TOWARDS ELIMINATION OF DOG MEDIATED HUMAN RABIES

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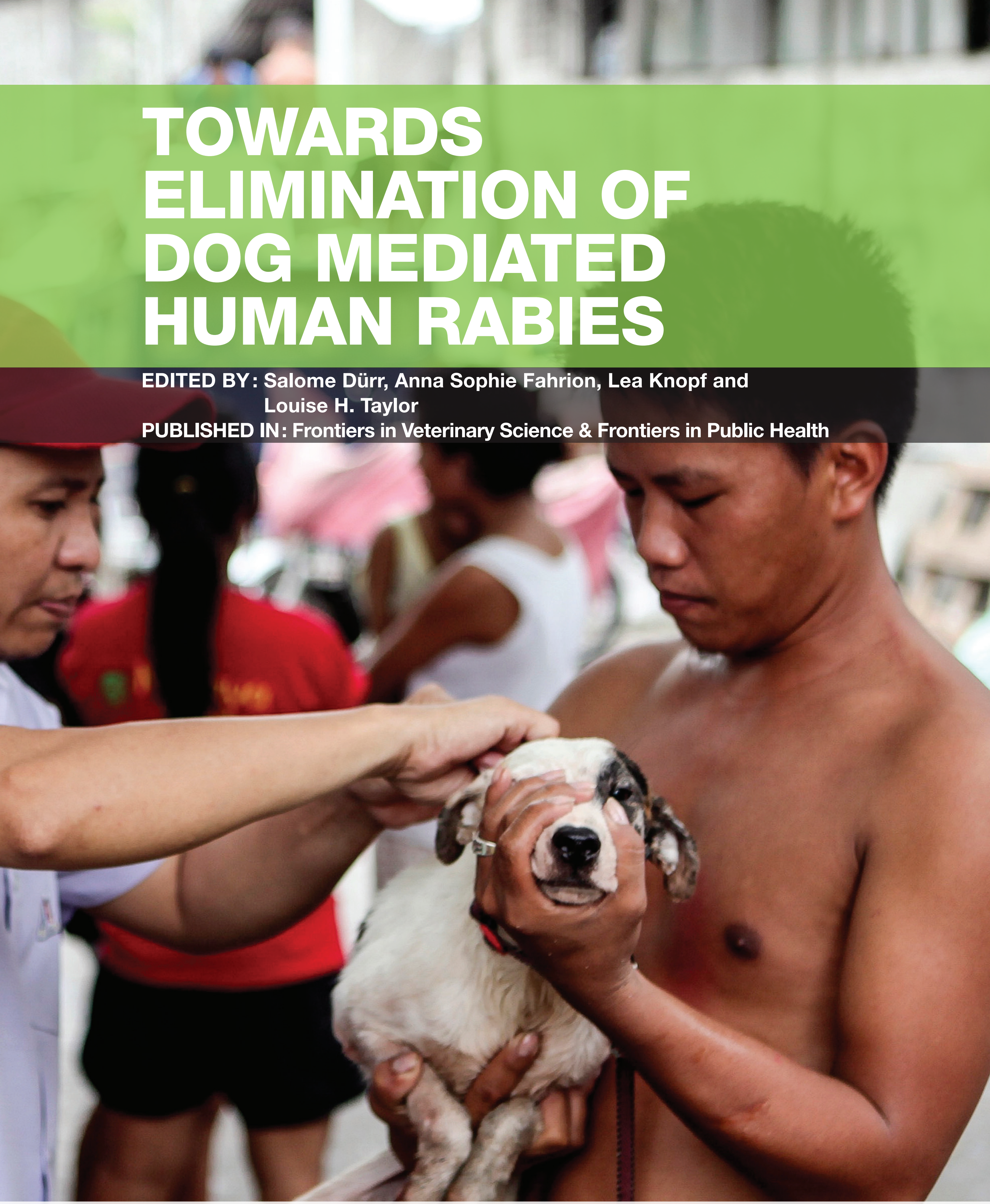

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TOWARDS ELIMINATION OF DOG MEDIATED HUMAN RABIES

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An owner has his dog vaccinated during a mass dog vaccination campaign in the neighbourhood of Payatas in Manila, Philippines.

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Rabies is an ancient zoonotic viral disease that still exerts a high impact on human and animal health. The disease is almost 100% fatal after clinical signs appear, and it kills tens of thousands of people per year worldwide, particularly in Africa and many parts of Asia. Although the disease in humans can be prevented by timely post-exposure prophylaxis, its access and affordability is limited in rabies endemic countries. With 99% of infections in humans caused by rabid domestic dog bites, controlling the infection in this reservoir population has been proven to be most effective to reduce and eliminate human rabies cases. In this context, this Research Topic invited contributions on the control and elimination of dog mediated human rabies. Publications on epidemiological, educational, policy-related and economic aspects of dog and human rabies surveillance, implementation of control in dogs and humans and scientific documentation of success stories were consolidated. We hope that these articles contribute to reaching the ambitious goal, set by key players in global health, of the elimination of dog mediated human rabies by 2030.

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EDITORIAL
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Editorial: Towards Elimination of Dog Mediated Human Rabies

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Editorial on the Research Topic

Towards Elimination of Dog Mediated Human Rabies

Rabies is a zoonotic viral disease with a high impact on human and animal health. The disease is almost 100% fatal after clinical signs appear and kills tens of thousands of people per year worldwide. About 99% of infections in humans are caused by rabid domestic dog bites. Human disease is related to poverty, with the highest burden in Asian and African low-income settings. Along with the group of neglected tropical diseases, increasingly recognized by high-level global health policy as indicators of functionality of health systems, rabies is scheduled for potential elimination as part of the UN sustainable development goals. In late 2015, the international rabies community, represented by more than 100 (mostly rabies endemic) countries, set a global target of eliminating human rabies mediated by dogs by 2030. Despite this momentum, rabies has received relatively less international attention compared with some of the other NTDs as of yet.

In this research topic, 123 authors contributed 15 articles (9 original research articles, 4 perspective pieces, and 2 reviews) from different regions in the world (4 from Australasia, 5 from Africa, 1 from Latin America, 4 global, and 1 theoretical) discussing various aspects of working towards the achievement of this goal. The collection brings together the experience and lessons learned from rabies control programs small and large, research aimed at improving the design and cost-effectiveness of rabies control programs, and analysis of the resources needed to expand rabies control efforts.

Our understanding of rabies control is sufficient, and the key tools are available to eliminate the disease. However, an overview by Fahrion et al. highlights the challenges and barriers to successfully *implementing* sustainable control of the disease. This article sets the scene for the whole collection, by discussing not just the gaps but also possible solutions for the socio-political, organizational, technical, and resource-linked issues that are being addressed by many different stakeholders. It highlights the need for applied research, a feature that has been taken up by most of the articles of this research topic.

Evidence that rabies can be locally eliminated has been built in recent years in a variety of settings, demonstrated here by Byrnes et al., Valenzuela et al., and Mpolya et al., describing successful state-wide programmes in Sikkim, India, Ilocos Norte, Philippines, and Southeast Tanzania and Pemba Island. All the programs were implemented by the government, in collaboration with one or more organizations, such as NGOs, WHO, OIE, national and international research institutes, and private foundations. Mass rabies vaccination in dogs and promotion of post-exposure prophylaxis (PEP) in humans were the common interventions, supported by dog population management (Byrnes et al.) and promotion of surveillance (Valenzuela et al.; Mpolya et al.), including the use of innovative methods such as mobile phone tools (Mpolya et al.), and the transition to intradermal PEP delivery (Mpolya et al.). Two facts were highlighted in all case studies, namely, the importance of a One Health approach demanding involvement of stakeholders from the veterinary and public health sectors

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and the challenge of sustaining progress in areas situated amidst rabies endemic areas.

From all projects there are lessons to be learned that can be used to support efforts elsewhere. This is particularly true for the coordinated approach to rabies control programs across Latin America and Caribbean (LAC), described by Del Rio Vilas et al., whose lessons derived are highly relevant to large-scale regional elimination goals. Although the target to eliminate rabies from LAC had to be reset four times since the implementation of the program in 1983 (it is currently set to 2022), a massive reduction of the human and animal rabies cases to (almost) 0 in most of the LAC countries has been achieved. One of the key messages is the need for adapted regional and national strategies to recognize that countries can vary enormously in their capacities.

Long-term intensive programs are required to achieve sustainable elimination and ensure that the reduction of cases is not followed by a resurgence of the incidence. The example from Morocco described by Darkaoui et al. demonstrates how inadequate implementation of the law, slack requests for responsibility from dog owners, and weak collaboration between Ministries impeded success in controlling rabies. Arief et al. also highlight the need for sustained control efforts in Bali, Indonesia, where dramatic reduction of rabies cases were achieved, but resurgence of disease has shown that elimination was still not possible.

What are the knowledge and action gaps that need to be addressed to implement sustainable rabies control programs at small and large scales? Concrete examples are addressed in articles of this research topic:

- The availability of high-quality surveillance data to support control efforts is absolutely vital. Unified reporting platforms have to be established (such as the epidemiological rabies bulletin for Africa proposed by Scott et al.) and sustainable community engagement has to be ensured for effective surveillance (Brookes et al.). The latter can only be achieved by the use of culturally adapted communication pathways.
- For concrete planning of control programs, detailed questions must be answered. For example, which subpopulation of dogs should be targeted in specific environments to reach the overall goal of elimination of rabies from the population? Theoretical modeling approaches can be used to answer such questions. In their setting, Leung and Davis identified the free-roaming owned dogs to be the most critical population to be vaccinated. Arief et al. conducted an observational study and identified puppies and dogs living in rural areas as having a higher risk of being unvaccinated, thus the focus should be set on these populations. Taylor et al. provide a comprehensive overview in their review on dog population management, an intervention for which evidence of its benefits with regards to rabies control is still lacking. The authors advocate for cost-effectiveness studies for dog population management and suggested that safe, effective, cheap, and injectable contraceptives for females should be a research priority to benefit management of dog populations.
- The important job of assessing the vaccination coverages achieved in free-roaming dogs is often neglected. Sambo et al. found that transect studies (counting vaccinated and unvaccinated dogs in the streets) soon after the campaign is cheap, quick, and provides good results. It is, therefore, more appropriate for routine monitoring of mass vaccination campaigns than household or school-based surveys.
- Not only in relation to rabies, but any control program, cost-effectiveness and identification of funding needs and options are crucial to ensure sustainability. Mindekem et al. found that a strategy that combines canine vaccination with the provision of PEP is more cost-effective in the long term than relying on PEP alone, particularly when communication across the human and veterinary health sectors is guaranteed to minimize unnecessary PEP application. Wallace et al. evaluated funding and capacity needs to reach the elimination of canine rabies globally and identified cheaper vaccine and increased efficiencies in vaccine delivery and application as ways to reduce these projected costs, but predicted that complementary dog population management interventions would markedly increase costs. Innovative financing mechanisms are needed to secure sufficient financial support, which is frequently a stumbling block to ensure that comprehensive vaccination plans can move forwards. Welburn et al. consider whether Development Impact Bonds could help to fill this funding gap. Such a finance model would enable investors taking on the risk of program delivery to ensure stricter management of implementation.

It is noteworthy that almost all contributions highlighted the need for an intersectoral approach involving all stakeholders, including the engagement of the communities. A One Health approach along the path to disease elimination (from resource allocation, to raising awareness, surveillance, implementation of control interventions, and eventual elimination) is a crucial requirement to realize the goal of 2030. To borrow words from Wallace et al., this research topic "hopes to stimulate and inform the necessary discussion on global and regional strategic planning, resource mobilization, and continuous execution of rabies virus elimination" that will be necessary to eliminate human-mediated canine rabies by 2030—a target that should not be reset.

AUTHOR CONTRIBUTIONS

All the authors were involved in writing the article and in editing contributions to this research topic. They all agree to the final version of this article.

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PERSPECTIVE
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The Road to Dog Rabies Control and Elimination—What Keeps Us from Moving Faster?

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Rabies, a vaccine preventable neglected tropical disease, still claims an estimated 35,000–60,000 human lives annually. The international community, with more than 100 endemic countries, has set a global target of 0 human deaths from dog-transmitted rabies by 2030. While it has been proven in several countries and regions that elimination of rabies as a public health problem is feasible and tools are available, rabies deaths globally have not yet been prevented effectively. While there has been extensive rabies research, specific areas of implementation for control and elimination have not been sufficiently addressed. This article highlights some of the commonest perceived barriers for countries to implementing rabies control and elimination programs and discusses possible solutions for sociopolitical, organizational, technical, and resource-linked requirements, following the pillars of the global framework for the elimination of dog-mediated human rabies adopted at the global rabies meeting in December 2015.

Keywords: rabies, dog rabies, neglected tropical diseases, zero human deaths, global framework, implementation

BACKGROUND

During the past decade, neglected tropical diseases (NTDs) have gained more recognition on the global health and development agendas (1–3). The transition from the Millennium Development Goals to the Sustainable Development Goals has renewed emphasis on ending the inequality that has deprived neglected communities from access to effective and affordable health care (Goal 3.8) and includes a specific goal to end NTDs by 2030 (Goal 3.3) (4).

Rabies, a viral disease categorized by the World Health Organization (WHO) as a NTD, kills tens of thousands of people every year, mostly among underserved populations in Africa and Asia; more than 95% of human rabies deaths result from the bites of infected dogs (5, 6). While the disease is almost 100% fatal, effective human and dog vaccines to prevent rabies are available. Elimination of dog-transmitted rabies as a public health problem is feasible (7, 8) by vaccinating dogs and providing post-exposure prophylaxis (PEP) to humans until dog rabies is eliminated (5).

Elimination of canine rabies is integral to the WHO–OIE[1]–FAO[2] tripartite collaboration, which works at the animal–human–ecosystems interface (9, 10). A joint global meeting (Geneva, December 2015) marked a milestone at which human and animal health sectors agreed a framework to eliminate canine rabies with the vision of ending dog-mediated human rabies by 2030 (8) (**Figure 1**). All 180 Member countries of the OIE affirmed this commitment in Resolution N.26 adopted by the World Assembly of Delegates of the OIE in May 2016.[3]

Rabies is widely recognized as a public health threat that warrants prioritization of control efforts in Asia (11–13), Africa (14), and among the least developed nations globally (15). Health leaders are increasingly aware that this fatal disease could be eliminated as a public health problem cost effectively in a relatively short time (7, 16), yet rabies remains neglected and progress remains slow.

While there has been extensive research on the rabies virus, a comparative lack of operational research has led to knowledge gaps in how to design and implement control and elimination programs where they are needed most (11, 17) and calls for a "science of rabies elimination" (18). What barriers remain to coordinated efforts within and among countries? What is needed to transform the increased public and political awareness into real progress on the ground? And ultimately, what is needed to translate existing knowledge into success against rabies in a country? This paper discusses aspects of the "science to policy gap," (perceived) barriers to progress and possible solutions (**Table 1**). It is structured according to the pillars of the Global framework for the elimination of dog-mediated human rabies (**Figure 1**), namely, sociocultural, technical, organization, political, and resources, reflecting a coordinated approach.

[1] World Organization for Animal Health.
[2] Food and Agriculture Organization of the United Nations.
[3] http://www.oie.int/fileadmin/Home/eng/About_us/docs/pdf/Session/2016/A_RESO_2016_public.pdf.

OVERCOMING BARRIERS TO RABIES ELIMINATION

Political or Sociocultural—Raising Public Awareness and Political Will

Making the Burden Visible, Demonstrating Impact

Prioritization of a disease is brought about through increasing public awareness and political will (19). One of the most important

FIGURE 1 | **Global framework for the elimination of dog-mediated human rabies**.

TABLE 1 | Key areas for improvement, necessary actions, and the stakeholders required to take action to support programmatic success for canine rabies elimination.

Pillar	Action	By who	Main target audiences/beneficiaries
POTENTIAL BARRIER: LACK OF AWARENESS AND PRIORITIZATION			
Political	Demonstrate the burden and impact	Epidemiologists, public health and veterinary services, program managers, international organizations[a]	Government policy makers, global health funders
Political	Declare the disease notifiable	Government lawmakers, World Health Organization (WHO), OIE	Health and veterinary professionals
Political	Implement adequate surveillance in both humans and animals	Policy makers, public health and veterinary authorities	Local authorities, health and veterinary professionals
Sociocultural	Build awareness of the risks and prevention methods	All stakeholders, but especially: health educators, media, program managers, international organizations[a]	General public, particularly children
Sociocultural	Build community engagement and responsible dog ownership	Policy makers, health communicators, communities, NGOs	Communities/general public, dog owners
POTENTIAL BARRIER: LACK OF NECESSARY GUIDANCE AT REGIONAL AND NATIONAL LEVEL			
Organizational	Plan effective interventions	Program managers with support of international organizations[a] and experienced countries with successful programs as examples	National implementation authorities
Organizational	Enable intersectoral collaboration at local and national levels	All relevant government sectors, NGOs and private partners, international organizations[a]	Program managers and health-care providers
Organizational	Regional collaboration	Regional networks and (economic) associations, direct country partnerships, international organizations[a]	Program managers
POTENTIAL BARRIER: CUMBERSOME METHODOLOGIES			
Technical	Simplify rabies diagnosis for surveillance	Researchers, test developers and producers	National and regional laboratory and surveillance personnel
Technical	Simplify access to vaccine	(Regional or national) responsibilities for procurement mechanisms, OIE and WHO vaccine banks	Government policy makers, global health funders, Program managers
Technical	Simplify vaccine regimen and delivery	Researchers, expert groups developing recommendations[b] and guidelines, logisticians	Health authorities, community health providers
Technical	Improve effectiveness of vaccination strategies	Program managers, epidemiologists/researchers	Program implementers
Technical	Assess and implement control and management of dog movement	Policy makers, veterinary authorities, researchers	Local authorities, dog owners
POTENTIAL BARRIER: INADEQUATE FUNDING			
Resources	Ensure adequate resources for a program	Governments and international and bilateral funding agencies [including (international) funding agencies, foundations, private donors/investors, etc.]	Government and local policy makers, global health funders, program managers
Resources	Build necessary capacity and expertise for sustained control	National capacity building agencies, international organizations[a]	Government health departments, local authorities, medical and veterinary officers
Resources	Build a business plan for global rabies elimination	WHO, OIE, FAO, GARC	Government policy makers, (global) health funders, program managers

[a]"International organizations" refers primarily to the FAO/OIE/WHO tripartite and global NGOs such as Global Alliance for Rabies Control (GARC). But these roles and principles are equally valid for other organizations working in rabies or zoonosis control.
[b]A WHO Strategic Advisory Group of Experts on Immunization (SAGE) working group on rabies vaccines and rabies immunoglobulins was established in 2016 and is currently reviewing the scientific evidence and relevant programmatic considerations on the use and scheduling of these. The proposed recommendations resulting from this work will be considered by SAGE during its October 2017 meeting.

means of convincing policy makers to prioritize a disease and invest resources is to demonstrate its impact on public health and the economy and the potential benefit of targeting the disease.

High-quality surveillance data are needed, but human rabies deaths are commonly underreported 100-fold (20–22), and the absence of data and solid evidence for estimates induces a cycle of neglect (23). Conversely, the onset of a control program that delivers better surveillance data is a precondition to increased awareness. Where quantitative assessments have been attempted, rabies has been ranked consistently among the top five zoonotic diseases, for example, in India (12), Mongolia (13), Jordan (24), Ethiopia (25), Myanmar (26), and Kenya (27).

Declaring a disease notifiable is crucial to establish functional reporting (28), and monitoring and surveillance of the disease should, therefore, be a central element of every rabies program. Rabies is also included in the OIE list of notifiable diseases.[4] Disease surveillance starts at the community level, where awareness about the disease needs to be complemented by clear guidance on reporting to the authorities, ideally integrated into the wider national health information and statistics systems. Pathways

[4]http://www.oie.int/en/international-standard-setting/terrestrial-code/access-online/.

must be included for transmission of data from the community level to the national level and to the OIE and WHO, resulting in feedback and action to keep individuals along the reporting chain informed and engaged. To ensure that data are comparable and informative, indicators should be well-defined and measurable. Novel technology such as notification *via* cell phones could be further explored (29).

Creating Public Awareness

Rabies burdens individuals, families, societies, and economies (6). As communities become aware of this threat, political pressure to act will accumulate. Building awareness and education about how to avoid and treat rabies exposures is, therefore, crucial in mobilizing a country to eliminate rabies. Champions at all levels (community to national) are central to this effort as they directly advocate and educate communities (7). World Rabies Day, recognized by the United Nations and commemorated every year on 28th September, celebrated its 10th anniversary in 2016 with 302 events in 57 countries (as of December 21, 2016). This annual awareness-raising event has shown a remarkable upwards trend since its inception and is an example of the dedication of innumerable people worldwide (30, 31).

Building an Engaged Society

An integral part of a regional or national plan is to build a proactive society that is fully engaged in the dog rabies elimination efforts of the country. Awareness of rabies at the community level alone is not enough to increase pressure on governments to improve their control efforts. Besides well-informed general public and responsible pet owners, committed, supportive policy makers are needed who will cohesively support national efforts to achieve and maintain freedom from rabies. Currently, most efforts to raise public awareness focus on promoting rabies information, which may not translate into the desired behavior, practices, and actions. Thus, it is important to invest in a national communication strategy and in impact monitoring that use the science of behavioral change and consider the diverse behavioral drivers, incentives, motivations, and larger sociocultural context of the target audience.

An example of behavioral change necessary for rabies control is that owners accept responsibility for their dogs and any offspring they may produce. This includes protecting dogs from rabies through vaccination and from unwanted reproduction. The promotion of such responsible dog ownership can be achieved only through a combination of adequate legislation, public awareness, and education, recognizing cultural and economic conditions. Public health and veterinary authorities, animal welfare organizations, and private veterinarians should work together to establish and maintain responsible dog ownership programs especially in communities at risk.

Organizational—Establishing Necessary Policies and Guidance

Effective Planning of Elimination Programs

National authorities are responsible for developing national strategies and implementing programs but they are frequently overwhelmed by multiple human and animal disease priorities and the challenges associated with programs stretched across sectors and administrative levels. It may be difficult to know where to start and what is needed—a potential barrier. Guidance for developing and monitoring control and elimination programs is, however, freely available. For example, the Stepwise Approach toward Rabies Elimination, which is embedded in the rabies blueprint,[5] follows the principles of enhancing intersectoral collaboration. This guidance has been used by countries across three continents, mostly at national or regional stakeholder consultations, to kick-start coordinated rabies control (32). Likewise, the rabies surveillance blueprint[6] provides guidance for planning of surveillance in particular. Knowledge about these tools needs to be disseminated and promoted more widely.

Intersectoral Collaboration

While the incremental benefits of a One Health approach for rabies control are established at the highest international level, its operationalization at national or local levels remains a challenge. Administrative and management structures may need to be harmonized across sectors according to different ministries and budget lines and coordinated with stakeholders from the private sector (33). National stakeholder consultations that convene all actors across ministries, local and national levels as well as the private and public sectors, however, have proven excellent platforms from which to build connections and trust and from where operational barriers and constraints to effective collaboration in rabies prevention as well as possible solutions can be explored. The outcome of these consultations is the drafting of integrated, multidisciplinary rabies action plans (34). For example, coordination at the national level can pave the way for integrated management of bite cases at the local level, jointly involving human and animal professionals to ensure reporting of bite and rabies incidents, proper risk assessments, and a coordinated response while at the same time sharing logistic resources (35, 36). Close involvement of social sciences, the education sector, and municipalities is now equally recognized, for example, as a powerful method for preventing dog bites in children, increasing knowledge and awareness about rabies, and in sustainably managing dog populations in affected communities (36).

Sharing and Comparing: Transparency and Regional Collaboration

International cooperation and coordination in planning, implementing, and evaluating rabies control programs at all levels is crucial for success and cost effectiveness (5). As canine rabies is a transboundary disease, collaboration, cooperation, and transparency between countries can provide new insights for tackling the disease. Authorities often perceive admitting public health problems as failure and prefer not to address endemic rabies at international level, thereby missing an opportunity to share information. Establishing contacts between public health and veterinary authorities of neighboring regions and countries and

[5]http://caninerabiesblueprint.org/.
[6]http://rabiessurveillanceblueprint.org/.

frequently exchanging information and data can be a first step toward building trust and more regular bilateral or multilateral interaction. WHO collaborating centers, OIE, and FAO reference laboratories and other organizations can help countries to share, compare, and learn from each other's experience (5, 37). Participation at international disease conferences can also attract more international attention at a political level.

A regional approach has been fundamentally important for the effective control of rabies in Western Europe (5) and, more recently, Latin America (38). Rabies control program managers from across Latin America and the Caribbean meet at meetings facilitated by the Pan American Health Organization (REDIPRA) and the large scale, parallel declines in dog and human rabies achieved are striking (39). In Asia, the Association of Southeast Asian Nations launched a joint Rabies Elimination Strategy that encapsulates a regional approach in 2015.[7] The Middle Eastern, Eastern Europe, Central Asia, and North Africa Rabies Experts Bureau has held meetings since 2010 (40) and has called for a strong regional initiative with high level political support (41). In sub-Saharan Africa, the Pan-African Rabies Control Network was created in 2015 and shows promise as a suitable platform to drive a regional approach to rabies control (37). Such regional approaches will be vital to implementing the global strategic framework to eliminate dog-mediated rabies and will, therefore, require further extension with strong participation and political support from all countries for success.

Technical—Ensuring Necessary Technology and Knowledge

Diagnostics

Diagnostic tests confirm animal rabies cases, allowing better PEP decision-making and monitoring the progress of control efforts. The reference, fluorescent antibody test, is not practicable in many endemic settings due to costs and enhanced laboratory requirements. Thus, alternative tools using less specialized equipment, such as Direct Rapid Immunohistochemical Test (42) and lateral flow devices (43), could play an important role provided further validation and quality approval.

Predicting the Need for Vaccine: Forecasting

Manufacturing cycles of both human and animal rabies vaccines require several years of appropriate forecasting by countries in order to supply the actual need. An absence of accurate data impairs forecasting and thereby resource allocation. The veterinary services of endemic countries often have insufficient knowledge of dog population size or ecology and human health services lack accurate data on bite case exposures. Both sectors thus suffer from procurement delays or stock shortages, which can result in less effective control of the disease and may force countries to turn to manufacturers selling vaccines that are overly expensive or may not meet international quality standards (44). Vaccine banks or stockpiles at regional levels as managed by OIE or WHO have become a solid mechanism for countries to maintain the supply of quality-assured vaccines and allow manufacturers to forecast and stabilize their production over years with lowered pricing through bulk purchase (45). Moreover, vaccine banks have contributed demonstrably to the scaling up and maintenance of local, national, or sub-regional programs in Asia and Africa (46) and incentivized recipient countries to increase data collection, as reporting on vaccine use and results is required. The opportunity of a potential investment from GAVI (the Vaccine Alliance) into human rabies vaccine from 2018 onward (47) could substantially facilitate low-income countries' access to affordable rabies vaccine and stimulate the necessary political will to tackle human rabies at a large scale.

Getting the Vaccines to the Community

Despite the encouraging improvements observed in the field of universal health coverage, poor accessibility to and affordability of PEP [particularly of rabies immunoglobulin (RIG)] remain in most rabies-endemic countries (48). Certainly, progress has been made, for example, on shortening PEP regimens (fewer health facility visits) and countries changing their policy to cost-saving intradermal administration of rabies vaccines as recommended by WHO (49). There is hope that new technologies currently under evaluation by WHO (thermostable rabies vaccine, monoclonal antibodies as an alternative to human and equine RIG) will facilitate cost-effective delivery of PEP as well as dog vaccine to where it is needed. The long needed scale up and adaption of mechanisms for supply and distribution of PEP has received a global push through discussions around a potential GAVI investment.

More Tailored Dog Vaccination Strategies

Rabies is integrally linked to the ways people live with their dogs. Its control requires an adequate understanding of the dog ecology and dog-keeping practices in a country in locally differing sociocultural contexts (e.g., urban vs rural, among different economic, religious, or ethnic groups). Factors that can profoundly affect rabies transmission and control are usually not sufficiently understood to design the most appropriate control strategy, and as a result, efforts and resources can be wasted. In most circumstances, almost all dogs can be handled and vaccinated by the parenteral route (50). In rare cases, however, dogs may not be accessible to parenteral vaccination, thus jeopardizing the coverage of vaccination campaigns. Improved dog capture and vaccination techniques, as shown through the establishment of rabies A-teams by FAO in Bali, can assist with reaching dogs that are difficult to capture and handle.[8] Oral dog vaccination using a hand-out model may be used effectively to immunize those inaccessible dogs while ensuring the safety of the vaccinators, the community, and non-target species. The best feasible solution for long-lasting marking of vaccinated dogs should be decided on during planning of campaigns (51).

The lack in dog movement control has been attributed as responsible for rabies spread in endemic areas and incursion in previously free countries or regions. Vaccinating at least 70% of

[7] http://vncdc.gov.vn/files/article_attachment/2015/3/endorsed-ares-final.pdf.

[8] http://www.fao.org/indonesia/news/detail-events/en/c/411271/.

animals in order to eliminate rabies from a free-roaming dog population is a widely acknowledged recommendation (8). However, empirical work [e.g., on area-specific basic reproductive ratio (R_0) (52)] suggests that different settings probably require different vaccination strategies and coverages to control rabies successfully. High vaccination coverage in high-risk areas may be more crucial than medium coverage across the whole country, but clear guidance on this is lacking. Better knowledge of area/country specific factors related to dog-keeping practices, dog population turnover, and contact rates between dogs and wildlife can help in determining a more flexible, realistic required dog vaccination coverage. This can help to optimize resource allocation (53, 54) and define the most appropriate vaccination strategies and financing (55), the best vaccination campaign frequency (52), and how to target vaccination to the highest risk areas and segments of the dog population.

Making Resources Available

As for any public health program, sustainable funding sources are a precondition to starting a rabies control program, and the absence of those sources is one of the main barriers. There are ways, however, to reduce the investments necessary for rabies control and to integrate rabies into existing streams of work and financing.

Recognizing rabies control as a public good and thus as the responsibility of national governments is key to a sustainable rabies elimination effort. Donor contributions should be structured so as to be catalytic to the establishment of the program, and long-term dependence on donor support should be avoided through a well-planned strategy for donor exit.

In most rabies-endemic countries, human PEP and vaccinating animals against rabies remain an "out-of-pocket" market. As they build on their commitments to universal health coverage and the sustainable development goals (56), governments need to step up their funding and integrate rabies control into sustainable health plans, ensuring dog vaccination, and PEP are available at the primary health-care level. Costs can be substantially decreased by using the intradermal route for human vaccines and tailoring dog vaccination to local circumstances (see above). Rabies surveillance and control in dogs should be integrated into existing infectious diseases reporting mechanisms and vaccination programs, requiring also more integration of funding streams. For example, in the Philippines, the ministry of health invests in dog vaccination as a public health measure, creating a leverage effect (57). Innovative mechanisms for financing and cost sharing can help to make vaccine purchase more affordable. To support funding bodies in planning and costing, WHO is currently developing in collaboration with FAO, OIE, and the Global Alliance for Rabies Control, a comprehensive business plan that encompasses both human and animal perspectives for achieving the 2030 target. In the longer term, investing in rabies prevention and control is cost-efficient, saving both lives and money (16, 58). It is possible to start small and then unlock more investment by demonstrating value.

Capacity building is an investment in human resources with crucial importance for the sustainability of a project. Parallel to the technical efforts made by the country, plans to build related capacity through training, professional development, and/or continuing education will ensure quality at implementation and ensure future sustainability. This contribution to health systems' strengthening can be a legacy that rabies control efforts leave to a nation.

CONCLUSION

This paper describes some of the main technical, organizational, and political challenges that countries encounter when implementing measures to control and eliminate rabies. However, there are solutions to many of these perceived barriers and opportunities to fill existing gaps. As summarized in **Table 1**, health officials, program managers, donors/investors, and all those involved in development of strategies should be aware of those applicable to their local, national, and regional contexts as early as possible, to make coordinated, informed decisions and successfully fight this devastating disease.

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BA-R, LT, and AF prepared the initial concept for this paper. All the authors contributed equally to the further development of the content, delivered specific paragraphs for the paper from their area of expertise, and reviewed and complemented the manuscript. AF coordinated and collated the coauthor's input.

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REFERENCES

1. WHO. *Working to Overcome the Global Impact of Neglected Tropical Diseases. First WHO Report on Neglected Tropical Diseases*. Geneva: WHO (2010).
2. *Uniting to Combat Neglected Tropical Diseases. London Declaration on Neglected Tropical Diseases* (2012). Available from: http://unitingtocombatntds.org/london-declaration
3. WHO. *WHA66.12 Sixty-Sixth World Health Assembly Resolution on Neglected Tropical Diseases 2013* (2013). Available from: http://www.who.int/neglected_diseases/mediacentre/WHA_66.12_Eng.pdf
4. *United Nations. Sustainable Development Knowledge Platform: Goal 3 2015* (2015). Available from: https://sustainabledevelopment.un.org/sdg3
5. WHO. *WHO Expert Consultation on Rabies, Second Report*. Geneva: World Health Organization (2013).

6. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
7. WHO. *Rabies: Rationale for Investing in the Global Elimination of Dog-Mediated Human Rabies*. Geneva: World Health Organization (2015).
8. WHO, OIE. Global elimination of dog-mediated human rabies: the time is now! *Report of the Rabies Global Conference 10-11 December 2015, Geneva, Switzerland*. Paris: World Health Organization and World Organisation for Animal Health (2016). p. 27. Available from: http://apps.who.int/iris/bitstream/10665/204621/1/WHO_HTM_NTD_NZD_2016.02_eng.pdf?ua=1
9. OIE. Forum: rabies is a tripartite (WHO-OIE-FAO) priority – collaboration between animal and human health sectors. *Bulletin de lOIE* (2014) 3:3–4.
10. FAO/OIE/WHO. *The FAO-OIE-WHO Collaboration. Sharing Responsibilities and Coordinating Global Activities to Address Health Risks at the Animal-Human-Ecosystems Interfaces. A Tripartite Concept Note*. Hanoi: FAO/OIE/WHO (2010).
11. Abbas SS, Kakkar M. Rabies control in India: a need to close the gap between research and policy. *Bull World Health Organ* (2015) 93(2):131–2. doi:10.2471/BLT.14.140723
12. Sekar N, Shah NK, Abbas SS, Kakkar M; Roadmap to Combat Zoonoses in India Initiative. Research options for controlling zoonotic disease in India, 2010-2015. *PLoS One* (2011) 6:e17120. doi:10.1371/journal.pone.0017120
13. McFadden AM, Muellner P, Baljinnyam Z, Vink D, Wilson N. Use of multicriteria risk ranking of zoonotic diseases in a developing country: case study of Mongolia. *Zoonoses Public Health* (2016) 63:138–51. doi:10.1111/zph.12214
14. Grace D, Songe M, Knight-Jones T. Impact of neglected diseases on animal productivity and public health in Africa. *21st Conference of the OIE Regional Commission for Africa 16th-20th February*. Rabat, Morocco (2015).
15. GAVI. *Rabies Vaccine Investment Strategy Background document #44*. Geneva: GAVI (2013).
16. Shwiff S, Hampson K, Anderson A. Potential economic benefits of eliminating canine rabies. *Antiviral Res* (2013) 98(2):352–6. doi:10.1016/j.antiviral.2013.03.004
17. Yin W, Dong J, Tu C, Edwards J, Guo F, Zhou H, et al. Challenges and needs for China to eliminate rabies. *Infect Dis Poverty* (2013) 2(1):23. doi:10.1186/2049-9957-2-23
18. Zinsstag J. Towards a science of rabies elimination. *Infect Dis Poverty* (2013) 2(1):22. doi:10.1186/2049-9957-2-22
19. Mangen MJ, Batz MB, Käsbohrer A, Hald T, Morris JG, Taylor M, et al. Integrated approaches for the public health prioritization of foodborne and zoonotic pathogens. *Risk Anal* (2010) 30(5):782–97. doi:10.1111/j.1539-6924.2009.01291.x
20. Taylor LH, Hampson K, Fahrion A, Abela-Ridder B, Nel LH. Difficulties in estimating the human burden of canine rabies. *Acta Trop* (2017) 165:133–40. doi:10.1016/j.actatropica.2015.12.007
21. Cleaveland S, Fevre EM, Kaare M, Coleman PG. Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries. *Bull World Health Organ* (2002) 80:304–10.
22. Fahrion AS, Mikhailov A, Abela-Ridder B, Giacinti J, Harriesa J. Human rabies transmitted by dogs: current status of global data, 2015. *Wkly Epidemiol Rec* (2016) 91:13–20.
23. Taylor LH, Nel LH. Global epidemiology of canine rabies: past, present, and future prospects. *Vet Med* (2015) 6:361–71. doi:10.2147/VMRR.S51147
24. Sorrell EM, El Azhari M, Maswdeh N, Kornblet S, Standley CJ, Katz RL, et al. Mapping of Networks to Detect Priority Zoonoses in Jordan. *Front Public Health* (2015) 3:219. doi:10.3389/fpubh.2015.00219
25. Pieracci EG, Hall AJ, Gharpure R, Haile A, Walelign E, Deressa A, et al. Prioritizing zoonotic diseases in Ethiopia using a one health approach. *One Health*. (2016) 2:131–5. doi:10.1016/j.onehlt.2016.09.001
26. FAO. *New Myanmar One Health (OH) Strategy*. (2016). Available from: http://www.fao.org/ag/againfo/programmes/en/empres/news_170316b.html
27. Munyua P, Bitek A, Osoro E, Pieracci EG, Muema J, Mwatondo A, et al. Prioritization of zoonotic diseases in Kenya, 2015. *PLoS One* (2016) 11:e0161576. doi:10.1371/journal.pone.0161576
28. Taylor LH, Knopf L; Partners for Rabies Prevention. Surveillance of human rabies by national authorities – a global survey. *Zoonoses Public Health* (2015) 62(7):543–52. doi:10.1111/zph.12183
29. Zaidi SM, Labrique AB, Khowaja S, Lotia-Farrukh I, Irani J, Salahuddin N, et al. Geographic variation in access to dog-bite care in Pakistan and risk of dog-bite exposure in Karachi: prospective surveillance using a low-cost mobile phone system. *PLoS Negl Trop Dis* (2013) 7(12):e2574. doi:10.1371/journal.pntd.0002574
30. World rabies day 2016: educate, vaccinate, eliminate. *Vet Rec* (2016) 179(12):297. doi:10.1136/vr.i5066
31. Balaram D, Taylor LH, Doyle KAS, Davidson E, Nel LH. World rabies day – a decade of raising awareness. *Trop Dis Travel Med Vaccines* (2016) 2(19). doi:10.1186/s40794-016-0035-8
32. Coetzer A, Kidane AH, Bekele M, Hundera AD, Pieracci EG, Shiferaw ML, et al. The SARE tool for rabies control: current experience in Ethiopia. *Antiviral Res* (2016) 135:74–80. doi:10.1016/j.antiviral.2016.09.011
33. Jerolmack C. Who's worried about Turkeys? How 'organisational silos' impede zoonotic disease surveillance. *Sociol Health Illn* (2013) 35(2):200–12. doi:10.1111/j.1467-9566.2012.01501.x
34. Anonymous. *An Introduction FAO's Rabies Stakeholder Consultations – Tool I*. Rome: FAO (2016).
35. Pudjiatmoko P, Kandun IN. *Integrated Bite Case Management (IBCM) in Bali: One Health in Action*. Republic of Indonesia. p. 1–24. Available from: http://www.pmaconference.mahidol.ac.th/dmdocuments/PMAC_2013_PPT_%20PS3.4%20Pudjiatmoko.pdf
36. Lapiz SMD, Miranda MEG, Garcia RG, Daguro LI, Paman MD, Madrinan F, et al. Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol rabies prevention and elimination project. *PLoS Negl Tro0070 Dis* (2012) 6:e1891. doi:10.1371/journal.pntd.0001891
37. Scott TP, Coetzer A, de Balogh K, Wright N, Nel LH. The Pan-African rabies control network (PARACON): a unified approach to eliminating canine rabies in Africa. *Antiviral Res* (2015) 124:93–100. doi:10.1016/j.antiviral.2015.10.002
38. Vigilato MA, Clavijo A, Knobl T, Silva HM, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368(1623):20120143. doi:10.1098/rstb.2012.0143
39. Vigilato MA, Cosivi O, Knobl T, Clavijo A, Silva HM. Rabies update for Latin America and the Caribbean. *Emerg Infect Dis* (2013) 19:678–9. doi:10.3201/eid1904.121482
40. Aylan O, El-Sayed AF, Farahtaj F, Janani AR, Lugach O, Tarkhan-Mouravi O, et al. Report of the first meeting of the Middle East and Eastern Europe rabies expert bureau, Istanbul, Turkey (June 8-9, 2010). *Adv Prev Med* (2011) 2011:812515. doi:10.4061/2011/812515
41. Aikimbayev A, Briggs D, Coltan G, Dodet B, Farahtaj F, Imnadze P, et al. Fighting rabies in Eastern Europe, the Middle East and Central Asia – experts call for a regional initiative for rabies elimination. *Zoonoses Public Health* (2013) 61:219–26. doi:10.1111/zph.12060
42. Durr S, Naissengar S, Mindekem R, Diguimbye C, Niezgoda M, Kuzmin I, et al. Rabies diagnosis for developing countries. *PLoS Negl Trop Dis* (2008) 2:e206. doi:10.1371/journal.pntd.0000206
43. Léchenne M, Naïssengar K, Lepelletier A, Alfaroukh IO, Bourhy H, Zinsstag J, et al. Validation of a rapid rabies diagnostic tool for field surveillance in developing countries. *PLoS Negl Trop Dis* (2016) 10(10):e0005010. doi:10.1371/journal.pntd.0005010
44. Abela-Ridder B, Martin S, Gongal G, Engels D. Rabies vaccine stockpile: fixing the supply chain. *Bull World Health Organ* (2016) 94(9):635–635A. doi:10.2471/BLT.16.183012
45. WHO, OIE. *Human and Dog Rabies Vaccines and immunoglobulins. Report of a Meeting. Geneva, 12-13 October 2015*. Geneva: WHO (2015).
46. *From Concept to Completion: The Rabies Control Pilot Project Supported by the Bill & Melinda Gates Foundation*. World Health Organization (2015). Available from: http://www.who.int/rabies/bmgf_who_project_outcomes/en/
47. Mohammadi D. Moves to consign rabies to history. *Lancet Infect Dis* (2016) 16(10):1115–6. doi:10.1016/S1473-3099(16)30342-5
48. Hampson K, Cleaveland S, Briggs D. Evaluation of cost-effective strategies for rabies post-exposure vaccination in low-income countries. *PLoS Negl Trop Dis* (2011) 5(3):e982. doi:10.1371/journal.pntd.0000982
49. Gongal G, Wright AE. Human rabies in the WHO southeast Asia region: forward steps for elimination. *Adv Prev Med* (2011) 2011:383870. doi:10.4061/2011/383870
50. Morters MK, McKinley TJ, Horton DL, Cleaveland S, Schoeman JP, Restif O, et al. Achieving population-level immunity to rabies in free-roaming dogs in Africa and Asia. *PLoS Negl Trop Dis* (2014) 8:e3160. doi:10.1371/journal.pntd.0003160

51. Tenzin T, McKenzie JS, Vanderstichel R, Rai BD, Rinzin K, Tshering Y, et al. Comparison of mark-resight methods to estimate abundance and rabies vaccination coverage of free-roaming dogs in two URBAN areas of south Bhutan. *Prev Vet Med* (2015) 118:436–48. doi:10.1016/j.prevetmed.2015.01.008
52. IR D, G M. Concepts of infectious disease epidemiology. In: Dohoo IR, Martin W, Stryhn H, editors. *Veterinary Epidemiologic Research*. Charlottetown, Canada: VER Inc (2009).
53. Durr S, Meltzer MI, Mindekem R, Zinsstag J. Owner valuation of rabies vaccination of dogs, Chad. *Emerg Infect Dis* (2008) 14:1650–2. doi:10.3201/eid1410.071490
54. Sparkes J, Körtner G, Ballard G, Fleming PJ, Brown WY. Effects of sex and reproductive state on interactions between free-roaming domestic dogs. *PLoS One* (2014) 9(12):e116053. doi:10.1371/journal.pone.0116053
55. Durr S, Mindekem R, Kaninga Y, Doumagoum Moto D, Meltzer MI, Vounatsou P, et al. Effectiveness of dog rabies vaccination programmes: comparison of owner-charged and free vaccination campaigns. *Epidemiol Infect* (2009) 137:1558–67. doi:10.1017/S0950268809002386
56. Fitzpatrick C, Engels D. Leaving no one behind: a neglected tropical disease indicator and tracers for the Sustainable Development Goals. *Int Health* (2016) 8(Suppl 1):i15–8. doi:10.1093/inthealth/ihw002
57. Anonymous. *Report of the Sixth Meeting of the International Coordinating Group of the World Health Organization and the Bill & Melinda Gates Foundation Project on Eliminating Human and Dog Rabies*. Geneva: World Health Organization (2015). Contract No.: WHO/HTM/NTD/NZD/2015.3.
58. Zinsstag J, Dürr S, Penny MA, Mindekem R, Roth F, Menendez Gonzalez S, et al. Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc Natl Acad Sci U S A* (2009) 106(35): 14996–5001. doi:10.1073/pnas.0904740106

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Tribulations of the Last Mile: Sides from a Regional Program

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In Latin American and Caribbean (LAC) countries, the number of cases of dog-mediated human rabies is at its lowest since the onset of the Regional Program for Rabies Elimination in 1983, a commitment from LAC countries to eliminate dog-mediated rabies coordinated by the Pan American Health Organization. Despite minor setbacks, the decline in the number of human cases has been constant since 1983. While many LAC countries have significantly reduced rabies to a level where it is no longer significant public health concern, elimination has proven elusive and pockets of the disease remain across the region. In the 33-year period since 1983, the region has set and committed to four dates for elimination (1990, 2000, 2012, and 2015). In this paper, we ponder on the multiple causes behind the elusive goal of rabies elimination, such as blanket regional goals oblivious to the large heterogeneity in national rabies capacities. Looking ahead to the elimination of dog-mediated rabies in the region, now established for 2022, we also review the many challenges and questions that the region faces in the last mile of the epidemic. Given the advanced position of the Americas in the race toward elimination, our considerations could provide valuable knowledge to other regions pursuing elimination goals.

Keywords: rabies, canine mediated, America, regional program, elimination

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INTRODUCTION

In 1983, when dog-mediated rabies in the American region was the cause of over 200 human deaths and 12,000 dog cases per year, representatives from the countries, gathered at the first Regional Meeting of Rabies Program Directors (REDIPRA) (1) coordinated by the Pan American Health Organization (PAHO/WHO), had the vision of a future free of dog-mediated rabies. Armed with nerve tissue vaccine for dogs, they launched a region-wide plan leading to mass dog vaccination campaigns across the region and set up the first elimination goal for the Americas, by 1990. Three other elimination goals followed in 2000, 2012, and 2015. Although the goal was not achieved by 2015, the coordinated regional efforts toward elimination led to the control of dog-mediated rabies in most of the Americas. At the time of writing, eight dog-mediated human rabies cases have been reported across the region in 2016, all in Haiti.

In the following, we ponder on the possible reasons that may have contributed to the four missed elimination goals to date, and specifically target the final years of the regional control program. We then speculate on the main challenges that lay ahead. Our considerations, necessarily from a regional perspective, are based on the experience of the region in the race toward elimination and could provide valuable knowledge to other regions pursuing similar goals.

CHALLENGES PAST AND FUTURE

On Program Management

At the announcement during the last REDIPRA meeting in 2015 (1) that the fourth elimination goal was not going to be achieved, PAHO and the countries did not establish another deadline, but agreed on a pathway toward the definition of the next goal. Two possible future goals were discussed: (i) elimination of canine rabies or (ii) elimination of dog-mediated human rabies. Countries chose the latter, as they did on the previous four occasions. Regardless of the scope of the goal, countries agreed to the recommendation that the new date for elimination had to be based on the systematic evaluation of countries' rabies capabilities. This approach to goal setting differs from the previous four that led to arbitrary elimination dates that failed to recognize the heterogeneous development of rabies capabilities among countries.

