

ORIGINAL ARTICLE

Towards Canine Rabies Elimination in South-Eastern Tanzania: Assessment of Health Economic Data

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Summary

An estimated 59 000 people die annually from rabies, keeping this zoonosis on the forefront of neglected diseases, especially in the developing world. Most deaths occur after being bitten by a rabid dog. Those exposed to a suspect rabid animal should receive appropriate post-exposure prophylaxis (PEP) or risk death. However, vaccination of dogs to control and eliminate canine rabies at the source has been implemented in many places around the world. Here, we analysed the vaccination and cost data for one such campaign in the area surrounding and including Dar es Salaam, Tanzania and estimated the cost per dog vaccinated. We also estimated the cost of human PEP. We found that the cost per dog vaccinated ranged from \$2.50 to \$22.49 across districts and phases, with the phase average ranging from \$7.30 to \$11.27. These figures were influenced by over purchase of vaccine in the early phases of the programme and the significant costs associated with purchasing equipment for a programme starting from scratch. The cost per human PEP course administered was approximately \$24.41, with the average patient receiving 2.5 of the recommended four vaccine doses per suspect bite. This study provides valuable financial insights into programme managers and policymakers working towards rabies elimination.

Introduction

Globally, the majority of human rabies deaths occur as a result of being bitten by an animal that is commonly owned and encountered by humans: dogs. An estimated 59 000 people die annually as a result of canine rabies (Hampson et al., 2015). Most victims are children in Asia and Africa (Knobel et al., 2005; WHO, 2013a, Hampson et al., 2015). The global cost of canine rabies has been estimated at \$8.6 billion in direct economic losses (Hampson et al., 2015) and \$120 billion USD in aggregate losses including both economic losses and the value of statistical life lost

(Anderson and Shwiff, 2013). Direct and indirect costs include human post-exposure prophylaxis (PEP), animal diagnostic 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 wound care, rabies vaccine administration and infiltration of rabies immune globulin (RIG). As the relationship between humans and dogs is the main epidemiological driver, the elimination of canine rabies is considered the major cost-effective approach to prevent human rabies (Zinsstag et al., 2009; Fitzpatrick et al., 2014).

In individual households, factors such as rabies awareness, vaccine accessibility, income and the nature of the relationship with their dogs influence animal vaccination status (Kaare et al., 2009; Davlin and VonVille, 2012). 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' (Santerre and Neun, 2012).

Unlike private individuals, governments and public stakeholder groups are expected to consider the total benefits 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 prevention and 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 surveillance 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 (Pastoret and Brochier, 1998; Schneider et al., 2007; Shwiff et al., 2008). Collective, inter-sectoral cooperative strategies are theoretically the most successful in eliminating canine rabies and reducing the associated financial burden (Bögel 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.

Rabies is enzootic in Tanzania, causing a range of estimated annual human deaths from 345 (Hampson et al., 2015) to 1499 (Cleaveland et al., 2002). Currently, there are only two large-scale rabies prevention and elimination projects in the country. The Carnivore Disease Project began with the Serengeti Vaccination Campaign during 2003, which has focused on annual canine vaccination against

rabies, among other diseases, to create a buffer zone surrounding Serengeti National Park (Cleaveland et al., 2003). In 2010, south-eastern (SE) Tanzania, together with two other sites (in South Africa and the Philippines), became a canine rabies vaccination demonstration site, supported by the Bill and Melinda Gates Foundation (BMGF). Outside these programmes, there are no ongoing state-supported mass vaccination efforts and intervention is limited to rabies outbreak management, with routine dog vaccinations being paid for by the owners. Human PEP is provided by the government at a subsidized price or free of charge and is available at state run bite clinics. Sambo et al. (2013) find that PEP was provided free of charge to less than 20% of bite victims within their study area, with the rest paying a subsidized cost of \$12 per dose for rural patients and \$8 per dose for urban patients.

Our objectives were to estimate the cost per animal vaccinated and the cost per human vaccine administered, utilizing data for the BMGF project collected during 2011–2013 by various Tanzania government agencies. We also identify the minimum number of human lives that must be saved for the programme to be determined cost effective according to WHO guidelines, as well as a potential cost per life saved. A health economic data assessment is a crucial component of disease management and is useful for several reasons. At a broad level, this analysis can guide management decisions by highlighting the potential costs of intervention strategies, especially when comparing this analysis to other such studies from other programmes.

