

# The people's prescription

Re-imagining health innovation  
to deliver public value

October 2018

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## October 2018

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[www.stopaids.org.uk](http://www.stopaids.org.uk)

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# Foreword

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## by Mariana Mazzucato

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and Public Purpose

Innovation is a collective process; it takes a very long time and is highly uncertain. In the health sector, this collective high-risk effort is shared between different types of actors: private businesses (big pharma and small biotech), public institutions (like the National Institute of Health (NIH) in the US and the Medical Research Council (MRC) in the UK), and civil-society-based organisations (eg, patient groups, charities). The public sector also plays a key role on the demand side through its purchase of health products and building of health systems. This report asks how these different actors can come together across the innovation chain to increase not only the rate of innovation, but also its direction so that it is steered towards the areas most needed to create public value.

Outcomes are key. Health innovation is about making new treatments and cures available to the people that need them. Profits might be earned, but not at the cost of doing what the health system is meant to do: heal.

We should act with the same urgency toward improving health as we do when it comes to defence: through mission-oriented thinking. Mission setting requires asking ambitious questions but also very practical ones: What are we trying to achieve? What does winning mean? What is preventing us from achieving the goal? What regulatory changes and new instruments can be used to inspire progress towards a goal, while also enabling bottom-up experimentation?

It also requires being ambitious and taking risks. The mission to go to the moon and back again in one generation required government to dream big and coordinate investments across the entire innovation chain – as much on the supply side as on the demand side. This combination of top-down direction-setting and bottom-up experimentation and exploration is something we can use to stimulate health innovation. And while going to the moon was a purely technological feat, health missions will also require significant social, regulatory, behavioural and political changes. And what is at stake is of the utmost importance: the human right to health, which includes access to essential medicine.

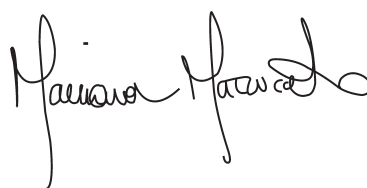
Transforming the current system in a more mission-oriented way requires rethinking the role of policy away from simply patching up market failures, towards co-creating and shaping markets to deliver public value. Key questions are:

- How should different actors distribute themselves across the innovation chain to increase the *rate of innovation*?
- How can concepts of public purpose and public value best ensure that the *direction of innovation* is aimed at those areas most needed by the public?
- How can upstream investment tools be used to negotiate better terms downstream, including affordable prices?
- How can patents be structured to create an effective knowledge governance system that increases innovation rather than blocking scientific collaboration?
- What are the key changes needed to move the sector from one based on profit maximisation towards one based on public value maximisation, for example by using alternative incentives to high prices to encourage innovation?

These questions are key to rethinking the direction of innovation – as well as the way in which the different actors work collectively along the entire innovation chain. The first part of the report outlines the key problems health innovation is facing, and the fundamental pillars that solutions must address: directed innovation and ‘mission’ setting, collaboration and transparency, affordability and access, and finally long-term horizons and patient finance. Part two considers solutions and how to implement change, first by highlighting immediate changes to lower drug prices through pricing strategies and rules around patents. Then more radically considering how to transform the system so that prices are not linked to costs, and how to bring a mission-oriented objective to the way innovation is done in health. Fundamentally, the report learns lessons from actual experiments around the world, with the goal of scaling up those lessons for system change. Lessons are drawn from the US Biochemical Advanced Research and Development Authority (BARDA), the Cuban mission around biotechnology, and the non-profit drug research and development (R&D) organisation Drugs for Neglected Diseases *initiative* (DNDi).

The point is not to cut and paste any particular solution, but to learn from them with an open mind – less ideology and more urgency to do better.

This visionary yet practical report is, in sum, a platform for how we can and must do better.



**MARIANA MAZZUCATO**

# Executive summary

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A thriving health innovation system should generate new health technologies that improve public health and ensure access to effective treatments for the people who need them.<sup>1</sup> However, our current health innovation system fails to direct innovations towards the greatest health needs, and is fraught with inefficiencies: when innovation happens, it happens more slowly and at great cost.<sup>2</sup>

Driven by profit rather than public health, the pharmaceutical sector is incentivised to set high prices and deliver short-term returns to shareholders, rather than focus on riskier, longer-term research which leads to critically needed therapeutic advances. The high prices of medicines are causing severe patient access problems worldwide, with damaging consequences for human health and wellbeing.<sup>3</sup>

These are symptoms of an innovation model that is broken. This report maps the fault lines of this system and sets out principles for a new one. While it does suggest some quick fixes that policymakers can implement in the short term, crucially it proposes concrete policy actions that can be taken in the long term to actively shape and co-create a health system that delivers real public value.

## Diagnosis

Continuing with business as usual is not an option, as our current health innovation model is expensive, inefficient and unsustainable. The first step to addressing these problems is to diagnose the problems of the system and outline the principles for how our health innovation system can be better designed to build a health innovation model that delivers public health.

### Problems with the current health innovation system

Our current health innovation system is failing on multiple fronts, affecting both the rate and the direction of innovation. Such failings affect patient health, innovation and the economy:

#### R&D priorities are not determined by public health needs

A wide range of critical health needs are either not being met or are sidelined, in high-income, middle-income and low-income countries alike. A system driven by profits ignores diseases prevalent mostly in the global south, such as tuberculosis which kills millions.<sup>4</sup> It also incentivises development

of 'me-too' drugs that offer little therapeutic advance and primarily serve to prolong patent protection. Studies have found that more than half of approved medicines in recent years offered no additional medical benefit.<sup>5,6</sup>

#### Lack of transparency and stifled collaboration

As the major incentive for innovation in our current system, intellectual property rights (IPR) need to encourage innovation rather than stifle it. The fact that patents have been made increasingly hard to license, much broader than the downstream area of innovation, and too easy to extend, has led to patents blocking learning, diffusion and dynamic collaborations. Additionally, a systemic lack of transparency (and public accountability) in the underlying research data and methods, in both pre-clinical and clinical trial stages, has severe implications not only for the research process, but also for patient health. A 2016 meta-analysis of 28 studies documenting clinical trial results found that unpublished documents were much more likely to report the occurrence of adverse events than published ones.<sup>7</sup>

## Out-of-reach drug prices

There are no safeguards within the current R&D model to guarantee that medicines – including those developed with public funding – are affordable for the patients who need them. Patent monopolies negate competition, allowing companies to charge the price the market will bear. High prices put pressure on national health budgets and have led to rationing of treatments, for example on breakthrough medicines for hepatitis C and cancer in the UK.<sup>8,9</sup> Pharmaceutical companies argue that prices are proportionate to the intrinsic value of drugs – that is, the costs to society if a disease is not treated or is treated with the second-best therapy available (value-based pricing). According to this argument, higher prices represent more value, with health systems willing to pay now for better future health outcomes from a therapeutic advance. However, this argument obscures the key political-economic drivers of higher prices: short-term financial pressures to increase prices, and monopoly power to set prices at the upper limits of what health systems can bear.

## Short-termism and financialisation

Pharmaceutical companies are increasingly focused on maximising short-term financial returns to shareholders. A common tactic is companies buying back their own shares to boost the value of the remaining ones, hence also boosting the value of stock options. From 2007 to 2016, the 19 pharmaceutical companies included in the S&P 500 Index in January 2017 spent US\$297 billion repurchasing their own shares, equivalent to 61% of their combined R&D expenditures over this period.<sup>10</sup> The use of these funds to boost shares and options, rather than investing in technology and production, leads to value capture by shareholders at the expense of health advances in the public interest.

## Principles for a health innovation model that delivers public value

Recognising the deep dysfunctionality of the current model, we have drawn up core principles that could nurture a better health innovation ecosystem:

### Directed innovation and mission setting

Innovation should be directed towards public health outcomes. This means designing an incentive structure that rewards public health advances rather than market return. This can be achieved through a 'mission-oriented' approach, in which public actors set the directions for innovation aimed at key public health milestones, and policy levers are used to welcome bottom-up experimentation to achieve those goals. Indeed, these are the processes that got us to the moon!<sup>11</sup>

### Collaboration and transparency

Tackling public health needs requires a collaborative environment where actors – public, private and civil society – work together and share knowledge in new and dynamic ways to accelerate innovation. This requires transparency as well as an intellectual property system that incentivises innovation rather than blocking it (eg, the use of narrow patents that are easily licensed).

### Affordability and access

Affordable and accessible medicines are fundamental to the realisation of the human right to health.<sup>12</sup> There is also a clear socio-economic case for supporting these actions in terms of securing a healthy workforce and the positive ripple effects on the economy as well as tax revenues.

### Long-term horizons and patient finance

Innovation is uncertain and can take time; public and private actors thus need to commit to long-term goals. It is also necessary to identify forms of finance that are 'patient' and capable of providing reliable funding to sustain the innovation process, allowing collective learning to accumulate over time while at the same time bearing high risks and inevitable failures.

## Remedies

Solutions to the problems of the current system cannot all be implemented overnight. While some can be implemented almost immediately, others require a more radical transformation of the system. The latter can be based on existing experiments worldwide, which at scale could be used to foster system change.

### **Immediate policy actions: Getting better prices today**

In the short term, immediate actions are needed to address the ongoing crises of access to medicines. Governments should urgently implement pricing strategies and measures based on managing intellectual property rights (IPR) to improve the affordability of vital medicines. These include pooled and volume-based procurement, and increasing transparency around prices – both these measures can improve the bargaining power of public buyers. Policy makers can also make intellectual property work for public health by ensuring that stringent patentability criteria are applied to prevent overly broad patents,<sup>13</sup> as well as making information on patents accessible to increase transparency. Governments can also negotiate agreements around voluntary licenses to improve access to affordable medicines. When this is not possible, compulsory licenses (and government or Crown use) should be actively used. Governments should not implement intellectual property rules that go beyond what is required by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).<sup>14</sup>

### **Transformational change: Re-imagining our health innovation system to deliver public value**

In the longer term, governments must do more than simply treat the symptoms of this fundamentally flawed system, and should instead adopt transformative approaches aimed at a radical shift in the innovation ecosystem to better serve public needs. The transformative proposals listed below are built on the principles of how innovation flourishes.

## **A mission-oriented approach to improving health outcomes**

Governments can set the direction of health innovation by focusing the energy of state, civil society and private sector actors on clearly articulated public health goals. This ‘mission-oriented’ approach has been successful in other areas, driving everything from technological advances in aviation and aerospace to the creation of the internet.<sup>15</sup> We believe the same approach can marshal unprecedented coordination in innovation for health. Government advocacy for long-term targets can also help secure the long-term financial investment required to support complex research and development processes. Mission-driven organisations can also collaborate internationally to address global health challenges. Social movements can play a key role in fostering mission-driven innovation contributing to meeting health challenges.<sup>16</sup>

### **Delinking incentives from high prices**

The current incentive system for drug development is failing to deliver optimal health outcomes and must be reformed. A critical first step is to ‘delink’ the cost of R&D from the price of any resulting product. Innovation can instead be supported through grants or subsidies and rewarded by a variety of prizes, including innovation inducement prizes, market entry rewards, or open source dividends. Because these financing options are public in nature, they can be used to reward the achievement of R&D milestones and stipulate that results be made affordable, creating an innovation system driven by agreed health priorities and dedicated to access. The potential savings from this delinked system, in which new medicines enter the market at non-monopoly generic prices, are vast.<sup>17</sup> We propose steps that can help transition health innovation towards such a model.

### **Achieving public return through conditionality**

If value is created collectively through the involvement of different actors, then the rewards should also be shared to ensure sustainable capital and resources for continued innovation. Instead, under the current system, the public sector plays an essential role



in funding the upstream high-risk research, while the downstream profits disproportionately go to the private sector.<sup>18</sup> A more just sharing of rewards needs to be based on a reinvigorated concept of ‘public value’ – in other words value that is both created *and* shared by the public. This could happen in various ways, including attaching conditions on public funding such as reinvesting profits from innovative products to support future R&D (rather than being hoarded);<sup>19</sup> a commitment to share knowledge and fully disclose data related to R&D, including expenditures and data from failed clinical trials; the possibility of the public retaining a golden share from IPR (and on occasion equity of profits);<sup>20</sup> and a requirement that manufacturers supply treatments on reasonable terms.

### **Changes to corporate governance: Beyond shareholder value**

Transforming innovation requires rethinking the role of the public sector beyond its ‘market failure’ box – acknowledging its role in actively creating markets, not just fixing them. Additionally, the private sector can be better structured. Corporate governance is key. The assumption that companies must maximise shareholder value can be rethought.<sup>21</sup> We should consider, for example: limiting share buybacks that extract value out of healthcare systems to reward shareholders; tying executive compensation to the delivery of therapeutic advances rather than stock price increases; giving taxpayers and patients a voice on corporate boards at pharmaceutical companies; and promoting alternative governance models such as co-operatives, ‘B-Corporations’, community interest companies, and other models with an explicit public value orientation.

### **Conclusions: A practical radical approach**

While this report is visionary, its recommendations are not based on fantasies. There are practical experiments around the world that can serve as stepping stones. This report analyses certain key state-directed, mission-oriented initiatives which incorporate the principles set out in this report. The US government’s Defense Advanced Research Projects Agency (DARPA) and Biochemical

Advanced Research and Development Authority (BARDA) show how government can set the direction of research and provide risk-tolerant funding to support that direction while working with the existing private ecosystem. DARPA is geared to embrace uncertainty and risk of failure in generating ground-breaking innovations for defense purposes, and BARDA puts the mitigation of health threats at the heart of its mission for the public. Examples from Cuba and Germany highlight contrasting processes in delivering missions: Cuba’s state-led, top-down biotech mission illustrates the role the state can play in the creation of an integrated innovation system that ensures access, while Energiewende in Germany shows the importance of combining bottom-up consensus-building and experimentation in civil society with a high-level political agenda in driving mission-led innovation. While governments may differ substantially in how they set about achieving missions, the common lessons in the primacy of the mission-oriented approach in delivering public value resonate across borders.

The report is both radical in its recommendations while also being practical, building on what has worked around the world in health and in other sectors to propose a series of policy recommendations designed to create a more efficient, collaborative, innovative and equitable model for developing effective medicines and ensuring access to them. A key aspect of the proposals is the way they steer and incentivise research investments that deliver public value, through a dynamic network of public, private and non-profit organisations across the entire innovation chain from the supply side to the market-creating demand side (eg, procurement).

As a whole, the report proposes a system of developing and ensuring access to medicines that increases the rate of innovation while also directing it towards health needs, and ultimately creates better value for money than the model we have today. As the number of countries struggling to afford new medicines grows, and patients are increasingly denied access to treatments that could heal them, the question for political leaders and policymakers is not whether they should initiate action to deliver a public-value-centred health innovation model, but when.

# Introduction

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The health sector produces goods and services that are vital for health and well-being; it is from this perspective, first and foremost, that the sector must be understood. Medicines are not luxuries, and access to medicines is paramount to achieving the right to health. Yet the economics of the sector as it stands does not support the Sustainable Development Goal of *producing healthy lives for all at all ages* (SDG 3).<sup>22</sup>

Innovation has both a *direction* (that is, where research efforts are focused) and a *rate* (how quickly research is translated into usable outcomes). Our current health innovation system fails to direct its innovative efforts towards the greatest public health needs, and is fraught with inefficiencies. Firstly, it drives research and development (R&D) priority-setting in the direction of greatest profit, rather than public health priorities or true medical benefit. This can result in prohibitively high prices.

Secondly, the system is not maximising the rate of innovation given available resources. Current economic and regulatory incentives have created a highly inefficient pharmaceutical sector that spends more on marketing than R&D.<sup>23</sup> The sector has become more financialised: an increasing percentage of net income is spent on companies buying back their own shares in order to increase the value per share and boost dividend payouts.<sup>24</sup> And while the justification for share buybacks is often the 'lack of opportunities' for investment, with over 50% of new medicines reaching the market not representing any added therapeutic advance for patients,<sup>25,26</sup> the real issue here is missed opportunities.

Those missed opportunities mean a wide range of critical health needs are not being met or are sidelined. This is the case in high-income, middle-income and low-income countries. In wealthy countries, there is too much focus on 'me-too' drugs (drugs that offer little or no therapeutic advance on existing drugs but are sufficiently different to obtain patent protection) and patent extensions on existing drugs. Disease prevention, vaccines

and much-needed new cures are often sidelined in favour of high-incidence chronic or life-long treatments (such as diabetes), as the latter offer better prospects for sales. There is also a severe lack of investment for conditions that mainly affect people in low-income countries, because these markets are not considered lucrative enough.<sup>27</sup> Ultimately, this is a business model driven by profits rather than public health objectives. In making forecasts for the biotech and pharmaceutical sector, Goldman Sachs analysts aptly asked: "is curing patients a sustainable business model?"<sup>28</sup>

## US National Institutes of Health funding contributed to the basic research associated with all of the 210 new drugs approved by the Food and Drug Administration from 2010–16.