Proactively coordinated, the aggregated evaluation of countries' rabies capacities, and their improvement plans toward disease elimination should inform the earliest date at which the region would be able to eliminate the disease. Moreover, the aggregation of gaps from all countries would inform the regional demand for specific capacities, e.g., rabies vaccine, some of which could be more efficiently provided by a regional mechanism (e.g., PAHO's Revolving Fund) (1).

The development of a systematic evaluation framework of the countries capacities is thus critical. Such a framework would require the definition of regional standards and indicators as well as clear requirements regarding the nature and quality of the evidence needed to support control and elimination claims. A PAHO review of indicators used by the countries to monitor the performance of their rabies programs identified large heterogeneity, in the number of indicators per country, from just a few to more than 100, and in the nature of them, from process indicators to outcome indicators (2).

The importance of the regular REDIPRA meetings, which constitute the strategic governance platform of rabies programs in the region, cannot be underestimated. Group dynamics prevalent at these meetings exercise great influence on strategic issues that cannot be replicated remotely. Specifically, we stress the importance of peer-pressure among countries. In addition, regional coordination requires formal structures to facilitate regular networking in the interval between REDIPRA meetings, e.g., via working groups around specific products such as interlaboratory proficiency exercises (1).

On coordination, we must mention stakeholder engagement, even if briefly, and specifically one of the most salient actors in recent years, i.e., animal rights groups. The engagement of officials with these groups was not always productive and, at times, led to departures from the real focus on rabies control. But a change at both camps appears evident in recent years. Both sides have learned to moderate their message, and now understand that negotiation and not confrontation leads to better outcomes for all. Official programs start to recognize that these groups need to be brought to the discussion table at the planning stages, as they can deliver niche-specific approaches to local problems.

On Evidence

The impact of interventions can only be monitored with reliable data. Since 1998, PAHO has been collecting data via questionnaires to the countries on their programs' performance prior to the regular REDIPRA meetings. It was only at the most recent REDIPRA in 2015 that a thorough analysis of the data could be presented (1).

Earlier reports stated that a number of Latin American and Caribbean (LAC) countries were conducting excellent rabies surveillance (3). These results seem to concur with those reported by zoonosis managers to a survey in early 2015 who replied that they were satisfied with the sensitivity of their rabies surveillance (4). However, to the best of our knowledge, and with the exception of Haiti (5), there is no systematic evaluation of rabies surveillance in the region, and we are not aware of recent patient chart reviews of acute encephalitis or sensitivity estimation of dog surveillance. Specifically on the latter, the region, by large, follows the recommendation of sampling a proportion of the dog population (3). This, at best, has facilitated discussions on the importance of targeting dogs for early warning and, at worst, has drained resources without informing the epidemiology of the disease. Recent work supported by PAHO questions this approach to surveillance and suggests more efficient alternatives (6). These studies also show the importance of variant identification, especially at the end game, and are a reminder that some countries in the region still lack this capacity in-house, or even nimble mechanisms to acquire it elsewhere for prompt response to cases.

The investigations that followed the recent occurrence of multiple dog cases in Brazil (7), spanning to more than one local authority, highlighted fundamental structural problems, not rabies-specific, for the generation of sound evidence, i.e., the absence of a common standard for data gathering across administrative units. This is likely to resonate in other countries, and it highlights the need for a standard epidemiological report. To that effect, the region will benefit from the ongoing efforts by Brazil toward the harmonization of processes across its network of zoonosis' surveillance units.

The regional rabies database, SIRVERA (8), despite all its shortcomings, has played a critical role in the success of the regional program. A perhaps overlooked contribution is that SIRVERA is the most tangible product of the program across its many years and participating countries. Together with other "brands" of the program (e.g., REDIPRA), SIRVERA has bundled the countries around the regional goal. That is, those countries that contribute data to it. Three countries where rabies is still endemic have consistently failed to report to SIRVERA. Such failure to report not only impacts on the ability of the program to monitor regional progress, but it has important consequences on neighboring areas pursuing control and elimination as they struggle to assess the risk of incursion from such countries. Like the other capacities, SIRVERA needs to change to adapt to the end game too and become the exhaustive repository of rabies programs performance indicators in the region. In other words, it must not just chase cases but also track and identify substandard capacity planning and deployment that constitute the best early warning of rabies risk.

On Resources

A prolonged epidemic tail, consecutive goal failures and farther in time goals, contribute to investors' fatigue (in the case of the Americas, these are mainly government budget holders, with external donors playing a much limited role, except for Haiti). It is a well-described fact that short-term goals lead to greater willingness to invest (9). The opposite can lead to reduced donor engagement. Efforts to attract resources must contemplate breaking down long-term regional goals, to reduce the long payback period, into country and area-specific objectives with short- and medium-term deliverables linked to enhanced capacity deployment to attract more investors/donors seeking quick returns. In other words, investment opportunities need to be indexed to processes and capacities that are fully measurable, tractable, and prone to direct influence. Moreover, short-term successes, e.g., the declaration of an increasing number of rabies-free countries and areas along the way, would reduce the perception of uncertainty around the overall investment for regional elimination, farther ahead.

Efforts to attract investment must also recognize that at the end game, there is little room for inefficiencies. As a result, optimization of regional and national resource allocation schemes, e.g., by country or geographical area vs. by capacity, merits study to prevent underperforming assets from receiving undeserved support (10, 11). This tendency may stem from failure to accept underperforming capacities relative to others, or a lack of appreciation of the full scope of opportunity costs. This might well be the case of devoting scarce resources to dog sterilization, an intervention that delivers a much lesser punch at a much greater cost than dog vaccination. Inefficient investment will only prolong the tail end of the epidemic, directly resulting in further cases and unnecessary deaths and, as a result, increasing the risk of goal fatigue. Other inefficiencies, either at the national or regional level, could occur as a result of maintaining vaccine production facilities for reduced domestic demand, unsubstantiated dog surveillance strategies that lead to no useful evidence for decision making, or the current prophylaxis schemes (PEP), promoting intramuscular administration, prevalent across the region.

On Vaccination

Notwithstanding occasional problems, all countries in the region, except for those that have been free from rabies for years, plan the purchase of vaccine (for humans and dogs) in their annual budgets. This, in comparison with other regions, is a feast. Not all, though, manage to acquire the vaccine at all (most notably Haiti), or in the quantities and timelines needed. The insufficient deployment of vaccine, whether in control or elimination stages, is the ultimate reason as to why rabies persists in some of those countries. Insufficient dog vaccine deployment, due to deficient population coverage, untested vaccine quality, mismanagement of batches, and non-compliance with protocol, translates into failure to consistently achieve herd immunity in a number of scattered locations that remain endemic, even if undetected. Occasional donations and exchanges of vaccines between countries, whether brokered by PAHO or not, have been the norm in the past to supply vaccine to areas in acute need (3, 12). This solidarity may be threatened as more areas reach elimination in the region, and hence reduce the size of their rabies programs and vaccine stockpiles. In such a scenario, where one single exposure may delay the region's goal, a regional mechanism to guarantee rapid deployment of rabies vaccines merits consideration.

Following on our remarks about the limited appetite for inefficiencies at the last mile, dog vaccine application must seek ways to reduce repeated vaccination of easy-to-reach animals. Beyond the financial implications, these animals contribute to vaccine coverage indicators, despite bringing no additional immunity, and may lead to a false sense of achievement about herd protection in the targeted dog population.

Rabies programs across the region have benefited from the incorporation of human rabies vaccine in the countries' regular acquisition of biologicals through PAHO's purchasing mechanisms. In 2014, following recommendations from REDIPRA (13), PAHO also included the dog vaccine in its portfolio of biologicals on offer through the PAHO revolving fund. Via large purchases, PAHO guarantees the provision of quality vaccine at competitive prices, and, most importantly, promotes regular budgeting practices in the countries. Improvements are possible, for example, by incorporating human rabies vaccine in the well-established logistical systems of the Expanded Programme on Immunization in country. This is a work in progress after a communication by PAHO to that effect was sent to the countries last year.

Despite seeing the lowest human case count in over 30 years, the demand for human rabies vaccine is on the rise. If human vaccine sold by PAHO's purchasing mechanisms is a good proxy for the overall use across the region, bearing in mind that not all the LAC countries buy through PAHO, we have noted an average increase of over 55,000 doses of human vaccine every year for the period 2005–2015. In 2015 alone, circa of 900,000 doses were acquired via PAHO's revolving fund. Although alternative dog surveillance systems, such as those based on tracking exposures after reported bites, could lead to more efficient PEP application (6), rabies programs must prepare for long-lasting demand of PEP even in the absence of canine rabies cases for quite some time.

On Awareness

In contrast to the evident scars left by smallpox, or other diseases with obvious sequelae, rabies does not leave living bearers to remind us of its occurrence. Together with the declining incidence, awareness of the disease will wane. This phenomenon will only get worse, and it would be important to regularly monitor the levels of awareness among the population in risk areas. Activities to that effect, e.g., knowledge-attitudes and practices surveys, may deliver collateral benefits by capturing heightened risk perception among the population that may provide sufficient reason, in the absence of adequate surveillance, for policy intervention.

A decrease in awareness may also lead to reduced uptake of preventive measures as seen in other diseases, e.g., measles vaccine. For rabies, the impact might be twofold: leading to reduced dog vaccination, and PEP uptake and prescription by health staff after exposure. The latter was the target of the recent rabies alerts issued by PAHO after a number of cases in the region (14). However, no similar alerts were issued after evidence of insufficient dog rabies vaccines coverage in risk areas. This, again, highlights the reactive nature of the program chasing cases and not capacities (or their absence).

FINAL REMARKS

It has been said that the regional rabies elimination program is a victim of its own success, as reduced disease incidence leads to relaxation of controls, and new evidence needs at the end game challenge attitudes and practices that worked well during the control phase, but may not do so well during the last mile. Given the regional success, some resistance to accept innovations tested in other settings, as is the case of intradermal human rabies vaccine or the use of capture–recapture methods to estimate dog vaccine coverage, is expected. Transferring successful approaches from well-controlled projects in local settings elsewhere is not without difficulty as managers tend to dismiss them as generated from different contexts of little applicability to their own. This may be true, given well-known limitations in external validity of even the most robust investigations (15). However, the merit of these well-controlled studies elsewhere is undeniable, and the region is now benefiting from such findings in the formulation of canine surveillance guidance and area level classification.

Basic problem structuring theory identifies two types of complexities in every problem and decision setting to its resolution: technical or analytical complexities, and organizational complexities (16). For rabies in the Americas, where effective tools are available for its control and elimination, disease persistence is due to organizational failure at the planning, implementation, or evaluation of the rabies program. Specifically, failure to (i) gather and properly present the evidence about disease risk and vulnerabilities to budget holders, (ii) systematically generate synergies with other programs and stakeholders to ensure efficient capacity deployment, and (iii) conduct thorough risk assessment on the sustainability of the rabies program. We recognize the impact of externalities on any disease program, but for dog rabies and the Americas, the authors believe that contextual factors play a critical role in one country alone: Haiti.

Improvements are underway. The regional program has now developed a framework for evaluation of rabies capacities, commissioned research to robustly guide dog surveillance requirements (5) and classify areas based on a composite measure of risk (17), and recently released a new SIRVERA platform capable of managing all the evidence needs in the elimination phase (8). These tools come with a price. They need increasing amounts of quality and timely data to provide the required precision, around results of interventions such as dog vaccine coverage, to support robust and opportune decision-making.

Reaching out to countries to promote reporting as per the new data standards and to support the shift in focus toward monitoring capacities and vulnerabilities, and not just cases, will require increased resources by the regional program. The additional resource will have to be distributed across endemic, at risk and free areas. Although the most obvious targets are the endemic and at risk classes, the region must also capitalize on those areas that achieve freedom. To that effect, the regional program needs to formalize the processes around rabies elimination and maintenance of such status and demand thorough risk analysis by countries that contemplate interventions beyond their borders in collaboration with areas still posing a risk.

Good as a planned approach may be, elimination requires more than cold preparation. Failure to reach the 2015 elimination goal should have generated a state of crisis to justify major transformational changes in the regional program. Without such changes, in the form of a state of urgency to propel the commitment to prompt elimination, the risk of apathy is real. Without consideration of the intangible benefits stemming from elimination, mostly of a political nature, the cold calculations around the diminishing returns of additional disease control measures at this stage may lead to the perpetuation of the current situation. This would betray the vision of those colleagues over 30 years ago. Without the pressure of an imminent goal, there are no regional consequences as a result of a new case, beyond the tragic death of a human being by a shameful disease.

The recently approved "Plan of Action for the elimination of neglected infectious diseases and post-elimination actions 2016–2022" (18), should deliver the new impetus, and the resources, to reach rabies elimination by 2022. Of mention is the inclusion in this plan, for the first time, of a reference to the elimination of canine rabies transmission.

AUTHOR CONTRIBUTIONS

VV conceived and wrote the work. All the authors have critically reviewed and revised the manuscript and approved it for publication.

REFERENCES

1. Pan American Health Organization (PAHO/WHO). *Regional Meeting of National Rabies Programme Managers in the Americas (REDIPRA)*. (2015). Available from: http://www.paho.org/panaftosa/index.php?option=com_content&view=article&id=211&Itemid=397
2. Del Rio Vilas VJ, Burgeño A, Montibeller G, Clavijo A, Vigilato MA, Cosivi O. Prioritization of capacities for the elimination of dog-mediated human rabies in the Americas: building the framework. *Pathog Glob Health* (2013) 107(7):340–5. doi:10.1179/2047773213Y.0000000122
3. Vigilato MAN, Clavijo A, Knobl T, Tamayo Silva HM, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368(1623):20120143. doi:10.1098/rstb.2012.0143
4. Maxwell MJ, Carvalho MJ, Del Rio Vilas VJ. Building the road towards a regional zoonoses strategy: a survey of zoonoses programs in the Americas. *Online J Public Health Inform* (2015) 8(1). doi:10.5210/ojphi.v8i1.6436
5. Wallace RM, Reses H, Franka R, Fenelon N, Orciari L, Etheart M, et al. Establishment of a canine rabies burden in Haiti through the implementation

of a novel surveillance program. *PLoS Negl Trop Dis* (2015) 9(11):e0004245. doi:10.1371/journal.pntd.0004354
6. Hampson K, Brunker K, Mancero T, Caldas E, Carvalho M, Castro A, et al. Surveillance to establish elimination of transmission and freedom from dog-mediated rabies. *Proceeding of the 2016 RITA (Rabies in the Americas) Meeting*. Belem, Pará, Brazil (2016).
7. Arruda da Silva W, Campos Ametlla V, Soares Juliano R. Raiva canina no municipio de Corumba-MS, 2015: relato de caso. *Acta Veterinaria Brasilica* (2015) 9(4):386–90.
8. Rocha F, Molina Flores B, Buzanovsky L, Santos AG, Carvalho M, Vigilato MAN, et al. SIRVERA: Atualizaçao Para Melhoria Da Qualidade De Informaçao Sobre Raiva Nas Americas. *Proceeding of the 2016 RITA (Rabies in the Americas) Meeting*. Belem, Pará, Brazil (2016).
9. Conlon D, Garland H. The role of project completion information in resource allocation decisions. *Acad Manage J* (1993) 36:402–13. doi:10.2307/256529
10. Scharfstein D, Stein J. The dark side of internal capital markets: divisional rent-seeking and inefficient investment. *J Finance* (2000) 55(6):2537–64. doi:10.1111/0022-1082.00299
11. Bromiley P. A prospect theory model of resource allocation. *Decis Anal* (2009) 6:124–38. doi:10.1287/deca.1090.0142
12. Millien MF, Pierre-Louis JB, Wallace R, Caldas E, Rwangabgoba JM, Poncelet JL, et al. Control of dog mediated human rabies in Haiti: no time to spare. *PLoS Negl Trop Dis* (2015) 9(6):e0003806. doi:10.1371/journal.pntd.0003806
13. Pan American Health Organization (PAHO/WHO). *Regional Meeting of National Rabies Programme Managers in the Americas (REDIPRA)*. (2013). Available from: http://www.paho.org/panaftosa/index.php?option=com_content&view=article&id=211&Itemid=397
14. Pan American Health Organization (PAHO/WHO). *Rabies Epidemiological Alert*. (2014). Available from: http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=25409&Itemid=270
15. Wandersman A, Alia K, Cook BS, Hsu LL, Ramaswamy R. Evidence-based interventions are necessary but not sufficient for achieving outcomes in each setting in a complex world: empowerment evaluation, getting to outcomes, and demonstrating accountability. *Am J Eval* (2016):1–18. doi:10.1177/1098214016660613
16. McNamee P, Celona J. *Decision Analysis for the Professional*. Stanford, CA: SmartOrg Inc (2008). 225 p.
17. Rysava K, Mancero T, Caldas E, Carvalho M, Gutierrez V, Haydon D, et al. Surveillance tools to guide rabies elimination programmes. *Online J Public Health Inform* (in press).
18. Pan American Health Organization (PAHO/WHO). *Plan of Action for the Elimination of Neglected Infectious Diseases and Post-Elimination Actions 2016-2022*. (2016). Available from: http://www.paho.org/hq/index.php?option=com_content&view=article&id=12547%3Aamericas-aim-to-eliminate-8-neglected-infectious-diseases-control-5-other-next-6-years&catid=8882%3A55-dc-news&Itemid=42099&lang=en

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Eliminating Dog-Mediated Rabies in Sikkim, India: A 10-Year Pathway to Success for the SARAH Program

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A third of the world rabies burden is in India. The Sikkim Anti-Rabies and Animal Health (SARAH) program is the first state-wide rabies program in India and demonstrates a successful One Health model of dog-mediated rabies elimination. The SARAH program was created in 2006 as a collaboration between the Government of Sikkim and international non-government organizations—Vets Beyond Borders and Fondation Brigitte Bardot. Activities are directed to canine rabies vaccination, humane dog population control, community education, and treatment of sick and injured animals. In 2005, there were 0.74 human rabies deaths per 100,000 (4 deaths) within Sikkim, and from 2006 to 2015, there were no human rabies deaths. In 2016, two human rabies deaths were reported near the West Bengal border region. From 2005 to 2010, the incidence of animal rabies is unknown; from 2010 to 2016, eight cases of animal rabies were reported. Major challenges for the program are continued commitment to rabies control in the face of 0 to low human rabies incidence and the risk of rabies incursions. Effective intersectoral communication between Health, Veterinary, Forestry, and Police officers is essential to enable rapid response to animal bite incidents and possible rabies incursions. An integrated One Health approach needs to be maintained with enhanced active rabies surveillance. Other states must establish similar programs if India is ever to achieve a goal of eliminating dog-mediated human rabies.

Keywords: SARAH program, Sikkim India, rabies elimination, One Health, mass dog vaccination, dog population management, animal welfare, surveillance

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INTRODUCTION

Globally, the incidence of human rabies deaths transmitted from dogs is estimated at 59,000 people, and a third of the world rabies burden is in India (1, 2). In India, there is no national strategy for the elimination of rabies (1), and rabies is not a notifiable disease. Recently, pilot programs for rabies control have commenced in the states of Tamil Nadu and Haryana (3–5), and a number of animal-welfare groups throughout the country include canine rabies vaccination in their activities. The state of Sikkim has implemented a state-wide One Health rabies program since 2006. Sikkim is a small Himalayan state in North East India bordered by Nepal, China, and Bhutan (**Figure 1**), with a population of 610,000 (2011 census) (6). The core components of the Sikkim Anti-Rabies and Animal Health (SARAH) program (the Program) are canine rabies vaccination, dog population management, and rabies prevention education, which have been shown to control and prevent

FIGURE 1 | Map of Sikkim, India—rabies incursions occurred near border of South and West Sikkim and West Bengal border.

rabies leading to elimination (7, 8). It also provides health care to street dogs and aims to foster a compassionate attitude toward all animals. The Program enjoys strong community support within Sikkim for its efforts in rabies control and improvements in animal welfare.

The SARAH program was created as a collaboration between the Government of Sikkim, Australian non-government organization (NGO)—Vets Beyond Borders (VBB), and French NGO—Fondation Brigitte Bardot (FBB) in response to the public of Sikkim requesting that mass shooting of street dogs cease and a more humane method of controlling the dogs be implemented. In 2005, human rabies incidence in Sikkim was 0.74 deaths per 100,000 persons, totaling 4 human deaths (**Table 1**). From 2006, there were no reported cases of human rabies until 2016. Two animal cases were reported in 2010; no further animal cases were reported until 2015. Data for reports of animal rabies cases are poor prior to 2010.

This paper provides a perspective on the implementation of the SARAH program for the control and elimination of dog-mediated human rabies in Sikkim and the benefits and challenges of a One Health approach (7, 9, 10).

DOG KEEPING IN SIKKIM

Sikkim is largely rural, with 47% of the state under forest cover. Seventy-five percent of the state's population reside in rural areas. The main urban center is Gangtok (**Figure 1**) with 100,000 people. Sikkim is a multiethnic state with strong influences of Buddhism (the state religion until Sikkim became an Indian state in 1975) and Nepalese Hindu. The majority of the population is Nepalese (11), and Nepali is the most common language spoken (12).

Dogs in Sikkim are traditionally kept outside as protectors against wildlife intrusion such as Himalayan bear, but also against bad spirits and adverse life events (13, 14). With increased standard of living most village households now keep one or more dogs. In villages, young puppies are often kept inside, and when older are kept outside and handled little. In urban areas, there is an increasing incidence of western-style pet ownership with dogs living inside as members of the family. Workers brought into Sikkim for contract jobs associated with construction of hydro-electric plants usually keep three to four dogs per household. These dogs are kept outside, free roaming and are often difficult to handle. When the contract is finished, the workers move away and usually leave the dogs on the street.

Free roaming dogs are common in Sikkim, and the supervision and responsibility felt for these dogs is on a continuum from nothing to full responsibility. Many family owned dogs are allowed to roam freely. A culture of quasi-ownership has been described in the city of Ranchi, India (15) where people feed roaming dogs but do not take responsibility for vaccination or sterilization, and dog catching with butterfly nets is required for vaccinating these dogs. Over the lifetime of the SARAH program, use of butterfly nets has reduced, and most dogs can now be caught by hand by the SARAH team or community members. While 42% of dogs were reported as stray in Tamil Nadu (5), on average in Sikkim 18% of the total dog population are unsupervised dogs for which no one takes responsibility and which require capture with butterfly nets. In South Sikkim where there are many contract workers, the unsupervised roaming dog population is 27% (**Table 2**).

There is also a population of feral dogs in the forests in the China border regions, which is likely to be derived from abandoned puppies from army camp dogs. Efforts are made to vaccinate and surgically sterilize these dogs in a trap and release program. The army has permitted access to army camps for the surgical sterilization and rabies vaccination of camp dogs to enable a buffer zone of vaccinated neutered dogs. The army has cooperated with improved garbage control in army camps thus eliminating a food source for feral dogs.

COMMUNITY ENGAGEMENT

Sikkim Anti-Rabies and Animal Health community education on rabies prevention have been designed around core Buddhist and Nepali Hindu religious beliefs including animal sentience, the cherished relationship between people and dogs, and the role of dogs in providing security, and their loyalty and friendship. The Program recognizes that human–animal relationships are "economic, cultural, and emotional in nature" (16, 17) and that dog keeping practices and norms of responsible pet ownership vary in different localities and cultures and can change over time. Animal-welfare lessons were incorporated into early school syllabus in 2009, and further lessons will be incorporated in the 2018 syllabus. The Program has been very careful to address the felt needs of the community to generate community participation.

TABLE 1 | Program data on activities and incidence of dog bites and rabies cases, program funding, and volunteers.

Year	Rabies vaccine doses given	Nos. surgical sterilizations	No. of sick/injured animals treated	No. of public awareness events	Dog bite incidents	Suspect human rabies cases reported	Suspect animal rabies cases reported	Fondation Brigitte Bardot funding (Euro)	Government of Sikkim funding (Euro)	Vets Beyond Borders volunteers (weeks)
2003	0	0	n/a	n/a	n/a	1	n/a	0	0	0
2004	0	0	n/a	n/a	n/a	2	n/a	0	0	0
2005/2006	1,400	830	n/a	n/a	853	4	n/a	12,410	0	81
2006/2007	7,006	4,942	n/a	n/a	n/a	0	n/a	109,000	70,000	103
2007/2008	8,514	5,618	n/a	n/a	n/a	0	0	63,981	57,400	115
2008/2009	7,523	4,364	n/a	n/a	2,320	0	0	70,000	58,212	111
2009/2010	4,941	2,797	n/a	n/a	1,082	0	0	23,000	71,400	79
2010/2011	16,807	3,283	611	n/a	1,334	0	2	21,600	28,000	42
2011/2012	18,611	4,060	1,123	n/a	1,348	0	0	20,500	74,200	47
2012/2013	17,466	2,947	1,581	72	3,315	0	0	14,500	74,900	92
2013/2014	23,669	4,289	2,245	120	n/a	0	0	13,000	61,600	39
2014/2015	23,706	4,300	1,925	86	n/a	0	4	18,000	21,000	39
2015/2016	24,571	5,487	2,304	190	n/a	2	2	22,976	62,300	40

n/a, not available. Dog bite data provided by Sikkim Department of Health include potential rabies exposure associated with animals such as drinking milk from a cow bitten by a dog or jackal.

TABLE 2 | Estimated number of dogs and canine rabies vaccination in four districts of Sikkim.

Year	Number dogs vaccinated	Dog population	Number dogs vaccinated	Dog population	Number dogs vaccinated	Dog Population	Number dogs vaccinated	Dog population
	East (% vac East)	East	South (% vac South)	South	North (% vac North)	North	West (% vac West)	West
2011	9,567 (50)	19,000	3,108 (31)	10,000	1,286 (32)	4,000	2,846 (36)	8,000
2012	12,504 (69)	18,200	2,931 (32)	9,200	635 (16)	4,000	2,541 (35)	7,200
2013	12,848 (69)	18,500	2,341 (25)	9,500	598 (15)	4,000	1,679 (22)	7,500
2014	14,458 (76)	19,000	4,932 (49)	10,000	828 (21)	4,000	3,451 (43)	8,000
2015	14,927 (83)	18,000	4,720 (45)	10,500	1,037 (26)	4,000	3,022 (36)	8,500
2016	14,361 (85)	17,000	5,916 (54)	11,000	733 (18)	4,000	3,561 (40)	9,000

Vaccination coverage is based on dog population size estimates provided by village councils and Department of Animal Husbandry field officers. Feral dogs in forests are excluded from the data estimates.

As trust in the Program has developed, the community is more aware of rabies, and societal norms of animal welfare have changed. Community members will now bring dogs for vaccination and sterilization or describe where they can be found enabling many of the unsupervised dogs to be vaccinated and sterilized. Family planning in women in Sikkim has been actively promoted by the Government (18), and the potential benefits of "family planning" in dogs in reducing the number of unwanted puppies and associated animal-welfare problems were quickly recognized by the community; the community reports fewer dog fights particularly during the breeding season. An increase in dog bite incident reports is seen twice yearly in dog breeding season (March/April and September/October), during the major festival in September/October and following rabies education activities.

Community participation and cooperation is integral to the Program. Key messages to encourage participation are (1) canine rabies vaccination is needed for control of human rabies, (2) surgical desexing will reduce dog roaming and fighting, and hence the risk of rabies, (3) canine rabies vaccination and sterilization are provided free of charge, (4) sterilization will reduce the number of unwanted puppies, and (5) if your dog is unvaccinated and bites a person, you may be held responsible by the Panchayat (local village council) and the affected person for the cost of PEP for the affected person. PEP is available free from public hospitals, but if it is unavailable at the hospital, it must be purchased from a private medical store. In the last 2 years, Panchayats have placed the onus of financial responsibility for PEP on the owners of unvaccinated dogs.

STAGES OF DEVELOPMENT

The SARAH program has developed over 10 years with capacity building and government commitment from a small NGO-managed program relying substantially on international volunteers to a state-wide government program, providing a One Health model of sustainable dog-mediated rabies elimination.

INITIAL STAGE

Initially, Program administration, veterinary volunteers, and training were delivered through VBB with a VBB Program manager present in Sikkim and 2–3 international volunteers assisting with the work throughout the year. FBB provided funding on a matching grant arrangement with the Government of Sikkim with the expectation that after 3 years the project would be taken over by the government. Government provided facilities for clinics and public education, accommodation for volunteers, and local staff for the project. A SARAH clinic was established for surgical sterilization, rabies vaccination, and treatment of sick and injured street dogs; mobile units enabled the Program to be extended to rural regions.

Initial and subsequent training activities had a strong emphasis on animal welfare and have been critical for community acceptance of the Program and cost control. Extensive training of local veterinarians in veterinary surgery and medicine, and local staff in animal handling and dog catching occurred through the formal VBB VetTrain© program. Volunteers provided mentoring, on-the-job training, and train-the-trainer programs to local staff. Important elements for community support for the Program were the adoption of humane catching methods, which cause minimal distress to animals and demonstrate a recognition of animal sentience and the significance of dogs in the community, good surgical outcomes with a low rate of surgical complications (<0.003%), rapid return of dogs to their home territory (within 24 h for healthy dogs), and commitment to treat all sick/injured street dogs.

In 2009, the Program became a Division of the Department of Animal Husbandry. VBB volunteers continued to participate, but VBB had a reduced role in Program administration; FBB provided reducing financial support (**Table 1**).

INTERMEDIATE STAGE

Multisectoral cooperation is essential for sustained rabies elimination (19), accordingly, a seminar on rabies and emerging zoonotic diseases was held in 2009. Representatives from the government veterinary and medical fraternity of the State Government were invited; few medical personnel attended. There were two major outcomes from the meeting. The first was the establishment of the Wildlife Conservation and Feral Dog Program to prevent the spread of wildlife rabies into the dog population in Sikkim by creating a buffer zone of rabies vaccinated dogs in the border regions adjacent to China and Nepal.

The second decision was to implement an annual state-wide rabies vaccination campaign each September with World Rabies Day activities incorporated (pet shows, school activities, and media releases). Critically, the implementation of state-wide rabies vaccination extended the Program to the rural regions of Sikkim. Canine rabies vaccine is provided free of charge; annual rabies vaccination of pet dogs is compulsory under state legislation. House-to-house vaccination was needed initially, but central vaccination posts are now feasible in most villages. A catch-vaccinate-release-resight program is undertaken for street dogs with marking of vaccinated dogs with paint. An annual dog census is correlated with village council knowledge of dog numbers facilitating 70% vaccination coverage to be achieved in East Sikkim (20–22). Vaccination coverage by district is shown in **Table 2**.

A distemper outbreak occurred in 2012 resulting in the death of thousands of dogs and community fear that distemper was caused by rabies vaccine. Extensive community education was undertaken to ensure participation in subsequent rabies vaccination campaigns and encourage owners to vaccinate dogs for distemper.

A One Health Intersectoral Rabies Committee was established in 2012 to transcend sectoral boundaries, comprised of Departments of Health, Animal Husbandry, Forestry, Urban Housing & Development, Police, and Army. The tasks of the committee were to prepare a proposal for rabies to be a notifiable disease in Sikkim, formulate procedures for restrictions of cross-border dog movement, formulate procedures for dog registration, work with the National Centre for Disease Control to establish a State Surveillance Laboratory for rabies control, develop a surveillance system for achieving rabies, and improve garbage control. A major achievement was rabies becoming a notifiable disease in Sikkim in 2014 for animals and humans (23). Garbage management has improved with daily rubbish collection in major towns, and weekly rubbish collection in regional districts.

CURRENT STAGE AND ONE HEALTH OUTBREAK RESPONSES

Both human and canine rabies were controlled in Sikkim during 2006–2015. Complacency developed about rabies as the perception of disease risk was low. The Health Department stopped stocking PEP and rabies immunoglobulin (RIG), and the need for rabies surveillance and development of laboratory capacity was given low priority. This occurred in the face of complex ecological interactions including wildlife habitat disruption associated with road construction, socioeconomic change, and a migratory workforce located in Sikkim who bring unvaccinated dogs with them and are on the fringe of Sikkim civil society.

In December 2014, two people and a number of dogs were bitten by a jackal in a village close to the West Bengal border. Dog brain samples were sent interstate for testing, but the results were inconclusive. In February 2016, there were reports of a jackal attacking cows near the West Bengal border. Two cows tested positive for rabies (**Table 1**). Subsequently, two suspect human rabies deaths were reported in a nearby village. One person had been bitten by an unvaccinated pet dog, refused medical treatment, and died. The other person had no history of dog bite and died in hospital. Laboratory confirmation was not undertaken reflecting problems previously identified in effective surveillance of rabies programs (24): inadequate training in sample collection, difficulties in getting samples to a diagnostic laboratory from Sikkim, and family reluctance to allow postmortem diagnosis.

DISCUSSION

Vaccination and Dog Population Control

Rabies vaccination of dogs is the cornerstone of rabies control (25, 26). The logistics of a state-wide vaccination campaign in the Himalayas are difficult. Cooperation of villagers, Panchayats, and Department of Animal Husbandry field officers is essential. Human-mediated dog movement and gaps in coverage are problems in effective rabies programs (27). Recent rabies incursions in South Sikkim occurred in areas where there is human-mediated dog movement, where they have been gaps in vaccine coverage (**Table 2**), and which is adjacent to West Bengal with no rabies program. A Program team is now permanently located in South Sikkim to improve vaccination coverage and dog population management.

Dog population management is important for the Program goals of improved animal welfare (28, 29) and rabies control; the numbers of dogs sterilized annually are approximately 20% of the dogs vaccinated in Sikkim each year (**Table 1**). It is also important because it addresses community concerns about dog fighting and nuisance, and unwanted puppies. Improved animal welfare supports a more stable dog population. Community assistance with dog catching enables a minimal although highly skilled dog catching team. The aides who assist with surgery are also the dog-catching team. This has enabled control of a major cost, for the size of the dog catching team can be a significant cost in a dog population management program (3).

Intersectoral Coordination, Community Engagement, and Animal Welfare

Intersectoral coordination and communication, essential for rabies control (10, 19), is an ongoing challenge. The establishment of a One Health Intersectoral Committee provided the authority for SARAH to seek cooperation at district and village level. The perceived success in controlling rabies and dog population management together with wide community support facilitated cooperation at all levels, although an unanticipated outcome was the Department of Health's interim decision to stop stocking PEP and RIG.

Education on animal welfare and the obligation to care and value dogs has been associated with increased community participation and support for the Program. There is a temptation to assume that the animal welfare emphasis of the Program will only work in Sikkim where animal sentience is accepted and the complex relationship between people and dogs is acknowledged in festivals such as Tihar (Deepawali). It has been suggested that the important role of dogs in Hinduism may be an impediment for successful program adoption (30), but in Sikkim, it has facilitated program adoption. An increase in empathy and improved attitudes to animals has been shown to increase empathy to humans and facilitate prosocial behavior (31–36), which may in turn motivate health behaviors including participation in vaccination campaigns (28). A critical feature in the SARAH program is the recognition of the significance of human–animal relations and culturally appropriate framing of community education messages.

Challenges Facing the SARAH Program

Recent suspect rabies cases highlighted the need for formal and regular intersectoral communication at community level, the need for improved epidemiological data, for enhanced active surveillance related to animal bites, training for appropriate medical response to suspect rabies dog bite, the logistical difficulties in getting both human and animal samples from Sikkim to a laboratory for confirmation of rabies, and the ongoing risk of rabies incursion and sylvatic rabies.

The seasonal pattern of the recent rabies outbreaks occurring at the border during winter when food sources are scarce suggests rabies incursions into Sikkim, rather than ongoing circulation of rabies within Sikkim. An effective surveillance system with tracing back of suspect animals is needed to confirm this hypothesis (37, 38). Increasing human wildlife conflict in Sikkim (6) may increase the risk of rabies transmission. If rabies were controlled in domestic dogs in surrounding areas, it is not known if jackal could sustain the circulation of rabies although Lembo (20) concluded that dogs were the only species essential for rabies persistence in the Serengeti. There are clear limitations in the accuracy of vaccination coverage estimates based on dog population size estimates provided by village council knowledge. However, the data suggest that vaccination coverages of 70% are likely to be feasible in Sikkim, as shown by consistently high estimates achieved in East Sikkim.

The SARAH program is a State Government supported program and lacks the international resources available to national programs. Effort is being directed at establishing low cost enhanced active rabies surveillance (37). The Rapid Test (BioNote) is used in the field when available. Discussions are being held with counterparts in West Bengal for extension of the rabies program into West Bengal, but resources are limited for both parties.

CONCLUSION

The Sikkim Government, together with SARAH partner NGO—VBB and FBB, has made a considerable investment to eliminate dog-mediated rabies. The recent re-emergence of rabies in Sikkim highlights the imperative of an integrated One Health approach to increase the sensitivity of rabies surveillance and to ensure interruption of rabies transmission. The SARAH program is a model of rabies control in a predominantly rural environment with limited resources. It is also an example of the challenges encountered in maintaining rabies control in a landlocked state. Other Indian states must establish similar programs if India is ever to achieve a goal of eliminating dog-mediated human rabies.

AUTHOR CONTRIBUTIONS

HB has been involved in the SARAH program since 2006. HB and AB researched, designed, and wrote this paper. TB has been local coordinator for the program since inception and provided expert and local knowledge about the paper subject.

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REFERENCES

1. Fahrion AS, Mikhailov A, Abela-Ridder B, Giacinti J, Harries J. Human rabies transmitted by dogs: current status of global data, 2015. *Wkly Epidemiol Rec* (2016) 91(2):13–20.
2. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
3. Abbas SS, Kakkar M, Rogawski ET. On behalf of the roadmap to combat zoonoses in India. I. Costs analysis of a population level rabies control programme in Tamil Nadu, India. *PLoS Negl Trop Dis* (2014) 8(2):e2721. doi:10.1371/journal.pntd.0002721
4. *National Rabies Control Program National Health Portal India*. (2017). Available from: http://117.239.178.13/national-rabies-control-programme
5. Fitzpatrick MC, Shah HA, Pandey A, Bilinski AM, Kakkar M, Clark AD, et al. One health approach to cost-effective rabies control in India. *Proc Natl Acad Sci U S A* (2016) 113(51):14574–81. doi:10.1073/pnas.1604975113
6. *Sikkim Human Development Report 2014*. New Delhi: Routledge (2014).
7. Cleaveland S, Beyer H, Hampson K, Haydon D, Lankester F, Lembo T, et al. The changing landscape of rabies epidemiology and control. *Onderstepoort J Vet Res* (2014) 81(2):2014. doi:10.4102/ojvr.v81i2.731
8. Knobel DL, Lembo T, Morters M, Townsend SE, Cleaveland S, Hampson K. *Chapter 17 – Dog Rabies and Its Control A2 – Jackson, Alan C. Rabies*. Third ed. Boston: Academic Press (2013). p. 591–615.
9. Lechenne MMM, Zinsstag J. Integrated rabies control. In: Zinsstag JSE, Waltner-Toews D, Whittaker M, Tanner M, editors. *One Health: The Theory and Practice of Integrated Health Approaches*. CAB International (2015). p. 176–89.
10. Cleaveland S, Lankester F, Townsend S, Lembo T, Hampson K. Rabies control and elimination: a test case for one health. *Vet Rec* (2014) 175(8):188–93. doi:10.1136/vr.g4996
11. *Demographic Features: Home Department, Government of Sikkim*. Available from: http://sikkim.nic.in/homedept/demog.htm (accessed October 31, 2016; February 21, 2017).
12. *Sikkim in Brief*. Gangtok: Department of Economics, Statistics, Monitoring & Evaluation, Government of Sikkim (2005).
13. Ekvall R. The role of the dog in Tibetan nomadic society. *Cent Asiatic J* (1963) VIII:163–73.
14. Vargas I. Snake-kings, boars' heads, deer parks, monkey talk: animals as transmitters and transformers in Indian and Tibetan Buddhist narratives. In: Waldau P, Patton K, editors. *A Communion of Subjects: Animals in Religion, Science, and Ethics*. USA: Columbia University Press (2006). p. 217–37.
15. Gibson AD, Ohal P, Shervell K, Handel IG, Bronsvoort BM, Mellanby RJ, et al. Vaccinate-assess-move method of mass canine rabies vaccination utilising mobile technology data collection in Ranchi, India. *BMC Infect Dis* (2015) 15:589. doi:10.1186/s12879-015-1320-2
16. Rock M, Buntain BJ, Hatfield JM, Hallgrimsson B. Animal-human connections, "one health," and the syndemic approach to prevention. *Soc Sci Med* (2009) 68(6):991–5. doi:10.1016/j.socscimed.2008.12.047
17. Porter N. Bird flu biopower: strategies for multispecies coexistence in Việt Nam. *Am Ethnol* (2013) 40(1):132–48. doi:10.1111/amet.12010
18. Sciences IIfP. *District Level Household and Facility Survey (DLHS-4), 2012-13: India. Sikkim*. Mumbai: International Institute for Population Sciences (2014).
19. Lapiz SM, Miranda ME, Garcia RG, Daguro LI, Paman MD, Madrinan FP, et al. Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol rabies prevention and elimination project. *PLoS Negl Trop Dis* (2012) 6(12):e1891. doi:10.1371/journal.pntd.0001891
20. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
21. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14(3):185–6. doi:10.1016/0264-410X(95)00197-9
22. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7(3):e1000053. doi:10.1371/journal.pbio.1000053
23. *Sikkim Government Gazette, No. 554. Sect. No. 27/AH&VS Adm*. (2014).
24. Taylor LH, Hampson K, Fahrion A, Abela-Ridder B, Nel LH. Difficulties in estimating the human burden of canine rabies. *Acta Trop* (2017) 165:133–40. doi:10.1016/j.actatropica.2015.12.007
25. Betsch C, Böhm R, Chapman GB. Using behavioral insights to increase vaccination policy effectiveness. *Policy Insights Behav Brain Sci* (2015) 2(1):61–73. doi:10.1177/2372732215600716
26. Wa OIE. *Global Elimination of Dog-Mediated Human Rabies – The Time Is Now. Report of the Rabies Global Conference, 10–11 December 2015*. Geneva, Switzerland. Available from: http://apps.who.int/iris/bitstream/10665/204621/1/WHO_HTM_NTD_NZD_2016.02_eng.pdf?ua=12016 (accessed November 2, 2016).
27. Townsend SE, Sumantra IP, Pudjiatmoko, Bagus GN, Brum E, Cleaveland S, et al. Designing programs for eliminating canine rabies from islands: Bali, Indonesia as a case study. *PLoS Negl Trop Dis* (2013) 7(8):e2372. doi:10.1371/journal.pntd.0002372
28. International Companion Animal Management Coalition. *Are We Making a Difference: A Guide to Monitoring and Evaluating Dog Population Management Interventions*. International Companion Animal Management Coalition (2015). Available from: http://www.icam-coalition.org/downloads/ICAM_Guidance_Document.pdf (accessed August 15, 2016).
29. Yoak AJ, Reece JF, Gehrt SD, Hamilton IM. Disease control through fertility control: secondary benefits of animal birth control in Indian street dogs. *Prev Vet Med* (2014) 113(1):152–6. doi:10.1016/j.prevetmed.2013.09.005
30. Devleesschauwer B, Aryal A, Sharma BK, Ale A, Declercq A, Depraz S, et al. Epidemiology, impact and control of rabies in Nepal: a systematic review. *PLoS Negl Trop Dis* (2016) 10(2):e0004461. doi:10.1371/journal.pntd.0004461
31. Ascione FR, Weber CV. Children's attitudes about the humane treatment of animals and empathy: one-year follow up of a school-based intervention. *Anthrozoos* (1996) 9(4):188–95. doi:10.2752/089279396787001455
32. Hergovich A, Monshi B, Semmler G, Zieglmayer V. The effects of the presence of a dog in the classroom. *Anthrozoos* (2002) 15(1):37–50. doi:10.2752/089279302786992775
33. Tissen I, Hergovich A, Spiel C. School-based social training with and without dogs: evaluation of their effectiveness. *Anthrozoos* (2007) 20(4):365–73. doi:10.2752/089279307X245491
34. Sprinkle JE. Animals, empathy, and violence can animals be used to convey principles of prosocial behavior to children? *Youth Violence Juvenile Justice* (2008) 6(1):47–58. doi:10.1177/1541204007305525
35. Zasloff RL, Hart LA, Weiss JM. Dog training as a violence prevention tool for at-risk adolescents. *Anthrozoos* (2003) 16(4):352–9. doi:10.2752/089279303786992044
36. Arkow P. The impact of companion animals on social capital and community violence: setting research, policy and program agendas. *J Sociol Soc Welf* (2013) 40(4):33–56.
37. Wallace RM, Reses H, Franka R, Dilius P, Fenelon N, Orciari L, et al. Establishment of a canine rabies burden in Haiti through the implementation of a novel surveillance program. *PLoS Negl Trop Dis* (2015) 9(11):e0004245. doi:10.1371/journal.pntd.0004245
38. Banyard AC, Horton DL, Freuling C, Muller T, Fooks AR. Control and prevention of canine rabies: the need for building laboratory-based surveillance capacity. *Antiviral Res* (2013) 98(3):357–64. doi:10.1016/j.antiviral.2013.04.004

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frontiers in Veterinary Science

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A Century Spent Combating Rabies in Morocco (1911–2015): How Much Longer?

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Rabies has no known beginning in Morocco and to date, government control efforts and plans fail to eradicate the disease. A review and analysis of available epidemiological data are crucial to learn lessons from the past and to propose effective actions. Legally, animal rabies is a notifiable disease since 1913 and legislation has been updated periodically since. Dogs have always been considered as both the disease's vector and reservoir, while cattle, other herbivores, and humans are victims. Animal rabies cases evolution from 1942 to 2015 is characterized by ascending phase then decreasing one following structured rabies control plan implementation in 1980s. Indeed, from 1986 to 2010, three rabies control plans have been conducted based on free of charge rabies vaccination of owned dogs through mass campaigns. The geographical distribution of rabies is stable over the years with highest cases number in rich rural areas and around cities. Human rabies cases are decreasing over the time (1976–2015) thanks to the opening of new antirabic treatment centers in the last decade which permit the administration of more PEPs. After a century of rabies control, Morocco registered an average of 301 animal cases and 21 human cases annually for the last decade (2005–2015). Few reasons led to those limited results. The lack in law enforcement and, moreover, the fact that the law do not take into account responsible dog ownership aspect are of importance. Lack of dog population knowledge and management and intersectoral coordination deficiency are additional failure reasons. The gathered data will help to build a new strategy with a focus on a "One Health" approach. Dog population ecology parameters' study is of primary importance. We estimated dog population to be 2.8 million dogs based on human:dog ratio. Enhancing vaccination coverage of dog population is feasible by combining parenteral vaccination and complementary oral vaccination. Updating legislation by inclusion of responsible dog ownership and law enforcement are crucial. Over the last century, Morocco registered a slow decreasing tendency in the number of animal and human rabies cases. Urgent strategy need to be implemented because rabies elimination is an achievable goal in Morocco.

Keywords: rabies, Morocco, epidemiology, dog, one health, vaccination coverage, dog population management

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INTRODUCTION

Rabies has no known beginning or starting point in Morocco (1). Several epidemiological studies have focused on this disease since the beginning of rabies vaccination among dogs in 1927 (2). They have provided a wealth of documentation covering a century of rabies surveillance in Morocco. Compilation and analysis of data are of importance to learn lessons from the past and to propose actions to be included in any new strategy.

Efforts to control rabies in Morocco began as early as 1911, year of the first human and canine rabies vaccination by a local vaccine manufactured at Institute Pasteur of Tangier (IPT) (1). Since that, routine antirabies vaccination of people and animals was practiced but without any improvement in the number of victims. The World Health Organization first launched initiatives to set up a rabies control program, supported by international experts, in 1980s (3–5). The program had an objective of rabies elimination through a certain number of actions related to human health, veterinary sector, and municipalities. The limited results led to other control strategies in 1990 and 2001. Despite these efforts, Morocco still recorded an average of 21 human rabies cases per year (2005–2015) (6) and since 1923, official documents have recorded the death of over 1,046 humans due to rabies and the exposure of over 838,660. The number of people having been given postexposure prophylaxis (PEP) is enough to fill a big-sized town such as Sale (city in north-west of Morocco, has a population of 850,403 according to the census of 2014, and is the fifth biggest city of country).

