

## BHUTAN

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Bhutan is a small country with a population of approximately 800,000 people that has made a significant effort toward Rabies elimination. Many areas have controlled the disease. However, Rabies is still endemic in Southern Bhutan near the Indian border. This not only is a public health issue in the affected areas but also could lead to a national problem where re-emergence of Rabies could occur in disease-free zones. Notably, sporadic cases of rabies have been reported in the interior of the country, which could indicate that this is happening. Over 5000 bite exposures occur each year and 17 deaths due to Rabies were reported in the past 10 years.

Control of Rabies in Bhutan is mainly due to the Government's commitment to an applied "One-health" approach that uses multi-sectoral activities in the implementation of their national plan for Rabies elimination by 2020. Important strategies that have been key to Bhutan's success are: 1) the provision of free Rabies vaccines and immunoglobulins (RIG) at health facilities; 2) extensive rabies, bite exposures and anti-rabies treatment surveillance; 3) a continuing mass dog vaccination program compassed within a dog population management program and 4) targeted research strategies. Currently, post-exposure prophylaxis (PEP) for rabies exposures costs of 82,500 USD per year to the public health system. Yet, these costs are likely to rise as more people seek healthcare after rabies exposures following rabies education campaigns and increased PEP access and uptake in "high-risk" rural areas.

As Bhutan is one of the few countries where rabies still occurs in selected regions that dispense PEP free-of-charge, it provides the unique opportunity to elucidate the factors, aside from direct treatment costs, that influence health-seeking behavior. Currently, Gavi and the WHO, in collaboration with the Ministry of Health and the Department of Livestock in Bhutan, are undertaking studies in the rabies endemic areas to evaluate the program in its current state in its capacity for averting human rabies deaths. Information will be gathered to 1) assess the direct costs incurred by the health system of a decentralized, and free, PEP treatment program; and 2) establish Rabies transmission networks, via contact-tracing, from PEP seeking index cases to collect more accurate information on rabies exposure socio-demographics, PEP seeking behavior, details of PEP treatment received and the indirect costs incurred.

The information gathered will identify program successes and areas of improvement to support, not only, national policy-making in Bhutan but the study results could positively impact the global strategy for Rabies elimination, where countries could use Bhutan's example to develop their own comprehensive disease targeted plans.

## KENYA

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Kenya is a country with a high rabies burden that counts the disease as one of its top 5 zoonotic diseases. Recent estimations denote that 523 rabies-related deaths occur each year. This statistic is likely to be higher given the large numbers of bite exposures within the country of at least 336 bites per 100,000 people per year (compiled from passive surveillance data between 2012-2016). With an ever-expanding population, which has doubled in the past 25 years, more people, than ever, are now at risk of contracting the disease.

The Kenyan government has recognized the public health problem posed by Rabies and has responded by launching a strategic plan, in 2014, for the prevention and elimination of Rabies by 2030. Its strategy hinges on public health and rabies education campaigns, strong human and animal health strategies coordinated by the Zoonotic disease unit, and PEP vaccine and Rabies Immunoglobulin (RIG) availability. Extensive surveillance strengthening to evaluate disease incidence is incorporated into the program to allow for the measurement of successes, identify regions that require intensified efforts, as well as areas where disease has been controlled. Pilot elimination campaigns have commenced in Western Kenya in Kisumu and Siaya counties that have a high rabies burden and possess natural borders. The surveillance activities in Kenya use a multi-faceted approach to collect data, in addition to health facility statistics, all of which are managed by the Centers for Disease Control and Prevention-Kenya Health and Demographic Surveillance System (HDSS). Community interviewers gather bi-annual population health and demographic data and conduct verbal autopsies in communities. Other reporting streams, such as Community Health Volunteer (CHV) network and Toll-free number reporting by the general public provide additional surveillance information in real-time. Currently, patients seeking PEP incur both direct and indirect costs of treatment, which is likely to have an adverse impact on health-seeking behavior.

Siaya County, Kenya has been selected as a focus region for a fact-finding study undertaken by Gavi and the WHO in collaboration with its Kenyan partners in the field including the Kenya Medical Research Institute (KMRI), the Zoonotic Disease Unit and county public health and veterinary departments. The goal is to address the information gaps in Rabies burden in humans and animals and the needs for ensuring access to PEP treatment by bitten individuals. The study is incorporated within the HDSS that gathers both retrospective health facility patient data and is undertaking prospective studies of community-based surveillance information attained from surveying randomly selected households, as well as reports from the CHV and toll-free calls. Rabies transmission networks are being elaborated by contact-tracing, using index cases of rabies exposures reported to HDSS, by the methods as mentioned above, are interviewed to identify the animal's owner and other contacts potentially exposed. Additionally, captured animals responsible for bite exposures will have their rabies infection status confirmed using both the point-of-care lateral flow kits and the OIE recommended Direct Fluorescence antibody tests.