That new medicines are not meeting public needs is especially problematic given that many of them were researched and developed with public money, and public funds are also used to fund the markets (through procurement) for those drugs. The 2018 R&D budget for the US National Institutes of Health (NIH) is US\$37 billion,<sup>29</sup> and since 1938 it has spent a total of US\$742 billion.<sup>30</sup> NIH funding contributed to the basic research associated with all of the 210 new drugs approved by the Food and Drug Administration from 2010–16. This amounted to more than US\$100 billion collectively.<sup>31</sup> In the UK, the Medical Research Council's (MRC) gross research expenditure in 2017–18 was £814.1 million, funded primarily through the public purse.<sup>32</sup> In effect, the public is 'paying twice' for many medicines: in 2016, the National Health Service (NHS) in England spent £1 billion purchasing medicines that had received public investment,<sup>33</sup> and globally some estimate that the public pays for between one- to two-thirds of upfront drug R&D costs.<sup>34,35</sup>

We must fundamentally rethink how we define and talk about health innovation (**box 1**) as well as the way in which the health innovation cycle operates, in favour of a more dynamic and 'directed' division of innovative labour which leads to better outcomes. This is not necessarily about spending more, but about structuring innovation so that it is aimed at public health needs, and inefficiencies are addressed so as to increase its rate of value-creation. Ensuring a fair distribution of risks and rewards among actors is crucial to sustaining further value creation. With research in the health sector heavily subsidised by the public, we need to ensure the public sees a greater return on its investment. Governments are often seen as passive 'market fixers'; but in fact they have the power and legitimacy to actively shape and create markets.<sup>36</sup> They can and should make strategic use of the tools at their disposal to design and incentivise a better health innovation system.

This report is intended to spur policymakers into action by providing ideas, principles and policy proposals to create a better health innovation system that delivers innovative medicines for all who need them. **Chapter 1** articulates the key problems of the current model of pharmaceutical innovation. **Chapter 2** presents the principles that would underpin a public-interest and health-driven approach to pharmaceutical innovation. **Chapter 3**

identifies immediate actions that governments can take today to tackle the urgent crisis in patient access to medicines, which demands solutions now. However, our health innovation system requires a longer-term and substantial overhaul. **Chapter 4** outlines a transformative approach based on mission-oriented research and innovation, learning from experiments across the world. This is used to develop three core policy proposals that embody the principles set out in **chapter 2** and form part of the 'mission' approach advocated here.

The analysis and proposals presented in this report build on the recommendations of the UN High-Level Panel on Access to Medicines<sup>37</sup> and the Lancet Commission on Essential Medicines for Universal Health Coverage.<sup>38</sup> They apply primarily to medicines but may also apply to health technologies in general (which, in addition to medicines, include devices, procedures, diagnostics and vaccines).

This report tackles the problems of our current health innovation system head-on, with a clear diagnosis and a strong prescription, all presented with a practical eye and optimistic spirit. The proposals in this report present practical policy steps to radically transform the incentives and structures of our current system to meet the needs of patients and of public health in general.

## Box 1. What is health innovation?

The WHO Health Innovation Group has adopted a comprehensive working definition of health innovation:

*Health innovation is to develop and deliver new or improved health policies, systems, products and technologies, and services and delivery methods that improve people's health. (...) Health innovation can be in preventive, promotive, therapeutic, rehabilitative and/or assistive care.<sup>39</sup>*

However, the current health innovation system does not match up to this comprehensive definition. On one hand, an excessive focus on 'novelty' (to allow research outcomes to be patented) or on what is 'technologically innovative' does not necessarily translate into improvements in health and patient outcomes. On the other hand, already known or patented compounds, which are not deemed to be inventive enough (and thus not patentable), are not being explored for their potential as medical breakthroughs.

Moreover, the focus on drug development largely overshadows other health technologies and interventions that might improve health and well-being. The importance of innovative ways to improve the adoption, affordability and availability of existing treatments (ie, innovations in access) should be in balance with the quest to invent new treatments.

# I. Diagnosis

The following chapters provide a detailed analysis of the problems with the way health innovation is currently conducted (**chapter 1**), followed by the principles to build a system that can deliver public value (**chapter 2**).

## 1. Problems with the current health innovation system

*We cannot achieve any real progress without acknowledging that the current patent-based business model (...) needs to change. The system is broken. Patent and intellectual property exclusivities are the only cornerstone of the current model. Companies can ask the price they like.*<sup>40</sup>

**Liliane Ploumen, Dutch Minister for Foreign Trade and Development Cooperation, and Edith Schippers, Minister of Health**

The Dutch Ministers' statement reflects the "consensus of dissatisfaction"<sup>41,42</sup> with the present health innovation system, with policymakers, researchers, health practitioners and patients all agreeing that something must change. The existing structure of incentives for innovation (**box 2**) fails to drive innovation towards meeting major health needs at affordable prices. Rather than acting as a 'reward' for carrying out high-risk research to meet a public health goal, these incentive mechanisms have been used as strategic defensive tools to deter competition and maintain a market monopoly.

Innovation is a cumulative process that takes a long time, in which value creation occurs through multiple actors taking risks and investing resources into a long-term uncertain process. The failure to place long-termism and collective value creation at the heart of the system threatens the sustainability of the innovation process itself, while skewing rewards toward a small group of actors. Existing incentives misdirect health innovation towards short-term accumulation for private pharmaceutical companies. The present model also diminishes the public value of therapeutic advances, and restricts access due to the high prices of the resulting medicines.

In this chapter we dissect each of the aspects mentioned above, showing why we must fundamentally and collectively rethink this model to harness society's scientific and technological progress to deliver needed health technologies that are accessible and affordable.

## Box 2. Patents – The right incentives for health innovation? <sup>43,44</sup>

The current system is based on incentivising health innovation through patents. Patents prohibit the manufacture, use or sale of an invention without the patent-holder's permission, for a minimum 20-year period. This market exclusivity is meant to incentivise innovation, and in exchange the invention is disclosed and the public is meant to benefit from the innovation. However, in reality patents provide excessive financial rewards to patent holders, mostly large pharmaceutical companies, as the monopoly created by the patent allows high prices to be set. Meanwhile, the way that patents are written and granted (allowing claims which are very broad) does not necessarily incentivise the innovation that is needed (**section 1.1**). Further, companies seek to extend patent terms beyond the minimum 20 years through practices such as 'evergreening' (**section 1.3**). The World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) is the most relevant international legal framework that sets minimum requirements for the protection of intellectual property for WTO Members.<sup>45</sup>

### 1.1 Research and development priorities are not determined by public health needs

The central goal of health innovation should be to develop novel therapies that represent a major advance in areas of unmet medical need. Yet on this essential measure, the current model of health innovation falls far short.

Disease areas that are not potential 'growth markets' are largely ignored. For example, between 2000 and 2011, only 37 of 850 (4%) of newly approved products were for neglected diseases that affect middle and low-income countries.<sup>46</sup> Conversely, many potential medical research avenues are not being explored simply because they are non-patentable, for example compounds that are already known, previously patented or not novel enough. As AstraZeneca's Craig Wegner has remarked, "Generic drugs found to work for a new disease are in a state of purgatory", since without the possibility to patent there is no financial incentive to bring them to market.<sup>47</sup> Disease prevention and vaccines are often sidelined over high-incidence chronic or life-long treatments (such as diabetes), as the latter offer better prospects for medicines sales.<sup>48,49</sup> The same applies to antibiotics, where the lack of market incentives has led to few investments to develop new compounds, despite an impending global public health crisis.<sup>50</sup> Our current system is structured around the development of single products (ie, new drugs); however, public health problems often require solutions that go beyond single drugs,

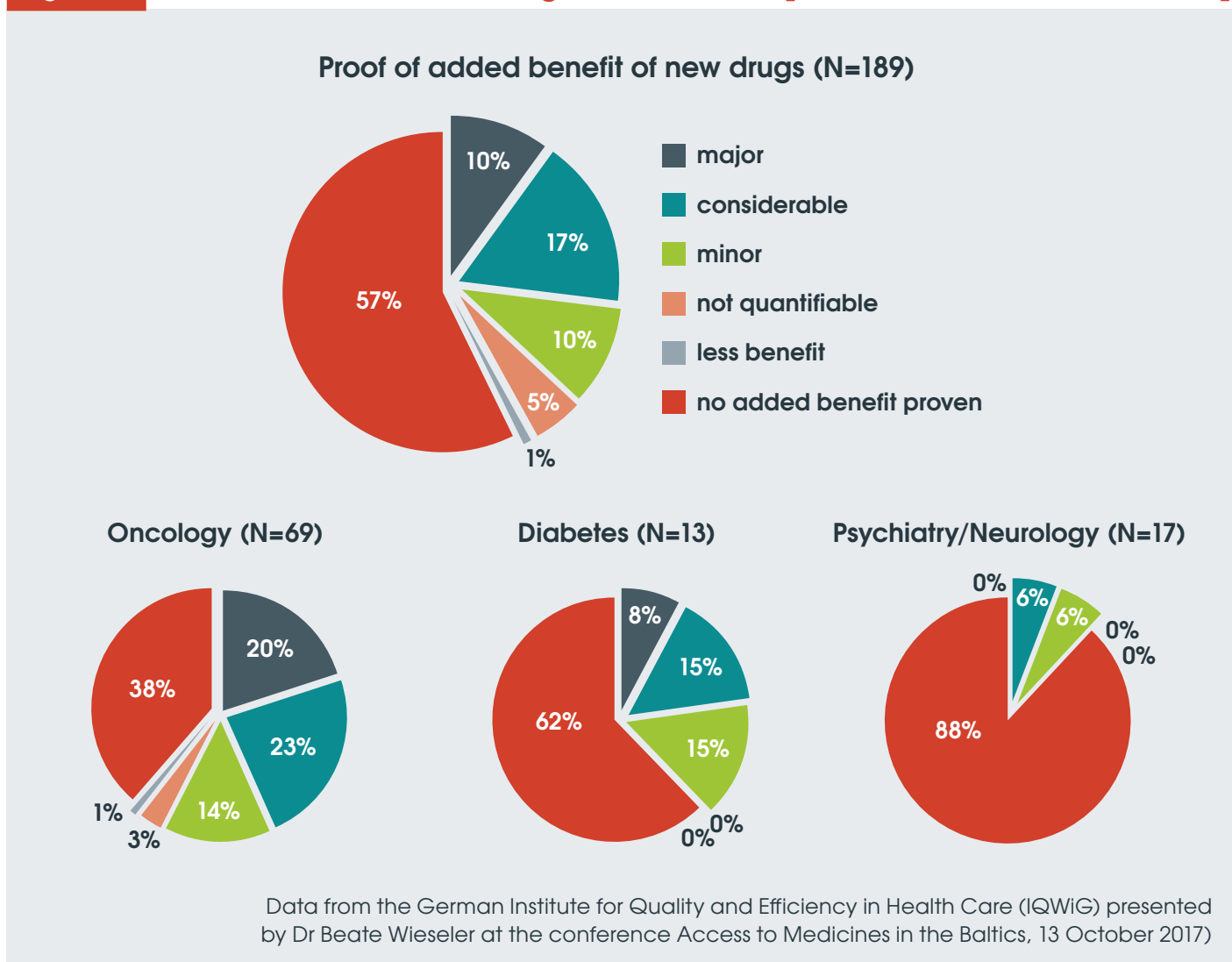
such as interventions and approaches which may include combinations of drugs (treatment regimens), knowledge of how best to administer drugs for different patients (eg children), and diagnostic tools to determine drug susceptibility to maximise patient benefit. Such a comprehensive approach is greatly needed but nevertheless lacking, particularly for drug-resistant infections such as tuberculosis (TB), which require a combination of drugs and where diagnostic solutions play an essential role in treatment design.

Indeed, less profitable non-drug interventions like lifestyle changes, as well as diagnostics and improvement of surgical treatments, are also given less priority over drugs, even when there is already scientific and technical progress that would support the development of these new technologies or methodologies. This is part of the growing trend of pharmaceuticalisation – an over-reliance on drugs to treat health, social and behavioural problems<sup>51</sup> – which contributes to the over-emphasis on drugs in health innovation over other areas like lifestyle or diagnostics.

***Reasonable people can disagree over where the fulcrum between speed and evidence should be placed. But a new drug is only innovative if lives are extended or improved, and we can't know if they will be without more data.***<sup>52</sup>

**The Editorial Board of the New York Times, June 2018**

**Figure 1 The extent that new drugs deliver therapeutic advance in Germany**



While critical medical needs remain unmet, a majority of new medicines developed have no added therapeutic value. In Europe, an analysis of 1345 new medicine approvals between 2000 and 2014 revealed that 51% of newly approved medicines were modified versions of existing medicines and did not offer any additional health benefits.<sup>53</sup> An analysis of the German health technology assessment agency came to a similar conclusion\* (**figure 1**).<sup>54</sup>

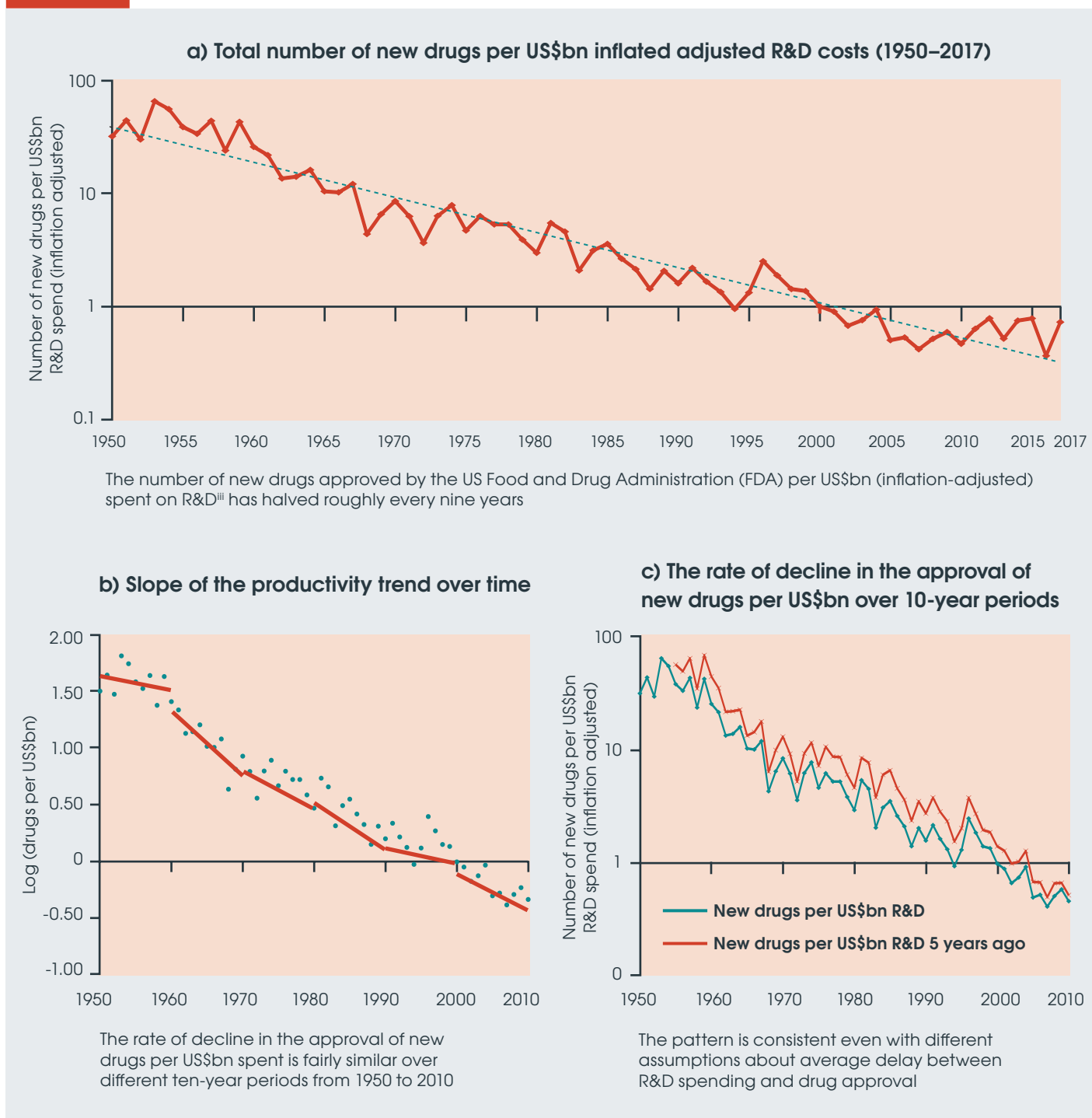
These medicines are known as ‘me-too’ drugs – drugs that offer little or no therapeutic advance in comparison to existing drugs, but which are sufficiently different to obtain patent protection. This situation has occurred due to the incentive mechanisms in the current system, as described in **box 2**, and has been further entrenched by

our regulatory environment. Indeed, to obtain marketing authorisation, sponsors are not required to demonstrate that their products offer therapeutic advance over existing therapies or are needed from a health point of view.<sup>55</sup>

Some industry players have been able to distort and undermine regulatory processes to meet short-term financial targets. Dependent on industry fees, regulatory agencies have become more vulnerable to industry demands for rapid regulatory reviews, which minimise checks on safety and efficacy.<sup>56,57</sup> Such a distorted system for pharmaceutical regulation has severe adverse effects on the health of patients, with less secure evidence about whether the marketed drugs work and many drugs being withdrawn from the market after approval for safety reasons.

