

ORIGINAL ARTICLE

Towards Canine Rabies Elimination in KwaZulu–Natal, South Africa: Assessment of Health Economic Data

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Summary

Rabies remains a significant problem throughout much of the developing world. An estimated 69 000 people die annually from exposure to rabies. Most of these deaths are the result of being bitten by a rabid dog. Mass vaccination campaigns targeting dogs have been implemented around the world in an attempt to control or eliminate canine rabies. We analysed the vaccination and cost data for a campaign in the KwaZulu–Natal province of South Africa; we found that the cost per dog vaccinated to be \$6.61 for mass campaigns and \$5.41 for local campaigns. We also estimated the cost of human post-exposure prophylaxis (PEP). The cost of PEP is approximately \$64.50 on average per patient, and \$333 on average for the 9% of patients who receive RIG. We also found that the districts that vaccinated the most dogs per capita experienced the highest rates of human treatment and thus had the highest PEP costs.

Introduction

The majority of human rabies deaths globally occur as a result of being bitten by one of the people's most trusted companions: dogs. It is estimated that approximately 69 000 people die annually as a result of canine rabies, and most victims are children on the continents of Asia, Africa and Latin America (Knobel et al., 2005; Rupprecht et al., 2011; Anderson and Shwiff, 2015; Shwiff et al., 2013; WHO, 2013). The estimated annual global cost of canine rabies may approach \$120 billion (Anderson and Shwiff, 2015; Shwiff et al., 2013). Direct and indirect costs include post-exposure prophylaxis (PEP), animal tests, dog vaccination, livestock losses and the cost of human mortality risk, which comprises the majority of the global burden of the disease. While the disease has a case-fatality rate of almost 100%, it is completely preventable with timely intervention of post-exposure rabies vaccine and immunoglobulin. As the relationship between humans and dogs is a main

epidemiological driver, the elimination of canine rabies is necessary to prevent human rabies (Hampson et al., 2009).

In individual households, factors such as rabies awareness, vaccine accessibility, income and the nature of the relationship with dogs influence animal vaccination status (Flores-Ibarra and Estrella-Valenzuela, 2004). Within any private market, individuals will choose to invest in dog vaccination and PEP up to the point where the expected private marginal benefits equal the expected private marginal costs (Beach et al., 2007). By their very nature, private markets provide neither an incentive nor a mechanism by which participants would consider the greater social costs or benefits of their rabies management actions. As a result, one would expect private individuals to underinvest in management from a social point of view. As the broader society would prefer greater investment in rabies management, this result is often referred to as a 'market failure'.

Unlike private individuals, governments and public stakeholder groups are expected to consider the total bene-

fits and costs of rabies mitigation and possible elimination. Given limited resources, especially in developing countries where canine rabies has the greatest impact, an investment in rabies control will depend on a demonstration of the cost and feasibility of the chosen strategy. Rabies management programmes initiated by governments and public stakeholder groups seek to achieve the optimal level of rabies control by factoring in a broader set of components including the impacts to overall disease containment in a region, impacts to canine and human health, and market impacts to consumers and the macroeconomy (Beach et al., 2007). In the developing world, additional barriers to successful vaccination campaigns include a lack of information about dog populations and location, poor monitoring and diagnostic facilities, and inadequate resources (Lembo et al., 2010; Hampson et al., 2011; Nel, 2013). However, government-led canine rabies elimination strategies have succeeded in many countries around the world, resulting in substantial fiscal savings (Schneider et al., 2007; Shwiff et al., 2008). Collective, inter-sectoral, cooperative strategies are most successful in eliminating canine rabies and

reducing the associated financial burden (Bogel and Meslin, 1990; Shwiff et al., 2008). Regardless of who initiates rabies management directed at animal populations, the economically efficient implementation of management efforts requires a comprehensive understanding of the costs associated with animal and human vaccination.

