2017.7467.).

Johnson & Johnson (2020). Johnson & Johnson celebrates role of scientists in society with 2020 Dr Paul Janssen Award for Biomedical Research, part of the Champions of Science initiative. Press release, 20 August. New Brunswick, NJ: Johnson & Johnson (www.pauljanssenaward.com/sites/default/files/pdf/DPJA%202020%20WINNER%20press%20release%208.20.20_FINAL.pdf).

Kourouklis D (2021). Public subsidies for R&D and public sector pharmaceutical innovation. Appl Econ.53(32):3759–3777.

Kremer M (2002). Pharmaceuticals and the developing world. J Econ Perspect.16(4):67–90.

Kremer M, Levin JD, Snyder CM (2020). Advance market commitments: insights from theory and experience. AEA Pap Proc.110:269–273.

Leone L (2012). Prize4Life Announces $50,000 ALS Prediction Prize Winners [blog]. In: Wazoku blog, 13 November (https://blog.wazoku.com/prize4life-announces-50000-als-prediction-prize-winners).

Levine R, Kremer M, Albright A (2005). Making markets for vaccines ideas to action. Report of the Center for Global Development Advance Market

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Commitment Working Group. Washington, DC: Center for Global Development.
Longitude Prize (n.d.a). About the Prize – Why innovation in point-of-care diagnostics is needed (https://longitudeprize.org/about-the-prize/, accessed 23 July 2023).
Longitude Prize (n.d.b). Longitude Prize teams (https://longitudeprize.org/teams/, accessed 23 May 2023).
Longitude Prize (n.d. c). Prize rules (https://longitudeprize.org, accessed 21 June 2021).
Love J, Hubbard T (2007). The big idea: prizes to stimulate R&D for new medicines. Chicago-Kent Law Rev.1519:1534–1543.
Love J, Hubbard, T (2009). Prizes for innovation of new medicines and vaccines. Ann Health Law.18(2):155–186.
Maurer SM (2005). The right tool(s): designing cost-effective strategies for neglected disease research. Report to WHO Commission on Intellectual Property Rights, Innovation and Public Health. Geneva: World Health Organization.
MDGH (2018). US FDA approves Moxidectin for the treatment of river blindness. Press release, 13 June. Southbank, VIC: Medicines Development for Global Health (www.medicinesdevelopment.com/news/u-s-fda-approves-moxidectin-for-the-treatment-of-river-blindness).
MMV (2018). Financial view to 31 December 2018. Geneva: Medicines for Malaria Venture (www.mmv.org/sites/default/files/uploads/docs/publications/2018/MMV_AR2018_Chapter8.pdf).
MMV (2023a). Funding and expenditure. Geneva: Medicines for Malaria Venture (www.mmv.org/about-us/funding-and-expenditure).
MMV (2023b). Clinical centre partners in endemic countries. Geneva: Medicines for Malaria Venture (www.mmv.org/partnering/clinical-centre-partners-endemic-countries).
MMV (2023c). Partnering. Geneva: Medicines for Malaria Venture (www.mmv.org/partnering-opportunities/our-partner-network).
MMV (2023d). Our work. Geneva: Medicines for Malaria Venture (www.mmv.org/our-work).
Monroe R, Greenberg A, Basey M (2015). Re:route: a map of the alternative biomedical R&D landscape. Washington, DC: Universities Allied for Essential Medicines (www.altreroute.com/assets/download/UAEM_Reroute_Report.pdf, accessed 23 May 2023).
Moran M (2005). A breakthrough in R&D for neglected diseases: new ways to get the drugs we need. PLOS Med.2(10):e376.
Moran M et al. (2005). The new landscape for neglected disease drug development. London: London School of Economics and Political Science and Wellcome Trust.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Mrazek MF, Mossialos E (2003). Stimulating pharmaceutical research and development for neglected diseases. Health Policy.64(1):75–88.

