



Beyond access to medicines: Eliciting high-income country support for a new global health research and development paradigm

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In recent decades, debates surrounding access to medicines have moved on to discussions on new ways of conducting research and development (R&D) to ensure equitable access from the outset. The market failure in the current R&D system and the need for new models has been apparent for decades [1,2]. A new framework for research and development to address health gaps primarily affecting low- and middle-income countries

(LMICs) is currently one of the most contentious issues being debated at the World Health Organization (WHO). While WHO member states agree that urgent action is needed, deciding upon models, implementation mechanisms and funding commitments has proven difficult [3].

The report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG), published in 2012, marks the most recent milestone in the search of a new R&D paradigm (Box 1) [7].

There is a need to move from the notion of R&D being the responsibility of high-income countries to it being a shared responsibility: low- and middle-income countries need to rise to the challenge of creating a new, sustainable global R&D model for the future. Globalisation and changing disease patterns necessitate a joint, global effort to battle, *inter alia*, antimicrobial resistance.

The CEWG was set the task of finding a solution to lack of funding for diseases that are not catered for by today's market forces, and they did so laudably, analysing various proposals in great depth and impressively dealing with conflicts of interest. Requiring nations to make final commitments is inevitably a difficult ask in today's economic climate. Even so, framing the recommendations as purely a set of models and mechanisms to close the gaps in accessible health care technology for the poor and failing to high-

light the benefits for high-income countries (HICs), may have undermined crucial support for a new R&D paradigm. We aim to point out the benefits HICs will accrue from adopting a new R&D framework. These benefits fall into three categories: increased investment by middle-income countries (MICs) into R&D so that HICs get increased returns on current investment; a more sustainable and efficient funding source for R&D; and direct benefits through the products of R&D into new antibiotics and vector borne diseases.

A new scheme for research and development (R&D) of medical technologies is needed. For decades the World Health Organization (WHO) has been the battlefield on which nations and non-state parties have attempted to improve access to essential medical technologies. In recent decades, debates surrounding access to medicines have moved on to discussions on new ways of conducting R&D to ensure equitable access from the outset. The report of the Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG) marks the most recent milestone in this endeavour. The CEWG proposed a global commitment to improve R&D funding and coordination for diseases primarily afflicting populations in low- and middle-income countries.

NO MORE FREE-RIDING – SHARED RESPONSIBILITY OF ALL NATIONS

One of the arguments for the globalisation of intellectual property (IP) rights through the World Trade Organization (WTO) agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) in 1994 was that LMICs were able to “free-ride” on the research conducted in HICs [8]. The proponents of this argument held the view that LMICs, whilst benefiting from the products of the translation of research, failed to contribute to it. By setting global standards for IP protection, this “free-riding” has been addressed to a degree; LMICs (particularly MICs) now largely abide by global IP protection standards, many due to the threat of economic sanctions [1]. However, this has come at a cost: access to essential medicines for the world’s poor has been jeopardised [2]. The impact of the globalisation of IP rights has been the subject of much debate. Many have questioned the wisdom of requiring countries that lack even basic health infrastructure to adhere to global standards in intellectual property [1,9]. Such debates have undoubtedly influenced the quest for new mechanisms to incentivise global health innovation [10].

Currently, the US is the world’s largest contributor to R&D addressing diseases that primarily afflict the poor. It is the only nation that meets the 0.01% of GDP minimum expenditure advocated by the CEWG [11]. Most MICs, despite having made significant gains in GDP, have arguably not contributed their fair share to R&D into diseases that primarily afflict their populations [11]. A global commitment to increase public R&D funding would enable pooling of funds from all participating nations, thus addressing the so-called free-rider problem. Countries which already contribute vast amounts would see a greater return on investment. Moreover, an equitable and sustainable model

would be created, replacing a framework based on charitable motives of HICs with one based on shared responsibility of all nations. It would also ensure that all contributing member states take ownership of investments and outcomes, a necessity for sustainability.

Knowledge created by research is a global public good. But for knowledge to be a true global public good, access has to be non-rivalrous and non-excludable: that is, without restrictions and freely available to all [12]. For this to happen, states have to take a greater part in upfront financing of research generated knowledge; legislative measures must be put in place to ensure that

such knowledge is in fact accessible to all [13]. By making knowledge derived from research more widely available, the global community has the potential to minimise – and perhaps in time eliminate – duplicative research [14]. Duplicative research slows the knowledge generating process and increases expenses associated with research [15]. According to Subra Suresh, Director of the United States National Science Foundation, “More nations recognize that innovation, driven by science and engineering (S&E), is the fuel for economic growth, prosperity, and social well-being.” [16]. As more actors from across the world increase contributions to the R&D landscape, minimising duplication of research will be ever more vital.