Methods

As part of the BMGF project, animal vaccination efforts were administered in 24 districts in SE Tanzania, as well as the island of Pemba, over three phases from 2010 to 2014 (Fig. 1). The districts were chosen to, as much as possible, exploit natural boundaries to facilitate the maintenance of a rabies-free area. These boundaries included the eastern coastline, the western Udzungwa Mountains and the Ruvuma River to the south. These districts comprise a variety of cultural settings, including coastal, urban, agro-pastoral and pastoral. The project in Tanzania is unique from the other BMGF project sites in that it includes a large wildlife protected area (the Selous Game Reserve), allowing for the examination of the role of biodiverse wildlife areas as buffers against infection. The inclusion of the Island of Pemba also allows for the comparison of canine rabies dynamics in island settings (WHO, 2010). Phase 1 spanned from May 2010 to April 2011, Phase 2 from October 2011 to July 2012 and Phase 3 from April 2013 to July 2014. Human PEP administration data were collected over a period from 2011 to 2013.

Tanzania Canine Vaccination Project Areas

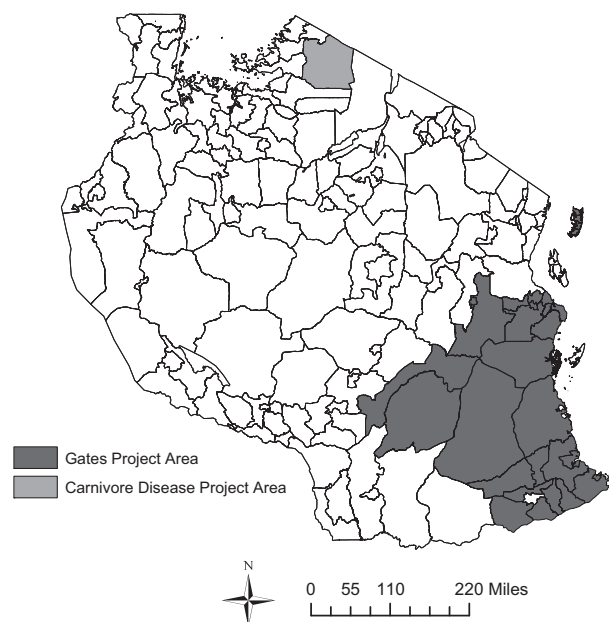


Fig. 1. Canine rabies vaccination programme areas.

Table 1. Parameters required to estimate animal and human vaccination administration and costs, their descriptions, and associated values and sources

Parameter	Definition	Value
Animal vaccine (V) ^{a,c}	Cost of all biologics used for animal vaccination campaigns	87 031
PEP (PEP) ^b	Cost of PEP vaccines and RIG	103 602
Consumables (C)	Cost of syringes, coolers and other equipment for biologics	
Animal campaign ^c		447 591
Human treatment ^b		214 529
Fixed assets (FA) ^a	Depreciated cost of all vehicles purchased for campaign use	220 382
Salaries (S)	Cost of salaries and other personnel costs	
Animal campaign ^a		701 156
Human treatment ^b		98 521
Awareness (AW) ^a	Cost of public notification efforts prior to vaccination campaign	43 371
Vehicles and transport (VT) ^a	Cost of vehicle maintenance, insurance and other transportation costs	89 714
Fuel (F)	Cost of fuel purchases for campaign efforts	
Animal campaign ^a		96 007
Human treatment ^b		66 330
Accommodation and supplies (AS) ^a	Cost of accommodation for staff and other supplies	24 592
Animals vaccinated (N_p) ^a	Total number of animals vaccinated	252 577
Vaccines administered (N_H) ^{b,d}	Total number of estimated human vaccines administered	23 546

^aMinistry of Livestock Development and Fisheries.

^bMinistry of Health and Social Welfare.

^cWorld Health Organization.

^dMobile Phone Survey.

