



One Health proof of concept: Bringing a transdisciplinary approach to surveillance for zoonotic viruses at the human-wild animal interface



Terra R. Kelly^a, William B. Karesh^b, Christine Kreuder Johnson^a, Kirsten V.K. Gilardi^a, Simon J. Anthony^{b,c}, Tracey Goldstein^a, Sarah H. Olson^d, Catherine Machalaba^b, PREDICT Consortium¹, Jonna A.K. Mazet^{a,*}

^a One Health Institute & Karen C. Drayer Wildlife Health Center, School of Veterinary Medicine, 1089 Veterinary Medicine Drive, University of California, Davis, CA, 95616, USA

^b EcoHealth Alliance, 460 West 34th Street, 17th Floor, New York, NY, 10001, USA

^c Center for Infection and Immunity, Mailman School of Public Health, Columbia University, 722 West 168th Street, New York, NY, 10032, USA

^d Wildlife Conservation Society, 2300 Southern Blvd., Bronx, New York, NY, 10460, USA

ARTICLE INFO

Article history:

Received 6 June 2016

Accepted 30 November 2016

Keywords:

Emerging infectious disease

Human-wildlife interface

One Health

Surveillance

Wildlife

Zoonotic

ABSTRACT

As the world continues to react and respond inefficiently to emerging infectious diseases, such as Middle Eastern Respiratory Syndrome and the Ebola and Zika viruses, a growing transdisciplinary community has called for a more proactive and holistic approach to prevention and preparedness – One Health. Such an approach presents important opportunities to reduce the impact of disease emergence events and also to mitigate future emergence through improved cross-sectoral coordination. In an attempt to provide proof of concept of the utility of the One Health approach, the US Agency for International Development's PREDICT project consortium designed and implemented a targeted, risk-based surveillance strategy 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 or food animals. Here, we share One Health approaches used by consortium members to illustrate the potential for successful One Health outcomes that can be achieved through collaborative, transdisciplinary partnerships. PREDICT's collaboration with partners around the world on strengthening local capacity to detect hundreds of viruses in wild animals, coupled with a series of cutting-edge virological and analytical activities, have significantly improved our baseline knowledge on the zoonotic pool of viruses and the risk of exposure to people. Further testament to the success of the project's One Health approach and the work of its team of dedicated One Health professionals are the resulting 90 peer-reviewed, scientific publications in under 5 years that improve our understanding of zoonoses and the factors influencing their emergence. The findings are assisting in global health improvements, including surveillance science, diagnostic technologies, understanding of viral evolution, and ecological driver identification. Through its One Health leadership and multi-disciplinary partnerships, PREDICT has forged new networks of professionals from the human, animal, and environmental health sectors to promote global health, improving our understanding of viral disease spillover from wildlife and implementing strategies for preventing and controlling emerging disease threats.

© 2016 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author.

E-mail addresses: trkelly@ucdavis.edu (T.R. Kelly), karesh@ecohealthalliance.org (W.B. Karesh), ckjohnson@ucdavis.edu (C.K. Johnson), kvgilardi@ucdavis.edu (K.V.K. Gilardi), sja2127@cumc.columbia.edu (S.J. Anthony), tgoldstein@ucdavis.edu (T. Goldstein), solson@wcs.org (S.H. Olson), Machalaba@ecohealthalliance.org (C. Machalaba), jkmazet@ucdavis.edu (J.A.K. Mazet).

¹ <http://www.vetmed.ucdavis.edu/ohi/predict/publications/Authorship.cfm>

1. Introduction²

Throughout history, societies have been plagued by emerging diseases and their rapid or insidious spread. Recent generations have borne the costs of HIV/AIDS, Severe Acute Respiratory Syndrome (SARS), and Middle Eastern Respiratory Syndrome (MERS), tallied in lives and livelihoods lost and profound impacts on broader-scale economies. The most recent emergence and spread of the Zika virus and Ebola virus disease (EVD) in West Africa demonstrate how ill prepared the world remains to respond to and control rapidly changing disease dynamics. The global panic resulting in significant financial and social consequences also illustrates the disappearing boundaries between the countries and continents working to protect their citizens. The majority of emerging infectious diseases (EIDs) are zoonotic, or those diseases caused by pathogens that are shared between people and animals (Jones et al., 2008). These diseases result in tens of thousands of deaths annually, and the economic losses from a single outbreak can amount to tens of billions of dollars (World Bank, 2012). While prevention and early control of outbreaks could be the key to reducing the impact of epidemics and potential pandemics, especially in less developed countries as demonstrated by the recent EVD epidemic in West Africa, the world still remains positioned only to respond, not to prevent.

Despite greater recognition of the importance of zoonotic diseases, little attention has been given to advancing the understanding of the underlying causes for emergence and drivers of spread (Murray and Daszak, 2013). A growing transdisciplinary community, often led by veterinarians and epidemiologists, has responded to this knowledge gap on disease dynamics by advocating for a more holistic or One Health approach that recognizes the need to expand disciplinary expertise in public health. From the beginning of the One Health movement, veterinarians have strongly advocated for an approach that considers all public, animal, and environmental aspects of health as a problem-solving paradigm (Cook et al., 2004). Notwithstanding the philosophical acceptance of the need for such an approach, the animal and environmental foundations of this three-legged stool often receive only cursory attention when major health problems are addressed in policy and practice.

