Institution: University of Glasgow

Unit of Assessment: Unit 5, Biological Sciences

Title of case study: Development of life-saving control strategies to eliminate rabies in Bali

1. Summary of the impact

Rabies is an infectious disease that kills at least 55,000 people annually, primarily in Asia and Africa, with infected dogs being the major source of infection in humans. In a recent rabies epidemic on the Indonesian island of Bali, between Dec 2008 and June 2011, over 130 human deaths occurred, because the actions of the local authorities were not sufficient to control the outbreak. Research undertaken at the University of Glasgow was instrumental in the development of an island-wide canine vaccination strategy between 2010 and 2013. These campaigns controlled the spread of rabies in dogs (villages reporting new cases) and reduced the incidence of human deaths by over 90% compared with the incidence before mass canine vaccination started, in late 2010. As of July 2013, Bali had gone 11 months without a human case of rabies. The research also contributed to advocacy, policy formulation and development of computer-based tools to support rabies control both within Bali and other developing countries.

2. Underpinning research

Domestic dogs represent the key reservoir of rabies viruses transmitted to humans, and in many parts of the world, mass vaccination of domestic dogs has successfully controlled rabies. Mounting evidence demonstrates that elimination of canine rabies is possible through sustained annual campaigns that attain 70% canine coverage. However, there are no operational guidelines on how to manage vaccination campaigns strategically in the face of an emerging epidemic.

Between 2009 and 2013, a team from the University of Glasgow, led by Professor Dan Haydon (Professor of Population Ecology and Epidemiology, 2007–present), including Dr Sunny Townsend (Postdoctoral Research Associate, 2010–present), Dr Katie Hampson (Research Fellow, 2009–present) and Darryn Knobel (Postdoctoral Research Associate, 2009–2010), designed a canine vaccination programme to eliminate a rabies epidemic that had begun on the island of Bali, Indonesia, in 2008. The team developed a computer model of this emerging rabies epidemic (referred to as the 'Bali model'), which they used to test different control strategies, and so identify the key targets that would need to be met to eliminate rabies from the island.

Determining the rate of rabies spread

A key requirement for the Bali model was determining the basic reproductive number (R_0), a parameter that encapsulates the invasion potential of a pathogen and has important implications for control measures. R_0 is a measure of the average number of secondary infections produced by an infected individual in a susceptible population. R_0 values of over 1 indicate a strong likelihood that disease will spread. Between November 2008 and March 2010, the team estimated that R_0 for rabies transmission between dogs in Bali was about 1.2, similar to the values reported for other populations, such as Tanzania, despite the dog density on Bali being at least 10-fold higher (over 250 dogs per km^2).[3] This estimate corroborated growing evidence that methods that aim to control rabies spread by reducing dog density (such as by culling), would not be effective.

Developing the Bali model

Between August and October 2010, the Bali model was developed by initially drawing upon parameters identified in earlier research by the University of Glasgow (of rabid dogs in Tanzania)[1] that quantified the incubation period of rabies, its infectious period, and the distance travelled by rabid dogs. The model simulated the spread of rabies on a map of Bali, starting with a single case where rabies entered the island.[2] This made it apparent that rabies could not have spread across the island as rapidly as it had without assistance from humans moving their dogs greater distances than dogs could move alone. Therefore a human-mediated dog movement parameter was added to the model.

Using the Bali model

The first result from the model was that approximately one in every 20 rabid dogs must have been

moved during the epidemic to explain the rapid spread of rabies. The model was then primarily used to explore key characteristics of vaccination campaigns, including (i) the percentage of vaccination coverage achieved across the island; (ii) the time taken to achieve this; (iii) the duration of vaccine-induced immunity; (iv) the effect of long-distance movement of dogs; and (v) the effect of unvaccinated 'gaps'.[3]

Using the Bali model, the University of Glasgow team showed that across a wide range of epidemiological scenarios, and even with high-density dog populations, the control and elimination of rabies epidemics from the island is feasible using canine vaccination. The model indicated that control depends upon reaching sufficient vaccination coverage (70%) across the dog population in successive campaigns and that success is not more likely when using more complex, reactive or synchronised campaigns. The model also indicated that even small 'gaps' in coverage (as few as three neighbouring villages of Bali's approximately 700 villages) could jeopardise campaigns; therefore, regional coordination and full participation in such campaigns is critical.[3]

As vaccination campaigns were implemented and data were made available, epidemics were simulated on the Bali-specific vaccination landscape. This was used to verify that the simulated epidemics matched the epidemic on Bali, and allowed real-time estimation of likelihood of elimination.[3] The team went on to use the model to establish minimum surveillance guidelines that would allow the effective management of rabies control. The ability to detect at least 5%, and preferably 10%, of all canine cases was recognised as key to initiating timely control interventions and to monitoring their on-going success. If surveillance is poor, then the regions supporting rabies transmission will be neglected, or insufficient numbers of campaigns will be implemented, leading to the persistence of rabies.[4]

