IIPP Policy Brief (March 2019)

Health innovation re-imagined to deliver public value

The people's prescription

Re-imagining health innovation to deliver public value

Professor Mariana Mazzucato
Director of UCL Institute for Innovation and Public Purpose

Henry Lishi Li
Research Associate, UCL Institute for Innovation and Public Purpose

This policy brief is based on the IIPP health innovation report *The people's prescription: Re-imagining health innovation to deliver public value.*

A thriving health innovation system is characterised by its ability to generate new health technologies that improve public health and ensure access to effective treatments for the people who need them (World Health Organization, 2018). However, the existing health innovation system is fraught with inefficiencies.

This policy brief provides a concise summary of the problems of the current health innovation system and sets out principles for a new one that delivers public value.

Diagnosing the problems with the current health innovation system

The current health innovation model is expensive, inefficient and unsustainable, facing problems regarding direction, rate, access and finance. Innovation is failing to direct research and development (R&D) towards the greatest health needs; and when it happens, it happens more slowly and at great cost (United Nations Secretary General's High-level Panel on Access to Medicines, 2016). Driven by profit, the pharmaceutical sector is incentivised to set high prices and focus on short-term returns to shareholders. This is at the expense of riskier, longer-term research, which leads to critically needed therapeutic advances and better public health outcomes. High prices of medicines cause severe patient access problems worldwide, with damaging consequences for human health and wellbeing (Gornall, Hoey and Ozieranski, 2016).

Problem with direction: R&D priorities are not determined by public health needs

A wide range of critical health needs (the direction) are either not being met or are sidelined in countries of all income level. A system driven by profits ignores diseases prevalent mostly in the global south, such as tuberculosis which kills millions (Wirtz, Hogerzeil and Gray et al., 2017). 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 (Année du medicament, 2015; Wieseler, 2017).

Problem with rate: 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 (Golder, Loke, Wright and Norman, 2016).

Problem with access: Out-of-reach drug prices creates barrier to access

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 (Table 1). 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 (Boseley, 2016; Hart, 2017).

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.

Problem with finance: Extensive financialisation leads to short-termism

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 USD $297 billion repurchasing their own shares, equivalent to 61% of their combined R&D expenditures over

Table 1. Public investment in biomedical innovation creates substantial private return (Mazzucato and Roy, 2017)

Health technology	Public investment	Manufacturer – prices/ revenues
Sofosbuvir-based treatments for hepatitis C	Pharmasset, the company that developed sofosbuvir (later acquired by Gilead) was based on 10+ years of Veterans Affairs and NIH (National Institute of Health)-funded research at Emory University as well as NIH-small business innovation grants.	Gilead Sciences – drugs priced at over $80,000 at launch, with over $50 billion in revenue as of Q2 2017.
CAR-T therapies for cancers	NIH invested more than $200 million to develop the CAR-T technology, 10+ years of investment across universities and research at central Bethesda campus. Novartis licensed technology from a publicly funded laboratory at the University of Pennsylvania, and Kite Pharma received significant support in running clinical trials from the NIH.	Novartis – drug approved in August 2017, prices set at $475,000; Gilead Sciences – after acquisition of Kite Pharma, prices set at >$325,000.
Paclitaxel, chemotherapy used to treat cancers	NIH/Florida State University spent $183 million developing the compound between the mid-1980s and the early 1990s, licensed the patent to BMS in 1991, and an additional $301 million on further development until 2002, making total investment $484 million; royalty payments to the NIH amounted to $35 million from 1991–2002.	Bristol Myers Squibb – over $9 billion in sales from 1992–2002.
Emtricitabine, a key component in major HIV/AIDS regimen	Drug developed by Schinazi and colleagues at Emory University with NIH funding, licensed to Triangle Pharmaceuticals (bought for $464 million by Gilead in 2004); from 1991 to 2002, Schinazi was a principle investigator in 64 NIH grants involving $10.5 million.	Gilead Sciences – total sales of emtricitabine containing regimens amounted to $33 billion between 2001 and 2011.
Infliximab used for autoimmune diseases (e.g. rheumatoid arthritis)	Publicly funded lab at NYU (lab of Jan Vilcek) worked during the 1970s and 1980s on immune-modulation to develop infliximab in collaboration with Centocor); United Kingdom, Medical Research Council (MRC) at Cambridge University provided long-term funding for the development of mono-clonal antibody research, with 65 percent of therapeutic antibodies using the intellectual property generated from this research.	Jannsen Pharmaceuticals (then Centocor) – cumulative sales of $85.5 billion through 2016 (4th highest selling medicine ever).

