Research Article

Pharma Can Shine Even More

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Abstract: Impressive in its innovative achievements, the pharmaceutical sector is also held back by three serious inefficiencies that new reward incentives could help overcome. The proposed Health Impact Fund would offer to reward new pharmaceuticals according to their health impact in exchange for their being sold without markup. This Fund would bring forth new pharmaceuticals against the heretofore neglected diseases of poverty and would ensure that these products are accessible to all and strategically deployed to reduce disease incidence. Giving innovators the additional option of claiming health impact rewards would greatly improve the cost-effectiveness of the pharmaceutical sector in terms of human health. Home to the vast majority of pharmaceutical innovators, the G20 has a special responsibility to help shape their incentives so that they can make their fullest contribution to human health.

Introduction

One respect in which humanity has made remarkable progress in recent decades is medicine and especially pharmaceuticals. Affluent people today can expect to live healthy and productive lives well into their 80s. And the recent COVID-19 pandemic has shown that the world's pharmaceutical innovators can tackle new challenges with astonishing speed and effectiveness. Yet, despite this spectacular success, it is evident that, better incentivised, the pharmaceutical sector could do even much better. Being home to most pharmaceutical innovations worldwide, the G20 has a responsibility to help shape the sector so that its innovative capacities can thrive and have their optimal impact on human health.

The most important rules structuring and guiding the global pharmaceutical sector are laid down in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement of 1994, which is Annex 1C of the founding treaty of the World Trade Organization (WTO).[1] This Agreement entitles innovators to 20-year product patents on their innovations (Articles 27.1 and 33). For the duration of such a patent, the patentee has a temporary monopoly on the sale and use of its product in the relevant jurisdiction:

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no one else can supply or use the patented innovation without the patent holder's permission. Thus protected from competition, innovators can sell their patented products at high markups or charge high licensing fees for rights to manufacture and sell these products. Such earnings allow innovators to recoup their up-front expenses for R&D, patenting, clinical trials and pursuing regulatory approval. These large fixed costs of innovation are thus, in effect, paid for by early users of approved pharmaceuticals, who buy these products while they are still under patent.

Three Main Inefficiencies of Monopoly Patents

This dominant reward mechanism attracts little research attention to diseases heavily concentrated among poor people, who cannot pay the high prices firms must charge to recover their fixed costs of bringing a new product to market. Paradigmatic for this category are the twenty WHO-listed "neglected tropical diseases," which together afflict over a billion people[2] but attract only 0.35 per cent of pharmaceutical-industry R&D (IFPMA, 2017: 15 and 21). Heavily concentrated among the poor are also tuberculosis (WHO, 2020), malaria (WHO, 2019), hepatitis,[3] and pneumococcal diseases,[4] which together kill some 7 million people annually, and then also measles, whooping cough and diarrheal diseases. The spectacular successes pharmaceutical innovators have achieved against COVID-19 give us a sense of what they could achieve against diseases of poverty if they really brought their ingenuity to bear upon them. As it is, these vast potential health gains remain unrealised because those diseases are simply not profitable targets for pharmaceutical R&D.

A second inefficiency arises from exorbitant markups on patented pharmaceuticals. Such exorbitance is partly explained by extreme economic inequalities, both between and within countries, which lead to highly convex demand curves, ensuring that a patented pharmaceutical's profit-maximising sales price tends to be far above what most households can afford. Firms do better selling at a very high price to the affluent or well-insured, a mere fraction of the patient population, than serving more patients at a lower price. A typical example is the important hepatitis-C drug sofosbuvir, sold under the brand name Sovaldi by patent holder Gilead Sciences.[5] While its production cost amounted to an estimated $68–136, Sovaldi was introduced in the United States at a price of $84,000 per 12-week course of treatment, that is, with roughly a thousand-fold – or 100,000 per cent – markup.[6] In poorer countries, where the upper classes are less affluent and less well-insured, the profit-maximising price is much lower. But because ordinary incomes are also much lower there, such international price differentiation does not alter the fact that most people around the world cannot afford advanced medicines – at least until their patents expire, which, with Sovaldi, will start happening in 2032. Each year, millions suffer and die from lack of access to medicines that could be mass-produced quite cheaply.

