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PREDICT NEPAL

One Health in action (2012-2020)



Enhancing One Health surveillance capabilities to detect (re)emerging diseases at the crossroads of Asia

NEPAL



PREDICT/Nepal is the country's first novel zoonotic virus surveillance program using a One Health approach. This project has been implemented by the Center for Molecular Dynamics-Nepal (CMDN) in close partnership with national stakeholders, private partners, and local communities since 2012. This project has systematically collected human and animal samples from both rural and urban wildlife interfaces to detect, track, and better understand the emergence of new zoonotic pathogens from wildlife that could pose a threat to human health. The PREDICT/Nepal team also collected information related to high-risk, human-animal interfaces as well as human activities and behavior with the potential to transmit and enhance spread of diseases. The PREDICT team established hospital-based syndromic surveillance, which enabled hospital assessments in addition to community-based surveillance.

PREDICT/Nepal conducted seasonal, concurrent sampling of animals and humans in rural and urban communities as well as year-

round, hospital-based syndromic sampling in clinical patients of Nepal. Altogether, 26,217 samples were collected from 3,293 animals (bats, birds, rodents and non-human primates) and 2,048 humans during eight years of the project. These samples were screened for five viral families—paramyxo-, corona-, influenza-, filo-, and flaviviruses. Behavioral data collected in the clinical and community settings will help identify potential behavioral risk factors that contribute to virus spillover.

Findings from the PREDICT project are shared with the national stakeholders and local partners regularly through reports, workshops, and meetings with an aim to improve recommendations for disease surveillance and prevention. Through analysis of project data and findings, the PREDICT project was able to identify risks and educate communities and health professionals on behavior change and intervention strategies designed to protect people and wildlife from disease threats.

PREDICT is a revolutionary project that has strengthened the country's emerging disease surveillance capacity, bolstered the One Health platform, and promoted collaborative work between the stakeholders and scientific communities for evidence-based policy in Nepal. PREDICT also organized Nepal's first One Health stakeholders' workshop to identify and promote collaboration among government and private agencies. PREDICT contributed to further develop One Health capacity by organizing workshops such as "Zoonotic Disease Pandemic Preparedness for South Asia." In addition to developing technical and human capacity for emerging disease surveillance, PREDICT has supported the government in outbreak investigation and contributed to One Health policy briefs at national and regional levels.

LOCAL PARTNERS

- Teaching hospitals at Patan of Kathmandu Valley and Bharatpur of Chitwan District
- Communities of rural and urban study sites
- Department of Livestock Services, Ministry of Agriculture and Livestock Services
- Central Veterinary Laboratory, Ministry of Agriculture and Livestock Services
- Department of National Parks and Wildlife Conservation, Ministry of Forests and Environment
- Epidemiology and Disease Control Division, Ministry of Health



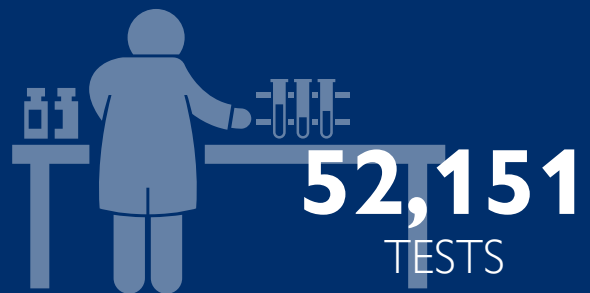
DEVELOPED the One Health Workforce by training more than 60 people in Nepal.



OPERATIONALIZED One Health surveillance and sampled over 5.2K animals and people, to identify ways to help minimize the spillover of zoonotic disease threats from animals into human populations.

LABORATORY STRENGTHENING

· Center for Molecular Dynamics Nepal/
Intrepid Nepal



DETECTED 19 unique viruses in both animal and human populations.



RAJINDRA NAPIT

Senior Research Associate
Center for Molecular
Dynamics Nepal

“PREDICT’s One Health Approach has been a great experience for me. I have been trained in biosafety, field epidemiology and surveillance and laboratory diagnostics and screening of various emerging pathogens using PCRs with high throughput sequencing. Using developed and optimized PREDICT protocols, we have been able to detect some emerging pathogens. PREDICT gave [me an] opportunity to work in community setting[s] with exposure from sample collection to final reporting. It has helped me understand the dynamics of zoonotic virus spillover, evolution, prevention and measures and practices that reduce disease transmission risk.”