Recent examples of emerging and re-emerging diseases, such as H1N1 pandemic influenza, H5N1 and H7N9 avian influenza, EVD, and Zika virus, serve as a reminder that the health of humans, animals, and ecosystems are interconnected and that early detection and response to emerging pathogens requires a coordinated, interdisciplinary, collaborative, cross-sectoral approach at local, regional, and global levels (Heymann and Dixon, 2013; Karesh et al., 2012; Morse et al., 2012). In addition to the burden on human and animal health, the economic impacts associated with emerging and pandemic pathogens can be catastrophic, including costs associated with decreased commerce, travel, and tourism, as well as those incurred from treatment and control efforts (Karesh et al., 2012; World Bank, 2012). As our world becomes increasingly connected through trade and travel, emerging infectious diseases pose a greater threat to the global community, requiring collaboration between ministries of health and institutions involved in health, trade, agriculture, and the environment (Mazet et al., 2014). The One Health approach presents important opportunities to reduce the impact of emergence events and also to prevent future emergence through improved knowledge and coordination.

In this article, we share One Health approaches applied by the US Agency for International Development's PREDICT project consortium to highlight the potential for successful One Health outcomes that can be achieved through developing cross-sectoral networks and establishing strong collaborative, transdisciplinary partnerships.

2. Observation of need at the human-wildlife interface

Arguably, veterinarians and veterinary epidemiologists have been among the most vocal advocates for the One Health approach. Pioneers of the One Health concept understood the value of comparative medicine and recognized the critical role that environmental factors play in the health of people and animals. Over the past decade, this concept was expanded to be much more inclusive of ecosystem health (Cook et al., 2004), due in part to the contributions of veterinarians witnessing firsthand the intimate connection among animal, human, and environmental health (Gibbs and Gibbs, 2013). For example, although veterinarians working in global health recognize the role that wildlife trade and consumption play in human nutrition and livelihoods in many countries around the world, they have expressed concern about the risks these practices pose with regard to spillover of zoonotic pathogens, as well as to conservation (Ahuka-Mundeke et al., 2011; Karesh et al., 2005; Karesh and Noble, 2009; Peeters et al., 2002; Smith et al., 2012; Wolfe et al., 2005). Human immunodeficiency viruses (HIV) types 1 and 2 are examples of pandemic infections resulting from cross-species transmission of simian immunodeficiency virus (SIV) from infected nonhuman primates to humans (Sharp et al., 2010). The documented spillover and pandemic potential of simian retroviruses illustrate the public health threat associated with close and frequent contact with wild animals, as occurs with wildlife trade and consumption (Switzer et al., 2012).

However, it should not be ignored that pathogens spill over in both directions, also threatening the health of wild animals. Tuberculosis in nonhuman primates and Asian elephants has long been associated with contact with infected humans (Mikota and Maslow, 2011; Montali et al., 2001). Investigation into a respiratory outbreak in mountain gorillas in Rwanda by PREDICT veterinarians revealed human metapneumovirus infection in affected individuals (Palacios et al., 2011). The source of the virus remains unknown; however, the strain was most recently described in human patients in South Africa and likely was transmitted to the gorillas by humans, illustrating the potential for bi-directional spillover of pathogens (Palacios et al., 2011). The parks where mountain gorillas reside are surrounded by very dense human populations, and research and ecotourism bring thousands of people into direct and indirect contact with the gorillas annually. Veterinarians documented 18 outbreaks of respiratory disease among these gorillas between 1990 and 2010 (Spelman et al., 2013). It is unclear if the increasing frequency and severity of respiratory disease outbreaks among mountain gorillas in the Virunga Massif (Spelman et al., 2013) are related to the growing human population surrounding the parks. Nevertheless, these findings provided further rationale for implementation of stricter visitation rules in some parts of the mountain gorillas' range in order to minimize the risk of disease transmission between visitors and wild human-habituated gorillas.

In Rwanda, an orphaned Grauer's gorilla confiscated from poachers and held in captivity for more than two years developed oral lesions. The consortium detected human herpes simplex virus Type 1 (HSV-1) in this individual (Gilardi et al., 2014), documenting spillover of another virus from humans into gorillas and further illustrating the need for targeted disease surveillance at the human-wildlife interface (Gilardi et al., 2014).

² Much of this review is based on material covered more thoroughly in *USAID PREDICT: Reducing Pandemic Risk, Promoting Global Health*, PREDICT Consortium, One Health Institute, University of California, Davis, December 2014 (www.report.predict.global).

3. One health on a regional scale: the PREDICT project

The US 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. In part because of their One Health leadership and research focused at the animal–human–environmental interface, the agency looked to veterinarians and epidemiologists to build a consortium to implement the surveillance and virus discovery component of the EPT program. The resulting PREDICT project focused on building transdisciplinary collaborations to identify potential zoonotic viral threats at high-risk transmission interfaces where pathogens are most likely to spill over. 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, like harvesting bat guano for agricultural fertilizer. Through a consortium of global and in-country partners, PREDICT 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 parts of Latin America. The consortium was able to overcome geographic and disciplinary constraints to public health protection by developing multidisciplinary partnerships and establishing networks and platforms for surveillance, diagnostics, and data sharing across stakeholders.

PREDICT, which was initially implemented in over 20 countries, improved early detection and response to disease threats through five main strategies: 1) building or strengthening zoonotic viral detection capabilities; 2) developing diagnostic laboratory and disease outbreak response capacities; 3) characterizing high-risk animal–human interfaces; 4) optimizing predictive models for disease emergence and spread; and 5) deploying information management and communication tools to advance a more integrated, global approach to sharing data from zoonotic virus surveillance.