Reflecting on this tragedy, one wishes for the lowest possible price, to make the relevant pharmaceutical affordable to everyone.[7] But, as illustrated by some very cheap generics, low retail prices can also impede access: by making it unprofitable to supply the product in small national markets or remote locations. For many patients, there exists

no price that would afford them access to needed pharmaceuticals – no price that is both low enough to make the product affordable and high enough to motivate sellers to supply it to them. And even when there is such a sweet price range, the actual price is most often outside this range, typically above. This leads to the second inefficiency: pharmaceuticals do not diffuse well and therefore achieve only a fraction of the health gains they would achieve if they were competently provided to all who need them. This loss of potential health impact is deeply regrettable because including the missed patients would greatly improve human health at extremely low cost (relative to the large fixed costs of creating the product in the first place).

A third inefficiency of monopoly patent rewards arises from their inattention to population effects. Imagine a firm choosing between two potential research projects, expected to result in new pharmaceuticals that will be equally good in their effects on the health of the patients treated with them. One of these products will have little effect on the evolution of the target disease, while the other will progressively reduce its incidence relative to how it would otherwise have evolved. Evidently, the public has strong reason to prefer that the latter product be pursued. But it is also evident that the pharmaceutical firm would find development of the former product more profitable because – while the profit-maximising sales price of the latter product might be slightly higher – its earnings would be depressed by lower sales volumes due to increasing shortfall in the number of patients. Even while we ardently hope that the firm will pursue the latter product, we have structured pharmaceutical markets to signal a clear preference for the former. We are penalising companies that, in addition to helping individual patients, design their research and marketing strategies toward effective reduction of the incidence of their target disease. And then we are astonished that, with all our scientific sophistication, all the trillions spent on pharmaceuticals, humanity has managed to eradicate only one lone disease, smallpox – and that over 40 years ago!

It must be said loud and clear that these three chief inefficiencies of patent rewards are not highlighted in support of some conspiracy theory or as a criticism of pharmaceutical firms. It is not in their best interest, either, that their incentives are structured as they are. To be sure, ***given*** these incentives, it is often in their best financial interest to make decisions that are not optimal for public health. But it is decidedly ***not*** in their best interest to be put into such morally conflicted situations, which expose them to temptations and suspicions of "putting profits over people." It would be much better for pharmaceutical firms if their financial interests were aligned with the public's interest in good health – if they could profitably decimate the disease burden weighing down the world's poor and could profitably design and market pharmaceuticals toward reducing the incidence of their target disease. If there were this alignment, then the question of whether firms put profits over people or people over profits would fade into insignificance: either way, they would make the same decisions. Pharmaceutical firms would do well by doing good.

Here we should also think of the people working in those firms and, more generally, in the pharmaceutical sector. Many are doing so because they want to benefit humankind. It deeply pains them to see their industry vilified in the media

and disrespected by the public. And it is even more frustrating for them to see their own firm make decisions that serve shareholder interests at the expense of public health. These employees would be much happier, and even more productive, if their pharmaceutical R&D successes had their fullest impact on the global burden of disease and if serving shareholder interests and serving public health both supported the same corporate decisions.

Finally, if the pharmaceutical sector were more efficient, and produced much greater health gains relative to inputs, then a healthier and wealthier global public would be ready to pay more into this sector. Inefficiency is the mother of opportunity: if we find a good way of overcoming it, then we can make everyone a winner.