The total cost (TC) of animal and human vaccination efforts for each phase is simply the sum of all cost components (see Table 1 for descriptions of each component) for each phase and was calculated using the following equations:

$$TC_{A,id} = V_{id} + C_{D,id} + FA_{id} + S_{A,id} + AW_{id} + VT_{id} + F_{A,id} + AS_{id}$$

$$TC_{H,id} = PEP_{id} + S_{H,id} + C_{H,id} + F_{H,id}$$

The cost per animal vaccinated and the cost per PEP administered are then defined as:

$$\text{Cost per animal vaccinated}_{id} = \frac{TC_{A,id}}{N_A}$$

$$\text{Cost per human vaccine administered}_{id} = \frac{TC_{H,id}}{N_H}$$

where N indicates the total number of either humans or animals vaccinated, the indexes A and H indicate the animal or human campaign costs, i indicates the campaign phase, and d indicates the district.

This economic analysis of the vaccination programme was requested by the BMGF after the programme was already implemented. This means that data were collected

Table 2. Proportion of total cost by component and phase for the animal vaccination campaign

Cost component	Phase 1	Phase 2	Phase 3	Total
Fuel	3.5%	5.7%	6.8%	5.6%
Vehicles and transport	5.2%	5.0%	4.8%	5.2%
Awareness	2.9%	2.3%	1.3%	2.5%
Accommodation and supplies	1.9%	1.1%	1.1%	1.4%
Salaries	38.3%	39.2%	40.3%	41.1%
Vaccine	5.9%	5.3%	5.4%	5.1%
Consumables	29.1%	28.6%	28.9%	26.1%
Fixed assets	13.1%	12.8%	11.3%	12.8%

after the fact from various sources, including the WHO Tanzania country office, the Tanzanian Ministry of Health and Social Welfare, the Tanzanian Ministry of Livestock, and a mobile phone surveillance programme (Table 2). Data collected from each source were verified by the authors to be unique to avoid duplication. All costs were converted from Tanzanian Shillings (TZS) to USD using average annual exchange rates from each phase. Exchange rates were as follows, 2010: 1563TZS/1USD; 2011: 1562 TZS/1 USD; 2012: 1583 TZS/1 USD; 2013: 1583 TZS/1 USD.

Animal vaccination, dose administration, estimated dog population records and animal vaccination administration costs were collected from the Tanzanian Ministry of Livestock Development and Fisheries which compiled the data over the course of the BMGF vaccination campaign (2010–2014). While initially this study was intended to only analyse dog vaccination efforts, a significant number of cats were also vaccinated under the campaign. Cats represented 15.5% of all animals vaccinated over the course of the campaign. For this reason, cats were included in the analysis. Animal vaccine and consumable cost data were collected from the WHO country office. Cost data for all components were available by phase and by district, while data for consumables was only available as an aggregate across districts for each phase. To assign this lump sum to each district, it was proportioned based on the number of animals vaccinated in each district (e.g. if 15% of all animals vaccinated in a certain phase were vaccinated in Ilala, then 15% of that phase's consumables cost would be assigned to that district). This allowed for a district-level cost estimate for each phase. A one-way analysis of variance (ANOVA) test is also performed to determine whether the observed costs per dog vaccinated across phases are statistically different.

Estimates for the total number of human vaccinations administered and the number of human vaccines distributed within each district over the period 2010–2014 were collected from the Tanzania Ministry of Health. Estimates on PEP schedule completion rates and the proportion of bite victims receiving RIG were obtained from a

mobile phone surveillance programme, recently established in Tanzania. The surveillance programme was implemented to improve distribution of PEP based on needs and to monitor mass animal vaccination campaign progress. Four primary health facilities from each district, a total of 112 health facilities, were given mobile phones and were encouraged to collect information on each bite victim (Mtema, 2013). Table 2 illustrates the sources used for each of the parameter values.

Using the average number of PEP vaccinations that patients received in each district, and dividing that number by the total number of vaccines distributed, less assumed wastage of 25%, the number of people given PEP was estimated. An assumed wastage of 25% is a rough average of estimates from the literature. For example, Salve et al. (2014) found that 20.8% of distributed PEP doses were wasted in rural Haryana, India. Similarly, Abbas et al. (2014) assumed a wastage rate of 30%, when estimating the costs of rabies control in Tamil Nadu, India. Estimated cases (bite victims) in this analysis are most likely lower than the actual number of cases in Tanzania. In Tanzania specifically, human rabies deaths have been estimated to be under-reported by a factor of 100 times or more (Cleveland et al., 2002). The island of Pemba is made up of four separate districts, but not all required data could be ascertained and was therefore excluded from the PEP analysis.