The KwaZulu–Natal (KZN) province of South Africa has had an ongoing programme for control of enzootic canine rabies since the late 1970s (Nel and Rupprecht, 2007). This province is the second most populated province of South Africa with more than 10 million residents and is located in the south-east portion of the country along the coast (Fig. 1). There were 473 confirmed animal rabies cases, with six reported human deaths related to rabies in the project area when the programme was augmented in 2007.

The dog vaccination campaigns have intensified since 2007, with the appointment of a provincial coordinator and single point of reference for rabies control, and since 2009, when the project, together with two others (in Tanzania and the Philippines), became demonstration sites supported by the Bill and Melinda Gates Foundation. Our



Fig. 1. Location of the KwaZulu–Natal province, South Africa.

objectives were to estimate the cost per dog vaccinated, cost per PEP administered and cost per human life saved using data collected during 2010–2012 from the KZN project. A health economic data assessment such as we present here is a crucial component of disease control. This analysis can guide management decisions by highlighting cost-effective strategies and illustrating the potential savings associated with avoided PEP costs. At a broader level, it will provide information to policy makers and other stakeholders regarding both the feasibility and public health benefits of the elimination of canine rabies. While it may be infeasible to eliminate rabies on a global scale, it is certainly feasible to eliminate or provide maintenance on a regional scale. It is important to understand cost-effectiveness, which varies by region to allocate resources where they are most productive and stretch the furthest.

Methods

In 2010, the KZN project intensified dog vaccination campaigns in 11 districts (Ugu, uMgungundlovu, uThukela, Ilembe, Sisonke, eThekweni, uMzinyathi, Amajuba, Zululand, uMkhanyakude and uThungulu) and data on the cost of dog vaccination were collected. Calculation of the cost of dog and human vaccination required estimates of a number of parameters (Table 1). Data related to the number of dog vaccines and both the number and cost of human PEP were

Table 1. Parameters required to estimate dog and human vaccination costs

Parameter	Definition
Dog vaccination costs (<i>V</i>)	All biologics used for dog vaccination campaigns
Diagnostics (<i>Dg</i>)	Testing animals for rabies
Disposables (<i>D</i>)	Syringes, coolers and other equipment associated with the use of biologics
Fuel (<i>F</i>)	Fuel for vehicles to travel to vaccination sites
Awareness (<i>Aw</i>)	Public notification efforts prior to vaccination campaign
Salaries (<i>S</i>)	Associated with veterinary professional time
S&T (<i>ST</i>)	Per diem for staff and professionals
Accommodation (<i>Ac</i>)	Accommodation for mass vaccination events and refer to room and board for staff
Number of dogs vaccinated (<i>N_D</i>)	Total number of dogs vaccinated in 2010
Total cost of human vaccination (<i>TC_{PEP}</i>)	Sum of hospital and clinic cost records
Number of humans vaccinated (<i>N_H</i>)	Total number of human treatment cases
Total cost of dog vaccination campaigns (<i>TC_D</i>)	$V + Dg + D + F + Aw + S + ST + Ac$

collected during 2010–2012. PEP data were collected from vaccine distribution lists of the central medical stores in KZN.

Two types of dog vaccination campaigns were used during the study period. Local campaigns were performed in day trips and did not require accommodations. Mass campaigns were performed in areas that required extended or difficult travel and field accommodation of staff. For local campaigns, salaries were the largest expenditure and the second largest was media outreach or awareness (Fig. 2). For mass campaigns, salaries again represented the largest single cost to the programme followed by awareness and accommodations (Fig. 3). Notably, vaccine and consumables for vaccination represented a minority of the expenses.