DHIRAJ PURI

Field Officer
Center for Molecular
Dynamics Nepal

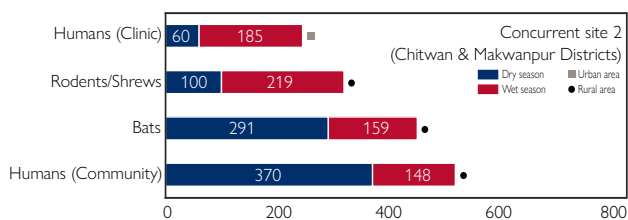
“As a vet technician, initially I [had] knowledge on poultry. But with PREDICT, I expand[ed] my knowledge about primates, rodents, ducks, bats, use of PPE, and skills on handling and collecting samples from these animals. I am also able to use [the EIDITH software] to enter and analyze sample data. In a word, PREDICT plays [a] vital role to increase my working area and [I] would like to thank [them] for providing [these] opportunities.”

ACHIEVEMENTS

- PREDICT/Nepal has generated the largest collection of animal (bats, birds, rodents and non-human primates) and human specimens in Nepal viral surveillance history.
- PREDICT enhanced characterization of fevers of unknown origin in patients by collaborating with healthcare workers at hospitals in two concurrent study sites.
- PREDICT supported Nepal’s first workshop, “Feasibility of One Health (OH) initiative in Nepal for surveillance of emerging and re-emerging zoonotic diseases of public health importance.”
- PREDICT/Nepal expanded testing for antimicrobial resistance (AMR) testing and established proof-of-concept for a One Health approach to AMR surveillance by which animal, human, and environmental samples are concurrently obtained to investigate AMR patterns in a community with intensifying livestock production.
- We established working relationships with the government agencies and local partners to implement a One Health project and integrate reporting across human, animal, and environmental health platforms.
- PREDICT assisted in drafting the National Strategies for Wildlife Disease Control through its partnerships with local government and private stakeholders by providing assistance in organizing and implementing a cross-disciplinary workshop focused on wildlife policy, “Strategic Planning Workshop for Improving Wildlife Health Capacity in Nepal” in 2016.
- PREDICT/Nepal further supported One Health platforms and pandemic preparedness in the country by facilitating One Health research in South Asia by implementing another workshop, “Zoonotic Disease Pandemic Preparedness for South Asia,” in 2017.
- The project also assisted the government in strain characterization during the H5N8 influenza outbreak in 2017.

ONE HEALTH SURVEILLANCE

CHITWAN & MAKWANPUR

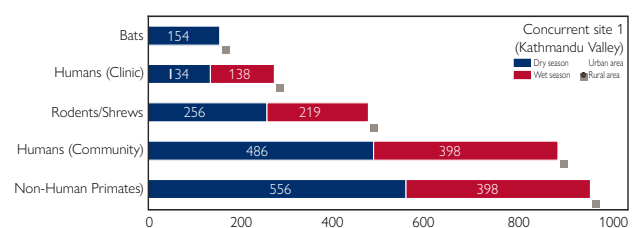


Numbers of individual taxa sampled during dry and wet seasons in Chitwan and Makwanpur Districts

Our team also conducted surveillance in a rural area south of the Kathmandu Valley in Makwanpur District inhabited primarily by the Chepang ethnic community. The Chepang traditionally farm and raise livestock and animals, but also hunt bats and are engaged in the wildlife value chain, selling animals or animal products to wildlife restaurants and markets. For syndromic surveillance, we worked with a teaching institution at Chitwan District that serves areas including Makwanpur.