this period (Tulum and Lazonick, 2018). 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

Core principles that nurture a better health innovation ecosystem therefore need to overcome the problems with direction, rate, access and finance (Table 2):

Directed innovation and mission setting

Directing innovation towards public health outcomes 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 (Mazzucato, 2018).

Collaboration and transparency

Tackling public health needs require 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 e.g. 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 (Office of the High Commissioner for Human Rights, 2018). 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 patient finance that are 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.

Proposals for a health innovation system that delivers public value

Solutions to the problems of the current system cannot 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.

In the short term, immediate actions are needed to address the ongoing crises of access to medicines. Governments can implement pricing strategies and measures based on 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. Policymakers can also make intellectual property work for public health by ensuring that stringent patentability criteria are applied to prevent overly broad patents (Musungu, Villanueva and Blasetti, 2004), 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 and consider the option of using compulsory licenses. In addition, governments should more carefully consider the implications of implementing intellectual property rules that go beyond what is required by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) (United Nations Secretary-General, 2016).

Table 2. Moving towards an alternative health innovation model

	What we have now	Feature/Pillar of an alternative model
Direction	R&D priorities are not determined by public health needs	Direction for innovation is set towards purpose-led missions for maximising health outcomes
Rate	Lack of collaboration and knowledge sharing	Dynamic, collaborative system at a global level with transparent and publicly accountable scientific data at all stages, including clinical study design and outcomes
Access	High drug prices for new drugs and increasing prices for already approved drugs	Affordability for patients and better access to medicines and health technologies
Finance	Short-termism based on financialised practices to meet the expectations of near-term and continual growth	Long-term horizons supported by patient finance

In the longer term, governments need to move beyond simply treating the symptoms of this fundamentally flawed system, and 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 core principles of a better health innovation system set out in Table 2.

Lord Jim O'Neill, Chair of Chatham House (formerly of the Review on Antimicrobial Resistance), opens the report launch

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 (Mazzucato, 2017). The same approach can marshal unprecedented coordination in innovation for health. Top-down initiatives, such as governments' plans and targets for long-term goals in health innovation can help secure the long-term financial investment required to support complex research and development processes. Mission-driven organisations, exemplified by the Biochemical Advanced Research and Development Authority (BARDA), the Defense Advanced Research Projects Agency (DARPA) and the proposed Health Advanced Research Projects Agency (HARPA), can set the direction of research towards public health needs and provide risk-tolerant funding to support that direction while working with the existing private ecosystem. Furthermore, bottom-up consensus-building and experimentation in civil society have a critical role in shaping high-level political agenda and fostering mission-driven innovation contributing to meeting health challenges (Leadbeater, 2018).

Delinking incentives from high prices

A critical first step to enhance collaboration in R&D is to rethink how R&D can be better incentivised. 'Delinkage' models exemplified by Drugs for neglected Diseases Initiative (DNDi) delink the cost of R&D from the price of any resulting product. This model shows how an alternative innovation system can be supported through grants or subsidies and rewarded by a variety of prizes, including innovation inducement prizes, market entry rewards and 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 (United States Legislative Information, 2017).

Achieving public return through conditionality

As value is created collectively through the involvement of public and private actors, the rewards of innovation should also be shared to ensure sustainable capital and resources for continued innovation. 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 (Lazonick and Mazzucato, 2013). Co-sharing of risks and rewards by all actors in the innovation system is 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 (Mazzucato, 2013); 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 intellectual property rights and on occasion equity of profits (Burlamaqui, 2012); 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 the market failure box. The public sector is not just a repairer of markets when it fails: it actively co-create and co-shape markets with all types of actors. Additionally, the private sector can be better structured. Corporate governance is key. The assumption that companies must maximise shareholder value can be rethought (Lazonick, Hopkins, Jacobson, Sakinç and Tulum, 2016). Options for governments to consider include: 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.