The Health Impact Fund

To meet the opportunity created by the three inefficiencies, a Health Impact Fund that, jointly supported by many countries, would invite innovators to register any of their new pharmaceuticals for participation in 10 consecutive annual payouts, each divided among registered products according to health gains achieved in the preceding year. With these rewards enabling innovators to recoup their R&D expenses and to make appropriate profits, the price of registered products would be capped to covering their costs of manufacture and distribution. Registrants would also agree to their registered product going generic after its 10-year reward period, even if it still has unexpired patents.[8] Some variant of quality-adjusted life years (QALYs), as widely employed and refined in recent decades, could be used as a common metric for comparing and aggregating health gains across diverse diseases, therapies, demographic groups, lifestyles and cultures.[9] To reassure funders and/or innovators, a maximum and/or minimum reward per QALY could be stipulated.

The Health Impact Fund might get started with annual pools of $6 billion – less than one per cent of the $800 billion *per annum* that the world currently spends on branded pharmaceuticals. This contribution would be offset by savings on registered medicines and other health care costs, as well as by gains in economic productivity and associated tax revenues.

Innovators would remain free to charge patent-protected high prices in non-contributing affluent countries. This would give innovators more reason to register products with the Health Impact Fund, and affluent countries more reason to join the funding coalition. Over time, the Fund would grow – through economic growth in contributing countries, accession of new countries, or agreement to raise the contribution percentage – and would then attract an increasing number of new pharmaceutical products.

With annual reward pools of $6 billion, each registered product would participate in $60 billion worth of disbursements over its 10-year reward period. A commercial innovator would register a product only if it is expected to make a profit over and above recouping its R&D expenses. There is some controversy over what these fixed costs of innovation typically amount to. The Health Impact Fund would throw light on this question by revealing in what range registrations will settle. An equilibrium at about 20 products, with two entering and two exiting in a typical year, would show that the prospect of $3 billion over ten years is seen as satisfactory – neither windfall nor hardship. This is so because the Health Impact Fund's reward rate

is self-adjusting: when innovators find it unattractive, a decline in the number of registered products will raise this rate; and when innovators find the reward rate highly attractive, a rise in the number of registered products will lower it. Such automatic adjustment provides reassurance to both sides: innovators can be sure that the reward rate will not fall to the point where their efforts are unprofitable, and contributors to the Fund can be sure that the reward rate will be limited by competition among companies. In any given year, all registered products would be rewarded at the same $/QALY rate: each product's earnings would then be proportional to its health impact, which in turn would depend on the quality of the product and on how well and widely it is marketed. Some products would earn more by delivering greater therapeutic value or by benefitting more people.

Tackling the Main Inefficiencies

The addition of the Health Impact Fund would most straightforwardly address the second inefficiency: any pharmaceutical registered with the Fund would be available without markup from day one, its price capped at the lowest feasible cost of manufacture and distribution. As a result, any such new pharmaceutical would quickly become accessible to nearly all patients who need it – in contrast to new pharmaceuticals rewarded with monopoly patents, which in their early years are accessible only to the affluent or well-insured. In both reward systems, the affluent cover the lion's share of R&D costs and appropriate innovator profits. In the patent regime, they do so through markups: by purchasing pharmaceuticals at exorbitant prices or, more commonly, by buying expensive insurance policies that cover high-priced pharmaceuticals. The patent regime thus excludes all those who cannot afford such high prices or appropriate insurance.

In the Health Impact Fund regime, R&D costs and appropriate innovator profits are covered by health impact rewards, financed from ordinary progressive taxation. This makes little difference to the affluent, who again pay the lion's share. But it makes all the difference to the non-affluent: rather than flowing through markups, health impact rewards preclude markups and thereby avoid excluding the poor. Even better, because the premiums complementing sales revenues are based on health gains achieved, innovators would, despite the non-profit price, have strong incentives to bring registered products to remote and impoverished places, with clear local-language instructions and adherence support for patients and medical staff. They would have incentives even to sell their product below the price cap to very poor patients, insofar as the additional health gains thereby achieved promised rewards exceeding the subsidy. By assigning more value to the health and survival of poor people than what they themselves can afford to pay, the Health Impact Fund ensures that really all human beings can benefit from its new pharmaceutical products – that no one is left behind.[10]