With the financial crisis sweeping the world, limited resources are available for R&D. These resources have to be coordinated effectively and prioritised to meet the greatest health challenges posed by the global burden of disease [17]. The CEWG suggested a convention under the auspices of WHO to ensure sustainable global governance for R&D, whereby member states, through a coordinating organ will be given the responsibility of prioritising and allocating funding.

HICs already have significant experience in advanced research, innovation, and technology transfer. They could benefit from a model with pooled funds, because the funds are likely to flow into existing research facilities, which could bring a boost for existing research projects and incentivise new ones.

MOVING TOWARDS SUSTAINABLE HEALTH RESEARCH FUNDING

Pharmaceuticals comprise a significant proportion of health expenditure; the pharmaceutical bill across the OECD

countries was estimated to have reached more than US\$ 700 billion, accounting for around 19% of health spending. In an attempt to cut overall health costs, many European countries made efforts to control pharmaceutical expenditure before the economic recession through a mix of price and volume controls directed at physicians and pharmacies, as well as policies targeting specific products [18]. In this context, it is vital that the process of pharmaceutical R&D is made as efficient as possible.

The traditional models of incentivising innovation are not delivering, even for HICs [19]. The current IP system does not incentivise innovation on the basis of need, but possible profit. Lifestyle drugs and me-too drugs flourish whereas much-needed treatments receive little funding [20]. Many companies secretly pursue similar lines of research hoping to be the first to get a product patent. Pharmaceutical companies, which are primarily responsible to their shareholders, cannot solely be blamed. Structural mechanisms that do not reward needs-driven innovation must be rectified. Moving to a system that encourages openness by its very nature would reduce inefficiencies and cut costs [14,21,22]. The problem, then, would lie with incentivising translation of basic research to commercial products [10]. HICs, therefore, have an interest in ensur-

ing that a significant proportion of the pooled funds end up as prize funds accessible to both private and public institutions. If such a model, based on openness, proves successful and minimises inefficiencies, there is potential for expanding the model.

IN THE SAME BOAT – HOW GLOBALISATION TRANSFORMS DISEASE PATTERNS

Globalisation plays an increasingly important role in human health and security [23]. With modern transportation technologies, migration and travelling have become vastly easier than a decade or two ago. People move easily between continents and, consequently, so do diseases. Indeed, many communicable diseases can now spread across countries and continents within their incubation periods, exemplified by the severe adult respiratory syndrome outbreak in 2002 and 2003, when only a concerted international effort prevented the spread from reaching pandemic proportions [24]. It is not just infectious diseases that easily traverse borders; it seems sedentary lifestyles and habits spread almost as easily. The rise of non-communicable diseases is a major global public health threat that must be



Photo: Courtesy of Sadie Regmi, personal collection

Box 1 The Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG)**WHAT**

The CEWG was established by the 63rd World Health Assembly in 2010 and consisted of professionals with a wide variety of expertise. The final report was published in April 2012 and included a set of key recommendations to address the gaps in health R&D [4].

WHY

Securing access to affordable health technologies in low- and middle income countries continues to be among the greatest challenges in global health. Underpinning the challenge is a systematic market failure in health R&D which leads to an underproduction of public goods. Incentives such as intellectual property (IP) rights have traditionally been used to address this underproduction. However, the IP model, which incentivises private industry to invest in health R&D provided they get a monopoly on the end product, has failed to provide incentives for the development of health technologies addressing diseases that primarily affect the poor.

KEY RECOMMENDATIONS

Approaches to R&D:

- Open knowledge innovation, equitable licensing and patent pools should be embraced

Funding mechanisms:

- Countries should commit to spend 0.01% of GDP on government funded R&D to meet the health needs of the poor

Pooling resources:

- 20–50% of the funds raised should be channelled through a pooled mechanism

Coordination:

- A global health observatory under the auspices of WHO should be established [5,6]

Implementation:

- A binding global instrument for health R&D and innovation should be implemented
- Formal negotiations on an international convention should be initiated.

CHALLENGES

All member states agree that the market failure in health R&D is a pressing global health challenge. However, member states, in particular high-income countries, have been reluctant to support concrete, binding commitments. The most contentious issues have been the financing commitment of 0.01% of GDP and the suggested implementation through a binding convention.

addressed through shared global action, both when it comes to prevention and treatment [17].

