excerpts from

*Reducing Pandemic Risk, Promoting Global Health*

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MAJOR GLOBAL ACHIEVEMENTS
PREDICT conducted the most comprehensive zoonotic disease surveillance capacity development program in the world, unprecedented in scope and productivity. The PREDICT consortium, led by the UC Davis One Health Institute, EcoHealth Alliance, Metabiota, the Wildlife Conservation Society, and the Smithsonian Institution, developed and stewarded the five year project starting in 2009.

PREDICT was implemented in Africa (Cameroon, Gabon, Republic of Congo, Democratic Republic of Congo, Tanzania, Uganda, and Rwanda), Asia (Bangladesh, Cambodia, China, Indonesia, Laos, Malaysia, Nepal, Thailand, Vietnam), and Latin America (Bolivia, Brazil, Mexico, and Peru) as part of USAID’s global Emerging Pandemic Threats (EPT) program.

DESIGNED AND IMPLEMENTED HIGHLY TARGETED RISK-BASED SURVEILLANCE

PREDICT designed and implemented a highly 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. To discover potentially pathogenic viruses before they emerge, surveillance efforts were focused on wildlife taxa most likely to serve as reservoirs for emerging zoonotic viruses (i.e. bats, rodents, and nonhuman primates) at human-animal interfaces with high-risk potential for disease transmission (see Surveillance Strategy section). High-risk interfaces are situations where people have frequent, direct, and often intense contact with these wild animals, such as when they are hunted for food or trade and where wildlife raid crops, share water sources, or enter and live in human dwellings. In addition, land-use changes were assessed in the context of how they could modify the risk of pathogen spillover by perturbing the dynamics of viruses in wildlife and/or by bringing naive animal species (including humans) into close contact. Samples specific to human-wildlife contact and likely routes of disease transmission were collected and tested for viruses related to genera or taxonomic families known to cause epidemics and pandemics in people to maximize detection of viruses of major public health importance.

PREDICT trained local project staff and their colleagues, as well as university and government partners, to safely and humanely sample more than 56,340 nonhuman primates, bats, rodents, and other wild animals (including from bushmeat) at animal-human interfaces with heightened opportunity for viral spillover from wildlife hosts to humans. To further assess human risk at these high-risk interfaces, PREDICT piloted a number of human disease surveillance efforts in Uganda, the Democratic Republic of Congo, Cameroon, Gabon, Malaysia, China, and Indonesia.
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. The protocols were implemented in 32 labs in the 20 countries selected by USAID for the EPT program. Uptake of these methods by in-country partners has built long-term capacity and partnerships for identifying known and novel viruses of animal and human origin.

PREDICT’s success in building local capacity to detect hundreds of viruses in wild animals, coupled with a series of on-going cutting-edge modeling and analytical activities evaluating the risk of emerging viral zoonoses, have significantly improved the world’s baseline knowledge on the pool of zoonotic viruses and the risk of exposure to people.

Since 2009, PREDICT has detected a total of 984 unique new and known viruses in wild animals and humans in regions where diseases are mostly likely to emerge (Table 1; see Virus Detection and Discovery section for breakdown of viruses detected by viral family).

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Viruses Detected in Animals and Humans*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>631</td>
</tr>
<tr>
<td>Africa</td>
<td>420</td>
</tr>
<tr>
<td>Latin America</td>
<td>73</td>
</tr>
</tbody>
</table>

*Note: numbers of viruses do not total to 984, as some viruses have been found in more than one region.
All viral genetic sequences are being deposited in the GenBank database for public access. Analyses incorporating all virus detections (i.e. all virus families combined) globally for PREDICT to date validate our surveillance strategy. For example, results show 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 (see Figure 1 for proportion of positive test results by animal host taxonomic groups sampled).

Figure 1. Proportion of positive test results for viruses detected to date among animal host taxonomic group sampled.

Among the 6,787 positive test results (out of 419,919 tests conducted to date), PREDICT detected 959 unique viruses in wild animals (in addition to the 34 viruses detected in human pilot studies). 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, our samples from animals have yielded 812 novel viruses (85%) and 147 known viruses (15%).
Among positive test results, approximately 58% were positive for novel viruses and 42% were positive for known viruses. Pilot work on samples collected from humans for disease surveillance in Uganda, the Democratic Republic of Congo, Cameroon, Gabon, Malaysia, China, and Indonesia, have so far yielded 31 known and 3 novel viruses (some of the known viruses were also found in animal samples) with testing still on-going (Table 2).

