Hed: What COVID-19 Drug Development Can Learn From Neglected Diseases

Dek: Global health partnerships offer lessons for developing drugs and vaccines in the current pandemic.

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The COVID-19 pandemic highlights how few drugs are available for treating infectious diseases. Such diseases are often neglected by national and international public health authorities and the global pharmaceutical industry, despite regular calls from the World Health Organization (WHO) and other supranational groups—and thus there has been little innovation in developing drugs, vaccines, and diagnostic tools to fight them.

We argue that COVID-19 drug and vaccine development can build on lessons from drug-development partnerships that *do* tackle neglected diseases. [These partnerships have shown success as “systems integrators](https://www.sciencedirect.com/science/article/pii/S0040162519300411?via%3Dihub),” which bring together expertise from many different stakeholders. Further success can be achieved by managing the relationships among these stakeholders, and this will require meeting challenges involving power, trust, governance, and risk.

The shortfall of innovation for neglected and infectious diseases traces to four key factors. First is a general lack of interest. Historically, most infectious diseases have been considered poverty-related. Ninety percent of deaths from infectious diseases occur in developing and less developed countries, and there is little motivation for political leaders and the pharmaceutical industry in developed countries to work on them. Two examples that resulted from this lack of interest are the [United Kingdom’s decision not to implement key findings of a 2016 pandemic-planning exercise](https://www.theguardian.com/politics/2020/mar/29/uk-strategy-to-address-pandemic-threat-not-properly-implemented), and the United States’ decision in 2018 to disband [the National Security Council’s unit that dealt with global health and security](https://www.washingtonpost.com/news/to-your-health/wp/2018/05/10/top-white-house-official-in-charge-of-pandemic-response-exits-abruptly/). Both actions made clear that preparing for a pandemic involving infectious diseases was not a top priority.

Lack of adequate funding for research and development is the second factor. The pharmaceutical industry is simply not incentivized to develop new drugs and vaccines for neglected diseases. In 2010, total global investment in R&D on neglected diseases was approximately $2.4 billion (in US dollars), [which was about 1% of the overall health R&D investment](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61046-6/fulltext). The limited funding for R&D is most strikingly reflected in the small number of new products for neglected and infectious diseases. Between 1975 and 1999, [only 16 new drugs were developed and registered for neglected diseases](https://www.sciencedirect.com/science/article/pii/S0140673602090967), out of a total of 1,393 drugs emerging during that period. Between 2000 and 2011, [only 37 of 850 new drugs and vaccines were for neglected diseases](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(13)70078-0/fulltext)—and among the 25 drugs in this group, only four were newly developed chemical entities. More crucially, as of December 2011, only 1% of clinical trials were for neglected diseases.

Lack of ownership and leadership is the third reason. The United Nations established the World Health Organization to exercise leadership in the global health field, but WHO does not currently play that role. The global health innovation system has undergone significant changes, especially since 2000. Nongovernmental, private, and major philanthropic organizations have arrived with the overarching aim of integrating research, development, and delivery of health interventions. These changes have been critical for developing products for neglected diseases, but they result from WHO’s diminishing central role.

Lack of coordination and collaboration is the fourth reason. Even as the global health system goes through major changes, various stakeholders have begun to collaborate to further scientific knowledge for neglected and infectious diseases. Against this backdrop, public-private partnerships (PPPs) have begun to play a greater role. Among these are product development partnerships (PDPs), which aim to develop pharmaceutical solutions particularly for low- and middle-income countries. In recent years, PDPs have emerged as key organizations to drive innovation for neglected diseases and ensure that new drugs are affordable and accessible.

[One example of the power of partnerships can be seen in the development of the antimalarial treatment ASMQ](https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-12-68), which combines the two existing drugs of artesunate and mefloquine. Starting in 2002, WHO partnered with groups including the nonprofit Drugs for Neglected Diseases Initiative to raise money, develop the drug combination, and make it available as a first-line treatment for malaria in South America and Southeast Asia. The partnership was successful because it brought together multiple actors in the global health innovation ecosystem: for-profit and nonprofit organizations, government institutions, and individuals including public health researchers, patients, and policy-makers.

In this global product innovation ecosystem, PDPs serve as the system integrators for bringing together expertise from different stakeholders. On one hand, the PDPs work toward attracting and generating funds from key funders, including philanthropic organizations. On the other hand, they tap into the scientific and technical knowledge base of partners from academia, public and private-sector organizations, and various international agencies in long-term partnerships to leverage each other’s strengths to reach the common goal of developing a new drug.

In most instances, PDPs work as virtual nonprofit R&D organizations that possess technical expertise and provide oversight both upstream (in research and discovery) and downstream (in clinical trials and manufacturing). Like any large pharmaceutical company, PDPs actively manage a portfolio of product development projects. In the process, they spread their risk and increase the chances of success. Some, such as the Medicines for Malaria Venture and the Global Alliance for TB Drug Development, focus on a single disease; others, such as the Drugs for Neglected Diseases initiative, have a broader remit.

PDPs share a number of distinctive features. They are nonprofit organizations with no shareholders pressuring for growth and revenue. They aim to develop new medical products that can improve public health. They engage and leverage diverse resources and capabilities of various players in the R&D chain. And they have the technical expertise to manage a number of R&D projects.

We argue that [this focus on using system integrators is key to successful drug innovation and development](https://journals.aom.org/doi/abs/10.5465/amp.2019.0023). Understanding how PDPs perform that role is important, yet there has been very little research into their strategic management and organization. As PDPs show, there are many actors in the global health system that need to work together smoothly—but they are intertwined in complex, dynamic, and shape-shifting relationships.

As mentioned, effectively managing PDPs involves balancing issues of power, trust, governance, and risk. Power is skewed in favor of key funders in most cases. Therefore, it is critical that PDPs form and manage their relationships based on mutual trust—particularly competence trust, which is one partner’s trust in the resources and capabilities of the other partner. A transparent and smooth governance structure contributes to generating trust in the drug development ecosystem. And risk is a distinctive component in these complex relationships because multiple actors spanning different countries and sectors must work together in an area that is characterized by high attrition rates and failure. The development of the antimalarial treatment ASMQ provides a template for how a PDP can balance these four critical factors to effectively deliver solutions to “wicked problems” such as COVID-19.

And the challenges will be great. The effort to develop drugs and vaccines for COVID-19 is seriously fragmented. [Well over 100 vaccine candidates are being pursued](https://www.nature.com/articles/d41573-020-00073-5) without global coordination, and the same problem afflicts numerous drug candidates under investigation. A solution for COVID-19 will require more concerted global efforts in real time, just as any other major infectious disease does.

Key PDP relationships are beginning to emerge for COVID-19, such as the collaboration among partners from academia, industry, and government to test and develop the antiviral drug remdesivir. Similarly, a UK-based pharmaceutical company is working with industry and government partners in China to develop one of the vaccine candidates. The global health system should look to the example of PDPs to figure out ways to balance trust, control, and risk among the many groups working to develop drugs and vaccines against COVID-19.

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