The rabies situation in Morocco affects not only Moroccan citizens but also neighboring countries. The density of trade with Europe exchanged by road is a source of rabies contamination for several rabies-free European countries. A number of cat and/or dog owners illegally smuggle their pet(s) into Europe mostly by road through Spain, disregarding all the legal provisions concerning the transportation of animals into Europe and not declaring their animal(s) to the customs officials or veterinary border control staff (7–10). From 2001 to 2015, 12 rabies alerts have been notified in Europe originating from Morocco (eight in France, one in Belgium, one in Germany, one in the Netherlands, and one in Spain) (10).

An analysis of the experience of the past century should reveal lines of action in order to make better headway; future strategies should also be able to benefit from scientific and technical progress in the field of rabies control (11). Morocco is a developing country and should choose the most efficient means of control in order to reduce the costs incurred by rabies (12) and eliminate the risk of exposing the Moroccan population to this fully preventable disease.

MATERIALS AND METHODS

Rabies Regulations

A review of the regulatory texts on rabies published between 1913 and 2014 in Moroccan official journal[1] is realized with focus on the legal status of rabies. The key points of each text are presented and general evolution of legislation related to rabies is discussed.

[1] http://www.sgg.gov.ma.

Epidemiological Analysis

Epidemiological data concerning animal and human rabies cases were collected from published bibliographical references and epidemiological reports issued by the competent public authorities, and more especially those of Morocco's National Food Safety Office (ONSSA) for animal rabies cases and the Ministry of Health for human cases. In the event of contradictory data from different sources, the highest figure has been chosen due to the substantial risk of underreporting (13). The epidemiological characteristics of animal rabies in Morocco are discussed for the period from 1928 to 2015. There follows a presentation and discussion of the rabies patterns in Morocco (reservoir, animal species affected, seasonal changes, and geographical distribution) as well as measures taken at different times to tackle the disease and the suggestions of various authors in order to improve the situation. Mapping of the evolution of the number of animal rabies cases in the Moroccan provinces was performed using ArcGIS 10.1 software. The number of human rabies cases reported annually from 1974 to 2015 is analyzed and discussed. There is a discussion on the geographical distribution of cases of human rabies. The provided PEP protocol is discussed as well as the laboratory diagnosis. Propositions of improvement are formulated. A review of the genetic characterization of rabies virus isolates in Morocco is realized. Molecular epidemiology data are compared with classical epidemiology findings.

National Rabies Control Plans (NRCPs)

Different NRCPs are presented. The achievements and deficiencies of plans are presented and the causes of their limited success analyzed.

Moroccan Dog Population

It is crucial to remain informed about the dog population in order to draw up a realistic and effective canine rabies control plan. A synthesis of the studies that are interested in the size of the Moroccan canine population is carried out in order to have an estimate of this population. This is based on a comparison between the results of estimations of the dog population in the framework of an amendment to the 1993 rabies control plan, the NRCP of 2001–2010 and other international studies or studies in Maghreb countries. The data are extrapolated depending on the human:dog ratio chosen in order to estimate the size of the dog population. Demographic data were provided by official Moroccan authorities (Health Ministry website: http://www.sante.gov.ma). The current state of dog population control and suggestions for improvement are also presented.

Vaccination Coverage of the Dog Population

The vaccination coverage of the dog population is estimated by combining data on vaccination in urban areas by private veterinarians with that in rural areas following government-run mass vaccination campaigns. Dog population data are related to the estimated human:dog ratio. Vaccination coverage is analyzed and suggestions put forward on how to improve the situation. Data on vaccination in urban areas were extrapolated from the number of doses of rabies vaccine sold between 2009 and 2015 to veterinarians in the private sector. The data were obtained from veterinary pharmaceutical companies with a rabies vaccine registered in Morocco[2] during the same period. Propositions for dog population vaccination coverage amelioration are formulated with reference to Moroccan experiments in oral dog rabies vaccination.

Application of the "One World, One Health" Concept

The "One World, One Health" concept is highlighted by international organizations such as FAO, OIE, and WHO as the most efficient way of controlling zoonotic diseases. The actions taken in Morocco are assessed in the light of this concept, examples, and suggestions given.

RESULTS AND DISCUSSION

Rabies Regulations in Morocco

Morocco has a wealth of regulations on animal rabies control with a new text every 9 years. These regulations were first focused in people treatment after rabies exposition on IPT (14) and at antirabies institute of Marie-Feuillet hospital in Rabat (15). The measures were also concentrated on prevention of exposure to rabid animals either imported (16) or locally by instigating measures (17) to control stray dogs in both urban settings (18) and the countryside (19). Parenteral vaccination of dogs was already mandatory in 1928 (20) early and quickly after OIE 1927 conference on rabies and mandatory antirabies vaccination of cats was instaured on 1934 (21).

This basic regulatory framework has been updated in several occasions either within mandatory notifiable animal diseases list update in 1977 (22) or by updating specific measures to control rabies in 2000, 2005, and 2014 (23–25).

This regulation evolves from the vizirial orders in 1915, 1927, 1928, 1934, 1936, to decrees in 2000, 2005, and 2014, which have more regulatory weight.

The regulations cover mandatory rabies vaccination of dogs and measures to be taken in the event of contamination but they do not cover management of the dog population or the concept and actions of "responsible dog ownership". The latter concept implies registering and identifying dogs, preventing their negative impact on society and controlling breeding. The legislation should also cover mass control actions for stray dogs (means of capture and humane euthanasia) in accordance with OIE rules on animal welfare (26).

It should be noted that national regulations are not fully applied. The mandatory vaccination of dogs is not monitored and there are no legal sanctions should a dog be found to be unvaccinated (25).

Epidemiological Analysis

The first rabies vaccination was performed in Morocco in 1911 by a rabies vaccine for human and veterinary use produced at IPT (1, 27). Since that, exposed people were treated and from 1923 to 1932 a total of 361 people received PEP in IPT (21). The number of exposed treated people increased to reach an average of 1,500 person per year between 1951 and 1958 (28).

Veterinary authority started dogs preventive antirabies vaccination in 1928 and an average of 671 dogs per year were vaccinated between 1928 and 1933 (27, 29). This number increased to reach 10,000 dogs per year between 1945 and 1965 (30).

An average of 302 (minimum 68 and maximum 663) animal rabies cases was registered between 1942 and 1968 (28, 31–33) demonstrating an active animal rabies surveillance system based on Casablanca laboratory.

Table 1 summarizes the data relating to the 1971 to 2015 period concerning animal rabies, the number of dogs vaccinated and culled, the number of human cases, and the number of people given PEP. We can identify an increasing trend of animal rabies cases number up to 1982 from where this trend decreases. This can be visualized in **Figure 1**, which traces evolution of animal rabies cases, number of vaccinated and culled dogs from 1942 to 2015. The animal rabies cases number follows a distribution with an ascending phase in which the number of animal rabies cases increases and a descending phase from 1982. The year 1982 coincides with start of WHO rabies fight in Maghreb zone (3). Those efforts led to first NRCP (1986–1990) launch. **Figure 1** shows also that the number of vaccinated dogs per year increases considerably in the beginning of the control plan rising from 2,730 dogs in 1982 to 25,000 dogs in 1983 and 229,231 dogs in 1989. This figure then dwindled before increasing once again during the amended rabies control plan of 1994, reaching 325,780 dogs. Similarly, a peak of 450,917 dogs vaccinated was reached in 2005 under the 2001–2010 rabies control program. This evolution in the number of vaccinated dogs in peaks during the maximal activity of different rabies control plans is characteristic. The decrease in the number of vaccinated dogs is thought to be linked to the veterinary services efforts to control other livestock diseases (**Figure 1**) (5, 34).

Up to 1992, the number of dogs culled was always greater than the number of dogs vaccinated. Since 1992, the culling of dogs has been stopped in the context of rabies control but is still practiced to limit the problem of stray dogs in urban environments (**Figure 1**).

Several studies have investigated the epidemiological status of rabies in Morocco. We selected the nine that we considered most relevant and which cover the period (1928–2015) (2, 6, 28, 29, 33, 35, 37, 56, 57). Several of the epidemiological characteristics of rabies in Morocco appear stable over the studied period (1928–2015).

Rabies Reservoir and Affected Animal Species

Table 2 contains data on the different species involved in animal cases from 1951 to 2015.

Since the very first epidemiological studies on rabies in Morocco (2, 29), dogs have been shown to be the reservoir and dog bites the primary source of human contamination. Since 1951, a number of 8254 dogs in all have been diagnosed as rabid, accounting for 51% of all animal notifications (**Figure 2**). The proportion of dog cases in the total animal rabies in Morocco

[2] www.onssa.gov.ma.

TABLE 1 | Number of animal rabies cases, number of vaccinated dogs and culled dogs, number of PEPs, and number of human rabies cases from 1971 to 2015.

Year	Number of animal rabies cases (reference)	Number vaccinated dogs (reference)	Number of culled dogs (reference)	Number of PEPs (reference)	Number of human rabies cases (reference)
1971	508 (35)[a]	4,492 (35)	21,952 (35)	9,011 (36)	
1972	606 (35)[a]	6,524 (35)	22,477 (35)	9,045 (36)	
1973	583 (35)[a]	ND (35)	11,676 (35)	10,209 (36)	
1974	635 (35)[a]	1,866 (35)	8,924 (35)		67 (4)
1975	525 (35)[a]	3,095 (35)	14,671 (35)		12 (4)
1976	370 (37)	1,303 (35)	9,379 (35)		14 (4)
1977	326 (35)[a]	ND (35)	6,788 (38)	11,109 (38)	15 (4)
1978	438 (37)[a]	3,511 (35)	17,375 (35)	15,769 (38)	50 (38)
1979	455 (37)[a]	6,250 (35)	28,502 (38)[a]	16,789 (38)	38 (4)
1980	479 (35)[a]	3,700 (35)	22,478 (38)	16,557 (38)	50 (4)
1981	417 (35)[a]	2,106 (35)	22,273 (38)	16,123 (38)	52 (39)[a]
1982	512 (35)	2,730 (35)	42,660 (38)	16,822 (38)	25 (39)[a]
1983	381 (37)	25,000 (3)	42,928 (38)	14,549 (38)	15 (39)[a]
1984	280 (40)		43,000 (3)[a]	14,960 (38)[a]	20 (39)[a]
1985	430 (40)		50,989 (38)	15,441 (38)	34 (4)[a]
1986	493 (5)	0 (5)	79,580 (38)[a]	15,954 (38)	34 (38)[a]
1987	433 (5)	18,569 (5)	59,958 (38)[a]	14,678 (41)	28 (4)[a]
1988	555 (5)	176,981 (5)	73,570 (5)	16,704 (41)	27 (4)[a]
1989	356 (5)	229,231 (5)	258,224 (5)	12,905 (41)	17 (39)[a]
1990	271 (5)	20,355 (5)	77,767 (5)	11,660 (41)	16 (39)
1991	384 (5)	3,527 (5)	50,666 (5)	10,496 (41)	18 (39)
1992	423 (5)	4,785 (5)	79,433 (5)	15,204 (41)	20 (39)
1993	287 (5)	265,731 (5)	65,986 (5)	11,562 (41)	24 (39)
1994	263 (5)	325,780 (5)	62,599 (5)	12,636 (41)	16 (39)
1995	317 (5)	264,739 (5)	74,425 (5)	14,700 (41)	29 (39)
1996	406 (5)	0 (5)	92,356 (5)	13,035 (41)	18 (39)
1997	369 (5)	0 (5)	59,562 (5)	13,906 (42)	21 (39)
1998	476 (5)	21,729 (5)	55,224 (5)	14,726 (42)	20 (5)[a]
1999	455[b]	60,839 (43)	4,145 (43)	13,742 (44)	30[a,b]
2000	474[b]	53,941 (43)	3,153 (43)	13,539 (45)	15[b]
2001	572[b]	68,548 (43)	5,470 (43)	14,196 (46)	26[b]
2002	446[b]	45,976 (43)	4,317 (43)	15,188 (47)	23[b]
2003	467[b]	124,688 (43)	47,799 (43)	15,425 (48)	17[b]
2004	425[b]	378,519 (43)	28,102 (43)	19,529[c]	23[a,b]
2005	360[b]	450,917 (43)	43,125 (43)	23,564[c]	25[b]
2006	335[b]	267,794 (43)	30,646 (43)	25,857[c]	16[b]
2007	355[b]	254,753 (43)	22,614 (43)	29,580[c]	31[b]
2008	313[b]	123,612 (49)		32,214[c]	24[b]
2009	294[b]	125,495 (49)	90,870 (49)	30,350[c]	17[b]
2010	269[b]	54,172 (50)	48,288 (50)	28,097[c]	19[a,b]
2011	253[b]	62,851 (51)	58,867 (51)	27,885[c]	18[b]
2012	337[b]	114,790 (52)	61,006 (52)	30,365[c]	19[b]
2013	310[b]	115,274 (53)		32,692[c]	24[b]
2014	299[b]	105,181 (54)		35,279[c]	20[b]
2015	248[b]	80,613 (55)		32,547[c]	19[b]

[a]*Discordant data.*
[b]*Data provided by the ONSSA/DSV Epidemiology and Health Monitoring Service.*
[c]*Data provided by the Epidemiology and Disease Control Directorate of the Moroccan Ministry of Health.*
ND, not determined.
Blue color: data for the period before implementing the first NRCP.
Orange color: data for the period after implementing the first NRCP.

decreases over the time passing from 82% in 1951 to 20% in 2015 (1951: 82%, 1964: 76%, 1973–1983: 52%, 2000: 45%, 2007: 32%, 2010: 25%, and 2015: 18%). This can be explained by the fact that veterinary services give more attention to rabies diagnosis on livestock because of its economic value (35) and concentrate less on the known vector (i.e., dog).

All the authors agree that herbivores (cattle, sheep, goats, equids, or camelids) are victims. Notifications of rabies in cattle come second to notifications concerning dogs in all the studies (4,244 cases, i.e., 26% of animal rabies cases). Contrary to the tendency evolution in dogs, diagnosis pressure on herbivores (cattle, ovine, goat, horses, and camels) is growing over the time passing from 12% in 1951 to 79% in 2015 (1951: 12%, 1964: 19%; 1973–1983: 43%, 2000: 47%, 2007: 64%, 2010: 65%, and 2015: 79%). This is probably, as previously said, because of economic value of livestock (35) that imposes a close surveillance.

Several studies have emphasized the role of cats in human contamination (21, 33, 35). In all, 800 cats have been notified as rabid and account for 5% of total registered animal rabies cases between 1951 and 2015.

Rats are regularly mentioned in diagnosed cases and even quoted as a rabies reservoir in natural surroundings (33, 37), but since 1980s, they have no longer been named in reports and are classified in the "Others" category of **Table 2**. Indeed, WHO considers that this species does not play an epidemiological role and is rather an epidemiological dead end (59).

Morocco is the natural environment for some 30 bat species (order *Chiroptera*, families *Rhinopomatidae*, *Emballonuridae*, *Nycteridae*, *Rhinolophidae*, *Hipposideridae*, *Vespertilionidae*, and *Molossidae*) (60, 61). To date, as far as we know, rabies has never been detected among these species, and no bats have never been reported as a source of human contamination in Morocco.

Seasonality of Rabies

In 1959, Chevrier (28) noted an annual cycle of animal rabies cases, with one peak in the spring and another in the autumn. The link between the cyclical nature of cases and the sexual cycle of bitches was only described in 1985 (35). To date, this seasonal variability is stable.

Several authors (28, 38) have pointed out a cyclical increase in the incidence of rabies every 6–8 years. No explanations have ever been provided for this cycle, which appears to have been broken after the instigation of the first NRCP from 1986 to 1990.

Geographical Distribution

No regions of Morocco are free from the disease. Rabies is a rural disease, 80% of notifications originating in the countryside and only 20% in towns. In rural areas, it is most often found in a 30–50 km perimeter around major towns rather than in remote areas of the countryside or mountainous regions where there are fewer people (28). Chevrier's observations have been confirmed by all the studies that have followed and are still relevant today (6).

The close relationship between the density of the human population and that of the dog population is also highlighted as a risk factor, because the denser the human population, the denser the dog population too and the higher the risk of exposure

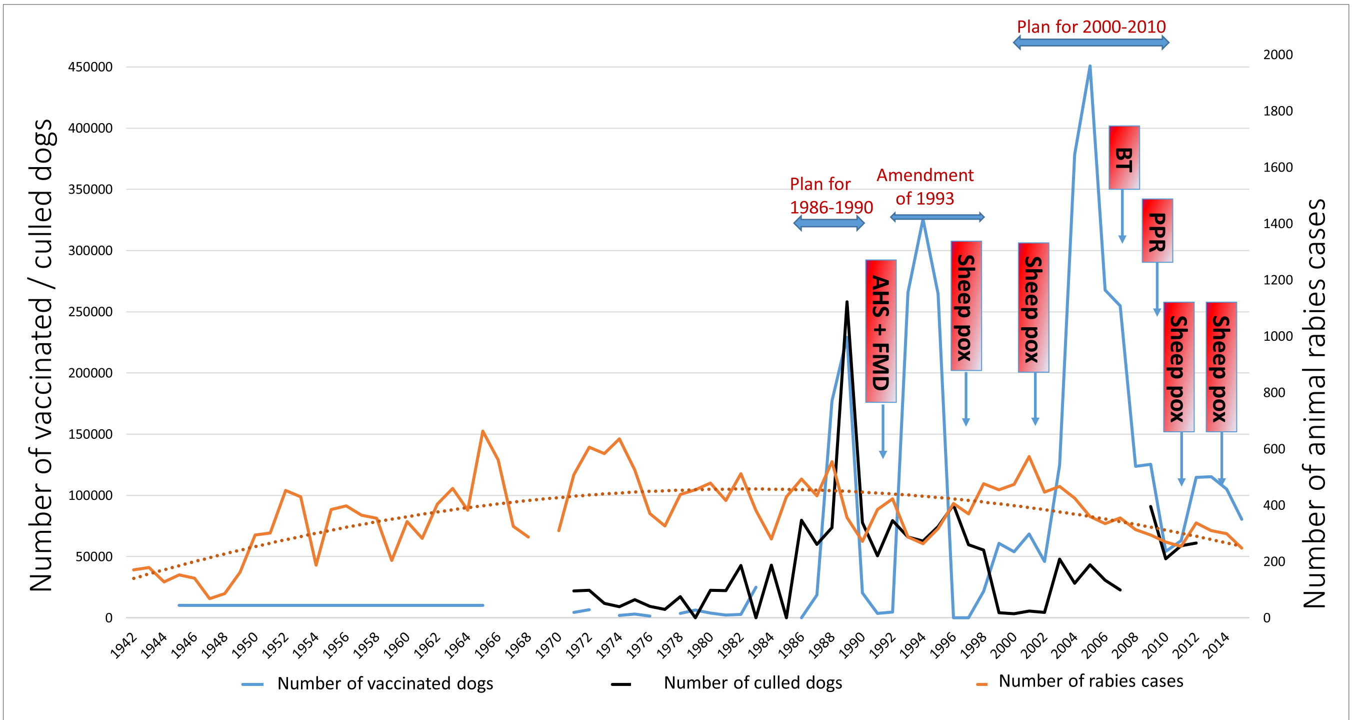

FIGURE 1 | Evolution of animal rabies cases, number of vaccinated and culled dogs (1942–2015). AHS, African Horse Sickness; FMD, Foot and Mouth Disease; BT, Bluetongue disease; PPR, Peste des petits ruminants disease.

TABLE 2 | Animal rabies cases per species from 1951 to 2015.

Species	1951 (28)[a]	1952 (28)[a]	1953 (28)[a]	1954 (28)[a]	1955 (28)[a]	1956 (28)[a]	1957 (28)[a]	1958 (28)[a]	1964 (33)[a]	1965 (33)[a]	1966 (33)[a]	1967 (33)[a]	1968 (58)	1973–1983 (37)
Dogs	248	224	193	154	189	191	299	268	291	304	293	236	231	2675
Cattle	22	38	37	18	33	14	34	16	57	75	11	59	36	1404
Cats	17	10	6	13	3	5	14	64	19	14	23	20	17	225
Equids	8	9	6	1	3	5	11	4	10	17	1	5	0	502
Sheep/goats	3	2	0	0	1	0	2	1	4	4	7	1	3	273
Camelids	3	1	2	1	2	1	3	1	1	1	1	3	0	15
Others	0	0	0	0	1	0	0	0	0	0	0	1	0	21
Total	301	284	244	187	232	216	363	354	382	415	336	325	287	5115

Species	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Dogs	167	201	194	215	255	192	173	153	106	103	113	100	95	66	64	91	62	64	44
Cattle	98	134	128	133	156	140	148	129	114	113	117	115	106	92	97	149	154	139	128
Cats	21	26	33	33	24	26	14	27	21	16	12	11	12	22	15	12	8	8	9
Equids	67	90	82	79	108	73	85	83	86	83	89	68	58	75	60	74	67	80	48
Sheep/goats	14	21	14	13	26	13	47	28	24	17	22	16	22	9	15	9	16	8	19
Camelids	0	4	3	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Others	2	0	1	1	1	2	0	5	9	3	2	3	1	5	2	2	3	0	0
Total	369	476	455	474	572	446	467	425	360	335	355	313	294	269	253	337	310	299	248

[a]*Data related to laboratory confirmed animal cases in Casablanca laboratory.*
Data from 1997 to 2015 provided by the ONSSA Epidemiology and Health Monitoring Service.

to rabies (28). The dissemination of the rabies virus along road networks was revealed by Fassi-Fehri et al. (37). These data were later confirmed by molecular biology research in 2010 (62).

Figure 3 shows geographical distribution of animal rabies in Morocco provinces for 1997–2001, 2002–2006, 2007–2011, and 2012–2015. The five most badly affected provinces according to 1976–2015 period data were Sidi Kacem (703 cases), Kenitra (608 cases), Safi (532 cases), Casablanca (492 cases), and Meknes (488 cases) [(35) and ONSSA Epidemiology and Health Monitoring Service]. The geographical distribution of cases shows that rabies is endemic to the whole of Morocco with the exception of desert regions (southern provinces). It may be seen that the distribution of rabies cases is related to the intensity of farming activities, thus confirming that Chevrier's observation in 1959 (28) is still valid in 2015.

Human Rabies

The vaccination of humans following exposure to the rabies virus was first practiced in Morocco by IPT (1). From 1923 to 1932, 361 people in all were treated (21) and from 1951 to 1958, this figure increased to 1,500 people treated on average per year (28) and continued to rise from 3,156 in 1964 to 10,209 in 1973 (36). The number of people treated per year was more or less stable between 1977 and 2003, averaging 13,789 (38, 41, 42, 44–48). From 2004, this figure more than doubled, reaching an average of 29,163 people from 2004 to 2015 (data provided by the Epidemiology and Disease Control Directorate of the Moroccan Ministry of Health). The human rabies is a notifiable disease in Morocco since 1967 (63).

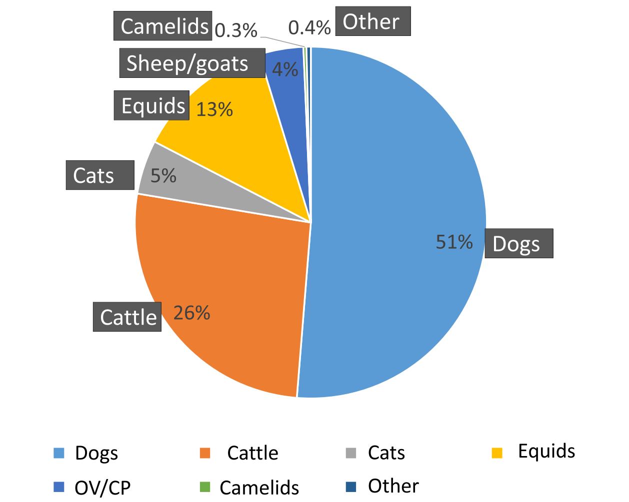

FIGURE 2 | **Animal rabies by species (1951–2015).**

Table 1 and **Figure 4** present the annual number of human rabies cases and the number of persons who received PEP from 1971 to 2015. The number of human rabies cases is slightly decreasing over time: the annual mean of human cases for 1976 to 1985 is 31 (min = 14 and max = 52), dropping to 23 (min = 16 and max = 34) for 1986 to 1995, then 22 (min = 15 and max = 30) for 1996 to 2005, and finally 21 (min = 16 and max = 24) for 2006 to 2015. The number of persons who received PEP increased in the same time: from 1986 to 2005, there were 14,633 PEPs per year on average (min = 10,496 and max = 23,564), but this figure has more than doubled, reaching an annual mean of 30,687 (min = 25,857 and max = 35,279) for the period from 2006 to 2015. This is no doubt thanks to the efforts of local communes which, under the impetus of the Ministry of the Interior (64), have opened new rabies treatment centers, whose numbers have risen from 120 in 2008 to 147 in 2012 (56, 63).

Up to now, Morocco has applied the 2-1-1 protocol for PEPs by the intramuscular route (63). This could increase by 60–80% the number of people treated for the same budget in rural areas if it used the intradermal delivery of fractioned doses recommended by WHO (65). It has been proven that poor people often do not spend time and money traveling to receive PEP (66).

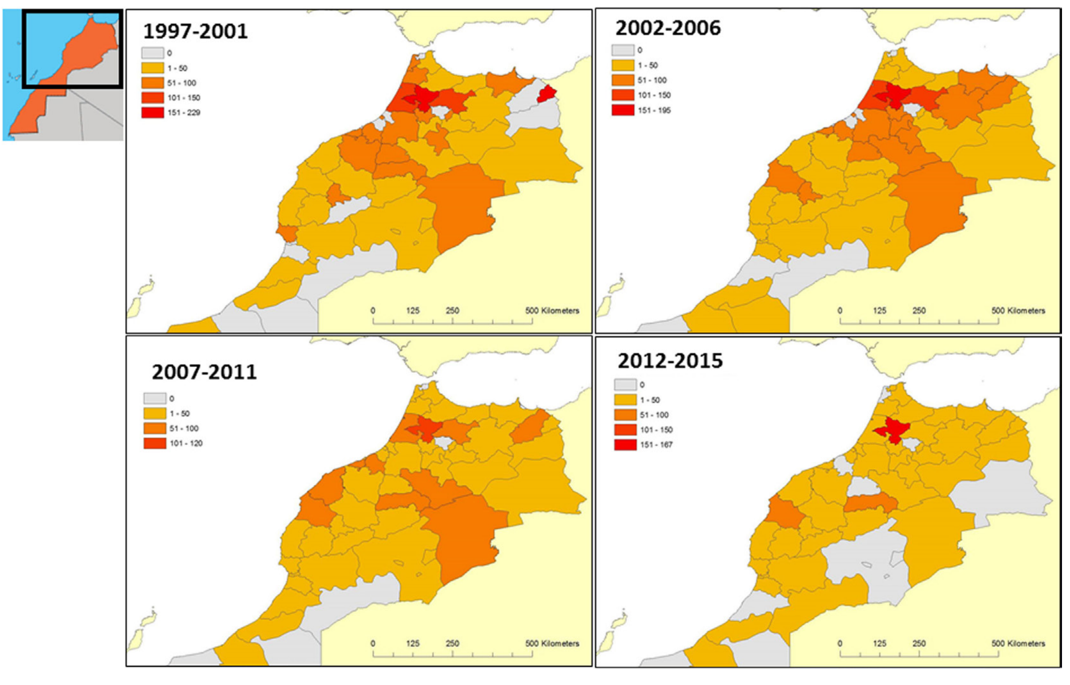

FIGURE 3 | **Geographical distribution of animal rabies in Morocco (1997–2015).**

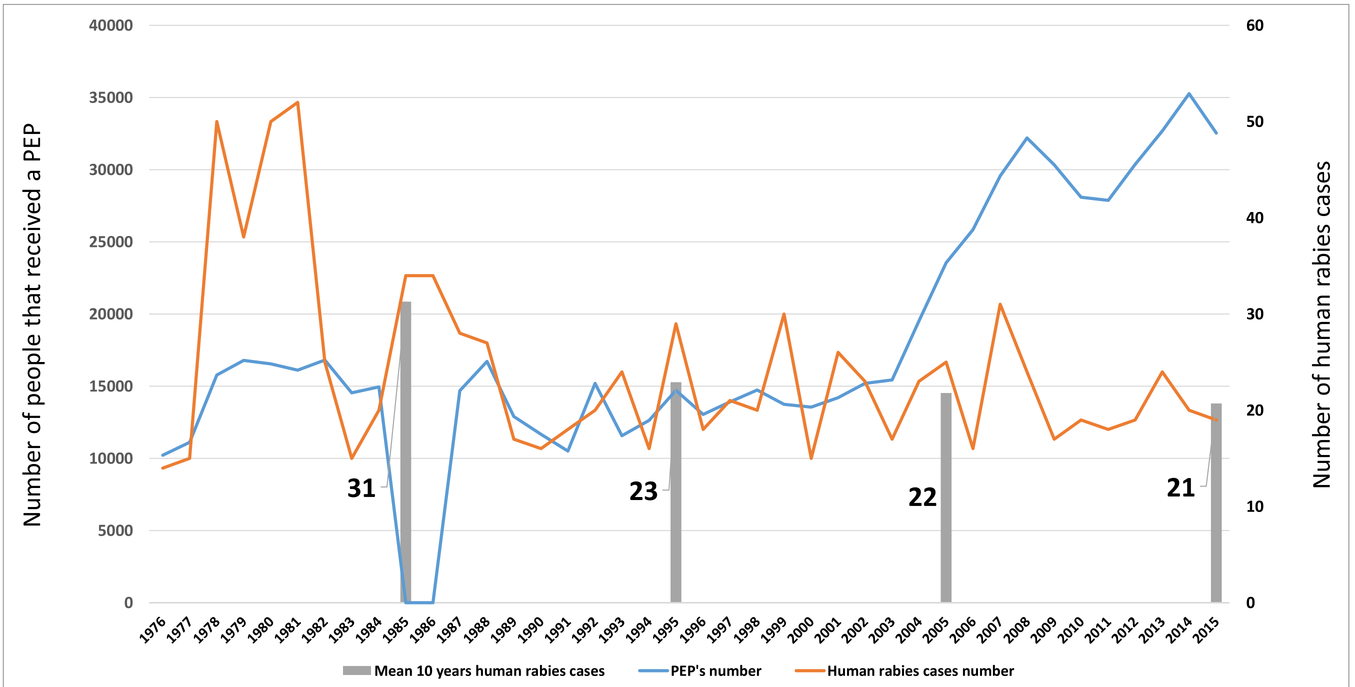

FIGURE 4 | **Number of human rabies cases and number of people who received postexposure prophylaxis (PEP) (1964–2015).**

Generally speaking, human rabies in Morocco matches the geographical distribution of animal rabies (35). Dogs are the main species responsible for human contamination (91% in 1935, 80% in 1965, 95% in 1973, and 80% in 1985) (2, 30, 35, 37). The frequency of contamination is greater among the male population (around 80%) and among young people (around 40% among children less than 15 years old). Bites often involve the legs (around 45%), face (around 15%), and hands (around 35%), all other locations (such as the neck or genitals) being rarer (35, 37, 38).

Although, as previously said, the number of human rabies cases of rabies is decreasing, it should be remembered that official notifications are generally underestimated (13) and that they may only concern hospital cases (37). There is a need to investigate the origins of underreporting and give feedback after detailed analysis over several years of the files on human deaths. This would reveal weaknesses in the system and possible means of improvement. One of the reasons of underreporting could be the population's refusal to allow an autopsy of their loved ones for cultural reasons. Alternatives to autopsy by non-invasive methods such as skin biopsies or supraorbital sampling could lead to an increase in the number of rabies cases reported and provide the diagnostic laboratory with precious samples (66). A report following a 2-week WHO expertise carried out in 2001 in different places of Morocco (67) as well as a study (39) revealed that human deaths are linked to an inadequate prophylaxis and suggest an improvement of training of physicians in antirabic centers.

Morocco has one diagnostic laboratory for human rabies, which only uses postmortem analytical methods. It confirms about 30% of clinical cases (63). The use of quick new reliable tests (lateral flow or immunohistochemical methods) in local, non-specialized laboratories (66) could help increase the rate of laboratory confirmations.

Genetic Variability of the Rabies Virus

Since the rabies virus was first sequenced in 1995, the Moroccan strains have been identified as belonging to genotype Africa 1 (68). The RabMed Control project included a phylogenetic study of 133 samples of canine rabies from 28 Moroccan towns between 2004 and 2008 (62). This study revealed:

- that rabies transmission in Morocco does not correspond to a rabies virus transmission model for a wild canine population;
- that the spatial dynamics of the rabies virus in Morocco is better described by mean road distance between outbreaks (51 km, with a minimum of 34 and maximum of 72 km per year), suggesting human intervention in the transmission of the rabies virus through the movement of rabid dogs (62).

National Rabies Control Plans

Since 1980s, several different NRCPs have followed in succession:

– *NRCP covering 1986–1990:* plan drawn up as part of the WHO rabies control program in Maghreb countries (3, 4). An interministerial committee was set up to draft a NRCP, whose broad lines included:
  - Raising awareness among the public and providing health education (causes, seriousness and consequences of rabies, reasons for and scope of the control measures proposed).

  - Health prophylaxis: eliminating stray domestic carnivores through stray dog culling campaigns. Reducing the availability of food for stray domestic carnivores. Monitoring suspected and biting animals. Checking the movements of wild and domestic carnivores. Making diagnosis of animal rabies regional rather than national.
  - Medical prophylaxis: targeted vaccination of 80% of 700,000 dogs (this being the estimated number of owned dogs at that time) with a stable, low-cost vaccine already proven to be harmless. A government veterinary vaccine company named Biopharma developed an inactivated rabies vaccine for animal use by the parenteral route in the framework of the plan (35). The maximum number of dogs vaccinated under this plan was in reality 229,231 in 1989 (5).
- *Amendment of 1993:* actions focused on vaccinating owned dogs (325,780 dogs vaccinated in 1994), while reducing the culling of stray dogs to the necessary minimum as this measure leads to an increase in the rate of replenishment of the dog population and thus an increase in the proportion of young unvaccinated dogs, not to mention its negative impact on the participation of owners in vaccination campaigns. This explains the need to limit culling to "true stray dogs" (i.e., feral dogs).

  As the plan progressed, this component was not strictly and constantly applied. From 1991 to 1992, the general rabies vaccination campaigns were not carried out because this period coincided with the outbreak of both African horse sickness and foot-and-mouth disease, which mobilized substantial human and material resources (**Figure 1**). From 1996 to 1998, the rabies vaccination of dogs was limited to campaigns isolated both geographically and over time (5). Consequently, the results fell well below the vaccination coverage targets set by the NRCP (i.e., 70–80% of the dog population).
- *NRCP covering 2000–2010:* this plan aimed to reduce the number of rabies cases within 5 years. The longer-term objective was to eliminate rabies within 10 years and ensure that the country then remained rabies-free. The strategy proposed, which is based on a generalization of medical prophylaxis supported by targeted health prophylaxis, required a change in regulations, regular awareness-raising activities among the general public, training, and retraining of the main players and the setting up of a national epidemiological surveillance network.

  Finally, a system to assess the proposed strategy was set up (5). This plan led to the vaccination of a maximum of 450,917 dogs in 2005 (5). The apparition of various health crises in the livestock sector led to veterinary services control efforts to combat or prevent the diseases by intensifying surveillance and/or vaccination campaigns (sheep pox vaccination campaigns in 2002, 2004, and 2006, avian influenza surveillance in 2005 and 2006, bluetongue vaccination campaign in 2007, and PPR vaccination campaigns in 2008, 2009, and 2010) (34). This prevented the plan from reaching its objectives.

Despite the limited effect of these different plans on the status of rabies in general, they nonetheless laid the foundation for future actions:

- Creation of an interministerial rabies control committee.
- The local production of an inactivated rabies vaccine for veterinary use produced on cells (69).
- Initiation of an operational epidemiological surveillance system (5).
- Development of a laboratory network comprising seven regional laboratories able to diagnose rabies using different OIE reference techniques (immunofluorescence, cell or mouse inoculation, and molecular biology). Of these, three (at Fes, Marrakech, and Rabat) accredited their rabies diagnosis analyses to standard ISO 17025 in 2012. **Table 3** shows the number of samples of animal rabies analyzed by laboratories between 1932 and 2015, data concerning the periods from 1932 to 1934, 1952 to 1958, 1963 to 1967, and 2010 to 2015. It may be seen that the mean percentage of samples confirmed positive by laboratory analysis has increased over time from 26% (minimum 20%, maximum 29%) for 1932–1934 to 62% (minimum 52%, maximum 74%) between 1952 and 1958, 70% (minimum 57%, maximum 86%) for 1963–1967 up to 104% (minimum 70%, maximum 168%) for the 2010–2015 period. Several rates exceed 100% for the latter period, probably due to the fact that several samples sent to a laboratory concern the same rabies outbreak. Nonetheless, an average of 20% (minimum 12%, maximum 30%) of cases were reported following clinical signs but not confirmed by a laboratory during the 2012–2015 period, which goes against OIE recommendations (70).

Since 2014, WHO, OIE, and FAO—supported by the Institut Pasteur network—have launched an initiative to eradicate rabies

TABLE 3 | Number of declared animal rabies cases and number of animal rabies laboratory-confirmed cases from 1932 to 2015.

	Year (reference)										
	1932 (2)	**1933 (2)**	**1934 (2)**	**1952 (28)**	**1953 (28)**	**1954 (28)**	**1955 (28)**	**1956 (28)**	**1957 (28)**	**1958 (28)**	**1963 (33)**
Official declaration	80	91	129	452	390	334	381	398	563	479	493
Laboratory confirmed rabies cases	23	18	38	284	243	185	232	207	363	354	365
Percentage	29	20	29	63	62	55	61	52	64	74	74
		1964 (33)	**1965 (33)**	**1966 (33)**	**1967 (33)**	**2010 (50)**	**2011 (51)**	**2012 (52)**	**2013 (53)**	**2014 (54)**	**2015 (55)**
		446	663	651	–	269	253	337	310	299	248
		382	405	374	325	453	346	297	243	210	204
		86	61	57	–	168	137	88	78	70	82

in North Africa in general, and Morocco in particular, by around 2020. This initiative is supposed to materialize the implementation of the concept (71). Since the initial kickoff workshop in 2014, the actions in the framework of this initiative have not yet been communicated.

The parenteral vaccination of owned dogs in rural settings has been the key measure in rabies control programs in Morocco since 1911 (1). However, this measure was rapidly revealed to be insufficient in the light of the tiny proportion of dogs vaccinated compared to the size of the total dog population. The culling of dogs as a means of controlling the dog population was suggested in 1935 (2). This twofold mechanism, involving the vaccination of dogs and culling of stray dogs, is still carried out today in Morocco.

Several reasons for the failure of this strategy have been identified from 1938 on and are still relevant today:

- Vaccinating dogs against rabies has a moral and sentimental rather than economic aspect to it compared to other livestock vaccinations. Vaccinating dogs is considered a luxury (29).
- The culling of stray dogs is not enough and only affects a few isolated cases. The mobility of stray dogs and their relations with the unvaccinated dogs found in douars (tent villages) are too frequent to allow this measure to fully succeed (28).
- By religious conviction, Moroccans refuse to destroy life, which explains why the dog population is so big (28).
- Moroccan farmers usually know the fatal issue of bite-related street rabies, yet refuse to sacrifice infected dogs by negligence or superstition (33).
- The rabies control program in terms of medical and health measures is insufficient (6).
- There are many players and they do not work closely enough together (6).
- There are insufficient resources (6).
- The socioecology of dogs is not yet well known (6).
- The management of rubbish dumps has to be rethought for the whole of the kingdom (6).
- Dog owners are not sufficiently aware of the problem and their responsibilities (6).

Several judicious proposals have been put forward by various authors from 1935 on to improve the situation and are still relevant:

- Vaccinate community dogs that roam free (2).
- Inform dog owners as actively as for other livestock vaccinations (2).
- Think of possible actions by kennel clubs, animal protection services, and even public hygiene services (2).
- Limit the number of dogs in douars (28).
- Instigate mandatory registration and vaccination of pet dogs (28).
- Investigate canine socioecology (56).
- Study the feasibility of oral vaccination as a complement to parenteral vaccination (6, 56).
- Regularly educate and raise awareness of rabies among the general public (6, 28).
- Associate/involve communes in the combat to control rabies (6).
- Strengthen intersectoral cooperation and give fresh impetus to the provincial rabies control centers (6).
- Improve infrastructures: rural slaughterhouses and public rubbish dumps (6).

Moroccan Dog Population

Several authors (5, 13, 72–74) have underlined the importance of a good estimation of the dog population in the success of rabies control programs. According to WHO, the size of the dog population may be estimated through the human:dog ratio (59). Studies of the dog population carried out in Morocco in 1993 assessed the human:dog ratio at 5.93 in rural settings and 25.36 in urban settings. In 1999, the ratio was found to be 7.93 in rural settings and 80.94 in urban settings (5). More recently in 2013, estimations of this ratio for North Africa gave 3.84 in rural settings and 9.83 in urban settings (73) and for Africa in general, 7.40 in rural settings and 21.20 in urban settings (13).

To estimate the current dog population, we chose the mean of national dog population estimates obtained in 1990s and international estimates obtained in 2005 and 2013, giving a human:dog ratio of 6.14 in rural settings and 34.33 in urban settings. This value is no doubt biased but the bias is acceptable. By applying the calculated human:dog ratio and taking into account Moroccan demographic data (the Moroccan population being estimated in 2015 at 34,271,622 in all, including approximately 13,458,258 in rural settings and 20,813,364 in urban settings) (data from target populations of health programs. Health Ministry website http://www.sante.gov.ma), we may conclude that the dog population is estimate to stand at 2,798,126 (of which 2,191,930 in rural settings and 606,195 in urban settings). This number could be overestimated but we consider that it is better to overestimate the target population rather to underestimate it.

It should be noted that generally speaking, there are few data about Moroccan dog population features (sex ratio, mean age, and life expectancy of an owned or stray dog). Although Moroccan legislation requires dog owners to vaccinate their pets, it remains silent on the management of this population, as mentioned earlier. Neither does it inspire responsible ownership in order to prevent dogs creating a nuisance within the community.

Managing the dog population is a complementary measure in rabies control and reducing the dog population does not directly affect the transmissibility rate (R0, i.e., the reproduction number) of the rabies virus (75). This runs contrary to the idea that canine rabies can be eliminated by reducing the density of the dog population (59, 66). This reduction in density is frequently achieved through culling campaigns that often prove counterproductive and have a major impact on animal welfare (11). Indeed, dog owners frequently begin hiding their dogs, moving them to other areas, or indeed acquiring new dogs to replace those killed. This behavior is linked to the need for dogs, itself related to their function. In Morocco, dogs are mainly used as guard dogs, to watch over livestock (31%), a combination of both (87%) or to hunt (2%) (76). Dog movements help disseminate the rabies virus, as reported in Indonesia (75) and North Africa, including Morocco (62). Furthermore, dogs that are easy to vaccinate are those that are the easiest to cull, thus reducing the dog population's immunity (66).

Dog sterilization campaigns are a key tool in the management of unwanted dogs. They reduce the trouble caused by dogs, along with their aggressive behavior and thus dog bites. They improve the human population's acceptance of free-roaming dogs and improve the health and life expectancy of dogs in a roaming population (77). Sterilization would increase the effectiveness of vaccination campaigns by stabilizing the size of the dog population and reducing its renewal rate. It is an important complementary measure in a rabies control program whose key thrust is vaccination coverage (66).

Currently, Moroccan communes are responsible for taking measures to prevent animals from roaming free. They must collect, check, and impound stray dogs in compliance with article 50 of the Communal Charter (64).

However, these functions are not fulfilled in most towns and those communes where they have developed various systems:

- Some communes organize armed hunts with hunting associations following citizens' complaints about the number of stray dogs. These hunting parties are held in daytime in urban settings. Communities and the press are increasingly hostile to this system (78, 79).
- Other communes lay strychnine-poisoned baits. This very dangerous method is illegal because the use of strychnine is regulated by Moroccan law (80). Furthermore, the use of this poison has a major ecological impact due to the harm it can cause to both wildlife and groundwater.
- Communes organize the capture of dogs in cooperation with the town's veterinary services or animal defense organizations. The veterinary services then put the animals down humanely using barbiturates (81).

There are several possible ways of getting out of this situation, alone or in conjunction depending on local conditions:

- Stimulate the networking of animal protection associations through contract programs (82). Several animal welfare associations are active in different regions of Morocco, the oldest having been active since 1916 (83–90). One example is an association working in the town of Essaouira that captures, identifies, sterilizes, and vaccinates against rabies then frees the stray cats and dogs captured at the place they were found (91). This model could be followed and extended to other towns in order to manage the stray cat and dog population. The Department of Agriculture is very experienced in monitoring and implementing contract programs with professional associations (92), an experience that could be capitalized on to develop contract programs with animal protection associations in order to manage the stray cat and dog population while still complying with departmental prerogatives and respecting animal welfare criteria.
- Delegate the management of municipal pounds and the impounding of stray dogs to the private sector. The experience of Madrid, Spain, in this area has recently been presented to the elected officials of Khemisset in the framework of the international partnership between Morocco and Spain on hygiene and public health (93).
- Raise awareness of dog owners about what being a responsible owner involves, especially with respect to the future of puppies from unwanted litters. This suggestion had already been put forward in 1959 (28).
- Use chemical or hormonal sterilization in conjunction with rabies vaccinations (94–97). It would be very useful to stimulate research into this possibility in the Moroccan context.

Vaccination Coverage of the Dog Population

The most efficient means of preventing human rabies cases is to reach a 70% vaccination coverage of the dog population (12, 66). The vaccination coverage rate of the dog population in Morocco can be estimated by dividing the total number of vaccinated dogs by the total dog population, calculated by adding together the following two figures:

- The number of dogs vaccinated in rural settings, which corresponds to the number of dogs vaccinated during free mass vaccination campaigns organized by the government. The rural dog population represents 78% of the total dog population, as previously estimated in this study.
- The number of dogs vaccinated in urban settings, which shall be estimated using the number of rabies vaccines sold by the veterinarian pharmaceutical companies authorized in Morocco to private veterinarians, divided by two. This is because the government-organized mass vaccination campaigns are not held in urban settings, and a dog living in town will only be vaccinated if its owner has it vaccinated by a private veterinarian. In practice, owners do not all follow the same vaccination protocol for their dog, despite the indications of vaccine manufacturers and private veterinarians. An owner may take his dog to the veterinarian only once for the primo-vaccination, or twice for a primo-vaccination divided into two injections, or take his pet for its annual booster only once in its life or never again after the primo-vaccination (personal observation). We consider that with a bias we accept that an owned dog in an urban setting is injected with rabies vaccine on average twice during its life. So the number of town-dwelling dogs, therefore, corresponds to the number of doses of rabies vaccines sold divided by two. The rabies vaccine is sold to private veterinarians by seven veterinary establishments. The list of products authorized per company is available on the ONSSA website (98). The vaccines marketed in Morocco are all inactivated adjuvanted vaccines prepared using different strains (VP12, G52, PV, Flury LEP, VP13, and CVS). The number of doses sold annually from 2009 to 2015 was provided by the companies themselves (**Table 4**). The number of sold doses increases by almost 5% each year.

It should be noted that the vaccination coverage from 2009 to 2015 never exceeded 6% of the total dog population. Urban vaccination coverage fluctuates between 6.51 and 8.25%, while rural vaccination coverage fluctuates between 2.47 and 5.73%

TABLE 4 | Number of rabies vaccine doses sold to veterinarians in the private sector from 2009 to 2015.

Year	Number of doses
2009	68,530
2010	71,040
2011	86,920
2012	70,200
2013	86,660
2014	85,640
2015	100,020

for the same period. The highest coverage rate in a rural setting was obtained during 2001–2010 NRCP, with 20.64% in 2005. The other national plans resulted in a maximum of 15.79% in 1994 and 11.41% in 1989. The data for urban vaccination coverage are not available before 2009. In any case, whether urban, rural, or total, the vaccination coverage rates are too low to break the transmission cycle of rabies virus. These data serve to confirm that since the first canine rabies vaccination in 1928, Morocco has only managed to vaccinate a tiny part of its dog population and is a very long way off the 70% vaccination coverage recommended by international organizations OIE and WHO (59, 70). Chevrier's observation in 1965 that "this vaccination is of no prophylactic benefit compared to the total dog population, so the issue needs to be completely reviewed" is just as true today (30). This operation has always been carried out with the same strategy, using government officials for vaccinations in rural areas and private veterinarians in towns. In addition, all previous official rabies control plans have always targeted to vaccinate owned dogs population rather than targeting the whole sensitive population (i.e., total dog population) and those plans did not propose any strategy to vaccinate the stray dogs. This led to the described limited results of vaccination coverage and rabies control failure.