3.1. Identifying threats at the human–wildlife interface

PREDICT’s surveillance strategy was designed to address the need for a more holistic, proactive approach to pandemic prevention, in which pathogens are discovered before they emerge or spread widely in people (Karesh et al., 2012; Morse et al., 2012). The strategy targeted high-risk disease transmission interfaces or conditions where people have frequent and direct contact with wild animals (Morse et al., 2012). To maximize discovery of zoonotic viruses, PREDICT focused surveillance activities on wildlife taxa for which there is scientific evidence of pathogen spillover to humans based on recent emerging and re-emerging viral zoonoses. The consortium drew on the diverse expertise of professionals across multiple disciplines, including human and veterinary medicine, epidemiology, ecology, economics, and environmental health to identify a range of high-risk interfaces and wildlife taxa to target for the project’s surveillance activities.

By linking networks of key stakeholders in a wide range of government ministries, scientific institutions, and local organizations, PREDICT helped integrate surveillance activities across the animal, human, and environmental health sectors with the aim of breaking down traditionally siloed approaches that currently serve as barriers to understanding the complex ecological and social changes that contribute to infectious disease emergence and therefore, the best interventions to prevent pathogen spillover (Mazet et al., 2014). The consortium worked with in-country partners to enhance capacity for wildlife disease surveillance, including field activities led by veterinarians and specialists experienced in the handling and sampling of wild animals to ensure safe and humane non-lethal methods.

To inform on a strategy designed to detect pathogens prior to spillover into people, the consortium examined the animal hosts and modes of transmission involved in previously reported zoonotic virus spillover events. Settings with diverse animal host assemblages and human activities facilitating cross-species disease transmission posed the highest risk for zoonotic virus spillover and were, therefore, important targets for surveillance for viruses of zoonotic potential (Johnson et al., 2015). Investigation into historic EID events revealed variation in major transmission pathways according to drivers of disease emergence (e.g., land-use change). These findings provided insight into how regional predominance of drivers can help with prioritization of pathways to target surveillance activities (Loh et al., 2015). Because pathogens circulating at high-risk interfaces often share modes of transmission (Loh et al., 2015), focusing on transmission pathways for surveillance and implementation of intervention strategies has the potential to prevent spillover from occurring.

To further inform a strategy best targeted for zoonotic virus discovery, PREDICT and its partners examined published virus detection data to compare the discovery potential of syndromic surveillance of diseased animals and active surveillance of apparently healthy animals (Levinson et al., 2013; Olson et al., 2012a). Compared to other mammalian taxa, there were fewer reports of clinical signs with viral infection in bats and rodents, providing further evidence that they serve as important healthy wildlife reservoirs to target for surveillance activities (Levinson et al., 2013). In addition, a mixed surveillance strategy of actively sampling healthy suspected wildlife reservoirs and animals involved in morbidity and mortality events, especially susceptible primates, was found to be the best for maximizing virus detection and discovery (Levinson et al., 2013; Olson et al., 2012a).

3.2. Assessing needs

At the beginning of the project, the consortium worked with partners to assess capacity for zoonotic pathogen surveillance in wildlife. Capabilities in each country were evaluated to identify needs for infrastructure and human capacity strengthening and to provide baseline information for monitoring change in capacity over time. As part of this process, wildlife officials and in-country PREDICT project scientists were surveyed to better understand perspectives regarding opportunities, challenges, and priorities for capacity development (Schwind et al., 2014a). Survey results indicated that enhancing coordination across agencies and sectors and increasing human and diagnostic laboratory capacities presented the most important opportunities for capacity strengthening (Schwind et al., 2014a). This information, as well as input from other in-country partners, was then used to target capacity enhancement priorities for the project.

3.3. Optimizing noninvasive sampling techniques

Priorities identified for capacity strengthening by stakeholders acknowledged the need to overcome logistical challenges of wildlife sampling in remote regions and when hands-on sampling was not ethically justified, feasible, or permitted. For example, many primate species inhabit areas that are logistically difficult to access, challenging for safe application of field anesthesia, or where their capture is not permitted. PREDICT developed a non-invasive sampling technique to obtain saliva samples from primates via a rope soaked in a fruit-based attractant (e.g. jam). The primate was allowed to chew on the rope that was subsequently retrieved for laboratory analysis (Smiley Evans et al., 2015). PREDICT also helped develop a noninvasive method to detect antibodies against Ebola virus in gorilla feces (Reed et al., 2014). In coordination with this effort, the consortium determined optimal sampling strategies for

detection of fecal samples from great apes in Central Africa (Olson et al., 2012b). In addition to improving early detection of circulating virus, these methods will aid in identifying immunologically naïve populations of wild apes that are vulnerable to EVD and could benefit from prevention measures (Reed et al., 2014).

3.4. Strategies for maximizing discovery of zoonotic viruses and understanding drivers of viral diversity

PREDICT's strategy for virus detection and discovery centered around the need for a cost-efficient approach that can concurrently detect known and novel viruses and be effectively implemented in resource-constrained regions. Because technologies used for viral discovery can be prohibitively expensive and require a high level of expertise, PREDICT virologists compiled a set of relatively simple and inexpensive protocols for the detection of known and novel viruses within viral families that had previously been recognized in animal hosts and known to cause human disease outbreaks, and coupled this cost-effective approach with the selected application of high through-put sequencing (Anthony et al., 2015; Anthony et al., 2013a; Goldstein et al., 2013). Using this strategy, the team detected hundreds of known and novel viruses. For example, the consortium first isolated and characterized a SARS-like coronavirus from a Chinese horseshoe bat (*Rhinolophus sinicus*; Ge et al., 2013). The virus was found to bind to the human ACE-2 cell receptor, suggesting that direct transmission to humans from bats would be possible. During the 2003 SARS outbreak, it was originally thought that bat viruses infected people through civets serving as intermediate hosts. However, this discovery provided compelling evidence that an intermediate host may not be necessary and that mitigation strategies should focus on decreasing human-bat contact (Ge et al., 2013).

