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From PREDICT to prevention, one pandemic later



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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic began only a few weeks after the end of PREDICT-2, the last-standing United States Agency for International Development (USAID) Emerging Pandemic Threats funding programme, which supported a decade of virology, ecology, and epidemiology around the world. Since 2009, PREDICT worked with more than 60 countries to build capacity and strengthen zoonotic pathogen surveillance, and identified at least 931 novel virus species from 145 000 samples of wildlife, livestock, and humans.^{1,2} The end of PREDICT leaves the closely connected Global Virome Project and a much broader coalition of multidisciplinary research in the lurch; one virologist observed to *The New York Times*³ that “PREDICT needed to go on for 20 years, not 10”. Despite a lack of immediate causation, the coincidental timing with the emergence of COVID-19 has not gone unnoticed, especially on social media; the issue even gained traction in the 2020 Democratic Party presidential primaries, with Senator Elizabeth Warren’s plan for COVID-19 response explicitly mentioning the need to restore PREDICT.

Rescuing research on the emergence of zoonotic viruses is a priority—but our field, as currently positioned, is still not ready to stop current or future pandemics. In no case is this clearer than the priority placed over the past decade on discovering novel viruses in wild mammals and birds—a task that has been described as “the beginning of the end of the pandemic era”⁴ and sometimes awarded a singular status as the solution to viral emergence. History tells us viral discovery is not enough to prevent pandemics: influenza was first isolated in 1933, Zika in 1947, chikungunya in 1952, and amid the emergence of severe acute respiratory syndrome coronavirus in 2003 and Middle East respiratory syndrome coronavirus in 2012, nearly two decades of wildlife sampling has turned up hundreds of new coronavirus species.⁵ Despite these scientific achievements, the present pandemic of SARS-CoV-2 has still grown over an order of magnitude beyond its 2003 counterpart.

Is this a success or failure of the scientific programmes that aim to predict and prevent the next pandemic? Previous critiques have identified a common rhetorical link between viral discovery and pandemic prevention that oversells basic science (especially wildlife virology

and ecology), and detracts funding and attention from the need to build surveillance, diagnostics, primary health care, and effective health security measures.⁶ The transition to new funding programmes could endanger or disrupt the zoonotic surveillance and capacity building efforts that USAID Emerging Pandemic Threats programmes spent a decade building. At the same time, our knowledge of the mammalian virome has grown by several orders of magnitude in the past decade, and as a result we can more rapidly contextualise where, how, and why new human viruses originate in wildlife. This new knowledge has had a noticeable impact during the current SARS-CoV-2 outbreak: PREDICT-funded work has contributed to the sequence libraries (along with rapid isolation of the virus, and global data sharing) that allowed taxonomists to rapidly classify SARS-CoV-2 and propose candidate origins.

Nonetheless, disciplinary tensions around accountability and rhetoric suggest that academic research on emerging wildlife viruses could be better positioned for a broader overall impact. Although PREDICT almost certainly discovered hundreds of potential zoonoses, their true zoonotic potential is almost impossible to assess, leading to the surprising statistic that the programme only led to one conclusive discovery of a zoonosis, the Bas-Congo virus.⁷ For now, the only real way to tell the 10 000 potentially zoonotic mammalian viruses apart from their 40 000 low-risk counterparts⁸ is to observe a human infection. This is not for lack of trying, with several recent studies having developed statistical or machine-learning approaches to predicting zoonotic potential. Those models have helped identify gaps in wildlife sampling,⁹ wildlife reservoirs (such as bats), viral groups with the highest zoonotic potential (such as betacoronaviruses),¹⁰ and viral traits that predict human-to-human transmissibility (such as absence of a lipid envelope).¹¹ However, all of these models are trained on a small handful of datasets, which mostly capture known zoonoses and well described wildlife viruses with relatively complete data on viral traits and traits of associated host species. No current approaches are designed to assess the zoonotic risk of an individual wildlife virus only known from a handful of genetic sequences—the sort of viral observations that account for most of the data generated by PREDICT.

With 99% of the wildlife virome still undescribed,⁸ viral discovery remains a seemingly boundless scientific endeavour. But to prevent future pandemics, and to build on the US\$207 million foundation of PREDICT, our field needs a renewed ambition and a refined focus. Collaboration is needed among disease ecologists, wildlife virologists, and data scientists to develop models that integrate new data streams (like genomic and metagenomic sequencing, or host and vector competence experiments) and more complex virological data (eg, host receptor use and associated viral structures). In doing so, the next generation of zoonotic risk assessment tools might be the first to identify and call attention to future threats before the first human infection. Despite some skepticism about whether such a scientific revolution will happen any time soon, smaller methodological proof-of-concept studies already exist.^{12,13} As new funding opportunities pick up where PREDICT left off, making this work a priority will help move the field towards risk assessment that supports targeted prevention efforts, like targeted surveillance for candidate zoonoses in high-risk populations, or the development of universal vaccines for high-risk groups like betacoronaviruses. In the meantime, the SARS-CoV-2 pandemic remains its own problem, months or years past the stage where wildlife virology could have made the most difference.

I declare no competing interests.

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