Leaving no one behind is a moral imperative. But it is also collectively advantageous and thereby helps tackle the third inefficiency. This is especially evident in the case of communicable diseases, which would likely be the most attractive targets for drugs registered with the Health Impact Fund. By decimating such a disease even among the poor, we protect everyone from the threat it poses. This is a great improvement over the *status quo*, under which new pharmaceuticals against

communicable diseases are priced out of reach of the poor, thus ensuring that many avoidably remain sick and continue to spread the disease. This often causes more dangerous drug-resistant strains to emerge because patients – desperate and poor – take less than the full course of treatment or self-medicate with drugs in diluted dosage. Drug-resistant disease variants constitute a rising share of the global disease burden and pose grave dangers to public health, including that of the affluent.

The rewards of the Health Impact Fund are fully attuned to these population-level concerns. Registered pharmaceuticals are rewarded according to the reduction they achieve in the burden of disease. This includes health gains for individual patients, of course. But it also includes achieved reductions in the incidence of the target disease.

The Health Impact Fund would motivate innovators to develop effective products that could be deployed strategically to rapidly reduce disease incidence as cost-effectively as possible. Collaborating with national health systems, international agencies and NGOs, such an innovator would seek to build a strong public-health strategy around its product, involving diagnostics and other factors relevant to treatment outcomes, bolstered by real-time monitoring to recognise and address possible impediments to uptake or therapeutic success. It is unlikely, to be sure, that an innovator can deploy a new pharmaceutical to eradicate a disease within ten years. But it would nonetheless work very hard in this direction – collecting massive rewards for its impact on the incidence of the disease even while having ever fewer patients left to serve.

Last but not least, the Health Impact Fund would also address the first inefficiency of the current regime: the systematic neglect of diseases heavily concentrated among the poor, including tuberculosis, malaria, hepatitis, pneumococcal diseases, HIV/AIDS, diarrheal diseases, measles, whooping cough, diphtheria, tetanus, sexually transmitted diseases and neglected tropical diseases. These diseases tend to score highly in the four dimensions that predict how cost-effective new R&D will prove to be in terms of health gains: they are widespread and severe, thus imposing substantial disease burdens available for reduction; they have been less researched in the past and therefore afford superior chances of important pharmacological advances; and these diseases, being mostly communicable ones, allow new R&D efforts also to achieve meaningful reductions in their incidence.

The Health Impact Fund does not favor diseases of poverty or infectious diseases as such. It simply draws R&D funding toward the diseases against which the most cost-effective health gains can be achieved.[11] This favors diseases of poverty because the current regime discriminates against them. The Health Impact Fund compensates for this discrimination by correcting two distortions: it rewards all health gains equally, irrespective of the socio-economic position of their beneficiaries, and it rewards health gains from preventing infection as much as health gains from treating disease.

The paramount focus on achieving cost-effective health gains would have another noteworthy effect. Reducing disease with pharmaceuticals is complicated and involves many stages – from research lab to patient care. All these stages and components are

interdependent, posing a highly complex global logistics problem. Optimal impact requires not merely the solution of many disparate tasks but also harmony among solutions. Early decisions about conceiving and pursuing R&D projects should already anticipate the challenges of successful deployment. How to identify the patients who can benefit most and, for infectious diseases, those whose timely treatment would do most to slow contagion? How to work with health systems so that the product reaches and benefits patients in remote and impoverished locations? How to build a strong collaborative public-health strategy around the product? How to fashion the best plan toward eradicating the disease worldwide? The Health Impact Fund would train innovators toward such holistic thinking, toward achieving cost-effective health gains through a well-coordinated global strategy of disease containment.

Through the new pharmaceuticals it pulls onto the market, the Health Impact Fund would be a valuable counterpart to national health systems, the Global Fund, GAVI, MSF, UNITAID, UNAIDS and PEPFAR by making available to them, at very low prices, the novel pharmaceuticals they need. The Health Impact Fund would also engender deeper and broader knowledge about such diseases and greater capacities for developing additional, more targeted responses quickly. Innovators would thus be much better prepared to supply or develop medicines suitable for confronting emerging threats such as Ebola or COVID-19.