Preliminary results have already demonstrated that community-based surveillance methods capture a more accurate picture of suspected rabies exposures with three-fold more cases being observed than those reported by health facilities. Of the patients who presented for health care, the patient's unwillingness to pay for PEP was minimal, and in fact, a high 38% were not treated due to unavailability of rabies vaccines at the point of care. As the study progresses, the information gathered will identify program successes and areas of improvement to support in further developing and expanding the 2014 Strategic plan for the prevention and elimination of human rabies into the rest of Kenya. Globally, the data generated will inform the strategies for global Rabies elimination. Countries developing national plans for Rabies elimination could use Kenya's example to develop their own comprehensive disease targeted plans.

## VIET NAM

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Vietnam currently reports 70 cases of rabies-related deaths per year and administers more than 300,000 post-exposure prophylaxis treatments for rabies exposures using their extensive decentralized rabies treatment system. The country has also conducted mass dog vaccination campaigns aimed at decreasing rabies disease incidences in reservoir animals to further impact rabies disease incidence rates.

Currently, patients seeking health care following rabies exposures may be treated at one of the 63 Provincial Preventative medical centers (PPMCs) or District Medical Centers, accounting for a total of 254 locations around the country where subsidized rabies vaccines can be available. Often, however, unavailability of biologics leads to patients resorting to treatment at private clinics where they must pay, if they can afford it. Interestingly, health facilities in Vietnam more often than not procure rabies vaccines and RIG directly from suppliers and information on patients seeking treatment after bite exposures are more likely to be filed at the point of care. These practices hamper the ability for the Ministry of Health to gather comprehensive surveillance data on the actual burden of rabies in the country and does not facilitate modeling for the needs for and availability of PEP within the country. Coupled with these points, expanded rabies education targeted at promoting the value of dog vaccination in preventing disease transmission and more information provided to “at-risk” populations on the appropriate measures to be taken after suspected rabies exposures would help decrease the dog to human transmission rates in Viet Nam. Furthermore, intensified efforts at rabies elimination in the Northern and Highland regions are needed as address regional issues related to fewer health facilities that are geographically harder for patients to travel to and the lower financial capacity to pay for treatment.

The rabies elimination program in Viet Nam is currently being expanded by the MoH National Rabies control program at the National Institute of Hygiene and Epidemiology (NIHE) in collaboration with the USCDC to pilot integrated bite case management (IBCM) in Phu Tho. Gavi and the WHO are currently performing studies in Phu Tho, Nghe An, Quang Ngai, and Binh Phuoc in Northern Viet Nam, where there is a high rabies burden, to gather information on 1) the demographics of suspected rabies exposures, rabies-related deaths, health seeking behaviors, PEP treatment regimens administered and failures to complete treatment; 2) Completing PEP survey at health facilities and with Vietnamese rabies biologic suppliers to evaluate the availability, procurement, cost of treatment, storage, administration, adverse events; and barriers to PEP availability; 3) Conducting prospective community-based surveys to capture further rabies epidemiological data and health seeking practices in Vinh city and Nghia Dan that are representative high rabies burden areas in urban or rural settings, respectively.

Using national aggregate data a total of 2683 deaths due to rabies were reported over the 22 year period between 1994 and 2016. Unsurprisingly, Most deaths occurred in the North and Highlands areas as compared to Central zones with a corresponding increased risk of 2.2 and 2.1 fold, respectively. Viet Nam has used approximately 10 million doses of rabies vaccines in the last 22 years, with PEP administration higher in the more affluent Southern and Central regions. Importantly, a decrease in vaccine administration was observed following the introduction of the substantially more expensive cell culture derived vaccines, which is likely to be linked to an inability for patients to incur the financial costs. Further information is still being gathered and will, in no doubt, provide essential information into how successful the Vietnamese decentralized rabies control program is at rabies elimination and highlight weaknesses.

The data will, not only, support the implementation of the National Rabies control plan for 2016-2020 in Vietnam and inform the development of the strategic framework of the ASEAN rabies elimination strategy by 2020, but it provides essential lessons for the elimination of Rabies worldwide by 2030.

## CAMBODIA

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Cambodia has the highest reported incidence of rabies globally with a previously reported rabies-related death rate of around 800, in 2007 and an estimated 700,000 people are being bitten by suspected rabid dogs every year. These statistics are extrapolated from modeling data and are unlikely to represent the real situation of rabies in Cambodia. Several factors including a high human to dog ratio of 3:1, a lack comprehensive rabies vaccination programs and the fact that PEP is only available in 2 centers located in the Capital of Phnom Penh are negatively influencing rabies burden. PEP expertise is provided by the Institut Pasteur du Cambodge (IPC) and National Institute of Public Health (NIPH). Using a centralized model for treatment after rabies exposures limits patients from rural or areas of significant distance from the capital having access to rabies PEP and leads to considerable indirect treatment costs in addition to the direct financial contribution they must pay. Individuals who do present themselves to local hospitals, are often turned away due to stigma and lack of education and may die if they have, in fact, contracted the disease.

