Biologia Futura (2021) 72:129–138
https://doi.org/10.1007/s42977-020-00025-5

REVIEW

Pharmaceutical drug development: high drug prices and the hidden role of public funding

Stephanie Annett[1]

Received: 20 February 2020 / Accepted: 11 June 2020 / Published online: 22 June 2020

Abstract

In 2019, the record for the most expensive drug was broken at US$2.1 million per patient. The high costs of new drugs are justified by the pharmaceutical industry as the expense required for maintaining research and development (R&D) pipelines. However, this does not take into account that globally the public pays for between one to two-thirds of upfront R&D costs through taxpayers or charitable donations. Governments are effectively paying twice for medicines; first through R&D, and then paying the high prices upon approval. High drug prices distort research priorities, emphasising financial gains and not health gains. In this manuscript, issues surrounding the current patent-based drug development model, public funding of research and pharmaceutical lobbying will be addressed. Finally, innovations in drug development to improve public health needs and guaranteeing medication access to patients will be explored.

Keywords Pharmaceutical drug development · Public funding · Drug pricing · Pharmaceutical pricing

Introduction

The latter half of the twentieth century was a highly successful period for biomedical innovation. The polio vaccine has resulted in a 99% reduction in cases, triple drug antiretroviral therapy transformed AIDS from a death sentence to a chronic disease and scientists are developing new cancer therapies based upon genetic discoveries [1–3]. In spite of many key advances, progress is increasingly leaving many patients worldwide behind who are unable to access these benefits. Cost is one of the key determinants of access, both in patients paying out of pocket and when governments ration treatments. Those who lack access are disproportionately poor, with three quarters living in middle-income countries [4]. Individuals living in high-income countries also face challenges in accessing treatments, particularly for non-communicable diseases [5, 6].

The increasing cost of new drugs is putting pressure on health services in low-, middle- and high-income countries alike. A thriving drug development model should generate new medicines that both improves public health and ensure access to patients. However, the current patent-based drug development model fails to direct innovations towards the greatest health needs. In this manuscript, we will focus on how governments are effectively paying twice for medicines; first through R&D, and then paying high prices for the medicine developed, despite being subsidised through public funding. Furthermore, we will explore how high drug prices distort research priorities, emphasising financial gains and not health gains, and how drug access problems worldwide have damaging consequences for human health and wellbeing. Short- and long-term provisions need to be taken to ensure that public funding leads to the development of life-saving medicines that are accessible for all.

Drug development overview

The traditional model of drug development translates basic biological research into clinical therapies. The discovery of information on disease pathogenesis leads to the development of candidate therapies based upon the fundamental role of many receptors, enzymes and disease-related pathways [7, 8]. This research is funded largely by the public sector and principally conducted at academic or government research institutes [7]. Private sector funding advances the potential drug candidates through the regulatory approval processes

✉ Stephanie Annett
stephanieannett@rcsi.com

[1] School of Pharmacy and Biomolecular Science, RCSI University of Medicine and Health Sciences, Dublin, Ireland

and conducts the manufacturing, distribution and marketing [8, 9]. This is funded primarily by profits generated from previous drugs sales and capital investments [9].

In 1986, negotiations leading to the establishment of the World Trade Organisation (WTO) commenced and fifty countries did not provide patent protection on pharmaceutical products [10]. In 1995, a new unpreceded era of global intellectual property began with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) which provided a 20-year period of patent protection for health technologies [10]. WTO members were required to implement the TRIPS agreement as a condition of membership; however, this presented a policy dilemma. The agreement had major economic benefits for global trade, but the obligation to grant patents affected the availability and affordability of health technologies. In addition, human rights laws binding through international treaties require governments to 'progressively realize the highest attainable standard of health', and therefore, safeguards and flexibilities were included in the agreement [11]. This agreement then created the current system based upon incentivising health innovation through patents. However, it has also created a system in which patents provide excessive financial rewards to patent holders, mainly large pharmaceutical companies, as the monopoly created allows unrestricted high prices to be set. In other consumer markets, prices are normally constrained by supply and demand, but medicines are essential and health systems/insurers have little choice but to accept the prices in order to meet their public health obligations.