Still, gaps in our knowledge of the viral diversity in wildlife hosts and the mechanisms involved in spillover and spread impeded the consortium's ability to fully implement a science-based surveillance strategy, including setting sample size targets for virus discovery. To investigate the potential pool of zoonotic viruses in target wildlife hosts and the effort required to better understand the diversity of mammalian viruses, the consortium investigated viral diversity in *Pteropus giganteus* fruit bats and the sampling effort needed to evaluate viral richness. PREDICT and its partners repeatedly sampled the bats and used PCR with consensus viral primers for nine viral families to saturate the discovery of new viruses in the species (Anthony et al., 2013b). Using statistical techniques similar to those used for estimating vertebrate diversity, the total viral richness within the nine viral families examined in this host was estimated to be 58 viruses. In addition, it was estimated that there is a minimum of 320,000 mammalian viruses that have yet to be discovered in these nine viral families. Sample size targets calculated from this information indicated that while approximately 7000 samples would need to be analyzed to identify 100% of these new viruses, a much more feasible target of 1300 samples would be needed to identify 80% of the novel viruses (Anthony et al., 2013b).

As a first step toward improving our understanding of how environmental drivers influence viral diversity in wildlife hosts and whether it might be possible to anticipate changes in viral communities, the consortium assessed whether viral communities identified in macaque feces were assembled through predictable or stochastic (unpredictable) processes (Anthony et al., 2015). Viral communities occurred mostly in non-random patterns between sites and within individuals, suggesting that forecasting changes in viral diversity in wildlife hosts in the face of environmental drivers of disease emergence might be possible (Anthony et al.,

2015). The ability to predict shifts in viral communities in wildlife reservoir hosts could allow us to evaluate various intervention strategies aimed at mitigating the risk of zoonotic pathogen emergence.

3.5. Assisting governments with zoonotic disease outbreak investigations

Because of the project's commitment to advancing the cutting edge of surveillance science, some in-country governments invited PREDICT team members to serve on national task forces and to provide technical assistance during disease outbreak response and prevention efforts. For example, consortium members helped inform on the science-based foundation for the Government of Rwanda's One Health Steering Committee, which aims to improve cross-sectoral coordination for human and animal disease outbreak response. PREDICT assisted with the Steering Committee's formulation of a One Health policy statement, which serves as an important platform for promoting and operationalizing One Health approaches. During disease outbreak investigations, consortium teams worked with local governments on strategies for and implementation of wildlife disease surveillance. PREDICT also collaborated with ministries on pathogen detection and characterization during outbreaks when traditional diagnostic assays for specific viral pathogens provided inconclusive results.

Results from PREDICT's viral discovery efforts have also been used to direct wildlife surveillance activities during human disease outbreak investigations. For example, PREDICT's discovery of a betacoronavirus (b-CoV) with 96.5% amino acid identity to Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) in a bat in Mexico informed on the target species for sampling in Saudi Arabia during MERS outbreak investigations (Anthony et al., 2013a). Sampling led to the discovery of a MERS-CoV sequence in a Saudi Egyptian tomb bat with 100% nucleotide identity to the virus from the MERS human index case (Memish et al., 2013). The consortium also generated evidence-based recommendations for disease surveillance during a series of human Ebola outbreak investigations in Africa, focusing mainly on strategies for animal sampling during resource-constrained response efforts, target species, and which diagnostics should be prioritized to rapidly screen for the presence of virus in animal hosts (Olson et al., 2012a). The consortium also provided technical assistance to governments through pathogen detection and characterization during a number of human-only disease outbreaks. For instance, the team developed and optimized a new, highly sensitive technique to reconstruct the genome of a novel rhabdovirus (Bas-Congo virus, or BASV) associated with three human cases of acute hemorrhagic fever in Democratic Republic of Congo (Grard et al., 2012). Although the rhabdovirus family had never been documented to cause hemorrhagic fever in people, they are now included in the list of viruses evaluated during hemorrhagic fever outbreaks (Grard et al., 2012).

3.6. Improving early recognition of disease events through innovative tools

PREDICT partnered with HealthMap, an established global leader in digital disease event monitoring, to develop a public platform to share sampling data and viral testing results and to contribute to the variety of data sources that HealthMap brings in to increase awareness regarding the state of infectious diseases. Once the project's virus detection results were shared with and approved for public release by in-country governments, the results (including reporting of negative findings) were uploaded into the HealthMap system for open, public access.

In addition to digital media's value for early event detection, there is also potential for its use as an early warning system through

monitoring drivers of disease emergence (Olson et al., 2015). The consortium developed a scientific framework for a digital disease driver surveillance platform (Olson et al., 2015). The platform has the potential to identify locations and periods of time with elevated infectious disease risk with alerting of public health officials to the need for active surveillance and intervention prior to pathogen spillover events.

PREDICT also worked with in-country partners to explore the value of local media to enhance surveillance and early recognition of disease events (Schwind et al., 2014b). Over a 16-week evaluation period, health reports in local media sources were compared to reports in the global HealthMap system to identify unique health event coverage. Selected media sources were reviewed to ensure they were not already feeding into main aggregation sites, including HealthMap. The local media surveillance was found to fill gaps in digital surveillance coverage of events through valuable localized information on risk and disease events and by supporting diverse languages. This effort demonstrated the utility of local media surveillance as an addition to active digital surveillance networks in regions with less-developed capacity for disease detection and response (Schwind et al., 2014b).