\*Because of the pharmaceutical single market, one can assume that these studies are representative of the pharmaceutical innovation levels in the EU.

**Figure 2 Decline of R&D efficiency**<sup>61,i,ii</sup>



- i) Data used is from Scannell, J.W., Blanckley, A., Boldon, H. and Warrington, B. (2012) 'Diagnosing the decline in pharmaceutical R&D efficiency', *Nature Reviews Drug Discovery*, 11(3), pp.191-200 and updated data was received from Jack Scannell.
- ii) In this context, efficiency and productivity refer to the number of new drugs approved per R&D spending.
- iii) R&D costs accounted for here are based only on the Pharmaceutical Research and Manufacturers of America (PhRMA) Annual Survey 2011, which does not include all drug and biotechnology companies. Therefore the PhRMA figures underestimate R&D spending at an industry level. New drugs include the total number of new molecular entities and new biologics approved by the US FDA from all sources, not just PhRMA members. For additional details and main assumptions, see Scannell, J.W., Blanckley, A., Boldon, H. and Warrington, B. (2012) 'Diagnosing the decline in pharmaceutical R&D efficiency', *Nature Reviews Drug Discovery*, 11(3), pp.191-200.

## 1.2 Lack of collaboration and knowledge sharing

In addition to the problem of innovation not being directed to socially useful ends, the current system also fails to optimise the rate of innovation. In other words, it is inefficient. On one hand, many promising biotechnological discoveries are not fully translated into clinical advances.<sup>58</sup> On the other hand, R&D productivity pertinent to scientific discovery – measured by the number of new drugs approved for a given value of R&D spend – has been steadily falling (**figure 2**).<sup>59,60,61</sup> A key reason for such inefficiency is the highly disintegrated nature of the current system, with each actor working in isolation on a specific part of the process, with strong upstream intellectual property rights, leading to insufficient collaboration. This way of working fails to address the complex, non-modular and non-linear problems faced in pharmaceutical R&D.<sup>62</sup>

The biggest players in this market are increasingly specialising away from ‘breakthrough innovations’ in order to maximise profits in the short term. This means disinvesting from riskier upstream research, accessing products that are already in later clinical trial stages through acquisitions, and focusing more on development and patenting.<sup>63,64</sup> These practices are not making the most efficient use of the industry’s vast resources, and in the long term will harm the technical capabilities of the innovation systems.

***Intellectual property in the form of patents should be thought of as a very useful tool with a relatively narrow applicability rather than as a means for owning ever larger swathes of human knowledge which is the way it is being driven at the moment.***<sup>65</sup>

### **Sir John Sulston, 2002 Nobel Prize for Physiology or Medicine**

As the major incentive for innovation in our current system, intellectual property rights (IPR) encourage a protectionist attitude around research, with each actor working in secrecy and isolation. As a result, much research data is not published or shared, which wastes financial resources and causes duplication of scientific efforts in both public and private research. This makes the research process less efficient, and exposes research and its outcomes to bias in favour

of actors’ specific interests (be they financial or scientific). Additionally, patenting is increasingly moving upstream in the research process, so that not only are products being patented, but the tools and processes for research that might lead to those discoveries are being patented as well. This is a trend to which both the private and the public sector have contributed – blocking the ability of new, basic science to be fully disseminated, diffused and translated into future innovation.<sup>66</sup> Nelson and Mazzoleni argue that to incentivise innovation, patents should protect only the area that is fundamentally new (what they call ‘narrow’ patents), and be focused downstream so as to avoid tools and processes being privatised while at the same time enabling licensing and diffusion (what they call ‘weaker’ patents).<sup>67</sup>

A systemic lack of transparency (and public accountability) in the underlying research data and methods both in pre-clinical and in clinical trial stages has severe implications not only for the research process, but also for patients’ health.

Substantial evidence published over the last 20 years shows that drug companies are responsible for commercial bias in drug design, testing and interpretation of results. Comparative efficacy studies may be designed to favour a new, profitable drug by various means.<sup>68,69,70</sup> In the EU, industry must provide detailed trial reports (Clinical Study Reports) to the European Medicines Agency (EMA), but many companies refuse to share these with other public agencies and independent scientists.<sup>71</sup> A 2016 meta-analysis of 28 studies documenting clinical trial results found that unpublished documents were much more likely to report the occurrence of adverse events than published ones.<sup>72</sup>

## 1.3 Out-of-reach drug prices

When the breakthrough treatments do make it to market, they often have price tags that prevent people and health systems from affording them. High drug prices also force difficult choices on national health systems, such as diverting funds or rationing. For example, research indicates that the pricing threshold the NHS uses to assess cost-effectiveness for a medicine – £30,000 for a drug that gives a patient a year of good-quality life – is too high: the authors argue that spending this much on medicines can result in other patients having to experience inferior treatment due to lack of financial resources.<sup>73,74</sup>



### Box 3. Examples of high-priced medicines

**Harvoni** (ledipasvir-sofosbuvir), Gilead's breakthrough hepatitis C drug, is listed\* at £39,000<sup>77</sup> for a 12-week course. This has forced NHS England to ration access to the drug. Patients were told to return for treatment when their condition worsened, with dramatic consequences for an extremely vulnerable patient population.<sup>78</sup>

**Lomustine** (CCNU) is a 40-year-old anti-cancer drug to treat brain tumours and Hodgkin's disease. It was available for years at a price of approximately US\$50 a capsule for the highest dose. Bristol-Myers Squibb sold the medicine to another company in 2013 and its price has been hiked up nine times since and is now priced at US\$768 per pill.<sup>79</sup>

**Deltyba** (delamanid) is one of the first two new anti-tuberculosis (TB) compounds to have become available in over four decades, and is potentially life-saving for patients with multi-drug resistant forms of TB. It costs US\$1700 per six-month treatment. Treatment regimens for drug-resistant forms of TB include several other drugs, some of which are also expensive. Médecins Sans Frontières (MSF) estimates a cost of US\$1000–4500 per treatment course, without delamanid; adding US\$1700 for one single component of the regimen is prohibitively high.<sup>80</sup>

**Phenytoin sodium** is an anti-epilepsy drug manufactured by Pfizer and distributed by Flynn Pharma. In 2012, 100mg packs of phenytoin sodium increased from £2.83 to £67.50 in the UK, a 2600% price rise, after the drug was deliberately de-branded in 2012, making it no longer subject to price regulation. As a result, NHS expenditure on these drugs increased 25-fold in 2013 compared to the previous year.<sup>81</sup>

In recent years, drug prices have soared even further, beyond the reach of patients and public health systems in high-income, middle-income and low-income countries alike, putting pressure on national health budgets (**box 3**).<sup>75,76</sup>

High prices of medicines can have ripple effects beyond public health. The World Bank estimates that high medicine prices lead to an additional 100 million people every year being pushed below the poverty line, as they must choose to buy medicines over other necessities.<sup>82</sup> Overall today two billion people face significant barriers in accessing the medicines they need.<sup>83</sup> There are also economic impacts due to the loss in human capital<sup>84</sup> caused by a reduction in the taxable workforce due to personal ill health or having to take time off from work to become an unpaid carer.

Pharmaceutical companies have traditionally justified high prices by claiming they are necessary to recoup the costs of R&D and ensure investments in lengthy, failure-ridden R&D for future products. However, as described in **section 1.2** and **1.4**, evidence suggests that rights-holders typically spend modest and in some cases very low percentages of revenue on high-risk upstream R&D, compared to what is spent on areas like marketing and share buybacks (see **section 1.4**).<sup>85</sup>

Industry-supported research by the Tufts Center for Drug Development estimated the cost of bringing a successful therapy to market at US\$2.6 billion per newly approved molecule.<sup>86</sup> This figure has, however, been widely disputed.<sup>87</sup> Not-for-profit drug developers Drugs for Neglected Disease *initiative* (DNDi), for example, estimates the cost for the development of a new chemical entity at €100–150 million.<sup>88,89</sup> The lack of transparency around R&D costs (with items like opportunity costs included, which reflect the loss of other revenue-generating opportunities upon investing in R&D) makes it difficult to verify industry claims of high costs.<sup>90</sup>

Industry justifications for high drug prices are also undermined by the key role that public investment plays in R&D. It is estimated that, globally, public bodies pay between one- and two-thirds of all up-front R&D investment.<sup>91</sup> In spite of public funding of R&D, there are no guarantees that drugs developed from publicly funded research will be affordable and accessible. For example, the Innovative Medicines Initiative (IMI) is the EU's biggest public-private initiative on health R&D. The EU contributes 50% of total funding in cash disbursements, while members of the European Federation of Pharmaceutical

\*Actual price may be lower due to negotiated price but this is not publicly available.

## Table 1 Examples of public investment in biomedical innovation

(adapted from Mazzucato and Roy 2017)

Health technology	Public investment	Prices and revenues
<p><b>Sofosbuvir-based treatments for hepatitis C</b></p>	<p>Sofosbuvir was the product of over 10 years of research funded by the US Department of Veterans Affairs and NIH-funded research at Emory University as well as NIH small business innovation grants.<sup>92</sup> Pharmasset then developed sofosbuvir, and was later acquired by Gilead Sciences.</p>	<p>Sofosbuvir was originally marketed at US\$84,000 in the US by Gilead Sciences for a 12-week course at 1 pill a day. In the UK, the list price for a course of treatment was nearly £35,000 (excluding VAT).<sup>93</sup></p> <p>These prices presented a significant barrier to access even in wealthy countries.</p> <p>Sofosbuvir-based products had generated over US\$50 billion in sales for Gilead by the end of 2017.<sup>94</sup></p>
<p><b>Infliximab</b> A monoclonal antibody treatment for autoimmune diseases (eg, rheumatoid arthritis)</p>	<p>A publicly funded lab at New York University, run by Jan Vilcek, worked during the 1970s and 1980s on immune-modulation to develop infliximab in collaboration with Centocor (later, Janssen Pharmaceuticals).</p> <p>The UK Medical Research Council Laboratory of Molecular Biology (MRC LMB) in Cambridge provided long-term public funding for the development of monoclonal antibody research. Today, 65% of therapeutic antibodies use the technology generated from this research.<sup>95</sup></p>	<p>Infliximab, manufactured by Janssen Pharmaceuticals, is the 4th-highest selling medicine of all time, with cumulative sales of US\$85.5 billion through 2016.<sup>96</sup></p> <p>In 2016/2017,<sup>97</sup> it represented the 4th-highest expenditure on a single medicine in the NHS, at £186 million.</p>
<p><b>Abiraterone</b> A treatment for prostate cancer</p>	<p>Abiraterone was discovered by the Institute of Cancer Research (ICR). ICR receives 38% of its funding from charities and the UK Medical Research Council, 16% from royalties and 14% from other government funding and from tuition fees.<sup>98</sup></p>	<p>The NHS spent £172 million on abiraterone from 2014 to 2016. The drug was made available after 5 years of negotiations when Janssen put the price just below the National Institute for Clinical Excellence (NICE) upper limit of acceptable costs.<sup>99</sup></p> <p>By the end of 2016, Janssen's global sales of abiraterone had reached US\$9.7 billion (£7.5 billion).<sup>100</sup> This is in stark contrast to the Institute for Cancer Research, which had earned just £137 million in revenues by the end of 2017, or about two percent of Janssen's sales.<sup>101</sup></p>

Industries and Associations contribute 50% of funding through 'in-kind' (that is, mainly non-cash) contributions. The IMI has been criticised<sup>99</sup> for its lack of measures to safeguard affordable access for the end products from the research.

**Table 1** provides examples of public investment in pharmaceutical innovation and the subsequent high prices of those treatments. The ability to

charge high prices is based on the monopoly protection granted through patents on new drugs. In the absence of competition, companies can essentially charge whatever prices they think the market can bear. In other consumer markets, setting prices is normally constrained by the laws of demand and supply: as suppliers hike up prices, consumers can walk away. But medicines are not

like consumer goods: they are essential for health and wellbeing, and insurers and health systems have little choice but to accept high prices in order to meet their obligations to public health.

## 78% of new medicine patents corresponded to drugs already on the market

The problem of monopoly protection is further exacerbated by the widespread use of 'evergreening' practices to extend patent protection beyond the minimum 20-year period. 'Evergreening' refers to the practice of making minor modifications to an existing invention and then applying for a secondary patent, thus enabling companies to continue extracting monopoly rents through high prices. The HIV drug zidovudine, for example, has had patent protection for decades through evergreening practices.\*<sup>102,103</sup> A study of 1,304 patent claims listed in the US Food and Drug Administration (FDA) Orange Book, which details all new approved drugs, found that the average patent life extension of new medical entities was 6.7 years as a result of secondary patenting.<sup>104</sup> And the practice seems to be on the rise. A recent study reports that, on average, 78% of new medicine patents corresponded to drugs already on the market, with the number of drugs adding a patent almost doubling during the period of the study (2010–15).<sup>105,106</sup>

### Value-based pricing: Is value in the eye of the beholder?

In addition to using R&D investment as a way to account for high drug prices, the industry is also now using a narrative centred on the methodology of Value Based Pricing. They now argue that prices are proportionate to the intrinsic value of drugs – that is, the costs to society if a disease is not treated or is treated with the second-best therapy available. Drug prices are then said to reflect the degree to which new drugs create health and economic value compared to prior standards of care. According to this argument, higher prices represent more value, with health systems willing to pay now for better health outcomes from a therapeutic advance. The companies' appeal to value-based pricing has been criticised on various grounds:

*First, it is far from clear that high prices do in fact reflect social value.* This argument obscures the key political-economic drivers of higher prices: short-term financial pressures to increase prices and monopoly power to set prices at the upper limits of what health systems can bear. Large publicly traded pharmaceutical companies are valued on their projected profit growth over time. Because new product development in health innovation takes many years, companies resort to price rises to generate growth, both on an annualised basis for already approved drugs and when bringing new therapies to market.

This creates an escalator phenomenon for drug prices, with each price setting the floor for the next price. Thus a price for a new health technology may seem 'cost-effective' compared to a prior option, but only because the prior option may have been already priced excessively high. In analysing cancer drugs, health policy scholar Peter Bach observed: "Expensive drugs can still seem deceptively cost-effective, because of the long upward spiral we have seen in the prices of cancer treatments".<sup>105</sup> This upward spiral is possible because of the monopoly power of patents. Companies capitalise on the temporary absence of competition to set high prices. Asymmetry of information on pricing and R&D costs between governments and patent holders puts patients and health systems in a weak position to argue that prices are inflated or to negotiate better prices. Hence prices are artefacts of financial market expectations and monopoly power used to maximise short-term growth, rather than reflective of health improvements.

*Second, even if high prices do reflect the social value, it does not follow that this value should flow entirely to the company that holds the patent and/or exclusive rights.* Value creation is a complex and dynamic process involving many actors. It is untrue to suggest that the value has been 'created' solely by the company that holds the exclusive rights to market it, and hence unwarranted to claim that the company should be able to capture all that value through drug prices. In the long run, this logic actually undermines value creation by short-changing public and non-profit actors who make vital contributions to the innovation process.<sup>108</sup>

\* It should also be noted that GSK publicly announced in 2006 that it would not enforce its AZT drug combination patents.