In reality, the patent process has not necessarily incentivised innovation and has led to profit driven research priorities. Disease areas which are not potential 'growth markets' are ignored, particularly diseases that affect low and middle-income countries [12]. In addition, many potential medical research avenues are not explored if they are not patentable such a generic drugs [13]. Diseases of high incidence that are chronic in nature, such as diabetes, are prioritised resulting in the side-lining of disease prevention or vaccines [14, 15]. Less profitable non-drug interventions, such as lifestyle changes and surgical treatments, are also given less priority leading to the trend of pharmaceuticalisation—the reliance on drugs to treat health, social and behavioural problems [16].

Today, the majority of new medicines have limited therapeutic value. In Europe, an analysis of 1345 new drug 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 benefit, and only 1% were considered a therapeutic advancement [17]. This analysis was reproduced by a German health technology assessment agency that reached similar conclusions, and the data is summarised in Fig. 1 [18–20]. These medicines have been termed 'me–too' drugs or drugs that have limited therapeutic advantage in comparison with existing drugs but are sufficiently different to obtain patent protection [21]. Indeed, to obtain a marketing authorisation, sponsors are not required to demonstrate their products offer a therapeutic advantage [22]. To sell these products, most drug companies spend more on marketing than on R&D [23].

Regulatory agencies are dependent upon industry fees making them vulnerable to industry demands for rapid reviews [20, 22]. The Orphan Drug Act has undoubtedly stimulated the development of drugs for rare diseases that would otherwise not be profitable and they currently dominate new drug approvals [24]. However, it is increasingly leading to a distorted system with less secure evidence of efficacy and safety, tax breaks and abruptly raising the price of medicines procured through smaller company acquisitions [25]. Furthermore, there is concerns that companies exploit the benefits of the Act by artificially subdividing diseases to create subgroups of patients that fall under the orphan drug prevalence threshold—a practice referred to as "salami slicing" [26]. A classic example of 'salami slicing' is the drug Epogen (epoetin alpha) which received orphan drug designation from the FDA for anaemia associated with end-stage renal disease, however, the drug was prescribed off label to a wide variety of anaemia patients and Epogen became a blockbuster drug generating billions [26].

The patent-based monopoly system also fails to optimise the efficacy of drug innovation. The R&D productivity, as measured by the number of new drugs approved by a given R&D spend, has halved every nine years since the 1950s [27]. This has led to major pharmaceutical companies moving away from 'breakthrough' innovations to tactics to maximise profits in the short term [28]. In addition, intellectual property rights promotes a culture of protectionism and therefore research data is not published or shared leading to a waste of financial resources and potential scientific duplication [20, 29]. This systemic lack of transparency and public accountability in data and methods hinders efficiency of the drug development process. Furthermore, in 2016, a meta-analysis of 28 studies found that unpublished studies were much more likely to report adverse events than published ones [30]. Furthermore, there is a disinvestment from high-risk research in house produced by large pharmaceutical companies to accessing experimental drugs that are already in clinical trials stages through acquisitions of smaller companies [31].

The problems of drug patent protections are further exacerbated by companies seeking to extend the patent terms beyond 20 years through a process of 'evergreening'. Evergreening is the practice of introducing a minor alteration to an existing invention and then applying for a secondary patent [32]. A study reported that on average 78% of new medicine patents correspond to drugs already on the market

