# Always the Bridesmaid…

**Although research and development for neglected diseases now commands a significant amount of attention, a new financial modeling tool shows that there is still a major funding gap.**

*By Gavin Yamey*

The recent progress in global health has been extraordinary. To give just one example, spurred on by the Millennium Development Goals, the global health community managed to cut the global child mortality rate by over half during 1990 to 2015. However, we are now in an even more ambitious era. The level of ambition is reflected in the United Nation's Sustainable Development Goals (SDGs), which include the target of ending "the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases" and ending "preventable deaths of newborns and children under 5 years of age" by 2030. Achieving these zero targets will almost certainly be impossible unless we step up our investments in neglected disease R&D to develop new, game-changing technologies. There is no credible empirical research showing that the world can reach these zero targets for global health with today's technologies alone.

Scaling up investments in neglected disease product development is a responsibility for everyone in the global

health community across the public, philanthropic, and private sectors – including pharma companies. Of the many barriers to such scale-up, a major one is the lack of consolidated information about which product candidates (drugs, vaccines, diagnostics, etc) are currently in the pipeline and at what stage, the estimated costs to move these candidates through the pipeline, and the likely product launches. If such information were more readily available it would highlight gaps in the pipeline – i.e., which diseases have no or few products under development – and enable investors and advocates to more easily drive change by targeting their investment decisions. What we ultimately need is an open access platform that has complete information on the pipeline. Such a platform would be highly valuable to public, philanthropic, and private health investors, allowing them to focus their funding on the areas of greatest need.

At Duke University's Center for Policy Impact in Global Health in the US, we are trying to put the spotlight on the need to finance R&D for neglected global health conditions. Recently, we conducted a study that aimed to shed light on the pipeline process (1). We looked at current candidates in the R&D pipeline, including vaccines, drugs, diagnostics, vector control products, contraceptives and multipurpose prevention technologies, across 35 neglected diseases. To estimate the cost of pushing these candidate products through the pipeline, we used a new, user-friendly financial modeling tool, Portfolio-to-Impact (P2I). P2I is a custom-built, public costing model developed by the WHO's TDR (the Special Programme for Research and Training in Tropical Diseases). The tool can estimate both the funding required to take candidate products from preclinical phases to launch, and the likely launches that would result. The tool shows us where the pipeline is most robust and where the real gaps are – crucial information if we, as an international health community, want to give a boost to the development of products available for the treatment, prevention and control of neglected diseases.

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## Enter the void

We initially identified 685 neglected disease product candidates as of August 31, 2017, of which 538 candidates met inclusion criteria for input into the P2I model. Of these 538 candidates, three diseases dominated the product pipeline process: HIV, malaria and TB. Specifically, they made up 57 percent of product candidates in the development pipeline, which reflects the fact they received around 70 percent of all funding for neglected disease product development. Certainly, these therapeutic areas are crucial as they contribute to an enormous number of deaths, but there are many other high-burden diseases that require attention, such as hookworm, leprosy, lymphatic filariasis, and giardiasis. Many of these just had one or two product candidates under development (and we all know the rough odds of such a small number of candidates leading to a commercialized product). For hookworm, an estimated 450 million people are infected worldwide; how can we ever hope to control the burden if it only receives 0.001 percent of total R&D funding? Our study found only two candidate products for hookworm in the pipeline.

The P2I tool estimated that it would cost around $16.3 billion to move these 538 candidates through the drug pipeline and estimated that it would result in about 128 product launches. Three-quarters of the costs incurred would be in the first five years. Around 40 percent of these launches would be diagnostics for HIV, malaria and TB – reflecting the higher probability of success for diagnostics in general compared with other product types.

Unfortunately, our study also suggests that we are unlikely to see launches by 2030 (the target year for SDGs) of 18 critically needed technologies: highly efficacious vaccines against HIV, TB, malaria, and hepatitis C (such vaccines are technologically difficult to develop and the success rates are low); a combined vaccine against multiple diarrheal diseases; a complex new chemical entity for TB; and new chemical entities for twelve neglected tropical diseases: Buruli ulcer, Chagas disease, dengue, human African trypanosomiasis, hookworm, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma, and trichuriasis.

And we are also facing a funding void. The P2I model estimates that an additional cost ranging from $13.6 billion to $21.8 billion (depending on product complexity) would be required to launch these missing 18 candidates.

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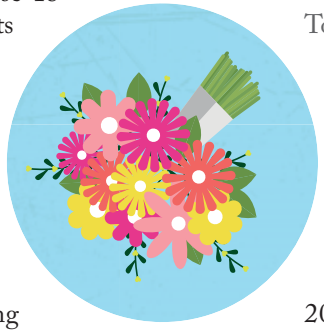
Of these additional costs, about $10.3 -16.6 billion would need to be spent in the first five years (an annualized average of $2-3.3 billion). Thus, overall, in the first five years, total estimated costs to move all current candidates through the pipeline and develop these 18 prioritized missing products would be around $4.5-5.8 billion per year. The annual G-FINDER surveys have shown that annual spending on neglected disease product development since 2008 has been around $3 billion (2), suggesting that the annual funding gap is at least $1.5-2.8 billion short. This figure is likely to be an under-estimate, as our model only looks at advanced pre-clinical to phase III costs, and does not include many other R&D costs, such as early preclinical development, regulatory review and marketing authorization.



To action!

The pharma industry is significantly under-investing in neglected disease R&D. Out of the $3.2 billion dollars invested in neglected disease product development in 2016, around 64 percent came from the public sector, 21 percent from the philanthropic sector, and just 15 percent from industry. In other words, total industry investment was just $497 million in 2016. Companies can and must do

better. The health, social, and economic returns of investing in global health R&D are enormous, representing some of the largest returns in all of global development. As one example of how huge the returns can be, consider the development of the polio vaccine. The initial development cost was roughly $26 million, and since routine vaccination was introduced, treatment cost savings have generated a net benefit of around $180 million in the US alone (3). This is an astonishing rate of return, not to mention the impact on global health and wellbeing.

I feel that the wider research community for neglected diseases has been left out of the loop by the pharma and health research industries. In particular, much of the information about neglected disease candidates that are at the preclinical research phase, and company information on product development costs, is under lock and key due to propriety interests and non-disclosure agreements. If an attitude of openness and transparency were fostered in the health research community, I think we would be better positioned to make a difference. If industry was more willing to share more information on its own neglected disease portfolio, we would be able to make more accurate estimations about the cost of moving candidates through the pipeline and the likely launches. I'd love to see other interested parties, including pharmaceutical companies, exploring tools like P2I to see how they can adapt it to create their own scenarios. And importantly, we should all be sharing the results so that we can inform the global healthcare community and devise new processes for supporting R&D for neglected diseases.

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*References*

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