3.7. Addressing re-emerging disease threats of major global importance

Lessons learned during recent disease outbreaks, such as EVD and highly pathogenic avian influenza (HpaI), highlight the need for a new paradigm focused on interruption of pathogen transmission prior to human spillover. However, this new paradigm is only plausible with an improved understanding of the biological and ecological factors driving disease emergence and mitigation strategies aimed at these underlying drivers. Following a series of HPAI outbreaks in the countries where PREDICT was active, the consortium worked in collaboration with partners to improve our understanding of how and where HPAI strains are emerging. Researchers evaluated data on influenza A viruses reported in the public domain in 32 different countries over a 12-year period (2000–2011; Rejmanek et al., 2015). Virus evolution was found to be higher in Asian countries, especially in East Asia, relative to North America, providing further evidence of an increased risk of emergence of novel pathogenic strains in East Asia. In addition, large gaps in reporting of influenza A virus activity were identified in Africa and South America. Reporting effort and health care spending (indicator of economic development) were strong predictors of subtype diversity at the country level, emphasizing the need to increase sampling and reporting efforts in under-sampled regions in order to better understand the underlying drivers of influenza A infections around the world (Rejmanek et al., 2015).

PREDICT also assisted partners during the 2013 influenza A (H7N9) outbreak investigation in China. Morbidity associated with H7N9 infection had not been previously reported in people, and little was known about this subtype in wild bird populations. To inform on the investigation and potential role of wild birds as sources of the human infections, the consortium examined the prevalence and distribution of influenza A (H7N9) virus previously reported in wild bird populations and the sample size needed to detect this strain in wild birds (Olson et al., 2013). The prevalence of H7N9 in wild birds was very low, requiring high sample sizes (>30,000 wild birds) for detection. Given the low prevalence in wild birds, PREDICT and its partners recommended targeted risk-based surveillance as an efficient and cost-effective strategy to monitor wild bird populations as a potential source of continued H7N9 infections in poultry and people (Olson et al., 2013).

3.8. Scaling and sustaining one health initiatives

Despite the substantial progress made in recent years, challenges to implementing and sustaining One Health initiatives remain. Successful One Health approaches require cross-sectoral coordination in which partners look beyond their disciplines to function as a team, despite their diverse organizational mandates, funding sources, and standard operating procedures (Mazet et al., 2014). One Health initiatives often arise from shared threats requiring a multi-agency, cross-sectoral response (Rubin et al., 2014). For example, the H5N1 HPAI outbreak, which brought together a diverse network of partners from the animal and human health sectors, fostered a number of One Health achievements, including a coordinated tripartite surveillance system, which has enabled improved information and data sharing and joint risk assessment (Rubin et al., 2014). However, sustaining effective coordination once the threat has diminished presents a significant challenge. Strong collaborations built during these periods of necessary cooperation, can provide a platform for scaling successful approaches into sustainable One Health programs. The One Health Strategic Plan for Rwanda (https://www.google.com/?gws_rd=ssl#q=one+health+strategic+plan+rwanda) provides another good example of how a clearly defined strategy and a fundamental understanding of the specific roles and mandates of the partners involved can be an effective approach for scaling and sustaining One Health initiatives.

4. Conclusions

The examples above, as well as the seriousness of the risks associated with viral spillover among hosts, has led to the recognition of the utility of a One Health approach in the design and implementation of emerging infectious disease surveillance strategies. PREDICT's One Health consortium has advocated for inclusion of multiple and diverse disciplines to shift the world's currently reactive approach (once a disease is spreading in populations) toward a proactive, predictive approach for emerging infectious disease prevention and timely control. The general lack of specific medicines and vaccines for new and spreading zoonotic viruses puts a premium on developing non-pharmaceutical interventions based on a detailed understanding of when, where, and how zoonotic viruses are moving among wildlife, domestic animals, and people. The PREDICT consortium provides just one example of the potential for success that can be achieved by a collaborative, transdisciplinary team.

Through integrated efforts to promote health, effective natural resource management, and economic development, the PREDICT project and its partners have advanced One Health capacity and infrastructure in over 20 countries considered to be hotspots for zoonotic disease emergence. PREDICT worked cooperatively with a wide range of government ministries, scientific institutions, local organizations, and other stakeholders to further local and global One Health initiatives by enabling a structure for effective collaboration across disciplines and geographic boundaries in countries where PREDICT was active. Utilizing a One Health approach, PREDICT focused its efforts on strengthening surveillance and laboratory capacity to detect known zoonotic pathogens and novel viruses at the wildlife-human interface, monitoring human-wildlife interactions for the potential spillover of viral pathogens posing a health threat, and investigating ecological drivers of pathogen spillover into people with the ultimate aim of improved prevention of zoonotic disease emergence. By emphasizing the links among human, animal, and environmental health, PREDICT enabled and supported integrated efforts to promote public health,

effective natural resource management, and socio-economic development.

Acknowledgements

This work was made possible by the generous support of the American people through the United States Agency for International Development (USAID). The contents are the responsibility of the PREDICT Consortium and do not necessarily reflect the views of USAID or the United States Government. Special thanks to the PREDICT partners in and the governments of Bangladesh, Bolivia, Brazil, Cambodia, Cameroon, China, Gabon, Democratic Republic of Congo, Indonesia, Laos, Malaysia, Mexico, Nepal, Peru, Tanzania, Uganda, Republic of Congo, Rwanda, Thailand, and Vietnam. The success realized by the PREDICT project, documented herein, would not have been possible without the valuable contributions of Dennis Carroll, Andrew Clements, Alisa Pereira, and August Pabst.