Not all persons bitten by suspect rabid animals die from rabies, for a variety of reasons, including the route of exposure and the severity of the bite. Therefore, estimation of the cost per human life saved requires information on the number of patients that received PEP that would have succumbed to rabies, had they not received prophylaxis. The most recently published data for such a parameter come from Hampson et al., 2015; which estimates that 34 240 patients receive PEP in Tanzania annually resulting in an estimated 4789 lives saved annually. These estimates indicate that approximately 13.9% (4789/34 240) of the patients receiving PEP in Tanzania would have died from rabies, had they not received prophylaxis. For simplicity, we assumed no PEP failure (100% patient survival), even if the full PEP series was not obtained. Applying this same probability to the number of patients receiving PEP during the BMGF project (7965), we calculated that the number of people who would have died from rabies over the study period to be 1107. The Hampson et al. (2015) estimates used to derive the 13.9% rate assumed an animal vaccination coverage level of 0.5% annually, far below what was achieved during this campaign. We assume that animal vaccination indirectly influences the number of human deaths by reducing the number of actual human exposures, and thus, the number of people who would have died without PEP. As the individual influence of each intervention cannot be distinguished, we include the cost of both PEP

and animal vaccination campaigns to calculate the cost per life saved. The total cost of PEP and animal vaccination for each district was divided by the estimated number of persons who would have developed rabies had they not received prophylaxis and had animal vaccination not occurred.

We identify the conditions under which this intervention could be considered cost effective by estimating the minimum number of human lives that must have been saved during the programme due to animal and human side interventions. Hampson et al. (2015), estimated that rabies causes 21 548 disability-adjusted life years (DALYs) and 345 deaths in Tanzania annually. This led to an estimate of approximately 62.46 DALYs per death. The WHO cost effectiveness guidelines state that health interventions are cost effective if the cost per DALY averted is less than three times the GDP per capita of the country, or very cost effective for a cost per DALY averted of less than one GDP per capita. The GDP per capita of Tanzania was US\$694.77 in 2013 (World Bank data). Dividing the total cost of the PEP administration campaign by US\$2084.31 (3X GDP per capita) yields the minimum number of DALYs that must be averted for the campaign to be considered at least cost effective. This number can then be divided by the above DALYs per death to find the minimum number of lives that must be saved. This exercise can be repeated using one GDP per capita for minimum values required for the programme to be very cost effective.

Results

The costs on which the analysis of cost per dog and cost per human PEP are given in Table 1.

Over the course of the three phases, an estimated 252 577 animals were vaccinated at a total cost of almost \$1.8 million. The overall cost per animal vaccinated fell from \$11.27 (95% CI \$9.38-\$13.16) during Phase 1, to \$8.24 (95% CI \$7.01-\$9.48) during Phase 2, and \$7.30 (95% CI \$5.95-\$8.66) during Phase 3. Using an ANOVA test, the costs per animal for each phase were determined to be statistically different at the 99% level (P -value = 0.0007). The cost per dog vaccinated over the whole programme was \$8.43. The over purchase of dog vaccines, of which 47% went unused in phase 1, and 16% in phase 2, led to increased purchase costs in those periods. Many of the unused vaccines from the previous two phases were still available during phase three, resulting in no new vaccine purchases needed for 16 of the vaccinated districts during phase 3. This resulted in an unused vaccine rate of 9.6% in phase 3 and reduced vaccine purchase costs (WHO, 2015a, b). Assuming an unused animal vaccine rate of 10%, the cost per animal vaccinated would have ranged from \$5.85 to \$7.66 for all three phases.