Case study

Health Advanced Research Projects Agency (HARPA)

Dr Geoffrey Ling, Founder and Former Director of the Defense Advanced Research Projects Agency (DARPA) Biotech Office, has recently called for a HARPA that models on DARPA's success. 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. 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 National Institute of Health (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.

Dr Ling explains that "HARPA, like DARPA, would be performance-based, milestone-driven and timeline-driven with the efforts determined by the government".

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

Key features of the proposed HARPA

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 rather than 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.

Conclusion

This policy brief has summarised the main propositions for a more efficient, collaborative, innovative and equitable model for developing effective medicines—one that directs innovation efforts towards public health needs, enhances collaboration, ensures access and delivers sustainable rewards over the long-term.

The foregoing policy recommendations are radical and at the same time practical, building on what has worked around the world in health and in other sectors. 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. Transforming the current system through a mission-oriented approach requires fundamentally rethinking the role of policy away from simply patching up market failures, towards co-creating and shaping markets to deliver public value. Ultimately, 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.

References

Année du médicament. (2015). Rev Prescrire 35 (376), pp. 132-136. English summary available online: Prescrire International. (2015) 'New drugs and indications in 2014. Some advances this year, but many drugs are poorly evaluated, too expensive, or more dangerous than useful' 24(159), pp. 107-110. [Online] Available at: http://bit.ly/1Amp61o (Accessed 10 September 2018).

Boseley, S. (2016). NHS abandoning thousands by rationing hepatitis C drugs. *The Guardian*, 28 July [Online]. available at https://www.theguardian.com/society/2016/jul/28/nhs-abandoning-thousands-by-rationing-hepatitis-c-drugs (Accessed 7 September 2018).

Burlamaqui, L. (2012). Knowledge Governance: An Analytical Approach and its Policy Implications in Burlamaqui, L., Castro, A. C. and Kattel, R. (eds.) *Knowledge Governance: Reasserting the Public Interest*. London: Anthem Press, pp. 3-26.

Golder, S., Loke, Y. K., Wright, K. and Norman, G. (2016). Reporting of adverse events in published and unpublished studies of health care interventions: A systematic review. *PLoS Medicine*, 13(9), e1002127.

Gornall, J., Hoey, A. and Ozieranski, P. (2016). A pill too hard to swallow: How the NHS is limiting access to high priced drugs. *British Medical Journal*, 354, i4117.

Hart, R. (2017). Drugs are too expensive for the NHS – and people are paying with their lives. *The Guardian*, 20 December. Available at: https://www.theguardian.com/science/2017/dec/20/drug-giants-hefty-prices-nhs-vital-medication-pharma-profits (Accessed 7 September 2018)

Lazonick, W. and Mazzucato, M. (2013). The risk-reward nexus in the innovation-inequality relationship: Who takes the risks? Who gets the rewards?' *Industrial and Corporate Change*, 22(4), pp. 1093–1128.

Lazonick, W. Hopkins, M. Jacobson, K. Sakinç, M.E. and Tulum, O. (2016). U.S. Pharma's Business Model: Why It Is Broken, and How It Can Be Fixed. Submission to the United Nations Secretary-General's High-Level Panel on Access to Medicines 28 February [Online]. Available at: https://highlevelpaneldevelopment.squarespace.com/inbox/2016/3/1/the-academic-industry-research-networkb

Leadbeater, C. (2018). Movements with missions make markets (IIPP Working Paper 2018-07) [Online]. Available at: https://www.ucl.ac.uk/bartlett/public-purpose/publications/2018/aug/movements-missions-make-markets (Accessed: 10 September 2018).

Mazzucato, M. (2013) *The Entrepreneurial State – Debunking Public vs. Private Sector Myths*. Anthem Press.

Tulum, Ö., Lazonick, W. (2018). Financialized corporations in a national innovation system: The US pharmaceutical industry. *International Journal of Political Economy*, in press

Mazzucato, M. (2017). Mission-oriented innovation policy: Challenges and opportunities (IIPP Working Paper 2017-01) [Online]. Available at: https://www.ucl.ac.uk/bartlett/public-purpose/sites/public-purpose/files/iipp_working_paper_rethinking_value_in_health_innovation_1.pdf (Accessed: 10 September 2018).

