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Zika virus and the need for pharmaceutical preparedness

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Epidemics are on the rise given globalisation, increasing vector populations, and rapid mutations of known viruses, yet our pharmaceutical development has largely played catch-up to the serious outbreaks of the past few years. While tactics such as rapid diagnostics, health systems strengthening, and epidemiologic response have attempted to mitigate the consequences of epidemic disaster, a fundamental restructuring of pharmaceutical research and development incentives is urgently needed to revolutionise our future preparedness for the next potential pandemic.

Zika virus: a failure of pharmaceutical innovation

Most recently, Zika virus is a prime example of this problem. As of April 2017, 48 countries/territories in the Americas have been noted to have Zika cases, and over 60 countries worldwide. While the public health response to Zika has been robust, thanks to lessons learned from the preceding Ebola outbreak, the questions remain: could we have been better prepared for the Zika epidemic, and how are we going to prepare for future related epidemics?

Zika virus emerged quickly, with relatively little warning given the rarity of serious epidemics from the virus in the past several decades. Without significant prior threat, there were weak incentives to develop a vaccine or therapy for Zika virus until it became a pandemic declared as a global emergency by the WHO. Now, drug development is far behind the pandemic, playing catch-up to the spreading disease without a single approved Zika-specific therapy. While control efforts, such as mosquito elimination and rapid diagnostics are essential, the need for therapeutics and vaccines is unmistakable.

Suggestions for rapid Zika therapeutic development include drug repurposing, utilising existing FDA-approved therapies to test their antiviral properties against Zika virus; the movement toward open-access data for related diseases, such as dengue, which could help researchers advance development quickly for Zika; and the utilisation of an in vitro assay for high throughput screening of vaccine/drug candidates. The anti-Hepatitis C drug sofosbuvir has been suggested for potential repurposing for Zika given an 80% overlap in the amino acids of Zika and hepatitis C virus RNA. In a screening of 774 FDA-approved drugs, over 20 showed anti-Zika virus activity. Proposals for Zika vaccine development have been multifold, and acknowledge the complexity of following routine human safety protocols given active outbreaks with potentially high mortality and morbidity.

Another avenue through which drug development could be incentivised is the FDA's Priority Review Vouchers for

neglected tropical diseases, which allow pharmaceutical companies to recoup some of their R&D costs by bringing another drug to market earlier through expedited review times. With pandemics like Ebola and Zika, the market for needed drugs develops over-night, meaning the potential for profits is not necessarily the major issue as it is for orphan drugs, for instance. The conundrum lies with the fact that this market develops only once an outbreak occurs, at which point many lives are lost before a vaccine or therapy can be developed. Advanced market commitments and compulsory licensing are other mechanisms that have been written about previously for addressing drug demands in emergency situations, such as pandemics.

Preparing for pandemics before they happen

While these approaches are important, a system of addressing pandemics before they occur is what is most critically needed. The USAID Emerging Pandemic Threats (EPT) program, started in 2009, and now extended until 2019 as "EPT-2", was designed for the early detection of disease threats, reduction in disease emergence, and enhancement



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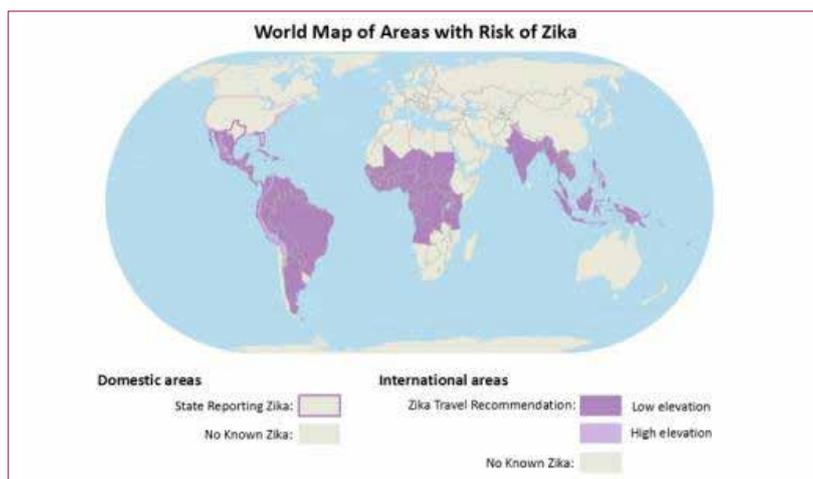


Image adapted from CDC: <https://www.cdc.gov/travel/files/zika-areas-of-risk.pdf>

of national response preparedness. Nonetheless, this program does not address the need for pharmaceutical investment and development in emerging pandemics that are primarily developing in Sub-Saharan Africa, the South/Central Americas, and Asia.

To truly address pandemics pre-emptively, we must create financial incentives in the pharmaceutical sector. Given that most pandemics start off as a few cases of disease primarily afflicting the poor, we must recognise that the existing paradigm of pharmaceutical research and development discourages pandemic preparedness at its earlier stages. If there had been Zika cases in affluent nations, or in countries in which tourism attracted people from developed economies, we would likely already have a vaccine developed many years ago. Thus, Zika and other pandemics are a reflection of the lack of public health attention for the poor at a global level, now manifesting more widely because of globalisation and international travel.

Mechanisms to truly re-structure the pharmaceutical patent system are relatively few, but greatly needed. The **Health Impact Fund (HIF)** is one such solution that has **been written about previously** as a truly transformative approach for developing drugs for diseases primarily affecting the poor. The HIF could have had an immense impact by incentivising early R&D efforts against Ebola and the Zika virus. The HIF is fundamentally an alternative route for pharmaceutical companies to develop medicines that would not be profitable in the traditional patent system because they treat diseases primarily affecting the poor. Funded by developed and developing countries, the HIF would offer any pharmaceutical innovator the opportunity to be rewarded according to the health impact of

an innovation, provided this innovation is sold at no more than the cost of manufacture and distribution. With this reward model, diseases concentrated among the poor would become far more lucrative targets for pharmaceutical research; and pharmaceutical innovators would have stronger incentives to work on diseases like Ebola and Zika long before they begin posing a threat to affluent populations.

Concluding thoughts

After Ebola virus became a global pandemic, much of the retrospective criticism focused on the lack of an organised, efficient, and prescient approach to controlling, treating, and managing spread of the disease. Yet little was done by way of improving vaccine and drug development as is evidenced by our response to Zika virus. The **final results of the vaccine trial were released in December 2016**, nearly 3 years after the pandemic took hold, thankfully showing 100% efficacy. In the process, we witnessed thousands of deaths worldwide, a death toll that could easily have been many times greater. Similarly, we may see many more children suffering from microcephaly, or as yet unknown effects in the future before a Zika vaccine is brought to market. Even when this happens, given high R&D costs, the vaccine will be unaffordable to most developing countries without assistance from GAVI and other international agencies. Furthermore, there may not be a traditional market for a Zika vaccine if the epidemic is brought under control prior to vaccine approval. Zika virus is another urgent reminder that our global pharmaceutical incentives are in need of fundamental restructuring such that we can be better prepared for pandemics.