References

- Ahuka-Mundeke, S., Mbala-Kingebeni, P., Liegeois, F., Ayoub, A., Lunguya-Metila, O., Demba, D., Bilulu, G., Mbenzo-Abokome, V., Inogwabini, B.I., Muyembe-Tamfum, J.J., Delaporte, E., Peeters, M., 2011. Identification and molecular characterization of new simian T cell lymphotropic viruses in nonhuman primates bushmeat from the Democratic Republic of Congo. *AIDS Res. Hum. Retrovir.* 28, 628–635.
- Anthony, S.J., Ojeda-Flores, R., Rico-Chávez, O., Navarrete-Macias, I., Zambrana-Torrel, C.M., Rostal, M.K., Epstein, J.H., Tipps, T., Liang, E., Sanchez-Leon, M., Sotomayor-Bonilla, J., Aguirre, A.A., Ávila-Flores, R., Medelín, R.A., Goldstein, T., Suzán, G., Daszak, P., Lipkin, W.I., 2013a. Coronaviruses in bats from Mexico. *J. Gen. Virol.* 94, 1028–1038. <http://dx.doi.org/10.1099/vir.0.049759-0>.
- Anthony, S., Epstein, J., Murray, K., Navarrete-Macias, I., Zambrana-Torrel, C.M., Solovoyov, A., Ojeda-Flores, R., Arrigo, N., Islam, A., Ali Khan, S., Hosseini, P., Bogich, T., Olival, K., Sanchez-Leon, M., Karesh, W., Goldstein, T., Luby, S., Morse, S., Mazet, J., Daszak, P., Lipkin, W., 2013b. A strategy to estimate unknown viral diversity in mammals. *MBio* 4, <http://dx.doi.org/10.1128/mBio.00598-13>, e00598-13.
- Anthony, S.J., Islam, A., Johnson, C., Navarrete-Macias, I., Liang, E., Jain, K., Hitchens, P.L., Che, X., Solovoyov, A., Hicks, A.L., Ojeda-Flores, R., Zambrana-Torrel, C., Ulrich, W., Rostal, M.K., Petrosov, A., Garcia, J., Haider, N., Wolfe, N., Goldstein, T., Morse, S.S., Rahman, M., Epstein, J.H., Mazet, J.K., Daszak, P., Lipkin, W.I., 2015. Non-random patterns in viral diversity. *Nat. Commun.* 6, 8147. <http://dx.doi.org/10.1038/ncomms9147>.
- Cook, R., Karesh, W., Osofsky, S., 2004. One World, One Health: Building Interdisciplinary Bridges to Health in a Globalized World. *Wildlife Conservation Society*, Bronx, New York, USA. <http://www.oneworldonehealth.org/sept2004/owoh.sept04.html> (Accessed 18 April 2016).
- Ge, X.-Y., Li, J.-L., Yang, X.-L., Chmura, A.A., Zhu, G., Epstein, J.H., Mazet, J.K., Hu, B., Zhang, W., Peng, C., Zhang, Y.-Y., Luo, C.-M., Tan, B., Wang, N., Zhou, Y., Cramer, G., Zhang, S.-Y., Wang, L.-F., Daszak, P., Shi, Z.-L., 2013. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* 503, 535–538.
- Gibbs, S.E.J., Gibbs, E.P.J., 2013. The historical, present, and future role of veterinarians in One Health. In: Mackenzie, J.S., Jeggo, M., Daszak, P., Richt, J.A. (Eds.), *One Health: The Human-Animal-Environment Interfaces in Emerging Infectious Diseases. The Concept and Examples of a One Health Approach*. Springer-Verlag, Berlin Heidelberg.
- Gilardi, K.V.K., Oxford, K.L., Gardner-Roberts, D., Kinani, J.F., Spelman, L., Barry, P.A., Cranfield, M.R., Lowenstine, L.J., 2014. Human herpes simplex virus type 1 in confiscated gorilla. *Emerg. Infect. Dis.* 20, 1883–1886.
- Goldstein, T., Mena, I., Anthony, S.J., Medina, R., Robinson, P.W., Greig, D.J., Costa, D.P., Lipkin, W.I., Garcia-Sastre, A., Boyce, W.M., 2013. Pandemic H1N1 influenza isolated from free-ranging Northern Elephant Seals in 2010 off the central California coast. *PLoS One* 8, e62259. <http://dx.doi.org/10.1371/journal.pone.0062259>.
- Grard, G., Fair, J.N., Lee, D., Slikas, E., Steffen, I., Muyembe, J.-J., Sittler, T., Veeraghavan, N., Ruby, J.G., Wang, C., Makuwa, M., Mulembakani, P., Tesh, R.B., Mazet, J., Rimoin, A.W., Taylor, T., Schneider, B.S., Simmons, G., Delwart, E., Wolfe, N.D., Chiu, C.Y., Leroy, E.M., 2012. A novel rhabdovirus associated with acute hemorrhagic fever in central Africa. *PLoS Pathog.* 8, e1002924. <http://dx.doi.org/10.1371/journal.ppat.1002924>.
- Heymann, D.L., Dixon, M., 2013. The value of the One Health approach: shifting from emergency response to prevention of zoonotic disease threats at their source. *Microbiol. Spectr.* 1, 1–11. <http://dx.doi.org/10.1128/microbiolspec.OH-0011-2012.f1>.
- Johnson, C.K., Hitchens, P.L., Evans, T.S., Goldstein, T., Thomas, K., Clements, A., Joly, D.O., Wolfe, N.D., Daszak, P., Karesh, W.B., Mazet, J.K., 2015. Spillover and pandemic properties of zoonotic viruses with high host plasticity. *Sci. Rep.* 5, <http://dx.doi.org/10.1038/srep14830>.
- Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Balk, D., Gittleman, J.L., Daszak, P., 2008. Global trends in emerging infectious diseases. *Nature* 451, 990–994. <http://dx.doi.org/10.1038/nature06536>.
- Karesh, W.B., Noble, E., 2009. The bushmeat trade: increased opportunities for transmission of zoonotic disease. *Mt. Sinai J. Med.* 76, 429–434.
- Karesh, W.B., Cook, R.A., Bennett, E.L., Newcomb, J., 2005. Wildlife trade and global disease emergence. *Emerg. Infect. Dis.* 11 (7), 1000–1002.
- Karesh, W.B., Dobson, A., Lloyd-Smith, J.O., Lubroth, J., Dixon, M.A., Bennett, M., Aldrich, S., Harrington, T., Formenty, P., Loh, E.H., Machalaba, C.C., Thomas, M.J., Heymann, D.L., 2012. Ecology of zoonoses: natural and unnatural histories. *Lancet* 380, 1936–1945. [http://dx.doi.org/10.1016/S0140-6736\(12\)61678-X](http://dx.doi.org/10.1016/S0140-6736(12)61678-X).
- Levinson, J., Bogich, T.L., Olival, K.J., Epstein, J.H., Johnson, C.K., Karesh, W., Daszak, P., 2013. Targeting surveillance for zoonotic virus discovery. *Emerg. Infect. Dis.* 19, 743–747. <http://dx.doi.org/10.3201/eid1905.121042>.