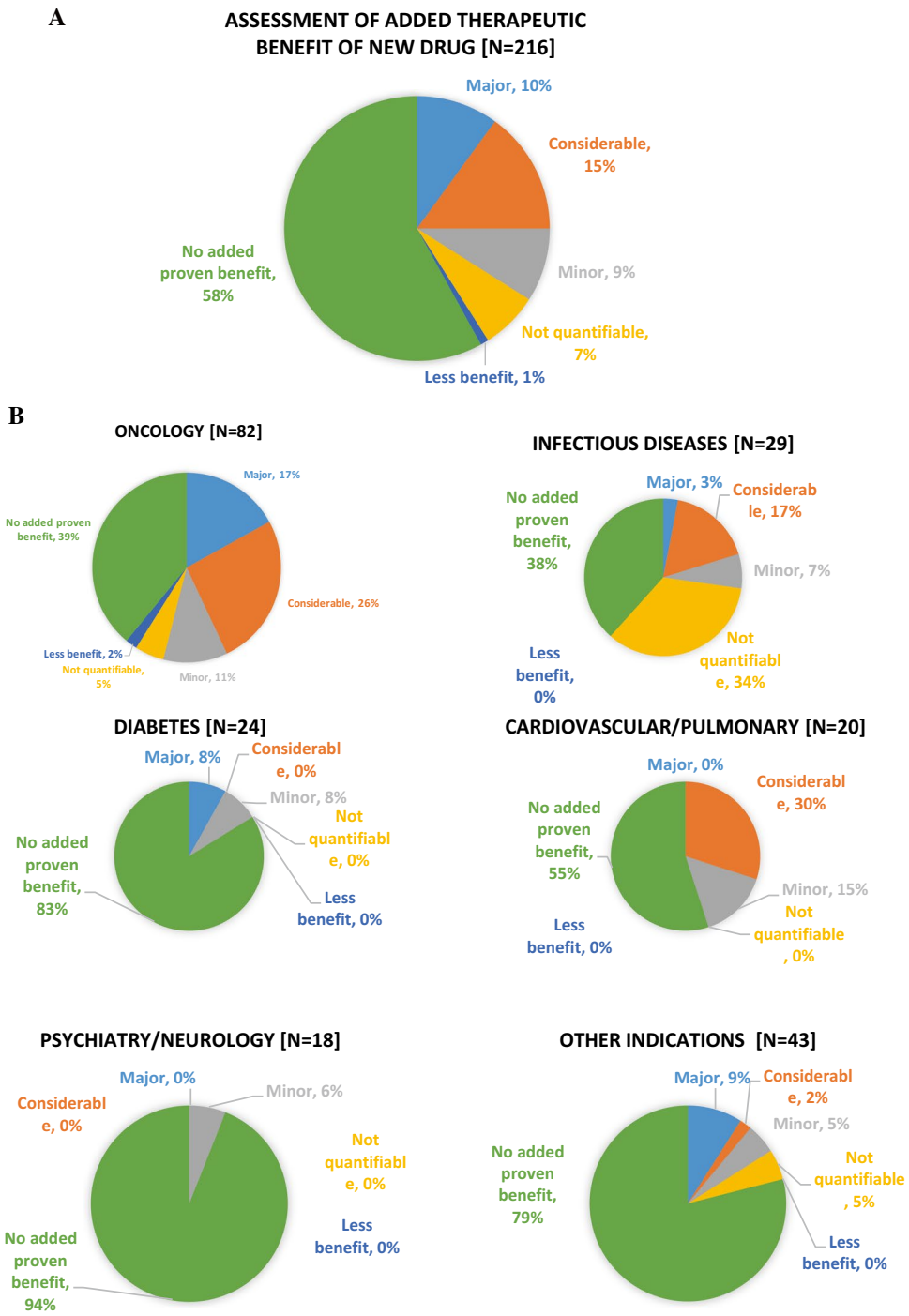

Fig. 1 Assessment of added benefit versus standard care of drugs entering the German market from 2011 to 2017 for all drug and by each indication (Adapted from [18]). **a** Assessment of added benefit of all drugs entering German market between 2011 and 2017 ($n=216$). **b** Assessment of added benefit versus standard care (assessments of drugs entering the German market 2011–2017) by indication; Oncology ($n=82$), Infectious Diseases ($n=29$), Diabetes ($n=24$), Cardiovascular/Pulmonary ($n=20$), Psychiatric/neurology ($n=18$) and Other indications ($n=43$)

with the number of drugs adding a patent almost doubling from 2010 to 2015 [33].