The process of value creation is often catalysed and sustained by an entrepreneurial, risk-taking state; yet value-based pricing mechanisms do not ensure a return on this investment for the state's value-creating organisations, such as national R&D laboratories. Furthermore, return on investment that goes to pharmaceutical companies primarily benefits shareholders' short-term expectations, through buybacks and dividends, rather than being invested in needed future health technologies (see **section 1.4**).

'Value-based pricing' then becomes a metric not for measuring improved health outcomes, but a method to maximise value extraction. Biotech financial investor Jack Scannell puts it baldly: "value-based pricing evolved as a way of charging customers more."<sup>109</sup>

***What's the value of life? (Value-based pricing) is good for luxury goods because you have a choice ... if I'm sick with cancer, what's the choice? We think value-based pricing is not feasible for products that are indispensable.***<sup>110</sup>

**Dr. Marie-Paule Kieny, Assistant Director-general of Health Systems and Innovation at WHO from 2012 to 2017**

## **1.4 Short-termism and financialisation**

Another challenge to the health innovation system is the way in which pharmaceutical companies are driven by a need to maximise shareholder value, often measured in quarterly financial returns. This 'short-termism' is at odds with the patient, long-term horizons needed for the discovery and development of genuine therapeutic breakthroughs.

**■ This chapter has examined the problems of the current health innovation model and demonstrated that it is inefficient, produces unaffordable medicines, and is not delivering the truly innovative medicines that we need to address public health needs. This model is economically and socially unsustainable, and we cannot afford to ignore this any longer. We need an immediate response to tackle the crisis in patient access to medicines, and also to work towards longer-term systemic change.**

**The next chapter explores the principles that would underpin a better health innovation system.**

**In the last ten years Pfizer has spent US\$139 billion on share buybacks and dividends compared to US\$82 billion on R&D**

Large publicly traded pharmaceutical companies are valued by stock market analysts based in part on their profits, but more so on the anticipation of *growth* in their profits over time. This expectation of near-term and continual growth, signalled through share price, has become the core metric by which shareholders evaluate a company's performance. In order to meet the short-term expectations of stock markets and shareholders, large companies have placed financial manoeuvres at the heart of their business models.<sup>111</sup>

Rather than reinvest accumulated capital into needed R&D, companies are increasingly focused on boosting near-term share price. One of the most common tools to do this is share buybacks, in which companies buy back their own shares to boost the value of the remaining ones to shareholders in equity markets.<sup>112</sup> Pfizer, a company that benefits immensely from government spending on life sciences research and subsidies for drug development, has spent US\$139 billion on buybacks and dividends in the past decade, compared to US\$82 billion on R&D and US\$18 billion in capital spending.<sup>113,114,115</sup> From 2007 to 2016, the 19 pharmaceutical companies included in the S&P 500 Index in January 2017 (and publicly listed from 2006 through 2015), spent US\$297 billion repurchasing their own shares, equivalent to 61% of their combined R&D expenditures over this period.<sup>116</sup> In the case of the pharmaceutical industry, excessive share buybacks have diverted funds from productive activities like R&D, which creates value. They have helped only to artificially inflate the price of an existing asset. By buying back their own shares, companies are effectively passing on their monopoly profits to today's shareholders rather than investing them in future innovation.

## 2. Principles for a health innovation model that delivers public value

Health innovation policy must build on the key characteristics of how innovation comes about. First, innovation is **uncertain**. Results – including the odds of success – are not known at the outset. Serendipitous discoveries, when the search for one thing leads to the discovery of another, are common. For example, the serendipitous discovery of penicillin by Alexander Fleming<sup>117</sup> changed the course of medicine. Some estimates say that 35% of all anticancer drugs in clinical use in 2012 were discovered by serendipity.<sup>118</sup> This means there is no linear process from basic research to commercialisation, which in turns means innovative actors must be able to bear failure and take detours to succeed.

Second, innovation is **cumulative**. Today's efforts rest on what was learned yesterday, and future achievements crucially depend on present (and past) ones. This means that information silos are detrimental to future innovation – sharing knowledge is essential.

Third, innovation is **collective**. Maximising the efficiency of the innovation system means creating ways for diverse actors, from the public, private and non-profit sectors, to work together dynamically, and to share rewards in proportion to the risks taken.<sup>119</sup> Rather than promoting the financial practices of *value extraction*, an equitable sharing of risks and rewards contributes to public value creation.

Finally, innovation requires **long-term commitment and investment**. Because innovation is uncertain, it requires an accumulation of knowledge over time and collective action by diverse actors, as well as long-term horizons to achieve desired outcomes.<sup>120</sup>

In this chapter we propose a thought experiment in order to define the key pillars of a new, alternative health innovation model that delivers public value:

- **Directed innovation and 'mission' setting:** Innovation should be directed towards public health outcomes. Missions are a powerful way to do this. Mission-oriented approaches for health innovation can help in designing an incentive structure that rewards public health advances rather than market return.

- **Collaboration and transparency:** Tackling public health needs requires a collaborative environment where actors work together in new, dynamic ways and share knowledge to accelerate innovation.
- **Affordability and access:** It is imperative that affordability and access are an explicit objective within the innovation process.
- **Long term horizons and 'patient' finance:** We need to identify forms of finance that are 'patient', namely capable of providing reliable funding to sustain the long and uncertain innovation process.<sup>121</sup>

Mirroring the problems discussed in **chapter 1**, we propose ways in which each of these problems can be transformed (**Table 2**) into an opportunity to build a dynamic, sustainable, inclusive health innovation ecosystem that delivers public value (**box 4**).

We envision public funding playing a far more strategic role in steering and shaping health innovation than it does today, in directions that more closely meet the needs of the public health system. A mission-oriented system is just as much about the direction as it is about the relationships: giving governments the opportunity to negotiate much better deals.<sup>122</sup> A stronger public steer driven by social value would be effective in building pressure to create a more long-termist approach, and to reverse the problems of financialisation, short-termism and profit-driven innovation. Thus, the role of public policy should not be seen as an 'intervention' but as a dynamic part of shaping and creating markets that meet public health needs.

***Making public value better justified, appreciated and evaluated would potentially open up a new vocabulary for policy makers. Rather than being mere 'regulators' of health care or the digital agenda, as co-creators of that care and digital transformation policymakers would have a more justifiable right to make sure that the benefits are accessible to all.***<sup>123</sup>

Mazzucato 2018, *The Value of Everything*

## Box 4. What is public value?

Policies that create public value improve the lives of citizens and society more broadly in ways that would not otherwise occur in pure market economy focused on maximising market (or shareholder) value. Public value can be enhanced by governments and citizens co-creating policies and shaping markets, reflecting the mutual obligations of one party to another.<sup>124</sup>

In this sense, the concept of public value is broadly aligned with that of public interest, albeit much more specific. The concept of public interest is an ideal for the wellbeing of society as a whole, but it is not tied to any specific action or policy. By contrast, public value is connected to specific public policies, and in many cases can be measured and evaluated.

Public value goes beyond the notion of public good. Public goods refer to a class of products whose consumption is non-rivalrous (consumption by one individual does not impede that by another) and non-excludable (consumption is fully open to everyone), such as street lighting or national defence. They are subject to free-riding, which means people can access and utilise public goods without paying for them. As a result, the market has little incentive to produce sufficient public goods (a market failure), making their provision largely reliant on the state.

Public value provides a new way to frame public policies: rather than fixing market failures, the state proactively co-creates and co-shapes markets with multiple actors to deliver societal benefit.<sup>125</sup>

**Table 2** Moving towards an alternative health innovation model

What we have now	Feature/pillar of an alternative model	Benefits of the new health innovation model
Research and development (R&D) priorities are not determined by public health needs	Direction for innovation is set towards purpose-led missions for maximising health outcomes ( <b>section 2.1</b> )	Urgent public health needs are prioritised Innovation that delivers true therapeutic advance is encouraged Interests of patients are safeguarded over private interests
Lack of collaboration and knowledge sharing	Dynamic, collaborative system with transparent and publicly accountable scientific data at all stages, including clinical study design and outcomes  International solidarity to tackle global health issues ( <b>section 2.2</b> )	Increased rate of innovation Interests of patients worldwide are safeguarded over private interests
High drug prices for new drugs and increasing prices for already approved drugs	Affordability for patients and better access to medicines and health technologies ( <b>section 2.3</b> )	Access to medicines for all, worldwide
Short-termism based on financialised practices to meet the expectations of near-term and continual growth	Long-term horizons supported by 'patient' finance ( <b>section 2.4</b> )	Sustainable R&D and innovation process capable of bearing scientific failures

## 2.1 Directed innovation and 'mission' setting

Innovation has not only a rate but also a direction. Indeed, periods of high innovation have often been times when innovation was not an inevitable outcome left to markets, but a result of strategic decision-making by both governments and business. Setting directions for health innovation through purpose-led missions (**box 5**) involves decisions about what disease areas to address or prioritise, and identifying unmet health needs that require new treatment options.

The direction for health innovation can learn from how missions have been set in other policy areas (eg, some aspects of defence and energy policy), with national or social problems driving the agenda. In these cases, a direction is set by public institutions with clear targets, with collaborations required across multiple sectors, with government levers (eg, prizes, procurement etc) used to nurture bottom-up experimentation and learning that are critical to a healthy innovation system.

Mission-oriented research and innovation requires a new lens on the role of government. Innovation that has led to general-purpose technologies has often been the result of large public investments aimed at solving important societal and technological problems. The technologies that have made Apple's i-products 'smart' were initially funded by different

public-sector mission-oriented institutions: the internet by the Defense Advanced Research Projects Agency (DARPA); global positioning system (GPS) by the US Navy; touchscreen display by the Central Intelligence Agency (CIA); and the voice-activated personal assistant Siri also by DARPA.<sup>126</sup> Given the amount of public funds in the health innovation system, there is a need to make sure that such funds are more explicitly directed at meeting problems set by public health needs, with metrics in place to evaluate the outcomes based on whether public value was achieved.<sup>127</sup>

In the health sector, the degree to which research can be 'directed' toward meeting public health objectives depends upon the incentive structures and regulatory environment that underpin it. Incentives to carry out innovation must be configured so that actors are rewarded for socially optimal benefits such as allowing the open flow of knowledge and ensuring the affordability of their innovations (see **section 4.2**). Similarly, regulation should support the right type of therapeutic innovation while at the same time safeguarding patients' health and interests. In other words, market approval should be granted to products that have been subjected to transparent, gold-standard comparative clinical trials that demonstrate an added therapeutic advance for patients (unless exceptions should be made.)\* Ultimately, governments have the power and the responsibility to set up, promote and safeguard a regulatory system that prioritises public health interests.

### Box 5. Mission-oriented innovation policy (from Mazzucato 2018)<sup>128</sup>

Mission-oriented policies can be defined as systemic public policies that draw on frontier knowledge to attain specific goals, or "big science deployed to meet big problems".<sup>129</sup> Missions provide a solution and an approach to address the numerous challenges that people face in their daily lives. Whether that is to have clean air to breathe in congested cities, to have access to digital technologies that improve public services, or to have better and cheaper treatment of diseases like cancer or obesity. To engage research and innovation in meeting such challenges, a clear direction must be given, while also enabling bottom-up solutions. The debate about directionality should involve a wide array of stakeholders, each contributing to the key questions: What are the key challenges facing society? How can concrete missions help solve those challenges? How can the missions be best designed to enable participation across different actors, bottom-up experimentation and system-wide innovation? The missions approach is currently guiding the way in which the European Commission is framing and guiding its innovation funding towards social challenges (in the Framework 9 Horizon Programme).

\*Exceptions should be made where accelerated approval is required for urgent access or when it relies on good predictors of clinical outcomes. Additionally, exceptions could be made for medicines or diseases where such a trial was agreed to be impossible or extremely difficult (eg, small patient populations).

## 2.2 Collaboration and transparency

It is collaboration and transparency that maximise the rate of innovation.<sup>130</sup> Tackling public health problems requires a collaborative environment where actors – public, private and civil society – work together in new and dynamic ways.<sup>131</sup> There is no such thing as a clear-cut division of labour where the public sector focuses *only* on scientific research, while the private sector *only* does applied research and development. Rather, the process involves actors interacting across the *whole* innovation chain, with public funding covering both upstream and downstream areas, and profits from private initiatives being reinvested back into further innovation.<sup>132,133</sup> A key feature of collective endeavours is continuous exchange within and across sectors, which allows the creation and diffusion of knowledge. While patents may be required to incentivise innovation by allowing firms to profit from inventions, overprotection can stifle innovation by locking away know-how that the next generation of inventions needs to build on. This is because innovation thrives when knowledge is diffused and shared.<sup>134</sup>

A knowledge commons perspective (**box 6**) that promotes open knowledge, transparency, collaborative innovation and an ability to share creative, scientific and technological resources is key to turning fundamental discoveries into new treatments.<sup>135,136</sup> This is particularly important in high-risk early-stage drug discovery. Given the low marginal costs of sharing knowledge, access to knowledge should be maximised to drive innovation rather than restricted and privately owned. This can be done through tools and platforms for sharing data and information. The legal right to use patented knowledge could be facilitated by setting up patent pools (see **section 3.2**). It has been argued that the knowledge economy is a key part of the global economy, so ensuring the flow of knowledge is paramount.<sup>137</sup> Periods in history which saw the most innovation have often been ones where knowledge-sharing was maximised.<sup>138</sup> And in many sectors, such as open-source or free software, patenting is strongly discouraged and not commonly used.<sup>139,140</sup>

### Box 6. What is the commons? <sup>141,142,143</sup>

The term ‘commons’ refers to shared resources that are not privately owned but are managed collectively for the good of the wider community. The commons can be tangible resources like air and water or intangible resources like scientific knowledge or cultural heritage. Across a range of sectors, from Wikipedia to renewable energy cooperatives, from open access academic publishing to urban agriculture, from carpooling to patent pooling, people are creating ways to enlarge the commons. Value, knowledge and resources are created and shared for the community rather than kept private for individual profit and competitive advantage.

Collaboration between different countries is also an important aspect of creating a public-health-driven innovation system. Given the impact of high drug prices on high-income, middle-income and low-income countries alike, and the fact that many health problems are global – let alone the global nature of the industry itself – a new health innovation model needs to work for all countries. The development of such a global R&D framework requires international collaboration and a commitment to a multilateral approach. The SDGs related to health require global solutions, and the UN High-Level Panel on Access to Medicines recommends the UN secretary-general initiate “a process for governments to negotiate global agreements on the coordination, financing, and development of health technologies. This includes negotiations for a binding R&D Convention ... to promote access to good health for all.”<sup>144</sup>

## 2.3 Affordability and access

Access to essential medicines<sup>145</sup> is fundamental to the realisation of the right to health, which is well-founded in international law.\* There is little public value in having medicines which are so expensive that only a limited number of people can access them. It is imperative, therefore, that affordability is an explicit objective within the health innovation process.

\* The right to health first emerged as a social right in the World Health Organization (WHO) Constitution 1946, the Universal Declaration of Human Rights 1948, and the International Covenant on Economic, Social and Cultural Rights 1966.



For example, the global scale-up in access to antiretroviral treatment (ARV) for HIV, a pandemic that was killing over two million people per year,<sup>146</sup> was only possible thanks to the dramatic reduction in treatment prices from over US\$10,000 to less than US\$100 per patient per year – achieved through generic production and competition.<sup>147</sup> In the ten years from 2007–16, that treatment averted an estimated nine million deaths worldwide.<sup>148</sup> This was, in part, achieved thanks to global pressure from civil society, patients and campaigners, demonstrating how social movements can impact on political leadership to set health-related missions that deliver widespread public benefit (see **section 4.1**).

While there is an indisputable moral and ethical imperative to promote affordability and access, there is also a clear socio-economic case for supporting these actions as an integral part of a mission-oriented approach to health innovation. Indeed, affordable and accessible medicines not only have direct positive health benefits to the individual but also wider socio-economic benefits in terms of a healthy workforce, and the ripple effects on human capital as well as tax revenues. This is exemplified by the effort to tackle AIDS, where the case for a concerted global response was underpinned by research detailing the significant positive impact delivering access to ARVs had on the economy,<sup>149</sup> education system,<sup>150</sup> and employment.<sup>151</sup> These effects, which can be replicated across healthcare and underline the importance of ensuring access and affordability, are central to our medical innovation model.