- Loh, E.H., Zambrana-Torrel, C., Olival, K.J., Bogich, T.L., Johnson, C.K., Mazet, J.A.K., Karesh, W., Daszak, P., 2015. Targeting transmission pathways for emerging zoonotic disease surveillance and control. *Vector-borne Zoonotic Dis.* 15, 432–437.
- Mazet, J.A.K., Uhart, M., Keyyu, J., 2014. Stakeholders in one health. *Rev. Sci. Tech. Off. Int. Epizoot.* 33, 443–452.
- Memish, Z.A., Mishra, N., Olival, K.J., Fagbo, S.F., Kapoor, V., Epstein, J.H., Alhakeem, R., Asmari, M., Al Islam, A., Kapoor, A., Brie, T., Daszak, P., Rabeah, A.A., Al Lipkin, W.I., 2013. Coronavirus in bats, Saudi Arabia. *Emerg. Infect. Dis.* 19, 1819–1823.
- Mikota, S., Maslow, J.N., 2011. Tuberculosis at the human-animal interface: an emerging disease of elephants. *Tuberculosis* 91, 208–211.
- Montali, R.J., Mikota, S.K., Cheng, L.L., 2001. *Mycobacterium tuberculosis* in zoo and wildlife species. *Rev. Sci. Tech. Off. Int. Epizoot.* 20, 291–303.
- Morse, S.S., Mazet, J., a, K., Woolhouse, M., Parrish, C.R., Carroll, D., Karesh, W.B., Zambrana-Torrel, C., Lipkin, W.I., Daszak, P., 2012. Prediction and prevention of the next pandemic zoonosis. *Lancet* 380, 1956–1965. [http://dx.doi.org/10.1016/S0140-6736\(12\)61684-5](http://dx.doi.org/10.1016/S0140-6736(12)61684-5).
- Murray, K.A., Daszak, P., 2013. Human ecology in pathogenic landscapes: two hypotheses on how land use change drives viral emergence. *Curr. Opin. Virol.* 3, 79–83. <http://dx.doi.org/10.1016/j.coviro.2013.01.006>.
- Olson, S.H., Reed, P., Cameron, K.N., Ssebide, B.J., Johnson, C.K., Morse, S.S., Karesh, W.B., Mazet, J., Joly, D.O., 2012a. Dead or alive: animal sampling during ebola hemorrhagic fever outbreaks in humans. *Emerg. Health Threats J.* 5, 9134.
- Olson, S.H., Reed, P., Ondzie, A., Joly, D., 2012b. Maximizing nonhuman primate fecal sampling in the Republic of Congo. *J. Wildl. Dis.* 48, 888–898.
- Olson, S.H., Gilbert, M., Cheng, M.C., Mazet, J.A.K., Joly, D.O., 2013. Historical prevalence and distribution of avian influenza virus A(H7N9) among wild birds. *Emerg. Infect. Dis.* 19, 2031–2033. <http://dx.doi.org/10.3201/eid1912.130649>.
- Olson, S.H., Benedum, C.M., Mekar, S.R., Preston, N.D., Mazet, J.A.K., Joly, D.O., Brownstein, J.S., 2015. Drivers of emerging infectious disease events as a framework for digital detection. *Emerg. Infect. Dis.* 21, 1285–1292.
- Palacios, G., Lowenstine, L.J., Cranfield, M.R., Gilardi, K.V.K., Lukasik-Braum, M., Kinani, J., Mudakikwa, A., Nyirakaragire, E., Bussetti, A.V., Savji, N., Hutchison, S., Egholm, M., Lipkin, W.I., 2011. Human metapneumovirus infection in wild mountain gorillas, Rwanda. *Emerg. Infect. Dis.* 17, 711–713. <http://dx.doi.org/10.3201/eid1704100883>.
- Peeters, M., Courgnaud, V., Abela, B., Auzel, P., Pourrut, X., Bibollet-Ruche, F., Loul, S., Liegeois, F., Butel, C., Koulagna, D., Mpoundi-Ngole, E., Shaw, G.M., Hahn, B.H., Delaporte, E., 2002. Risk to human health from a plethora of simian immunodeficiency viruses in primate bushmeat. *Emerg. Infect. Dis.* 8, 451–457.
- Reed, P.E., Mulangu, S., Cameron, K.N., Ondzie, A.U., Joly, D., Bermejo, M., Rouquet, P., Fabbio, G., Bailey, M., Shen, Z., Keele, B.F., Hahn, B., Karesh, W.B., Sullivan, N.J., 2014. A new approach for monitoring ebolavirus in wild great apes. *PLoS Negl. Trop. Dis.* 8, e3143. <http://dx.doi.org/10.1371/journal.pntd.0003143>.
- Rejmanek, D., Hosseini, P.R., Mazet, J.A.K., Daszak, P., Goldstein, T., 2015. Evolutionary dynamics and global diversity of influenza A virus. *J. Virol.* 89, 10993–11001. <http://dx.doi.org/10.1128/JVI.01573-15>.
- Rubin, C., Dunham, B., Sleeman, J., 2014. Making One Health a reality—crossing bureaucratic boundaries. *Microbiol. Spectrum* 2 (1), <http://dx.doi.org/10.1128/microbiolspec.OH-0016-2012>, OH-0016-2012.
- Schwind, J.S., Wolking, D.J., Brownstein, J.S., Consortium, P., Mazet, J.A.K., Smith, W.A., 2014b. Evaluation of local media surveillance for improved disease recognition and monitoring in global hotspot regions. *PLoS One* 9, e110236. <http://dx.doi.org/10.1371/journal.pone.0110236>.
- Schwind, J.S., Goldstein, T., Thomas, K., Mazet, J.A.K., Smith, W.A., Consortium, P., 2014a. Capacity building efforts and perceptions for wildlife surveillance to detect zoonotic pathogens: comparing stakeholder perspectives. *BMC Public Health* 14, 1–8.
- Sharp, C.P., LeBreton, M., Kantola, K., Nana, A., Le Doux Diffo, J., Djoko, C.F., Tamoufe, U., Kiyang, J.A., Babila, T.G., Ngole, E.M., Pybus, O.G., Delwart, E., Delaporte, E., Peeters, M., Soderlund-Venermo, M., Hedman, K., Wolfe, N.D., Simmons, P., 2010. Widespread infection with homologues of Human Parvovirus B19, PARV4, and Human Bocavirus of chimpanzees and gorillas in the wild. *J. Virol.* 84, 10289–10296.
- Smiley Evans, T., Barry, P.A., Gilardi, K.V., Goldstein, T., Deere, J.D., Fike, J., Yee, J., Ssebide, B.J., Karmacharya, D., Cranfield, M.R., Wolking, D., Smith, B., Mazet, J.A.K., Johnson, C.K., 2015. Optimization of a novel non-invasive oral sampling technique for zoonotic pathogen surveillance in nonhuman primates. *PLoS Negl. Trop. Dis.* 9, e0003813. <http://dx.doi.org/10.1371/journal.pntd.0003813>.
- Smith, K.M., Anthony, S.J., Switzer, W.M., Epstein, J.H., Jia, H., Sanchez, M.D., Huynh, T.T., Galland, G.G., Shapiro, S.E., Sleeman, J.M., McAloose, D., Stuchin, M.,