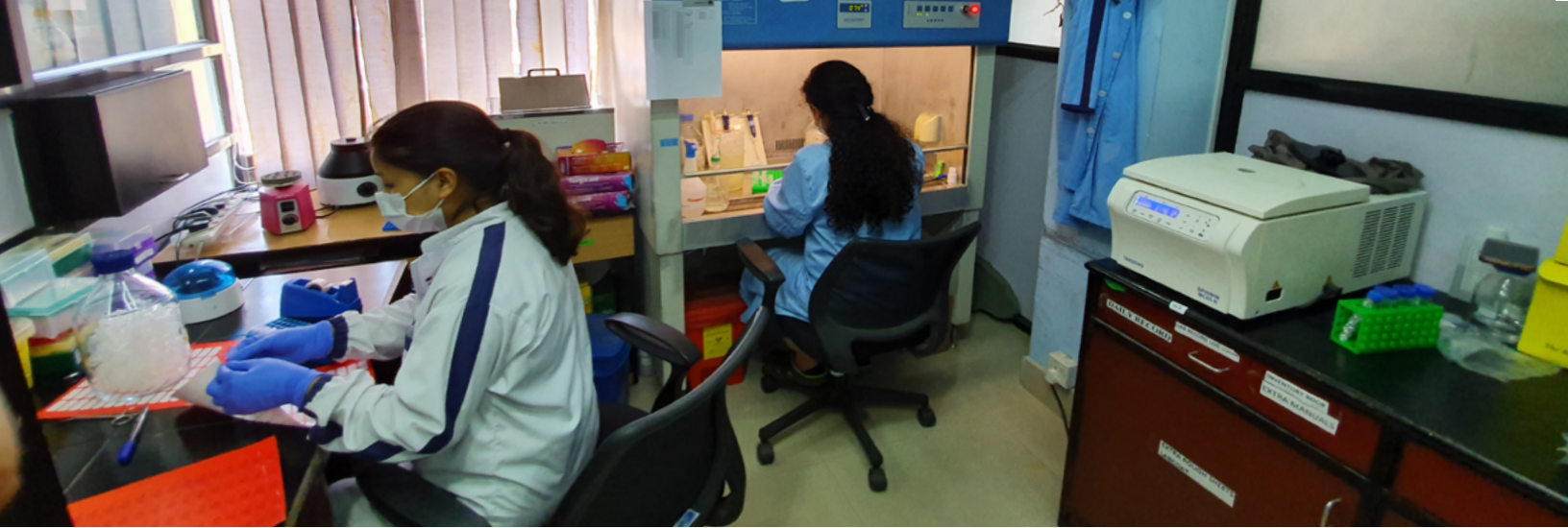
The PREDICT project's One Health surveillance approach was designed to train, equip, and enable the workforce to collect data and build the evidence base for zoonotic diseases and emerging viral threats in vulnerable areas. PREDICT is the first systematic project in Nepal to use the One Health approach for viral surveillance in both animal and human populations. Our team safely and humanely sampled wildlife, domestic animals, and people concurrently, targeting high risk communities for virus spillover and spread in urban and rural areas of Nepal. In addition, we implemented syndromic surveillance of febrile patients at major hospitals near our at-risk surveillance sites. We also used molecular tools to confirm the species of sampled wildlife (30 bats and 146 rodents), and identified five species of rodents along with three species of bats.

KATHMANDU VALLEY



Numbers of individual taxa sampled during dry and wet seasons in Kathmandu Valley

Our team conducted surveillance at low-income informal settlements situated along urban rivers in Kathmandu. At these sites, residents raise animals, grow food in urban gardens, and engage in a variety of livelihood activities. These sites are considered vulnerable due to the close contact between animals and people and lack of infrastructure, improved sanitation, and availability of health services. In addition, we sampled macaques at two temple heritage sites that attract local and international tourists. For syndromic surveillance, our team worked with a public not-for-profit tertiary academic institution that receives patients from all over the country.



VIRUS DETECTION

Virus discovery efforts have an important role to play in preparing for future epidemics. These activities are contributing to a global health paradigm shift by incorporating a more proactive approach to surveillance and pandemic preparedness. By finding viruses in wildlife before they emerge in humans, we stand to learn more about the ecology and evolution of viral diversity and transmission risk of potentially pandemic strains.

The PREDICT project's viral detection uses broadly reactive consensus (genus/family level) PCR supplemented with high throughput sequencing. These powerful tools produce specific, high-resolution data, allowing for detection of known and new potential pathogens. Between 2012 and 2019, 19 unique viruses were detected in animals and people.

In Nepal, our findings of novel paramyxoviruses and coronaviruses in rodents are good examples of how we are operationalizing this proactive paradigm. During the first phase of the project (2012-2014), we sampled wildlife in urban areas of Kathmandu and detected corona-, paramyxo-, hanta-, and rhabdoviruses in rodents and shrews; henipa- and retroviruses in macaques; and coronaviruses in bats.

In the second phase of the project (2014-2019), we sampled animals and people in Kathmandu Valley, as well as in Chitwan and Makwanpur Districts. We detected a total of 10 unique viruses belonging to 4 viral families (corona-, paramyxo-, flavi-, and influenza viruses) within humans, rodents, shrews, and mallards.