## 2.4 Long-term horizons and 'patient' finance

The R&D process to develop a medicine or vaccine takes 10–15 years and has an extremely high failure rate: less than 1 in 10,000 compounds reaches the

market approval phase, a success rate of <0.01%.<sup>152</sup> When successful, often the search for one product leads to the discovery of a completely different one, in a process characterised by serendipity.<sup>153,154</sup> This does not mean that innovation in health is based on luck, but rather on long-term strategies and targeted investments requiring patient, committed finance to support them.

In re-thinking our health innovation model, public and private actors need to commit to long-term goals. We also need to identify forms of patient finance that are capable of providing continuous funding to sustain the innovation process, allowing collective learning to accumulate over time while at the same time bearing high risks and inevitable failures.<sup>155</sup>

The public sector already plays a crucial role both as a source of patient finance and in attracting and leveraging long-term private investment, by creating new technological and industrial landscapes for such investment. An 'entrepreneurial state' often serves as the investor of first resort, before private pharmaceutical/biotechnology companies or venture capitalists.<sup>156</sup> For example, the biotechnology sector grew out of US NIH investments in molecular biology in the 1970s, with venture capital coming only after the market potential for new technologies was made visible through public investment.<sup>157</sup> States can use this power to direct investment in new areas, to incentivise innovation on matters important to their citizens.

The sources of finance affect the direction of what is financed.<sup>158</sup> As we saw in **section 1.4**, the rise of a 'shareholder value mentality' has deeply shaped, and arguably distorted, the direction of innovation in the pharmaceutical sector. Therefore it is particularly important to identify the nature of financing required to collectively and effectively address urgent public health needs.

■ **By bringing together actors from across public, private and non-profit spheres, we can redesign our medical innovation ecosystem such that it catalyses the right type of innovation and creates the conditions for access to that innovation. A more dynamic, impactful health innovation sector has the potential to pay for itself, as innovation is a key driver of economic growth,<sup>159,160</sup> and a healthier population is necessarily a more productive one.**

**To get there, visionary political leadership is necessary. States will play a critical role, not only by investing in health innovation, but by setting directions for health innovation while improving corporate governance and recalibrating the relationship between industry, public health research institutions and policymakers. This means profound changes in the way that governments currently relate to innovation. As access to essential medicines is a human right, these are changes worth making.**

# II. Remedies

The next two chapters set out a concrete plan for transforming the innovation system into one that creates value for all. We begin with immediate steps that policymakers can take to address the urgent problem of high drug prices that prevent patient access (**chapter 3**). This is followed by proposals for transformative change (**chapter 4**) to radically re-orientate the system to deliver innovative outcomes that benefit all. The proposals build on actual experiments around the world which, if scaled up and learned from systematically, could help to transform health innovation to meet public value and get a better public return for public investment.

## 3. Immediate policy actions: Getting better prices today

The crisis in patient access due to high drug prices demands immediate action. This chapter identifies a range of actions that policymakers can take in order to address these urgent problems. Building on real examples, we propose pricing strategies and intellectual-property-based measures and reforms that governments can implement *today* that can improve affordability of vital medicines.

### 3.1 Pricing strategies

Price negotiations are important in obtaining better prices for medicines. Policymakers should adopt measures to help improve the bargaining power of the public sector within the current system in order to procure drugs at better prices. Key elements of obtaining better prices are: pooled or volume-based procurement and improving transparency of prices. The following proposals provide further details of these two strategies with examples of where they have been used:

#### **α) Actively explore opportunities for volume-based and pooled procurement to help drive down medicine prices**

By procuring greater volumes of medicines and/or by pooling procurement needs between countries (and/or purchasing through international agencies that use pooled procurement systems), governments can help to lower prices while providing drug companies with a secure and larger market. A fundamental problem of volume-based

and pooled procurement is that governments are usually negotiating with a monopoly supplier, and their leverage on price is limited by the lack of suitable alternative options. Nonetheless, continued efforts to develop these collaborations could bear fruit, especially if countries use other tools to strengthen their bargaining power – for example by stating their willingness to seek alternative suppliers through compulsory licensing (see **section 3.2**).

These pricing strategies are already in use by some governments and international agencies and the following provides some examples of their use and effectiveness:

- To get around the high price of the hepatitis C drug sofosbuvir (brand name Sovaldi), the Australian government entered into a unique volume-based price agreement with Gilead to treat 62,000 people at a cost of AUS\$1 billion over five years – an average price per treatment of AUS\$16,129 (US\$11,715 / £8,234) if all 62,000 people are treated.<sup>161</sup> This compares with the list price of £34,982 for a 12-week course and £69,965 for 24-week course (excluding VAT) in England.<sup>162</sup> This deal creates an incentive for Australia to diagnose and treat as many people as possible while providing a high revenue for Gilead, which is the main incentive for them entering into the deal.
- Over at least the past decade, pooled procurement strategies have been promoted globally, particularly between international agencies in order to serve the needs of developing countries. For example,

through the Global Drugs Facility – set up by the Stop TB Partnership – pooling markets helped to lower the price of the most expensive treatment for multi-drug resistant TB by 26% between 2011 and 2013.<sup>163</sup> The Pooled Procurement Mechanism of the Global Fund aggregates order volumes on behalf of participating grant recipients to negotiate prices and delivery conditions with manufacturers. In 2017, the Pooled Procurement Mechanism managed US\$1 billion in orders, serving grant recipients in 63 countries.<sup>164</sup>

- Recently there have also been unprecedented attempts by EU nations to coordinate and share information on drug pricing and procurement. The BeNeLuxA<sup>165</sup> and Valletta Declaration<sup>166</sup> groupings, comprising a dozen European countries, aim to build collective power to increase access to medicines at fair prices. The initiatives were established in explicit response to the extremely high prices of new medicines, and the threat they pose to sustainable health systems. Two BeNeLuxA partners, Belgium and the Netherlands, announced their first negotiation result in July 2018 with Biogen for a muscular atrophy drug, Spinraza, after getting the price down to an ‘acceptable level’. The negotiated price remains confidential, but has dropped from €83,300 per injection, the initial price Biogen demanded.<sup>167</sup> The Dutch Healthcare Institute had previously advised the health minister that Spinraza should not be reimbursed unless its price (currently listed at €88,298 per vial)<sup>168</sup> dropped by at least 85% and encouraged him to enter price negotiations with the company.<sup>169</sup>

## **b) Undertake measures to ensure medicine price transparency**

Another way that governments can improve their bargaining power during price negotiations with industry is to address the lack of transparency of prices that other countries are paying for medicines.<sup>170</sup> While the ‘list price’ of a medicine is usually known, the actual price agreed, including rebates, is kept secret. This creates an asymmetry of knowledge in negotiations, where companies know what prices they can obtain in which markets but governments do not. Policymakers could take action to make this information publicly available.

The following examples show where steps have been taken in this direction:

- Across the US, around 30 states have introduced pricing legislation in recent years, many of which have specific demands for transparency on pricing. Oregon is the latest state to approve transparency legislation<sup>171</sup> that mandates advanced warning and disclosure of price increases over a certain amount. It also requires manufacturers who impose such price increases to disclose R&D and marketing spend, profits and prices charged in other countries.
- The efforts of the BeNeLuxA and Valletta groups in Europe, which have sought to build information-sharing and cooperation in decision-making on medicine purchases, are steps in the right direction towards increased pricing transparency.<sup>172</sup>
- Recent studies modelling estimates of profitable generic prices for patented medicines could also allow health decision-makers to make more informed choices on their willingness to pay the prices demanded for new medicines.<sup>173</sup>

## **30 US states have introduced pricing legislation in recent years**

The bargaining power of public procurers can also be improved by governments’ willingness to deploy the flexibilities in patent law (‘TRIPS Flexibilities’ such as compulsory licensing) in case of high-priced patented medicines. This is covered in the next section, along with other intellectual-property-based actions that can be taken in the short term.

## **3.2 Making intellectual property rules work for public health**

Alongside pricing strategies, there are also a range of strategies around the existing intellectual property system that can be adopted to mitigate high drug prices. These involve adopting stringent patentability criteria; improving the use of voluntary and compulsory licences; making information on patents more accessible; and avoiding the implementation of TRIPS-plus provisions in patent and medicines law. The following subsections provide further details with examples of where these policies have been applied:

## **α) Policymakers to ensure the strict application of stringent patentability criteria by patent offices, consistent with the TRIPS Agreement**

Ensuring that patents are only granted for real innovations can help to prevent the granting of overly broad patents and the evergreening of pharmaceutical patents. Article 27 of the TRIPS Agreement states that: “patents shall be available for any inventions ... provided they are new, involve an inventive step and are capable of industrial application.”<sup>174</sup> This gives countries room to specify how ‘new’ is defined. Therefore countries are given the flexibility to define the scope of an invention. For example, they can exclude new uses of already known compounds from patentability under their national law.<sup>175</sup> Further, TRIPS allows for exceptions. Countries may exclude from patentability diagnostic, therapeutic and surgical methods for the treatment of humans. The Final Report of the UN High-Level Panel on Access to Medicines emphasises the flexibility the TRIPS Agreement offers, encouraging WTO Members to apply rigorous patentability criteria to ensure only true innovations are rewarded.<sup>176</sup> To support this, and to bolster the quality of patents, national laws should facilitate robust opposition processes so that any party can oppose patent claims before they are granted, as well as allowing any party to oppose a patent after it has been authorised. Patent applications should therefore be published on the patent office’s website in a timely manner.

As outlined in the examples below, a global movement is building around national patent law reform, with some countries introducing more stringent patentability criteria so that patents are only granted for genuine innovations.

- Argentina,<sup>177</sup> Brazil<sup>178</sup> and India<sup>179</sup> have taken steps towards more stringent patentability criteria. South Africa has adopted a new IP policy which is expected to lead to substantive changes in the way the country deals with patent applications. The policy calls for a much more thorough and substantive examination of patent applications prior to granting patents.<sup>180</sup>

- The European Commission – following the Council conclusions of June 2016 on strengthening the balance in pharmaceutical systems in the EU and its Member States<sup>181</sup> – is conducting reviews of the impact of IP-related incentives, including Supplementary Protection Certificates (SPCs), data and market exclusivity and orphan drug regulation. This review is expected to lead to legislative change in the EU.
- Civil society organisations in high and middle-income countries have successfully used patent grant oppositions to limit patent claims or overturn patents of essential medicines.<sup>182,183</sup> For example, groups in Brazil, Argentina and France have successfully opposed patents on HIV medicines.<sup>184</sup>

## **b) Governments to negotiate voluntary licenses and actively use legal powers (eg, compulsory licensing agreements) to improve access to affordable medicines**

Patents as such do not need to form a barrier to access so long as licenses are available for others to use and to exploit the innovation against the payment of a remuneration. Voluntary and compulsory licenses are consistent with the WTO’s TRIPS Agreement and the Doha Declaration. Non-voluntary or compulsory measures are important legal safeguards to ensure governments can take measures to protect public health and promote access to medicines.<sup>185</sup>

A voluntary license is one granted by a patent holder (eg, a pharmaceutical company) to (usually) a generic manufacturer to use and/or sell the invention on mutually agreed terms including royalty payments. Negotiating voluntary licenses through patent pools (see below) has been used effectively, for example to improve access to low-cost generic HIV medication.

Additionally, increased use of compulsory licences, granted by the government without the consent of the patent holder, would serve as an effective check on unreasonably high prices being demanded by industry. Compulsory licences can ensure access to a medicine at an affordable price, while still rewarding the patent holder through payment of a fair royalty on the sales of the medicine. As well as ensuring access to the drug in question, they can also have a deflationary effect on the prices of other medicines, as companies seek to price at a level that will avert further use of these flexibilities.

The following are examples where voluntary and compulsory licencing approaches have been used:

- Patent pools, such as the Medicines Patent Pool (MPP),<sup>186</sup> are mechanisms that can be used to negotiate **voluntary licences**. The MPP negotiates patent licences for middle and low-income countries to ensure the availability of sources of low-cost generic production of patented products. As of January 2018, the MPP has signed agreements with nine patent holders for thirteen HIV drugs, one HIV technology platform, an anti-TB drug treatment and two HCV direct-acting antivirals. In 2018 the MPP announced its mandate had further expanded to include all other WHO essential medicines that are patented.
- **Compulsory, or public non-commercial use licences** have been used by governments worldwide to secure affordable access to medicines over 100 times since the Doha Declaration was agreed.<sup>187</sup> In 2016, for example, the German courts awarded a compulsory licence on the HIV drug Isentress.<sup>188</sup> Recently the Italian government raised the prospect of utilising compulsory licences during negotiations with the drug company Gilead over the high price of the hepatitis C treatment sofosbuvir.<sup>189</sup> In several high-income countries, civil society organisations have asked their governments to issue compulsory licenses to deal with high prices of medications. The United States and Canada also threatened to use a compulsory licence during negotiations with the supplier of a treatment for anthrax poisoning in 2001.<sup>190</sup> In 2018 Just Treatment launched a campaign calling for the Scottish government to issue a compulsory licence to secure affordable access to the breast cancer medicine pertuzumab, which is currently not available in Scotland due to the high price.<sup>191</sup>

Finally, other legal avenues to control prices can be pursued by national governments. The 1980 US Bayh-Dole Act provided researchers the ability to obtain patent rights for federally financed research inventions. (Prior to this, the government retained patent rights for research it had funded.) The idea was that this would provide a stronger incentive to commercialise innovative scientific discoveries, typically by licensing the patents to large manufacturers. The Act also left the government

with rights to intervene when federally funded inventions were either not developed, not put on the market on reasonable terms, or otherwise used in way that has an adverse impact on the public. Under these circumstances, the US government agency that provided the research funding can 'march in' and license the patent to a third party. However, in reality these rights have never been exercised, in spite of growing pressure to do so. In 2016, 51 members of Congress<sup>192</sup> urged the US government to use its existing powers under the Bayh-Dole Act to authorise the generic production of expensive medicines by activating their 'march in' rights on products developed with public funds.

### **c) Patent offices and patent holders/ applicants to make information on medicines patents accessible**

The patent status of pharmaceuticals should be published in an accessible format and should include the generic or International Nonproprietary Name (INN) of the product where possible, so as to aid generic production.<sup>193</sup> This will make it easier to ascertain the patent status of medicines around the world, informing countries when a generic could be bought to market. National and regional patent offices have an important role to play in increasing transparency in the patent status of medicines.

The following are examples of information on patents being made more accessible:

- MedsPal is a patents and licences database created by the Medicines Patent Pool to provide information on the intellectual property status of selected HIV, hepatitis C, tuberculosis and other patented essential medicines in middle and low-income countries. In 2017, the MPP expanded its Patent and Licensing Database, MedsPaL, to all patented treatments on the World Health Organization (WHO) Model List of Essential Medicines (EML).<sup>194</sup> To support the updating of MedsPal, the MPP has signed collaborative agreements with various regional and national patent offices. The more patent offices that collaborate with the MPP, the more effective the database will be as a tool for facilitating strategies to improve access.

- The World Intellectual Property Organisation (WIPO), with the pharmaceutical industry, has announced the publication of a medicines patent database to be available late September 2018.<sup>195</sup>
- The WHO and UNITAID have published patent status information for hepatitis C and TB medicines.<sup>196,197</sup>

### Box 7. Going beyond TRIPS in the EU

Data exclusivity means generic companies cannot use the originator's clinical test data to gain marketing authorisation for a generic medicine for a certain period, which in the EU is eight years. After eight years have passed, the regulatory authorities can process the generic company's application for marketing authorisation, but the product may still not be put on the market until ten years have passed since the initial marketing authorisation of the originator product, which is known as market exclusivity. These rules essentially prolong existing monopolies by making it harder for generic medicines to gain marketing approval.<sup>198</sup>

### d) Governments should not adopt TRIPS-plus provisions in patent or medicines law

TRIPs-plus provisions are rules that go beyond what is required in the TRIPS agreement. These provisions can further strengthen monopolies, as well as create legal barriers to implementing TRIPS flexibilities, thereby exacerbating access problems. The EU's data and market exclusivity rules are examples of TRIPS-plus (see **box 7**). These rules not only prevent the production of generic medicine in the absence of a patent, but can also interfere with the effective use of compulsory licensing because they prohibit the registration of generic medicines.

These TRIPS-plus measures should not be included as demands in negotiations of free trade agreements. The US and the EU pursue TRIPS-plus provisions with their trading partners. These demands in general meet with opposition, but in the end are agreed as part of a larger trade deal. The Trans-Pacific Partnership (TPP) was a proposed multilateral trade agreement between Australia, Brunei, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore, Vietnam and the US. The developments in the TPP negotiations after the US withdrew from the agreement provide interesting insights. In November 2017, the remaining countries suspended the controversial TRIPS-plus provisions in the intellectual property section of the agreement, which would have harmed patient access to medicines.<sup>199</sup> It was then renamed the Comprehensive and Progressive Agreement for Trans-Pacific Partnership.