- Amato, G., Lipkin, W.I., Karesh, W.B., Daszak, P., Marano, N., 2012. Zoonotic viruses associated with illegally imported wildlife products. *PLoS One* 7, e29505, <http://dx.doi.org/10.1371/journal.pone.0029505>.
- Spelman, L.H., Gilardi, K.V.K., Lukasik-Braum, M., Kinani, J.F., Nyirakaragire, E., Lowenstine, L.J., Cranfield, M.R., 2013. Respiratory disease in mountain gorillas (*Gorilla beringei beringei*) in Rwanda, 1990–2010: outbreaks, clinical course, and medical management. *J. Zoo Wildl. Med.* 44, 1027–1035.
- Switzer, W.M., Tang, S., Ahuka-mundeki, S., Shankar, A., Hanson, D.L., Zheng, H., Ayouba, A., Wolfe, N.D., Lebreton, M., Djoko, C.F., Tamoufe, U., Esteban, A., Heneine, W., Peeters, M., Wright, L.L., Muyembe-tamfum, J.J., Wemakoy, E.O., Mulembakani, P., Hoff, N.A., Rimoin, A.W., 2012. Novel Simian Foamy Virus Infections from Multiple Monkey Species in Women from the Democratic Republic of Congo., pp. 1–15.
- Wolfe, N.D., Daszak, P., Kilpatrick, A.M., Burke, D.S., 2005. Bushmeat hunting, deforestation, and prediction of zoonoses emergence. *Emerg. Infect. Dis.* 11, 1822–1827.
- World Bank, 2012. People, Pathogens and Our Planet: the Economics of One Health, <http://documents.worldbank.org/curated/en/2012/06/16360943/people-pathogens-planet-economics-one-health> (Accessed 18 April 2016).