Going Beyond the Pharmaceutical Sector

The Health Impact Fund constitutes a meta-innovation, an innovation that rewards innovations. Its basic idea can work in any domain where a ***uniform*** metric of ***social*** value can be formulated, such as health gains (pharmaceuticals), pollution reduction (green technologies), knowledge and employment (education), nutrient yield and reduced use of fertilisers and pesticides (agriculture). Five key features of the impact-fund model are:

- While monopolies reward innovation in a way that ***impedes diffusion***, Impact funds ***delink*** the sales price from the cost of innovation.
- Impact funds also ***supplement*** what innovators earn from the sales price, by rewarding ***performance***, of which diffusion is an integral part.
- While monopoly rewards tempt innovators to put profits over people, impact funds bring profits into ***alignment*** with human needs: innovators do well by doing good.
- Impact funds organise ***competition*** across a whole domain of innovation, thereby sustaining a broad quest for the lowest-hanging fruits.
- Impact funds train innovators to work ***holistically***: to optimise the entire chain from allocating research efforts to serving end-users.

Any impact fund should ideally be global to serve more people at lower *per-capita* cost. Richer people and societies should contribute more, as they do under the current regime, but without excluding the poor. By promoting innovations and their diffusion together, impact funds fully include poor people in the orientation and benefits of innovation and thereby massively increase its social value and cost-effectiveness.

It is worth understanding how the impact fund model might work in the domain of green technologies. The

looming climate disaster has obvious similarities with the COVID-19 crisis. Both dangers have a tendency to grow exponentially. Both threaten a global catastrophe from which individual countries or regions cannot safely insulate themselves. In both cases, plausible counter-measures require concerted international collaboration; individual countries and national governments have self-interested reasons to defect from the collectively optimal collaborative plan; powerful economic interests block the path toward a global solution; and innovation is a key element in any plausible and realistic solution.

These parallels suggest that, like in the pharmaceutical sector, we are foolish to use patent monopolies to reward green innovations because we are thereby inhibiting their use. When green innovations are expensive to use, rational producers of electricity, cement or steel may well decide to do without, since this decision's fallout will mostly be externalised as the additional pollution will harm other, including future people and the rest of our planet.

It would be much smarter to reward green innovations through an Ecological Impact Fund (Pogge 2010). This approach makes sense when two conditions are fulfilled: use of the incentivised innovation serves a morally or socially desirable purpose, which makes public expenditure appropriate; and contributions to this purpose can be quantified for proportional disbursement. The Health Impact Fund fulfills the second condition through a general measure of health impact (e.g., QALYs). An Ecological Impact Fund can fulfill it by employing a suitable metric of pollution averted, which assigns weights to the various greenhouse gases, pesticides, aerosol particles, plastics, etc. Green innovators would be asked to allow cost-free use of their innovation in exchange for annual reward payments proportioned to their innovation's ecological impact. A well-financed Ecological Impact Fund would promote widespread use of green innovations while also encouraging green R&D and guiding innovators toward the specific R&D projects that can yield the most cost-effective ecological-harm reductions.

Monopoly patent rewards turn innovators into jealous spies, scouring the Earth to find possible patent infringers, who may be using their innovation without license. Impact funds do the opposite: they encourage innovators actively to promote widespread and effective deployment of their innovation so as to enlarge its impact. Wider deployment can be promoted by adding one's innovation to a patent pool, for instance, or by subsidising its use among the poor even below variable cost. More effective deployment can be promoted by various means that guide and help users to get the most value out of the product. Greater effectiveness, insofar as potential buyers care about it, also promotes wider use.

Piloting the Health Impact Fund Idea

The proposed Health Impact Fund is a large agency with an annual budget in the billions. Because it works with long-term incentives, its funding must be secured for many years into the future. To win governments' support for such an ambitious project, a significant pilot is essential. With funding from the European Research Council and active collaboration by RIS, there has already been one small pilot in India, focused on data collection for health impact assessment.[12] The next pilot should be

much larger and involve real rewards, showing how innovators respond to incentives and how much can be achieved with a given pool of reward funds.

