excerpts from
Reducing Pandemic Risk, Promoting Global Health

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EXECUTIVE SUMMARY
The appearance and spread of diseases, such as HIV/AIDS, Severe Acute Respiratory Syndrome (SARS), Ebola virus disease (EVD), and pandemic influenza, have had profound global health impacts and adverse ramifications for human livelihoods and broader scale economics. The lives lost and financial consequences have illustrated our vulnerability to the emergence and re-emergence of infectious diseases and the disappearing boundaries between the developing and developed world.

Zoonotic diseases caused by pathogens that are shared between people and animals result in millions of deaths annually, and the economic losses from a single outbreak can amount to tens of billions of dollars. Prevention and early control of outbreaks is key to reducing the impact of epidemics and pandemics, but there remains a critical need to improve global capacity to effectively implement these mitigating activities, especially in developing countries, as demonstrated by the 2014 EVD epidemic in West Africa.

Despite greater recognition of emerging infectious diseases (EIDs), there is limited understanding of the underlying causes for emergence and spread of zoonotic pathogens in people. Viral diseases originating from wildlife have been responsible for most zoonotic EIDs in recent history. The seriousness of the risks associated with viral spillover from animals to people has led to the recognition that a shift from a conventional, reactive approach (once a disease is spreading in human populations) toward a proactive, predictive approach is necessary for EID prevention and timely control (Figure 1). The general lack of specific medicines and vaccines for new zoonotic viruses puts a premium on developing non-pharmaceutical interventions based on a detailed understanding of when, where, and how zoonotic viruses are moving from wildlife to people.

The United States Agency for International Development (USAID) initiated the Emerging Pandemic Threats (EPT) program in 2009 with the goal of strengthening capacities in developing countries to prevent, detect, and control infectious diseases. PREDICT, a surveillance and virus discovery component of the EPT program, focused on building capacity to identify potential zoonotic viral threats at high-risk wildlife-human pathogen transmission interfaces where diseases are most likely to emerge. These interfaces occur in many cultural contexts and regions and usually result from necessary daily activities, such as animal-based food production/acquisition and other income-generating activities, such as preparation or harvesting guano for agricultural fertilizer from structures constructed to attract bats (photo on previous page). Through a consortium of global and in-country partners, PREDICT’s efforts focused on early detection and response to potentially high-consequence animal viruses in regional “hotspots” for EIDs, such as central Africa, South and Southeast Asia, and Latin America. The consortium developed robust mechanisms for overcoming geographic and disciplinary constraints to public health protection by developing multidisciplinary collaborations and establishing networks and platforms for surveillance, diagnostics, and data sharing and interpretation across stakeholders.
PREDICT, implemented in over 20 countries, improved early detection and response to disease threats through five main objectives: 1) strengthening viral surveillance; 2) improving virus detection and discovery by developing laboratory and disease outbreak response capacities; 3) characterizing high-risk animal-human interfaces, behaviors, and drivers of pathogen spillover from animals to people; 4) optimizing predictive models for disease emergence and spread; and 5) deploying cutting-edge information management and communication tools to advance a more integrated, global approach to sharing data from zoonotic virus surveillance.
By enhancing in-country capacity for detection, response, and prevention of pathogen spillover and increasing connectivity among government sectors (wildlife, livestock, and human health), PREDICT effectively engaged 59 government ministries and hundreds of scientific institutions, local organizations, and other stakeholders to significantly advance One Health capacity. Our team trained 2,500 government personnel, physicians, veterinarians, resource managers, laboratory technicians, hunters, and students on biosafety, surveillance, laboratory techniques, and disease outbreak investigation. With USAID support, we equipped, supplied, and trained staff in 32 diagnostic laboratories around the world to safely and properly process and test wildlife samples for viral pathogens of known and unknown zoonotic potential. This capacity-building effort led to the safe and humane sampling of more than 56,340 nonhuman primates, bats, rodents, and other wild animals (including samples from bushmeat). PREDICT detected 959 viruses in wild animals and 34 viruses in human pilot studies (some viruses detected in both humans and animals). Viruses were classified as novel (genetically divergent from known strains and species) or known (sufficiently similar to known viruses) based on genetic sequencing. Thus far, samples have yielded 815 novel viruses and 169 known viruses.
To achieve these successes, PREDICT developed and optimized low-cost viral family-level consensus PCR methods and synthetic controls for the detection and discovery of known and new viruses in laboratories operated by our in-country partners. Our efforts resulted in the detection of more viruses in just five years than the total number of viruses previously recognized in mammals by the International Committee on Taxonomy of Viruses (ICTV; last version from ICTV in 2009 at the beginning of PREDICT). On the list of viruses detected thus far are many important human and animal pathogens, such as SARS- and Middle East respiratory syndrome (MERS)-related coronaviruses in bats, a novel rhabdovirus (Bas-Congo virus, or BASV) in humans that was associated with acute hemorrhagic fever, and Ebola viruses in humans during multiple EVD outbreaks in Africa. In fact, PREDICT has detected new coronaviruses numbering almost twice those previously acknowledged (both approved and proposed) by the ICTV by the end of 2009.