Following the TRIPS Agreement and in the context of the AIDS pandemic at that time, WTO members had not reached a consensus on how to interpret and apply the flexibilities within the agreement. An accord was reached and embodied in the Doha Declaration on the TRIPS agreement [34]. The Doha Declaration stresses that the TRIPS "can and should [be] interpreted and implemented" to support the "right to protect public health [and] promote access to medicines for all". However, the signatories of the TRIPS have not pursued implementation of the flexibilities that protect the health with the same rigour as enforcement of intellectual property protections [34]. The government of Thailand between 2006 and 2008 decided to grant government licences to enable the import and production of generic versions of medicines that were patent protected, including for anti-retro viral and cancer drugs [35]. The US

and European Commission, despite having signed the Doha Declaration, sought to exert political pressure on Thailand including the threat of trade sanctions [35]. This has led to the UN calling for governments and the private sector to refrain from threats and tactics that undermine the right of WTO members to use TRIPS flexibilities [34].

How much does it cost to make a new medicine?

When new therapies make it to market, they often have a price that prevents patients from accessing them. In the USA, the price of a new cancer medicine has doubled from a decade ago averaging from US$5000 to 10,000 per month and of the 12 cancer drugs approved by the FDA in 2011, 11 of them were over US$100,000 per year [36]. The UK NHS assesses a new therapy by cost effectiveness through a body called The National Institute for Health and Care Excellence (NICE). It has a threshold of approx. £20–30, 000 per year with a good quality of life [37]. However, research indicated that this limit is too high and can result in patients experiencing inferior treatment due to lack of financial resources in other areas of the NHS [37]. High drug prices have an effect beyond public health with the World Bank estimating that it pushes an additional 100 million people every year below the poverty line as they chose to buy medicines over other necessities [38]. Globally, 2 billion people cannot access the medicines they need, and this also has economic impacts due to loss of a taxable workforce because of ill health [20, 39].

The familiar narrative that the pharmaceutical industry has used to justify high drug prices is claiming they are necessary to recoup the high R&D costs and ensure sufficient capital for R&D investments for the future [20]. However, evidence suggests that only a modest amount will be spent on high risk R&D compared to what is spent in other areas such as, marketing and share buybacks [20]. The lack of transparency in drug developments means there is a profound lack of published data on the cost to produce a new medicine and only broad estimates are available. The most widely cited study, conducted by the industry funded Tufts Centre for Drug Development, estimated that the cost of bringing a new medicine to market is US$2.6 billion [40]. However, this figure has been contested, and the study has been widely criticised for biased and erroneous errors in methodology [41]. The not-for-profit drug developers, Drugs for Neglected Diseases Initiative (DND*i*) estimated the cost of a new chemical entity at €100–150 million [42]. Furthermore, analysis of ten cancer drugs by two oncologists found the median cost of developing a single cancer drug was £480 million [43].

In addition to using the narrative of R&D investment to account for high drug prices, the industry is now using 'Value Based Pricing' [20]. This is defined as the price of drug is proportionate to the intrinsic value of the drug i.e. the cost to society if a disease is not treated [20]. This methodology drives prices to the upper limit of what health systems can pay. Not surprisingly, value-based pricing has received criticism on a number of grounds. Large publicly traded pharmaceutical companies are valued on their projected profit growth over time. Biomedical research takes many years, and therefore, companies resort to drug price rises to generate growth [20]. In addition, rather than reinvesting capital, R&D companies have increasingly focused on boasting near term share price using share buyback—a method in which companies buy back their own shares to boast the value of remaining shares to shareholders in equity markets [44]. From 2007 to 2016, the 19 pharmaceutical companies in the S&P index in January 2017 spent $297 billion repurchasing their own shares, equivalent to 61% of combined R&D expenditures [44]. Overall, share buy backs have diverted R&D funds—which invest in future innovation—to passing on monopoly profits to today's shareholders [44]. Value-based pricing is not a metric to improve health outcomes but a method to maximise value extraction from society and charge health providers more [20]. In addition, industry justifications for high drug costs are undermined by the key role that public funding plays in fundamental R&D.