During the period 2010–2012, over 1.3 million dogs were vaccinated (Table 2). The 2011 decline in the number

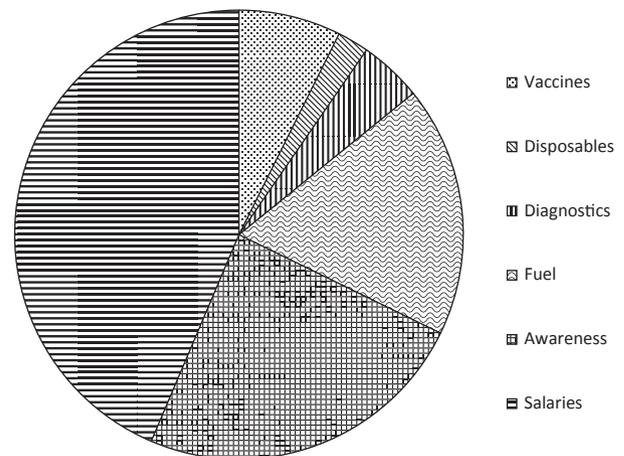


Fig. 2. Relative breakdown of component costs for local campaigns.

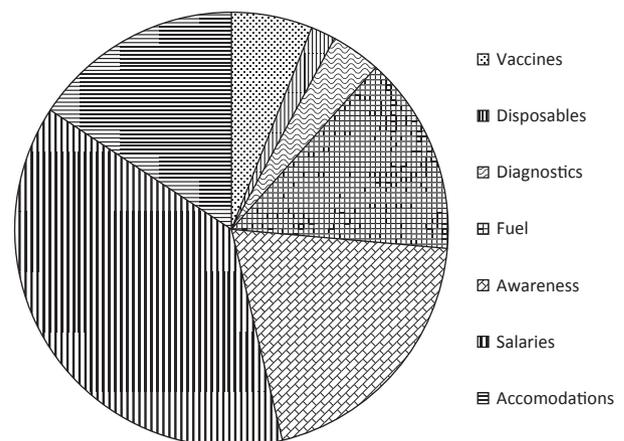


Fig. 3. Relative breakdown of component costs for mass campaigns.

Table 2. Total number of dogs vaccinated under mass and local campaigns by district and year

District	2010	2011	2012	Total
Amajuba	19 020	17 761	39 309	76 090
eThekwini	132 792	57 360	154 377	344 529
Ilembe	35 582	25 615	34 634	95 831
Sisonke	48 507	8 720	44 829	102 056
Ugu	47 177	38 017	61 101	146 295
uMgungundlovu	33 734	11 738	52 125	97 597
uMkhanyakude	30 509	16 700	36 528	83 737
uMzinyathi	23 861	12 681	38 260	74 802
uThukela	30 828	22 610	64 995	118 433
uThungulu	43 110	30 211	74 005	147 326
Zululand	14 978	16 494	38 229	69 701
Total	460 098	257 907	638 392	1 356 397

of dogs vaccinated was primarily due to staff shortages as a result of foot and mouth disease outbreaks, which pulled resources from the rabies programme. In the absence of these limitations and with increasing political and public awareness, an overall increase in the number of vaccinations in all but two districts (both Ilembe and Sisonke saw declines in the number of dogs vaccinated between 2010 and 2012) occurred in 2012. While accurate dog vaccination numbers were available for all 3 years, cost data proved to be unreliable or incomplete for 2010 and 2011. The cost data for 2012 more fully and accurately represented the true cost of the programme and was therefore used to estimate total costs for 2010 and 2011. Mass campaigns were used to vaccinate the majority of dogs (61% in 2010 and an estimated 50% in 2012, with the remainder having been vaccinated under the local campaigns).