Following the agreements between the ASEAN Health and Agriculture Ministers for the elimination of rabies in South East Asia by 2020, and after a workshop in 2015, the Cambodia Rabies Elimination Strategy was developed with support from the FAO, OIE, WHO and the US-CDC. Its goal is to eliminate Rabies in Cambodia by 2020. For rabies elimination to come to fruition, information on the current rabies situation related to disease epidemiology and health seeking behaviors of rabies-exposed individuals in Cambodia as well as accurate mapping of PEP delivery, procurement, and cost-effectiveness of vaccine regimens will facilitate the formulation and implementation of new guidelines and activities, into the national plan. In fact, the Ministry of Health and the Communicable Disease Department of Cambodia (CDCC), with support from the WHO country office, IPC, and the Ministry of Agriculture, Forestry and Fisheries have developed new guidelines for surveillance and rabies case management embracing the concept of “one health”. New standardized operating protocols for the evaluation and provision of PEP for suspected rabies cases are also complete. Validation will be sought at a rabies stakeholders meeting in the near future. In recognizing the high demand suspected rabies exposure treatment, a new bite management and the prudent use of biologics training series is underway for health care professionals. The MoH are gathering information on the current system of procurement, delivery, logistics of EPI and rabies vaccine, as well as the willingness to pay within the public and private sectors, which will hopefully lead to streamlining the procedures and a decrease in cost to the patient.

The IPC is evaluating the epidemiology of Rabies regarding human and dog demographics, incidence, bite exposures, PEP characteristics using retrospective data collected between 2002 and 2015, as well as prospective community surveys of known dog owners and randomly selected households in Kandal Province. Preliminary results show that 274,072 patients received PEP over the 12 year period with children less than 15 years old, women, and those injured by dogs accounting for 51.5, 48.0, and 95% of all cases, respectively. Given their expertise in rabies PEP administration and the high number of patients arriving every day IPC is evaluating alternative the cost-effectiveness of a shortened 3-session Intradermal PEP regimen.

All of the information gathered, coupled with new policies that incorporate a multi-sectoral approach, and the implementation of capacity building, and the expansion of dog vaccination pilot programs nationwide will facilitate Cambodia’s goal of Rabies elimination. Given, the extensive rabies disease problem within the country, their ability to successfully decrease rabies exposures and deaths will showcase how it may be achieved.

## INDIA

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India has a very high rabies burden with 17.4 Million rabies exposures per year and an estimated 20,000 rabies-related deaths reported during a multi-centric rabies study that was performed in 2003-2004. Since then, India has made many improvements to their rabies control and treatment programs which may have impacted rabies disease burden within the country. These efforts may be partially linked to the industrious nature of the country where they have switched to cell-derived vaccines and established in-house production facilities for both vaccines and RIG. Furthermore, the implementation of cost-saving intradermal vaccine administration regimens at government hospitals further decreases rabies exposure treatment-related costs and serve as surveillance centers for rabies disease. Advances in the socio-economic status of the Indian population as a whole has also provided better access to healthcare through improved infrastructure and transport, and higher education levels facilitate rabies awareness campaigns.

Following a 2015 call by the WHO for the elimination of rabies by 2030, India is mobilizing to make this a reality in their country. The Association for Prevention and Control of Rabies in India (APCRI), the National Center for Disease control, Delhi, and other national partners are re-launching the National Rabies Control Programme, and its elimination strategy is being updated to encompass multi-sectoral activities and implement a “one health” approach. As there is a lack of accurate, up to date surveillance information on the current rabies situation in India the APCRI has developed a very ambitious fact-finding study to be completed with the support of the WHO and Gavi. The study assesses recent data on PEP and RIG for cost-effectiveness in urban and rural settings, determines current procedures in place ensuring PEP vaccines and RIG are available in health facilities, conducting a market landscape analysis for Indian suppliers of rabies biologics, and determining the applicability of new technologies in the health system. Community surveys evaluating the epidemiology of rabies in high and low dog vaccination coverage area, confirming the rabies free status of Andaman, Nicobar and Lakshadweep Islands, as well as identify risk factors associated with non-compliance to treatment regimens is essential to implement the activities laid out in the Rabies elimination programme re-launch.

All of these points, as well as information derived from expert consultations, will lead to the drafting of a policy paper for the Indian Government to ensure that new guidelines and implementation strategies incorporated into the new version of the National Rabies Control Programme will have been developed using an evidence-based, informed process and will provide activities that will, when implemented, dramatically impact rabies burden in India. If India, can successfully eliminate, or even lower the risk of human deaths due to rabies, given its large size and high population, it will encourage other countries to follow suit.