Role of public money in drug development

It is estimated that globally, public bodies pay between one and two-thirds for all up-front costs of R&D (Fig. 2) [45]. Cleary et al. [9] reported in PNAS that National Health Funding contributed to published research associated with every drug approved by the FDA from 2010 to 2016. Collectively, the funding totalled $100 billion and > 90% of this funding was for basic research related to the biological targets for drug action [9]. Public investment underpins the breadth of scientific discoveries leading to new therapies, and if public research funding is reduced, the pipeline for new drugs is slowed. The following case studies give an overview of the drug development process and the role of public funding from discovery through to commercialisation.

Abiraterone

The Institute of Cancer Research (ICR) is a college of the University of London in partnership with the Royal Marsden NHS Foundation Trust. It is funded by individual donations and endowments, research grants from charities, funding from royalties and government funding [46]. Researchers in the Institute of Cancer Research (ICR) in the early 1990s noted that the anti-fungal drug ketoconazole supressed androgen synthesis and was effective in treating prostate

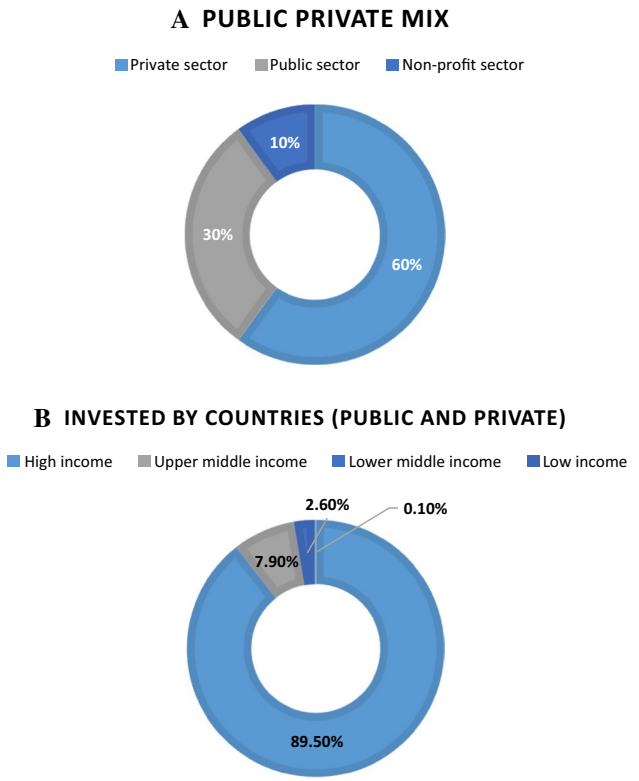

Fig. 2 Investment in research and development during 2009/2010 (Adapted from [34]). **a** An analysis of spending in wealthy countries in health research and development (R&D) found that 60% is derived by private sources and 40% from public and not-for-profit sources. The percentages were reversed for R&D in diseases that mainly affect low- and middle-income countries including HIV, TB and malaria. **b** Health research investments (public and private) by income level of country

cancer [47]. However, it had numerous undesirable effects which limited the drugs clinical applicability, and several molecules based upon ketoconazole were synthesised [48]. With grant funding from the charity Cancer Research Campaign (later known as Cancer Research UK) a novel compound with a similar mechanism of action to ketoconazole was synthesised and became known as abiraterone. Phase I, II and III trials were led by the ICR and with multiple public funders as well as industry funding [49]. Janssen, which is part of Johnson & Johnson, acquired albiraterone for approximately £600 million in 2009 [49]. It received marketing authorisation in the EU and USA in 2011, and it was due to be finished patent protection in 2018 [50, 51]. However, due to a further patent protecting the use of abiraterone with a steroid—the method of which it is licensed—the patent was extended, and therefore, generic competition has been prevented until 2027 [49].