Analyses incorporating all virus detections validated our surveillance strategy – showing that PREDICT’s target wildlife taxa (i.e. bats, nonhuman primates, and rodents) were significantly more likely to test positive for a virus than other taxonomic groups sampled. A significant benefit of the PREDICT strategy is that it extends beyond the detection of viruses in wildlife and can be successfully applied in other areas – such as the diagnosis of mystery illnesses in medical hospitals and veterinary laboratories where testing capacity has historically been limited. Continuing use of our viral detection and discovery methods by in-country partners illustrates the establishment of long-term capacity for identifying known and novel viruses and should be increasingly useful in diagnosing outbreaks of diseases of unknown origin, thus speeding up the detection of EID events.

PREDICT’s risk-based surveillance strategy was focused on situations where people have frequent, direct contact with wild animals. These high-risk disease transmission interfaces have occurred where diverse groups of wildlife viruses are available to infect susceptible humans or their domestic animals, as was seen with SARS emerging from wildlife markets, EVD and HIV/AIDS from butchering or handling of wild primates, and new strains of influenza in people.

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Figure 2. Epidemiologic network map illustrating high-risk disease transmission interfaces for zoonotic viruses transmitted from wildlife to humans. High-risk interfaces are shown with node size proportionate to the number of viruses (red) reported for each transmission interface, categorized according to 1) direct contact with wildlife (blue); 2) indirect contact with wildlife (green); and 3) transmission by vector (yellow). From Johnson et al. 2014.
handling poultry. More broadly, high-risk interfaces reported in zoonotic disease transmission of viruses from wildlife to humans in the literature include contact with wildlife in and around human dwellings and during hunting or consumption of wildlife, in addition to occupational exposures including veterinarians; researchers; and workers in laboratory settings, agricultural fields, wildlife management, zoos, and sanctuaries (Figure 2). These high-risk interfaces are important targets for pathogen surveillance and may be critical points for implementation of disease prevention and control measures. Other interfaces were also targeted by surveillance to more fully investigate and rank risks for potential virus transmission, including wild animal farms; markets and restaurants; other sites on the food value chain; sites with ecotourism; and wildlife preying on livestock, raiding crops, and causing public safety hazard.

While PREDICT surveillance activities were not designed to specifically target influenza A viruses, our diagnostic strategy did include protocols to detect influenza viruses. Thus PREDICT contributed protocols for testing to laboratories and facilitated influenza A screening of wildlife and human samples in collaborating laboratories. In order to understand the role wild birds play in the emergence of zoonotic influenza viruses, PREDICT scientists examined 11,870 sequences from the National Institutes of Health genetic sequence database, GenBank, and gathered data from 50 studies and over 250,000 birds to provide a baseline inventory and insight into patterns of global influenza A subtype diversity and richness in wild birds. Over 116 influenza A strains occurred in wild birds globally, which is approximately twice the number found in domestic birds. In an effort to understand factors driving the evolution and diversity of all high-risk influenza A virus subtypes and more accurately identify hotspot areas of emergence to better design diagnostic strategies, PREDICT investigators also evaluated mutation rates of high priority influenza A subtypes detected globally as well as socio-economic, biodiversity, and agricultural drivers that may be associated with subtype diversity and reassortment. Results indicated that potentially pathogenic influenza A strains may be more likely to evolve in East Asia, reinforced by the fact that the majority of subtypes that have caused disease and mortality in humans in recent years, including H5N1 and H7N9, were first detected in China and Hong Kong. In addition, PREDICT researchers assisted partners in China and investigated potential source populations and the conditions for the genesis of the 2013 H7N9 virus outbreak using active surveillance, screening of virus archives, and evolutionary analyses. This research revealed that the H7N9 outbreak lineage originated from reassortment of H7 viruses and enzootic H9N2 viruses and that the H7 viruses likely transmitted from domestic ducks to chickens in China during two separate events. An important recommendation for diagnostic testing was to revise current strategies of targeted surveillance for specific influenza subtypes – instead performing broader testing to detect all subtypes in order to better understand the total diversity globally and to facilitate the early detection of emerging subtypes and strains.
PREDICT improved our understanding of the underlying causes for disease emergence by building upon previous research to assess temporal and spatial patterns of disease emergence globally. The newly developed risk map (Hotspots II depicted at left) focuses on emerging zoonotic viruses from wildlife and provides a more refined projection of EID risk globally. The new Hotspots II model independently confirmed that the risk for zoonotic disease emergence increases with higher mammal diversity. Land-use type and land-use change are the other most important factors predicting emergence of zoonotic diseases of wildlife-origin.