3. References to the research

1. Hampson K. *et al*. (2009) Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* 7: e1000053. doi:10.1371/journal.pbio.1000053.
2. Putra AA *et al*. (2013) Response to a rabies epidemic, Bali, Indonesia, 2008-2011. *Emerg Infect Dis.* 19: 648–651. doi: 10.3201/eid1904.120380.
3. Townsend SE *et al.* (2013) Designing programs for eliminating canine rabies from islands: Bali, Indonesia as a case study. *PLoS Negl Trop Dis* 7: e2372. doi:10.1371/journal.pntd.0002372.
4. Townsend SE *et al*. (2012) Surveillance guidelines for disease elimination: a case study of canine rabies. *Comp Immunol Microbiol Infect Dis* 36: 249–261. doi:10.1016/j.cimid.2012.10.008.

4. Details of the impact

In Bali, the first cases of rabies in humans and dogs were reported in 2008. The initial response of local authorities to the emerging epidemic was a combination of mass dog culling and low-coverage (<25%) canine vaccination. The outbreak, however, was not controlled, and rabies spread quickly through the dog population, reaching all nine regencies of the island by 2010. In the 3 years between the beginning of the outbreak and June 2011, (the month following completion of the first island wide dog vaccination), 130 human deaths from rabies had been reported and more than 130,000 doses of post-exposure prophylaxis (PEP) – a course of vaccination which is given as a treatment – delivered to bite victims. In total, these control measures cost around US$17 million.

In 2009, the University of Glasgow research team was approached by the World Society for the Protection of Animals (WSPA), which had been supporting a local non-government organisation (NGO) called the Bali Animal Welfare Association (BAWA). The aim was to demonstrate the feasibility of mass canine vaccination in Bali, by initiating a small-scale, but high-coverage, pilot vaccination programme between December 2009 and June 2010.[a] Between 2010 and 2013, the University of Glasgow team advised WSPA, BAWA and other NGOs, successfully drawing upon their research to:

- Add significant scientific weight to the design of control strategies, which was needed by

WSPA and BAWA to successfully lobby the local government to abandon canine culling and adopt mass vaccination as the official control policy
- Influence the design, implementation and evaluation of measures to direct island-wide vaccination strategies, to control the spread of rabies and to reduce the human death toll.

Achieving control of a rabies epidemic

The involvement of University of Glasgow researchers was key to developing Balinese government confidence and support for the Memorandum of Understanding between the Governor of Bali and BAWA in 2010, which ensured that the first island-wide mass canine vaccination project would not be de-railed by continued dog culling.[b,c]

> '*Glasgow's involvement provided credibility to the concept of mass vaccination as being sufficient for rabies control without the need to cull apparently healthy dogs – such a concept coming from animal welfarists alone would not necessarily have been believed*.' – Scientific Advisor, WSPA.[b]

In August 2010, WSPA invited Haydon, Townsend and Hampson to Bali to help guide strategic choices in planning Bali's first island-wide mass vaccination campaign (which took place from October 2010 to March 2011). Townsend trained members of the Bali provincial government and BAWA in data collection, including mapping vaccination delivery points, statistics and rabies epidemiology; Townsend then worked with local government scientists to analyse the data. Using data from the pilot vaccination campaign on Bali, the model was used to define the parameters of a successful campaign and address logistical questions raised by the campaign funders (WSPA) and operators (BAWA and local government staff) about a mass vaccination strategy.

> '*Under severe pressure from the regional mayors and head of animal husbandry [a Bali government office] we really needed some scientific back up. The Glasgow team was exactly what we needed…I believe we succeeded to run our program on time and on budget because we had Glasgow's experts to back us up. It also gave us the courage to continue with our plan even under extreme stress.'* – Director, BAWA.[d]

In the first mass vaccination campaign, 249,429 dogs were vaccinated, a coverage of 70% at the village level.[2] The result was a 70% decrease in the number of human deaths (from 82 cases in 2010 to 24 cases in 2011) and a 75% reduction in the number of observed canine rabies cases (36 cases per month in 2010 to about 7 cases per month in 2011).[2] Convinced by these outcomes, the Indonesian Directorate of Animal Health reached out to the Food and Agriculture Organization (FAO) of the United Nations for technical support with continued control strategies. The University of Glasgow team described their findings in a report to the FAO.[c] Mass vaccination significantly reduced the number of canine rabies cases in villages where culling had previously had no effect; mass vaccination protected dogs in villages from re-infection for an average of 6 months; and the size of outbreaks in villages decreased with increasing vaccination coverage within the village. This report concluded with recommendations for a second mass vaccination.[c]