In the UK, abiraterone was initially assessed for use in metastatic hormone-resistant prostate cancer patients, however, it was deemed not cost effective [52]. After significant pressure, Janssen offered a discount and it was recommended as a second line following chemotherapy failure in 2012 [53]. Despite the significant role of UK public funding in R&D, the NHS spent £172 million on abiraterone from 2014 to 2016 [49]. In 2016, Janssen's global sales for abiraterone were $9.7 billion whilst the ICR has earned £137 million in revenue, approx. 2% of sales [49]. In 2019, the World Health Organisation added abiraterone to the Essential Medicine List (2019) [54]. There is a disproportionately high rate of prostate cancer mortality in black African men and access to treatment is limited by costs [55]. Prostate cancer caused 7.8 deaths per 100,000 worldwide, but in sub-Saharan Africa and the Caribbean, the mortality rate is 2.5–3% higher [55]. Abiraterone is not publically available in South Africa and the private cost is the similar to the UK, despite an 8 times lower average income [49]. Based upon the price of raw albiraterone exported from India, the generic cost of estimated to be approximately US$4.08 per day [49]. Countries in Asia have been using ketoconazole instead due to prohibitive costs, however, it has potential side effects and is not approved for prostate cancer [49].

Monoclonal antibodies

Antibodies are proteins produced by human immune cells that attach to 'foreign' identities such as bacteria [56]. Monoclonal antibodies (MCA) are artificially created to bind to specific disease targets and have been revolutionary in modern medicine, particularly in cancer and autoimmune diseases [56, 57]. There are > 40 MABs available and they have generated 6 of the 10 medicines with the all-time highest sales [58]. The basic technology for producing MABs was developed at the UK Medical Research Council Laboratory which is funded primarily by the taxpayer funded UK Medical Research Council (MRC) [59]. Geoff Hale and Herman Waldmann who developed alemtuzumab, a MAB for leukaemia, wrote that the decision not to patent some of the early discoveries at MRC regarding MABs "probably did more than anything else to facilitate the widespread use of monoclonal antibodies" [49, 60]. The MRC only received a small royalty of the revenues from companies selling these very expensive medicines [61]. The recent Lancet Commission on Essential Medicines Policies considered that "monoclonal antibodies used to treat cancers [are] another example of medicines whose prices present affordability challenges to all countries, regardless of income level" [49, 62]. In South–east Asia, only 15% of eligible patients receive the monoclonal antibodies bevacizumab and cetuximab for colorectal cancer or trastuzumab for breast cancer. However, there is hope for increased access and decreased cost of MABs though the production of biosimilars [63].

It is without doubt that taxpayer and charity funded research has led to breakthrough advances in medicines in

the past decades. Despite the lack of transparency surrounding drug development, it is clear that the pharmaceutical industry makes substantial profits from medicines developed from taxpayer and charity funded R&D. The transferring of intellectual rights of medical advances from public institutes and small companies to large multinational pharmaceutical companies who then use patent monopolies to generate large profits. Whilst it has financially benefited pharmaceutical companies, the health budgets of all countries is under unprecedented strain. Any royalties paid to public institutes in the development of new medicines is dwarfed by the cost to public health systems.

Recommendations on findings

Ensuring accessibility and affordability of medicines is of global concern, and there has been influential reports published including the UN Secretary Generals High Level Panel on Access to Medicines [34], the Lancet Commission of Essential Medicines Policies [62] and the Council of the European Union [64]. A summary of the collective recommendations are discussed below.

Public interest conditions and intellectual property licenced to safeguard access to medicines

The conditions attached to R&D grants financed through public funding or charitable donations are not sufficient to guarantee access to the final medicine at a reasonable price [49]. Public funding agencies often attach provisions for open access to research grants but not conditions related to pricing or accessibility of assets derived from R&D spending [49]. To avoid taxpayers 'paying twice', conditions related to affordability and access should be attached to the funding.

To strengthen the pharmaceutical sectors commitment to long-term public health policy, public funding could be contingent on a number of conditions. This, for example, could be a requirement to reinvest a share of profits into a public innovation funds or the public receiving a share of financial returns from successful innovations [20]. In most cases today, royalties are mediocre for public agencies contributing to the discovery. For example, the cancer drug Taxol was discovered at the US taxpayer funded National Institute of Health (NIH) and marketed by Bristol-Myers Squibb, yet the NIH received just 0.5% in royalties [65].