In our opinion, one of the ways of improving canine vaccination coverage would be to involve private veterinarians in the free government-run vaccination campaigns, whether in rural or urban settings, as part of a public–private partnership. The synergy between ONSSA and private veterinarians during an action program to vaccinate sheep and cattle was successful in tackling various livestock diseases (PPR vaccination campaigns in 2008, 2009, and 2010; bluetongue vaccination campaign in 2007; sheep pox vaccination campaigns in 2011 and 2013, and foot-and-mouth disease vaccination campaign in 2015) (34). This public–private partnership managed on more than one occasion to successfully vaccinate 19.5 million sheep and 3.2 million cattle (92) within 3–4 months, resulting in a vaccination coverage of about 97% (34). The pathway to participation of private veterinarians has already been cleared through a decree establishing government remuneration of veterinarians in the private sector for the vaccination of dogs and cats in January 2015 (99).

Oral vaccination is another promising possibility currently under investigation for dogs. WHO has proposed various application scenarios, such as door-to-door vaccination, distribution at a central point, or a wildlife model (100). The latter involves jettisoning baits from aircraft, which is not very practicable for the oral vaccination of dogs. Unlike wildlife, the dog's habitat is closely linked to that of humans, making aerial distribution such as practiced in un- or little-populated areas where wildlife live unrealistic for dogs. Unlike injectable rabies vaccines, which are inactivated and often contain adjuvants, oral rabies vaccines are live attenuated vaccines or recombinant protein vaccines. Several oral rabies vaccines have market authorizations, yet only two are considered sufficiently safe by WHO (59, 100) to be used in proximity to people. One is Rabigen SAG2™, produced by Virbac SA, France (101), and the other is Raboral V-RG®, produced by Merial Inc., USA (102). The other commercial vaccines have residual virulence that can induce rabies, in target and non-target species (103, 104).

Studies have been carried out on the use of V-RG on dogs in Morocco, investigating the appetence of the bait and its efficacy under controlled conditions, but the study results were limited (49, 105). This had already been observed by other authors (72). Further research would be beneficial to investigate the efficacy of this vaccine on dogs and cats.

The results of a pilot study carried out in Morocco on the use of SAG2 for oral vaccination of dogs in field conditions were promising. The dog population in the study zone was composed of 70% of owned dogs and 30% of stray dogs. Using the door-to-door model (59), 77% of owned dogs ate the bait. Using the wildlife immunization model (59) in stray dogs, up to 73% of baits disappeared and 68% of the capsules containing the SAG2 vaccine were found pierced (106). Further research is needed to fine-tune the distribution strategy before large application in the field.

In our opinion, the oral vaccination of dogs is a way forward in conjunction with parenteral vaccination as recommended by WHO (59). It would reach stray dogs or dogs that are inaccessible due to their aggressive behavior and could be organized during mass parenteral vaccination campaigns. It would also be possible to distribute baits to well-informed owners so that they themselves give their dog the bait (on the condition that is in individual wrapping and kept at 4°C for no more than a few days), with strict instructions on giving the bait as soon as it has been opened. If not consumed straight away, it must be destroyed.

The use of new technologies has given good results by allowing real-time monitoring of mass vaccination campaigns (107). Several parameters can be assessed in real time, such as the number of dogs vaccinated, the proportion of dogs vaccinated compared to the total population, the GPS position of vaccination locations, and a map of the vaccination coverage per region for the whole country (107, 108). This should be able to be used in Morocco, one of the main advantages being that it would enable resources and vaccination teams to be redeployed in real time without having to wait for the end of a campaign before drawing conclusions.

All these difficulties underline the peculiarities of rabies compared to other livestock diseases, where often just one vaccination campaign is enough to improve the situation. For rabies, substantial efforts have to be made over several consecutive years on a sufficient large range of dog population, each interruption losing the benefits accrued up to then. This shows the importance of political determination and coordinated efforts. Rabies should never be accepted as banal. Even though it is not a disease with a direct economic impact (dogs generally not having an "economic" value), political efforts must be kept up over a long period so that the enthusiasm of vaccination teams does not wane year after year. Vaccination initiatives must be maintained in the light of an ever-increasing dog population and efforts should not be allowed to be diverted to other health priorities.

Application of the "One World, One Health" Concept

The "One World, One Health" concept was initiated in 2008 by FAO, OIE, and WHO with the support of the United Nations Children's Fund, the United Nations System Influenza Coordination, and the World Bank (109). It aims to develop a joint strategic network for coordinating medical, veterinarian, and environmental health policies to face up to the risks associated with the emergence or reemergence of zoonoses (109, 110). The major advantage of this concept lies in the economies of scale afforded through the efficiency of control and elimination measures, which is why it is so advantageous for low-income nations (66).

Latin America is a successful example of the "One World, One Health" concept as regards rabies. The strong political will of all the countries in that region was channeled into national public health and animal health action plans. Mass dog vaccination campaigns were held (59). The cooperation with NGOs, animal welfare organizations, and a close public–private partnership supported by efficient communication with local communities which were also heavily involved were the keys to the success of this rabies elimination program (66). Results were visible after a few years, by which time animal and human rabies cases had dropped by 90% (59).

The bases for this "One World, One Health" approach already exist in Morocco. The interministerial committee on rabies control is just one proof. The action of this committee should be supported by new legislation that gives it broader powers. Kenya, for example, created a "One Health Office" in 2011 in order to develop control strategies for the country's priority zoonoses, including rabies (111).

Since 2009, Morocco has celebrated World Rabies Day (112), an initiative launched in 2007 by the Global Alliance for Rabies Control. Held on September 28 each year, World Rabies Day seeks to focus the attention of the international community on rabies prevention and control measures (113). The World Rabies Day events from 2009 to 2013 were organized jointly by the National Food Safety Office, ONSSA, and the Hassan II Agronomics and Veterinary Institute, with the participation of other ministerial departments such as the Moroccan Ministry of Health, the Ministry of the Interior, the Ministry of National Education, and the Ministry of Islamic Affairs, in addition to local authorities, the Moroccan Association of Veterinary Professors–Researchers, the Society for the Protection of Animals and Nature along with the media. Various rabies-related actions were held on these occasions, including a rabies science day, the vaccination of dogs, information on rabies targeting elected officials in the communes, Friday sermon on rabies throughout all the mosques in Morocco, educating and informing primary school children about rabies, awarding of a prize to the journalist having done the best report on rabies, a radio broadcast, and inclusion on the news of the main TV channel (112). All these local and national events have raised awareness among the general public, especially young people, and will bear fruit in the long term.

CONCLUSION

Despite the fact that the first rabies vaccination for dogs dates back to 1911 in Morocco, rabies is still endemic. Despite an annual decline in the number of cases, the situation is alarming, and 19 deaths by rabies registered in 2015 is too high a price to pay. The epidemiological characteristics of the disease have been stable for the past century: dogs remain the vector and the reservoir of the disease, while other animal species are its victims. There are two peaks in the number of cases each year: one in the autumn and the other in the spring, in keeping with the sexual cycle of bitches. Rabies is endemic throughout Morocco, with a higher concentration of cases in areas where the human population is denser. The disease is mainly rural. The circulating virus is genetically homogeneous and belongs to the Africa 1 genotype. Several rabies control plans have been implemented, all with the same strategy of vaccinating owned dogs, opening rabies treatment centers, and increasing the budget for PEP. Unfortunately, the results are limited.

Morocco did not develop any strategy for dog population management, either owned dogs or stray dogs. Only a few old data exist about dog population characteristics. The Moroccan legislation does not deal with the concept of responsible dog owner, and rabies control strategies need to be developed and tested with all stakeholders' contributions to control and stabilize dog population.

In our opinion, the major reasons of failure of Moroccan strategies to control rabies are as follows:

- Lack of dog population knowledge and control
- Failure to implement any rabies control strategy in the event of another livestock health crisis
- Problem of human rabies case management
- Lack of coordination between departments
- Lack of law enforcement especially regarding antirabies dog vaccination
- Absence of the concept of dog responsible owner

Morocco needs a new approach to rabies control based on scientific advances and success stories in other parts of the world. Such an approach should include the following elements:

- Implementing an integrated approach in keeping with the "one world, one health" concept,
- Using a public–private partnership to extend the vaccination coverage of dogs and manage dog pounds,
- Updating current legislation to include:
  - the notion of a responsible owner;
  - sanctions if the law is not applied.
- Initiating contract programs with animal protection associations to sterilize dogs,
- Managing the dog population while complying with human population needs and animal welfare principles,

- Studying the socioecology of dogs (size and structure of the dog population) to fine-tune control strategies to be routinely implemented before each campaign,
- Combining parenteral and oral vaccination in preselected areas,
- Using new technologies to disseminate information better, including awareness of the general public,
- Improving and updating knowledge of professionals involved in rabies prevention and control by organizing regular trainings,
- Drafting and assessing the strategy chosen using international models,
- Estimating the annual economic cost of rabies (animal control and human prevention)

Rabies is not a fatality with which we have to live, but a fully preventable disease. Each day spent considering and refining strategies is another day of needless deaths.

AUTHOR CONTRIBUTIONS

SD, FC, MB, and OF-F: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content; and final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. MW, ER, and NA: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work and drafting the work or revising it critically for important intellectual content.

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REFERENCES

1. Matter H, Blancou J, Benelmouffok A, Hammami S, Fassi-Fehri N. Chapter 14: Rabies in North Africa and Malta. *Historical Perspective of Rabies in Europe and the Mediterranean Basin. Historical Perspective of RAbies in Europe and the Mediterranean Basin*. Paris: OIE (World Organization for Animal Health) (2015). p. 185–99. Available from: http://www.oie.int/doc/ged/d11246.pdf
2. Velu H. *La prophylaxie de la rage au Maroc*. Casablanca, Maroc: Direction Générale de l'Agriculture, Service de l'Elevage (1935).
3. OMS. *Rapport de la réunion OMS sur la lutte contre la rage canine au Maghreb*. Geneva, Switzerland: WHO (1985). Available from: http://apps.who.int/iris/bitstream/10665/62499/1/VPH_1985_fre.pdf
4. OMS. *Réunion OMS sur la lutte contre la rage dans les pays Maghrebins*. Alger: WHO (1990). Available from: http://www.who.int/rabies/animal/en/vph9092fr.pdf
5. Direction de l'Elevage. *Stratégie nationale d'éradication de la rage (2001-2010)*. Rabat, Maroc: Direction de l'Elevage, Ministère de l'Agriculture et de la Pêche Maritime (2001).
6. Amraoui F. *Situation épidémiologique de la rage au Maroc*. (2016). Available from: http://www.rr-africa.oie.int/docspdf/en/2016/REMESA/12th-REMESA-Rabies-Morocco.pdf
7. Napp S, Casas M, Moset S, Paramio JL, Casal J. Quantitative risk assessment model of canine rabies introduction: application to the risk to the European Union from Morocco. *Epidemiol Infect* (2010) 138:1569–80. doi:10.1017/S0950268810000415
8. Gautret P, Ribadeau-Dumas F, Parola P, Brouqui P, Bourhy H. Risk for rabies importation from North Africa. *Emerg Infect Dis* (2011) 17:2187–93. doi:10.3201/eid1712.110300
9. Cliquet F, Picard-Meyer E, Robardet E. Rabies in Europe: what are the risks? *Expert Rev Anti Infect Ther* (2014) 12:905–8. doi:10.1586/14787210.2014.921570
10. Ribadeau-Dumas F, Cliquet F, Gautret P, Robardet E, Le Pen C, Bourhy H. Travel-associated rabies in pets and residual rabies risk, Western Europe. *Emerg Infect Dis* (2016) 22:1268–71. doi:10.3201/eid2207.151733
11. Franka R, Smith TG, Dyer JL, Wu X, Niezgoda M, Rupprecht CE. Current and future tools for global canine rabies elimination. *Antiviral Res* (2013) 100:220–5. doi:10.1016/j.antiviral.2013.07.004
12. Shwiff S, Hampson K, Anderson A. Potential economic benefits of eliminating canine rabies. *Antiviral Res* (2013) 98:352–6. doi:10.1016/j.antiviral.2013.03.004
13. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda MEG, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83:360–8. doi:10.1590/S0042-96862005000500012
14. Anonyme. *Avis du 20 juin 1913 autorisant l'Institut Pasteur de Tanger à traiter les personnes mordues par des chiens ou autres animaux enragés ou suspects*. (1913). Available from: http://81.192.52.100/BO/fr/1913/bo_34_fr.pdf
15. Le Commissaire Résident Général, Commandant en Chef. *Arrêté résidentiel du 4 mai 1915 au sujet du fonctionnement de l'institut antirabique à Rabat*. (1915). Available from: http://81.192.52.100/BO/fr/1915/bo_133_fr.pdf
16. Le Commissaire Résident Général. *Dahir du 18 Chaabane 1332 (12 Juillet 1914) édictant des mesures de police sanitaire vétérinaire à l'importation des animaux et produits animaux*. (1914). Available from: http://81.192.52.100/BO/fr/1914/bo_92_fr.pdf
17. Le Commissaire Résident Général. *Dahir du 19 Chaabane 1332 (13 Juillet 1914) édictant les mesures pour garantir les animaux domestiques contre les maladies contagieuses*. (1914). Available from: http://81.192.52.100/BO/fr/1914/bo_92_fr.pdf
18. Ministère Plénipotentiaire Délégué à la Résidence Générale. *Arrêté viziriel du 20 Juillet 1915 prescrivant des mesures à prendre contre la rage (7 Ramadan 1333)*. (1915). Available from: http://81.192.52.100/BO/fr/1915/bo_145_fr.pdf
19. Ministère Plénipotentiaire Délégué à la Résidence Générale. *Arrêté viziriel du 29 Juillet 1927 (29 Moharrem 1348) prescrivant des mesures à prendre contre la rage et portant modification à l'arrêté viziriel du 20 juillet 1915 (7 ramadan 1333)*. (1927). Available from: http://81.192.52.100/BO/fr/1927/bo_774_fr.pdf
20. Ministère Plénipotentiaire Délégué à la Résidence Générale. *Arrête viziriel du 17 Juillet 1928 (29 moharrem 1347) complétant les arrêtés viziriels des 20 juillet 1915 et 29 Juillet 1927 prescrivant les mesures à prendre contre la rage*. (1928). Available from: http://81.192.52.100/BO/fr/1928/bo_823_fr.pdf

21. Remlinger P, Bailly J. La vaccination du chat contre la rage. *Presse Med* (1934):22.
22. Le Premier Ministre. *Dahir portant loi 1-75-292 du 5 choual 1397 (19 Septembre 1977) édictant des mesures propres à garantir les animaux domestiques contre les maladies contagieuses*. (1977). Available from: http://81.192.52.100/BO/fr/1977/bo_3388_fr.pdf
23. Ministère de l'agriculture du développement rural et des pêches maritimes. *Arrêté du ministre de l'agriculture du développement rural et des pêches maritimes n°12-00 du 30 ramadan 1420 (7 janvier 2000) édictant des mesures complémentaires et spéciales pour la lutte contre la rage*. (2000). Available from: http://81.192.52.100/BO/fr/2000/bo_4784_fr.pdf
24. Ministère de l'agriculture, du développement rural et des pêches maritimes. *Arrêté du ministre de l'agriculture, du développement rural et des pêches maritimes n°166-05 du 10 rabii I 1426 (19 avril 2005) modifiant l'Arrêté du ministre de l'agriculture du développement rural et des pêches maritimes n°12-00 du 30 ramadan 1420 (7 janvier 2000) édictant des mesures complémentaires et spéciales pour la lutte contre la rage*. (2005). Available from: http://81.192.52.100/BO/fr/2005/bo_5314_fr.pdf
25. Ministère de l'agriculture, du développement rural et des pêches maritimes. *Arrêté du ministre de l'agriculture, du développement rural et des pêches maritimes n°2271-13 du 17 moharrem 1435 (21 novembre 2013) relatif aux mesures complémentaires et spéciales pour lutter contre la rage animale*. (2014). Available from: http://81.192.52.100/BO/FR/2014/BO_6218_Fr.pdf
26. Aidaros H. *Monitoring and control of dog populations*. (2016). Available from: http://www.oie.int/eng/A_RABIES/presentations_rage/S4-5%20ControlOfDogPopulation_Prof%20Aidaros.pdf
27. Bailly J. La vaccination antirabique dans la pratique vétérinaire. *Rec Méd Vét* (1931) 107:929–40.
28. Chevrier L. Epidemiologie de la rage au Maroc. *Rev Elev Med Vet Pays Trop* (1959) 12:115–20.
29. Remlinger P, Bailly J. La vaccination antirabique des animaux au Maroc en 1933. *Maroc Med* (1934):12.
30. Chevrier L. *Evolution de la pathologie animale au Maroc de 1945 à 1965*. (1965). Available from: www.abhatoo.net.ma/content/download/41987/915487/version/1/file/Evolution+de+la+pathologie+animale+au+Maroc+de+1945+%C3%A0+1965.pdf
31. Ramon G. La lutte contre la rage chez les animaux et chez l'homme. Mesures sanitaires et vaccination. *Bull Off Int Epizoot* (1954) 41:1011.
32. Service Vétérinaire de Rabat. *Lutte Contre Quelques Maladies Frequentes Au Maroc Et Transmissibles A L'homme*. Rabat, Maroc: Service Vétérinaire (1956). Available from: www.abhatoo.net.ma/content/download/41902/913447/version/1/file/LUTTE+CONTRE+QUELQUES+MALADIES+FREQUENTES+AU+MAROC+ET+TRANSMISSIBLES+A+L%E2%80%99HOMME.pdf
33. Fassi-Fehri M, Morchid M. Quelques remarques sur l'épidémiologie de la Rage au Maroc. *Maroc Med* (1968) 48:624–30.
34. El Abrak A. *Privatisation de la médecine vétérinaire et concept du mandat sanitaire au Maroc*. (2015). Available from: http://www.rr-africa.oie.int/docspdf/en/2015/PPP/17.EL_ABRAK.pdf
35. Bakkali MM. Epidémiologie et Prophylaxie de la Rage au Maroc. In: Kuwert E, Mérieux C, Koprowski H, Bögel K, editors. *Rabies in the Tropics*. Berlin, Heidelberg: Springer Berlin Heidelberg (1985). p. 371–86.
36. Erroughi A. *Les complications des vaccinations antirabiques à propos de cinq cas*. (1976). Available from: www.abhatoo.net.ma/content/download/41563/905329/version/1/file/LES+COMPLICATIONS+DES+VACCINATIONS+ANTIRABIQUES+A+PROPOS+DE+CINQ+CAS.pdf
37. Fassi-Fehri N, Bikour H. L'endémie rabique au Maroc de 1973 à 1983. *Rev Sci Tech Off Int Epiz* (1987) 6:55–67. doi:10.20506/rst.6.1.287
38. Sebban A. *La rage et les traitements antirabiques au Maroc de 1977 à 1987 Thèse Doct. Méd.* Université Hassan II, Faculté de Médecine et de Pharmacie de Casablanca, (1988).
39. Bouchrit N, Khyatti M, Nourlil J, Dardari R, Ibrahimy S, Tordo N, et al. Déterminants de la rage humaine au Maroc: variabilité génétique, qualité du vaccin ou prise en charge insuffisante. *Méd Mal Infect* (2002) 32:508–13. doi:10.1016/S0399-077X(02)00407-9
40. Fassi-Fihri O. *Historique et situation epidémiologique de la rage au Maroc*. Rome: FAO (2008).
41. Ministère de la Santé. *Bulletin epidemiologique N°28*. Rabat, Maroc: Ministère de la Santé (1996). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
42. Ministère de la Santé. *Bulletin Epidemiologique Bilan 1998*. Rabat, Maroc: Ministère de la Santé (1998). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
43. Anonymous. *Situation épidemiologique de la rage animale au Maroc*. (2008). Available from: www.abhatoo.net.ma/content/download/14854/257974/version/1/file/SITUATION+EPIDEMIOLOGIQUE+DE+LA+RAGE+ANIMALE+AU+MAROC.pdf
44. Ministère de la Santé. *Bulletin Epidémiologique Bilan 1999*. Rabat, Maroc: Ministère de la Santé (1999). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
45. Ministère de la Santé. *Bulletin Epidémiologique, Bilan 2000*. Rabat, Maroc: Ministère de la Santé (2000). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
46. Ministère de la Santé. *Bulletin Epidémiologique, 4ème Trimestre 2001*. Rabat, Maroc: Ministère de la Santé (2001). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
47. Ministère de la Santé. *Bulletin Epidémiologique Bilan année 2002*. Rabat, Maroc: (2002). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
48. Ministère de la Santé. *Bulletin Epidémiologqie, Bilan année 2003*. Rabat, Maroc: Ministère de la Santé (2003). Available from: http://www.sante.gov.ma/Publications/Bulletins/Pages/Bulletin-epidemiologique.aspx (accessed January 9, 2016).
49. Zouine K, Ezzahra Lahkak F, Demerson JM, Fassi-Fehri O, Darkaoui S, Id Sidi Yahia K, et al. Situation, perspectives de lutte, faisabilité de la vaccination orale des chiens contre la rage. *Troisièmes Rencontres du bureau des experts de la rage du continent africain (AfroREB), Casablanca, 23–26 mai 2011* (2011).
50. ONSSA. *Rapport annuel ONSSA 2010*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2011). Available from: www.abhatoo.net.ma/content/download/44544/966087/version/1/file/Rapport+annuel+ONSSA++2010+.+Synth%C3%A8se+des+r%C3%A9alisations+physiques+des+structures+r%C3%A9gionales+et+centrales+de+l%E2%80%99Office+National+de+S%C3%A9curit%C3%A9+Sanitaire+des+produits+Alimentaires+%28ONSSA%29.pdf
51. ONSSA. *Reporting ONSSA 2011*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2012). Available from: www.abhatoo.net.ma/content/download/44545/966111/version/1/file/Reporting+ONSSA+2011+.+Synth%C3%A8se+des+r%C3%A9alisations+physiques+des+structures+r%C3%A9gionales+et+centrales+de+l%E2%80%99Office+National+de+S%C3%A9curit%C3%A9+Sanitaire+des+produits+Alimentaires+%28ONSSA%29+au+titre+de+l%E2%80%99ann%C3%A9e+2011.pdf
52. ONSSA. *Reporting ONSSA au titre de l'année 2012*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2013). Available from: www.abhatoo.net.ma/content/download/44546/966135/version/1/file/Reporting+ONSSA+au+titre+de+l%E2%80%99ann%C3%A9e+2012+.+Synth%C3%A8se+des+r%C3%A9alisations+physiques+et+financi%C3%A8res+des+structures+r%C3%A9gionales+et+centrales+de+l%E2%80%99Office+National+de+S%C3%A9curit%C3%A9+Sanitaire+des+produits+Alimentaires+%28ONSSA%29.pdf
53. ONSSA. *Reporting ONSSA au titre de l'année 2013*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2014). Available from: www.abhatoo.net.ma/content/download/44547/966159/version/1/file/Reporting+ONSSA+au+titre+de+l%E2%80%99ann%C3%A9e+2013+.+Synth%C3%A8se+des+r%C3%A9alisations+techniques+et+financi%C3%A8res+des+structures+r%C3%A9gionales++et+centrales+de+l%E2%80%99Office+National+de+S%C3%A9curit%C3%A9+Sanitaire+des+produits+Alimentaires.pdf
54. ONSSA. *Faits et chiffres 2014 – ONSSA*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2015). Available

from: http://www.onssa.gov.ma/fr/images/Publications/faits-marquants-2014.pdf
55. ONSSA. *Faits et chiffres 2015 – ONSSA*. Rabat, Maroc: Office National de Sécurité Sanitaire des produits Alimentaires (ONSSA) (2016).
56. El Harrak M. *Epidemiological Situation of Rabies in Morocco and Control Strategy*. (2008). Available from: http://www.rabmedcontrol.org/Communication/SadatCity-19April07/Rabies%2520in%2520Morocco.pdf (accessed April 23, 2014).
57. LNEZ. *Situation Epidemiologique De La Rage Animale Au Maroc*. (2008). Available from: http://www.fve.org/news/presentations/taiex/2008/2008_4_12_situationmaroc_nationallaboratoire.pdf
58. MARA. *Laboratoire de recherches du service veterinaire et de l'elevage rapport – annuel 1968*. Ministère de l'Agriculture et de reforme Agraire, Direction des Services Vétérinaires et de l'Elevage (1969). Available from: www.abhatoo.net.ma/content/download/31915/692577/version/1/file/LABORATOIRE+DE+RECHERCHES+DU+SERVICE+VETERINAIRE+ET+DE+L%27ELEVAGE++RAPPORT+-+ANNUEL+1968.pdf
59. WHO. WHO expert consultation on rabies. Second report. *World Health Organ Tech Rep Ser*. Geneva: WHO Press, World Health Organization (2013). p. 1–139.
60. Thevenot M, Aulagnier S. Mise à jour de la liste des mammifères sauvages du Maroc. Janvier 2006. *Go South Bull* (2006) 3:6–9.
61. Benda P, Jaroslav Č, Konečný A, Reiter A, Ševčík M, Uhrin M, et al. Some new records of bats from Morocco (Chiroptera). *Lynx (Praha)* (2010) 41:151–66.
62. Talbi C, Lemey P, Suchard MA, Abdelatif E, Elharrak M, Jalal N, et al. Phylodynamics and human-mediated dispersal of a zoonotic virus. *PLoS Pathog* (2010) 6:e1001166. doi:10.1371/journal.ppat.1001166
63. AFROREB. *Situation de la rage 2012*. (2013). Available from: http://searg.info/fichiers/afroreb/2013/posters/Maroc.pdf
64. Le Premier Ministre. *Loi n° 78-00 portant charte communale*. (2002). Available from: http://www.sgg.gov.ma/CodesTextesLois/Loiportantchartecommunale.aspx
65. OMS. *who-rabies-bulletin.org*. (2014). Available from: http://www.who-rabies-bulletin.org/about_rabies/classification.aspx
66. Cleaveland S, Lankester F, Townsend S, Lembo T, Hampson K. Rabies control and elimination: a test case for one health. *Vet Rec* (2014) 175:188–93. doi:10.1136/vr.g4996
67. Aubert M, Cliquet F. *Evaluation du programme de contrôle de la rage au Maroc*. Maroc: OMS (2001).
68. Kissi B, Tordo N, Bourhy H. Genetic polymorphism in the rabies virus nucleoprotein gene. *Virology* (1995) 209:526–37. doi:10.1006/viro.1995.1285
69. Darkaoui S, Fassi Fihri O, Schereffer JL, Aboulfidaa N, Wasniewski M, Zouine K, et al. Immunogenicity and efficacy of Rabivac vaccine for animal rabies control in Morocco. *Clin Exp Vaccine Res* (2016) 5:60. doi:10.7774/cevr.2016.5.1.60
70. OIE. *OIE Fiche d'information générale*. (2016). Available from: http://www.oie.int/fileadmin/Home/fr/Media_Center/docs/pdf/Disease_cards/RABIES-FR.pdf
71. Cohen N. *Lutte Antirabique A L'institut Pasteur: L' Histoire Continue …. Lett Pasteur*. Casablanca: Institut Pasteur du Maroc (2014). 16 p.
72. Fassi-Fehri N. *Contribution à l'étude épidémiologique de la rage canine au Maroc. Influence du Programme National de Lutte contre la Rage. Evolution de l'immunité humorale protectrice post vaccinale. Thèse Doct., Univ. Claude-Bernard, Lyon I*. (1993). Available from: http://cat.inist.fr/?aModele=afficheN&cpsidt=154607
73. Belsare AV, Gompper ME. Assessing demographic and epidemiologic parameters of rural dog populations in India during mass vaccination campaigns. *Prev Vet Med* (2013) 111:139–46. doi:10.1016/j.prevetmed.2013.04.003
74. Conan A, Kent A, Koman K, Konink S, Knobel D. Evaluation of methods for short-term marking of domestic dogs for rabies control. *Prev Vet Med* (2015) 121:179–82. doi:10.1016/j.prevetmed.2015.05.008
75. Townsend SE, Sumantra IP, Pudjiatmoko, Bagus GN, Brum E, Cleaveland S, et al. Designing programs for eliminating canine rabies from islands: Bali, Indonesia as a case study. *PLoS Negl Trop Dis* (2013) 7:e2372. doi:10.1371/journal.pntd.0002372
76. Fassi Fihri O. Un monde, une santé dans la lutte contre les zoonoses majeures: cas du projet ICONZ au Maroc. Exposé présenté à la réunion "La rage tue, jusqu'à quand?, Kenitra, Maroc (2013). 28 Septembre 2013.
77. FAO/GARC. *Developing a Stepwise Approach for Rabies Prevention and Control. Proceedings of the FAO/GARC Workshop*. Rome, Italy: FAO (2013). Available from: http://www.fao.org/3/a-i3467e.pdf
78. Reda M. *Sit-in devant le parlement contre l'abattage des chiens errants*. (2016). Available from: http://test.telquel.ma/2016/03/07/sit-in-devant-parlement-contre-labattage-chiens-errants_1486265
79. SOS Animaux Du Soleil. *Cagnotte: Refuge pour les animaux du soleil – Leetchi.com*. (2016). Available from: https://www.leetchi.com/c/local-de-sos-animaux-du-soleil
80. Le Directeur de l'Agriculture et des forêts. *Arreté du directeur de l'Agriculture et des forêts du 8 octobre 1955 modifiant l'arréêté du directeur général de l'Agriculture, du commerce et de la colonisation du 1er mars 1930 déterminant les vertébrés pour la destruction desquels les substances portées au tableau A annexé au dahir du 2 décembre 1922 peuvent être utilisées*. (1955). Available from: http://81.192.52.100/BO/fr/1955/bo_2242_fr.pdf
81. Tohry F-Z. *Aux anciens abattoirs, l'inévitable extermination des chiens errants*. L'Economiste (2015). Available from: http://www.leconomiste.com/article/968855-aux-anciens-abattoirs-l-inevitable-extermination-des-chiens-errants
82. RAPAD. *Gestion de la population canine Au Maroc Rapport effectué par l'ONG RAPAD Maroc*. Marrakech, Maroc: Réseau Associatif pour la protection animale et le développement durable au Maroc (RAPAD) (2016). Available from: http://rapadmaroc.org/wp-content/uploads/2016/04/GESTION-DE-la-POPULATION-CANINE-AU-MAROC-RAPAD.pdf
83. UMPA (Union Marocaine de Protection Animale). (2017). Available from: http://www.umpa-maroc.com/
84. SPANA (Société Protectrice des Animaux et de la Nature). (2017). Available from: http://spana.org.ma/
85. ADAN (Association de Défense des Animaux et de la Nature). (2017). Available from: www.adan-asso.com
86. AHPAE. (Association Hanane pour la Protection des Animaux et de l'Environnement). (2017). Available from: www.ahpae-maroc.com
87. fhh-sos-animaux. *SOS animaux au Maroc (Helga Heidrich Foundation)*. (2017). Available from: www.fhh-sos-animaux.com
88. Le coeur sur la patte. (2017). Available from: www.lecoeursurlapatteagadir.com
89. Lea Pollux. (2017). Available from: https://www.facebook.com/pages/Lea-Pollux/165918773565810
90. Le Sanctuaire de la Faune. (2017). Available from: https://www.facebook.com/Le-Sanctuaire-de-la-Faune-de-Tanger-SFT-131959403651870/
91. HSAM (Help the Street Animals of Morocco). (2016). Available from: http://www.hsam.org.uk/
92. MAPM. *Suivi de la mise en oeuvre des contrats programmes Gouvernement/Professionnels dans le cadre du Plan Maroc Vert*. Département de l'agriculture – Ministère de l'agriculture et de la pêche maritime. Ministère Agric Pêche Marit – Dép Agric (2014). Available from: http://www.agriculture.gov.ma/pages/actualites/suivi-de-la-mise-en-oeuvre-des-contrats-programmes-gouvernementprofessionnels
93. Morcillo AA, Vicario JMC, Howlett MG, Arco JJR, Rodríguez MFB. *Programa de Cooperacion Internacional Marruecos – España Concerniente A La Higiene Y La Salubridad Pública*. (2015). Available from: http://www.mastercongresos.com/sesa2015/imagenes/O-91.pdf
94. Yoder CA, Miller LA, Fagerstone KA. Population modeling of prairie dog contraception as a management tool. *Proc. Vertebr. Pest Conf*. (2015). p. 229–34. Available from: http://www.researchgate.net/publication/43279430_Population_modeling_of_prairie_dog_contraception_as_a_management_tool/file/d912f509408b2ef65c.pdf
95. Wu X, Franka R, Svoboda P, Pohl J, Rupprecht CE. Development of combined vaccines for rabies and immunocontraception. *Vaccine* (2009) 27:7202–9. doi:10.1016/j.vaccine.2009.09.025
96. Levy JK. Contraceptive vaccines for the humane control of community cat populations. *Am J Reprod Immunol* (2011) 66:63–70. doi:10.1111/j.1600-0897.2011.01005.x
97. Vargas-Pino F, Gutiérrez-Cedillo V, Canales-Vargas EJ, Gress-Ortega LR, Miller LA, Rupprecht CE, et al. Concomitant administration of GonaCon™ and rabies vaccine in female dogs (Canis familiaris) in Mexico. *Vaccine* (2013) 31:4442–7. doi:10.1016/j.vaccine.2013.06.061

98. ONSSA D. *Liste positive des médicaments vétérinaires*. (2016). Available from: http://www.onssa.gov.ma/fr/images/sante_animale/mv/liste-positivem-vaout2016.pdf
99. Ministère de l'agriculture et de la pêche maritime, Le Ministre de l'économie et des finances. *Arrêté conjoint du ministre de l'agriculture et de la pêche maritime et du ministre de l'économie et des finances N°4486-14 du 19 Safar 1436 (12 décembre 2014) fixant le montant des honoraires servis par l'Etat aux vétérinaires du secteur privé munis du mandat sanitaire et les modalités de son attribution*. (2015). Available from: http://81.192.52.100/BO/Fr/2015/BO_6326_Fr.pdf
100. WHO. *Oral Vaccination of Dogs Against Rabies*. Geneva: WHO (2007). Available from: http://www.who.int/rabies/resources/guidelines%20for%20oral%20vaccination%20of%20dogs%20against%20rabies_with%20cover.pdf
101. Cliquet F. Oral vaccines used for rabies control programmes: types, storage, quality control and performance in different species. *Meeting on enhancing rabies eradication in the EU: international co-operation, Helsinki, Finland*. (2006). Available from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.577.8853&rep=rep1&type=pdf
102. Blancou J, Artois M, Brochier B, Thomas I, Pastoret PP, Desmettre P, et al. Innocuité et efficacité d'un vaccin antirabique recombinant des virus de la vaccine et de la rage administré par voie orale au renard, au chien et au chat. *Ann Rech Vet* (1989) 20:195–204.
103. Hostnik P, Picard-Meyer E, Rihtarič D, Toplak I, Cliquet F. Vaccine-induced rabies in a red fox (*Vulpes vulpes*): isolation of vaccine virus in brain tissue and salivary glands. *J Wildl Dis* (2014) 50:397–401. doi:10.7589/2013-07-183
104. Vuta V, Picard-Meyer E, Robardet E, Barboi G, Motiu R, Barbuceanu F, et al. Vaccine-induced rabies case in a cow (*Bos taurus*): molecular characterisation of vaccine strain in brain tissue. *Vaccine* (2016) 34:5021–5. doi:10.1016/j.vaccine.2016.08.013
105. Youssef Y. *Etude comparative entre la vaccination orale et parentérale contre la rage chez des chiens en captivité*. (2011).
106. Darkaoui S, Boue F, Demerson JM, Fassi-Fihri O, Id Sidi Yahia K, Cliquet F. First trials of oral vaccination with rabies SAG2 dog baits in Morocco. *Clin Exp Vaccine Res* (2014) 4:220–6. doi:10.7774/cevr.2014.3.2.220
107. Gibson AD, Ohal P, Shervell K, Handel IG, Bronsvoort BM, Mellanby RJ, et al. Vaccinate-assess-move method of mass canine rabies vaccination utilising mobile technology data collection in Ranchi, India. *BMC Infect Dis* (2015) 15:589. doi:10.1186/s12879-015-1320-2
108. Banyard AC, Horton DL, Freuling C, Müller T, Fooks AR. Control and prevention of canine rabies: the need for building laboratory-based surveillance capacity. *Antiviral Res* (2013) 98:357–64. doi:10.1016/j.antiviral.2013.04.004
109. Operationalizing CDC. *"One Health": A Policy Perspective – Taking Stock and Shaping an Implementation Roadmap*. (2011). Available from: https://www.cdc.gov/onehealth/pdfs/atlanta/meeting-overview.pdf
110. Vallat B. Un monde, une seule santé. *Organ Mond Santé Anim* (2016). Available from: http://www.oie.int/fr/pour-les-medias/editoriaux/detail/article/one-world-one-health/
111. Mbabu M, Njeru I, File S, Osoro E, Kiambi S, Bitek A, et al. Establishing a one health office in Kenya. *Pan Afr Med J* (2014) 19:106. doi:10.11604/pamj.2014.19.106.4588
112. Bouslikhane M, Lhor Y, Fassi Fihri O. Le partenariat Institut Agronomique & Vétérinaire Hassan II (IAV) – Office National de Sécurité des Produits Alimentaires (ONSSA): Un modèle de collaboration prometteur en matière de lutte contre la rage au Maroc. *Lett Pasteur* (2014) 16:8–11.
113. Briggs D, Hanlon CA. World rabies day: focusing attention on a neglected disease. *Vet Rec* (2007) 161:288–9. doi:10.1136/vr.161.9.288

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Toward Elimination of Dog-Mediated Human Rabies: Experiences from Implementing a Large-scale Demonstration Project in Southern Tanzania

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A Rabies Elimination Demonstration Project was implemented in Tanzania from 2010 through to 2015, bringing together government ministries from the health and veterinary sectors, the World Health Organization, and national and international research institutions. Detailed data on mass dog vaccination campaigns, bite exposures, use of post-exposure prophylaxis (PEP), and human rabies deaths were collected throughout the project duration and project areas. Despite no previous experience in dog vaccination within the project areas, district veterinary officers were able to implement district-wide vaccination campaigns that, for most part, progressively increased the numbers of dogs vaccinated with each phase of the project. Bite exposures declined, particularly in the southernmost districts with the smallest dog populations, and health workers successfully transitioned from primarily intramuscular administration of PEP to intradermal administration, resulting in major cost savings. However, even with improved PEP provision, vaccine shortages still occurred in some districts. In laboratory diagnosis, there were several logistical challenges in sample handling and submission but compared to the situation before the project started, there was a moderate increase in the number of laboratory samples submitted and tested for rabies in the project areas with a decrease in the proportion of rabies-positive samples over time. The project had a major impact on public health policy and practice with the formation of a One Health Coordination

Unit at the Prime Minister's Office and development of the Tanzania National Rabies Control Strategy, which lays a roadmap for elimination of rabies in Tanzania by 2030 by following the Stepwise Approach towards Rabies Elimination (SARE). Overall, the project generated many important lessons relevant to rabies prevention and control in particular and disease surveillance in general. Lessons include the need for (1) a specific unit in the government for managing disease surveillance; (2) application of innovative data collection and management approaches such as the use of mobile phones; (3) close cooperation and effective communication among all key sectors and stakeholders; and (4) flexible and adaptive programs that can incorporate new information to improve their delivery, and overcome challenges of logistics and procurement.

Keywords: Rabies Elimination Demonstration Project, mass dog vaccination, Southeastern Tanzania, One Health, SARE

BACKGROUND

Rabies is one of the oldest known zoonosis, which is defined as an acute progressive encephalitis that almost inevitably results in death without timely intervention (1). Rabies can be transmitted by several hosts, but domestic dogs are the main species that transmit the disease to humans (2). With a growing recognition of the need for One Health approaches to tackle zoonotic diseases (3), it has been recognized that a paradigm shift is required to tackle human rabies in low- and middle-income countries (LMICs), by focusing on immunization of the primary reservoir hosts, the domestic dogs.

In terms of the disease burden, rabies is responsible for an estimated 59,000 human deaths globally, about 96.0% of which occur in Africa and Asia (4). Particularly, Asia contributes 59.6% of annual deaths due to rabies, while Africa contributes 36.4% of annual deaths (4). The escalation of dog rabies across much of Asia and Africa is mainly due to the low priority given to control of the disease. This low priority is in turn due to a lack of awareness of the true scale and magnitude of the disease burden as well as misperceptions as to the feasibility, cost-effectiveness, and public health benefits of dog rabies control (5, 6).

Since most LMICs still focus on post-exposure prophylaxis (PEP) as the only means to prevent human deaths from rabies (4), there is a clear need for greater focus on dog vaccination as a more sustainable and cost-effective way of addressing rabies in humans (7–9). Within this context, a demonstration project in Tanzania was initiated to prevent human rabies through the control and eventual elimination of canine rabies while improving the delivery of PEP to exposed patients, as well as surveillance and diagnostics. Finally, the project aimed to build a strategy to ensure sustainability of the rabies-free status beyond the project duration as illustrated in the Stepwise Approach towards Rabies Elimination—SARE (10).

Critical milestones of the project were therefore the progressive reduction and eventual elimination of human deaths due to dog rabies together with decreased numbers of PEP doses delivered. These should be concomitant with a reduction of dog rabies cases and/or positivity rate of dog samples tested in the laboratory, coupled with increasing immunization coverage in the dog population and evidence of rabies-free status. In light of these milestones, we present our experiences of implementing this large-scale rabies control project.

METHODOLOGY

Project Areas

The project site in Tanzania included the mainland regions of Dar es Salaam, Lindi, Mtwara, Morogoro, and Pwani, as well as Pemba Island. This covered a total of 28 districts including 4 from Pemba, and 459 wards, as of the year 2010, with more than 8 million inhabitants. Initially, the area was estimated to have about 400,000 dogs, based on dog-to-human ratios generated from other areas of Tanzania extrapolated to the districts in Southern Tanzania with similar population characteristics (11). Through household and post-vaccination surveys, the actual number of dogs was subsequently determined to be between 100,000 and 150,000 with much more variable human-to-dog ratios within districts.

The area of implementation was selected to exploit natural boundaries to facilitate the establishment and maintenance of a rabies-free area, including the coastline to the east, Udzungwa Mountains to the northwest, and Ruvuma River to the south. The Dar es Salaam–Mbeya highway to Morogoro and railway line to Kilosa defined the northern boundary of the project zone (**Figure 1**).

Project Management

The project was implemented collaboratively and primarily by bodies relevant to the animal and human health sectors with other sectors having a secondary role. The project organizational structure involved a national coordinator based at the World Health Organization (WHO)—Country Office of Tanzania. The National Coordinator worked with a multisector steering advisory committee, which consisted of representatives from key Tanzanian ministries dealing with livestock and human health through their focal persons, the WHO, the Sokoine University of Agriculture (SUA), and the University of Glasgow. Two laboratories dealt with diagnostic tasks: the Tanzania Veterinary Laboratory Agency (TVLA) in Dar es Salaam and the Sokoine

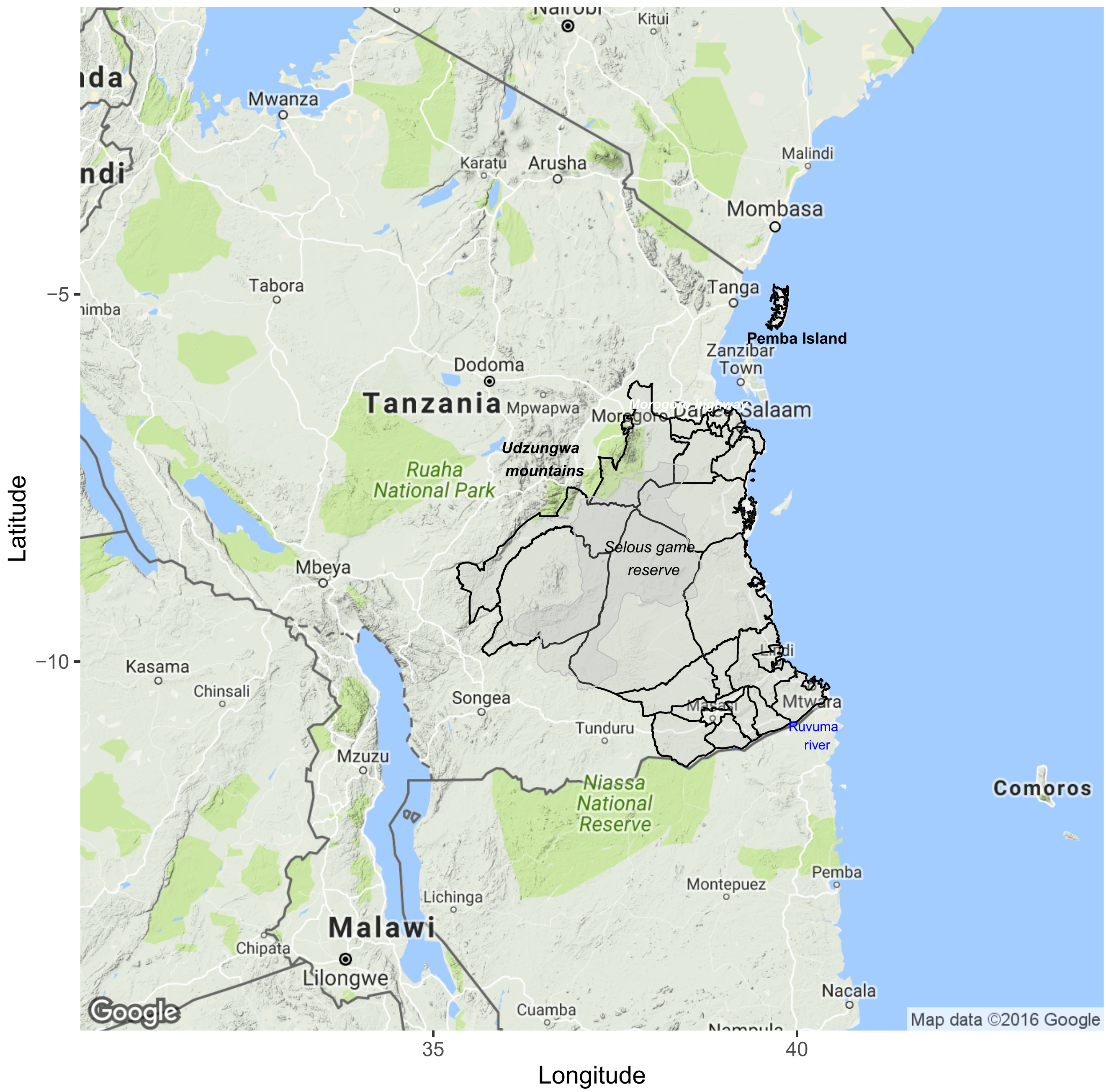

FIGURE 1 | Project area consisting of 28 districts from mainland Tanzania and Pemba Island. Districts within the project area are demarcated in black with natural boundaries highlighted including the highway and railway in the north, the coastline in the east, mountains to the west, and the Ruvuma River in the south. The Selous Game Reserve is shaded in gray.

University of Agriculture's (SUA) Faculty of Veterinary Medicine Laboratory in Morogoro.

Project Launch and Implementation

The project was internationally launched in 2009 when there was no large-scale rabies control program in Tanzania. In 2010, the project was initiated officially in Tanzania. Between 2009 and 2010, the necessary human and material resources for the project were set up, including infrastructure for implementation and working relationships between relevant sectors. With the aim to revaccinate each district annually, training sessions were delivered to district veterinary officers, district medical officers, health workers, and laboratory staff. In addition, standard operating procedures were established for control, prevention, and surveillance activities. Health information relevant to rabies was continuously delivered to community leaders, students, teachers, and the general public throughout the project.

Mass dog vaccination campaigns were conducted in phases, according to logistic constraints. Initially, the vaccination project focused on urban areas and then expanded to the entire project area, aiming to revaccinate each district annually. Household surveys and post-vaccination transects were used at different times during the project to estimate dog populations and vaccination coverage. Training and materials for sample collection and for diagnostic capacity were also provided by the project to district veterinary officers and livestock field officers. Fluorescent microscopes at the two laboratories were also refurbished with the support of the US Centers for Disease Control.