PREDICT’s effort in just five years resulted in more viruses detected than the total number of viruses previously recognized in mammals by the International Committee on Taxonomy of Viruses (ICTV). On the list of viruses detected thus far are many important human and animal pathogens such as Severe Acute Respiratory Syndrome (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 ebolaviruses in humans during multiple outbreaks in Africa. PREDICT is continuing to prioritize which of these viruses should be targeted for further characterization and has been combining these discoveries with data on types and rates of human-wildlife contact in order to assess risk and inform on future surveillance strategies and critical points for implementation of disease prevention and control measures. As part of the viral detection effort, PREDICT developed “viral discovery curves” to estimate the number of undiscovered viruses that exist in a given population, as well as the sample size required to maximize discovery (see Virus Detection and Discovery section). These discovery curves filled a knowledge gap critical for ensuring that surveillance strategies for potential zoonotic threats in wildlife populations are optimal for both viral discovery and cost effectiveness.

Table 2. Viruses detected and discovered to date by taxonomic groups sampled.

<table>
<thead>
<tr>
<th></th>
<th>Bats</th>
<th>Nonhuman Primates</th>
<th>Rodents and Shrews</th>
<th>Humans</th>
<th>Other taxa**</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novel</td>
<td>431</td>
<td>234</td>
<td>143</td>
<td>3</td>
<td>9</td>
<td>820</td>
</tr>
<tr>
<td>Known</td>
<td>80</td>
<td>55</td>
<td>15</td>
<td>31</td>
<td>1</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1002*</td>
</tr>
</tbody>
</table>

*Note: numbers of viruses do not total to 984 as viruses have been found in more than one host taxa.

**Other taxonomic groups sampled include carnivores (e.g. bears, civets), lagomorphs (e.g. pikas), pangolins, and ungulates.

Over the span of the project, PREDICT developed and applied a number of innovative modeling and analytical techniques to investigate the risk of emerging infectious diseases, with a focus on emerging zoonoses from wildlife (see Modeling and Analytics section). For example, 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. This new model (Hotspots II) focuses on emerging zoonotic viruses from wildlife and provides a more refined projection of EID risk globally.

In addition, PREDICT provided evidence for epidemiologic mechanisms that have long been suspected to promote disease emergence by examining common transmission pathways shared by animal hosts and high-risk activities at transmission interfaces. Mathematical modeling explored viral traits, host species, and high-risk interfaces as predictors of susceptible host taxonomic range, human-to-human transmission, and geographic spread of viruses. Ongoing analyses of the influence of animal-to-human interfaces based on PREDICT test findings by viral family will
also yield information on high-risk behaviors that could be involved in disease transmission for specific viruses detected. In addition, analyses that are underway for the Deep Forest study (see Deep Forest section) will enhance our understanding of the ecological factors that drive zoonotic disease emergence due to land-use change.

**ENHANCED ONE HEALTH CAPACITY**

PREDICT worked closely with nearly 60 government ministries and hundreds of scientific institutions, local organizations, and other stakeholders to significantly advance One Health capacity and infrastructure in these countries. We trained 2,500 government personnel, physicians, veterinarians, resource managers, laboratory technicians, hunters, and students on biosafety, surveillance, laboratory techniques, and disease outbreak investigation (training materials freely available at: [http://www.vetmed.ucdavis.edu/ohi/predict/predict_publications.cfm](http://www.vetmed.ucdavis.edu/ohi/predict/predict_publications.cfm)). With USAID support, the team 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.

PREDICT developed robust mechanisms for overcoming geographic and disciplinary constraints to public health protection by developing multidisciplinary collaborations and establishing systems for procurement and data sharing and interpretation across stakeholders. The project actively engaged partners in PREDICT surveillance and diagnostic testing activities. In fact, as a testament to the degree to which PREDICT and its partners truly advanced systems for wildlife surveillance and supported scientific excellence and transparent communications, in-country staff were 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 Ebola virus disease outbreaks.

*PREDICT conducted surveys in communities surrounding Ebola virus disease and yellow fever outbreaks to better understand types of contact people have with wildlife.*
SHARE AND DISSEMINATED INFORMATION

Once cleared for release by host country governments, PREDICT surveillance data were integrated with HealthMap’s digital surveillance data and spatial information generated from PREDICT’s disease hotspots modeling and shared on the PREDICT public site (www.healthmap.org/predict). The open access, online platform is presented in a user friendly format for a broad audience, providing users with a tool to visualize PREDICT surveillance along with disease events worldwide. As mentioned above, all viral genetic sequences obtained during the project are being deposited in GenBank for public access.