Transparency requirements attached to public R&D funding

Companies defend the high drugs cost but do not provide details on the drug development costs, and in many cases, information on public funding of R&D is not readily available. The confidentiality that clouds R&D costs, as well as final price agreements between national governments, creates an uneven playing field for negotiators [20]. In addition, it also reduces the power of citizens, society and the media to engage in conversations over the final price [20, 49]. A greater transparency in drug development and commercialisation is a key step towards a fairer system, and this could be introduced and mandated by a state. For example, the US state of Oregon has approved transparency legislation that mandates disclosure of price increases and requires manufactures who impose price increases to disclose R&D and marketing spend, profits and prices charged to other countries [66].

Furthermore, any public funding should stipulate participation in open data repositories from basic research to late stage clinical trials. The human genome project is a prime example of what can be achieved through publically funded open access research; unprecedented scientific discovery funded by the public and safeguarded for public benefit [20, 67]. Innovations in gene editing made possible by the Human Genome Project are the subject of fierce patent battles, despite research into the breakthrough gene editing technology, CRISPR, being publically funded [20].

The price of medicines delinked from R&D costs

Using prize incentives to encourage inventors to solve problems is not a new idea. The Longitude Prize was sponsored by the British Government and awarded in 1737 to John Harrison for his novel, clock-based solution for determining a ships longitude [68]. Innovation prizes then fell out of academic and political fashion for the twentieth century (with the exception of the Soviet Union) as patents and intellectual property rights became the main drivers of technological innovation [68]. Recently, there has been a resurgence of interest in replacing intellectual property rights with prizes, particularly within the field of drug development. Novel medicines are expensive because of monopolies and when medicines are supplied generically, the price generally falls dramatically. The concept of delinking the cost of R&D from the price of medicine includes paying for R&D up-front through grants and prizes and then allowing the competitive production of the medicine [34]. Delinking allows for ownership of medicines to be kept in public, and so public health is prioritised rather than corporate profit [20]. The Drugs for Neglected Diseases Initiative (DND*i*) is a prime example of a delinked R&D model which prioritises accessibility and affordability [69]. The DND*i* was established in 2003 as a non-profit to develop treatments for neglected diseases funded through both government and private donations [69]. To date, DND*i* has brought to market eight new treatments (two for malaria; two for visceral leishmaniosis;

two for African trypanosomiasis; one for paediatric HIV/TB co-infection and one for Chagas disease) [69]. Furthermore, in 2016 DND*i* and WHO launched a not-for-profit organisation called the Global Antibiotic Research and Development Partnership (GARDP) to develop and improve new antibiotics whilst ensuring sustainable access. DND*i* builds in and considers accessibility and affordability from the beginning of the R&D process. The anti-malarial treatment artesunate/amodiaquine was developed by a partnership between DND*i* and Sanofi and was launched at a price of US$1 per adult treatment course and US$0.50 per paediatric treatment course [20].

The delinked model of drug development could be applied to other conditions outside of neglected diseases, particularly those less profitable. However, a key discussion is if delinkage could work for more profitable disease areas? Potential savings in a delinked system are vast with new medicines entering the markets at non-monopoly, generic prices. In the UK, it is estimated that the NHS cancer fund bill could be reduced by between 75 and 99.6% if it could be procured as generics on a competitive market [70]. In the US, in 2017, Senator Bernie Sander's proposed a Medical Innovations Prize Fund which 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 [71]. In 2016, this would have amounted to US$102 billion, but by supporting the R&D of affordable generic medicines, this delinked prize would have generated US$92 billion in savings during 2016 [20, 71]. In addition, the features of the delinked model such as collaboration, transparency and open access are key principles in their own right for thriving drug development. The estimated US$102 billion prize fund would be almost double the reported spend on pharmaceutical research in the US in 2018, and the key questions are; is it a large enough incentive to replace the current monopoly system? [20]. Interestingly, the DND*i* has recently extended its definition of 'neglected diseases' to include areas where drugs are increasingly not affordable including in high-income countries. For example, it has began development of an alternative treatment regimen for hepatitis C (sofosbuvir and ravidasvir) with a target price of US$300 for a 12 week course, much lower than the current price of approx. €40,000 for the branded drug [72].