MSF (2020). Analysis and critique of the advance market commitment (AMC) for pneumococcal conjugate vaccines. Technical brief. Geneva: Médecins Sans Frontières (https://msfaccess.org/analysis-and-critique-advance-market-commitment-amc-pneumococcal-conjugate-vaccines).

Mueller-Langer (2013). Neglected infectious diseases: Are push and pull incentive mechanisms suitable for promoting drug development research?. Health Econ Pol Law 8:185–208 (https://doi.org/10.1017/S1744133112000321).

Munoz V et al. (2015). Can medical products be developed on a non-profit basis? Exploring product development partnerships for neglected diseases. Sci Public Policy.42:315–338 (https://doi.org/10.1093/scipol/scu049).

NBR (2014). The value of product development partnerships. An interview with Rob Lin. Seattle, WA: National Bureau of Asian Research (www.nbr.org/publication/the-value-of-product-development-partnerships/).

OECD (2016). Tax incentives for R&D and innovation. In: OECD Science, Technology and Innovation Outlook 2016. Paris: Organisation for Economic Co-operation and Development (https://doi.org/10.1787/sti_in_outlook-2016-24-en).

Outterson K (2006). Patent buy-outs for global disease innovations for low-and middle-income countries. Am J Law Med.32(2–3):159–173.

Outterson K, McDonnell A (2016). Funding antibiotic innovation with vouchers: recommendations on how to strengthen a flawed incentive policy. Health Aff (Millwood).35(5):784–90 (https://doi.org/10.1377/hlthaff.2015.1139. PMID: 27140983.).

Outterson K, Samora JB, Keller-Cuda K (2007). Will longer antimicrobial patents improve global public health? Lancet Infect Dis.7(8):559–66.

Philanthropy News Digest (2008). XPRIZE Foundation plans tuberculosis-diagnostics prize with Gates support – October 2008. New York, NY: Candid (https://philanthropynewsdigest.org/news/x-prize-foundation-plans-tuberculosis-diagnostics-prize-with-gates-support, accessed on 23 May 2023).

Pogge T (2005). Human rights and global health: a research program. Metaphilosophy.36(1–2):182–209. (https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1467-9973.2005.00362.x).

Policy Cures Research (2021a). G-FINDER: tracking funding for global health R&D. Surry Hills, NSW: Policy Cures Research (https://gfinderdata.policycuresresearch.org).

Policy Cures Research (2021b). Neglected disease R&D scope. Surry Hills, NSW: Policy Cures Research (https://gfinder.policycuresresearch.org/staticContent/pdf/G-FINDER_ND_R%26D_scope.pdf).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

Policy Cures Research (2023). Neglected diseases data visualisation. Surry Hills, NSW: Policy Cures Research (https://gfinderdata.policycuresresearch.org/pages/data-visualisations/allNeglectedDiseases).

Pugatch Consilium (2017). Charting the course to sustainable innovation in neglected diseases globally. Geneva: International Federation of Pharmaceutical Manufacturers & Associations (www.ifpma.org/publications/charting-the-course-to-sustainable-innovation-in-neglected-diseases-globally/).

Radhakrishnan R (2016). Patent buyout in a model of endogenous growth. Economics Discussion Papers, No. 2016–51 (http://dx.doi.org/10.2139/ssrn.2815628).

Rao A (2011). R&D tax credits – a tool to advance global health technologies? Washington, DC: Results for Development Institute.

Ridley BD, Grabowski HG, Moe JL (2006). Developing drugs for developing countries. Health Aff.25(2):313–324.

Robertson AS et al. (2012) The impact of the US priority review voucher on private-sector investment in global health research and development. PLOS Negl Trop Dis.6(8):e1750 (https://doi.org/10.1371/journal.pntd.0001750).

Robinson L, Ritchie E, Kenny C (2020). Aid-Financed Mechanisms for Technology Development. CGD Policy Paper 176. Washington, DC: Center for Global Development (www.cgdev.org/publication/aid-financed-mechanisms-technology-development).

Romer PM (1990). Endogenous technological change. J Polit Econ.98(5):71–102.