VIRUS TABLE

| VIRAL FAMILY | VIRUS | SPECIES | SAMPLING LOCATION | # OF POSITIVE INDIVIDUALS | | |
|-----------------|---------------------------------|-------------------|--|---------------------------|------------|------------|
| | | | | TOTAL | WET SEASON | DRY SEASON |
| Coronavirus | Alphacoronavirus NL63 | Human | Makwanpur District | 2 | 2 | 0 |
| | Coronavirus 229E (Human strain) | Human | Kathmandu Valley | 2 | 0 | 2 |
| | Murine coronavirus | Black Rat | Kathmandu Valley | 3 | 0 | 3 |
| | Duck coronavirus | Mallard | Kathmandu Valley | 16 | 0 | 16 |
| Paramyxovirus | Infectious bronchitis virus | Mallard | Kathmandu Valley | 3 | 0 | 3 |
| | Human parainfluenzavirus 3 | Human | Makwanpur District | 1 | 0 | 1 |
| | PREDICT_PMV-83 | Asian House Shrew | Kathmandu Valley | 3 | 0 | 3 |
| Influenza virus | Newcastle disease virus | Mallard | Kathmandu Valley | 8 | 0 | 8 |
| | Influenza A | Human, Mallard | Kathmandu Valley, Clinic (Kathmandu), Makwanpur District | 21 | 4 | 17 |
| Flavivirus | Dengue virus serotype 2 | Human | Clinic (Chitwan) | 1 | 0 | 1 |
| Total | | | | 60 | 6 | 54 |

EPIDEMIOLOGIC & BEHAVIORAL RISK

The PREDICT project deployed a multidisciplinary One Health surveillance approach, working with local communities to evaluate animal-human interactions, animal distributions, human demographics, behaviors, and activities at sampling sites. Between September 2016 and September 2018, 2,046 individuals participated in clinic and community-based surveillance activities. Samples were collected from all participants to screen for viruses, and interviews were conducted to collect survey data to shed light on potential drivers and risk pathways for zoonotic virus spillover and spread. Both epidemiological and ethnographic methods were used in data collection and analysis to generate insights.

CLINIC-BASED SURVEILLANCE

Clinic-based surveillance aimed to detect viruses causing illness in people. Specifically, we targeted patients with undifferentiated or undiagnosed fever (temperature $\geq 38^{\circ}\text{C}$ (100.4°F)) and tested individuals for coronaviruses, filoviruses, flaviviruses, influenza viruses, and paramyxoviruses.

At the time of sampling, most participants had acute fever of 1-5 days' duration. In addition to fever, patients reported a range of other symptoms, including cough (30.9%), diarrhea and/or vomiting (41.6%), headache and/or joint pain (77.7%), convulsions and/or altered consciousness (2.9%) or a combination of these symptoms. Fever with cough was more common in patients at the Kathmandu clinic (73.8%) compared to patients sampled at the Chitwan clinic (26.2%). Symptoms did not vary by gender and age-class of patients sampled, except for fever with headache and/or joint pain, which was significantly more common in patients >11 years old.

PARTICIPANT CHARACTERISTICS ACROSS ALL SURVEILLANCE SITES

| | Clinic-based surveillance (n=543) | | Community-based surveillance (n=1,503) | |
|-------------|-----------------------------------|--------------------------|--|----------------------------|
| Study Sites | Clinic (Kathmandu) (n=275) | Clinic (Chitwan) (n=268) | Urban (Kathmandu) (n=946) | Rural (Makwanpur) (n=557)* |
| Gender | | | | |
| Female | 117 (42.5%) | 134 (50.0%) | 604 (63.8%) | 336 (60.3%) |
| Male | 158 (57.5%) | 134 (50.0%) | 342 (36.2%) | 221 (39.7%) |
| Age (years) | | | | |
| 0-10 | 38 (14.2%) | 56 (20.4%) | 80 (8.5%) | 72 (12.9%) |
| 11-20 | 49 (18.3%) | 57 (20.7%) | 367 (38.8%) | 203 (36.4%) |
| 21-40 | 86 (32.1%) | 75 (27.3%) | 240 (25.4%) | 104 (18.7%) |
| 41-60 | 63 (23.5%) | 53 (19.3%) | 77 (8.1%) | 55 (9.9%) |
| 61+ | 32 (11.9%) | 34 (12.4%) | 182 (19.2%) | 123 (22.1%) |

*2 did not participate in the behavior survey

Participants enrolled in the hospital setting were most commonly students (Kathmandu Clinic: 36.4%; Chitwan Clinic: 32.8%), agricultural workers (Kathmandu Clinic: 25.0%; Chitwan Clinic: 22.9%), non-animal business workers (Kathmandu Clinic: 19.6%; Chitwan Clinic: 12.7%), or homemakers (Kathmandu Clinic: 12.7%; Chitwan Clinic: 27.6%). Among agricultural workers sampled, the majority were involved in crop production (48.4%) or did both animal and crop production (40.0%), and the remaining were engaged in animal production alone.