Under current national policy in Tanzania, PEP is distributed only to district hospitals. However, for this project, decentralized provision of PEP was established through training of staff and distribution of vaccines to four additional health facilities in each district. Health-care workers were trained in the more immunogenic and cost-effective intradermal (ID) administration of vaccine to animal bite victims (12) and in the use of human rabies immunoglobulins (RIG). PEP was provided free of charge to bite victims across the project areas.

Data Collection

The Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC) routinely records animal bites and human rabies deaths throughout Tanzania and numbers of human vaccinations administered and distributed within each district. These data were initially compiled before the project began to assess vaccine needs. During the project, the Ministry of Agriculture, Livestock and Fisheries (MALF) collected data on dog vaccination, and estimated dog populations and vaccination administration costs (13).

From 2011 onward, a mobile phone-based surveillance system was established to collect more detailed information needed for evaluation of project progress (14). Phones were distributed to the four health facilities responsible for district-level provision of PEP and to the district livestock officers. Livestock field officers and health workers were trained on how to report using mobile phones, enabling more rapid collection of extensive data than routine paper-based approaches. Variables collected included animal bite patient records, human rabies deaths (based on clinical criteria), PEP doses (demand and shortages), animals vaccinated during village-level vaccination campaigns, and results from laboratory investigation of samples and rabies suspect cases for animals. Livestock field officers and health workers collected and submitted these data as events occurred (vaccination campaigns, suspect rabid animals identified, animal bite patients reported to clinics). Researchers from Ifakara Health Institute monitored these records and followed up with users if they identified gaps without any submissions or if they received calls on a helpline indicating that difficulties had been encountered. The mobile phone-based surveillance provided relevant government stakeholders with more detailed accessible data for evaluation of the project.

The mobile phone-based system was also used to record the responses of a household survey conducted to assess initial vaccination coverage achieved and to review dog population estimates. A minimum of 30 households were sampled per village within 6 randomly selected villages for each district. Following campaigns conducted from 2013 onward, post-vaccination transects were completed by trained enumerators in each village. Transects were walked in every village on the day after the campaign in that village (~2 h duration) recording collared dogs (vaccinated) and dogs without collars (unvaccinated). Further details of these transects are provided in Sambo et al. (this issue).

In eight mainland districts in Southern Tanzania and on Pemba Island, contact tracing methods were followed to investigate declines in the numbers of bite patients. Contact tracing involved compiling bite records from mobile phone-based surveillance, and visiting households to interview bite patients and identify the status of the biting animal based on clinical criteria and circumstances of the bite. All subsequent and previous exposures and suspect rabies cases were also traced following established methods (15).

Here, we compile these data, describe progress, and discuss challenges and successes of the project, including lessons for scaling up large-scale rabies control and prevention activities elsewhere.

RESULTS

Mass Vaccination of Domestic Dogs

When the project was officially launched in Tanzania in 2010, mass dog vaccination campaigns were planned and delivered only in urban centers in Dar es Salaam and Morogoro as well as Ulanga and Kilombero districts where vaccination campaigns were ongoing in collaboration with the Ifakara Health Institute (**Figures 2** and **3**). However, operations were rapidly scaled up with mass vaccinations conducted across the rural areas of the project area in 2011. This was the first time that such large-scale mass dog vaccination campaigns had been conducted against rabies in Tanzania. The country in general, and project areas in particular, had no prior experiences with controlling rabies at this level or scale.

Relatively low numbers of dogs were vaccinated in some rural areas in the first phase of implementation and not all

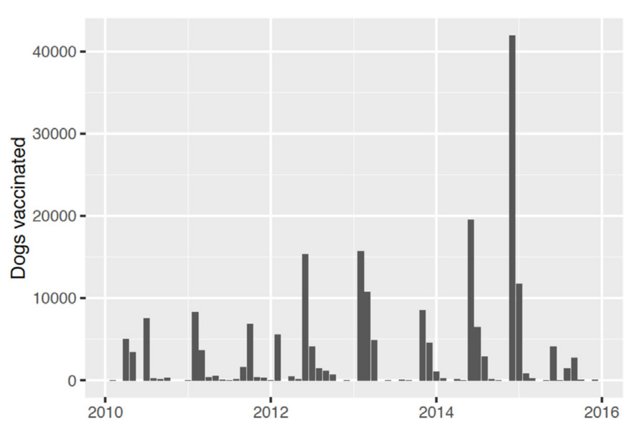

FIGURE 2 | **Numbers of dogs vaccinated by month during each year of the project.**

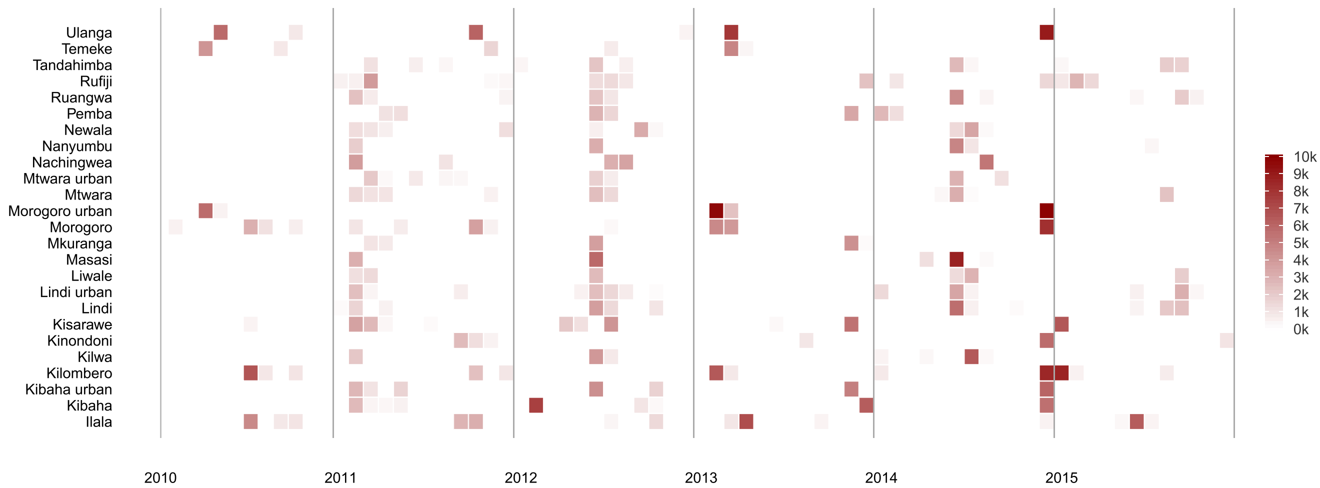

FIGURE 3 | **Dogs vaccinated in each district by month during each year of the project**.

district-level campaigns included every village; therefore, gaps in coverage were evident. Transects conducted from 2013 until 2015 indicated an average of 65% coverage in villages where campaigns were conducted (detailed analyses of these data are underway). Coverage was probably lower than this as transects tend to miss young puppies and campaigns were not completed in every village; however, given that substantially more dogs (and villages) were vaccinated than during the initial campaigns, this represented a major improvement in implementation.

Lessons learned in these early mass dog vaccination campaigns were incorporated into subsequent campaigns leading to an increase in dogs vaccinated as time went on (**Figure 2**). However, probably the single largest challenge to implementation was ensuring procurement and distribution of dog rabies vaccine within government and international systems. The initial plan was that dog vaccinations be conducted in each district annually. In practice, procurement challenges led to vaccination campaigns being conducted in phases involving a subset of local government authorities (**Figures 2** and **3**) and sometimes with long intervals between campaigns (**Figure 4**).

Logistical challenges included personnel changes in the WHO country office (16) and changes in vaccination procurement systems. A project officer was replaced, but recruitment was not immediate. With the absence of a project officer, several processes took longer to be implemented. Before the new procurement system, vaccines were procured internationally by the international project coordinator at the WHO headquarters, who then arranged shipment to the WHO country office in Tanzania. With the new system, all purchases related to government projects were required to go through a procurement process involving several procedures such as competitive tendering, deliberations by the procurement teams and selection of the supplier. These procedures meant that the purchase of vaccines was no longer straightforward, which led to disruptions in the vaccination schedule of the project. Lengthy intervals between campaigns were not ideal (**Figures 3** and **4**) and likely reduced their effectiveness. Detailed analyses of these data are underway to assess the impacts of these vaccinations and how this was affected by the disrupted schedule. A study to estimate the cost-effectiveness of the program in Tanzania found that the cost-per-dog vaccinated ranged from USD 2.5 to 22.49 across districts and phases with the average cost per phase falling from USD 11.27 in the first phase to USD 7.3 in the third phase (13). In comparison to other rabies elimination demonstration sites of KwaZulu-Natal and Cebu in the Philippines (17, 18), Tanzania had the highest cost-per-dog vaccinated mainly because of the

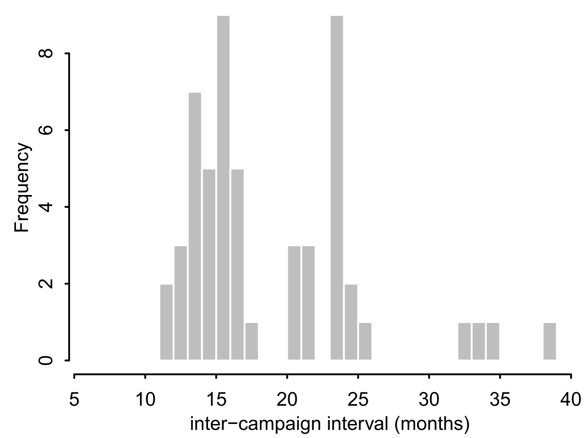

FIGURE 4 | **District-level inter-campaign intervals between mass dog vaccination campaigns**. Campaigns were initially intended to occur in every district 12 months apart. However, the actual distribution of intervals between consecutive campaigns varied from 11 months to over 30 months for some intervals in districts which only completed three campaigns within the 60-month period of study (2011–2015).

over purchase of the vaccine in the early phases of the program and purchasing equipment for a program starting from scratch.

Suspected Rabies Incidence, Bite Exposures, PEP Use, and Human Rabies Deaths

From January 2011 until December 2015, there were over 23,800 patient visits to clinics in the project area due to animal bites, with corresponding use of 22,295 doses of PEP. The age distribution of reported bite patients was consistent with previous findings from Tanzania and elsewhere, with younger people bitten more than adults (19–21). Overall, 45% of the bitten population was aged between 0 and 15 years of age, while over 50% of the bitten population was less than 20 years old.

The number of reported bite patients increased from 2011 to 2012 from just over 1,600 bite patients to more than 2,700 (**Figure 5**). From 2012 onward, bites declined, but fluctuations occurred particularly in 2014. When the project started in 2010, PEP was being administered solely through the intramuscular (IM) route, which has a maximum of five doses. However, following training of health workers, a rapid shift of delivery from IM to ID—which has a maximum of four doses—was observed. The average number of PEP doses received per bite patient was 2.4. The overall reduction in bite patients led to markedly less use of PEP. The concurrent transition to ID administration (**Figure 6**) means that less vaccine was needed for the same number compared to IM administration. The main issue encountered during the transition related to procurement and distribution of appropriate syringes. However, even with the shift to ID administration, shortages of PEP occurred, with Ulanga and Kilombero districts in Morogoro region the worst affected. Although training in RIG and its supply from external sources were also provided, RIG was used only infrequently (<1.5% of patients) due to scarcity, and most patients given RIG were treated between 2011 and 2013.

The areas with the largest dog populations (Morogoro region in central Tanzania) had the highest bite incidence and demand for PEP, whereas the most notable declines in bites were observed in the most southerly districts in Lindi and Mtwara regions (**Figure 7**). A cost-effectiveness study estimated that the cost per human PEP administered was approximately $22.41, while the cost per life saved ranged on average from $862 to $7,859 (13). Detailed contact tracing of suspect rabies cases from bite patient records indicated that rabies was locally eliminated on Pemba island, falling from 42 suspect animal rabies cases based on clinical criteria before vaccination campaigns in 2011 to just 2 in 2014 (**Figure 8**). No suspect rabies cases were identified on Pemba since May 2014 despite follow-up of all bite patients, until a recent incursion was detected in August 2016. Contact tracing in the southernmost districts of Tanzania also indicated major declines in suspect rabies cases.

Prior to the demonstration project, very little data on human deaths due to rabies were available. With the project implementation, more systematic follow-up of suspected human rabies cases was practiced throughout the project areas; however, none were laboratory confirmed. In 2010, 17 deaths due to rabies were recorded in the project areas. In the following year of 2011, there were 11 recorded deaths, which further declined to 3 in 2012. There were no suspect rabies deaths recorded in 2013. However, in years 2014 and 2015, the number spiked to 4 suspect rabies deaths for both years and just 2 in 2016. This decline was likely due to mass dog vaccinations reducing incidence in dogs, while awareness campaigns encouraged increased health seeking by dog bite victims and PEP accessibility improved. Among the recorded human rabies deaths, some bite victims did not seek treatment until symptom onset, whereas others sought care, but were unable to obtain vaccines.

Despite the training and materials for sample collection and diagnosis provided by the project, relatively few samples were submitted for testing. Local livestock officers reported considerable logistical difficulties in sample collection, including lack of resources and materials. Logistical disruptions to the project were known to have influenced sample collection during 2012 and 2013. However, despite these challenges and in comparison to the situation before the project started, more samples were collected and analyzed during the course of this project. Almost 98% of samples collected—submitted as heads of dead animals—came from domestic dogs, with the remaining 2% from cats, cows,

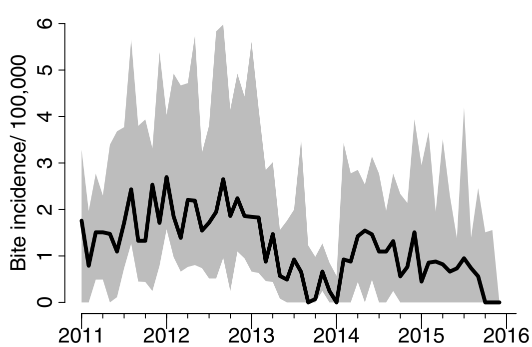

FIGURE 5 | **Average bite incidence/100,000 persons per month in the project area across districts and interquartile range of district-level bite incidence**.

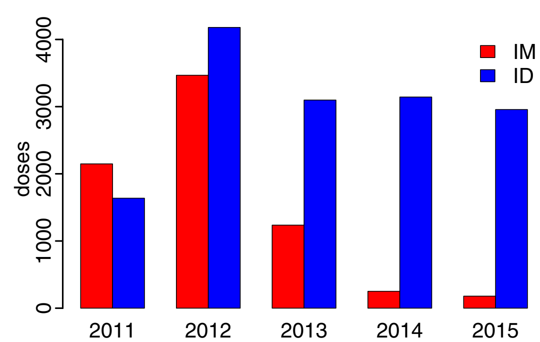

FIGURE 6 | **Transition from intramuscular (IM) to intradermal (ID) administration of post-exposure prophylaxis following training of health workers in 2010**.

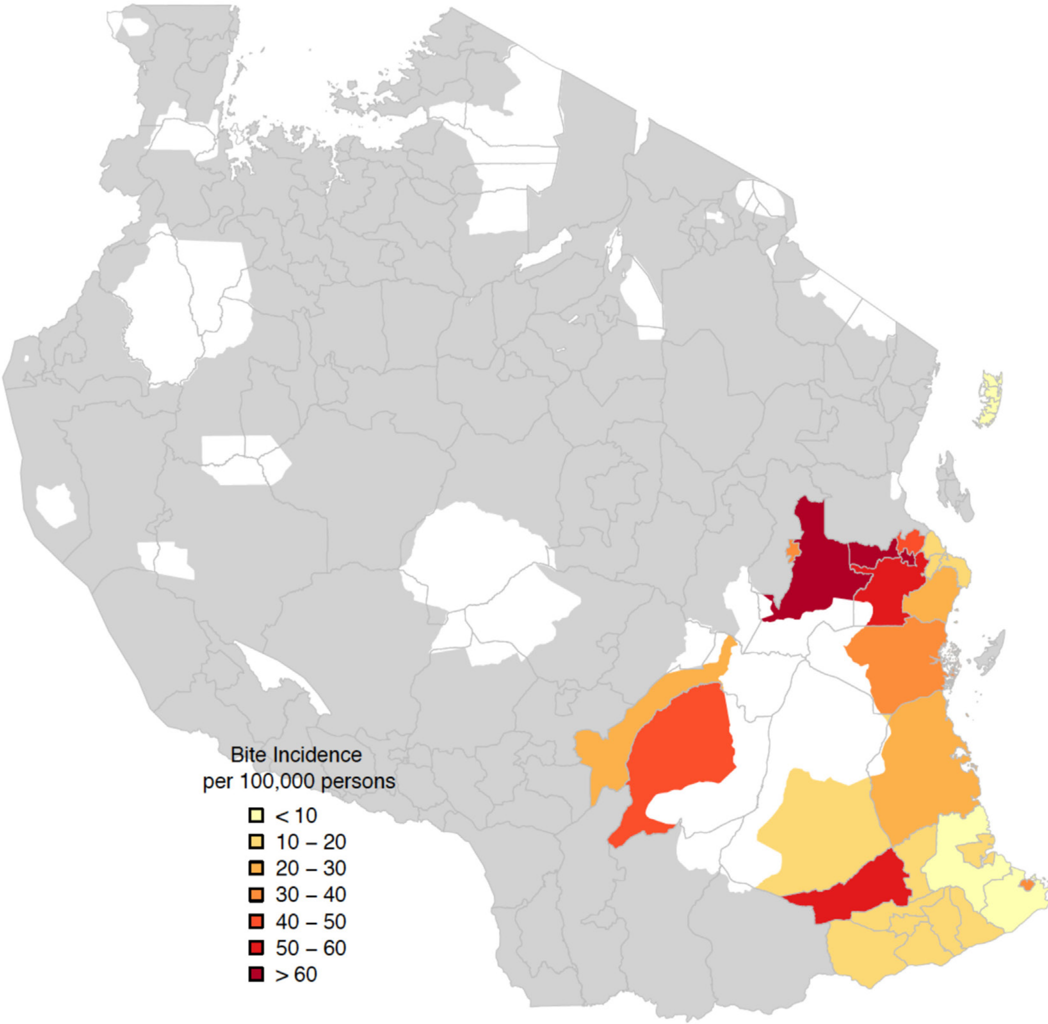

FIGURE 7 | Spatial distribution of average annual bite incidence/100,000 persons in districts in Southern Tanzania. White zones correspond to national parks.

goats, hyenas, jackals, and mongoose. The total number of samples per year showed an increasing trend with a few disruptions; there were a total of 22 samples in 2010, 40 samples in 2011, 60 samples in 2012, 22 samples in 2013, 150 samples in 2014, and 140 samples in 2015, making an average of 72 samples per year. About a quarter of all samples were diagnosed at the SUA laboratory, while three-quarters were diagnosed at the TVLA laboratory. While the number of samples submitted for diagnosis increased over the project duration, the proportion of rabies-positive samples decreased over time (**Figure 9**). Further analysis is underway to determine whether this fall in the number of rabies-positive samples was a direct effect of mass dog vaccination campaigns.

Impacts on Policy

The Rabies Elimination Demonstration Project in Tanzania brought about major changes in policy. The heightened awareness of rabies among policy makers led to the establishment of offices as well as guidelines focusing on rabies elimination. For the first time, a One Health Coordination Unit was formed in the Prime Minister's Office to coordinate health interventions of diseases and conditions whose management requires a multisectoral approach, such as rabies. In addition, a multisectoral body of experts coming from universities, ministries, research institutions, and the private sector finalized a National Rabies Control Strategy which envisions elimination of rabies in both humans and dogs in Tanzania by 2030 and takes many lessons from this demonstration project (22). To achieve the vision of elimination of rabies in Tanzania by 2030, the National Rabies Control Strategy follows the Stepwise Approach towards Rabies Elimination (SARE) (10).

DISCUSSION

Tanzania was among the three countries globally implementing the Rabies Elimination Demonstration Project through financial and technical assistance from the Bill and Melinda Gates Foundation (BMGF) and WHO. Activities were implemented through the MALF and the MoHCDGEC. The 5-year project

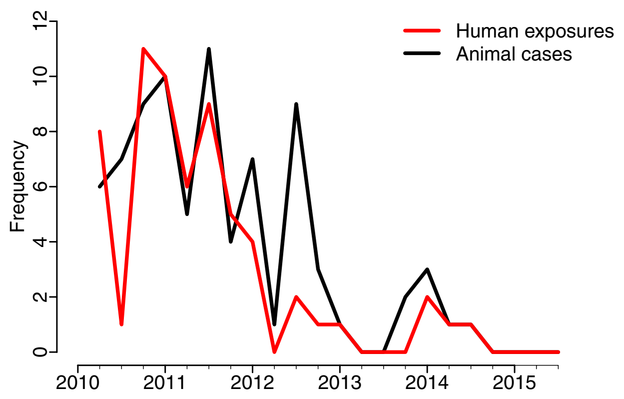

FIGURE 8 | Suspect rabies cases in animals and human exposures on Pemba Island by quarter (exposure, in the context of rabies, refers to being bitten by a possibly rabid dog).

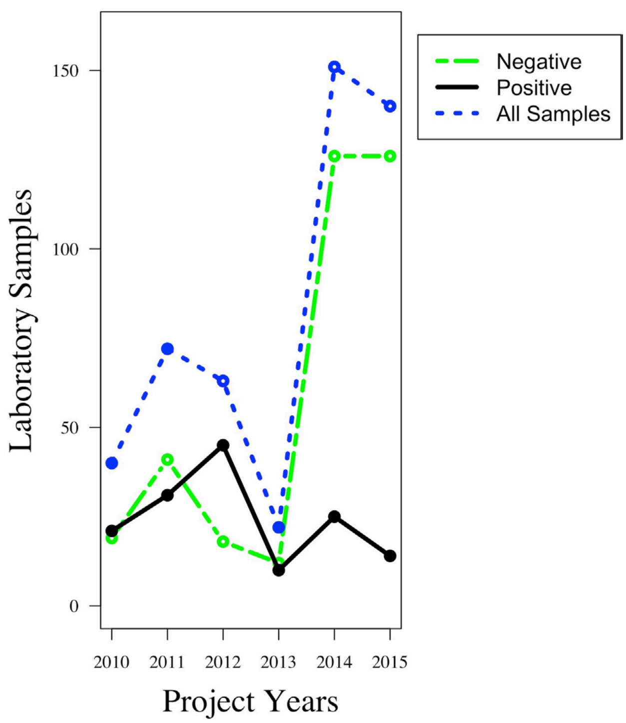

FIGURE 9 | Trends in the number of animal samples collected and analyzed between years 2010 and 2015. Before the project begun, only a handful of samples were collected and analyzed. That number rose steadily with the full installation of the project infrastructure, and in subsequent years, the proportion of rabies-positive samples showed a decline.

aimed at controlling and eliminating rabies in domestic dogs, thereby improving surveillance and diagnostics and providing targeted delivery of PEP to rabies-exposed patients. Five regions in Southern Tanzania including Pemba Island benefited from this project. Pemba Island was included for comparison of canine rabies elimination dynamics in island and inland settings.

The Rabies Elimination Demonstration Project in Southern Tanzania has achieved major successes. Since the project inception, major declines in dog bites and suspect rabies cases have been observed, with a concomitant fall in the demand for PEP, and a shift to more cost-effective ID administration of PEP. However, rabies is yet to be eliminated entirely from the project area. Moreover, the project encountered many challenges, mainly logistical from which lessons must be learnt for the future successful elimination of rabies from Tanzania and from across sub-Saharan Africa.

This was the first large-scale One Health project in the country, with major infrastructure and human resource challenges. These included unreliable estimates of the dog population needed to purchase vaccines and consumables, shortcomings in governance capacity that hindered coordination and implementation between and within animal and human health agencies, and a lack of experience in planning and delivering dog vaccination campaigns and in routine data collection to monitor their implementation. Lack of experience was rapidly overcome as livestock field officers and health workers became familiar with project activities and were supported by follow-up provided through the surveillance system. However the structural hurdles, such as unresponsive and overly bureaucratic procurement and distribution systems, and a lack of intersectoral coordination mechanisms were more problematic. These must be critically addressed for the future success of One Health programs in sub-Saharan Africa.

Difficulties were encountered in ensuring that budgets assigned to districts were not diverted to other local competing priorities and therefore those activities were conducted as required and scheduled, given the decentralized government structure. This was most apparent in the timing of vaccination campaigns, which were not conducted annually as initially planned. Interruption in campaign implementation is a recurring issue in LMICs, with problems encountered in the other project demonstration sites (23), but less than in Tanzania. An important question to address in future is therefore how such interruptions impact on progress toward rabies elimination and how these can be minimized.

Implications of overestimating the dog population in the project proposal were quite important, especially as Tanzania was allocated a large proportion of the total BMGF 5-year funding for rabies pilot projects. Its impact on the cost-effectiveness of the program is obvious considering that the actual dog population to be immunized was about a third of the initially estimated target population size. As a consequence, larger than needed quantities of dog vaccines were procured and stored for long periods of time. Moreover, funds for dog vaccination campaigns were kept unused with the possibility of being reallocated to more pressing activities, though for a large part excess dog vaccines (and budget) were available for future years. Subsequent vaccination campaigns and post-vaccination monitoring enabled assessment of coverage and informed future vaccine purchase (21). However, procurement obstacles for both vaccines and consumables were considerable. Partly, this was due to a lack of continuity in project leadership and shortcomings in organizational capacity (16). These challenges highlight the catalytic role that mechanisms such as the OIE rabies vaccine bank can play in overcoming bureaucratic challenges such as the tendering process to ensure a reliable supply of low-cost, high-quality vaccines.

Similar arguments apply to the supply of lifesaving PEP, which could be transformed if rabies post-exposure vaccines were incorporated within the portfolio of vaccines supported by the GAVI, the Vaccine Alliance. ID administration of PEP is cheaper than IM (reducing costs by at least 60% due to savings in vaccine) and equally immunogenic (12, 24–27). The rapid transition to ID administration demonstrated that health workers were capable of implementing this more cost-effective vaccine-sparing approach. Provision of free PEP administered intradermally to bite victims attending local health facilities greatly improved the PEP access across project areas. Nonetheless, even with this improved provision, PEP shortages still occurred, even at district hospitals, and this continues to be a challenge across the country more generally. Improved approaches are therefore needed for the distribution of lifesaving human rabies vaccines, given the unpredictability of demand, potential for epidemics, and urgency with which they must be administered.

Critically, many lessons spanning management, logistics, organization, implementation, and technological areas were learned through this project, which should be applied to the roll out of rabies elimination programs elsewhere in Tanzania and sub-Saharan Africa. These include the need to have a dedicated management unit with focused responsibilities to deal with rabies, for close cooperation of key sectors and stakeholders involved, and for flexible and responsive procurement and distribution systems. The Tanzanian government recognized the need for intersectoral financing and coordinating mechanisms and recently established the One Health Coordination Unit under the Prime Minister's Office to deal with endemic and emerging epidemics (28). Major costs for implementing the program were attributed to *per diem* payments for livestock field officers conducting campaigns out of their offices (13). This has prompted investigations into more efficient delivery methods for mass dog vaccination campaigns. The use of innovative methods such as mobile phones to support comprehensive surveillance infrastructure with timely data collection also improved decision-making. Spatial visualization of surveillance data and feedback from frontline health workers and livestock field officers captured through the mobile phone-based system were used to communicate to policy makers the role of local government and the differences in implementation and results across the project area (14).

Overall, it is clear that the program delivered valuable public health benefits, but it is also evident that if dog vaccinations are not continued these gains will be lost. The recent incursion on Pemba highlights this situation, where no vaccination campaigns were conducted since early 2014. However, the improved surveillance resulted in early detection and prompted a strong outbreak response. Moreover, it appears as though there is now only limited circulation of rabies in the southernmost districts in Tanzania and that elimination across a wider region is within reach. The ultimate success of the project will be seen in whether the sustainability plan for continued mass dog vaccinations is achieved and whether this leads to rabies elimination across the project area and spurs progress toward the elimination of rabies nationally.

ETHICS STATEMENT

This was a demonstration project that involved mass dog vaccination campaigns. However, aspects of mobile phone surveillance, since they involved humans, were granted ethical clearance by the Institutional Review Board of Ifakara Health Institute and the Medical Research Coordinating Committee of the National Institute for Medical Research of Tanzania (NIMR/HQ/R.8a/Vol.IX/946).

AUTHOR CONTRIBUTIONS

EAM conceived the general structure of the paper, analyzed data, and wrote the manuscript; TL contributed in writing the manuscript; SM and SL contributed by providing information about logistic challenges of the program; MM contributed by providing information about program implementation and challenges; CN contributed by providing information related to diagnostics part of the program; JC contributed by providing information about the implementation of the mobile phone surveillance; ZM contributed by providing information about the mobile phone surveillance; MS contributed information about estimation of human:dog ratio and program implementation; GM contributed information about implementation from the health sector; KL, SM, LS, GJ, CN, JC, ZM and MS all contributed to data collection and processing; KR, RM and ST contributed through data analysis and graphics; KL contributed information about project implementation; AN contributed information about project implementation from the WHO side; F-XM provided information about the early stages of the program; BA-R contributed information about project implementation and logistics; GJ contributed information about project implementation's challenges and success; EMM contributed ministry-specific information; and RK, TL, SC, and KH made substantial contributions to the conception of design, data analysis, and general layout of the work. RM contributed in reviewing and proof-reading the manuscript; LS contributed in field-specific information; ST contributed in project challenges-specific information.

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REFERENCES

1. Garg SR. *Rabies in Man and Animals*. New Delhi: Springer (2014).
2. WHO. *WHO Expert Consultation on Rabies: Second Report*. Geneva: World Health Organization (2013).
3. Nel LH, Taylor LH, Balaram D, Doyle KA. Global partnerships are critical to advance the control of neglected zoonotic diseases: the case of the global alliance for rabies control. *Acta Trop* (2015) 165:274–9. doi:10.1016/j.actatropica.2015.10.014
4. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
5. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda MEG, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83(5):360–8.
6. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
7. Kaare M, Lembo T, Hampson K, Ernest E, Estes A, Mentzel C, et al. Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* (2009) 27(1):152–60. doi:10.1016/j.vaccine.2008.09.054
8. Zinsstag J, Schelling E, Roth F, Bonfoh B, de Savigny D, Tanner M. Human benefits of animal interventions for zoonosis control. *Emerg Infect Dis* (2007) 13(4):527–31. doi:10.3201/eid1304.060381
9. Zinsstag J, Dürr S, Penny MA, Mindekem R, Roth F, Gonzalez SM, et al. Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc Natl Acad Sci U S A* (2009) 106(35):14996–5001. doi:10.1073/pnas.0904740106
10. Taylor L. Developing a stepwise approach for rabies prevention and control. *Proceedings FAO/GARC Workshop*. Rome (2014).
11. Knobel DL, Laurenson MK, Kazwala RR, Boden LA, Cleaveland S. A cross-sectional study of factors associated with dog ownership in Tanzania. *BMC Vet Res* (2008) 4(1):1. doi:10.1186/1746-6148-4-5
12. Ambrozaitis A, Laiškonis A, Balčiuniene L, Banzhoff A, Malerczyk C. Rabies post-exposure prophylaxis vaccination with purified chick embryo cell vaccine (PCECV) and purified Vero cell rabies vaccine (PVRV) in a four-site intradermal schedule (4-0-2-0-1-1): an immunogenic, cost-effective and practical regimen. *Vaccine* (2006) 24(19):4116–21. doi:10.1016/j.vaccine.2006.02.036
13. Hatch B, Anderson A, Sambo M, Maziku M, Mchau G, Mbunda E, et al. Towards canine rabies elimination in South-eastern Tanzania: assessment of health economic data. *Transbound Emerg Dis* (2016). doi:10.1111/tbed.12463
14. Mtema Z, Changalucha J, Cleaveland S, Elias M, Ferguson HM, Halliday JE, et al. Mobile phones as surveillance tools: implementing and evaluating a large-scale intersectoral surveillance system for rabies in Tanzania. *PLoS Med* (2016) 13(4):e1002002. doi:10.1371/journal.pmed.1002002
15. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7(3):e1000053. doi:10.1371/journal.pbio.1000053
16. WHO. *Report of the Fourth Meeting of the International Coordinating Group of the Bill & Melinda Gates Foundation–World Health Organization Project on Eliminating Human and Dog Rabies in Cebu City, Philippines, 2–4 October 2012*. Geneva (2013). Available from: http://apps.who.int/iris/bitstream/10665/79216/1/WHO_HTM_NTD_NZD_2013.1_eng.pdf
17. Miranda L, Miranda M, Hatch B, Deray R, Shwiff S, Roces M, et al. Towards canine rabies elimination in Cebu, Philippines: assessment of health economic data. *Transbound Emerg Dis* (2015) 64(1):121–9. doi:10.1111/tbed.12350
18. Shwiff S, Hatch B, Anderson A, Nel L, Leroux K, Stewart D, et al. Towards canine rabies elimination in KwaZulu-Natal, South Africa: assessment of health economic data. *Transbound Emerg Dis* (2014) 63(4):408–15. doi:10.1111/tbed.12283
19. Cleaveland S, Fevre EM, Kaare M, Coleman PG. Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries. *Bull World Health Organ* (2002) 80(4):304–10.
20. Hampson K, Dobson A, Kaare M, Dushoff J, Magoto M, Sindoya E, et al. Rabies exposures, post-exposure prophylaxis and deaths in a region of endemic canine rabies. *PLoS Negl Trop Dis* (2008) 2(11):e339. doi:10.1371/journal.pntd.0000339
21. Sambo M, Cleaveland S, Ferguson H, Lembo T, Simon C, Urassa H, et al. The burden of rabies in Tanzania and its impact on local communities. *PLoS Negl Trop Dis* (2013) 7(11):e2510. doi:10.1371/journal.pntd.0002510
22. United Republic of Tanzania. *National Rabies Control Strategy*. Dar es Salaam: United Republic of Tanzania through the Ministry of Agriculture Livestock and Fisheries (MALF) (2017).
23. WHO. *Report of the Fifth Meeting of the International Coordinating Group of the World Health Organization and the Bill & Melinda Gates Foundation Project on Eliminating Human and Dog Rabies in Dar es Salaam, United Republic of Tanzania, 8–10 October 2013*. Geneva (2014). Available from: http://apps.who.int/iris/bitstream/10665/102317/1/WHO_HTM_NTD_NZD_2014.2_eng.pdf?ua=1
24. Hampson K, Cleaveland S, Briggs D. Evaluation of cost-effective strategies for rabies post-exposure vaccination in low-income countries. *PLoS Negl Trop Dis* (2011) 5(3):e982. doi:10.1371/journal.pntd.0000982
25. Khawplod P, Wilde H, Tepsumethanon S, Limusanno S, Tantawichien T, Chomchey P, et al. Prospective immunogenicity study of multiple intradermal injections of rabies vaccine in an effort to obtain an early immune response without the use of immunoglobulin. *Clin Infect Dis* (2002) 35(12):1562–5. doi:10.1086/344954
26. Suntharasamai P, Warrell M, Viravan C, Chanthavanich P, Looareesuwan S, Supapochana A, et al. Purified chick embryo cell rabies vaccine: economical multisite intradermal regimen for post-exposure prophylaxis. *Epidemiol Infect* (1987) 99(03):755–65.
27. WHO. *Report of a WHO Consultation on Intradermal Applications of Human Rabies Vaccines, Geneva, 13–14 March 1995*. Geneva: WHO (1995).
28. Afrique One Alliance. *Control of Epidemic Disease in Tanzania: Dr Sayoki Mfinanga Presented the Contribution of Afrique One-ASPIRE*. (2016). Available from: http://afriqueoneaspire.org/activities/control-of-epidemic-disease-in-tanzania-dr-sayoki-mfinanga-presented-the-contribution-of-afrique-one-aspire/

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The Ilocos Norte Communities against Rabies Exposure Elimination Project in the Philippines: Epidemiological and Economic Aspects

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As canine rabies control in Africa and Asia transitions from research-led proof-of-concept studies to government-led programs for elimination, experience and evidence of their impact and costs must be shared for the benefit of future programs. The Ilocos Norte Communities against Rabies Exposure project was implemented in April 2012 by the provincial veterinary and health offices and supported by many other partners. It delivered a comprehensive dog vaccination program and increased awareness of the need for postexposure prophylaxis (PEP), aiming to eliminate human and animal rabies cases from Ilocos Norte by 2015. Prior to the intervention, confirmed rabies cases in dogs were between 19 and 50 per year (2008–2011). The primary outcome of the project was a reduction in rabies cases in both dogs and humans to 0 in 2014 and 2015, which has subsequently been maintained. Animal bite consultations increased significantly during the project. Economic data for the dog vaccination and PEP components of the project were collated for two sites: Laoag City (an urban setting) and Dingras Municipality (a rural setting) between 2012 and 2014. The average programmatic cost of vaccinating each dog was $4.54 in Laoag City and $8.65 in Dingras, and costs fell as the project reached more dogs. The average costs of providing PEP were $69.72 per patient and $49.02 per patient for the two sites, respectively, again falling as the project reached more people. External donor contributions contributed less than 20% of dog vaccination costs and less than 1% of PEP costs. The project demonstrated that rabies elimination can be achieved in a short period of time, with concerted effort across multiple sectors. A lack of clear dog population estimates hampered interpretation of some aspects of the programme. From 2016, the provincial government has assumed complete responsibility for the programme and must now continue the vaccination and surveillance efforts. Although safeguards are in place, reintroduction from surrounding areas remains a threat, and vigilance must be maintained.

Keywords: canine rabies, rabies elimination, dog vaccination, Philippines, anti-rabies vaccine costs

INTRODUCTION

Most canine rabies-endemic countries have been implementing rabies control efforts for decades. However, incomplete provision of postexposure prophylaxis (PEP) to dog bite victims, a lack of comprehensive dog vaccination campaigns, and weak collaboration between animal and human health sectors have prevented elimination of the disease (1). An estimated 59,000 human deaths a year still occur as a result of canine rabies (2).

Over the last decade, research-led proof-of-concept studies have provided theoretical and practical evidence that canine rabies elimination is feasible even in Africa and Asia where the disease still exerts a heavy burden (3–6). Success at scale has been achieved in Latin America, where major canine vaccination efforts have led to the elimination of the public health threat in many countries (7). In Africa and Asia, however, only a small number of countries or provinces have enacted effective mass dog vaccination programmes, for example, in KwaZulu-Natal in South Africa and SE Tanzania (5), Sri Lanka (8), and Bohol (9) and the Visayas region in the Philippines (5).

Research-led disease interventions focus on detailed data collection to gain an understanding of disease control mechanisms. In contrast, government-led interventions tend to implement accepted techniques at a larger scale, seeking to deliver health benefits but with less detailed assessment of the actual impact. Particularly because of the zoonotic nature of the disease, there is a need to document the ways in which rabies programs have been structured, the partners that have contributed, and the lessons learned.

BACKGROUND AND RATIONALE

Despite the 2008 Call for Action toward the Elimination of Rabies in the ASEAN Member States by 2020 (10), little progress toward this goal has been achieved. In December 2015, an ambitious global goal of an end to dog-mediated human rabies by 2030 was set (6). The global framework for rabies elimination developed at the December 2015 meeting is based on five essential program pillars: socioeconomic, technical, organization, political, and resource, to reflect the range of interventions necessary to ensure successful elimination (11). Lessons learned from government-led programs in how they implement these pillars and their successes and costs will benefit rabies elimination programs planned elsewhere and enable the faster scale up of programs necessary to reach rabies elimination.

A previous rabies prevention and elimination project, which was implemented from 2007 to 2009 on the island of Bohol in the Philippines, proved effective within 2 years (9). The same multisectoral model was adapted for Ilocos Norte to test whether rabies could be eliminated in a province bordered by areas still endemic for canine rabies. All activities implemented were anchored on the Philippines National Rabies Prevention and Control Program, which is well supported by legislation.

ESSENTIAL ELEMENTS OF THE INTERVENTION

The Ilocos Norte Communities against Rabies Exposure (CARE) project was implemented from April 2012 until September 2016. The multisectoral program was spearheaded by the Provincial Rabies Control Committee, with the Provincial Veterinary Office (PVO) collaborating with the Provincial Health Office (PHO) and other local agencies such as interior and local government, the Department of Education, local police, medical associations, and universities. A donation of animal rabies vaccines was provided by World Animal Health Organisation (OIE) through the OIE Regional Vaccine Bank for Asia and in kind support was received from the Department of Agriculture-Bureau of Animal Industry as well as provincial and local government units. Technical input was provided by the Global Alliance for Rabies Control through the support of the UBS Optimus Foundation.

The project's goal was to improve the existing rabies control approach and eliminate canine-mediated human rabies cases in the province by 2015. The interventions not only focused on comprehensive mass dog vaccination aiming to reach 70% coverage across the province and raising community awareness of the risk of rabies in a variety of school- and community-based settings but also involved additional training in surveillance and diagnosis. Barangay health workers and other volunteers were trained to support the rabies project and paved the way to increasing the number of dogs vaccinated during the project intervention phase. Educational interventions included an early childhood intervention program to teach animal bite prevention in preschool day care centers, integration of rabies information into the grade school curriculum, training of rabies speakers for the community, and various media outreach (separate manuscript in preparation). The activities of the full program are summarized in **Table 1** and reflect in 2015 the inclusion of a more rigorous monitoring system and a more extensive training program to ensure sustainability of the program after its completion. To intensify the one health surveillance system, a multisectoral reporting mechanism was institutionalized such that highly suspicious rabid dogs located following bite reports were placed under observation. After the end of the CARE project period, the local government partners are continuing to implement the program's initiatives to ensure that the public health benefits are maintained.

Here, we present the key epidemiological findings and an economic evaluation to determine the programmatic costs of the dog vaccination and human PEP provision.

METHODS

Study Site

Ilocos Norte is a province of the Philippines in the Ilocos Region, located at the northwest corner of Luzon Island. Its total land area is 3,622.91 km^2 (12). It is bounded by four provinces to the east and south and the South China Sea to the west. There are 13 mountains in the province, almost all in the southeastern portion. It has 557 barangays (the smallest administrative division) in 21 municipalities and 2 cities.

The human population of Ilocos Norte in the 2015 census was 593,081, a density of 170 people/km^2 (13). The majority (81.3%) of the population resides in rural areas. The province has one of the lowest poverty incidences in the Philippines, at 12.3% in 2015 (14), and the average annual family income in 2012 was

TABLE 1 | Rabies prevention and control activities implemented as part of the Ilocos Norte Rabies project.

Activities	Implemented by	2012	2013	2014	2015
Establishment of Provincial Rabies Control Committee	PVO, PHO	■			
Intersectoral collaboration (universities, animal welfare organization, professional groups, and media)	PRCC	■	■	■	■
Mobilize BRBVs	PVO	■	■	■	■
Train BRBVs as vaccinators	PVO, GARC				■
Mass dog vaccination	PVO, CVO, MAO, DA-BAI, OIE Vaccine Bank, GARC, UPCVM	■	■	■	■
Dog registration	PVO, CVO, MAO	■	■	■	■
Dog Population Survey	PVO, GARC, MAO, PDRRMO, HSI	■	■	■	■
Human Rabies Case investigations	PHO	■	■	■	■
Institutionalization of "One Health" response system	PVO, PHO, GARC				■
Laboratory diagnosis training and biosafety	PVO, RITM, GARC		■		■
Training on use of nets and humane handling of dogs	PVO, HSI, Cebu City DVMF, GARC				■
Dog rabies case investigation training	DARFU I, PVO				■
Rabies Speakers' Bureau (to increase community participation and advocate for rabies control)	PVO, MMSU, MAO, MHO, GARC				■
Integration of rabies in the grade school curriculum	PVO, PHO DepED, GARC			■	■
Early Childhood Intervention Program in Pilot Day Care/Pre-School Centers	PVO, PSWD GARC, MMSU				■
Provincial quiz bee on rabies	PVO, PHO, DepEd		■	■	■
Information campaign to strengthen border control	PVO, PHO, DA-BAI, DOH, GARC				■
Region I Rabies Summit (to disseminate achievements)	PVO, PHO, DA-BAI, DARFU I, CHD Region I, GARC				■
Policy advocacy for local government executives	PRCC	■	■	■	■
Media Awareness Workshop	GARC		■		
Awards for best local government rabies implementers	PRCC				■
Community-based survey (including Knowledge, Attitudes and Practice)	GARC, PVO, MMSU	■		■	

Shaded sections indicate the years that the activities were completed.

Key to project partners: Cebu City DVMF, Cebu City Department of Veterinary Medicine and Fisheries; CHD Region I, Centre of Health for Development Region I; CVO, City Veterinary Office; DA-BAI, Department of Agriculture Bureau of Animal Industry; DARFU I, Department of Agriculture Regional Field Unit; DepED, Department of Education; GARC, Global Alliance for Rabies Control; HSI, Humane Society International; MAO, Municipal Agriculture Office; MHO, Municipal Health Office; MMSU, Mariano Marcos State University; OIE, World Organisation for Animal Health; PDRRMO, Provincial Disaster Risk Reduction Management Office; PHO, Provincial Health Office; PRCC, Provincial Rabies Control Committee; PSWD, Provincial Social Welfare Development; PVO, Provincial Veterinary Office; RITM, Research Institute for Tropical Medicine; UPCVM, University of the Philippines College of Veterinary Medicine; BRBV, Barangay Bantay Rabies sa Barangay Volunteers.

Philippine pesos (PHP) 254,923 ($5,275 US at current exchange rates) (15).

Legislative support for rabies control is very good in the Philippines, with the Republic Act 9482 (the Anti Rabies Act of 2007) providing a comprehensive legal framework for the implementation of rabies prevention measures from national to local levels. Provisions of the law include the target of rabies elimination in the country by 2020; policies on mass dog vaccination, responsible pet ownership, and access to PEP; roles of different national agencies and local government units; and penalties for violators. The Provincial Government of Ilocos Norte enacted Provincial Ordinance no. 82–97 (Ordinance Governing Rabies Control in Ilocos Norte) in 1997, which was revised in 2001 and 2008 to adapt to the Anti-Rabies Act of 2007. All municipalities, cities, as well as two barangays also have respective ordinances on rabies.

Before the project implementation, rabies control efforts involved sporadic vaccination campaigns in response to rabies outbreaks, most recently in 2010, together with provision of subsidized PEP at animal bite treatment centers. Surveillance data showed 19–50 confirmed rabies cases in dogs and around 2 human deaths per year in the province from 2008 to 2011.

Surveillance Data

Surveillance data from the project site were extracted from the relevant national databases in the Philippines. Data on numbers of animals tested and confirmed canine rabies cases were obtained from the Regional Animal Disease Diagnostic Laboratory 1. Dog brain testing was carried out using the gold standard fluorescent antibody test at the Provincial Animal Rabies Diagnostic Laboratory of the PVO. Starting in 2016, Municipal Agricultural Offices are required to submit monthly negative monitoring reports to the PVO. Field staff at the municipal level list the barangays they have visited in a month and indicate in the report that they have not encountered a highly suspect rabid animal in the places they have visited.

Data on human rabies cases was obtained from the Epidemiology Bureau of the Department of Health. Cases are classified as suspect, probable, or confirmed. Suspect cases are those presenting with clinical signs of furious and paralytic rabies leading to coma and death. Probable cases are suspect cases with contact with suspected rabid animals. Confirmed cases are those with laboratory confirmation, which is not yet fully implemented in the Philippines. Data on the number of Animal Bite Treatment Centre (ABTC) consultations were obtained from the Center for Health Development for Region I. Bite consultations are collated from eight ABTCs across Ilocos Norte by the PHO quarterly and then submitted to the Region 1 Center for Health Development.

Dog Vaccinations, Dog Population, and Vaccination Coverage

As part of the CARE project, mass dog vaccinations were carried out in a rolling program from March to November each year from 2012, using a fixed point and door-to-door vaccination strategy. The province takes advantage of the publicity and awareness campaigns of the March national Rabies Awareness Month (preceding the bite incidence peak in summer) to start the mass dog vaccination campaigns, which end before the December holiday period in the Philippines. The strategy implemented in a particular location was chosen to best suit the geographic setting and the preferences of the community. Records of the number of dogs vaccinated in each barangay each year were collated by the Ilocos Norte PVO.