Human vaccination data were aggregated across the 11 districts for 2010–2012 (Table 3). All human vaccinations were performed either in a hospital or clinic. South African

Table 3. Vaccines administered and total cost over the 3-year period. Estimated number of human rabies post-exposure prophylaxis cases and the population of each district (2011)

District	Cases	Vaccine	Cost	Population
Amajuba	3787	11 324	\$241 816	499 839
eThekwini	26 845	80 268	\$1 733 670	3 442 361
Ilembe	10 696	31 982	\$687 177	606 809
Sisonke	9136	27 318	\$578 429	461 419
Ugu	14 472	43 270	\$939 826	722 484
uMgungundlovu	11 265	33 681	\$728 108	1 017 763
uMkhanyakude	10 206	30 515	\$654 755	625 846
uMzinyathi	9341	27 931	\$603 162	510 838
uThukela	9466	28 304	\$608 064	668 848
uThungulu	19 212	57 443	\$1 238 168	907 519
Zululand	11 173	33 407	\$716 601	803 575
Total	135 600	405 443	\$8 729 777	10 267 301

policy is to follow Centers for Disease Control and Prevention (CDC) guidelines, which recommends four treatments for each patient post-exposure (CDC, 2010). Specific records were only available for a sample of all reported human vaccinations. These hospital and clinic records indicated that each individual received three treatments on average, with few completing an entire prophylaxis series. Records included the name of the individual, hospital or clinic name, geographic location of the bite incidents and dates for treatments received. There are many possible reasons why individuals do not complete treatment and these include a lack of understanding of the importance of the completion of the series, limited access to facilities and prohibitively high transportation costs. In some cases, treatment was discontinued due to the dog testing negative for rabies.

Using the average number of treatments that individuals received in this sample, we estimated the number of individual rabies PEP cases by dividing the total number of vaccinations reported by the average number of treatments obtained from the sample data (Table 3).

The estimation of the cost per life saved requires information on the number of patients who received PEP that were exposed to a rabid dog. This information was not available for South Africa, and the only published estimates come from two studies. One was conducted in the Philippines from 1995 to 2000 that indicated that approximately 3% of all patients receiving PEP were bitten by a rabid dog (Miranda, 2005; Partners for Rabies Prevention, n.d.). The other was conducted in Tanzania from 2002 to 2006 and indicates that the probability of developing rabies following exposure to a suspect animal is 2% in the Serengeti district and 12% in the Ngorongoro district (Hampson et al., 2008). In addition to assuming that 2–12% of all PEP patients would have developed rabies post-exposure to a suspected rabid dog, we also assumed that these patients received the full treatment series and that there was no treatment failure (100% patient survival post-treatment). The total cost for each district was then divided by the estimated number of persons who would have developed rabies post-exposure to a suspected rabid dog.

From the relationship between human PEP cases and dogs vaccinated, it is evident that the districts that vaccinated the most dogs also experienced the highest incidence of PEP interventions (Fig. 4). This might be due to population scaling effects. To further adjust for population, we derived estimates of dog vaccination intensity (DVI) and human treatment rate (HTR), which are measured in per capita terms. DVI was calculated as the number of dog vaccinations in each district divided by the total human population of the district. This indicates the number of dogs vaccinated per person, which is an approximation of the intensity of vaccination efforts. Higher DVIs imply more

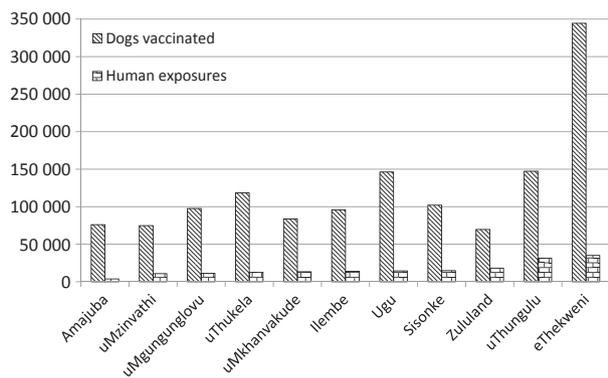


Fig. 4. Number of dogs vaccinated and the number of estimated human treatments to rabies by district.

dogs vaccinated per person. To calculate HTR, the number of human PEP cases was divided by the total population of the district.