COMMUNITY-BASED SURVEILLANCE

From 2016 to 2018, 1,503 individuals participated in One Health surveillance and behavioral risk investigations at community-based surveillance sites in urban Kathmandu and in rural areas. The majority of participants from the rural community were involved in both animal and crop productions whereas urban participants were mostly involved in animal production. There were significantly higher

numbers of unemployed people sampled in the urban community. However, more individuals reported not attending school in the rural community compared to the settlement in Kathmandu; therefore literacy rates in this area may be lower. Among people interviewed, contact with both wild and domestic animals was prevalent in both rural and urban communities. Participants involved in crop and animal production reported crop foods raided by rodents and shrews (18%), non-human primates (54%), and other wild animals.

The majority of people in rural and some from urban communities reported that they had eaten raw, sick animals, or animals found dead. Hunting of wild animals and selling of dead animals were observed only in the rural study site, where communities engaged in hunting were targeted for surveillance and where residents reported hunting, cooking, or handling bats. Other animals were also hunted in this community to mitigate crop and food raiding. Hunting of bats was most common in male and adult (20-60 years) participants. People who hunted bats were also more likely to report influenza-like symptoms in the past

year, compared to individuals who did not hunt bats. Respondents from the rural community provided important context for their contact with animals, including bats, in ethnographic interviews and focus group discussions.

In both communities, our findings highlight concerns over sanitation and hygiene, lack of knowledge on disease risks, and the prevalence of high-risk activities for virus spillover related to human-animal interactions. These behaviors and documented knowledge gaps show vulnerabilities to infectious diseases. At both sites, meetings were held in partnership with local authorities to raise awareness of zoonotic diseases and to identify potential strategies for risk reduction and disease prevention.

SELECTED EXCERPTS ON ANIMAL CONTACT AND HUNTING FROM ETHNOGRAPHIC INTERVIEWS AND FOCUS GROUP DISCUSSIONS

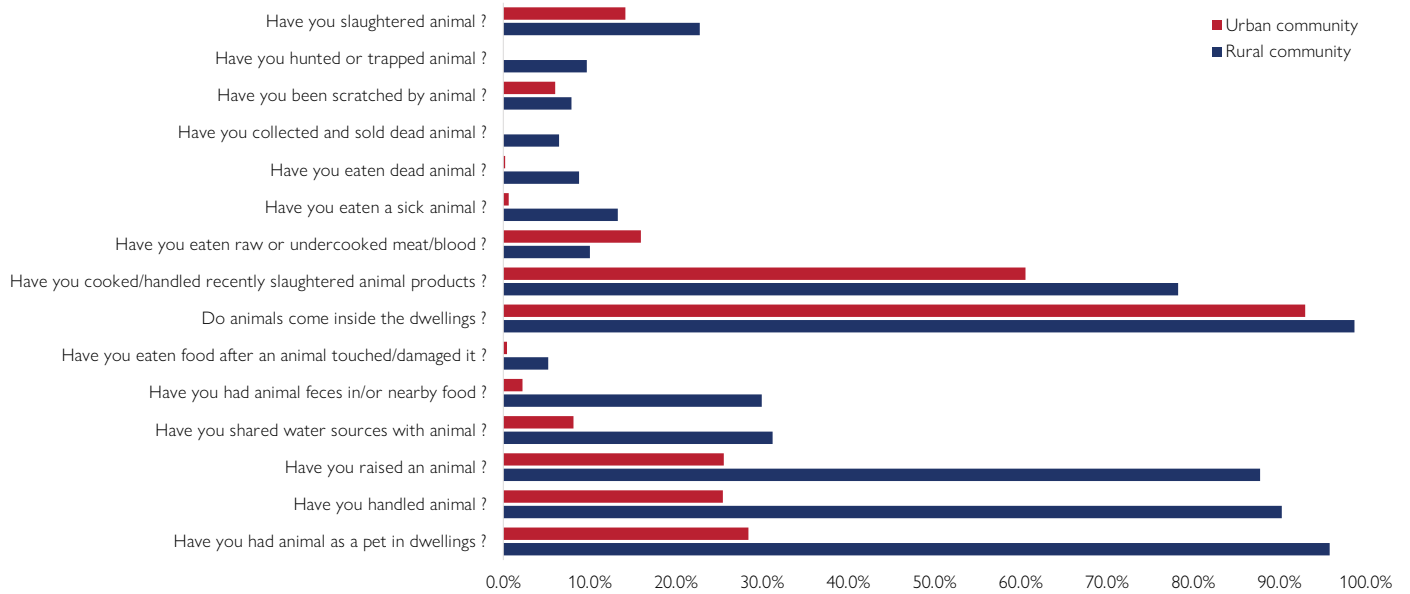
Who usually takes care of animals in the household?