## 4. Transformative proposals: Re-imagining our health innovation system to deliver public value

This chapter presents proposals for transformative change to radically re-orientate the system to prioritise public health. We begin by proposing that governments adopt a mission-oriented approach to health innovation (**section 4.1**). This approach involves governments setting a public health agenda to direct innovation. It fundamentally changes the role of the state in health innovation, from just fixing market failures to becoming an active creator and shaper of markets. A mission-oriented approach for health innovation incorporates the core principles that nurture innovation (as described in **chapter 2**).

By setting the direction for a solution, missions do not specify how to achieve success. Rather, they stimulate the development of a range of different solutions to achieve the objective. A mission is not a single project, but a portfolio of actions that can encourage multiple solutions.

To support policymakers in identifying practical recommendations which they can implement when designing health missions, we present three specific policy proposals that include concrete policy steps that support and form part of the missions approach. These are: delinking the funding of R&D from the revenues generated from sales (**section 4.2**), attaching conditions to the provision of public funding (**section 4.3**), and changing the rules of corporate governance (**section 4.4**).

Rethinking the role of the state as an active, strategic investor is central to each of these proposals. Alongside these policies, it is important that there are sufficient democratic safeguards and measures for participatory governance to ensure that public investment does deliver public value.

The mission-oriented approach and the policy proposals are all based on existing examples and experiences from around the world that provide useful lessons about radical change. Although discussed as separate areas, these ideas are not mutually exclusive but can be combined to fit different national, regional or international contexts.

### 4.1 A mission-oriented approach to improving health outcomes

Policymakers can draw important lessons from other sectors that have adopted a mission-oriented approach. Missions are a powerful tool to direct innovation to meet public health needs and solve specific problems that require multiple types of activities. They can provide the means to focus research, innovation and investment while laying the foundations for economic growth, resulting in positive spillovers across many sectors and spurring job creation.<sup>200</sup>

A mission-oriented approach would work as follows: governments, in consultation with experts and stakeholders (such as patient groups) discuss the key problems that require innovation to target. This health research agenda would be connected to key milestones and/or target products and supported by 'patient' capital – sources of finance that are risk-tolerant and not dependent on short-term success. This might, as has been the case in both defence and energy, require specific institutions to be created (see discussion of HARPA below). This approach would allow the state to set a direction for innovation, while focusing on nurturing collaborations with actors in the business sector, public sector and third sector – with government tools like procurement aimed at nurturing bottom-up experimentation. There are several models for how governments could connect financing and forge collaborations, but the principle of a public-interest focused and sustainably financed research agenda would remain the same.

The following sections describe some state-directed, mission-oriented initiatives that place directionality at the heart of fostering innovation, analysing the key features that made these experiences so successful. While these examples all share the focus on specific missions, they differ substantially in how governments set about achieving these missions. Our aim is not to advocate one approach over another but to illustrate the range of possible approaches and the lessons to be learned from each.

## **α) Learning from DARPA: Generating groundbreaking innovations to meet a societal problem while welcoming uncertainty and risk-taking**

There is much that the health sector can learn from the strategies through which the US government's Defense Advanced Research Projects Agency (DARPA) has funded defence-related innovation. DARPA's internal structure is designed in such a way to be guided by problem solving (mainly concerning national security) while welcoming the exploration of uncertain ideas, including the inevitable risk of failure in the process. DARPA's aim is to attract scientists and researchers keen to conduct path-breaking research without pressure to produce results in the short term. Its internal structure has been much studied, such as the use of secondment practices (for 4–5 years) to attract high-level scientists into public service.<sup>201</sup>

The DARPA approach has been successful for defence technology and has also resulted in substantial spillovers, providing the basis for many innovations in widespread use today. The internet, for example, was the result of the US Department of Defence (DoD) developing a decentralised communication network; had DARPA not targeted investment in it, the technology may never have been developed. The Global Positioning System (GPS) was an attempt to digitise worldwide geographic positioning to enhance the coordination and accuracy of deployed military assets.<sup>202,203,204</sup> What initially began in the 1970s as a strictly military-use-only technology is now ubiquitous.

Mission-oriented policies have more recently been used to set up dynamic public agencies in other areas of public interest, such as fighting climate change. The Advanced Research Projects Agency–Energy (ARPA-E), established in 2007 and modelled specifically after DARPA, is now leading US green investments in renewable energy.<sup>205</sup>

There is currently a push for the US government to introduce an equivalent of DARPA in the US Department of Health: a Health Advanced Research Projects Agency (HARPA) (**box 8**).

DARPA demonstrates how the state can play a role in developing groundbreaking innovation while enduring the uncertainty and risks inherent in the innovation process. In facilitating the channelling of investment to existing private actors, DARPA (and the proposed HARPA) are models whereby government imposes limited conditionality on the results of research and merely aims to recoup its investment

by taxing the resulting profits. These approaches need to be complemented with upfront stipulations to ensure that patient access and affordability are not jeopardised by any intellectual property associated with new innovations. As we explore in **section 4.3**, stricter conditionality could be one way of improving this model.

***If you want someone to do something revolutionary, you have to create a revolutionary apparatus for it. It can't be built within the same old structure.***<sup>206</sup>

**Dr Geoffrey Ling, Col. (ret.) Founder and Former Director, DARPA Biotech Office**

## **b) The experience of BARDA: Setting missions to tackle health threats for the US population**

The US government does have experience with this approach in the context of health innovation, through the US Biochemical Advanced Research and Development Authority (BARDA). BARDA was set up to procure and develop countermeasures against certain threats to the US population.<sup>214</sup> It does this by funding the research, development and stockpiling of vaccines and treatments that the government could use during public health emergencies such as chemical, biological, radiological or nuclear attacks. Setting the requirements for the medical countermeasures (MCMs) is decided by BARDA based on information from stakeholders throughout the government. Some of the main threats that have been under active consideration by the authority are pandemic influenza and emerging infectious disease threats such as Dengue, Ebola, SARS and Nipah virus, as well as antibiotic resistance (through the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, CARB-X).<sup>215,216</sup>

BARDA has established three Centers for Innovation in Advanced Development and Manufacturing (CIADM) to create manufacturing capability in response to health emergencies. These are funded by BARDA as public–private partnerships and based on long-term contracts with the private sector (up to 25 years).<sup>217</sup> Between 2007 and 2017, BARDA procured and stockpiled 21 products. New products produced include the only FDA licensed vaccine against anthrax disease and the only FDA licensed botulinum antitoxin (used for a paralytic illness), alongside others.



## Box 8. A Health Advanced Research Projects Agency (HARPA)

Dr Geoffrey Ling, Founder and Former Director of the DARPA Biotech Office, has recently called for a Health Advanced Research Projects Agency (HARPA) in the US, modelled on DARPA's success.<sup>207</sup> The initial focus for a HARPA would favour and speed up translation of key scientific discoveries into much-needed medicines and diagnostic tools, and their commercialisation.<sup>208,209</sup> As with DARPA, HARPA would also focus on bringing in multiple actors to solve government-set problems.

HARPA is not meant to compete with or duplicate the NIH nor any existing federal research efforts, but rather to work in synergy with them by fostering an innovation ecosystem where multiple actors – academic institutions, government and regulatory agencies, the commercial market, biotech and healthcare companies and venture capital and philanthropy – can work together synergistically and in a streamlined fashion.

"HARPA, like DARPA, would be performance-based, milestone-driven, timeline-driven with the efforts determined by the government"<sup>210</sup> says Dr. Ling.

Efforts to secure congressional support for HARPA are ongoing, but no executive order has been issued so far.<sup>211</sup> The budget proposed for HARPA is US\$2 to 3 billion,<sup>212</sup> the equivalent of about 10% of the NIH's US\$34 billion for 2017 and similar to that of the US ARPA-E.

### Key features of the proposed Health Advanced Research Projects Agency (HARPA)<sup>213</sup>

- **A flat, nimble, non-bureaucratic structure to ensure efficiency:** There will be no career programme managers, which will ensure that the agency is scientifically current and flexible to new avenues of investigation. A limited term for each programme manager (3–6 years) will ensure a fresh flow of ideas and prevent personal interests from influencing HARPA's interests.
- **Autonomous decision-making:** Decisions about which health problems to address will be taken purely within the agency. HARPA programme managers will design projects based on HARPA-initiated requests for proposals to solve a specific problem and choose partners across disciplines to reach that goal. HARPA proposals will be openly competed, but the HARPA programme managers select the winners and can assemble a portfolio of projects intended to achieve a particular goal.
- **Active risk-taking through a performance-based approach:** HARPA will invest in high-risk translational projects through contract-based (not grant-based) investments, with the autonomy to terminate projects at will should they fail to deliver.
- **Milestone-driven and timeline-constrained:** Setting firm performance milestones for every programme will create strict accountability and ensure that scientific progress is made in an efficient and timely manner.
- **Market creation:** HARPA programmes will be designed with regulatory demands and commercial transition strategies in mind from the start. Regulatory experts will join project design and selection, and integration of private-sector partners and co-funding agreements will be in place early.

In June 2018, BARDA launched a new initiative called the Division for Research, Innovation and Ventures (DRIVE). It aims to accelerate the development of innovative MCMs not only through the traditional BARDA model (ie, through providing grants), but also acting more like a strategic investor in private and public companies with which BARDA would like to partner, deriving value

by holding equity or equity-like instruments in the venture. Investing in opportunities in this manner offers a pathway to renew funds to reinvest into other ventures deemed essential to the national interest.<sup>218,219</sup> DRIVE will initially accelerate the development of innovative solutions in its first two target impact areas of sepsis, and pre-exposure, pre-symptomatic diagnostics.

BARDA is an example of setting a health mission to tackle health threats to the US population, and shows how the government can determine the direction of innovation and then coordinate with different actors across the innovation chain to deliver the desired outcomes. However, BARDA operates within existing US legislation that allows the private sector to retain IP protection, which could hamper patient access as well as knowledge sharing, collaboration and future innovation. Missions need to embed the principles of access and affordability to achieve public health goals.

### c) Cuba's biotech mission

The nationalisation of Cuba's pharmaceutical industry, although created out of necessity within a specific historical and political context, is another example of what can be achieved if there is political will to make public health a national priority. The Cuban government created a 'mission' to deliver the best and most affordable medical treatment to every Cuban.<sup>220</sup>

Cuba's health system has been widely recognised for its efficiency and the achievement of universal health coverage, in spite of limited resources and decades of economic sanctions. These achievements occurred not in spite of being state controlled but – crucially – because of it.

With the 2012 creation of BioCubaFarma, Cuba has now brought together its biotechnology research institutions and other centres of medicines production and marketing under one roof. This vertical integration, from research to manufacturing to commercialisation, has contributed to collaboration and the free flow of knowledge within the system and spurred further innovation.<sup>221</sup>

Cuba's health innovation model has allowed it to take the lead in south-south technology transfer and capacity building in other low-income countries.<sup>222</sup> Cuba has signed technology transfer deals as well as joint production agreements with firms in countries including Algeria, India, Brazil, China, South Africa, Mexico, Argentina, Vietnam and Malaysia.<sup>223</sup> For example, Cuba and Brazil entered into a joint venture agreement in 2010 to manufacture Cuba's meningitis B vaccine in Brazil to reduce cost to patients in Brazil.<sup>224</sup>

### d) Energiewende: The role of civil society in setting missions

While in some cases an innovation mission is set by government – the classic example of a top-down mission is John F Kennedy setting the mission to get a human to the moon and back – or philanthropic funders, in some other cases they have been the result of bottom-up social movements culminating in political leadership to set a clear, ambitious target (**box 9**). It is thus important to ask who sets the mission, and how a mission is established so that it is not just compelling but legitimate, especially when the goal is societal change.<sup>225</sup>

Energiewende in Germany is a concrete mission with the specific target to reduce carbon emissions, framed in the broader mission of fighting climate change, and it has been a result of a bottom-up process mediated via the green movement, which brought legitimacy in Germany for a green transformation of the country. Energiewende shows how missions may require consensus-building in civil society, combining the need to set directions from above with processes of bottom-up experimentation from below.<sup>226</sup> This has also shaped the financing and ownership models that have underpinned Energiewende. Germany has used public investment and subsidies to help 'crowd in' investment from citizens themselves, building a diverse ecosystem of community- and cooperatively-owned green energy suppliers. As a result, 46% of the resulting renewable capacity is owned by citizens, while only 5% is owned by the 'big four' power companies.<sup>227</sup>

Social movements have also been critical in the health sector. A global movement led by people living with HIV transformed the policy response to the AIDS pandemic in the 1990s and early 2000s, forcing a profound change in the market for antiretrovirals from a 'high price, low volume' business model to one which sees 21.7m people accessing treatment today.<sup>228,229</sup>

And while the development of the contraceptive pill looks like a straightforward story of corporate innovation, it was actually the result of a social-movement-driven innovation mission. For this innovation, the scientific and medical communities were nested within a larger social movement, the women's movement, which provided the overarching mission.<sup>230</sup>

## Box 9. What is the relevance of movements to mission-driven innovation?

(adapted from Leadbeater 2018)

Innovation movements play four important roles in mission-driven innovation contributing to meeting significant social challenges.

- Movements help to create, contest and shape the mission and purpose of innovation. They can challenge the direction of innovation in a dual sense. Movements often stem from frustration with how things are. They challenge a status quo which is regarded as unacceptable. But they also set a challenge to find a better solution.
- Movements help organise the supply side of innovation through the generation and circulation of ideas, knowledge and technology. Innovations often develop and spread within communities of scientists, engineers and technologists who cooperate, emulate and compete in devising new and better solutions to solve shared challenges.
- Movements with missions can make new markets when they crystallise consumer aspirations for better ways to live. Innovations often fail because they are too early for the market; consumers are not ready to take them up and do not know how to integrate them into daily life.
- The movements perspective provides a way to understand how entire systems change. Systems change, involving coalitions of players from the public, private and philanthropic sectors, is far more powerful as a form of innovation than the creation of a standalone product or service.

### Policy Step:

#### Adopting a mission-oriented approach

The initiatives and examples outlined above demonstrate what can be achieved when there is political will for the government to take an active role in directing and shaping innovation, and thus the potential for a better health innovation system. We have provided these international examples not to copy and paste them, but rather to learn from them and demonstrate how a mission-oriented approach could work in transforming health innovation.

Public health challenges are complex problems that are rarely purely technological or scientific in nature. In an interconnected world, they are also increasingly global. Tackling such challenges requires scaling up the mission-oriented approach described above, creating comprehensive, synergistic interventions through cross-sectoral, cross-country collaboration.

Proactive and explicit engagement with the missions approach internationally is crucial: it can significantly facilitate and accelerate the process of in-depth problem analysis and comprehensive solution mapping that is necessary to solve urgent public health challenges that cross national and sectoral boundaries.

The struggle to mobilise an international response to antimicrobial resistance (AMR), for example, is a striking example of what could have been. Mitigating AMR requires that interventions be implemented worldwide ranging from behaviour change to animal health to environmental management. But the policy response severely lagged behind the urgency of tackling the problem, and AMR has grown to be a global crisis. A cross-country, collaborative, mission-oriented approach to AMR could have helped speed the development of a comprehensive policy package suited to the urgency of the problem.

Governments should adopt a mission-oriented approach to health innovation. This can be done initially by testing mission-driven organisations within the health sector. The lessons learned nationally could then inform and guide international cooperation on shared health challenges in the longer term.

■ In the following sections we propose a range of key policies that policymakers can include when developing their missions for health innovation. These policies can provide the tools and strategies to deliver a flourishing health innovation system within a missions context.

## 4.2 Delinking incentives from high prices

The practice of charging high prices is encouraged through current incentives mechanisms which rely on market exclusivity, either through patents or through data or orphan drug exclusivities.<sup>231</sup> The incremental reforms to the patent system proposed in **section 3.2** can help to improve affordability and access *today*, but here we recommend something bolder: entirely replacing the idea of high prices as a reward for innovation. This concept is known as ‘delinkage’ – because it decouples the price of a needed medical technology from the cost of its R&D.

