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Commentary

Research & development in the dark: what does it take to make one medicine? And what *could* it take?

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ABSTRACT

Earlier this year a series of advertisements appeared in London's Westminster tube stations asking viewers to consider a seemingly simple question, 'what does it take to make one medicine?' But as it turns out, this question is not so simple to answer. In this commentary we highlight some key considerations and questions on what it takes to make one medicine, and what it could take to develop medicines that meet people's health needs and are accessible and affordable for all who need them.
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Earlier this year a series of advertisements appeared in London's Westminster tube stations asking viewers to consider a seemingly simple question, 'what does it take to make one medicine?' But as it turns out, this question is not so simple to answer.

Pharmaceutical company Pfizer, the sponsor of the advertisements, suggests that it takes 'more than a billion pounds', but taking a closer look at that figure leaves us with more questions than answers [1].

As a medical humanitarian organization, Médecins Sans Frontières (MSF) welcomes medical innovations that can help us and the Ministries of Health with whom we work better respond to people's health needs. But MSF teams regularly face a lack of medical tools—including drugs, vaccines and diagnostic tests—to provide appropriate care to people.

After more than 15 years of advocating for development of—and for access to—new and improved medical tools, including new antibiotics, a clear answer to the question of 'what does it take to make one medicine?' eludes us.

Lack of transparency

What does it take to make one medicine? The answer is not adhered to the walls of the London underground, but in the accounting books of innovators and developers. The answer is available, but not to the public. Instead we are encouraged to rely on industry-funded estimates based on confidential data. However, these estimates and the methods by which they were calculated have been widely criticised, including by some in the industry, like GlaxoSmithKline CEO Andrew Witty, who referred to the billion dollar figure as 'one of the great myths of industry' [2].

Although we do not know exactly how much it costs pharmaceutical companies to make one medicine, we do know that the estimates quoted by industry include the 'cost of failure', accounting for research and development (R&D) expenses for 'failed' or abandoned drug candidates that do not make it to market. In reality, there is probably significant variation in costs between different products developed and for different indications or diseases.

Additionally, up to half of the 'costs' of some industry-supported estimates represent the 'cost of capital', money not actually spent by anyone, but effectively counted as the potential return on investments that companies could have made, had they not invested in researching and developing new medical tools. Essentially, these estimates are inflated by the 'opportunity cost' of being a pharmaceutical company.

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[1] Dr Balasegaram submitted this piece during his tenure as the Access Campaign Executive Director of Doctors Without Borders/Médecins Sans Frontières. He stepped down from this position at the end of May 2016.

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Paying twice: public contributions to R&D

Despite the opacity and significant methodological concerns raised regarding existing estimates of R&D costs, these figures are used in an effort to justify the high prices charged to the public, who have often contributed significantly to the funding of R&D. People are effectively paying twice for the same product: first through public investment in medical R&D, and second through high prices.

Public funding contributes significantly to overall R&D efforts—constituting about 30% of direct funding [3], plus additional support through tax breaks and other incentives. About a quarter of new drugs originate in university laboratories, and that proportion is even higher when considering treatments addressing unmet medical needs [4]. In certain priority disease areas, like tuberculosis, most R&D funding comes from public institutions or philanthropic organizations [5].

Yet despite significant public funding for R&D and high prices for many drugs and vaccines, many priorities remain unaddressed in global health. In crises from Ebola to drug-resistant infections, we have been forced to respond virtually empty-handed, without effective treatments or vaccines. Companies too often prioritize products that offer limited additional therapeutic benefit, but that may offer substantial revenues. Prescrire's analysis of new drugs and indications approved in France over a decade found that the majority offered nothing new or were unacceptable [6]. At the same time, some major pharmaceutical companies are shuttering R&D facilities for areas of public health importance—like Pfizer's anti-infective R&D unit. When therapeutically significant drugs are developed, in too many cases—like the recently approved anti-methicillin-resistant *Staphylococcus aureus* antibiotics oritavancin and dalbavancin, which represent slight chemical modifications of the old drug vancomycin—they come with expensive price tags (up to several thousand dollars per vial in the case of these two drugs in the USA). Such high prices will not add to conservation, but do risk pricing them out of reach for those who need them most.

High prices are a global concern

The pharmaceutical industry is being increasingly challenged over expensive products, thanks to a growing recognition that the global problem of high medicine prices is unsustainable. In the USA, the Obama Administration has acknowledged 'deep concerns' about 'rapidly growing prescription drug prices', and is proposing measures to promote R&D transparency, among others [7]. In France, 110 oncologists recently spoke out against 'explosive' cancer medicine prices. Japan is similarly 'taking aim at ballooning drug prices' [8]. In April, demonstrators in 13 cities across the globe called on pharmaceutical companies to address the unaffordability of medicines.

More countries are now echoing the concerns that MSF and many others have raised over the past decade and a half—that today's medical R&D system, which incentivizes innovation primarily through monopolies, leaves tremendous needs underserved and creates significant barriers to access for millions of people. Policy discussions are escalating to global forums; the United Nations, the World Health Organization and the G7 are each considering innovation and access challenges with renewed interest.

Better models

Instead of promoting further measures that will not adequately work to address specific failures, we should ask how to deliver affordable, innovative products that meet public health needs. We should ask what it *could* take to make one new medicine.

We know from experience that more affordable and effective approaches could be possible. For example, the non-profit biomedical R&D organization Drugs for Neglected Diseases initiative estimates that the cost of developing a new chemical entity, based on their business model and experience bringing new treatments for infectious diseases to market, could be within 150 million euros, including the 'cost of failures' [9].

Conclusion

Instead of accepting the talking points of marketing campaigns, let us turn the question back on drug developers and policy makers: what does it really take to make one medicine? We need answers, and greater transparency on the costs and risks of medical R&D would help to inform the ongoing debates about how we can better deliver innovative products that are accessible to people who need them.

To start, companies can play a greater role by being transparent about their R&D costs and by pro-actively and systematically promoting access to their products. Realistic and transparent pricing, avoidance of excessive and abusive patenting strategies for medicines, fair and comprehensive voluntary licensing for developing countries, participation in patent pooling and investment in R&D that addresses public health needs are all essential to aligning medical R&D with people's health needs.

Governments should promote needs-driven innovation that protects access by supporting complementary R&D models. They should make every attempt to negotiate fair pricing and should make use of public health safeguards permitted in international trade rules. Governments should also work together to support calls for greater price and R&D transparency for medical tools, and to identify and fund innovation gaps and priorities. A global, pooled R&D fund would also be useful in providing long-term funding for key R&D priorities.

More fundamentally, governments and product developers must embrace incentives and models for R&D that do not put innovation and access into conflict, and that enable prioritization of disease areas that need urgent attention (e.g. neglected diseases, antibiotic resistance and emerging infectious diseases). For example, MSF and partners have proposed an innovative approach to financing and incentivizing R&D for new treatment regimens for tuberculosis that promotes data sharing, pools intellectual property and pays for the R&D costs up front, removing the link between these costs and the price of the products developed [10].

We all want to ensure that medical R&D both addresses public health needs and is optimally funded and incentivized. That is why we should all have an interest in understanding how to accomplish this as efficiently and effectively as possible—how to develop new medicines that are accessible to all who need them.

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