Our scientists also implemented the Deep Forest (DF) study to further enhance the understanding of ecological factors that drive zoonotic viral disease emergence due to land-use change. This work has and will continue to refine our approach in the global scale “hotspots” modeling, by providing detailed information about risk at a local level – a scale at which humans live and interact with wildlife and livestock. Characterizing known and unknown viral diversity and describing the relationship between viral diversity, host diversity, land-use change, and human ecology are critical for better understanding of the ecological processes behind zoonotic disease emergence so that disease outbreaks can be prevented or their impacts minimized. Mathematical modeling used in PREDICT has expanded knowledge of viral traits, host species, and high-risk interfaces as predictors of susceptible host taxonomic range, human-to-human transmission, and geographic spread of viruses.

Interpreting and sharing of information with the host governments in PREDICT countries highlighted the critical steps of data collection, management, validation, and verification that are often overlooked. All data were carefully examined upon integration into the purposefully-designed internal information management system. When test results (e.g. initial detection and subsequent sequence confirmation of viruses) were produced for a given specimen, the data were interpreted in light of all available scientific literature by PREDICT virologists. This iterative process ensured the highest quality, most robust data possible. After interpretation, results were provided to host governments for examination, used to inform policy, and approved for public sharing. Once cleared for release by host country governments, our surveillance data were integrated with HealthMap’s digital surveillance data and spatial information generated from PREDICT’s disease hotspots modeling and shared with the public on the PREDICT data site (www.healthmap.org/predict). The open access, online platform provides users with a tool to visualize PREDICT surveillance along with disease events worldwide. All viral genetic sequences obtained during the project are also being deposited in the GenBank database for public access.

The PREDICT consortium designed and implemented a targeted risk-based surveillance strategy as an approach to pandemic prevention based not on humans as sentinels of disease but on detecting viruses early, at their source, where intervention strategies can be implemented before there is opportunity for spillover and spread in people. As a testament to the degree to which PREDICT and its partners have truly advanced wildlife surveillance and supported scientific
excellence and transparent communications, in-country staff and partners have been requested to serve on national disease task forces and to provide technical and expert assistance for several high-profile disease outbreak investigation and response efforts, including H7N9 influenza A, Nipah virus, MERS, and multiple EVD outbreaks. PREDICT’s success in building local capacity to detect hundreds of viruses in wild animals, coupled with a series of ongoing cutting-edge modeling and analytical activities evaluating the risk of emerging viral zoonoses, have significantly improved the world’s baseline knowledge on the zoonotic pool of viruses and the risk of exposure to people. Further testament to the success and utility of the PREDICT project and the work of its team of dedicated One Health professionals are the resulting 90 peer-reviewed, scientific publications that improve our understanding of zoonoses and the factors influencing their emergence. The wide distribution of the project findings from these scientific publications is assisting in cutting-edge global health improvements, including surveillance science, diagnostic technologies, understanding of viral evolution, and ecological driver identification. Through its One Health leadership and highly productive partnerships, PREDICT has forged new networks of professionals from the human, animal, and environmental health sectors to promote global health, improving our understanding of high-risk interfaces for viral disease spillover from wildlife into people and implementing strategies for preventing and controlling emerging disease threats. In the next phase, the PREDICT consortium will focus on ranking risk of spillover, amplification, and spread of these newly detected viruses using all available virological, epidemiological, ecological, and host-specific data. A targeted approach will be used to identify risky human behaviors for transmission of zoonotic viruses, and potential hosts (animal and human) at high-risk interfaces will be evaluated in concert to document pathogen sharing. This approach will build on the findings and capacity built during the first phase of PREDICT to better target effective detection, diagnosis, intervention, and prevention of EIDs of pandemic potential.