Delinkage is based on the premise that the costs and risks associated with R&D should still be rewarded, but that the incentives for R&D can be provided by means other than financial returns from charging high product prices.<sup>232</sup> A model of delinkage involves paying for R&D through a combination of research grants, subsidies, and cash or other rewards for successful achievement of various objectives. The cash rewards have been described as ‘innovation inducement prizes’, ‘market entry rewards’, or ‘open source dividends’<sup>233</sup> and can be implemented as alternative innovation incentives to the granting of a monopoly and the associated high prices. In the absence of a market monopoly, generic competition can then drive the price of a product down, closer to the marginal costs of production.<sup>234</sup>

These alternative incentives can either replace patents or be used alongside them, since patents can be managed so as not to result in high prices.<sup>235</sup> For example, patents could play a role in terms of defining authorship of research and the claim to the prize or market entry reward revenues,<sup>236</sup> but the patent holder would freely license their technology or license it for particular purposes (eg, for use in public hospitals or by researchers). This would be included within the stipulations of the contract of the delinked mechanism in use, whether that is a research grant or a milestone prize. The crucial element is that the new incentives replace market exclusivity.

Under delinkage, governments and philanthropic donors provide the funding for R&D. As R&D financing no longer relies upon monopoly-protected high prices, directionality can be set more easily according to the public health needs identified by the funding agency.<sup>237,238</sup> This creates a much more efficient system, as it pays only for the meeting of defined R&D milestones.<sup>239,240</sup>

Any prize system that would effectively replace market exclusivity as an incentive mechanism would require large-scale funds.<sup>241</sup> However, funding a delinked model is not about finding additional financing, but about re-allocating money that is currently being spent on expensive, monopoly drug prices.<sup>242</sup> Prize funds are feasible when we consider the amount of public money currently spent procuring drugs. In 2017 the US spent an estimated US\$324 billion on medicines.<sup>243</sup> NHS spending on medicines in England has grown from £13 billion in 2010/11 to £17.4 billion in 2016/17 – an average growth of around 5% a year.<sup>244</sup>

### In 2017 the US spent an estimated US\$324 billion on medicines

Potential savings from switching to a delinked system, in which new medicines enter the market at non-monopoly generic prices, are vast. In the US market in 2017, patented medicines were on average 14.5 times more expensive than generic medicines.<sup>245</sup> The United States therefore stands to make significant savings by switching to a delinked model that would result in all new medicines being sold in a competitive generic market. Senator Bernie Sanders’s 2017 proposal for a Medical Innovation Prize Fund<sup>246</sup> required the US government to create a fund equal to 0.55% of US GDP to reward researchers and drug developers for reaching specific health objectives. In 2016 this would have amounted to US\$102 billion. By supporting the R&D of affordable generic medicines, this delinked prize fund would have generated US\$92 billion in savings in 2016.<sup>247</sup>

### The US could have saved US\$92 billion in 2016 if it had used a delinked R&D model

One key question is whether a US\$102 billion prize fund would be a large enough incentive to replace the monopoly incentive provided by the current system.<sup>248</sup> The Pharmaceutical Research and Manufacturers of America (PhRMA) members’ reported spend on R&D in 2016 in the United States was US\$65.5 billion.<sup>249</sup> The estimated US\$102 billion prize fund would have been nearly double this amount, and would have been equal to a US\$4.6 billion spend on R&D per novel drug approved by the FDA that year<sup>250</sup> (almost twice the industry’s own estimate of

US\$2.6 billion per new chemical entity developed).<sup>251</sup> The features of a delinked model, such as increased collaboration, transparency and open access, are key principles in their own right for health innovation to thrive (see **chapter 2**). These features, combined with the investments in R&D proposed in the delinkage model, can create a model that would “cost less, expand access, accelerate and improve innovation, and replace an incentive system that is expensive, inefficient and unsustainable.”<sup>252</sup>

## Prices for some cancer medicines in the UK could be reduced by 75% to 99.6% if they were procured as generics in a competitive market

Other countries are also likely to generate increased resources for R&D through the savings made by procuring generic medicines under delinkage. The prices the UK pays for some cancer medicines could be reduced by between 75% and 99.6% if they could be procured as generics in a competitive market,<sup>253</sup> giving an indication of the potential savings which could be made across the NHS drugs bill.

Examples of delinkage, such as the Drugs for Neglected Diseases *initiative* (DNDi, **box 10**) have demonstrated how changing incentives can enable research priorities to be determined by public health needs, encourage open research, and ensure that products are affordable and available.

It could be argued that DNDi has been able to operate under a delinkage model because their remit is neglected tropical diseases. These diseases are neglected because there is little market incentive to develop treatment for them; pharmaceutical companies are more open to sharing information, tools and data as there is no financial reason not to.

Could delinkage work for more profitable disease areas? DNDi has recently extended its definition of ‘neglected diseases’ to include areas where drugs are available but not affordable, which is also an increasing problem in high-income countries. For example, DNDi has started to develop an alternative treatment regimen for hepatitis C. The target price for this new treatment regimen (sofosbuvir and ravidasvir) is US\$300 for a 12-week treatment,<sup>257</sup> much lower than the existing brand name treatments for hepatitis C (see **Table 1**). In addition to DNDi and some companies in middle-income countries, Ravidasvir is also being licensed through the Medicines Patent Pool (MPP), which offers the potential for further generic manufacture.<sup>258</sup>

The delinkage model could be incorporated into mission-oriented approaches to address public health needs, as it creates the framework and incentives to drive broader innovations in health, including how best to develop and use different products together to maximise patient benefit. For example: developing drug combinations for drug-resistant infections rather than focusing on single drugs; or developing and integrating diagnostic tools that enable the design of optimal treatment regimens for patients from the outset. The proposed Life Prize project is an example of such an approach (**box 11**).

### Box 10. From theory to practice: The Drugs for Neglected Diseases initiative (DNDi) as an effective form of delinkage

The Drugs for Neglected Diseases *initiative* (DNDi) is a non-profit product development partnership established to develop drugs for diseases neglected by industry, such as sleeping sickness, Chagas disease, leishmaniasis, filaria, and later paediatric HIV/AIDS. DNDi relies on public (50%) and private (50%)<sup>254</sup> contributions to pay for R&D upfront. This allows them to keep their research agenda focused on priority public health needs, promote greater sharing of research data, and price products affordably.<sup>255</sup> DNDi has developed six new treatments since it was founded in 2003, and expects to complete 10–12 additional new treatments by 2023. In general DNDi does not patent its innovations, but DNDi’s IP policy foresees that at times this may be necessary to strengthen DNDi’s ability to ensure control of the development process and to negotiate with partners. However, its aim is to always ensure affordable, widespread access to the results of its research.<sup>256</sup>

## Policy Step:

### Testing delinkage mechanisms

To truly break the grip of the dysfunctional shareholder-driven pharmaceutical model, alternative models that are driven by public health interests need to be able to compete as mainstream players in areas with large and profitable markets. The following proposals provide a starting point for policymakers to move towards a delinked model that could be tested and scaled up to deliver public health benefits:

#### α) Undertake feasibility studies in different disease areas to explore how a delinked model might operate

The NGO Knowledge Ecology International has proposed a delinkage feasibility study for cancer treatments, the Cancer Innovation Fund (CIF) (**box 12**). Policy makers should support the CIF initiative, while conducting their own feasibility studies for using delinkage incentives for significant health challenges within their national or regional contexts.

### Box 11. The Life Prize – A proposed delinked model to tackle tuberculosis

Worldwide, tuberculosis (TB) is the leading cause from a single infectious agent (above HIV/AIDS). An estimated 10 million people fell ill with TB in 2017, of which 558,000 cases were drug-resistant (DR-)TB.<sup>259</sup>

Treating TB requires long and complex treatments containing multiple antibiotics, and for drug-resistant TB might take up to two years, with severe side effects for patients. Current DR-TB treatment regimens have low cure rates and no paediatric formulations are available for most of the drugs. New drug combinations for TB (and particularly for DR-TB) that are more effective and affordable are therefore urgently needed.<sup>260</sup>

Under the current system there is little financial return in treating a condition that mainly affects poorer countries, and the focus on single product outputs does not deliver the multi-drug regimens required for treating TB.<sup>261</sup>

The Life Prize, currently sponsored by the International Union against Tuberculosis and Lung Disease ('The Union'), is a project aimed at incentivising the collaborative development of better and more affordable TB treatment while encouraging companies and academic institutes to invest in TB R&D.

The mission of the Life Prize goes beyond single drug development and instead aims to create a suitable environment for delivering an affordable, short-course treatment regimen effective against all forms of TB – "a regimen that works for everyone, everywhere."<sup>262</sup>

The Life Prize aims to do this by promoting:

- An open, collaborative research environment where pre-clinical and clinical data are shared among actors. The possibility to test candidate compounds in combination at an early stage of drug development thanks to such open collaborative framework for R&D would accelerate the development of new drug combinations.
- Fair IP strategies to ensure streamlined development, affordability and access of final products.

Currently over 60% of funding for TB R&D comes from public sources.<sup>263</sup> By attaching conditions to the provisions of public funding (see **section 4.3**) to ensure an open R&D and fair IP strategies, the Life Prize project aims to speed up TB regimen development. The Life Prize ultimately aims to mobilise prize funding for drugs entering clinical trials that fulfil predefined criteria, including data and IP sharing, thereby completely delinking the R&D costs from the final price of the resulting treatment regimens, ensuring affordability.

The Life Prize is continuing to work with R&D actors and donors to implement the Life Prize principles. The project is promoted in the Political Declaration on the fight against TB, which will be endorsed at the first ever UN High-Level Meeting (HLM) on TB (September 2018, New York).<sup>264</sup>

## Box 12. The Cancer Innovation Fund (CIF)

The proposed Cancer Innovation Fund (CIF) would be a multi-country commitment to fund the R&D of new drugs, vaccines, cell-based treatments and diagnostic tests for cancer.<sup>265</sup> The feasibility study for the CIF would assess the level of funding required to present a robust alternative to the current system in terms of stimulating innovation and how this would be divided between countries, for instance as tied to GDP or GNI, health care expenditure, or spending on cancer treatment.

The study would then explore the most appropriate types of incentives, which could include: direct research grants, research subsidies, milestone prizes, end-product prizes and open source dividends. The latter involves the appointment of a panel who, once a product enters the market, decides which persons and entities should get credit for having shared their knowledge, data and technology to develop the product. These stakeholders share in the end product rewards, effectively having a royalty on the market entry or a financial prize. The objective is to provide an incentive to do what is socially optimal, which is to share and be open.<sup>266</sup> The feasibility study would also analyse the costs, processes and outcomes of the current way cancer R&D is conducted and use this data to compare the current system with the proposed one to establish which approach delivers the best treatment at the most affordable price.

### b) Commit to launching pilot delinked models for different missions

Cancer affects high and low-income countries alike, and would be a logical choice for a pilot delinkage scheme that would drive the needed R&D. A pilot would involve testing and combining various delinked incentives and a variety of financing schemes to achieve the appropriate funding combination. This demonstration project should be used to create a roadmap for how the principles of delinkage can be scaled up to eventually be a viable alternative to the current monopoly-driven model of pharmaceutical R&D.

■ Many prominent health reports have recommended delinkage, including the Lancet Commission on Essential Medicine<sup>267</sup> and the UN Secretary-General's High-Level Panel on Access to Medicines.<sup>268</sup> Many governments have also agreed that delinkage should be a key principle to guide new R&D for unmet health needs. This is evident in its inclusion in several WHO resolutions, such as the 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property<sup>269</sup> and the political declaration of the high-level meeting of the UN General Assembly on antimicrobial resistance.<sup>270</sup>

Some might argue that delinkage models give too much power to governments and other decision-makers to allocate resources, and that the market is the most efficient way to incentivise innovation.

However, as we argue in **chapter 1**, there is ample evidence that the health sector is not currently a well-functioning market. It is questionable whether monopoly profits to patent holders can ever be an effective way to finance the complex, collaborative process of innovation (or a morally justifiable one, given the life-saving nature of the products involved).

## 4.3 Achieving public return through conditionality

Innovation systems in which risks and rewards are shared fairly among all actors are vital for fostering the dynamic and sustainable investments that are needed across the long and uncertain process of health innovation, and for producing a symbiotic, collaborative environment for health innovation to flourish.<sup>271</sup> The existing paradigm of socialised risks and privatised returns needs to be replaced by one where public investment leads to public returns.

DARPA and BARDA show how government can set the direction of research and provide risk-tolerant funding to support that direction while working with the existing private ecosystem (see **section 4.1**). However, both allow private entities to retain IP protection, which is not ideal in terms of creating the knowledge governance that stimulates access, collaboration and future innovation. This means that direction-setting in a mission-oriented approach needs to be complemented by a contract that creates a symbiotic deal.

One way this can be done is by repositioning the way we structure public investments. Rather than simply setting the direction of the investment, mission-oriented policies could be bolder in setting conditions on how public benefit can be achieved in such key areas as:

- **Reinvestment** – ensuring profits of firms that benefit from public investment are reinvested back into innovation
- **Knowledge sharing** – ensuring that the benefits of new knowledge flow within the system as well as out to the public at large
- **Transparency of R&D costs** – ensuring informed discussion of pricing and R&D financing by clarifying the real costs of health R&D
- **Conditions for access and affordability** – ensuring taxpayers do not pay twice for medicines developed with public funds

Considering the large amount of public financing that goes into health R&D, governments have a responsibility to ensure that public money results in public benefit. Although these conditions are relevant to all health innovations, applying these conditions in the first instance to health innovation that has benefited from public funding provides an essential and practical first step that policymakers can take to start transforming and shaping the health innovation system.

## Policy Steps:

### Achieving public return on public investment

The following policy steps address each of the aforementioned key areas for condition-setting:

#### a) Conditions for reinvestment

To strengthen the pharmaceutical sector's commitment to long-term public health policy objectives – and mitigate the chances of value extraction through short-term, speculative finance – public funding could be contingent on certain conditions. These conditions could include, for example, requiring a company to reinvest a share of their profits into productive economic activities or a public innovation fund;<sup>272</sup> or the public receiving a share of the financial returns from successful innovations in which public funding played a major role (whether by retaining stakes in the companies concerned, holding intellectual property rights, or

receiving royalties on sales). Royalties can be used to finance future innovation or to help cover the losses that inevitably arise when investing in high-risk areas.

Examples of firms reinvesting in productive economic activities include Bell Labs in the US, which was created out of a condition imposed by the government on the telecoms monopolist AT&T.<sup>273</sup> These types of conditions can also be attached to procurement, requiring contractors to invest directly in productive economic activities, which is a common practice in defence-related innovations.<sup>274</sup> For example, in Brazil this mechanism has been adopted to ensure investment in medical manufacturing and technological capacities.<sup>275</sup>

Although many argue that the state already earns a return from its investments via taxation systems, this revenue is not well designed to support innovation. Royalties from publicly financed innovation could, by contrast, have a major impact on the sustainability and directionality of the health innovation process. In most cases today royalties are meagre, at best, for the public agencies that contributed to a discovery. The cancer drug Taxol was discovered by the NIH and marketed by Bristol-Myers Squibb. Yet the company pays the NIH just 0.5% in royalties for the drug.<sup>276</sup> The UK Medical Research Council receives royalties on many monoclonal antibody medicines developed based on their discoveries, but the royalties represent a very small proportion of the revenues earned by the companies selling the medicines.<sup>277</sup>

While the financial rewards eventually achieved by public funding agencies can offer an objective measure of success against which to hold governments accountable, it is crucial that the public sector's risk-taking occurs in a democratic context, to avoid replicating the problems of the current system where financial incentives rather than public health needs drive direction setting. This means ensuring adequate participatory governance and accountability measures to ensure decision-making on public investment indeed delivers public value.

#### b) Conditions for sharing knowledge

The public should retain not only a share of the *financial* flows that result from public funding, but also a share in the *knowledge* produced. As argued in **section 2.2**, wherever possible this should be treated as a shared resource, part of the 'knowledge commons'. This helps to ensure that the knowledge generated flows within the system as well as out to the public at



large, and is not captured by private actors. It also creates the open and collaborative environment which is essential for further innovation to thrive.

Public funding should support and stipulate participation in open data repositories, open access publishing and collaborative research initiatives. Intellectual property rights should either be avoided or shared via open licensing or participation in patent pools. Government could also retain a 'golden share' of patents developed with public funding, with patents governed in such a way to allow companies to recover their costs while spurring greater use of that specific innovation.<sup>278</sup> Ultimately, such a 'golden share' would allow the public to convert a property right previously granted into a general public licence, should the owner refuse to license broadly and fairly.<sup>279</sup>

The human genome project (**box 13**) is a good example of what can be achieved through publicly funded open access research: unprecedented scientific discovery was both funded by public money and then safeguarded for the public benefit. Such

models should be applied to as many steps of the drug discovery pipeline as possible, from basic research to late-stage clinical trials. Promoting open access platforms for sharing both the design and the outcomes of clinical trial data would allow detailed analysis and informed discussion by all interested parties, including scientists and health practitioners. Having clinical data available in the public domain (subject to ethical protections of patient identity details) would eliminate incentives and opportunities to exaggerate or underestimate evidence for profit.