From 2011 to 2013, an estimated 9834 people sought PEP at bite centres receiving an estimated 23 546 vaccinations at a total cost of \$482 983. Over this period, the average cost per vaccination was \$24.41. These costs varied significantly by district, with cost per vaccination ranging from a low of \$12.68 in Morogoro Urban to a high of \$39.71 in Liwale. This variation is due primarily to the number of patients being treated as fixed costs were similar across districts. If the patient received the average number of vaccination doses (2.5), the total cost was \$61.78 and \$97.63 if the recommended four vaccination doses were administered. Clinical records indicated that less than 1% of bite victims received RIG. On average, of those who received the first vaccination of the series of four, 60.9% returned for the second, 53% for the third and 30.9% for the fourth.

A breakdown of the total cost of animal and human vaccination campaigns by component over their respective study periods is presented in Table 2 and Fig. 2. Personnel and staff costs were pro-rated to account for the estimated time spent on rabies-related work and were based on interviews conducted with personnel. Within the animal vaccination campaign, salaries represented the largest single contributor to total costs, followed by consumables. Vaccine accounted for only 5% of total cost. In PEP administration, consumables represented 44% of the total cost, followed by the purchase of vaccine and RIG.

The estimated cost per life saved by region ranged from a low of \$862 in Kibaha to a high of \$7859 in Lindi Rural, with an overall estimate for the entire project area of \$2819. The minimum number of lives saved needed to achieve at least WHO-defined cost-effective status was 4 and 11 to be considered very cost effective. This is assuming the cost of the PEP campaign alone. If we include the cost of animal vaccination administration as well, the minimum number

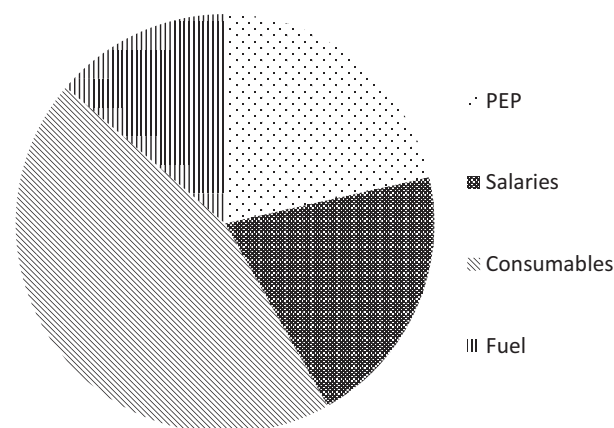


Fig. 2. Proportion of each cost component on the total cost of PEP administration, 2010–2013.

of lives saved needed for cost-effective status is 17 and 51 for very cost-effective status.

Discussion

Our analysis indicates that the cost of vaccinating animals under the BMGF campaign fell from \$11.27/animal during the first phase to \$7.30/animal during the third and final phase. At the outset of the project, preliminary estimates of the total dog population of the programme area, owned or otherwise, reached as high as 400 000. Throughout each phase of the vaccination campaign, improved dog population information was obtained leading to the preliminary estimate being revised downward (WHO, 2013b).

The observed costs per dog vaccinated in this analysis are higher than other estimates within Tanzania. Kaare et al. (2009) estimate a cost per dog vaccinated ranging from \$1.73 in agro-pastoral land to \$5.55 in pastoral communities. There are several possible reasons for this difference. Given the initial over estimation of the dog population, there was high vaccine over purchase in the first phase leading to higher overall cost per animal. This example of over-estimation highlights the ongoing challenge of estimating dog populations during canine rabies elimination projects. Often, when data are not available, the best method is trial and error through the vaccination campaign itself. The higher cost of animal vaccination could also stem from the fact that this project was the first government-led large-scale vaccination programme in Tanzania. This means that many of the required assets, such as the vehicles, had to be purchased for this campaign.

Cost per human vaccine administered was \$24.41, and average cost of a PEP course was \$62. The cost per life saved ranged from \$862 to \$7859 on average from 2011 to 2014. Comparing the relative costs of human PEP with dog vaccination provides insight into human- versus animal-focused intervention strategies. At the very least, it highlights the possible cost savings that could be achieved given the elimination of canine rabies and the subsequent reduction in human post-exposure treatment.

This analysis dealt exclusively with the direct costs of animal and human intervention. Indirect costs, however, do represent a significant burden in many cases in the form of travel, accommodation, lost work and other expenses. While these costs are important to understand, they were not considered, as the project did not perform surveys to obtain this data. Other studies indicate that the cost to the patient depends largely on whether they live in a rural or urban area, but can be more than \$100 USD for a complete PEP series (Sambo et al., 2013).