Results

All monetary values were provided in South African Rand (ZAR) and converted to US dollars (USD) using the appropriate exchange rate. Approximately 640 000 dogs were vaccinated in 2012 at a cost of roughly \$3.8 million. Dividing the total costs by the number of dogs vaccinated under each campaign indicates that local campaigns (\$5.41) offered a cost reduction relative to mass campaigns (\$6.61) (Table 4). This is a result of the lack of expenditure related to accommodations and per diem (S&T) associated with mass campaigns. Given the additional components, mass campaigns commanded a significant premium, costing \$1.20 more per dog than local campaigns. Using the cost per dog vaccinated by campaign and the percentage of dogs vaccinated under each campaign in each year, we estimated the total cost of vaccination in 2010 and 2011. This indicates that 2012 was the most expensive year for dog vaccination (Table 5). We find that these estimates are consistent with previously reported estimates of the cost per dog vaccinated in other parts of the world (Table 6).

Cost per human vaccination was estimated by dividing the total cost of vaccinations for each district by the number of vaccinations administered. These costs ranged from

Table 4. Total number of dogs vaccinated and cost for each campaign type in 2012

Category	No. of dogs	Total cost	Rate/dog
Mass campaign	319 196	\$2 108 497	\$6.61
Local campaign	319 196	\$1 727 899	\$5.41
Total	638 392	\$3 836 396	

Table 5. Total cost (TC) of vaccination programmes for 2010–2012 for each campaign type

Category	2010	2011	2012
Mass campaign	\$1 850 800	\$937 621	\$2 108 497
Local campaign	\$973 800	\$627 875	\$1 727 899
Total	\$2 824 600	\$1 565 495	\$3 836 396

2010 and 2011 are estimated.

Table 6. Summary of cost per dog vaccinated estimates

Location	Rate/dog	Study
Tanzania	\$1.73–5.55	Kaare et al. (2009)
Bhutan	\$1.66–6.36	Tenzin et al. (2012)
Chad	\$1.80–2.60	Zinsstag et al. (2009)
Philippines	\$1.19–4.27	Fishbein et al. (1991)
Tunisia/Thailand	\$1.30	Bogel and Meslin (1990)
South Africa	\$5.41–6.61	Shwiff et al. (2014)

\$21.17 to \$21.72 per vaccination, with an overall average of \$21.50. Assuming that on average each individual receives three treatments with an average cost of \$21.50 per vaccine, the total cost of treatment was \$64.50. Roughly 9% of individual cases received human derived RIG, bringing the total cost for three treatments to \$333. For individuals who completed the four vaccination series, the cost was \$86 without RIG and \$354 with RIG. The cost per human life saved ranged from an average of \$2565 using the 2% rabies contraction rate to an average of \$427 using the 12% rabies contraction rate.

The dog vaccination intensity (DVI) ranged from 0.09 to 0.22 with an overall average of 0.15 (Table 7). The HTR ranged from 0.76% to 2.12% with an overall average of 1.52%. A scatter plot of DVI against HTR allows for a cursory examination of the relationship between the intensity

Table 7. Dog vaccination intensity (DVI) and human treatment rate (HTR) during the period 2010–2012 for each district

District	DVI	HTR (%)
Amajuba	0.15	0.76
eThekwini	0.10	0.78
Ilembe	0.16	1.76
Sisonke	0.22	1.98
Ugu	0.20	2.00
uMgungundlovu	0.10	1.11
uMkhanyakude	0.13	1.63
uMzinyathi	0.15	1.83
uThukela	0.18	1.42
uThungulu	0.16	2.12
Zululand	0.09	1.39
Total or average	0.15	1.52

of dog vaccination campaigns and the number of humans who received post-exposure treatment (Fig. 5). The general upward sloping trend between DVI and HTR indicates that the districts that vaccinated more dogs per capita generally had higher human treatment rates.