Salter A et al. (2000). Talent, not technology: the impact of publicly funded research on innovation in the UK. Brighton: University of Sussex Science Policy Research Unit.

Seabury S, Sood N (2017). Toward a new model for promoting the development of antimicrobial drugs [blog]. In: Health Affairs Blog, 18 May (https://doi.org/10.1377/hblog20170518.060144).

Shavell S, Van Ypersele T (1999). Rewards versus intellectual property rights. J Law Econ.44(2):525–47.

Sloan FA, Hsieh CR (2017). Health economics. Second edition. Cambridge, MA: MIT Press, pp. 359.

Sonderholm J (2009). Wild-card patent extensions as a means to incentivize research and development of antibiotics. J Law Med Ethics.37(2):240–6.

Spellberg B et al. (2007). Societal costs versus savings from wild-card patent extension legislation to spur critically needed antibiotic development. Infection.35(3):167–74 (https://doi.org/10.1007/s15010-007-6269-7).

Spellberg B et al. (2008). The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

of America. Clin Infect Dis.46(2):155–164 (https://doi.org/10.1086/524891).
Statista (2021). Global pharmaceutical R&D spending 2010–2024. New York, NY: Statista Inc www.statista.com/statistics/309466/global-r-and-d-expenditure-forpharmaceuticals/).
Syed T (2009). Should a prize system for pharmaceuticals require patent protection for eligibility? IGH Discussion Paper No 2. New Haven, CT: Incentives for Global Health (www.healthimpactfund.com/files/DP2_Syed.pdf).
Tasslimi A et al. (2011). Cost effectiveness of child pneumococcal conjugate vaccination in GAVI–eligible countries. Int Health.3(4):259–269.
TB Alliance (2019). Audit of financial statements and supplemental schedule of expenditures of federal awards 2019. New York: TB Alliance (www.tballiance.org/sites/default/files/assets/TBAlliance_2019-Financial-Statement.pdf, accessed 23 May 2023).
TB Alliance (2020). Gaining ground: 2020 Annual Report. New York: TB Alliance (www.tballiance.org/sites/default/files/assets/TBAlliance_2020AnnualReport_0.pdf).
TB Alliance (2023). About us – donors. New York: TB Alliance (https://www.tballiance.org/about/donors).
Toole AA (2012). The impact of public basic research on industrial innovation: evidence from the pharmaceutical industry. Res Policy.41(1):1–12.
UK Government (2016). Vaccine research relief: expiry in 2017. Policy paper. London: HMRC (www.gov.uk/government/publications/vaccine-research-relief-expiry-in-2017/vaccine-research-relief-expiry-in-2017).
UK Government (2020). Research and development tax credits statistics, September 2020. London: HMRC/National Statistics (www.gov.uk/government/statistics/corporate-tax-research-and-development-tax-credit).
US Congress (1983). Public Law 97–414 – Orphan Drug Act. 97th Congress. Washington, DC: US Government Publishing Office (www.govinfo.gov/content/pkg/STATUTE-96/pdf/STATUTE-96-Pg2049.pdf).
US Congress (2007). S.2210 – Medical Innovation Prize Act of 2007. 110th Congress. Washington, DC: US Government Publishing Office (www.keionline.org/misc-docs/SandersRxPrizeFundBill19Oct2007.pdf).
US Congress (2009a). H.R.3156 – To amend the internal revenue code of 1986 to provide a credit against tax for expenses paid or incurred in non-clinical research for neglected diseases. 111th Congress. Washington, DC: US Government Publishing Office (www.congress.gov/bill/111th-congress/house-bill/3156/text).

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

US Congress (2009b). H.R.3156 – SEC. 41. Credit for increasing research activities, 111th Congress. Washington, DC: US Government Publishing Office (www.irs.gov/pub/irs-regs/research_credit_basic_sec41.pdf).

Wang O (2018). Buying and selling prioritized regulatory review: the market for priority review vouchers as quasi-intellectual property. Food Drug Law J.73(3):383–404.

Webber D, Kremer M (2001). Perspectives on stimulating industrial research and development for neglected infectious diseases. Bull World Health Organ.79(8):735–741.