Mazzucato, M. (2018). Mission-oriented research & innovation in the EU: A problem-solving approach to fuel innovation-led growth [Online]. Available at: https://ec.europa.eu/info/sites/info/files/mazzucato_report_2018.pdf (Accessed: 10 September 2018).

Office of the High Commissioner for Human Rights (2018) Fact Sheet No. 31, The Right to Health [Online]. Available at: https://www.ohchr.org/Documents/Publications/Factsheet31.pdf (Accessed 10 September 2018).

Mazzucato, M. and Roy, V. (2017). Rethinking value in health innovation: From mystifications towards prescriptions. IIPP Working Paper 2017-04 [Online]. Available at: https://www.ucl.ac.uk/bartlett/public-purpose/publications/2018/jan/rethinking-value-health-innovation-mystifications-towards-prescriptions (Accessed: 10 September 2018).

Musungu, S. F., Villanueva, S., & Blasetti, R. (2004). Utilizing TRIPS flexibilities for public health protection through South-South regional frameworks. Geneva: South Centre [Online]. Available at: http://apps.who.int/medicinedocs/collect/medicinedocs/pdf/s4968e/s4968e.pdf (Accesseed on 10 September 2018).

Secretary-General, U. N. (2016). The United Nations Secretary-General's High-Level Panel on Access to Medicines Report: Promoting innovation and access to health technologies [Online]. Available at https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/57d9c6ebf5e231b2f02cd3d4/1473890031320/UNSG+HLP+Report+FINAL+12+Sept+2016.pdf (Accessed: 10 September 2018).

United Nations Secretary General's High-level Panel on Access to Medicines. (2016). Promoting innovation and access to health technologies [Online]. Available at: http://www.unsgaccessmeds.org/s/UNSG-HLP-Report-FINAL-12-Sept-2016.pdf (Accessed: 10 September 2018).

United States Legislative Information. (2017). S.495 - Medical Innovation Prize Fund Act. Senator Sanders, B. [Online]. Available at: https://www.congress.gov/bill/115th-congress/senate-bill/495/ (Accessed: 18 September 2018).

Wieseler, B. (2017). Keynote address at the conference "Access to medicines in the baltics: Changing the narrative".

Wirtz, V. J., Hogerzeil, H. V., Gray, A. L., Bigdeli, M., de Joncheere, C. P., Ewen, M. A., Gyansa-Lutterodt, M., Jing, S., Luiza, V. L., Mbindyo, R. M., Möller, H., Moucheraud, C., Pécoul, B., Rägo, L., Rashidian, A., Ross-Degnan, D., Stephens, P. N., Teerawattananon, Y., 't Hoen, E. F. M., Wagner, A. K., Yadav, P. and Reich, M. R. (2017). Essential medicines for universal health coverage. *The Lancet*, 389(10067), pp. 403-476.

World Health Organization. (2018). What is a health technology? [Online]. Available at http://www.who.int/health-technology-assessment/about/healthtechnology/en/ (Accessed: 19 September 2018).

Further information

The full original report can be cited as follows:
UCL Institute for Innovation and Public Purpose (2018). The people's prescription: Re-imagining health innovation to deliver public value. IIPP Policy Report, 2018-10. London: IIPP, Global Justice Now, Just Treatment, STOPAIDS. Available at: https://www.ucl.ac.uk/bartlett/public-purpose/wp2018-10

We would like to acknowledge the authors of the report: Mariana Mazzucato (UCL Institute for Innovation and Public Purpose) with (in alphabetical order) Heidi Chow (Global Justice Now), Saoirse Fitzpatrick (STOPAIDS), Andrea Laplane (UCL Institute for Innovation and Public Purpose), Tiziana Masini (UCL Institute for Innovation and Public Purpose), Diarmaid McDonald (Just Treatment), Victor Roy (UCL Institute for Innovation and Public Purpose) and Ellen 't Hoen (Medicines Law & Policy).

We would like to thank the Open Society Foundations for funding our work on health innovation.

For further information, please contact:
Henry Lishi Li
henry.li@ucl.ac.uk and iipp-enquiries@ucl.ac.uk