Discussion

Our analysis indicates that the higher cost per dog vaccinated (\$6.61) for mass efforts versus local campaigns (\$5.41) was due to the added transportation and accommodation costs. There are many possible reasons for the higher dog vaccination cost in KZN relative to other projects. The KZN project required a large fleet of vehicles and field agents given the vast rural nature of the project site. The societal structure in KZN also differs from that of neighbouring provinces. Rather than having a village structure, the Zulu population tends to be more independent and spread out. This creates unique difficulties in disseminating information and vaccinating animals.

The cost per human treatment with PEP ranged from \$21.17 to \$21.72 (\$21.50 average), and the average estimated cost per human life saved ranging from \$427 to \$2565. Over the 3-year period, 1 356 397 dogs were vaccinated for slightly less than the cost of administering PEP to 179 274 humans. These results highlight a possible cost-saving opportunity: prevention (i.e. dog vaccination) may be more cost-effective than treatment (i.e. human vaccination). The majority of dog and human vaccination costs are likely borne by governments, and increasing the cost-effectiveness of management should be an important consideration for the governments in the developing world that may suffer chronic revenue shortages and that may already struggle to provide adequate services. It is important to note that these estimates are not necessarily universally applicable because they have been derived from a specific programme with unique characteristics. However, it is a rational premise that the principles of cost saving demonstrated here may be applicable for any canine rabies control

programme elsewhere in Africa and in the developing world in general.

Several possible conclusions can be drawn from the positive correlation between the human treatment rate and dog vaccination intensity. If resources are being effectively allocated to those districts that suffer a relatively greater burden of canine rabies, we expect that dog vaccination intensity would be higher in those districts. The relationship depicted in Fig. 5 may suggest that resources to vaccinate dogs are being allocated in an efficient manner. However, the positive correlation between the human treatment rate and dog vaccination intensity might also suggest that even if resources are being allocated efficiently, dog vaccination efforts are currently insufficient or have not been implemented for a long enough period of time to reduce human treatment rates in high-treatment districts to average levels. Finally, the positive correlation may not be indicative of any causative link. It is possible that higher estimated treatment rates are not indicative of a greater inherent threat from canine rabies, but are instead indicative of the availability of more resources, better accessibility to PEP or an increased awareness as a result of the presence and efforts of vaccination personnel. If the availability of resources that can be devoted to PEP is higher in certain districts, it is possible that there are also more resources available to vaccinate dogs. Therefore, relatively resource-rich districts may have higher numbers of PEP cases and higher dog vaccination intensities because the needed resources are available, but not because such districts face a greater threat from canine rabies.

Elimination of rabies depends entirely on efficient efforts. Our results allow for estimates of the resources needed to pursue future vaccination campaigns as well as elimination strategies. By understanding the relative contribution of each component to the final cost, it is possible to improve methods to reduce overall costs. Estimates of the cost of human PEP provide an understanding of the potential benefits given canine rabies elimination. We can deduce that if canine rabies cases were eliminated, no PEP expenditures would be needed, saving this province close to \$9 million dollars over a 3-year period, not including the reduced veterinary costs when moving from elimination to prevention of canine rabies reintroduction. Understanding the costs and benefits of rabies elimination also improves the ability to motivate the inter-sectoral cooperative strategies needed for elimination to be successful (Meslin and Briggs, 2013).

Successful elimination also depends on an understanding of the intra- and interspecies dynamics as well as the threat of canine rabies reintroduction from bordering provinces and countries (Hampson et al., 2009; Zinsstag et al., 2009). In the KZN province, wildlife does not play a significant role in the rabies epidemiology. Cases involving wildlife are rare

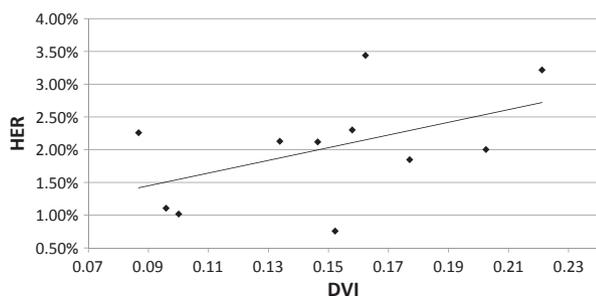


Fig. 5. Scatter plot of human treatment rate (HTR) against dog vaccination intensity (DVI) with line of best fit.