The planned pilot would involve one single reward pool of $100 million, raised from a few governments and foundations (India, US, South Korea, Germany, Italy, UK, Canada, Gates Foundation).[13] This is not enough to finance the full development of even a single new pharmaceutical. Instead, innovators would be invited to submit proposals to increase the use of existing patented pharmaceuticals in countries or regions where they have heretofore failed to obtain meaningful sales. As with the Health Impact Fund, in the pilot they would have to sell the product in the targeted countries at cost, and the reward would then pay for their efforts to get the product used widely and effectively. An expert committee would select the four best proposals based on, *inter alia*, anticipated incremental health gains, prospects for broad, equitable access especially by the poorest, susceptibility to reliable, consistent and inexpensive health impact assessment, and promise of follow-on social value. Selected proponents – which might include non-commercial innovators such as DNDi[14] and the TB Alliance[15] or commercial innovators such as Serum Institute of India[16] – would then be given three years for implementation. At the end of this period, achieved health gains would be assessed – according to pre-agreed criteria, by an agency like the Institute for Health Metrics and Evaluation[17] or the Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen[18] – and the reward pool be divided proportionately. If this pilot were reasonably successful, an international agreement on the establishment of the Health Impact Fund would become a real possibility. In any case, the pilot would bring its own substantial health gains and health policy insights.

The G20 has consistently provided important guidance to member countries to help align policies. The Health Impact Fund offers an opportunity for the G20 collectively to support a novel mechanism to address some of the deficiencies arising in the interaction between intellectual property and public health. The G20 effectively acted to launch the Global AMR R&D Hub,[19] recognising the challenging problems in antimicrobial resistance. The challenges in developing needed medicines for other diseases, including tuberculosis, malaria, and many neglected diseases, are at last equally pressing and cry out for action. The Health Impact Fund is a solution that works within the existing institutional architecture to bring meaningful new incentives to some of the most important problems humanity faces.

Endnotes

1. For details on Agreement on Trade-Related Aspects of Intellectual Property Rights (unamended), See WTO website.
2. For more on Control of Neglected Tropical Diseases, see WHO website.
3. See Wikipedia on Hepatitis.
4. See Wikipedia for Pneumonia.
5. See Wikipedia on Sofosbuvir.
6. Sachs. 2015. Pharmaceuticals for uncommon diseases can cost even much more: a gene therapy treatment for spinal muscular atrophy, Zolgensma, is selling for $2,125,000.
7. This wish manifests itself in frequent calls for compulsory licensing, as specifically permitted under Section 5 of the Doha Declaration. With a compulsory license, a government overrules a national patent by authorizing a company within its jurisdiction to manufacture and sell the patented product in this jurisdiction while paying a small share

of its earnings to the patentee. So constrained, compulsory licenses can bring relief only in countries in which suitable manufacturing capacity exists. Compulsory licenses are strongly discouraged and penalized by the U.S. and are therefore rarely used. For the pressure the U.S. applies, see OUSTR 2020 and the many hostile reference to compulsory licensing throughout this document and its predecessors.

8. For more information and extensive critical discussion on the Health Impact Fund.
9. See Wikipedia.
10. 'Leave no one behind' "is the central, transformative promise of the 2030 Agenda for Sustainable Development and its Sustainable Development Goals (SDGs)."
11. An innovator's profit margin is the Health Impact Fund's reward rate divided by the innovator's cost-per-QALY. To maximize profit, innovators will then focus on the R&D efforts with which they can achieve health gains at the lowest cost per QALY.
12. See Pogge for 'New Tracks for Drug Development'.
13. See Health Impact Fund Pilot Proposal.
14. For further details, see Drug for Neglected Diseases Initiative.
15. See TB Alliance.
16. See Serum Institute of India.
17. See IHME.
18. See Institute for Quality and Efficiency in Health Care.
19. See Global AMR R&D Hub.

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