Corporate lobbying

The recommendations of the UN High Level Panel on Access to Medicines (summarised above) was well received by the majority of national governments including Austria, Brazil, Portugal, Malaysia, Netherlands, India and South Africa [73]. However, the report has been strongly opposed by pharmaceutical companies as well as the US government, the European Commission, the United Kingdom, Switzerland, Japan and Germany—several of which have traditionally defended the interests of pharmaceutical companies in international negotiations [73]. The pharmaceutical industry is enmeshed at all levels of the health R&D process in developed countries such as the UK [49]. Professor John Abraham was centrally involved in the UK parliamentary inquiry called 'Inquiry into the Influence of the Pharmaceutical Industry' (2005) [74]. He notes that "the pharmaceutical industry was, and is, permitted to have privileged strategic access to, and involvement with, government regulatory policy over and above any other interest group." [49, 75]. In 2005, a House of Commons health select committee report stated "The Department [of Health] seems unable to prioritise the interests of patients and public health over the interests of the pharmaceutical industry" [49, 74]. The Department of Health was deemed jointly responsible for promoting the interests of pharmaceutical industrial companies and patients [49]. Personnel employed by the pharmaceutical industry have key positions in the UK tax payer funding agencies including the Medical Research Council, Biotechnology and Biological Sciences Research Council and the Council for Science and Technology which directly advises the Prime minister [49]. Furthermore, the Office for Life Science provides industry executives and lobbyists with direct access to ministers from the Department of Health and HM Treasury [49]. The current commercial officer for the Department of Health, Steve Oldfield has previously held senior roles in Sanofi and Teva and is a board member for the Association of British Pharmaceutical Industry [49]. In his role, he is responsible for negotiating drug prices with pharmaceutical companies despite writing openly to former prime minister David Cameron stating it "is a prevailing myth that medicines are expensive" [49, 76].

The Innovative Medicines Initiative (IMI) is a programme of public–private partnerships jointly managed by the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA) [77]. The EU contributes 50% of total funding in cash and the EFPIA members contribute 50% in 'in kind' (non-cash) contributions. The primary aim of the IMI is to make drug development cheaper, quicker and better, and it was allotted a budget of €5.3 billion between 2008 and 2020 [77]. However, it has had numerous criticism from project partners, academia, non-governmental organisations for allegedly acting as a large subsidy to the pharmaceutical industry and failing to safeguard access to an end product in research partnerships [49]. The German publication Speigel, Belgian newspaper De Standaard and Swiss broadcaster SRF jointly investigated the IMI and published a report in 2015 [78]. It stated "analysing IMI's structure, procedures and finances, [and interviewing] researchers, politicians and employees of pharmaceutical companies and non-governmental organizations"

the report found that the IMI is "funded with more than €2.5 billion […] in taxpayer money, [and] has been used almost exclusively to subsidise the pharmaceutical industry through the circuitous route of research" [49, 78]. According to non-profit campaign organisation Corporate Europe Observatory, "Big pharma enjoys semi-systematic access to decision-making in Brussels, facilitated by its vast lobby expenditure, complex web of actors, extensive meetings with policy-makers, and participation in advisory groups" [79]. In 2015, the declared lobbying spent by the pharmaceutical industry to the European Union was almost £35 million [49, 79].

Contact and collaboration between the pharmaceutical industry and the government is necessary for innovation but evidence indicates that the industry exerts an insidious and persuasive form of influence leading to bias. This bias towards corporate interests overrides public health interests leading to today's current problems of access and price. The persuasive influence of the pharmaceutical industry over government health R&D leads to questions on whether funding is in the interest of patients or if shareholders may be the greatest beneficiaries of publically funded R&D.

Conclusion

Patients worldwide are being denied access to medicines due to high costs, despite the vital role of public funding in their development. Driven by profit and share price rather than public health, the pharmaceutical sector is incentivised to set high prices and deliver short-term returns to investors, rather than focus on riskier, longer-term research which leads to much needed therapeutic advances. To break the dependence on the dysfunctional shareholder-driven pharmaceutical model, alternative models that are driven by public health interest such as delinking initiatives are required to disrupt the industry.

Funding No funding received for manuscript.

Compliance with ethical standards

Conflict of interest The author declares that they have no conflict of interest.

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