and stem primarily from the canine cycle. Rabies is transmitted almost exclusively from canine to canine or from canine to wildlife. In 2012, there was a rabies outbreak in the black-backed Jackal (*canis mesomelas*) population, which maintained the disease for roughly 4 months. Once the dog rabies problem was eliminated, rabies in the Jackal reservoir died out. There exists a rabies cycle within the Lagos Bat and a Mokola variant, which is of unknown origins, but currently these are purely of academic interest as they have proven to be insignificant problems. While wildlife may not play an integral role in the rabies epidemiology in KZN, wildlife can and does contribute to the overall cost of rabies elimination in many other parts of the world. A thorough cost-benefit analysis then must include these wildlife intervention strategies, if any, to present a more accurate picture.

Surrounding provinces and countries also pose a reintroduction threat. As KZN approaches elimination, efforts have begun shifting towards surrounding provinces where rabies is still relatively problematic as similar projects do not exist. The KZN project leaders have been working to establish similar elimination programmes in surrounding areas in order to expand the elimination area or, at the very least, to protect its borders. This is carried out by providing technical assistance, training and, where needed, small loans of essential equipment. An international animal vaccine bank was also recently established in KZN and has distributed close to 200 000 vaccines to surrounding areas. Vaccination efforts within KZN will move to a 3-year cycle targeting 70% coverage rather than annual efforts. Rabies will become a rapid response disease for the teams prepared for major disease outbreaks. These ongoing maintenance efforts are estimated by local staff and coordinators to cost roughly \$2 million per year including all surveillance, vaccination and trainings.

Other possible intervention strategies include population control and oral rabies vaccination (ORV) bait distribution. State-led sterilization programmes are ongoing in KZN. These efforts have failed to adequately influence the dog population due to budget limitations leading to too few animals being sterilized. As a result, there are trials being run on new types of canine contraceptives, which could make population control more achievable. There is no culling of dogs, and very small numbers are removed by welfare organizations. Given the relative insignificance of wildlife as a contributor of the problem, ORV baits are not used. Wild dogs are captured using specialized veterinary equipment, vaccinated and released.

The KZN project has proven to be extremely successful in reducing the prevalence of rabies. Animal and human case data dates back to 1979 when surveillance programmes were initiated. Animal and human cases steadily increased, peaking at 411 animal cases and 29 human deaths in 1995. Animal and human cases declined and remained steady at

roughly 200 animal cases and eight human deaths per annum from 1998 to 2007. There was a large spike in animal cases in 2007, which is due to increased surveillance efforts. The number of confirmed animal cases was 80 in 2013 with two reported cases per month for January and February of 2014. Human deaths have declined to 1 in all of 2013. The most recent death occurred in May of 2013 that was due to incorrect treatment at the clinic.

This study has several limitations. Much of the data obtained were not uniform, in that some data were broken down by district and year while other data were presented in aggregate form either for all districts or for all years. This restricted the depth of analysis, generally requiring a strict cross-sectional examination. Given the low number of observations and lack of uniform time series data, it is impossible to make reliable inferences as to the exact nature of the relationship between dog vaccination efforts and human treatment rates. The 3% exposure rate and 2–12% contraction rates used in the cost per life saved estimate may not reflect the situation in South Africa, although they were the only published estimates available at the time. Given the unique circumstances faced in the KZN project area, extrapolation of these findings, even to other South African provinces, should be avoided. Future studies related to canine rabies in South Africa could make use of additional data, which should enable a more complete assessment of both the costs and benefits of dog vaccination programmes.

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