Disease patterns in the world have changed significantly, not just because of the movement of people, lifestyles and norms, but also the movement of disease-carrying vectors due to a changing climate. For instance, West Nile Virus is spreading across the US at an increasing pace, having affected thousands of Americans in just a decade [25]. Similarly, the incidence rates of dengue fever in the US have increased greatly, and two types of mosquitoes capable of transmitting the dengue virus can now be found in 28 states. With further changes to the climate and the following rise in average temperature, this trend is expected to continue [26].

The spread of drug resistant microbes is another major global concern. There is a large discrepancy between the burden of infectious due to multidrug-resistant bacteria and investments into the development of new antibiotics. According to the Global Risks 2013 report issued by World Economic Forum the global risk of antimicrobial resistance is linked to the “failure of the international Intellectual Property (IP) regime” [27].

These public health concerns are not country-specific and dealing with them will require concerted global efforts. Indeed, with increased globalization, it is perhaps time we

moved beyond the notion of viewing some diseases and challenges as being *tropical*. Recent history suggests that diseases which today primarily afflict populations in LMICs can evolve into true global public health threats imposing significant financial strain on health care systems in high-income countries as well.

CONCLUSIONS

The world is in transition: countries which are powerful today will not necessarily remain as powerful tomorrow, diseases are moving beyond geopolitical borders, and the threat of common antimicrobials becoming ineffective is a pressing public health issue for all. Today's R&D system is clearly not optimal: drug pipelines are not aligned with global health needs, prices for end-products are becoming ever more unaffordable, and inefficiency and declining rates of true innovations are becoming hallmarks of the R&D process. These patterns have emerged over the last few decades and despite many perceptive analyses of the situation, action towards repairing the situation remains wanting.

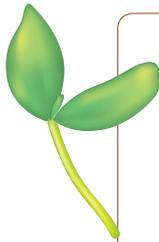
The new R&D framework suggested by the CEWG addresses some of the crucial problems in health R&D as it encompasses a number of models that could improve the existing system. Unfortunately, most HICs have so far expressed little will to truly explore the possibility of a global shift in

norms. We believe one factor contributing towards such a response is the failure to highlight the potential benefits for these countries.

There are still several unanswered questions concerning how such a new R&D framework could work: how much would each country have to contribute to make the fund large enough, and how much would need to be pooled? How many countries would need to participate? How will the coordinating organ be organised and whom should it consist of?

Wider political interest in global health has meant that the health community currently has the opportunity to debate

health R&D within a wider political arena; the CEWG's work is a solid platform on which to base these debates. WHO member states have started to identify promising demonstration projects that address the health R&D gaps through incorporation of open knowledge innovation mechanisms. This is a welcome start, but questions surrounding sustainable financing and ability or willingness to scale up such projects within a new normative framework still remain unanswered. A new R&D framework will not address every health challenge we face, but it could be a first step towards creating a sustainable system for pharmaceutical R&D where nation states bear shared responsibility for global public health.



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REFERENCES

- 1 Smith RD, Correa C, Oh C. Trade, TRIPS, and pharmaceuticals. *Lancet*. 2009;373:684-91. [Medline:19167054](#) [doi:10.1016/S0140-6736\(08\)61779-1](#)
- 2 Cohen-Kohler JC. The morally uncomfortable global drug gap. *Clin Pharmacol Ther*. 2007;82:610-4. [Medline:17898710](#) [doi:10.1038/sj.clpt.6100359](#)
- 3 Kiddell-Monroe R, Iversen JH, Gopinathan U, Medical R. D convention derailed: implications for the global health system. *Journal of Health Diplomacy*. 2013;1:1-6.
- 4 Röttingen JA, Chamas C, Goyal LC, Harb H, Lagrada L, Mayosi BM. Securing the public good of health research and development for developing countries. *Bull World Health Organ*. 2012;90:398-400. [Medline:22589577](#) [doi:10.2471/BLT.12.105460](#)
- 5 Röttingen JA, Regmi S, Eide M, Young AJ, Viergever RF, Årdal C, et al. Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory? *Lancet*. 2013. Epub ahead of print. [doi:10.1016/S0140-6736\(13\)61046-6](#)
- 6 World Health Organization. Draft working paper: A global health R&D observatory – developing a case for its development. Geneva: WHO, 2013. Available at: http://www.who.int/phi/documents/dwp1_global_health_rd_observatory_16May13.pdf. Accessed 3 October 2013.
- 7 World Health Organization. Research and development to meet health needs in developing countries: strengthening global financing and coordination. Geneva, Switzerland: WHO Press, 2012. Available at: http://www.who.int/phi/CEWG_Report_5_April_2012.pdf. Accessed: 10 October 2013.
- 8 Rechman JH. Intellectual property in international trade: opportunities and risks of a GATT connection. 1989. Available at: http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=1400&context=faculty_scholarship. Accessed: 10 October 2013.
- 9 Lopert R, Gleeson D. The high price of “free” trade: U.S. trade agreements and access to medicines. *J Law Med Ethics*. 2013;41:199-223. [Medline:23581666](#)
- 10 Regmi S. Improving global health: intellectual property rights and alternative ways of incentivizing innovation. In: Coggon J, Gola S. *Global Health and International Community*. London: Bloomsbury Academic, 2013.
- 11 Moran M, Guzman J, Ropars A-L, McDonald A, Jameson N, Omune B, et al. Neglected diseases research and development: how much are we really spending? *PLoS Med*. 2009;6:e30. [Medline:19192946](#) [doi:10.1371/journal.pmed.1000030](#)