Several methods of dog population estimation have been used in Ilocos Norte. Before 2013, the dog population was estimated based on vaccination activities in high-risk areas (those with human rabies cases and city centers) and assuming a 1:10 dog:human ratio in all other areas. This strategy was improved by obtaining the number of dogs from city and municipality dog registration records. In 2014, a community-based survey (CBS) conducted house-to-house interviews utilizing cluster sampling of households and completing a structured questionnaire. This determined the proportion of households that owned dogs, determined the mean number of dogs owned, and provided an estimate for the dog:human ratio.

A more comprehensive dog population survey (including both owned and unowned dogs) was conducted early in 2016. This employed household surveys and dog counts conducted in 36 1 km × 1 km randomly chosen grids, corrected for incomplete detectability and incomplete coverage of roads within grids, where relevant. Corrected dog counts were then compared to human density data from Oak Ridge National Laboratory's Landscan data layer for the Philippines (2013) to give dog:human ratios for three different density categories (0–1,000 people/km^2, 1,000–5,000 people/km^2, and >5,000 people/km^2). From here, the total dog population of the province was estimated.

Overall vaccination coverage was estimated indirectly by dividing the total number of dogs vaccinated by the total population as assessed by the different dog population surveys.

Economic Data

Economic data for the provision of the dog vaccination program and PEP administration were collated for two sites: Laoag City (highly urban) and Dingras Municipality (rural), for the years 2012–2014. Costs were obtained by interviewing key personnel at the PVO, City Veterinary Office, and Municipal Agriculture Office of Dingras for the dog vaccination costs and the PHO, City Health Office, Gov. Roque B. Ablan Sr. Memorial Hospital ABTC, and Dingras District Hospital ABTC for the costs of providing PEP to bite victims.

The costs of (salaried) personnel, awareness and social mobilization (including volunteer training), vaccines, rabies immunoglobulin, consumables, and other cost categories were used to calculate the programmatic cost of vaccinating each dog and providing each course of PEP, as well as to indicate the division of costs between different stakeholders.

One of the three ABTCs in Laoag City was located within a government-operated hospital, but managed by a private health provider in 2012 and 2013. The private provider covered some personnel costs during this time, but the remaining costs were paid by the government hospital. In 2014, the government took over the ABTC's full management, which has remained the case since. The remaining facilities were fully managed by the government throughout the time period analyzed.

Costs were converted from PHP to US dollars (USD) using an exchange rate of 1 PHP = USD0.022.

RESULTS

Surveillance of Animal Cases, Human Bites, and Human Cases

During the course of the project, between 32 and 48 dog brains were sampled each year (**Table 2**). In 2012, eight dogs (23%) tested positive, which fell to 1 (2%) in 2013 and then 0 subsequently. These figures represent significant reductions from the average of 35.5 confirmed dog cases and the average of 38.8% samples proving positive for rabies from 2008 to 2011 (**Table 2**). The program of monthly negative monitoring reports started in 2016 has yielded no further case reports.

According to the national clinical criteria, one or two suspect human cases per year were diagnosed from 2008 to 2011. Following the implementation of the project, two suspect human cases were reported in 2012 and one in 2013. Since then, no cases have been reported, as of October 2016 (**Table 2**). This corresponds to an annual incidence (per 100,000) of 0.352 human cases in 2012, falling to 0.176 in 2013 and then to 0 from 2014 onward (**Table 2**).

Animal bite consultations rose from 3,070 in 2012 to a peak of 5,908 in 2014 and then fell to 5,520 in 2015, and 40–43% of patients were younger than 15 years (**Table 2**). The proportion of bites attributed to dogs was 83–89%, and other bites were from cats and various small mammals. Likely due to increased rabies awareness efforts by the Philippines government and an increase in the number of ABTCs in the province, the number of ABTC consultations had been rising prior to the CARE project's implementation. However, during the project, the rate of increase in uptake of these services rose markedly (**Table 2**).

Dog Vaccinations and Coverage

Before the project, around 12,000 dog vaccinations were conducted per year, apart from in 2010 when an emergency intervention in response to rising rabies cases increased this to over 28,000 (**Table 2**). As part of the CARE project, mass dog vaccination campaigns increased the number of barangays covered from 61.0% in 2012 to 75–87% in subsequent years and the number of dogs vaccinated to an average of 38,276 each year (**Table 2**).

The vaccination coverage achieved was not routinely collected as part of the vaccination campaign, leaving only indirect assessments based on the estimated dog population. The total dog population was initially estimated in 2012 at 35,000, based on numbers from previous vaccination campaigns in high-risk areas, and a dog:human ratio of 1:10 elsewhere. Subsequently, dog censuses were conducted by the barangay rabies volunteers every first quarter of the year before the start of the annual mass dog vaccination. These records yielded estimates of the owned dog population of 76,628 for 2013, 68,655 for 2014, and 63,815 for 2015.

Realizing that the dog population may have been underestimated, CBS was conducted in 2014. These surveys found that 65.9% of houses owned dogs, with 71% of those houses owning one or two dogs and 5% more than four dogs. The calculated dog:human ratio was 1:3.8, generating an estimated owned dog population of the province of 149,748, of which 67% were free roaming.

Finally, a rigorous dog population survey in 2016 calculated the unowned, owned roaming, and owned confined dog populations for each of three human density categories. For the human density categories <1,000 people/km^2, 1,000–5,000 people/km^2, and >5,000 people/km^2, the estimated total dog:human ratios calculated were 1:2.03, 1:2.55, and 1:2.25, respectively (see Table S1A in Supplementary Material). It concluded an overall dog:human ratio of 1:2.24, a total owned dog population of

TABLE 2 | Indicators of animal and human rabies risks over the project period.

	Prior to project implementation				After project implementation			
	2008	2009	2010	2011	2012	2013	2014	2015
Animal and human cases								
Dog brain samples tested	123	87	90	66	36	45	48	32
Confirmed dog cases	50	29	44	19	8	1	0	0
% of samples positive	40.7	33.3	48.9	28.8	22.2	2.2	0	0
Suspect human cases	2	1	2	2	2	1	0	0
Annual incidence of suspect human cases per 100,000 (N = 568,017)	0.352	0.176	0.352	0.352	0.352	0.176	0.000	0.000
Patients seeking animal bite consultations	897	954	1,475	2,015	3,070	3,571	5,908	5,520
Number of children seeking animal bite consultations (%)	Not available				1,265 (42)	1,378 (43)	2,052 (40)	1,394 (41)
Dog vaccinations								
Number of barangays reached by the vaccination campaign	329	342	381	266	340	420	485	447
% Barangays reached (n = 557)	59.1	61.4	68.4	47.8	61.0	75.4	87.1	80.3
Number of dogs vaccinated	12,044	12,203	28,581	12,066	23,539	39,647	38,722	36,460
% Dogs vaccinated (assuming n = 76,628)[a]	15.7	15.9	37.3	15.7	30.7	51.7	50.5	47.6
% Dogs vaccinated (assuming n = 149,748)[b]	8.0	8.1	19.1	8.1	15.7	26.5	25.9	24.3
% Dogs vaccinated (assuming n = 278,691)[c]	4.3	4.4	10.3	4.3	8.4	14.2	13.9	13.1

A child is defined as anyone 15 years or younger.

[a]*Concluded from dog censuses in 2013.*

[b]*Concluded from community survey in 2014.*

[c]*Concluded from comprehensive dog population assessment in 2016.*

217,469 (53% free roaming), and an additional 61,222 unowned free-roaming dogs, giving a total dog population estimate of 278,691 (overall 36% confined by owners) (Table S1B in Supplementary Material).

The very different dog population estimates mean that the vaccination coverage achieved by the project is very hard to calculate with certainty. Using the estimated dog population from the 2013 dog census (76,628), the average coverage level from 2013 to 2015 was 50.0%, but using the estimated population from the 2014 CBS, the average coverage was 25.6%, and using the 2016 comprehensive dog population survey data, the average coverage was just 13.7% (**Table 2**).

Alternative estimates of vaccination coverage came from household surveys conducted during the 2016 rigorous dog population survey, which suggested that 38.8% of owned dogs (and therefore likely around 30% of all dogs) had been vaccinated against rabies during the previous year. This is consistent with the 38% vaccination coverage of owned dogs estimated from the 2014 CBS.

Cost per Dog Vaccinated

The programmatic cost of vaccinating dogs (including vaccine, salaries, equipment, and other costs) and the derived cost per dog are presented in **Table 3**. For Laoag City, the average vaccination cost per dog fell from $7.03 to $3.09 over the 3 years of the project as the number of dogs vaccinated increased (overall cost = $4.54 per dog; **Table 3**). Costs for the Dingras Municipality (overall cost = $8.65 per dog) also fell when higher numbers of dogs were vaccinated after 2012, but were on average higher than in Laoag City, likely due to the lower number of dogs vaccinated, especially in 2012 (**Table 3**).

The breakdown of cost into components and by project partner is provided in Table S2 in Supplementary Material and summarized in **Figure 1**. Personnel costs formed the bulk of the expenditure (73.4% for Laoag City and 84.0% for Dingras Municipality), followed by the cost of the vaccine (13.5% for Laoag City and 6.0% for Dingras Municipality) with consumables and awareness activities the next highest costs (**Figure 1**).

The majority of funding for dog vaccination in Laoag City came from the city and provincial governments (56.8 and 24.2%, respectively; **Figure 1**). For Dingras Municipality, the bulk of the funding was provided by the municipality and the provincial government (78.7 and 11.8%, respectively). In each case, these were the main sources of funding for the personnel costs (Table S2 in Supplementary Material). National and provincial governments provided a very small proportion of the total funds spent, and donors (Global Alliance for Rabies Control and the OIE vaccine donation) provided a total of 19 and 9% of the dog vaccination costs for Laoag City and Dingras Municipality, respectively.

Costs per Patient Provided with PEP

The programmatic cost (inclusive of salaries and other components necessary to deliver vaccines) of providing each PEP dose and the total cost per patient for the two sites are shown in **Table 3**. Across both sites, the costs per patient fell as the project progressed and higher numbers of patients presented at ABTCs.

TABLE 3 | Programmatic costs for dog vaccination and postexposure prophylaxis (PEP) provision in Laoag City and Dingras Municipality.

	2012	2013	2014	Overall
Dog vaccination costs for Laoag City				
Total cost of dog vaccination (PHP)	1,110,365	1,040,485	1,054,202	3,205,053
Total cost of dog vaccination (USD)	24,428	22,891	23,192	70,511
Number of dogs vaccinated	3,476	4,527	7,513	15,516
Cost/dog (USD)	7.03	5.06	3.09	4.54
Dog vaccination costs for Dingras Municipality				
Total cost of dog vaccination (PHP)	591,155	751,045	648,821	1,991,021
Total cost of dog vaccination (USD)	13,005	16,523	14,274	43,802
Number of dogs vaccinated	726	2,982	1,357	5,065
Cost/dog (USD)	17.91	5.54	10.52	8.65
PEP costs for Laoag City				
Total cost for PEP (PHP)	2,156,857	2,297,622	2,755,215	7,209,695
Total cost for PEP (USD)	47,451	50,548	60,615	158,613
Number of PEP doses provided	2,295	2,402	3,397	8093.13
Number of patients vaccinated	636	726	913	2,275
Average doses/patient	3.61	3.31	3.72	3.56
Cost per PEP dose (USD)	20.68	21.05	17.85	19.60
Cost per patient (USD)	74.61	69.62	66.39	69.72
PEP provision cost for Dingras Municipality				
Total cost for PEP (PHP)	183,976	404,390	755,128	1,343,494
Total cost for PEP (USD)	4,047	8,897	16,613	29,557
Number of PEP doses provided	202	507	1,207	1,917
Number of patients vaccinated	63	158	382	603
Average doses/patient	3.21	3.21	3.16	3.18
Cost per PEP dose (USD)	20.01	17.54	13.76	17.11
Cost per patient (USD)	64.25	56.31	43.49	49.02

PHP, Philippine pesos; USD, US dollars.
The overall column shows the totals from 2012 to 2014, except for the costs per dog, per patient or per dose where the mean is given.

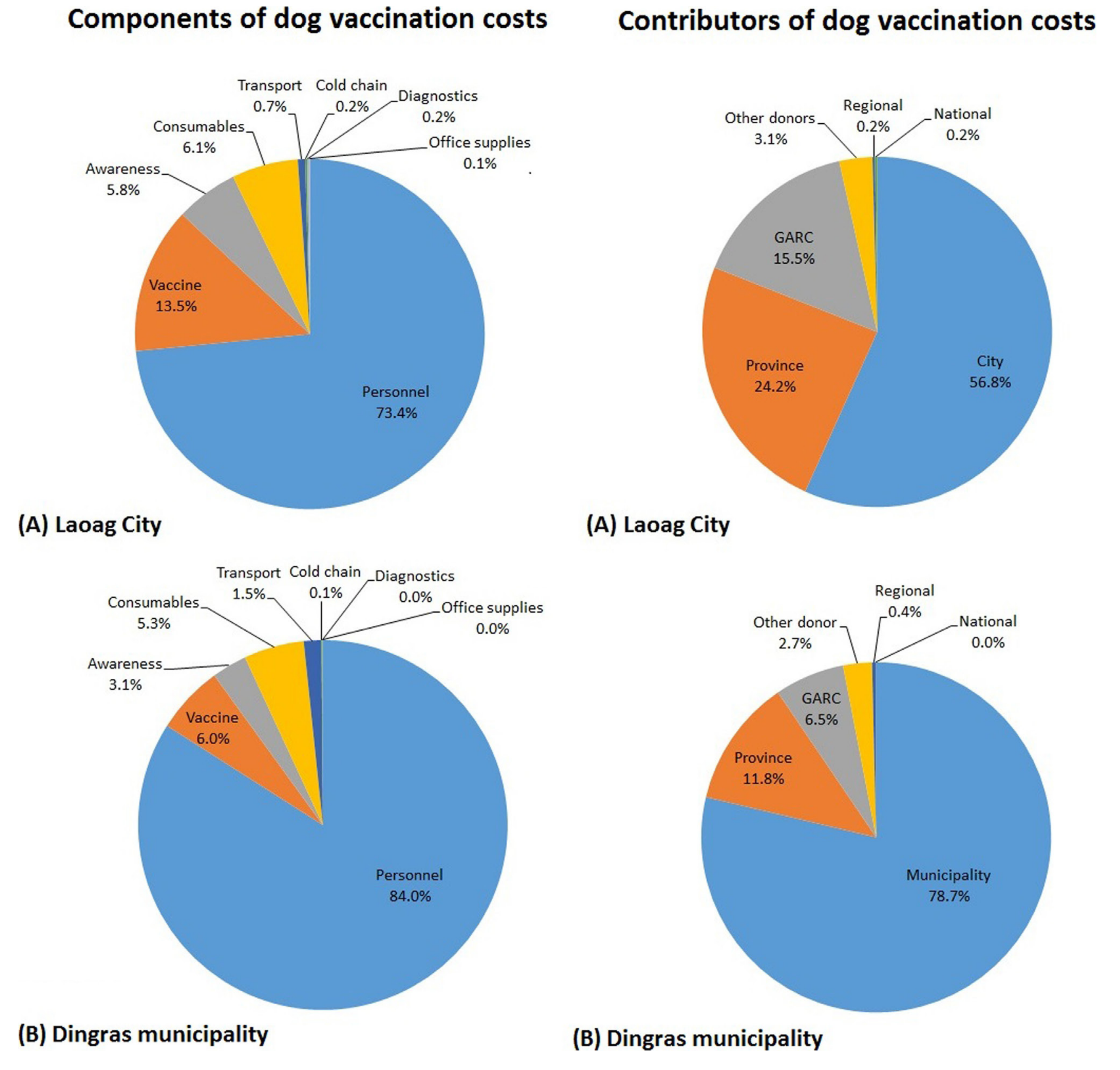

FIGURE 1 | **The cost of vaccinating dogs divided into the different components and between the different project contributors for (A) Laoag City and (B) Dingras Municipality from 2012 to 2014**.

Dingras, the rural municipality, had a lower average cost for providing PEP per patient than Laoag City (average of $49.02 per patient given PEP compared to $69.72 per patient), which is partly explained by the average number of PEP doses per patient being higher in the city, but also the price per dose of PEP being lower in Dingras (**Table 3**).

For PEP, the bulk of the costs for both project sites was attributable to the vaccine and biologics (69.6 and 80.0% for Laoag City and Dingras, respectively; **Figure 2**; Table S3 in Supplementary Material), with personnel the second highest component of cost (23.6 and 13.1%, respectively; **Figure 2**). The smaller proportion of personnel costs in Dingras compared to that in Laoag City may help to explain why the overall cost per PEP dose was lower.

At the time of this project, PEP was partially subsidized by the government, but patients still provided the most significant amount of the total cost of providing PEP (49.2 and 55.1%, respectively; **Figure 2**). Project donor contributions were insignificant (a small contribution toward awareness activities), and the bulk of the remaining costs were provided by local government with city and municipality supplying 38.0 and 23.8% of the costs to the sites, respectively (**Figure 2**).

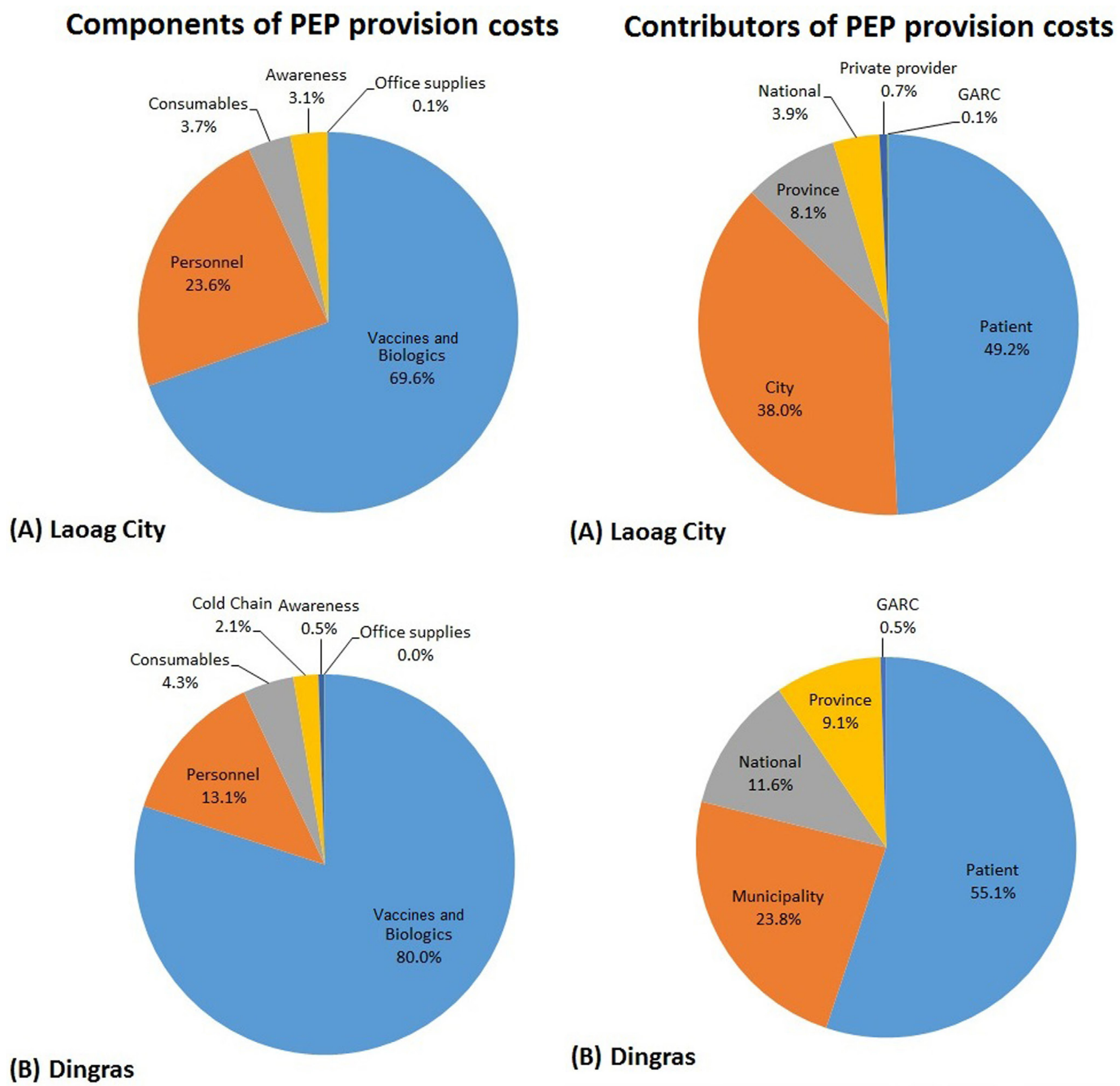

FIGURE 2 | The cost of providing postexposure prophylaxis (PEP) divided into the different components and between the different project contributors for (A) Laoag City and (B) Dingras Municipality from 2012 to 2014.

DISCUSSION

Governments in Africa and Asia are starting to translate research-led proofs of principle into practical rabies elimination interventions that save lives at scale. Although often not a priority, it is important to document such efforts for the benefit of rabies elimination programs evolving elsewhere.

Before the implementation of the CARE project, sporadic vaccination and emergency interventions produced some reduction in canine rabies case numbers, but failed to reduce them to zero. The CARE project demonstrated that more intensive dog vaccination efforts can break long-term cycles of rabies transmission. Consequently, human and canine case numbers were reduced to zero within 2 years. The trend in human rabies case numbers closely followed that of cases in dogs, as for previous rabies elimination programs (9, 16, 17), re-enforcing the value of focusing effort on dog vaccination. Other parts of the Philippines and other canine rabies-endemic countries could rapidly reduce their human rabies deaths by investing in more comprehensive canine vaccination.

The CARE program benefited from strong legislative and leadership support from the Philippines Government, strong intersectoral collaboration, and the regional and national surveillance systems able to provide a clear assessment of the progress of the project. Such supporting mechanisms facilitate the success and full evaluation of rabies control programs and should be prioritized during planning.

Of the total cost per dog vaccinated, a much higher proportion was attributed to personnel costs than to vaccine. Governments interested in conducting mass dog vaccination must invest in personnel costs and training, not just in the procurement of vaccines if campaigns are to succeed. Other provinces in the Philippines have access to vaccines from the national government, but do not have enough field staff to conduct effective vaccination campaigns, which needs to be addressed. The CARE project's use of volunteers such as barangay health workers who served as vaccinators, recorders, and community mobilizers could be replicated to enable limited personnel to be more effective and to facilitate higher community engagement, which delivers economies of scale.

One major drawback was the lack of accurate estimates of the total dog population, which seriously limited the estimations of the vaccination coverage, the surveillance effort, and the incidence of rabies in dogs. A number of other rabies control programs have suffered from initial dog population estimates that were too high [e.g., in Tanzania (18)], too low [e.g., KZN and Philippines (19)], or simply uncertain [e.g., Haiti (20)]. Reliable confidence intervals on dog population estimates are difficult to determine, but the conflicting data over coverage suggest that either the most detailed estimation of the dog population was too high (possible if the detailed survey was carried out in unrepresentative sites) or that the reporting vaccinations was not complete.

A valuable improvement for areas with poor data on dog populations would be to utilize mark–recapture assessments to provide estimates of vaccination coverage immediately after the first vaccinations are completed in a location (21, 22). This is labor intensive, but these data can very quickly provide "real-time" vaccination coverage data to guide catch-up or subsequent vaccination campaigns. Combined with accurate dog vaccination numbers, such surveys can also provide immediate feedback on the estimated dog population size.

Despite uncertainty over the exact vaccination coverage achieved, it is clear that the Ilocos Norte CARE project did break the cycle of rabies transmission with likely much lower than recommended (70%) vaccination rates in dogs. Lower than recommended vaccination coverages have also been noted in successful rabies control efforts in KwaZulu-Natal and the Philippines (6).

The recommended coverage of 70% is a conservative value (23), and it is possible that rabies in this province has a relatively low rate of spread. This could allow a modest increase in vaccination coverage achieved to still have a significant impact on transmission, which was suggested as possible in recent modeling studies (24). The estimated 36% of dogs that were kept confined by owners may have contributed to lower rabies transmission rates within the free-roaming dog population. However, the vaccination campaign was expected to have reached mostly owned dogs, and the estimated 22% of dogs without owners may not have been vaccinated. With only two private veterinary practices in Ilocos Norte, large numbers of privately vaccinated dogs are unlikely.

The reported dog cases were only those that were laboratory confirmed, so there is a risk that other cases could be missed. However, surveillance effort was consistent throughout the project, and the case numbers clearly decreased to zero, with monthly negative monitoring reports suggesting that this is still true. Through coordination between animal health and human health sector, animal bites from highly suspect rabid animals are investigated, and all suspect canine rabies cases in recent years have, after observation, been found to be negative.

Even as canine rabies cases fell, bite treatment numbers rose, a trend that has been found elsewhere (8, 9, 25, 26). The impact of educational and other community-based bite prevention activities usually increases the reporting rate of bites (seen here from 2012 to 2014) and could mask any effect of reduced numbers of bites occurring. However, given the extensive awareness exercises conducted in the CARE project, the availability of eight bite treatment centers, and the Philippines' government subsidy for PEP, a high percentage of patients were expected to seek treatment for bites by the end of the project. It is possible that the decrease in bite consultations between 2014 and 2015 may be a result of reduced number of bites, but this requires further data to confirm.

Lower costs per dog vaccinated with higher throughput and higher human density have been observed in other programs (18, 25), and overall costs fell in the middle and toward the higher end of the range of previously documented costs (27). In this project, a very small proportion of the costs of dog vaccination were from external donors, which is expected to be a good model for ensuring rabies control is sustained beyond the end of the project.

The cost per patient provided with PEP was consistent with other similar full programmatic cost assessments for Africa (18, 25, 26) and elsewhere in the Philippines (25). Interestingly in Ilocos Norte, the rural health center had lower costs on average than in Laoag City, explained by fewer PEP doses received per patient on average, and a lower programmatic cost per dose in Dingras. In Ilocos Norte, a large proportion of the costs were borne by the patients, similar to elsewhere in the Philippines, where patients paid around 50% of the total costs (25). This situation will change as the Philippines national government has agreed to pay for full courses of PEP for patients presenting from 2016 onward (28).

It is impossible to assess the relative value (and therefore cost-effectiveness) of each component of a mixed intervention. We know that canine vaccination is critical to halt rabies transmission, but education and awareness are critical to build trust and participation in the dog vaccination campaign, and to make sure that people seek PEP when needed. The relatively small investment in education campaigns (such as the training of Rabies Speakers in every municipality of Ilocos Norte) was likely a very cost-effective way to increase the program's impact.

From 2016 onward, annual mass dog vaccination campaigns will be planned and implemented by the provincial government. The established educational initiatives will continue to maintain high awareness and participation in vaccination programs, and the activities at borders, ports, and airports are expected to play an important role in preventing rabies being reintroduced into the province. There is evidence of increased investment in rabies control from the provincial government, which has invested in the renovation of Rabies Diagnostic Laboratories to enhance laboratory biosafety and biosecurity. One lesson learned already being acted upon is capacity building for vaccinators on the use of nets to catch free-roaming dogs to increase vaccination coverage in this high-risk population of dogs. The expertise gained and lesson learned from the CARE project are already being used to revise the National Rabies Program Manual of Operations, the Medium Term Plan which serve as the basis for the national elimination strategy.

Currently, the 38 nationally declared rabies-free areas in the Philippines are all islands. The absence of rabies in animals and humans for several years in Ilocos Norte has proven that rabies elimination at a provincial level in a landlocked area in one of the major islands of the Philippines is feasible. More active surveillance is now needed with an increase in the submission of dog samples to confirm continued rabies freedom. Laboratory confirmation of human cases is not yet carried out, but should be encouraged to enable viral genetic analysis that can differentiate reintroductions from local transmission. Such measures should be included in the national governmental guidelines to enable all areas in the Philippines to benefit from their application.

It is now a challenge to the national government to plan a more progressive zoning approach toward the elimination of rabies across other rabies-endemic provinces in the major islands of Luzon, Visayas, and Mindanao and to prevent incursions into rabies-free provinces.

CONCLUSION

A highly intersectoral model and widespread community engagement backed by national government support and surveillance systems provided the necessary boost to rabies control efforts to eliminate canine rabies from the province in a short time period. This occurred despite apparently low dog vaccination coverages. The programmatic costs were comparable to other recently published programmes and similarly showed decreasing costs as efforts were scaled. Donor funding comprised a small amount of the total investment, and local government support is sufficient that the results should be maintained going forward. However, as the province is still surrounded by endemic areas, vaccination and surveillance must be maintained to rapidly respond to possible reintroductions.

ETHICS STATEMENT

Veterinary and human health activities were conducted by the Provincial Veterinary Office and Provincial Health office under the implementation of the government's rabies elimination program and as such did not undergo a separate ethics review. All services provided were bound by Republic Act 9482 "Anti-Rabies Act of 2007," Republic Act 6713 "Code of Conduct and Ethical Standards for Public Officials and Employees," and Republic Act 9268 "The Philippine Veterinary Medicine Act of 2004." The data used in the study were based on records collated by the provincial veterinary and health offices.

AUTHOR CONTRIBUTIONS

LV and SJ oversaw the Ilocos Norte CARE project; AA, MC, DL, and RG-B collected and analyzed the data; and LT and LN lead the manuscript preparation. All authors contributed to drafting and editing of the manuscript and approved the final version.

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SUPPLEMENTARY MATERIAL

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REFERENCES

1. Lembo T, Attlan M, Bourhy H, Cleaveland S, Costa P, de Balogh K, et al. Renewed global partnerships and redesigned roadmaps for rabies prevention and control. *Vet Med Int* (2011) 2011:923149. doi:10.4061/2011/923149
2. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
3. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
4. Cleaveland S, Beyer H, Hampson K, Haydon D, Lankester F, Lembo T, et al. The changing landscape of rabies epidemiology and control. *Onderstepoort J Vet Res* (2014) 81(2):E1–8. doi:10.4102/ojvr.v81i2.731
5. WHO. *Rabies: Rationale for Investing in the Global Elimination of Dog-Mediated Human Rabies*. World Health Organization (2015). Available from: http://apps.who.int/iris/bitstream/10665/185195/1/9789241509558_eng.pdf
6. WHO, OIE. Global elimination of dog-mediated human rabies: the time is now! *Report of the Rabies Global Conference*, 2015 Dec 10-11, Geneva, Switzerland. Paris: World Health Organization and World Organisation for Animal Health (2016). Available from: http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Rabies_portal/EN_RabiesConfReport.pdf
7. Vigilato MA, Clavijo A, Knobl T, Silva HM, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368(1623):20120143. doi:10.1098/rstb.2012.0143
8. Harischandra PAL, Gunesekera A, Janakan N, Gongal G, Abela-Ridder B. Sri Lanka takes action towards a target of zero rabies death by 2020. *WHO South East Asia J Public Health* (2016) 5(2):113–6.
9. Lapiz S, Miranda M, Garcia R, Daguro L, Paman M, Madrinan F, et al. Implementation of an intersectoral program to eliminate human and canine rabies: The Bohol Rabies Prevention and Elimination Project. *PLoS Negl Trop Dis* (2012) 6(12):e1891. doi:10.1371/journal.pntd.0001891
10. ASEAN/OIE. *The South-East Asia Dog Rabies Elimination Strategy*. (2013). Available from: http://www.rr-asia.oie.int/fileadmin/SRR_Activities/SEA_Rabies_Strategy_-_OIE_Final_Draft.pdf
11. OIE. *Global Strategic Framework for the Elimination of Dog-Mediated Human Rabies*. (2016). Available from: http://www.oie.int/for-the-media/press-releases/detail/article/global-strategic-framework-for-the-elimination-of-dog-mediated-human-rabies/
12. Wikipedia. *Ilocos Norte*. (2016). Available from: https://en.wikipedia.org/wiki/Ilocos_Norte
13. Philippine Statistics Authority. *Population of Region I – Ilocos Region*. (2016). Available from: https://www.psa.gov.ph/content/population-region-i-ilocos-region-based-2015-census-population
14. Philippine Statistics Authority. *Poverty Incidence among Filipinos Registered at 26.3%, as of First Semester of 2015 – PSA*. (2016). Available from: https://www.psa.gov.ph/content/poverty-incidence-among-filipinos-registered-263-first-semester-2015-psa
15. Philippine Statistics Authority. *2012 Annual Average Income and Expenditure by Region and Province*. (2013). Available from: https://www.psa.gov.ph/content/2012-annual-average-income-and-expenditure-region-and-province
16. Ortiz-Prado E, Ponce-Zea J, Ramirez D, Stewart-Ibarra AM, Armijos L, Yockteng J, et al. Rabies epidemiology and control in Ecuador. *Glob J Health Sci* (2015) 8(3):113–21. doi:10.5539/gjhs.v8n3p113
17. Taylor LH, Nel LH. Global epidemiology of canine rabies: past, present, and future prospects. *Vet Med* (2015) 6:361–71. doi:10.2147/VMRR.S51147
18. Hatch B, Anderson A, Sambo M, Maziku M, McHau G, Mbunda E, et al. Towards canine rabies elimination in South-Eastern Tanzania: assessment of health economic data. *Transbound Emerg Dis* (2016). doi:10.1111/tbed.12463
19. WHO. *Report of the Fourth meeting of the International Coordinating Group of the Bill & Melinda Gates Foundation–World Health Organization Project on Eliminating Human and Dog Rabies*. Cebu City, Philippines (2013). Available from: http://apps.who.int/iris/bitstream/10665/79216/1/WHO_HTM_NTD_NZD_2013.1_eng.pdf?ua=1
20. Millien MF, Pierre-Louis JB, Wallace R, Caldas E, Rwangabgoba JM, Poncelet JL, et al. Control of dog mediated human rabies in Haiti: no time to spare. *PLoS Negl Trop Dis* (2015) 9(6):e0003806. doi:10.1371/journal.pntd.0003806
21. Lechenne M, Oussiguere A, Naissengar K, Mindekem R, Mosimann L, Rives G, et al. Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* (2016) 34(4):571–7. doi:10.1016/j.vaccine.2015.11.033
22. Gibson AD, Ohal P, Shervell K, Handel IG, Bronsvoort BM, Mellanby RJ, et al. Vaccinate-assess-move method of mass canine rabies vaccination utilising mobile technology data collection in Ranchi, India. *BMC Infect Dis* (2015) 15:589. doi:10.1186/s12879-015-1320-2
23. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14(3):185–6. doi:10.1016/0264-410X(95)00197-9
24. Fitzpatrick MC, Shah HA, Pandey A, Bilinski AM, Kakkar M, Clark AD, et al. One health approach to cost-effective rabies control in India. *Proc Natl Acad Sci U S A* (2016) 113(51):14574–81. doi:10.1073/pnas.1604975113
25. Miranda LM, Miranda ME, Hatch B, Deray R, Shwiff S, Roces MC, et al. Towards canine rabies elimination in Cebu, Philippines: assessment of health economic data. *Transbound Emerg Dis* (2017) 64(1):121–9. doi:10.1111/tbed.12350
26. Shwiff SA, Hatch B, Anderson A, Nel LH, Leroux K, Stewart D, et al. Towards canine rabies elimination in KwaZulu-Natal, South Africa: assessment of health economic data. *Transbound Emerg Dis* (2016) 63(4):408–15. doi:10.1111/tbed.12283
27. Elser JL, Hatch BG, Taylor LH, Nel LH, Shwiff SA. Towards canine rabies elimination: economic comparisons of three project sites. *Transbound Emerg Dis* (2017) 1–11. doi:10.1111/tbed.12637
28. Government of the Philippines. *Free Anti-Rabies Vaccines in 2016*. (2016). Available from: http://www.gov.ph/2016/01/05/free-anti-rabies-vaccines-in-2016/

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Qualitative Research to Design Sustainable Community-Based Surveillance for Rabies in Northern Australia and Papua New Guinea

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Given the proximity and recent spread of rabies in Indonesia, effective rabies surveillance in dogs is a priority in Northern Australia and Papua New Guinea (PNG). Reporting of potential cases requires community engagement; therefore, the value and acceptability of such a system is critical to ensure sustainable surveillance. We used qualitative research methods to identify factors that influence the acceptability and value of community-based rabies surveillance. Thirty-two semi-structured interviews were conducted with informants in 16 communities in East Arnhem, the Northern Peninsula Area, the Torres Strait in Australia, and in Western Province, PNG. Thematic analysis identified common themes including the importance of verbal communication, particularly *via* radio, community meetings, and direct conversation. We also found that dogs have high value to community members through connection to culture, economic (especially hunting), and companionship. The greatest barrier to the reporting of sick dogs was insufficient veterinary services and the subsequent lack of treatment response. In some regions, acceptance that sick dogs are a normal daily occurrence and lack of trust of authorities were also barriers to reporting. The findings from this study will be used to design sustainable rabies surveillance in Northern Australia and PNG by utilizing traditional communication channels and building on existing and valued animal-management services. The methods and findings of this study complement previous quantitative research, so as to target surveillance to high-risk areas within these regions.

Keywords: rabies, canine, dog, participatory epidemiology, qualitative, interviews, surveillance, one health

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INTRODUCTION

After almost a century of endemic rabies infection in the Greater Sunda Islands in Indonesia (Sumatra, Java, Borneo, and Sulawesi), canine-rabies has spread to historically free islands in the east during the previous two decades (1, 2). The Oceanic region is free of canine-rabies, but the most recently infected Indonesia islands—the southern Maluku Islands—are approximately 1,000 km from Papua New Guinea (PNG), the Torres Strait, and Queensland, Australia, and only 300 km from the coastline of the Northern Territory, Australia. While the drivers of the recent spread of rabies in Indonesia are unknown, infection of new islands has been attributed to movement of rabies-infected dogs associated with human activities such as fishing and visiting relatives (3). Sea trade routes and cultural links exist between people in the south-east Asian and Oceanic regions and although international regulations restrict the movement of dogs, risk assessments indicate that the probability of unregulated movement—and thus the entry of rabies-infected dogs—from Indonesia into Australia and PNG is not negligible (4).

The global burden of rabies is high—it is estimated that tens of thousands of human deaths occur annually, the majority of which are caused by bites from infected dogs (5). Dogs are abundant in Aboriginal and Torres Strait Islander (Indigenous) communities in both Australia and PNG. Although owned, they are usually allowed to roam freely (6). Additionally—and in contrast to other regions of the world in which rabies is endemic—Australia and PNG have feral and wild dog populations (7). Rabies is challenging to eliminate from dog populations (5, 8, 9); endemicity in either the domestic or wild dog populations in Australia and PNG could have devastating, long-term impacts on both human and animal health in these countries. Therefore, timely detection of a rabies incursion in PNG or Northern Australia is important to increase the probability of elimination and prevent human deaths.

A global framework for elimination of canine-rabies was recently jointly proposed by the World Health Organization, World Organisation for Animal Health (OIE), Food and Agriculture Organization of the United Nations, and Global Alliance for Rabies Control (10). Recommendations included a One Health approach requiring sustained resources, understanding of socio-cultural contexts, technical capacity, and organizational and political support to support elimination efforts. Effective rabies surveillance in dogs is an essential component of elimination efforts, required to facilitate control measures and prevent human deaths. The importance of surveillance was illustrated recently during an outbreak in Malaysia (11). An effective surveillance system needs to have high positive predictive value and timely detection. To achieve this, methods such as risk assessment and evaluation of diagnostic tests have been used to focus resources to high-risk pathways and address requirements for rapid diagnosis. However, a surveillance system must also be sustainable to ensure that collected data are of high quality with comprehensive geographic and temporal coverage. Key attributes of sustainable systems—for example, reliability, flexibility, and simplicity—are more difficult to incorporate into surveillance system design because they require an understanding of the acceptability and value of the surveillance to the individuals required to participate in the system. In the case of rabies surveillance, community participation is critical for the reporting of suspect cases; therefore, community acceptability and value of rabies surveillance is essential. This was demonstrated in a trial of community-based rabies surveillance in Kenya, in which high community engagement led to an increased rate of case detection (12).

Qualitative research methods such as ethnographic or interview-based studies can provide insights about the human-driven contexts and mechanisms that lead to, or influence, particular actions and outcomes (13). These methods can complement the findings of quantitative research such as observational and experimental studies and are now used widely in medical research to promote delivery of health services (14–16). In the context of animal health, informal interviews are included in the repertoire of methods used in the discipline of participatory epidemiology (17) and have been used to identify production constraints, disease impacts, and feasible control strategies for endemic diseases (18–20). These methods have also been used recently in the context of biosecurity research to evaluate the acceptability of existing surveillance systems using focus group discussions, interviews, and visualization approaches (21–23).

The objective of the current study was to use qualitative research methods to identify factors that will influence the acceptability and value of community-based rabies surveillance in PNG and Northern Australia. We aim to use the findings from this study to enhance existing non-specific surveillance and plan targeted, community-based, sustainable canine-rabies surveillance in PNG and Northern Australia. We also evaluate the use of qualitative research in this context.

MATERIALS AND METHODS

Overview

The core research for this study involved informal, semi-structured interviews, which were conducted with individuals or small groups (two to six participants) of informants in their homes or workplaces. Qualitative analysis of transcripts identified themes relevant to the design of sustainable surveillance for canine-rabies. The procedures used in this study were approved by the Human Research Ethics Committee of The University of Sydney (project number 2016/192).

Selection of Communities

The target population was residents of Indigenous communities in Northern Australia, the Torres Strait, and coastal Western Province, PNG. Sixteen communities were selected in East Arnhem in the Northern Territory, the Northern Peninsula Area (NPA) in QLD, the Torres Strait, and coastal Western Province in PNG (**Figure 1**). These regions have been identified to be at high risk of rabies incursion relative to other regions in PNG and Northern Australia in previous risk assessments [(4), B. Cookson, personal communication].

Demographic data about the Australian study regions were obtained from the Australian Bureau of Statistics, Census of Population and Housing 2011.[1] Population density was estimated to be 0.32, 2.23, and 9.5 people/km^2 in East Arnhem, the NPA, and the Torres Strait, respectively. The mean size of Australian communities included in this study was 588 people [median 375 people, range estimated 15–2,614 (Mata Mata and Thursday Island, respectively)]. In East Arnhem, the NPA, the Torres Strait, and the Australian general population, 60, 80, 72, and 79% of the population completed high-school education (year 10 or equivalent), respectively. The foundation-year 10 school curriculum is consistent throughout Australia.

Detailed population demographics were not available for the study region in PNG. The population density of South Fly, PNG was estimated to be 1.9 people/km^2. The estimated population size of Mabaduan was 2,000 people (Mabaduan village recorder, personal communication). In contrast to Australia, the human

[1] http://www.abs.gov.au/census.

development index (HDI) of PNG is low (0.505, ranked 158th in the world). Therefore, access to education and health services in rural regions are limited due to poor infrastructure and lack of resources. However, residents in South Fly have access to emergency health care in the Torres Strait (24).

Selection of Informants

Informants were selected purposively to obtain comprehensive information from a range of stakeholder groups. Informants were all older than 18 years. The stakeholder groups included the following:

- traditional leaders and elders,
- councilors (including divisional managers),
- veterinarians, environmental health workers (EHWs), and animal management workers (AMWs),
- biosecurity officers,
- health workers (HWs), including nurses and pharmacists,
- teachers,
- community residents.

Other information and perspectives were gained from people who were selected opportunistically during field-trips; for example, aircraft pilots, Animal Management in Rural and Remote Indigenous Communities employees,[2] and hospitality, building, and retail industry workers. Direct observations were also made

[2]http://www.amrric.org, accessed 13.09.16.

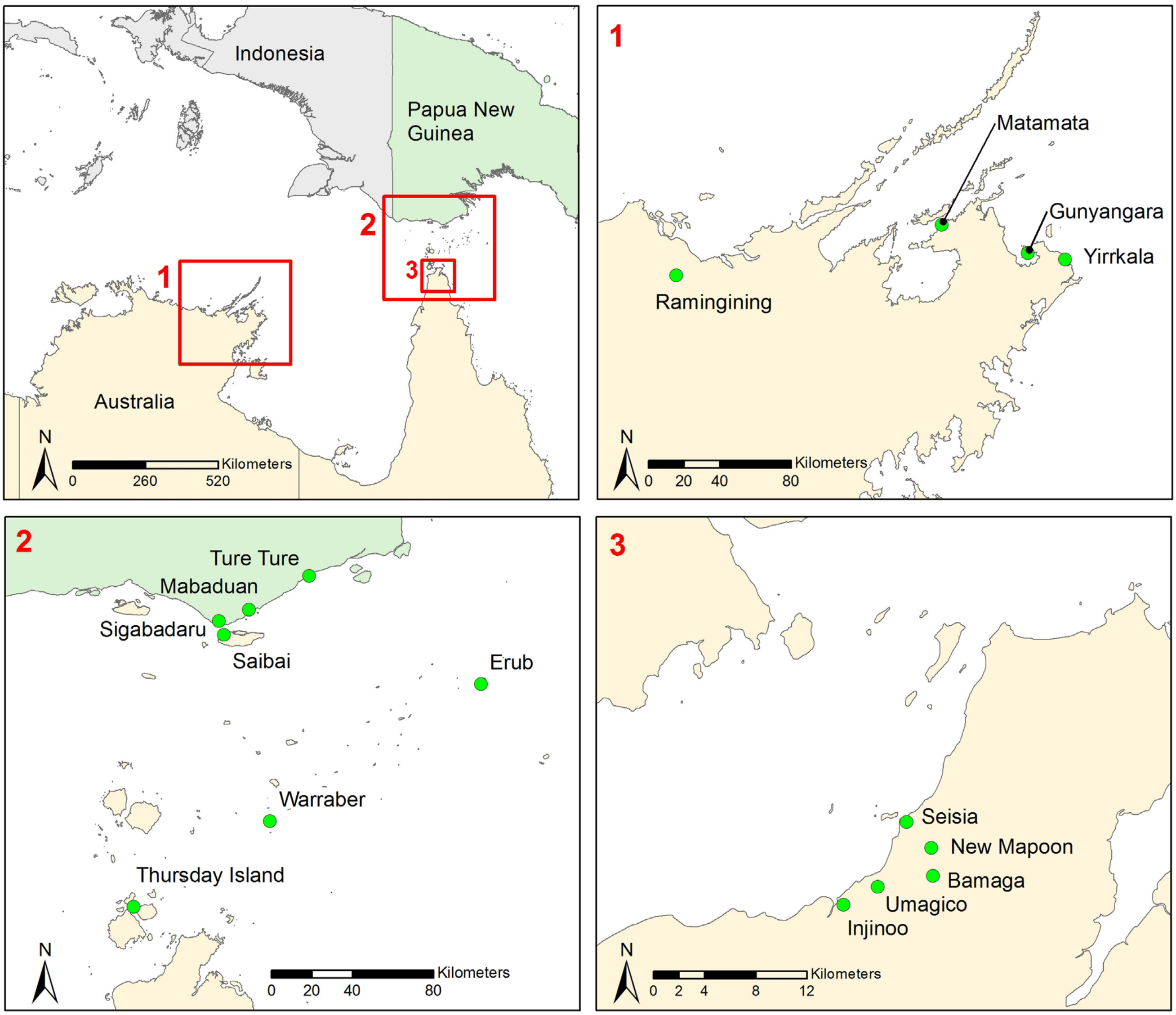

FIGURE 1 | Map showing location of communities included in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and Papua New Guinea.

during visits to communities regarding the general level of dog health.

Interview Structure and Data Collection

Data collection took place between February and June 2016. Informants were interviewed in their homes or workplaces. Interviews were semi-structured, so that informants could talk freely and about topics that they considered important. This flexibility also allowed researchers to investigate themes more thoroughly, dependent on informant experiences and perspectives. Interviews were guided by selecting open-ended questions relevant to stakeholder groups from a list of topics (**Table 1**). Time for each interview was determined by the informants' willingness to talk and was not limited by the researchers. Researchers were accompanied by community members who translated interviews when informants preferred to talk in languages other than English. Informants were offered parasiticides for their dogs, to thank them for participation in the study.

Data Analysis

Interview transcripts and opportunistically collected information and perspectives were collated using qualitative data analysis software (NVivo; QSR International Pty Ltd. Version 11, 2015). Themes within the topics in **Table 1** were identified in transcripts and triangulated between communities and regions and with peer-reviewed literature to assess consistency, divergence, and validity of themes.