Tanzanian policy is to follow Center for Disease Control (CDC) guidelines, which recommends four vaccinations for each patient after rabies virus exposure (CDC,

2010). The RIG is administered only for category III contact according to WHO guidelines, which is defined as 'single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches' (WHO). Assuming that WHO guidelines were followed within the project area, 1% of all exposures (bite patients) were category III. The PEP schedule completion rates were relatively low for all districts over the study period with an average of 30.9% finishing the recommended (four dose) series. Given that rabies has a case fatality of almost 100%, completion of the PEP schedule, if there exists a risk of viral exposure, is important.

There are several possible explanations for this non-compliance, including PEP shortages, budget constraints associated with travel or loss of work, time constraints or a lack of education regarding the importance of schedule completion. In addition, if roughly 80% of bite victims are also required to pay some of the vaccine cost, as found in Sambo et al. (2013); this represents another financial burden that many may not be able to afford. Another reason would be that the offending animal was restrained, observed and found to be rabies-free over the observation period, although the mobile phone survey suggests that surveillance of this kind is almost non-existent in this area. Further, some health authorities in Tanzania only recommend a 3-dose PEP regimen. The compliance problem leaves open the possibility for research into the factors contributing to non-compliance, to motivate policy aimed at improving the completion rates. Incomplete or delayed PEP may still result in rabies in some cases, while complete and appropriate PEP in a timely manner is close to 100% effective, particularly if RIG is administered (Hampson et al., 2008).

During the Tanzania project, the reported number of human rabies has declined, and within the project area itself, reported rabies deaths dropped from 7 in 2010 to 1 in 2012, and 0 reported deaths in 2013. Reported data on human deaths during 2011 were unavailable. The number of reported human deaths during these years are most likely well under the actual number of human deaths due to rabies as under-reporting in Tanzania is an issue (Cleaveland et al., 2002). However, surveillance is far from consistent within and around the project area. The decline in human deaths in the project area compared to the surrounding areas could be due to the animal and human vaccination efforts, but could also be due to natural canine rabies cycles (Hampson et al., 2007). Clearly, surveillance inconsistencies could have some impact together with a number of other factors. The limited reporting data prevents a greater in depth analysis of the programme effectiveness. This illustrates the importance of accurate, consistent and robust surveillance efforts prior to, during and post-intervention. Reliable surveillance provides better

estimates as to the burden of the disease as well as the potential benefits stemming from the intervention. Understanding the dynamics of human and canine rabies pre- and post-intervention would lead to much better cost effectiveness estimates.

This analysis was limited by several factors. Data collection was compiled post facto from different organizations, meaning that the data collection did not always match, making direct comparison difficult. For example, annual comparisons between animal vaccination phases and human PEP administration were not possible, as phases spanned multiple years beginning and ending at different months of the year, while data were collected on an annual basis leaving aggregate analysis as the only comparison option. Much of the personnel cost estimates relied on interviews, creating the possibility for recall bias. These results reflect the nature and challenges of the vaccination programme specific to Tanzania and may not be applicable to other countries or regions. If collection of the relevant data had been planned and coordinated during the project itself, higher quality data and more robust conclusions would have been available.

This article provides insight into the potential costs of administering large-scale canine vaccination campaigns and human PEP administration in SE Tanzania. This project was the first government-led, large-scale canine vaccination in Tanzania. By understanding the costs of rabies elimination efforts and the factors that influence those costs, future campaigns in Tanzania and elsewhere may be able to mitigate critical public health challenges and improve the efficiency of efforts.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Total number of animals vaccinated under mass campaign efforts by district and phase.

Table S2. Total cost in USD\$ of animal vaccination efforts by district and phase.

Table S3. Estimated number of human bite cases, the number of vaccines distributed with the average number of vaccines administered per patient, and total cost in \$USD by district over the 4 year period.

Table S4. Total cost per animal vaccinated by district and phase in USD\$.

Table S5. Estimated cost per PEP treatment, cost per person who receives the average number of treatments, and the estimated cost per life saved by district over the 4 year period in USD\$.

Table S6. Dog vaccination coverage rate by district and phase.