> '*The contributions provided by Glasgow University through Dr. Sunny Townsend's consultancy and subsequent collaboration with Dr. Townsend and Dr. Katie Hampson have been integral to the progress made in rapidly improving rabies control on Bali Island.'* – Chief Technical Advisor, FAO Emergency Centre for Transboundary Animal Diseases (ECTAD), Indonesia.[e]

A second mass vaccination campaign was conducted (June 2011 to August 2011), and the FAO contracted the University of Glasgow team as consultants to analyse the impact of this campaign. The Bali model was thus used to provide recommendations for future rabies control strategies in Bali.[f] In February 2012, these scenarios were formally presented by Townsend in discussions with Indonesian Government officials in Jakarta, as well as provincial government and campaign implementers in Bali. Subsequently, a third island-wide mass vaccination campaign was conducted (March 2012 to February 2013) followed by a fourth (April 2013 to June 2013); these were organised with continued consultancy from the University of Glasgow team.[e] Following the third round of vaccination, the incidence of human rabies cases (deaths) decreased by over 90%

compared with the incidence before mass canine vaccination started, in late 2010. As of July 2013, Bali has gone 11 months without a human case of rabies.[e]

Contributing to advocacy

After the first mass vaccination campaign in Bali, the model was used to evaluate the epidemiological and economic consequences of a range of vaccination scenarios in Bali.[c,f] Working with researchers from the Royal Veterinary College (London) on a report commissioned by WSPA, the Glasgow team used the Bali model to predict the outcome for Bali under different vaccination control scenarios.[g] This was used to calculate the economic costs of these outcomes over a 10-year period. Continued culling would lead to rabies becoming endemic, as it did on the neighbouring island of Flores following introduction of the disease in 1997. Rabies eradication can be achieved by vaccination strategies, and despite the costs involved these save the estimated US$4.25 million per year cost associated with providing rabies PEP treatment if it were endemic.[f] This helped WSPA develop a high profile evidence base for policy formulation and advocacy both within Bali and elsewhere.

> *'The predictive modeling provided by Glasgow was particularly effective in convincing Bali local government to continue with island-wide dog vaccination and the importance of achieving even coverage across all villages on the island.'* – Chief Technical Advisor, FAO ECTAD, Indonesia.[e]

Aiding global control (Wise Monkey Portal)

While the Glasgow team was undertaking research in Bali, it also collaborated with 'Wise Monkey Foundation' – a Seattle-based not-for-profit organisation – to produce the Wise Monkey Portal.[h] Established in 2012, Wise Monkey provides software support for NGOs and government offices that need ways to collect validated and structured data that are crucial for the surveillance of rabies and large-scale rabies control measures, such as mass vaccination programmes. The software allows data to be entered (or viewed) in any location, allowing cases to be detected and responded to in real time and allowing impact to be monitored and sustained.

In 2012, Townsend and Hampson were instrumental in driving the structure of this database and trained members of the Nias provincial government in Indonesia and government officers in several municipalities in the Philippines (Sorsogon, Illocos Norte and Manila) to use Wise Monkey for data management. In 2013, Hampson, Townsend and Haydon implemented Wise Monkey as a data management tool (recording rabies vaccinations, population, bite cases, etc.) supporting rabies-control demonstration projects with the charity Global Alliance for Rabies Control (GARC) in the Indian city of Jamshedpur, and likewise with GARC and Philippines government in Bohol province and Region VI (Western Visayas).[h]

5. Sources to corroborate the impact.

a. Knobel, D. & Hiby, E. (2009) Bali rabies control report and recommendations. WSPA; available on request.
b. Statement from the Science Advisor, World Society for the Protection of Animals (WSPA); available on request.
c. Knobel D, Townsend S, Hampson K, Hiby E. & Girardi J. (2011) Preliminary evaluation and recommendations from the Bali mass dog rabies vaccination campaign. Report commissioned by the United Nations Food & Agriculture Organisation; available on request.
d. Statement from the Director, Bali Animal Welfare Association (BAWA); available on request.
e. Chief Technical Advisor, United Nations Food and Agriculture Organisation (FAO), Emergency Centre for Transboundary Animal Diseases (ECTAD), Indonesia
f. Townsend, S. & Hampson, K. (2012) Impacts of island-wide mass dog vaccination in Bali, Indonesia and prospects for achieving freedom from rabies. Report commissioned by the United Nations Food & Agriculture Organisation; available on request
g. Häsler *et al*. (2011) Economic analysis of rabies control in Bali, Indonesia. Report commissioned by World Society for the Protection of Animals (WSPA) (p.11).
h. Information from the Director, Wise Monkey Foundation; available on request.