TABLE 1 | Topics and example questions used in semi-structured interviews in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and Papua New Guinea (PNG).

Topic 1: effective modes of communication within and between communities.

- If there is an important announcement for the community, how do you make sure that everybody knows about it?
- How do people communicate between communities?
- How do you think we could get people to tell us concerns about their dogs?

Topic 2: motivation and barriers to report concerns about dogs to other community members or organizations.

- What is the value of dogs to individuals; for example, is there connection to dogs through culture and what is the purpose of keeping dogs?
- What would motivate you to report health concerns about your dog?
- Why wouldn't you report health concerns about your dog?

Topic 3: levels of expectations about dog health.

- What diseases do you see in your dogs?
- Informants' descriptions of clinical signs associated with endemic differential diagnoses of rabies (for example, snake envenomation and cane-toad intoxication),
- Awareness and level of concern about dog health,
- Current level and perception of need for veterinary care in the community.

Topic 4: awareness of biosecurity regulations and rabies.

- Have you heard of rabies?
- When you travel, are you aware of quarantine zones and biosecurity requirements? This question was specific to PNG, Torres Strait and Northern Peninsula Area residents.

Topic 5: human health and perspectives on community dogs by health workers.

- Do residents seek treatment for bite wounds at health centers?
- Do you like community dogs and acknowledge them when they come with their owners to the clinic, or you visit patients in their homes?
- What do you think is the most appropriate way to deliver health messages to community members?

RESULTS

Thirty-two semi-structured interviews were conducted with 64 informants (**Table 2**), of whom 73% were Aboriginal or Torres Strait Islander peoples of origin within the study regions. All informants were resident in the study regions. Interview duration ranged from 20 min to 1.5 h. All informants were willing to talk about their personal and workplace experiences related to dogs.

The strongest theme for effective modes of communication both within and between communities was verbal communication. This theme was consistent among informants from all study regions and backgrounds. Informants commonly described this as "passing on the message." Verbal communication from elders, village leaders, or councilors to other community members and children was considered particularly important. Preferred modes of verbal communication for dissemination of information between and within communities included direct conversation, listening to the radio, or attending community meetings. Direct communication was the preferred method to inform other people about concerns such as poor dog health. In East Arnhem, informants were most likely to communicate concerns to elders and in other regions in this study, informants stated that they would speak to authorities, including biosecurity officers and AMWs or EHWs. Social media was also mentioned as potentially useful in some regions (East Arnhem) and with some participant groups (young adults and school children in the NPA and Torres Strait), highlighting that effective modes of communication should be re-assessed as the use of social media develops in these regions. Pictures were also thought to be a potentially useful method to disseminate information, but delivery of messages *via* written media (for example, leaflets and posters in health clinics) appeared less likely to be effective. Written media were not mentioned by Indigenous informants, and HWs said that leaflets and posters were largely ignored by patients and community members. In general, education about animal health and biosecurity was difficult to include in primary schools (teachers explained that there is insufficient space for these topics unless they support activities within the existing curriculum), and students in high school do not value agriculture-based classes.

TABLE 2 | Number of semi-structured interviews and informants in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and PNG.

	East Arnhem	NPA	Torres Strait	PNG
Community elders, leaders, residents	6/6	2/4	3/3	9
Veterinarians, animal and environmental health workers, rangers, biosecurity officers, council workers	3/8	2/6	5/11	0
Human health workers, teachers	2/3	3/9	3/5	0
Total interviews/informants	11/17	7/19	11/19	3/9

NPA, Northern Peninsula Area; PNG, Papua New Guinea.

Informants also stated that information about rabies surveillance should be delivered in local languages because English is not the first language of many residents. For example, most Torres Strait Islanders speak at least three languages (their local Indigenous language, Torres Strait Creole, and English). Excerpts from interview transcripts relevant to the theme of communication are shown in **Box 1**.

Dog value was a potential motivator to report health concerns about dogs. In the NPA and PNG, dogs are valued for hunting because they provide an important source of cheap protein (feral pigs, deer, or cattle). In East Arnhem, the cultural value of dogs was strong—informants described how harm to dogs can cause tangible pain to individuals for whom the dog is their totem. Informants in this region often noted that dogs are part of their family; researchers observed that some dogs had "skin names" and were included in the kinship system. Although the cultural value of dogs was more abstract in other regions, dogs were totems for individuals throughout the study regions (including PNG). In some circumstances, dogs also had economic value apart from hunting. For example, East Arnhem informants described payments to a dog's owner if a dog is killed because the dog can no longer protect the owner. Payments could also be made to custodians of dog dreaming if a dog is harmed so that pain to ancestors and people connected to dogs through their totem is avoided. Dogs were also valued as companions in all regions and to enhance the social status of the owner in some regions. This was particularly apparent in the Torres Strait, where residents were sometimes keen to acquire particular breeds of dog from the Australian mainland.

Informants said that the lack of veterinary services in most regions was the greatest barrier to reporting health concerns in dogs. This theme was consistent between all informants and regions in this study. In the context of this study, a veterinary service refers to availability of a registered veterinarian who is able to examine animals, provide diagnoses, and prescribe treatments. A veterinary service is available in East Arnhem, but comprehensive coverage is limited due to the size of this region (35,000 km^2) and the workforce available: one veterinarian based in a clinic in Yirrkala during the study period. In the Torres Strait, a veterinarian visits the region biannually and provides basic services such as dog population control. Veterinary services were not available in PNG and the NPA during and at least 2 years prior to the study period. Therefore, animal health care is generally limited to services provided by AMWs and EHWs, which include supply of parasiticides and disposal of dead dogs in some regions. Informants were aware of potential zoonotic disease transmission (another potential motivator)—for example, dogs with skin disease such as mange and ticks were perceived as a risk to family health. Throughout all regions, informants stated that parasitic skin disease in dogs was common and wanted parasiticides for their dogs. In Northern Australian regions, cane-toad poisoning and snake envenomation (both differential diagnoses for rabies) are sufficiently common in dogs that informants could describe clinical signs. Informants explained that there was no incentive to report these concerns because treatment was not available. This led to acceptance that unhealthy dogs are a normal, daily occurrence. Consistent with this theme, researchers observed that dogs appeared generally healthier in regions in which veterinary services were available intermittently (Torres Strait islands) or continuously (Yirrkala, East Arnhem).

BOX 1 | Excerpts from interview transcripts about modes of communication in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and Papua New Guinea.

Community elder: "Everybody listens to the radio."

Community elder: "We will help spread the message about the disease. On radio also."

Community elder: "It is easy to teach the children, to pass on the stories."

Community elder: "The people, they listen to Yolngu [people of East Arnhem] radio."

Community member: "Talking to people—by visits"

Community elder: "Information needs to be passed from elders and parents through the kinship system."

Health worker: "Radio is best for messaging… Everybody listens to [local radio] throughout Torres Strait and NPA."

Councillor: "We have public meetings about everything. Some people… they can get very intense."

PNG village leader: "We have meetings with the Torres Strait councillors… here and over there… to come up with solutions for our problems."

Health worker: "We are kinaesthetic learners, so pictures are really good."

Community elder: "I'm on Facebook, I like to stickybeak… some people poke me, but I keep quiet."

Teacher: "Agriculture is a dying subject… kids don't want to go outside."

Other themes about barriers to reporting were region-specific or less common. Lack of trust of authorities and fear of shame or recrimination within the community were both barriers to reporting concerns about dogs in East Arnhem. This was attributed to historical experiences such as inhumane dog control. Throughout all regions in the study there was also an apparent lack of concern for dog welfare by some community members, attributed to insufficient connection to culture, and therefore, lack of knowledge that dogs are part of family. Excerpts from interview transcripts relevant to motivation and barriers to reporting health concerns in dogs and level of expectations about dog health are shown in **Box 2**.

Indigenous informants were aware of the importance of biosecurity and stated that they complied with regulations when traveling between PNG, the Torres Strait and mainland Australia. Non-indigenous residents more commonly had either limited knowledge, lack of concern for regulations, or openly admitted non-compliance because the regulations were inconvenient. Although most people had heard of rabies, very few were aware of the risk of an incursion due to entry of infected dogs from endemic regions or the zoonotic potential and impact of rabies in humans. A few people recalled a picture of a rabid dog on biosecurity information for passengers in ferries and aircraft in the region. Human HWs were aware of rabies, but it was not something that they considered in their daily work—they were occupied with current health risks that included multi-drug resistant tuberculosis (in PNG residents seeking healthcare in

BOX 2 | Excerpts from interview transcripts about motivation and barriers to reporting health concerns in dogs, and level of expectations about dog health in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and Papua New Guinea.

Community elder: "This is dingo land. Dog is not alone from humans. Through the spirit, the journey, we feel them close…"

PNG leader: "I have two dogs (two females), with six babies… I like them. My totem is dog."

Councillor: "You can't restrict everybody to two dogs. Hunting is big here… they need more [than two] dogs…"

Health worker: "Dogs are a totem … here in the NPA, in Bamaga in particular, there is a high cohort of Umai [dog] totem. This comes from Saibai."

PNG community leader: "We look after our dogs like we look after our children because they also provide food for our children… dogs are valuable"

Councillor: "If you cull dogs, people get upset. Not because of cultural beliefs, but because they are attached to their dog."

Community elder: "If a dog gets sick you can put a blanket on it. There is nobody to help."

Community elder: "We need more [veterinary] service as well as awareness of disease."

Veterinarian: "We have to follow up cheeky [aggressive] dogs, but it can be difficult because people think we are going to take the dog away."

Health worker: "People worry that the dogs will get blamed if they [the people] have skin problems. They hide the dogs."

Community member: "She didn't want the ticks on the verandah because of the children [so she threw the boiling water at the dog]… she didn't realise it would be long-time pain."

Community elder: On reasons for animal cruelty and neglect, "Important song-lines are not shared. The young people don't know them."

BOX 3 | Excerpts from interview transcripts about awareness of biosecurity regulations, rabies and the interface between human and dog health in a study to identify factors that will influence the acceptability and value of community-based rabies surveillance in Northern Australia and Papua New Guinea.

Health worker: "So many times, people ask me to help with their dog… Other nurses say they don't want to have anything to do with the animals, but that affects their relationship with the families, because then they are not part of the holistic approach. Dogs are part of the family."

Health worker: "Dogs should be removed from the clinic waiting area… people should only be allowed one dog per household by law."

Health worker; "it is important to empower people through self-management of health… but this is a challenging approach for some HWs in a system which has traditionally advocated a custodial approach to Indigenous health."

Health worker; "We don't see many issues from dogs. Bites are rare… we see a few cat scratches on children."

Councillor: On the value of dogs in the community in comparison to other community issues, "Dogs are still important… it's all interrelated."

Non-indigenous community member: "When I visit my son on TI we take the dogs. We don't go through quarantine on the way back, but it's OK—the dogs don't go anywhere, they don't meet other dogs."

PNG community leader: "We have our control measures making sure we don't violate our [quarantine] guidelines and we maintain our treaty agreement…."

Torres Strait Island health clinics) and the recent outbreak of Dengue Fever in the Torres Strait region.

Health workers (most of whom were non-indigenous) estimated that the majority of people with dog-bite wounds would seek medical attention because wound infections are viewed as a common cause of more serious conditions such as septicemia. Consistent with this opinion, the few informants who had experienced dog-bite wounds had attended a health clinic for treatment. HWs' perceptions and level of acceptance of dogs in community were variable; some recognized dogs as part of the family and acknowledged and treated unhealthy dogs. Other HWs felt threatened by community dogs in public places, were unaware that free-roaming dogs in Northern Australia are owned, were not interested in dog health and perceived unhealthy animals as an indicator of lack of concern for dog welfare by Indigenous community residents. This variability was also found in other groups of non-indigenous informants such as teachers and hospitality industry workers. Excerpts from interview transcripts relevant to awareness of biosecurity regulations, rabies, and the interface between human and dog health are shown in **Box 3**.

DISCUSSION

Effective communication is vital for community-based surveillance; participants need to understand reporting requirements and reports need to be collected in a timely manner for analysis. The most consistent theme for this topic throughout all study regions was the importance of verbal communication and informants in this study commonly talked of "passing on the message" about rabies. This is consistent with the cultural background of Indigenous people in Northern Australia and PNG. Aboriginal and Torres Strait Islander lore has been passed down generations for tens of thousands of years by elders, using stories, ceremonies, dance, music, and art.[3] Story-telling (such as "sing-sings") is also a fundamental feature in PNG culture. For example, Mercer et al. (25) found that the impacts of a tsunami in 1930 on the north coast of mainland PNG were mitigated because residents knew stories—which had been passed down verbally through generations—that described warning signs and evacuation to higher ground. In contrast to Western culture in which information is commonly disseminated in written form and directed from authorities to children, we suggest that messages to enhance rabies surveillance in Northern Australia and PNG should be verbal and use traditional communication channels by engaging elders and councils to "pass on the message." These strategies also build on connection to culture and encourage traditional values such as care for dogs in community. Messages should be delivered in local languages. This has also been recognized as important for effective communication in sectors other than biosecurity. For example, the Queensland Government Department of Health provides an interpreter service which includes Tok Pisin, the PNG equivalent of Torres Strait Creole.

Although several modes of verbal communication were identified *via* which messages to enhance rabies surveillance might

[3]http://aiatsis.gov.au/, accessed 20.09.16.

be delivered, modes to report clinical signs were limited to direct communication. In addition, the preferred routes for reporting varied between regions. In the Torres Strait and NPA, informants stated that they would report concerns to AMWs or biosecurity officers; in these regions, there is comprehensive coverage by these groups, both geographically and temporally, and they are already familiar with the importance of animal health. However, in Western Province PNG, there are no animal health services, and in East Arnhem there is mistrust of authorities due to previous experiences of inappropriate responses to perceived animal health issues. This poses challenges for collection of high quality surveillance data over such a large region because the structure of data collection might need to be regionally customized. In regions such as PNG and East Arnhem, it is likely that community elders will need to be engaged to encourage reporting.

This study also highlighted other important challenges and barriers to rabies surveillance in Northern Australia and Western Province, PNG. We found that dogs are valued for a variety of reasons which can be intangible (for example, connection to culture and companionship) or tangible (for example, their value as hunting animals). This is consistent with the findings of Constable et al. (6). Although the value of dogs is a potential motivator to report health concerns about dogs, the lack of veterinary services was a major barrier. Without direct health benefits to dogs, reporting of clinical signs is unlikely to be sustainable. This is illustrated by the acceptance of the lower level of general dog health in communities in which veterinary services were unavailable. The importance of a returned value (perceived benefit) to those that report in surveillance systems has been highlighted previously by Syibli et al. (26) and illustrated by the development of a mobile phone reporting system in Indonesia.[4] Primarily, this system provides benefit to those involved directly in animal health (for example, farmers and veterinarians) and has a secondary purpose as a tool for syndromic surveillance. Preliminary reports suggest that the value of animal health care is a sufficient incentive to report clinical signs and achieve syndromic surveillance with good temporal and geographic coverage in some Indonesian regions (27). In addition to the lack of veterinary services as a barrier to reporting clinical signs, the specificity of clinical signs for rabies is low due to common endemic syndromes with similar clinical signs. As well as likely reducing sustainability through false-positive incursion alerts, this also has implications for messaging about surveillance; community-wide surveillance for rabies-associated clinical signs should be carefully considered so as not to induce panic about dogs with clinical signs which currently are more likely to indicate non-zoonotic syndromes, such as snake envenomation or cane-toad poisoning. Overall, we believe that unless veterinary services can be improved consistently throughout this region, community-wide surveillance of dog mortality and training of selected community leaders and workers to identify clinical signs is likely to be more acceptable and sustainable than community-wide surveillance for clinical signs consistent with rabies. This level of syndromic rabies surveillance has a number of advantages: it builds on the already valued service provided by EHWs and AMWs in some regions to dispose of dead dogs and it is 100% sensitive for rabies (all rabies-infected dogs die). In addition, messages to report dog mortality are unlikely to induce the same fear that reporting suspect cases of rabies would. Although mortality is not specific to rabies, increased incidence of dog mortality is a useful indicator of other important diseases such as distemper (endemic) and screw-worm fly (exotic).

We also identified potential gaps in community engagement for rabies surveillance. The Torres Strait is a cultural and geographic interface between PNG and mainland Australia, and compliance with biosecurity regulations is important to maintain freedom of movement for traditional purposes, while protecting human, animal, and plant health in this region (The Torres Strait Treaty).[5] We found that the level of awareness of the importance of these regulations was variable among informants, particularly non-indigenous residents such as HWs, teachers, and other industry workers. Understanding the value and acceptability of community-based rabies surveillance to engage non-indigenous residents was not an objective of this study. In particular, HWs and teachers are positioned to provide valuable surveillance of both animal and human health in these regions—there is an extensive network of human health care facilities and schools in Indigenous communities throughout Northern Australia, and residents in coastal Western Province PNG have access to emergency healthcare in the Torres Strait. However, informants in these groups were also sometimes unaware of the value of dogs to communities or the risk of rabies to the region and therefore, dismissed the importance of community dog health. Further studies to investigate methods to improve engagement of non-indigenous community residents in biosecurity practices and encourage a One Health approach to community health are worth pursuing. In addition to enhancing the sustainability and community-wide coverage of rabies surveillance, improved understanding of the value of dogs and the way in which they are kept in communities is also likely to promote trust between Indigenous community members and those of non-indigenous origin in regions such as East Arnhem. Among other benefits, this could also enhance reporting for community-based rabies surveillance.

Qualitative research asks questions that are fundamentally different to those studied in quantitative research (13, 14) to document and explain a range of views, needs, values, practices, and beliefs. For example, a qualitative study might investigate why people make decisions to report health concerns, whereas a quantitative study might investigate the proportion of people that report health concerns. Although lack of quantitative data obviously precludes evaluation of precision, assessments can be made concerning the internal and external validity of qualitative study findings. Limitations of the current study could include selection bias of communities and informants and information error due to interpretive bias by the researchers during thematic

[4] http://wiki.isikhnas.com/, accessed 20.09.16.

[5] http://dfat.gov.au/geo/torres-strait/Pages/the-torres-strait-treaty.aspx, accessed 20.09.16.

analysis of transcripts. However, the themes of the importance of verbal communication and traditional communication channels, the high value of dogs to Indigenous community residents, and the lack of veterinary services as a barrier to reporting were consistent throughout the study region across informants with a range of backgrounds. In addition, these themes are consistent with other research and Indigenous Australian and PNG history; this increases the generalizability of these findings across Northern Australia and Western Province, PNG. Divergent themes—for example, cruelty to dogs associated with lack of connection to culture in some communities or the use of social media for communication—are less generalizable. Quantitative studies could be used to investigate the importance of these themes, and methods from participatory epidemiology (which also include semi-structured interviews) could be used to determine the frequency of these activities relative to actions that promote dog welfare in communities (17). Perhaps a more important limitation of this study was the assessment of acceptability and value of community-based rabies surveillance out of context of competing community concerns. For example, health outcomes are poorer, levels of education achieved are lower, and a greater proportion of people serve custodial sentences in Aboriginal and Torres Strait Islander communities than other communities in Australia (28, 29), and the HDI in PNG is low (0.505).[6] Despite the improved sustainability of community-based surveillance that could be achieved using the findings of the current study, surveillance for animal health might ultimately be of insufficient value in comparison to other community concerns to achieve timely detection of a rabies incursion in these regions.

Consistent with previous studies (21–23), the qualitative methods used in this study provided important insights about the acceptability and value of community-based rabies surveillance in Indigenous communities in Northern Australia and Western Province, PNG. The findings of this study will inform design of communications materials—such as radio stories—to enhance appropriate syndromic (for example, dog mortality), community-based rabies surveillance using traditional communications channels. The qualitative methods used in this study complemented the quantitative methods used in previous studies in this region that identified the comparative risk of regions in Northern Australia and PNG (4, 30). Together, the findings of these studies can be used to design sustainable surveillance strategies targeted to high-risk regions and increase the probability of effective surveillance to limit outbreak size and detect disease in dogs before a human death occurs. However, it should be noted that sustainable surveillance will also depend on the integration of surveillance activities within the context of competing concerns in communities. As described by informants, community health requires a holistic approach because all aspects of community life are interrelated.

[6] http://hdr.undp.org/en/countries/profiles/PNG, accessed 20.09.16.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the Australian National Health and Medical Research Council's National Statement on Ethical Conduct in Human Research, the Human Research Ethics Committees of the Northern Territory Department of Health and The University of Sydney with informed verbal consent from all subjects. The protocol was approved by the Human Research Ethics Committees of the Northern Territory Department of Health and The University of Sydney (reference numbers 2016-2606 and 2016/192, respectively).

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and design of this study and acquisition of data. VB was responsible for analysis and interpretation of the data. All authors contributed to critical revision of this manuscript and agreed to be accountable for all aspects of this study.

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REFERENCES

1. Amaral AC, Ward MP, Freitas JDC. Estimation of roaming dog populations in Timor Leste. *Prev Vet Med* (2014) 113(4):608–13. doi:10.1016/j.prevetmed.2013.11.012
2. Ward MP, Hernandez-Jover M. A generic rabies risk assessment tool to support surveillance. *Prev Vet Med* (2015) 120(1):4–11. doi:10.1016/j.prevetmed.2014.11.005
3. Ward MP. Rabies in the Dutch East Indies a century ago – a spatio-temporal case study in disease emergence. *Prev Vet Med* (2014) 114(1):11–20. doi:10.1016/j.prevetmed.2014.01.009
4. Brookes VJ, Ward MP. Expert opinion to identify high-risk entry routes of canine rabies into Papua New Guinea. *Zoonoses Public Health* (2016). doi:10.1111/zph.12284
5. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
6. Constable S, Dixon R, Dixon R. For the love of dog: the human-dog bond in rural and remote Australian indigenous communities. *Anthrozoos* (2010) 23(4):337–49. doi:10.2752/175303710x12750451259336
7. Dwyer PD, Minnegal M. Wild dogs and village dogs in New Guinea: were they different? *Aust Mammal* (2016) 38(1):1–11. doi:10.1071/am15011
8. Tenzin T, Ward MP. Review of rabies epidemiology and control in South, South East and East Asia: past, present and prospects for elimination. *Zoonoses Public Health* (2012) 59(7):451–67. doi:10.1111/j.1863-2378.2012.01489.x
9. Townsend SE, Sumantra IP, Pudjiatmoko, Bagus GN, Brum E, Cleaveland S, et al. Designing programs for eliminating canine rabies from islands: Bali,

Indonesia as a case study. *PLoS Negl Trop Dis* (2013) 7(8):e2372. doi:10.1371/journal.pntd.0002372
10. Anonymous. Aiming for elimination of dog-mediated human rabies cases by 2030. *Vet Rec* (2016) 178(4):86–7. doi:10.1136/vr.i51
11. ProMED-mail. *Rabies* – Malaysia (Perlis): Canine, OIE, Archive Number: 20150825.3599775, Published Date: 2015-08-25 06:03:38 (2015). Contract No.: 20150825.3599775.
12. Kitala PM, McDermott JJ, Kyule MN, Gathuma JM. Community-based active surveillance for rabies in Machakos district, Kenya. *Prev Vet Med* (2000) 44(1–2):73–85. doi:10.1016/s0167-5877(99)00114-2
13. Christley RM, Perkins E. Researching hard to reach areas of knowledge: qualitative research in veterinary science. *Equine Vet J* (2010) 42(4):285–6. doi:10.1111/j.2042-3306.2010.00074.x
14. Britten N, Jones R, Murphy E, Stacy R. Qualitative research methods in general-practice and primary-care. *Fam Pract* (1995) 12(1):104–14. doi:10.1093/fampra/12.1.104
15. Pope C, Mays N. Reaching the parts that other methods cannot reach – an introduction to qualitative methods in health and health-services research. *Br Med J* (1995) 311(6996):42–5.
16. Pope C, Mays N. Critical reflections on the rise of qualitative research in health services research. *J Epidemiol Community Health* (2008) 62:A1–36.
17. Catley A, Alders RG, Wood JL. Participatory epidemiology: approaches, methods, experiences. *Vet J* (2012) 191(2):151–60. doi:10.1016/j.tvjl.2011.03.010
18. Birhanu A, Worku T, Benti D. Investigation of major cattle production constraints in Kembata Tambaro zone of Southern Ethiopia using participatory epidemiology methods. *Trop Anim Health Prod* (2016) 48(1):109–15. doi:10.1007/s11250-015-0928-y
19. Byaruhanga C, Oosthuizen MC, Collins NE, Knobel D. Using participatory epidemiology to investigate management options and relative importance of tick-borne diseases amongst transhumant zebu cattle in Karamoja region, Uganda. *Prev Vet Med* (2015) 122(3):287–97. doi:10.1016/j.prevetmed.2015.10.011
20. Kabaka W, Gitau GK, Mariner J, Abudiku N. The use of participatory epidemiology to determine the prevalence rate and economic impacts of PPR and CCPP in Turkana county of Kenya. *Bull Anim Health Prod Afr* (2012) 60(3):241–50.
21. Calba C, Antoine-Moussiaux N, Charrier F, Hendrikx P, Saegerman C, Peyre M, et al. Applying participatory approaches in the evaluation of surveillance systems: a pilot study on African swine fever surveillance in Corsica. *Prev Vet Med* (2015) 122(4):389–98. doi:10.1016/j.prevetmed.2015.10.001
22. Calba C, Goutard FL, Vanholme L, Antoine-Moussiaux N, Hendrikx P, Saegerman C. The added-value of using participatory approaches to assess the acceptability of surveillance systems: the case of bovine tuberculosis in Belgium. *PLoS One* (2016) 11(7):e0159041. doi:10.1371/journal.pone.0159041
23. Schulz K, Calba C, Peyre M, Staubach C, Conraths FJ. Hunters' acceptability of the surveillance system and alternative surveillance strategies for classical swine fever in wild boar – a participatory approach. *BMC Vet Res* (2016) 12(1):187. doi:10.1186/s12917-016-0822-5
24. Foreign Affairs Defence and Trade References Committee. *The Torres Strait: Bridge and Border*. Canberra: Commonwealth of Australia (2010). p. 978–971.
25. Mercer J, Gaillard JC, Crowley K, Shannon R, Alexander B, Day S, et al. Culture and disaster risk reduction: lessons and opportunities. *Environ Hazards Hum Policy Dimens* (2012) 11(2):74–95. doi:10.1080/17477891.2011.609876
26. Syibli M, Nurtanto S, Yulianti S, Yohana CK, Cameron AR, Muljono AT, et al. The power of one: realising the dream of an integrated animal health information system in Indonesia. *International Conference on Animal Health Surveillance 2 (ICAHS2)*. Havana, Cuba (2014).
27. Happold J. Tackling emerging disease threats at source: the Australian government's partnerships with Indonesia, Timor Leste and Papua New Guinea. *Australian and New Zealand College of Veterinary Scientists, Annual Conference*. Gold Coast (2016).
28. Department of the Prime Minister and Cabinet. *Closing the Gap: Prime Minister's Report 2016*. Canberra: Commonwealth of Australia (2016). Available from: http://closingthegap.dpmc.gov.au/assets/pdfs/closing_the_gap_report_2016.pdf
29. House of Representatives – Standing Committee on Aboriginal and Torres Strait Islander Affairs. *Doing Time – Time for Doing: Indigenous Youth in the Criminal Justice System*. Canberra: Commonwealth of Australia (2011). Available from: http://www.aph.gov.au/parliamentary_business/committees/house_of_representatives_committees?url=atsia/sentencing/report.htm
30. Brookes VJ, Ward MP. *Risk Assessment: The Entry of Canine-Rabies into Papua New Guinea via Land and Sea Routes*. Gold Coast, QLD: Australian and New Zealand College of Veterinary Scientists, Science Week (2016).

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Addressing the Disconnect between the Estimated, Reported, and True Rabies Data: The Development of a Regional African Rabies Bulletin

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It is evident that rabies continues to be a neglected tropical disease; however, a recent global drive aims to eliminate canine-mediated human rabies by 2030. Global efforts have been vested into creating and developing resources for countries to take ownership of and overcome the challenges that rabies poses. The disconnect between the numbers of rabies cases reported and the numbers estimated by prediction models is clear: the key to understanding the epidemiology and true burden of rabies lies within accurate and timely data; poor and discrepant data undermine its true burden and negate the advocacy efforts needed to curb this lethal disease. In an effort to address these challenges, the Pan-African Rabies Control Network is developing a regional rabies-specific disease surveillance bulletin based on the District Health Information System 2 platform—a web-based, open access health information platform. This bulletin provides a data repository from which specific key indicators, essential to any rabies intervention program, form the basis of data collection. The data are automatically analyzed, providing useful outputs for targeted intervention. Furthermore, in an effort to reduce reporting fatigue, the data submitted, under authority from the respective governments, can automatically be shared with approved international authorities. The implementation of a rabies-specific bulletin will facilitate targeted control efforts and provide measurements of success, while also acting as a basis for advocacy to raise the priority of this neglected disease.

Keywords: rabies, bulletin, DHIS2, data, surveillance, PARACON, reporting

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INTRODUCTION

Rabies has been a scourge for centuries. Despite the fact that this disease is fully preventable, the exemplary efforts that led to the elimination of dog rabies (e.g., in Western Europe, the United States, and Japan) have failed to be replicated across Asia and Africa. Significantly, the continued lack of impetus toward its control and elimination has resulted in the official recognition of rabies as a neglected tropical disease (1). The low priority status of rabies in the global community has resulted in a lack of interest from relevant stakeholders and national governments, despite the important socioeconomic and public health impact of the disease (2). Without a unified governmental and global effort toward rabies control, human lives will continue to be needlessly lost.

Many rabies endemic countries are afflicted by economic and political instability, resulting in a plethora of challenges. These circumstances make it even more difficult to assign sufficient resources toward rabies surveillance and intervention, especially when a host of other diseases competes for attention. Diseases are often prioritized according to those that are most visible or perceived to be emerging threats. Failure to command attention leads to a lack of resources required to implement an effective intervention strategy. A cycle of neglect is thus established, depriving the disease from the attention that it deserves (3). The absence of accurate data is considered as a foundational challenge in the prioritization of the fight against rabies (2, 4).

By providing decision makers, countries and regions with robust estimates as to both the burden of the disease (2) and the associated costs (5), a stronger case for rabies prioritization and intervention may be built. Therefore, an important next step would be for regional networks and the global community to improve data collection, quality, and analysis, among others, to inform the disease prioritization cycle.

DISCONNECT BETWEEN ESTIMATED AND REPORTED DATA

There is an inordinate disconnect between the data that are officially reported by governments and that of the estimates provided by predictive models (2). Furthermore, a plethora of data from grassroots levels (e.g., health-care facilities) is also available but is seldom reported and aggregated to the national level. It can be argued that these models provide the most useful and well-considered estimates for the burden of rabies to date, specifically in Africa and Asia where rabies reports, in those instances where reporting does occur, often appear to be haphazard or discrepant (6). Within Africa, for example, underreporting the actual numbers of human deaths can be as much as 100-fold, resulting in the misperception of the burden of rabies in individual countries and on the continent as a whole (7).

While a lack of reported data is problematic, poor-quality data can result in a conscious decision to mistakenly not address a disease. Poor-quality data can present a false picture of the situation, resulting in a false sense of security among governments and decision makers. Thus, improving data reporting should be a process that starts at the lowest governmental levels and aggregates up to the national level. The ultimate goal of each country and stakeholder involved in rabies control and elimination should be to drive accurate data collection, reporting, and analysis in order to ensure that the reported data reflect the true burden of rabies in their country.

HINDRANCES TO RELIABLE DATA COLLECTION

Many countries in Africa have functional surveillance systems, yet the data that are reported at a national level or to international organizations such as the World Health Organization (WHO) and World Organization for Animal Health (OIE) do not correlate with that from the community or district level (6, 8–11) as it is sourced from various sectors and databases within the country.

Cumbersome, complex, and time-consuming reporting systems contribute in large to poor data collection and reporting. A recent study showed that only 10/19 surveyed African countries reported human rabies data using an electronic database, but 18/19 countries still used paper-based reporting at some stage(s) within their reporting system (12). Rabies data reports are often late, or submission rates are low. A stand-alone rabies surveillance system was reported in 4/16 countries, meaning that reported data for the remaining 12 countries would likely be presented to an integrated disease surveillance system for multiple diseases within each ministry (12). As a result of the complex structuring of existing types of reporting systems, as well as the lack of any feedback mechanisms, those data misreported or unreported are not pursued, clarified, or questioned (9). These factors all contribute to a lack of confidence in rabies surveillance systems in Africa; only 3/19 countries deemed their rabies surveillance system adequate, despite its status as a notifiable disease in all 19 surveyed countries (12).

Apart from the obvious drawbacks associated with cumbersome reporting systems, the roles played by data managers should also be considered. Individuals responsible for reporting data are tasked with various other responsibilities. These include reporting morbidity and mortality statistics to international organizations and responsibility for reporting data for all of the notifiable diseases to various sectors, stakeholders and decision makers within a country. Additionally, there should be capacity for analysis and interpretation of raw data in order for it to be used for case follow-up, outbreak responses, targeted intervention campaigns, and the identification of disease incidence hotspots. Thus, data managers are often overburdened with a plethora of tasks and commitments, resulting in some health data being poorly reported. In this light, it would be most beneficial for data reporting as a whole if reporting systems could be made as simple and efficient as possible.

IMPROVING DATA REPORTING IN AFRICA

Formerly, two main international epidemiological reporting bulletins for rabies existed, namely the WHO Rabnet (13)—reporting on public health data—and the OIE World Animal Health Information System (WAHIS) (14)—reporting on veterinary health data. The Rabnet system closed in 2011 due to a lack of reported data (8). The WAHIS is a well-established global animal disease reporting system that reproduces the data that countries submit to OIE, but it is also limited by the underreporting issues inherent to the national reporting systems (7). A further disconnect exists in many places between human and animal health, with little or no cross-sectoral exchange occurring (8). Thus, the need for regional, One Health-oriented reporting networks has become evident (15). The creation of rabies-specific regional bulletins has been exceptionally successful in the Pan-American Health Organization region (SIEPI database) (16) and in Europe (WHO Rabies Bulletin Europe) (17). These bulletins have enabled countries to improve surveillance for targeted intervention and control measures, while also increasing advocacy and awareness about the disease situation. In Africa, no rabies-specific database existed, and only informal reporting occurred within regional networks (6, 12). Also, with the lack of a regional bulletin, data quality from the African region has remained poor or non-existent, emphasizing the need for such a tool.

Addressing the Disconnect in Africa: The Pan-African Rabies Control Network (PARACON) Bulletin

The PARACON was founded in 2014 under the secretariat of the Global Alliance for Rabies Control. PARACON unified various subregional networks and other independent countries into a single regional network for Africa, with the mandate to provide tools and support to Member countries (15). In light of this mandate, PARACON is developing and refining a regional, network-based reporting bulletin for rabies using a standardized set of critical indicators that are applicable to each country individually, as well as to the region as a whole. Furthermore, to improve reporting incrementally on a global scale, WHO is working closely with regional networks to improve rabies data collection (8). Thus, through the unification of rabies reporting systems in the region, and the creation of a single platform that can provide regional rabies data to global reporting systems, the burden of data reporting can be substantially reduced.

District Health Information System 2 (DHIS2): The Backbone of the PARACON Bulletin

The DHIS2 is an open-source platform specifically designed for health surveillance. It functions not only as a data collection and storage point but also as a versatile tool to aggregate and disaggregate data, manage individual patient records, perform analytics, and create useful and interactive visuals for data analysis. In addition, to facilitate the use and dissemination of the data, the DHIS2 system has an integral sharing functionality with mass communication and messaging capabilities, while maintaining strict access control and confidentiality. The DHIS2 can furthermore be adapted to any type of program requiring data gathering, analysis, and dissemination.

The DHIS2 has been implemented globally, including in 40 countries throughout Africa (18, 19) and is currently being used as an official Health Information System (HIS) in Malawi, Kenya, and Uganda, among others (19). In Africa, for instance, the implementation of the DHIS2 system in Zimbabwe resulted in timelier reporting, enhanced data quality, and improved report completeness for child health-related data (20). Similarly in Zambia, the DHIS2 system was used for a national malaria control program, resulting in improved case detection, improved diagnostic confirmation, and reduced numbers of unconfirmed malaria cases reported (21).

The PARACON Bulletin

As a new way of rabies data collection and dissemination, the PARACON bulletin uses the DHIS2 as its data collection platform. The PARACON bulletin will encourage the collection of rabies data from both the public and animal health sectors, promoting the One Health concept and intersectoral collaboration for improved rabies surveillance efforts. It is hoped that the simplicity of the Bulletin's use and design will lead to improved rabies data reporting with little input and expertise required. Initial feedback at the Beta launch of the PARACON bulletin in 2016 was positive: 65% (15/23) of West African PARACON workshop participants agreed that the bulletin is easily workable and could be utilized as a country-level solution. Subsequent to its launch in July 2016, the PARACON bulletin has been implemented at another workshop targeting five Anglophone PARACON countries, where all of the participants agreed that the PARACON bulletin is as an easy-to-use and useful rabies reporting system for their country. In addition, the PARACON bulletin will continue to be introduced to the remaining PARACON member countries in subsequent workshops, meetings and in-country visits. Outcomes from these workshops and visits have already shown continued data reporting for the end of 2016, with continuous follow-up for further data reporting.

The use of standardized data indicators is paramount to the consistent and accurate reporting of data for national, subregional, regional, and international uses. By initially focusing on basic indicators (**Table 1**) during the early phases of implementation, the Bulletin is designed to be easy to use and should provide the maximum output in exchange for a limited input. This will be essential to encourage countries to buy-in to the concept. The initial indicators will likely adapt as the bulletin continues to develop in line with the global needs and trends in data collection for rabies and are also subject to further consultation and refinement. As PARACON will work closely with WHO as well as other international collaborating centers and expert networks, the concept is to create a globally accepted, standardized set of indicators that will continue to be developed and refined. This standardized set of indicators will be focused on essential criteria to help guide countries in (further) developing their own surveillance and control strategies as they strive toward self-declaration of freedom from rabies.

On a regional scale, the use of a single reporting system can instigate interest and control efforts in neighboring countries through the evaluation of shared data, in the race for the first African country to declare freedom from canine-mediated human rabies by 2030. Furthermore, by sharing data internationally, countries can work together to control rabies cycles along international borders—something that is vitally important for a sustainable approach to rabies control (3). As the Bulletin is closely linked to the Stepwise Approach towards Rabies Elimination tool, as well as to key indicators for the WHO Global Health Observatory, this platform presents an easy means for countries to assess progress and program successes, while gathering essential data for the declaration of freedom from rabies in the future.

The PARACON bulletin has been designed to not only act as a regional platform for national rabies data but also can be adopted by countries as their own national and subnational rabies surveillance systems. The use of an electronic platform will enable users to access data instantly, resulting in an improved sense of ownership (25). To ensure that data quality is kept at the highest possible standards, several data quality checks will be available,

TABLE 1 | Description of and rationale for using initial basic indicators in the Pan-African Rabies Control Network bulletin.

Indicator	Disaggregation	Description	Rationale	Reporting period
Number of bite cases in humans	Age: <5 years, 5–14 years; ≥15 years; unknown age Sex: male, female; unknown Wound category: I, II, or III	Number of bite cases reported at a health-care facility, disaggregated by age, sex, and wound category	To determine at-risk populations (children, adults) and the numbers of people who have been potentially exposed to a rabid animal; this indicator influences decisions regarding human vaccine procurement and targeted education. This indicator also excludes snake bites	Annual
Doses of human vaccines purchased	None	Number of human vaccines purchased for the country	To determine the number of vaccines available in the country and whether this complies with PEP requirements	Annual
Cost per vaccine (US$)	Private sector Public sector	Cost per vaccine administered in a government institution (including all associated costs such as doctor's fees, consumables, etc.)	To determine the costs associated with procurement and administration of vaccine for budgetary purposes and to advocate the allocation of funds toward rabies control efforts	Annual
Doses of animal vaccine available	Purchased this year Viable vaccine carried over from previous year Vaccine administered	Number of animal vaccines administered, carried over, and purchased by the government for mass vaccination campaigns	To establish the number of vaccine doses available to the government; this indicator is also used for the eventual calculation of the estimated vaccination coverage for the country	Annual
Estimated total dog population	Human population: urban, rural Human:dog ratio: urban, rural Dog population: urban, rural	A means to determine an estimated dog population for the country based on the HDR method (4, 22–24)	In most countries where rabies is endemic, there is no information about their current dog population; this lack of knowledge inhibits the assessment of the effectiveness of mass dog vaccination campaigns and also prevents countries from purchasing the correct number of doses of animal vaccine to achieve 70% coverage	Annual
Dog vaccination coverage		A means to determine the estimated vaccination coverage for the estimated dog population for the country	To enable decision makers to determine whether sufficient vaccine has been purchased and administered and for countries to plan ahead for vaccine purchase for the next year	Annual
Animal rabies cases	Species: dog, cat, livestock, wildlife, bat Result: positive, negative Total: per species, per result	Determination of the number of suspect rabies cases submitted for laboratory confirmation. The results indicate the number of positive and negative cases per species, as well as the totals	Results to provide an indication of the effectiveness of a surveillance program by examining the positive:negative ratio	Biannual
Human rabies cases	Diagnosis: clinical, laboratory Result: positive, negative	The number of human rabies cases diagnosed clinically and by laboratory confirmation	To determine the burden of the disease and to determine the efficacy of disease intervention strategies	Biannual
Number of people receiving PEP	Sex: male; female; unknown Age: <5 years, 5–14 years; ≥15 years; unknown age Wound category: I, II, or III	Number of humans receiving wound care and at least one dose of rabies vaccine for PEP	To determine the number of people receiving at least one dose of PEP in a country	Annual

HDR, human:dog ratio; PEP, post-exposure prophylaxis.

including completeness, correctness, and timeliness of reporting. Reported data will thus remain of the utmost quality, ensuring its usefulness to decision makers and stakeholders. Customized reports can be created and tailored to each sector's needs—with only selected indicators included into each report—making them relevant to that specific sector or authority. Additionally, the PARACON Bulletin enables automatic analyses and visuals that can help target intervention programs toward high-risk areas in a country.

Often, donor-based funding projects that aim to improve surveillance initiate similar reporting bulletins, but they end abruptly if those donors discontinue support and maintenance and administration are not sustained (26). A bulletin hosted and administered by an independent organization that has no direct involvement in target countries, as is the case with the PARACON bulletin, would ensure the sustainability of programmes. The PARACON network enables countries to start small, making the initial steps toward improving surveillance a less daunting task.

Furthermore, direct international support will allow subregional focal points, WHO country offices and other subregional or national authorities to assist countries and contribute valuable data to this regional bulletin.

Although the PARACON bulletin will help to improve the surveillance networks of individual countries, it cannot compensate for a system lacking any basic surveillance. The first step toward collecting reliable and realistic data reflecting the true rabies situation is awareness at the community level and the subsequent collection of relevant data. While in some countries, surveillance is hampered because no laboratory confirmation exists, a lack of surveillance can generally be attributed to the logistical constraints associated with sample submission (27, 28). Without a surveillance foundation, any data collection system will be a redundant tool. Thus, countries will need to implement a collective plan for improving rabies surveillance concurrently with the implementation of the PARACON bulletin. What needs to be known and what minimum requirements are to be met to establish adequate rabies surveillance for both humans and animals has recently been compiled in the rabies surveillance blueprint (29). In doing so, the PARACON bulletin will build upon these foundational elements and can also be integrated into existing HIS to improve data flow.

CONCLUSION

The lack of awareness and knowledge about the true burden and impact of rabies within countries in mainland Africa remain the primary barrier to the control and elimination of this disease. With poor rabies surveillance throughout Africa, there remains little political will and motivation to prioritize rabies among other notifiable diseases, resulting in its continued neglect. Improved surveillance is likely to lead to increased interest and more targeted and sustainable control strategies.

Pan-African Rabies Control Network has committed to provide countries with an effective, simple, and free-to-use bulletin for rabies that aims to address the issues of poor reporting and data quality in Africa as a whole. With the successes of other regional rabies reporting bulletins, as well as the addition of the PARACON bulletin for Africa, the next step would be to extend these regional databases into a global collective. With the unification of national data reporting systems and the reduced need for redundant reporting and the use of streamlined and automated data management systems, the expansion of regional bulletins into a global rabies-specific disease database is practicable. As a result, reporting burdens will be relieved and with improved data, decision makers and stakeholders can be convinced that rabies elimination is feasible within their country. With these tools and the support from the international community, the recent global declaration for the elimination of canine-mediated human rabies by 2030 (30) seems a realistic target for countries to aspire toward.

AUTHOR CONTRIBUTIONS

All of the authors contributed equally to the conception, development and drafting of the manuscript.