### **c) Conditions for transparency of R&D costs**

Lack of transparency over the true costs incurred by pharmaceutical companies impedes both the effective functioning of markets and the ability to design fairer alternatives. Clarifying what the real costs of health R&D are would inform the national and international discussion on what constitutes a fair price, and how new models of R&D financing can be designed. Public funding could more actively stimulate this transparency.

## **Box 13. The Human Genome Project: The power of effective knowledge sharing**

In 1953 James Watson and Francis Crick discovered the chemical structure of DNA, setting the basis for understanding the detailed structure of the human gene (or human genome). A project that started with funding from the US Congress in 1990 grew into a large, collaborative international effort led by publicly funded institutes to map the genome.<sup>281</sup> Initially there was a private attempt to determine the structure and patent the results for private gain, but key scientists in the UK and the US ensured that the results of publicly funded research would be accessible in analysed form in public databases as they developed it.<sup>282</sup>

Perhaps the most interesting aspect of the project was how a large international team, mostly working in publicly funded institutes, was able to make rapid progress. The scale of equipment and resources, training and organisation in the public sphere was huge. Government bureaucracy did not stifle innovation. Efficient management and continuous monitoring supported scientists undertaking 'co-operative competition' – vying to have the best results, but also sharing lessons learned and supporting each other with specialised experiments.<sup>283</sup>

The genome project was funded and carried out internationally through public support with the long-term objective of improved human health and health care. Unquestionably, the implications of the project both now and for the future are very large. It represents an exemplary and inspiring public project for the public good.

Innovations in gene editing made possible by the discoveries of the Human Genome Project have recently become the subject of fierce patent battles, despite much of the work to develop the breakthrough gene editing technology CRISPR having been publicly funded. This appropriation has been criticised for putting at risk scientific utilisation of, and medical access to, a technology which many feel should be safeguarded for the public good just as the human genome was.<sup>284</sup>

Information on R&D costs could also empower procuring entities in price negotiations, for example through standardised financial reporting measures for each medicine (branded and generic) they procure. The state of Oregon is one of a number of US states to approve transparency legislation that not only mandates advanced warning and disclosure of price increases over a certain amount, but also requires manufacturers who impose such price increases to disclose R&D and marketing spend, profits and prices charged in other countries.<sup>280</sup> This example demonstrates that transparency measures can be introduced and mandated by the state, even in the absence of public funding contributions.

#### **d) Conditions for access and affordability**

To avoid taxpayers 'paying twice', conditions on affordability and access must be attached to public funding. One possible way to do so is through the adoption of fair pricing regulations. Although never utilised, the 1980 Bayh-Dole Act gives the US government the power to license a third party to produce a patented medicine developed with public funding, if it is not made available to the public *under reasonable terms*.<sup>285</sup> Effective use of these 'march in' rights by the US government and legislating to extend this provision to other states could help to control drug price inflation.<sup>286</sup> This proposal has increasingly gained support among members of the US Congress<sup>287</sup> and civil society organisations,<sup>288</sup> and could be adopted by other countries.

■ Managing the terms and conditions under which public and private actors negotiate funding provides powerful tools to ensure a fair and sustainable distribution of risks and benefits across the system. Crucially, these public-private relationships must be symbiotic rather than parasitic.<sup>289</sup> Ensuring a public return on public investment requires public agencies to develop the muscles and confidence to attach conditions to the provision of public funding that will create an environment where health innovation thrives and where patient access is assured.<sup>290</sup>

## **4.4 Changes to corporate governance: Beyond shareholder value**

To build a truly symbiotic public-private ecosystem, it is not enough to rely on public conditionality to constrain extractive private business models. We must also take positive steps to promote business

models that focus on value creation rather than value extraction; ownership models which share that value fairly between all stakeholders (including patients and health systems), not just shareholders; and governance models that give these stakeholders a say.

As we saw in **section 1.4**, short-termism and financialisation are increasingly pushing shareholder-owned companies towards extractive practices such as share buybacks, rather than towards public value creation. This problem is certainly not unique to the pharmaceutical sector, and many of the reforms we suggest could be applied to different industrial sectors too. However, there is a particularly strong case for applying them to the health sector, given that it is heavily financed by the public and controls products which are essential to human health.

### **Policy Steps:**

#### **Policymakers to promote value-creating business models**

##### **a) Introduce rules to limit share buybacks**

The most 'light touch' approach would be to limit or ban share buybacks. Though this would address only the symptoms rather than the causes of 'shareholder value mentality',<sup>291</sup> it would limit the amount of value that can 'leak' out of healthcare systems in excess rewards to shareholders. It would also hopefully 'nudge' companies towards reinvesting these resources in innovation. Of course, this alone would not prevent companies from simply building up cash piles.<sup>292</sup> As discussed below, deeper changes will likely be needed to incentivise the sustained financial commitment that is necessary to support long-term, high-risk R&D projects that can deliver true health innovation.

In the US, companies have been allowed to repurchase their shares on the open market with virtually no regulatory limits since 1982.<sup>293</sup> Limiting the practice of share buybacks for firms who have benefited from publicly funded research is a first, essential step to restoring stable and equitable economic growth while ensuring pharmaceutical R&D is focused on delivering true innovation and access to medicines.<sup>294</sup>

##### **b) Change executive compensation to incentivise investments in innovation**

Stock-based compensation rewards executives for draining earnings out of the company rather than mobilising earnings to invest in innovation. In recent years there has been growing criticism of this model,

with research suggesting that it fails to reward true performance and only serves to ratchet up executive pay.<sup>295,296,297,298</sup> The UK-based High Pay Centre has suggested that stock-based incentive plans should be phased out and that the balance should shift back towards basic salary rather than large performance-related bonuses. If such bonuses are to be paid, they recommend that they should be based on broader measures of performance.<sup>299</sup> In the case of pharmaceutical companies, new rules should require that any performance-related bonuses reward the success of the company in generating new medicines that deliver therapeutic advance, at affordable prices.

### **c) Take steps to improve stakeholder governance to align corporate interests with the public interest**

A more direct way to ensure companies incorporate the public interest into their ethos, decisions and actions is to give the wider public a stake in corporate governance. There is longstanding debate over the relative merits of the US/UK model of corporate governance, which prioritises shareholder interests, and the more corporatist model adopted by central European countries such as Germany, which includes a greater voice for workers and other stakeholders on corporate boards. In 2006, the UK attempted to respond to growing criticism of the shareholder model by introducing a requirement for companies to 'have regard' to the interests of other stakeholders.<sup>300</sup> Doubts have been expressed about the impact of this measure.<sup>301</sup> In proposing to give workers direct representation on company boards, the UK government acknowledged that the current system was not working for all stakeholders, although it later backed down from this proposal.<sup>302</sup> Similar concerns have been expressed in the US.<sup>303</sup>

There are two possible approaches to corporate governance reform. One is to place stakeholders representing taxpayers, workers and patients directly on corporate boards of publicly listed pharmaceutical companies. Governments could encourage or mandate companies to allocate a certain number of board positions to such stakeholder representatives. Another is to amend the legal duties of *all* company directors so that they are obliged to serve the

interests of a range of stakeholders, rather than to prioritise shareholders. These two approaches are not mutually exclusive. Elements of these ideas have recently been advanced by the United States Senator Elizabeth Warren, whose proposed bill 'Accountable Capitalism Act' stipulates that any US corporation with revenue over US\$1 billion should consider the public interests of all stakeholders through introducing federal chartering, ensuring at least 40% of board members are elected by employees, and limiting share buybacks.<sup>304</sup>

### **d) Promote alternative ownership and governance models that promote public value creation when partnering with the private sector**

The shareholder-owned corporation is not the only way to structure economic activity, although it has become the dominant one. As we saw in **section 4.1**, other ownership and governance models are possible. Mission-oriented approaches could be used to set up new public entities designed to work differently, ensuring the benefits of public investment automatically flow to the public purse. When partnering with the private sector, governments may wish to actively prioritise ownership and governance models that promote public value creation. Just as the German Energiewende created a thriving community energy sector and a new class of citizen owners (**section 4.1(d)**), governments financing health innovators could prioritise co-operatives, 'B-Corporations' (companies that are legally required to consider their impact on their workers, customers, suppliers, community and the environment), community interest companies, and other models with an explicit public value orientation. Where none exist, they could use tax breaks, procurement policies, seed funding and regulatory tools to help incubate them, with the aim of enhancing diversity in the system as a whole.

■ Collectively these policy steps will help to create a diverse eco-system of different actors within the health innovation sector, as well as shape corporate governance and ownership to incorporate public interest and value creation from the outset.

■ **Transforming our health innovation system will not happen by default. Policymakers must take intentional steps to make it happen. Adopting a missions-oriented approach including the three policy interventions proposed in this chapter will create the context for health innovation to thrive. These proposals are not intended as one-size-fits-all prescriptions but are intended to highlight that there are a range of mechanisms policymakers can use to achieve innovative and equitable outcomes for public health.**

# Conclusions

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The current debate about health innovation is characterised by a poor understanding of what drives innovation, and in particular the respective roles of public and private actors in the innovation process. Through its analysis of the current pharmaceutical model, this report highlights how the system is largely missing the essential elements required to deliver innovation with public value: public-health directionality, a collaborative research process with equitable sharing of risks and rewards among actors, and long-term horizons to deliver accessible products.

But rather than focusing on the problems, this report focuses on practical approaches and policies that policymakers can adopt, both in the short term and in the long term, to embed the principles that allow health innovation to thrive. What is needed now is political will and international collaboration. There are immediate actions that governments can take to stem the price inflation of drugs and mitigate the access problems caused by high drug prices (**chapter 3**). By implementing pricing strategies and intellectual-property-based measures and reforms, governments can act today to improve patient access.

In the longer term, governments can take bold steps to adopt a mission-oriented approach to completely overhaul the incentives in the system, and so direct innovation to meet public health needs. Inspired by lessons learned in sectors of strategic importance (eg, defence) and building on the experience of health-related experiments (BARDA, DNDi, Human Genome Project), governments can shape mission-oriented directions for health innovation, thus creating entirely new technological horizons. By working collectively and collaboratively

with public, private and civil society bodies, these organisations can attract an array of investment from various actors to address crucial health needs for patients while spurring sustainable economic growth (see **section 4.1**).

When designing their 'mission for health', governments can include the following policies within the mission:

- Use alternative 'delinked' incentive models that allow governments to play a bigger role in direction setting while encouraging collaboration between different actors. By taking on a more active role, governments can ensure that the management of intellectual property is conducive to access as well as delivering more affordable medicines. DNDi proves that R&D can be financed in a way that does not rely on high prices and can deliver impressive results without relying on market exclusivities. Policy makers should carry out feasibility studies to explore where delinkage could work for other disease areas of public health relevance, such as cancer (**section 4.2**).
- Build a symbiotic innovation ecosystem where risks and rewards are shared among actors to ensure sustainability and equitable outcomes. Public investment must lead to public returns, and strategies of value creation have to be promoted over strategies of value extraction (**section 4.3**).
- Transform corporate governance so that we move towards business models that promote value creation and ownership models which share that value fairly between all stakeholders (including patients and health systems), and give these stakeholders a say (**section 4.4**).

All the policy proposals in this report share a common premise: a more active role for the state in health innovation. Governments should not be limited to 'fixing market failures' – financing high-risk basic research where private investments are scarce and regulating high prices after they have been set. Instead they should be actively setting the directions for health innovation in the first place, in order to serve real public health needs. Policy makers would not start from zero. The public sector already plays a crucial role as a source of 'patient' finance and attracting the 'crowding in' of private investment. An entrepreneurial state often serves as the investor of first resort even before pharmaceutical/biotechnology companies or venture capital.<sup>303</sup>

While some of these proposals will initially incur increased costs for the state, they will also deliver significant savings in the long term by bringing spiralling drug prices under control. The impact of more targeted health research on neglected areas and concentrating on delivering products with added therapeutic benefits will also increase the public value of public R&D spending.

Making the case for an expanded role of the state does not, however, negate the participation of the private sector, but rather redefines its role. The proposals outlined here show that by setting up mission-oriented organisations, by changing the incentives to innovate, and by setting conditions on public investment, we can maximise the public value of private-sector contributions. A beneficial situation for all actors can be achieved if we can balance risk taking with adequate rewards, and incentivise what is socially optimal.

The real question is whether we can afford to continue with the dysfunctional status quo. The answer is no. We need to move from an increasingly financialised health innovation system to one that promotes collective strategies of *value creation*, where value is considered as 'public value'. A system that delivers innovative medicines and health technologies that are accessible and affordable for those who need them.

**Now is the time to re-imagine and re-structure our health innovation system so that it works for all.**

# Glossary

<b>Compulsory licensing</b>	A compulsory licence is an authorisation by a competent government authority to use a patented invention by a third party without the consent of the patent holder, against a payment of 'adequate remuneration'. A 'government use' license is a particular form of compulsory licence issued by the government for its own use or for the use of a third party.
<b>Delinkage</b>	A concept in public health wherein the cost of research and development on a new medicine is 'delinked', or independent from, the medicine's final market price. Several ways to achieve delinkage have been discussed, including pooled funding for research and development and cash prizes.
<b>Innovation 'direction'</b>	For the purposes of this report, we define direction as the space where research and development efforts are focused within a system of incentives for that research and development. A patent-based innovation system, for example, incentivises research in the direction of the greatest potential profits.
<b>Innovation 'rate'</b>	For the purposes of this paper, we define rate as how efficiently time and money spent on research is translated into useable results or outcomes.
<b>International Nonproprietary Name (INN)</b>	International Nonproprietary Names (INN) facilitate the identification of pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised and is public property. A nonproprietary name is also known as a generic name. <sup>306</sup>
<b>Intellectual Property Rights</b>	A legal right granted for the protection of the products of human ingenuity. The three major types are copyrights, trademarks, and patents, although there are others. For the purposes of this report, intellectual property primarily concerns patents. A patent is a form of intellectual property granted to an inventor for the creation of something new, non-obvious to a person who is knowledgeable in the field, and useful. During the patent term (minimum 20 years) the patent holder can prevent others from making, using, or selling the invention, thereby maintaining a monopoly position in the market.
<b>List price of a medicine</b>	List prices of medicines (also known as ex-factory prices) are set by manufacturers and are publicly available. However, they do not reflect the prices that countries actually pay, because confidential discounts are agreed. <sup>307</sup>
<b>Me-too drugs</b>	'Me-too' drugs are new molecular entities with very minor chemical modifications of the prototype, but sufficiently different, according to patent standards, to obtain patent protection. 'Me-too's' often offer little or no therapeutic advance on existing drugs. The name refers to the strategy of grabbing part of the profitable market of the 'first in class' without providing significant additional therapeutic advance over existing drugs. <sup>308</sup> It is argued that some 'me-too' drugs provide therapeutic substitutes and generate competition which can drive down prices. <sup>309</sup> However, there is also evidence that prices of drugs for the same condition, which are pegged against each other, often go up rather than down over time, with older drug prices increased to match the prices of new competitors. <sup>310,311,312</sup>
<b>Patient capital</b>	Financing sources that are highly risk tolerant and which do not require short-term returns on investment.
<b>Share buyback</b>	When a company buys its own shares back from shareholders, either in the market or by making a formal offer, normally at a premium to the market price. A share buyback cuts the number of outstanding shares and thus increases earnings per share.
<b>TRIPS-plus Provisions</b>	'TRIPS-plus' provisions are measures that require more stringent IP standards than those contained in the World Trade Organisation (WTO) Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), or that limit flexibilities inherent in TRIPS. 'TRIPS-plus' provisions have regularly featured in trade agreements with the US and/or EU. A common TRIPS-plus provision is data exclusivity, whereby originator companies' clinical test data cannot be used to register a generic competitor product for a certain period of time. Because this data is required by regulatory bodies to demonstrate the safety and efficacy of a drug, a long data exclusivity period (for example, eight years in the EU) delays market entry for more affordable generic drugs. Re-doing clinical trials is often prohibitively expensive for a generic company, and in most cases cannot be ethically defended. Other examples of 'TRIPS-plus' provisions include extending the term of a patent longer than the twenty-year minimum, or introducing provisions that limit the use of compulsory licences or restrict generic competition.

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