Since 2009, PREDICT staff have been invited to present on the project’s approach and findings in some of the world’s most respected and powerful institutions and convenings, including multiple presentations at the United States White House, the World Health Organization, the Food and Agriculture Organization of the U.N., the World Organisation for Animal Health, the United States National Academies of Science, and the United States Institute of Medicine. In addition, PREDICT also delivered presentations to the American Society of Microbiology, the Chatham House in London, Prince Mahidol Awards Conference in Thailand, the International One Health Congress, the American Association for the Advancement of Science, International Meeting for Emerging Diseases, International Society for Infectious Diseases, the Food Safety Summit, the American Society of Tropical Medicine and Hygiene, and the American Public Health Association.

PREDICT and the Consortium’s many in-country partners, have published more than 90 peer-reviewed, scientific manuscripts that improve our understanding of zoonotic pathogens and drivers of their emergence and that contribute to improvements in surveillance strategies, laboratory methodology, and pathogen discovery and characterization. These manuscripts have been published in Nature, the Proceedings of the National Academies of Science, The Lancet, Emerging Infectious Diseases, mBio, PLoS Pathogens, and numerous other peer-reviewed journals (see Highlights of PREDICT Publications section and http://www.vetmed.ucdavis.edu/ohi/predict/predict_publications.cfm).

IMPROVED OUTBREAK RESPONSE AND PREPAREDNESS

In coordination with USAID EPT partners, PREDICT responded to requests by host governments and other stakeholders to support disease investigations, laboratory diagnostics, supply procurement, and communications in 23 significant outbreaks affecting people, domestic animals, and wildlife, including MERS, H7N9 Influenza, and Ebola virus disease (see Outbreak Response section). PREDICT and EPT partners worked with key stakeholders to operationalize a One Health approach by integrating wildlife and domestic animal surveillance into outbreak investigations. Examples of PREDICT’s contributions to disease outbreak response include:

Minimized Response Times for Outbreaks of Human Disease

Over the course of the project, dramatic improvements in response and control times were recognized. Unfortunately, the PREDICT team was not engaged in the West African region where the largest Ebola outbreak in history occurred during the end of PREDICT activities in 2014. Tragically, due to numerous causes, including lack of diagnostic capacity and public health education and infrastructure, the seriousness of the outbreak was not recognized until months after the first case occurred there. In contrast, in the Democratic Republic of Congo, where PREDICT was actively engaged with the government and the public health infrastructure,
samples were tested and control measures implemented within three days of collection of the first samples in a concurrent, yet separate Ebola outbreak that was then rapidly controlled before substantial spread. The rapid response and ultimately extremely reduced death toll and control time are illustrative of what can be achieved when a local One Health workforce is trained, employed, and able to activate during outbreaks.

**Prevented Yellow Fever Outbreak in Bolivia**

PREDICT rapidly identified a yellow fever outbreak in March of 2012 after five primates were found dead in eastern Bolivia. Laboratory diagnostics revealed that they were infected with a flavivirus. The Ministry of Public Health was immediately notified, and genetic sequencing performed by PREDICT confirmed that the infections had been caused by two yellow fever viral strains, both related to human cases occurring in Trinidad and Tobago and Brazil. The speed with which PREDICT was able to collect and test samples and interpret results (eight days) allowed local authorities to promptly implement human yellow fever prevention strategies (e.g. vaccination campaigns, public outreach, and mosquito control), resulting in zero human cases of illness during the outbreak.

**A SUSTAINABLE MODEL FOR ENHANCED PREVENTION, DETECTION, AND RESPONSE TO VIRAL OUTBREAKS**

USAID has recognized PREDICT’s success in navigating the technical and management complexities of such a large-scale global initiative, citing the project’s strength in its innovation and success in forging a shared vision and coordinated actions to protect public health. Through its One Health leadership and highly productive partnerships, PREDICT built a sustainable model for in-country and regional capacities to prevent, detect, and respond to viral outbreaks. PREDICT forged new networks of professionals from the human, animal, and environmental health sectors to promote global health through improving our understanding of high-risk interfaces for disease spillover from wildlife into people and implementing strategies for preventing and controlling emerging disease threats.