Most of the time, we women take care of animals at home as men are mostly in the field to farm, but they sometimes help to feed animals. Men slaughter the animals.

Do you hunt/capture wild animals that you have said are seen in this area? Do you also hunt or consume them?

Ancestors used to hunt bats and we also learned from them. If the elder of the family hunts, then their family eats bats. Some occasionally sell them at the market. Bat tastes like pigeon meat. We do not eat the small bats that eat insects.

I have not hunted or eaten bats as there are no 'Chiuri' plants in our area but we hunt 'Gosya' a cat like animal that eats fruit.



Responses on animal contact compared across rural and urban community participants



RISK COMMUNICATION

Given the zoonotic risk identified in bats species from surveillance activities conducted throughout the PREDICT project, communities in the rural study sites were informed about the risks associated with bat hunting and consumption. Outreach and risk reduction campaigns were also conducted after the completion of field work through leaflets and booklets including PREDICT's

behavior change communication and risk reduction resource, *Living Safely with Bats*. These efforts helped increase awareness of the potential dangers of direct contact with bats and helped identify strategies for staying safe from exposure and infection, while ensuring the health and safety of the bats.



Cover of *Living Safely with Bats*

COMMUNITY ENGAGEMENT

By design, the PREDICT team engaged local communities to forge partnerships, build trust, and develop participatory One Health surveillance. Through these collaborations, local individuals are recruited to act as ambassadors and liaisons, and speak with their communities

about zoonotic diseases, transmission dynamics, risky behaviors and practices, and measures to mitigate risk. In these communities, PREDICT also improved access to healthcare, linking vulnerable populations with health professionals and needed services. In addition, the

PREDICT team shared resources and strategies with community partners of laboratory findings and surveillance summaries designed to reduce risks for virus transmission while balancing health and conservation goals.



PRACTICAL IMPLICATIONS

The PREDICT project's work in Nepal has been integral to establishing emerging virus disease surveillance using the One Health approach and strengthening One Health platforms in the country.

Pilot studies conducted by PREDICT in partnership with hospitals in Nepal have highlighted the importance of screening for emerging and re-emerging viruses in clinical settings.

Surveillance activities involving bats, rodents, and primates have strengthened the wildlife health capacity in Nepal and expanded the workforce with knowledge and skills needed to work with wildlife.

OUTBREAK PREPAREDNESS & RESPONSE

The PREDICT team provided technical expertise and support to government partners during the 2017 H5N8 poultry outbreak. The outbreak killed 3,650 birds, with another 2,550 suspected animals culled by rapid response teams; eggs, feed, and egg trays were also destroyed to control the spread. PREDICT's lab enabled rapid influenza subtyping by providing influenza detection primers with the Central Veterinary Laboratory (CVL), which conducted Influenza A testing on the dead poultry.

STRENGTHENING CAPACITY

Through hands-on trainings and experiential learning embracing the One Health approach to disease surveillance and detection, the PREDICT project has strengthened capabilities in Nepal to conduct behavior risk investigations, humanely and safely collect samples from animals and humans, safely transport samples to laboratories for testing, detect viruses and emerging disease threats, and develop disease prevention and risk communication strategies.

Since 2012, PREDICT has trained >65 individuals from multiple disciplines, including doctors, veterinarians, field biologists, epidemiologists, molecular biologists, sociologists, community leaders, para-veterinarians, and government officials. In addition, our team has trained 50 members of the global health workforce (20 interns and 30 visiting international students). Trainings were conducted through conferences, hands-on field and lab experiences, internships, and workshops.



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