WHO (2007). Sixtieth World Health Assembly. Geneva: 14–17 May 2007. Resolutions and Decisions Annexes. Geneva: World Health Organization (https://apps.who.int/gb/ebwha/pdf_files/WHASSA_WHA60-Rec1/E/cover-intro-60-en.pdf).

WHO (2010). Working to overcome the global impact of neglected tropical diseases: first WHO report on neglected tropical diseases. Geneva: World Health Organization (https://iris.who.int/bitstream/handle/10665/44440/9789241564090_eng.pdf?sequence=1).

WHO (2011). Knowledge Ecology International submission to the World Health Organization Expert Working Group on R&D Financing – Innovative Inducement Prizes. Geneva: World Health Organization (https://web.archive.org/web/20131030231300/https://www.who.int/phi/news/phi_2_kei_prizes_cewg_22june2011_en.pdf).

WHO (2012). Research and development to meet health needs in developing countries: strengthening global financing and coordination. Geneva: World Health Organization (www.who.int/publications/i/item/9789241503457).

WHO (2013). Sustaining the drive to overcome the global impact of neglected tropical diseases. Geneva: World Health Organization (https://iris.who.int/handle/10665/77950).

WHO (2015a). Proposal by Bolivia, Suriname and Bangladesh: prize fund for development of low-cost rapid diagnostic test for tuberculosis. Geneva: World Health Organization (https://web.archive.org/web/20220324021740/https://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_TBPrize.pdf).

WHO (2015b). Proposal by Bolivia, Suriname and Bangladesh: prizes as reward mechanism for new cancer treatments and vaccines in developing countries. Geneva: World Health Organization (https://web.archive.org/web/20190202190710/https://www.who.int/phi/Bangladesh_Bolivia_Suriname_CancerPrize.pdf).

WHO (2021a). Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030. Geneva:

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press

World Health Organization (www.who.int/teams/control-of-neglected-tropical-diseases/ending-ntds-together-towards-2030).
WHO (2021b). Governing health innovation for the common good. Council on the Economics of Health for All. Council Brief No.1. Geneva: World Health Organization (www.who.int/publications/m/item/governing-health-innovation-for-the-common-good, accessed 23 May 2023).
WHO (2021c). GAVI COVAX advance market commitment (AMC) summit. Press release, 2 June. Geneva: World Health Organization (www.who.int/news-room/events/detail/2021/06/02/default-calendar/gavi-covax-advance-market-commitment-(amc)-summit, accessed 23 May 2023).
WHO (2023). Global report on neglected tropical diseases 2023. Geneva: World Health Organization (https://iris.who.int/handle/10665/365729).
Widdus R (2005). Public-private partnerships: an overview. Trans R Soc Trop Med Hyg.99(1):S1–8 (https://doi.org/10.1016/j.trstmh.2005.06.005).
WIPO (2014). Committee on Development and Intellectual Property. Fourteenth Session. 10–14 November. Geneva: World Intellectual Property Organization (www.wipo.int/edocs/mdocs/mdocs/en/cdip_14/cdip_14_inf_12.pdf, accessed 23 May 2023).
XPRIZE Foundation (2020). Consolidated financial statements and independent auditor's report. 21 December. Culver City, CA: XPRIZE Foundation, Inc. and Subsidiaries (https://assets-us-01.kc-usercontent.com/5cb25086-82d2-4c89-94f0-8450813a0fd3/49dbbb00-f689-44f7-a6ce-9bd5b75f9f60/XPRIZE%20FOUNDATION%2C%20INC.-%20FINAL%20AUDITED%20FINANCIALS%202020.PDF).
XPRIZE Foundation (2023). Empowering personal healthcare. Culver City, CA: XPRIZE Foundation (www.xprize.org/prizes/tricorder).
Yin W (2008). Market incentives and pharmaceutical innovation. J Health Econ.27(4):1060–1077.

https://doi.org/10.1017/9781009746274.021 Published online by Cambridge University Press