- 12 Stiglitz JE. Knowledge as a global public good. In: Kaul I, Grunberg I, Stern MA. (Eds.). *Global public goods: International cooperation in the 21st century*. New York, NY: Oxford University Press, 1999. pp. 208–325.
- 13 Moon S. Medicines as global public goods: the governance of technological innovation in the new era of global health. *Global Health Governance*. 2009;2:1–23. Available at: http://blogs.shu.edu/ghg/wp-content/blogs.dir/109/files/2011/11/Moon_Medicines-as-Global-Public-Goods_Fall-2008-Spring-2009.pdf. Accessed: 10 October 2013.
- 14 Heller MA, Eisenberg RS. Can patents deter innovation? The anticommons in biomedical research. *Science*. 1998;280:698-701. [Medline:9563938](#) [doi:10.1126/science.280.5364.698](#)
- 15 Dasgupta P, Stiglitz J. Industrial structure and the nature of innovative activity. *Econ J*. 1980;90:266-93. [doi:10.2307/2231788](#)
- 16 Suresh S. Moving toward global science. *Science*. 2011;333:802. [Medline:21835985](#) [doi:10.1126/science.12110025](#)
- 17 Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Diseases Study. *Lancet*. 2012;380:2197-223. [Medline:23245608](#) [doi:10.1016/S0140-6736\(12\)61689-4](#)
- 18 Organisation for Economic Co-Operation and Development. *Health at a glance 2011, OECD indicators*. 2011. Retrieved from <http://www.oecd.org/els/health-systems/49105858.pdf#glance>.
- 19 Cressey D. Traditional drug-discovery model ripe for reform. *Nature*. 2011;471:17-8. [Medline:21368796](#) [doi:10.1038/471017a](#)
- 20 Gilbert D, Walley T, New B. Lifecycle medicines. *BMJ*. 2000;321:1341-4. [Medline:11090522](#) [doi:10.1136/bmj.321.7272.1341](#)
- 21 Cain C. Making the case for precompetitive clinical development. *Science-Business eXchange*. 2011;4:7-8.
- 22 Norman T, Edwards A, Bountra C, Friend S. The precompetitive space: time to move the yardsticks. *Sci Transl Med*. 2011;3:76cm10. [Medline:21451121](#) [doi:10.1126/scitranslmed.3002399](#)
- 23 Owen JW, Roberts O. Globalization, health and foreign policy: emerging linkages and interests. *Global Health*. 2005;1:12. [Medline:16053520](#) [doi:10.1186/1744-8603-1-12](#)
- 24 World Health Organization. Summary of probable SARS cases with onset illness from 1 November 2002 to 31 July 2003. Geneva: WHO, 2003. Available at: http://www.who.int/csr/sars/country/table2004_04_21/en/index.html. Accessed: 10 October 2013.
- 25 Center for Disease Control. West Nile virus disease cases and deaths reported to CDC by year and clinical presentation, 1999–2012. Atlanta (GA): CDC, 2013. Available at: http://www.cdc.gov/westnile/resources/pdfs/cummulative/99_2012_CasesAndDeathsClinicalPresentationHumanCases.pdf. Accessed: 10 October 2013.
- 26 Knowlton K, Solomon G, Rotkin-Ellman M. Fever pitch: mosquito-borne fever threat spreading in the Americas. 2009. Available at: <http://www.nrdc.org/health/dengue/>. Accessed: 10 October 2013.
- 27 World Economic Forum. *Global risks 2013 – eight edition*. 2013. Available at: <http://www.weforum.org/reports/global-risks-2013-eighth-edition>. Accessed: 10 October 2013.

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