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REFERENCES

1. WHO. *First WHO Report on Neglected Tropical Diseases: Working to Overcome the Global Impact of Neglected Tropical Diseases*. Geneva: (2010). Available from: http://apps.who.int/iris/bitstream/10665/44440/1/9789241564090_eng.pdf
2. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):1–20. doi:10.1371/journal.pntd.0003709
3. WHO. WHO expert consultation on rabies. 2nd report. *WHO Technical Report Series 982*. Geneva: World Health Organisation (2013). p. 1–141.
4. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda ME, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83(5):360–8. doi:10.1590/S0042-96862005000500012
5. Shwiff S, Hampson K, Anderson A. Potential economic benefits of eliminating canine rabies. *Antiviral Res* (2013) 98(2):352–6. doi:10.1016/j.antiviral.2013.03.004
6. Nel LH. Discrepancies in data reporting for rabies, Africa. *Emerg Infect Dis* (2013) 19(4):529–33. doi:10.3201/eid1904.120185
7. Taylor LH, Hampson K, Fahrion A, Abela-Ridder B, Nel LH. Difficulties in estimating the human burden of canine rabies. *Acta Trop* (2015) 165:133–40. doi:10.1016/j.actatropica.2015.12.007
8. Fahrion AS, Mikhailov A, Abela-Ridder B, Giacinti J, Harries J. Weekly epidemiological record relevé épidémiologique hebdomadaire. *World Health Organ* (2016) 91(2):13–20.
9. Mtema Z, Changalucha J, Cleaveland S, Elias M, Ferguson HM, Halliday JE, et al. Mobile phones as surveillance tools: implementing and evaluating a large-scale intersectoral surveillance system for rabies in Tanzania. *PLoS Med* (2016) 13(4):e1002002. doi:10.1371/journal.pmed.1002002
10. Meslin FX, Briggs DJ. Eliminating canine rabies, the principal source of human infection: what will it take? *Antiviral Res* (2013) 98(2):291–6. doi:10.1016/j.antiviral.2013.03.011
11. Halliday J, Daborn C, Auty H, Mtema Z, Lembo T, Bronsvoort BM, et al. Bringing together emerging and endemic zoonoses surveillance: shared

challenges and a common solution. *Philos Trans R Soc Lond B Biol Sci* (2012) 367(1604):2872–80. doi:10.1098/rstb.2011.0362

12. Taylor LH, Knopf L. Surveillance of human rabies by national authorities – a global survey. *Zoonoses Public Health* (2015) 62(7):543–52. doi:10.1111/zph.12183
13. WHO. Constant evolution of the online rabies information system, Rabnet. *Releve Epidemiologique Hebdomadaire* (2005) 80(7):63–4.
14. OIE. *WAHID Interface – OIE World Animal Health Information Database*. (2014). Available from: http://web.oie.int/wahis/public.php?page=home
15. Scott TP, Coetzer A, de Balogh K, Wright N, Nel LH. The Pan-African Rabies Control Network (PARACON): a unified approach to eliminating canine rabies in Africa. *Antiviral Res* (2015) 124:93–100. doi:10.1016/j.antiviral.2015.10.002
16. PAHO. *Epidemiological Information System*. (2016). Available from: http://siepi.panaftosa.org.br/Panel.aspx?Idioma=i
17. Freuling CM, Kloss D, Schroder R, Kliemt A, Muller T. The WHO rabies bulletin Europe: a key source of information on rabies and a pivotal tool for surveillance and epidemiology. *Rev Sci Tech* (2012) 31(3):799–807.
18. Venczel L. GHSA field perspectives: Vietnam. *CDC Global Health Security Agenda/Ebola Grantee Meeting*. Centres for Disease Control and Prevention (2016). Available from: http://www.cdc.gov/globalhealth/security/materials/pdf/day2/perspectives-from-the-field.pdf
19. WHO iERG. *Advancing Health Information Systems: Experiences from Implementing DHIS 2 in Africa*. (2012). Available from: http://www.who.int/woman_child_accountability/ierg/reports/11_Nielsen_HISP.pdf
20. Chidawanyika H, Nyika P, Katiyo J, Sox A, Chokuda T, Peter K, et al. Success in revitalizing weekly disease surveillance system in Zimbabwe using cell-phone mediated data transmission, 2009-2013. *Online J Public Health Inform* (2014) 6:2579. doi:10.5210/ojphi.v6i1.5171
21. Chisha Z, Larsen DA, Burns M, Miller JM, Chirwa J, Mbwili C, et al. Enhanced surveillance and data feedback loop associated with improved malaria data in Lusaka, Zambia. *Malar J* (2015) 14(1):222. doi:10.1186/s12936-015-0735-y
22. Knobel DL, Laurenson MK, Kazwala RR, Boden LA, Cleaveland S. A cross-sectional study of factors associated with dog ownership in Tanzania. *BMC Vet Res* (2008) 4:5. doi:10.1186/1746-6148-4-5
23. Cleaveland S, Beyer H, Hampson K, Haydon D, Lankester F, Lembo T, et al. The changing landscape of rabies epidemiology and control. *Onderstepoort J Vet Res* (2014) 81(2):1–8. doi:10.4102/ojvr.v82i2.731
24. Davlin SL, VonVille HM. Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* (2012) 30(24):3492–502. doi:10.1016/j.vaccine.2012.03.069
25. Manya A, Braa J, Øverland L, Titlestad OH, Mumo J, Nzioka C. National roll out of district health information software (DHIS 2) in Kenya, 2011 – central server and cloud based infrastructure. *IST-Africa 2012 Conference Proceedings*. Dar es Salaam (2012). p. 1–9.
26. FAO. Challenges of animal health information systems and surveillance for animal diseases and zoonoses. *FAO Animal Production and Health Proceedings*. Rome: FAO (2011).
27. Weyer J, Blumberg L. Rabies: challenge of diagnosis in resource poor countries. *Infect Dis J Pak* (2007) 16(3):86–8.
28. Tricou V, Bouscaillou J, Kamba Mebourou E, Koyanongo FD, Nakouné E, Kazanji M. Surveillance of canine rabies in the Central African Republic: impact on human health and molecular epidemiology. *PLoS Negl Trop Dis* (2016) 10(2):e0004433. doi:10.1371/journal.pntd.0004433
29. GARC. *Rabies Surveillance Blueprint*. (2014). Available from: http://rabies-surveillanceblueprint.org/
30. WHO, OIE. Global elimination of dog-mediated human rabies. *Report of the Rabies Global Conference*. Geneva (2015). Available from: http://www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/Rabies_portal/EN_RabiesConfReport.pdf

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Rabies Vaccination Targets for Stray Dog Populations

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The role of stray dogs in the persistence of domestic dog rabies, and whether removal of such dogs is beneficial, remains contentious issues for control programs seeking to eliminate rabies. While a community might reach the WHO vaccination target of 70% for dogs that can be handled, the stray or neighborhood dogs that are too wary of humans to be held are a more problematic population to vaccinate. Here, we present a method to estimate vaccination targets for stray dogs when the dog population is made up of stray, free-roaming, and confined dogs, where the latter two types are considered to have an identifiable owner. The control effort required for stray dogs is determined by the *type-reproduction number*, T_1, the number of stray dogs infected by one rabid stray dog either directly or via *any* chain of infection involving owned dogs. Like the basic reproduction number R_0 for single host populations, T_1 determines the vaccination effort required to control the spread of disease when control is targeted at one host type, and there is a mix of host types. The application of T_1 to rabies in mixed populations of stray and owned dogs is novel. We show that the outcome is sensitive to the vaccination coverage in the owned dog population, such that if vaccination rates of owned dogs were too low then no control effort targeting stray dogs is able to control or eliminate rabies. The required vaccination level also depends on the composition of the dog population, where a high proportion of either stray or free-roaming dogs implies unrealistically high vaccination levels are required to prevent rabies. We find that the required control effort is less sensitive to continuous culling that increases the death rate of stray dogs than to changes in the carrying capacity of the stray dog population.

Keywords: dog rabies, canine rabies, mathematical model, infectious disease modeling, zoonosis

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1. INTRODUCTION

Rabies is a preventable infectious disease in warm-blooded animals that causes acute encephalitis and death. The etiological agent is a virus belonging to the genus *Lyssavirus*. Canine rabies is the form carried by domestic dogs that is overwhelmingly responsible for approximately 59,000 human deaths per year (1) where transmission of the virus occurs via a dog bite.

Despite the presence of rabies control programs, rabies remains endemic in over 80 countries (2). The main component of these programs is vaccination, where the long-held World Health Organization (WHO) recommendation of a dog vaccination target of 70% (2, 3) is most often the aim. What we now increasingly appreciate is that differences in the local ecology of the dog population (4), and the dogs' relationships with the humans they live with (5), can determine the outcome of a control program (6, 7).

The efficacy of a vaccination program is expected to depend on vaccinated dogs living long enough for herd immunity to build up. A relatively rapid turnover in a dog population (where a population is largely made up of stray dogs, for example) ought to decrease the efficacy of a vaccination program (8, 9). Field studies that have measured turnover rates found they are higher in regions with higher dog density, and they are especially high in areas where the stray dog population is high (10). Such thinking and observations have led to the Animal Birth Control program implemented in India, for example, to sterilize the female dogs that were captured and vaccinated, conscious that this would improve the survival of these dogs (no costs of reproduction), reduce population turnover, and increase the impact of the vaccination effort (11, 12).

The proportion of the dog population that is stray (ownerless) varies considerably from one country to another, ranging from 5% in Tanzania (13), 19% in Sri Lanka (6), to as high as 60% in India (12). Stray dogs are typically wary of humans such that they cannot be held, and so vaccination of these dogs needs to be achieved either by physically capturing the dogs or by distributing oral baits (2, 14). In either case, reaching a sufficiently high vaccination coverage of the *whole* dog population becomes a more difficult and costly endeavor.

Another contributing factor to the success of vaccination programs is the relationships that dogs share with the humans they live with. Some owned dogs are fully confined, and others partially free-roaming (6). The degree of care humans provide for dogs ranges from none at all, to supplying food and/or shelter only (but not claiming ownership), to full adoption of the dog as a pet where the dog would be provided food, shelter, and health care (5). By contrast, some claim ownership but provide no care at all (15). These differences can have a considerable effect on the dog's health and exposure to diseases.

A widely used epidemiological measurement of infectious disease transmission is the basic reproduction number, or R_0, which describes the average number of secondary cases produced by a typical infectious individual in a completely susceptible population (16). It can be interpreted as the initial growth rate of the spread of an infectious disease. It follows that when $R_0 > 1$, the disease will cause an epidemic in the population, and when $R_0 < 1$, the disease will die out. Theoretical literature shows how R_0 is calculated and then applied to public health, such that a vaccination coverage of $1 - 1/R_0$ is expected to lead to the elimination of a disease (16, 17). However, this assumes that coverage occurs homogeneously across the population. In the context of dog rabies, this may not be the case since dog rabies vaccination campaigns typically target specific types of dogs, such as strays (11, 18). When control targets a single type of host then the required effort can be measured by the type-reproduction number (19).

The type-reproduction number, T_1, is an epidemiological quantity introduced by Roberts and Heesterbeek (19) that measures the effort required to prevent outbreaks when control targets a single type of host. For homogeneous populations, its threshold coincides with R_0. In a heterogeneous population, say, with three host types, the concept of T_1 supposes there is a single infectious type 1 host in an otherwise fully susceptible population; T_1 is the average number of type 1 infections caused by the primary case, either directly or via *any* chain of infection involving host types 2 and 3 (each chain starts with the initial infected type 1 host and ends in a second type 1 infection). Similar to R_0, the critical fraction of host type 1 vaccination coverage required to prevent outbreaks in the entire population is $1 - 1/T_1$. We use this relationship to present results on vaccination targets for stray dogs.

The key to interpreting T_1 and how it relates to vaccination coverage targets is that there are three cases to consider. The first is that $T_1 > 1$. This implies that $R_0 > 1$ (19) and that control efforts that target type 1 have the potential to bring an outbreak under control, or prevent outbreaks from occurring, provided a vaccination coverage of $1 - 1/T_1$ can be achieved. The second is where $T_1 < 1$ which implies that $R_0 < 1$ (20) so no control efforts need be applied to type 1 (or indeed to any type). The third and final case is where transmission between the other host types (types 2 and 3, for example) occurs enough such that even if *every* type 1 host were vaccinated or removed, outbreaks would still occur among the other types. Mathematically, this coincides with a single infected stray dog causing an infinite number of stray dog infections because the chains of infection in the owned dog host types never stop.

In this paper, we consider the control of canine rabies in a mixed dog population consisting of strays, owned free-roaming dogs, and owned confined dogs. In particular, we show how T_1 can be calculated from a differential equation model for rabies transmission, and how it is related to R_0. Our goal is to understand how vaccination targets for strays, determined by the quantity T_1, are affected by the composition of the dog population, the numbers of dogs (dog density), the vaccination coverage of the owned dog population, and the mortality rates of the stray population.

The mathematics we use is presented in discrete boxes and contained as figures. The reader will be able to "skip" the mathematics if they wish to do so and still follow the methods, results, and conclusions of the paper, provided they understand the epidemiological quantities, T_1 and R_0.

2. MATERIALS AND METHODS

Motivated by the studies of dog populations by Matter et al. (6) and Massei et al. (5), who both observed differences in dog ownership styles, our modeling approach divides the dog population into three ownership types: stray (type 1), owned free-roaming (type 2), and owned confined (type 3). In our mathematical model of dog rabies transmission, we define stray dogs to be ownerless, hence have no health care, and must forage for their own food. Owned free-roaming dogs are defined to be regularly fed by the community but are provided little to no health care. Owned confined dogs are regularly fed and have access to health care through their owners. Under these differences, stray, owned free-roaming, and owned confined dogs have short, medium, and long life spans, respectively.

A difference in life span between groups of dogs creates a slight epidemiological difference (12, 21) because high natural mortality or additional density-dependent mortality implies that an exposed stray could die of natural means before becoming rabid, whereas this is much more unlikely for an owned dog. The stronger epidemiological differences between the host types are in terms of exposure, and therefore biting rates and transmission to other dogs. Our premise is that an owned confined dog, unless it is momentarily free to roam during hunting or some other activity, will not normally be free to come across or attack other dogs, and hence, is assumed not to wander beyond their owner's property.

2.1. SEI Canine Rabies Model with Three Dog Ownership Types

We extend the susceptible-exposed-infectious (SEI) compartment model typically adopted for rabies (22–24) by sub-dividing the dog population into the three types and hence having nine equations (see **Figure 1**). Birth and death rates of type i are a_i and b_i, respectively (for type $i = 1, 2, 3$). Stray dogs face an additional per capita density-dependent death rate γN_1 (proportional to the stray dog population size). Susceptible (S) dogs become infected at a rate proportional to the number of infectious dogs of each type. Before becoming infectious (I), they enter the exposed (E) state, where they are infected but not yet infectious, for an average period of $1/\sigma$. Disease always ends in death at disease mortality rate μ. The flow diagram of the model is presented in **Figure 2**.

The transmission rates within and between the three types of dogs are given by the transmission matrix β, where the element β_{ij} represents the transmission rate to type i from type j, for i, $j = (1, 2, 3)$. Throughout the paper, we impose that owned free-roaming dogs and stray dogs both roam freely all of the time, so that they are at the highest risk of infection in terms of exposure. Confined dogs are at the lowest risk of infection as they spend minimal time outside their owner's property. Mathematically, the transmission rates between the three types of dogs (β_{ij}) are now determined by whether or not the dogs are confined. This simplifies the transmission matrix to contain three different rates: p, between two unconfined dogs; q, between one confined dog and one unconfined dog; and r, between two confined dogs.

Parameter values for the average life expectancy of a stray dog ($1/b_1 = 3$ years), average exposed ($1/\sigma = 25.5$ days), and infectious periods ($1/\mu = 5.7$ days) were taken from Hampson et al. (23). The average life expectancy of the confined dog ($1/b_3$) is set at 8 years, reasonably within the range Patronek et al. (25) determined for owned pet dogs. Owned free-roaming dogs live for 5 years on average ($1/b_2$), a value chosen to be between that of the average confined and stray dogs. Elements of the transmission matrix β remain fixed throughout the paper, at values chosen ($(p, q, r) = (0.4, 0.04, 0.004) \times 10^{-3}$ per dog per day) so that for a population size of 1,000 composed of 50% stray, 25% owned free-roaming, and 25% owned confined (these proportions are arbitrary), the model has an $R_0 = 1.62$, a value in line with other studies of dog rabies (8, 23, 26). We chose $p > q > r$ to reflect that an infectious owned confined dog is more likely to be restrained should the owner observe their dog exhibit uncharacteristic aggression. See **Table 1** for baseline values of the model.

Numerical integration of the system was performed using MATLAB (27) with an integration time of 125 years to allow the system to settle to its endemic equilibrium, which is the solution to the differential equations (where the numbers of dogs no longer change over time) in the presence of disease.

2.2. Calculation of R_0 and T_1 of the Model

To estimate R_0 for the model, and hence the control effort required to eliminate the virus, we define a next-generation matrix, K (28). This methodology has been used for numerous human and

Canine Rabies Model

The model for rabies in a population of dogs consisting of three host types is described by the following equations:

$$\begin{aligned}
\frac{dS_1}{dt} &= a_1N_1 - (b_1 + \gamma N_1)S_1 - (\beta_{11}I_1 + \beta_{12}I_2 + \beta_{13}I_3)S_1\,,\\
\frac{dE_1}{dt} &= (\beta_{11}I_1 + \beta_{12}I_2 + \beta_{13}I_3)S_1 - (\sigma + b_1 + \gamma N_1)E_1\,,\\
\frac{dI_1}{dt} &= \sigma E_1 - (\mu + b_1 + \gamma N_1)I_1\,,\\
\frac{dS_2}{dt} &= a_2 - b_2S_2 - (\beta_{21}I_1 + \beta_{22}I_2 + \beta_{23}I_3)S_2\,,\\
\frac{dE_2}{dt} &= (\beta_{21}I_1 + \beta_{22}I_2 + \beta_{23}I_3)S_2 - (\sigma + b_2)E_2\,,\\
\frac{dI_2}{dt} &= \sigma E_2 - (\mu + b_2)I_2\,,\\
\frac{dS_3}{dt} &= a_3 - b_3S_3 - (\beta_{31}I_1 + \beta_{32}I_2 + \beta_{33}I_3)S_3\,,\\
\frac{dE_3}{dt} &= (\beta_{31}I_1 + \beta_{32}I_2 + \beta_{33}I_3)S_3 - (\sigma + b_3)E_3\,,\\
\frac{dI_3}{dt} &= \sigma E_3 - (\mu + b_3)I_3\,.
\end{aligned}$$

Please see Table 1 and the main text for parameter descriptions.

FIGURE 1 | **System of equations for the model of canine rabies with three dog ownership types**.

wildlife disease systems such as Lyme disease (29). The matrix can be found via a system of differential equations (i.e., those in **Figure 1**) or by direct epidemiological reasoning (28). Such a matrix consists of elements k_{ij}, that enumerate, on average, how many infected of one type (type *i*) a single infected of another type (type *j*) would produce over its entire infectious lifetime (28). For example, the average number of confined dogs (type 3) infected by a single rabid stray dog (type 1) is given by k_{31}.

In creating a next-generation matrix, it is critical that type is not an attribute that a host can change over time. This means we must make the simplifying assumption that dogs do not change from one type to another over their lifetime, acknowledging this surely does occur to some degree. The simplification makes possible the explicit calculation of R_0 (see **Figure 3**) and, more importantly, the calculation of vaccination targets for the stray dog population (see **Figure 4**) without resorting to numerically solving large systems of differential equations.

Values of R_0 and T_1 were calculated for different compositions of dog types and different population sizes. The sizes were chosen to indicate the effects of higher density and therefore higher transmission (because the model assumes that contacts are density-dependent). Initial type population sizes (N_1, N_2, and N_3) were systematically assigned values from 0 to N by steps of 25, for $N = 1{,}000$, 2,000, and 5,000 dogs, where $N = N_1 + N_2 + N_3$. This allows the composition of each dog type to range from 0 to 100%, and all combinations of dog type composition are obtained. Birth rates of owned dogs (a_2 and a_3) and the strength of density-dependent mortality (γ) for stray dogs were determined by the assigned initial population size of each type and analytically derived by the expressions: $N_1 = S_1 = (a_1 - b_1)/\gamma$, $N_2 = S_2 = a_2/b_2$, $N_3 = S_3 = a_3/b_3$. Indeed, this is the disease-free equilibrium, which is the solution to the differential equations (where the numbers of dogs no longer change over time) in the absence of disease. For example, for initial population size $N = 1{,}000$ and $N_3 = 250$, we can use the relationship $N_3 = a_3/b_3$ (as the natural death rate b_i is fixed) to solve for the birth rate of owned confined dogs ($a_3 = N_3 \times b_3 \approx 0.0856$).

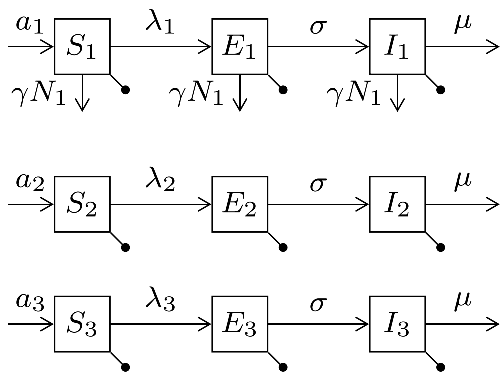

FIGURE 2 | Diagram of the canine rabies model with three dog ownership types. Type $i = (1, 2, 3)$ represent stray dogs; owned free-roaming dogs; and owned confined dogs, respectively. The bullets represent the natural death rates b_i. Infection of susceptible dogs occurs at a rate $\lambda_i = \beta_{i1}I_1 + \beta_{i2}I_2 + \beta_{i3}I_3$, also known as the force of infection. Stray dogs (type 1) face an additional density-dependent mortality at rate γN_1. See **Table 1** for parameter meanings.

3. RESULTS

We first visualize the results of solving the differential equation model given in **Figure 1** while varying the initial composition of the dog population and the initial size of the dog population. The initial proportions of dogs that are stray, free-roaming, and confined are varied but always sum to 1. This means that the effects of the composition of the dog population on R_0; the number of infected dogs at equilibrium; and rabies prevalence can all be visualized as ternary plots (see **Figure 5**). The corners of each of the pictured triangles represent dog populations at the extremes where there are only strays, or only owned free-roaming dogs, or only owned confined dogs. The sides of the triangle represent when the dog population is a mix of two dog types, and the region inside the triangle represents populations that are a mix of all three.

3.1. R_0 and Rabies Prevalence

The first row of panels in **Figures 5A–C** is ternary plots of R_0 and shows that the highest values occur when the dog population consists entirely of owned free-roaming dogs (top corners of the

TABLE 1 | Parameter meanings and baseline values of the SEI canine rabies model with three dog ownership types.

Parameter	Biological meaning	Baseline value	Reference
a_1	Per capita birth rate of stray dogs	0.0027/day	Assumption
a_2	Birth rate of owned free-roaming dogs	(variable) dogs/day	Assumption
a_3	Birth rate of owned confined dogs	(variable) dogs/day	Assumption
$1/b_1$	Average natural life span of stray dogs	3 years	(23)
$1/b_2$	Average natural life span of owned free-roaming dogs	5 years	Assumption
$1/b_3$	Average natural life span of owned confined dogs	8 years	(25)
$1/\sigma$	Average incubation period	25.5 days	(23)
$1/\mu$	Average infectious period	5.7 days	(23)
γ	Strength of density-dependent mortality	(variable)/(dogs × day)	
β	β_{ij}: transmission term that a dog of type *j* infects a dog of type *i* (*i*, *j* = 1, 2, 3)	$\begin{pmatrix} 0.4 & 0.4 & 0.04 \\ 0.4 & 0.4 & 0.04 \\ 0.04 & 0.04 & 0.004 \end{pmatrix} \times 10^{-3} / (\text{dog} \times \text{day})$	Assumption

*Parameters with values that vary throughout the paper are marked as (variable). See **Figure 5** for details on the form of the transmission matrix.*

An analytic expression for R_0

The next-generation matrix for the model is:

$$K = \begin{bmatrix} \theta\beta_{11}N_1^* & \epsilon\beta_{12}N_1^* & \alpha\beta_{13}N_1^* \\ \theta\beta_{21}N_2^* & \epsilon\beta_{22}N_2^* & \alpha\beta_{23}N_2^* \\ \theta\beta_{31}N_3^* & \epsilon\beta_{32}N_3^* & \alpha\beta_{33}N_3^* \end{bmatrix},$$

where

$$\theta = \sigma/[(a_1+\mu)(a_1+\sigma)],$$
$$\epsilon = \sigma/[(b_2+\mu)(b_2+\sigma)],$$
$$\alpha = \sigma/[(b_3+\mu)(b_3+\sigma)],$$

and N_i^* is the equilibrium of type $i = (1, 2, 3)$.

By imposing that type 1 and type 2 dogs have the same level of exposure, the transmission matrix simplifies to having three different values:

$$p = \beta_{11} = \beta_{12} = \beta_{21} = \beta_{22},$$
$$q = \beta_{13} = \beta_{31} = \beta_{23} = \beta_{32},$$
$$r = \beta_{33}.$$

With this pattern of transmission rates the transmission matrix $\boldsymbol{\beta}$ takes the form

$$\boldsymbol{\beta} = \begin{bmatrix} p & p & q \\ p & p & q \\ q & q & r \end{bmatrix}.$$

The basic reproduction number is then:

$$R_0 = \frac{1}{2}\left(\Lambda + \sqrt{\Lambda^2 + 4N_1^*\alpha(q^2 - pr)(N_2^*\epsilon + N_3^*\theta)}\right),$$

where

$$\Lambda = \theta p N_1^* + \epsilon p N_2^* + \alpha r N_3^*.$$

FIGURE 3 | **Analytic expression of R_0 using the next-generation matrix**.

triangles). Slightly lower values of R_0 occur when there is a mix of stray and owned free-roaming dogs, and R_0 drops rapidly when an increasing part of the dog population is owned and confined. These patterns are unaffected by higher initial population sizes; higher dog densities uniformly increase R_0. The peak R_0 value occurs when the entire population is owned and free-roaming (rather than when all dogs are stray) because owned free-roaming dogs have higher survival and hence an exposed dog is less likely to die of natural causes before becoming rabid.

The second row of panels in **Figures 5D–F** is ternary plots of the total number of infected dogs when the differential equation model settles to an equilibrium. In this case, there are interesting differences between the plots for different initial dog populations. At low densities the worst case scenario (highest numbers of infected dogs) occurs when the dog population consists mostly of stray dogs, whereas at higher densities higher numbers of infected dogs arise when the population consists mostly of owned free-roaming dogs. The contour line where there is one infected dog in the total population (**Figures 5D–F**) is roughly equivalent to when $R_0 = 1$ (**Figures 5A–C**). Where there is an "empty" triangle, the total number of infected dogs (in the "exposed" and "infectious" state) is less than one, which coincides with when $R_0 < 1$. This "empty" triangle becomes smaller for higher initial dog densities. There is a highly non-linear contour line at 30 infected dogs in **Figure 5F**. The differences in birth rates and life spans between the host types cause both the non-linear contour line and the shift from maximum numbers of infected dogs occurring when all dogs are stray (at $N = 1{,}000$) to all dogs are owned free-roaming (at $N = 2{,}000$ and $N = 5{,}000$). For the stray dogs, the lower population sizes are associated with higher density-dependent mortality and hence greater population turnover, while for the owned dogs their life spans are fixed, and only the birth rate varies when population sizes are lower or higher.

The final row of panels in **Figures 5G–I** is ternary plots of the proportion of the total number of dogs that are infected at equilibrium (prevalence). Again there is a shift from low density to high density with peak prevalence first corresponding to a large proportion of stray dogs, and then corresponding to a large

An analytic expression for T_1

T_1 is the type reproduction number introduced by Roberts & Heesterbeek (19) and calculated from the next-generation matrix as:

$$T_1 = e'K(I-(I-P)K)^{-1}e\,,$$

where for our canine rabies model, the prime denotes transpose, K is the next-generation matrix, I is a 3×3 identity matrix,

$$P = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix},$$

and

$$e = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix}.$$

Evaluating this formula gives,

$$T_1 = k_{11} + k_{12}\left[\frac{k_{21}}{1-k_{22}} + \frac{k_{23}M(k_{31}(1-k_{22})+k_{23}k_{21})}{(1-k_{22})^2}\right] + k_{13}M\left[k_{31} + \frac{k_{32}k_{21}}{1-k_{22}}\right],$$

where

$$M = \frac{1-k_{22}}{(1-k_{33})(1-k_{22})-k_{32}k_{23}}.$$

FIGURE 4 | **Analytic expression for the type-reproduction number in terms of the elements (the k_{ij}) of the next-generation matrix K.**

proportion of owned free-roaming dogs. For all model outcomes, the general pattern is that if the proportion of confined dogs is fixed, then model outcomes are largely insensitive to whether the remaining dogs in the population are strays or owned free-roaming dogs.

3.2. Impact of Stray Dogs in the Presence of Vaccination of Owned Dogs

We now suppose that a proportion of owned dogs (both free-roaming and confined) is vaccinated and ask what vaccination rate for strays is required to eliminate rabies. This vaccination target for strays, calculated as $1 - 1/T_1$, is shown in **Figure 6** where we again show results for three scenarios: when the initial size of the dog population is 1,000, 2,000, and 5,000. For the two higher dog densities, the vaccination targets for the stray dogs are always greater than 50%, compared to much more manageable targets for the low density scenario. **Figure 6** is a sharp reminder of the sensitivity of vaccination targets to dog density typically predicted when density-dependent transmission rates are assumed. The areas to the left of the lines indicate when rabies remains uncontrolled. For example, for $N = 5{,}000$ when 60% of owned dogs are vaccinated, rabies remains endemic even if all stray dogs were vaccinated. The points labeled A, B, and C in **Figure 6** indicate where the critical vaccination effort for stray dogs is equal to the vaccination effort for owned dogs. The region to the left of these points represent when the critical vaccination effort required for stray dogs is higher than the level of vaccination achieved in the owned dogs and hence further increasing the effort directed toward stray dogs would be inefficient, misguided, and unrealistic (because vaccinating stray dogs is far more costly and difficult than vaccinating owned dogs).

In **Figure 7**, we again use ternary plots to show how stray vaccination targets depend on the composition of the dog population when 70% of the owned dog population is vaccinated. As was the case for **Figures 5D–I**, there is a shift between the low density case ($N = 1{,}000$) and the higher density cases ($N = 2{,}000$ and $N = 5{,}000$) where higher vaccination targets change from being associated with a high proportion of strays to a high proportion of owned free-roaming dogs. The light blue areas on these plots represent where vaccination of the stray dog population is not required as vaccinating 70% of the owned population is enough to eliminate rabies. The region where the stray vaccination target is larger than 1 (labeled danger zone) indicates when $R_0 > 1$ despite a 70% owned dog vaccination rate (independent of the vaccination level of stray dogs). In this danger zone region, higher vaccination levels in the owned dog population are required before any effort directed toward the stray dogs could possibly be effective.

3.3. Effectiveness of Reducing the Stray Dog Population

We now consider the effects of varying the stray dog demographic parameters on the critical stray dog vaccination coverage; b_1 represents the background mortality rate and γ determines the strength of density-dependence which sets the carrying capacity of the stray dog population. The three panels of **Figures 8A–C** correspond to having an owned dog population of 500, 1,000, and

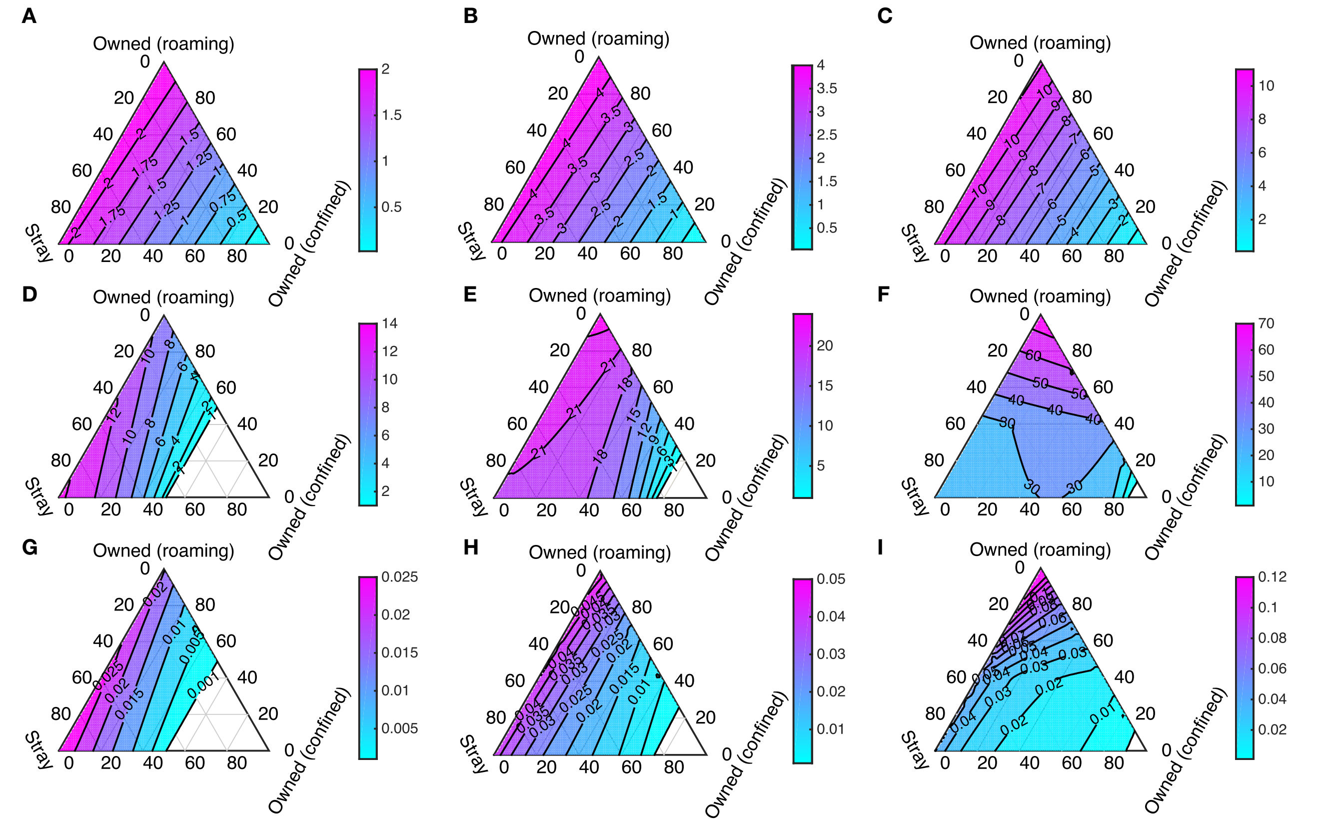

FIGURE 5 | **R_0 (first row: (A–C)), number of infected dogs at equilibrium (second row: (D–F)), and rabies prevalence (third row: (G–I)) calculated for three different initial total population size: 1,000 (first column: (A,D,G)); 2,000 (second column: (B,E,H)); and 5,000 (third column: (C,F,I))**. The corners of each triangle represent when populations contain only dogs of one type (as labeled). The edges represent when populations contain two dog types. The center of the triangle represents when the three dog types each make up an equal percentage of the population (totaling 100%).

2,500, respectively, and an owned dog vaccination rate of 70% is assumed.

The impact of a continuous stray dog culling program can, albeit simplistically, be modeled as an increase in b_1 (death rate), and modifications to the environment that *reduce* the stray dog carrying capacity (such as improving disposal of food) as an *increase* in γ. The top left corners of the panels in **Figure 8** correspond to $N_1 = 500$ (**Figure 8A**), 1,000 (**Figure 8B**), and 2,500 (**Figure 8C**). The variation in the vertical axis (γ) spans a decreasing carrying capacity by 33% from top to bottom. Similarly, the variation from left to right in the horizontal axis (b_1) is a 33% decrease in the average natural life span of a stray dog as representation of culling. For both parameters, increases result in reduced stray dog density but **Figure 8** shows that shifts in γ are more effective at bringing down the required vaccination rates for stray dogs. Note that on the vertical axis, γ is plotted in descending values to reflect an increasing carrying capacity.

4. DISCUSSION

We have used a differential equation model and the epidemiological quantity, T_1, introduced by Roberts and Heesterbeek (19), to explore how vaccination targets for stray dogs might be expected to depend on dog population size and composition, stray dog demography, and on the vaccination rate that is achieved in the owned dog population. Our study shows that an increase in public knowledge around rabies (such as proper disposal of garbage) can be effective in reducing the required vaccination targets for stray dogs. We have found that the required stray dog vaccination rate is sensitive to the proportion of the total dog population that is owned and free-roaming. Indeed, a dog population consisting wholly of free-roaming owned dogs is predicted to require a higher vaccination coverage to ensure it is rabies-free, compared to any other mix of types, and even compared to a population consisting entirely of stray dogs.

This is not to say that populations of owned free-roaming dogs are more challenging for rabies control because owned dogs can be handled and are therefore easier to vaccinate. With this consideration, populations of stray dogs are clearly the most problematic. However, for example, our findings do underline concerns about rabies entering Australia's northern communities where dog populations consist entirely of free-roaming dogs (30). There are typically no stray dogs in this population, but there are contacts with wild dogs (4). The insights we have presented here would predict that this mix of wild dogs and free-roaming domestic dogs could be highly vulnerable to a rabies incursion.

We emphasize that our modeling assumes that stray and owned free-roaming dogs have similar roaming behavior and hence similar exposure to infected dogs. The bottom right-hand corners of the ternary plots represent populations where a high proportion of the dog population is confined and these always correspond to the "safest" situations because the transmission rates of confined dogs are assumed to be much lower. The effect of higher proportions of stray dogs, which can be observed by traveling along the border of the ternary plot, is to subtly reduce R_0 (**Figures 5A–C**). This is because higher demographic turnover means that an exposed stray dog is slightly less likely to survive long enough to become rabid.

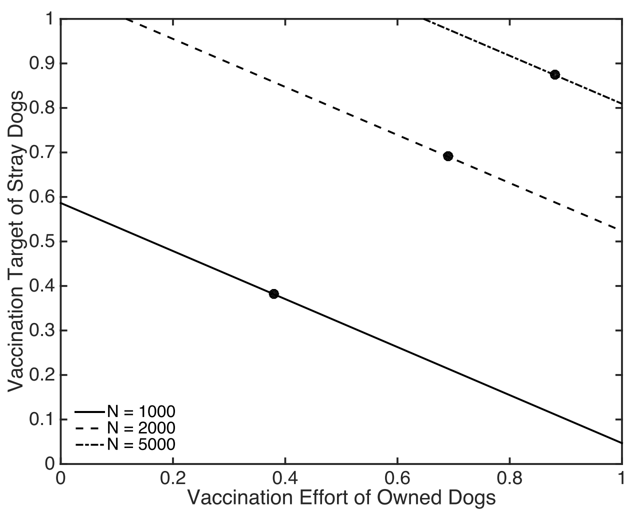

FIGURE 6 | **The critical proportion of stray dog vaccination coverage required to prevent outbreaks as a function of the proportion of vaccinated owned dogs for three total population sizes comprising 50% stray, 25% owned free-roaming, and 25% owned confined**. Filled black circles denote when the vaccination efforts are equal for owned and stray dogs. For $N = 1{,}000$, $(a_2, a_3, \gamma) = (0.1370, 0.0856, 3.6530 \times 10^{-6})$. For $N = 2{,}000$, $(a_2, a_3, \gamma) = (0.2740, 0.1712, 1.8265 \times 10^{-6})$. For $N = 5{,}000$, $(a_2, a_3, \gamma) = (0.6849, 0.4281, 7.3059 \times 10^{-7})$. Other parameters are specified in **Table 1**.

In general, the three types would likely exist to some degree in all populations of dogs, though for specific regions and countries one or two of the types might be in negligible numbers. Defining these three types of dogs is a simplification of the varied and complex relationships between dogs and humans. Whether an owned dog is confined or allowed to roam, and even whether a dog has an owner or not, will have answers that vary from yes to no to everything in between. We therefore acknowledge that in reality the composition of a dog population and the validity of allocating every member to one of three types will vary from one region to another. Similarly, it is clear that dog densities vary from location to location, and contact rates too, so while we can endeavor to be in the right "ball park" it is not easy to be more precise than we have been unless we parameterize the model for a particular region where dog density, dog composition, and R_0 are all known. Despite these caveats it is insightful to explore the consequences for rabies vaccination programs if there were groups of dogs that vary in their exposure (to bites from rabid dogs) as well as their freedom to infect other dogs should they become rabid.

The critical assumptions of this study are that dogs mix randomly at the population level, do not change from one type to another over their lifetime, and that every dog clearly belongs to one and only one type. The degree to which this is a simplification of reality, and what effect introducing further, more realistic, heterogeneity in the dog population would have on the epidemiological quantities that determine vaccination targets is unknown. Another core assumption is that the transmission rate between dogs has a linear relationship with density. This is a common feature of many rabies modeling studies (3, 23, 31); replacing the density-dependence with frequency-dependent contact in a standard SEIR compartmental model gives behavior that is discordant with observed dynamics (the dog population becomes extinct) (32), but there is conflicting evidence for density-dependent transmission and hence for the population thresholds one would expect to see as a result.

Our study highlights the importance of developing a better understanding of the dog ecology, such as dog population densities and degree of contact between the dogs, to guide future

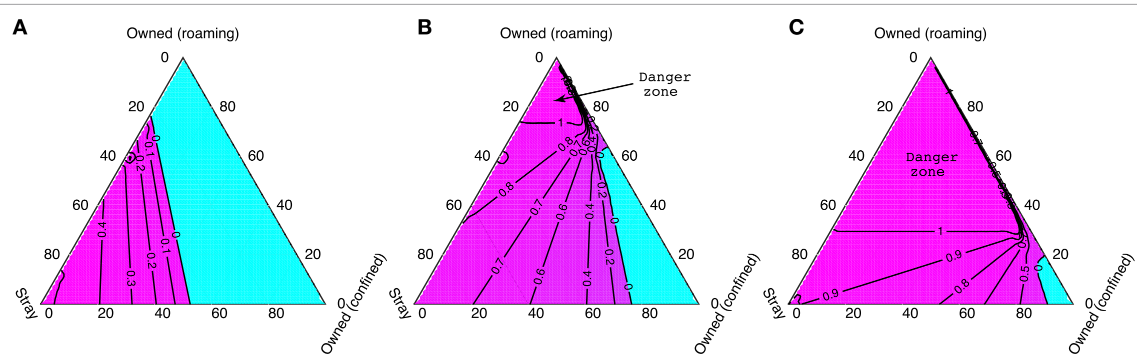

FIGURE 7 | **The critical stray dog vaccination targets for different total dog population sizes: (A) 1,000, (B) 2,000, and (C) 5,000, when 70% of owned dogs are vaccinated**. Corners of the triangle represent when the dog populations contain only dogs of one type (as labeled); the edges when populations contain two dog types only, and the center represents when the population is made up equally of all three types. The blue area shows when a 70% vaccination rate of owned dogs alone is sufficient to bring $R_0 < 1$. The region marked as "Danger zone" shows when vaccinating the entire stray dog population remains ineffective to control rabies despite a 70% owned dog vaccination rate.

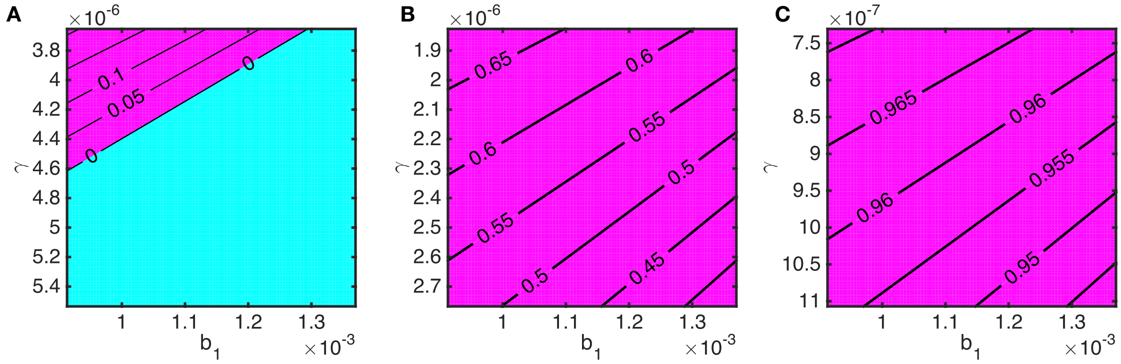

FIGURE 8 | The required stray dog vaccination targets to bring rabies under control in terms of natural death rate of stray dogs (b_1) and strength of density-dependent mortality (γ) for varying stray dog population size (determined by $N_1 = (a_1 - b_1)/\gamma$) when 70% of owned dogs are vaccinated. Owned dog population sizes are $N_2 = N_3 =$ **(A)** 250, **(B)** 500, and **(C)** 1,250. The blue area indicates when rabies is controlled without stray dog vaccination. The purple area shows the minimum proportion of stray dogs that must be vaccinated to bring $R_0 < 1$.

model development, improve model-based interpretation, and provide guidance to the design of vaccination programs. Our study provides a firmer scientific basis for vaccination programs aimed at stray or neighborhood dogs that cannot be handled and therefore cannot be brought to vaccination points. If the key dog ecology parameters can be estimated, then the theory provides definite vaccination targets, which can give greater confidence that a control program represents sufficient effort to eliminate canine rabies.

AUTHOR CONTRIBUTIONS

TL and SD together defined the research questions of the paper and designed the approach. TL performed much of the analytical work and obtained numerical solutions for the differential equations, created the figures, and helped write the manuscript. SD recovered many of the analytic results found by TL and led the writing of the manuscript.

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REFERENCES

1. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(5):e0003786. doi:10.1371/journal.pntd.0003786
2. World Health Organization. *WHO Expert Consultation on Rabies. Second Report*. (Vol. 932). Geneva: World Health Organization (2013).
3. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14(3):185–6. doi:10.1016/0264-410X(95)00197-9
4. Sparkes J, Fleming PJS, Ballard G, Scott-Orr H, Durr S, Ward MP. Canine rabies in Australia: a review of preparedness and research needs. *Zoonoses Public Health* (2015) 62:237–53. doi:10.1111/zph.12142
5. Massei G, Fooks AR, Horton DL, Callaby R, Sharma K, Dhakal IP, et al. Free-roaming dogs in Nepal: demographics, health and public knowledge, attitudes and practices. *Zoonoses Public Health* (2017) 64:29–40. doi:10.1111/zph.12280
6. Matter HC, Wandeler AI, Neuenschwander BE, Harischandra LPA, Meslin FX. Study of the dog population and the rabies control activities in the Mirigama area of Sri Lanka. *Acta Trop* (2000) 75:95–108. doi:10.1016/S0001-706X(99)00085-6
7. Tenzin T, Ahmed R, Debnath NC, Ahmed G, Yamage M. Free-roaming dog population estimation and status of the dog population management and rabies control program in Dhaka city, Bangladesh. *PLoS Negl Trop Dis* (2015) 9(5):e0003784. doi:10.1371/journal.pntd.0003784
8. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7(3):e1000053. doi:10.1371/journal.pbio.1000053
9. Kasempimolporn S, Sichanasai B, Saengseesom W, Puempumpanich S, Chatraporn S, Sitprija V. Prevalence of rabies virus infection and rabies antibody in stray dogs: a survey in Bangkok, Thailand. *Prev Vet Med* (2007) 78(3–4):325–32. doi:10.1016/j.prevetmed.2006.11.003
10. Kumarapeli V, Awerbuch-Friedlander T. Human rabies focusing on dog ecology – a challenge to public health in Sri Lanka. *Acta Trop* (2009) 112:33–7. doi:10.1016/j.actatropica.2009.06.009
11. Reece JF, Chawla SK. Control of rabies in Jaipur, India, by the sterilisation and vaccination of neighbourhood dogs. *Vet Rec* (2006) 159:379–83. doi:10.1136/vr.159.12.379
12. Totton SC, Wandeler AI, Zinsstag J, Bauch CT, Ribble CS, Rosatte RC, et al. Stray dog population demographics in Jodhpur, India following a population control/rabies vaccination program. *Prev Vet Med* (2010) 97(1):51–7. doi:10.1016/j.prevetmed.2010.07.009
13. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
14. Roberts MG, Aubert MF. A model for the control of *Echinococcus multilocularis* in France. *Vet Parasitol* (1995) 56(1–3):67–74. doi:10.1016/0304-4017(94)00655-V
15. Bardosh K, Sambo M, Sikana L, Hampson K, Welburn SC. Eliminating rabies in Tanzania? Local understandings and responses to mass dog vaccination in Kilombero and Ulanga districts. *PLoS Negl Trop Dis* (2014) 8(6):e2935. doi:10.1371/journal.pntd.0002935
16. Keeling MJ, Rohani P. *Modeling Infectious Diseases in Humans and Animals*. Princeton, NJ: Princeton University Press (2008). p. 864–65.
17. Fine PEM. Herd immunity: history, theory, practice. *Epidemiol Rev* (1993) 15(2):265–302. doi:10.1093/oxfordjournals.epirev.a036121

18. Yoak AJ, Reece JF, Gehrt SD, Hamilton IM. Disease control through fertility control: secondary benefits of animal birth control in Indian street dogs. *Prev Vet Med* (2014) 113(1):152–6. doi:10.1016/j.prevetmed.2013.09.005
19. Roberts MG, Heesterbeek JAP. A new method for estimating the effort required to control an infectious disease. *Proc Biol Sci* (2003) 270(1522):1359–64. doi:10.1098/rspb.2003.2339
20. Heesterbeek JAP, Roberts MG. The type-reproduction number T in models for infectious disease control. *Math Biosci* (2007) 206:3–10. doi:10.1016/j.mbs.2004.10.013
21. Schildecker S, Millien M, Blanton JD, Boone J, Emery A, Ludder F, et al. Dog ecology and barriers to canine rabies control in the Republic of Haiti, 2014-2015. *Transbound Emerg Dis* (2016). doi:10.1111/tbed.12531
22. Anderson RM, Jackson HC, May RM, Smith AM. Population dynamics of fox rabies in Europe. *Nature* (1981) 289:765–71. doi:10.1038/289765a0
23. Hampson K, Dushoff J, Bingham J, Brückner G, Ali YH, Dobson A. Synchronous cycles of domestic dog rabies in sub-Saharan Africa and the impact of control efforts. *Proc Natl Acad Sci U S A* (2007) 104(18):7717–22. doi:10.1073/pnas.0609122104
24. Zinsstag J, Dürr S, Penny MA, Mindekem R, Roth F, Menendez Gonzalez S, et al. Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc Natl Acad Sci U S A* (2009) 106(35): 14996–5001. doi:10.1073/pnas.0904740106
25. Patronek GJ, Waters DJ, Glickman LT. Comparative longevity of pet dogs and humans: implications for gerontology research. *J Gerontol A Biol Sci Med Sci* (1997) 52A(3):B171–8.
26. Zhang J, Jin Z, Sun GQ, Zhou T, Ruan S. Analysis of rabies in China: transmission dynamics and control. *PLoS One* (2011) 53(7):e20891. doi:10.1371/journal.pone.0020891
27. MATLAB. *Version 8.4.0 (R2014b)*. Natick, MA: The MathWorks Inc. (2014).
28. Diekmann O, Heesterbeek JAP, Roberts MG. The construction of next-generation matrices for compartmental epidemic models. *J R Soc Interface* (2010) 7(47):873–85. doi:10.1098/rsif.2009.0386
29. Davis S, Bent SJ. Loop analysis for pathogens: niche partitioning in the transmission graph for pathogens of the North American tick *Ixodes scapularis*. *J Theor Biol* (2011) 269(1):96–103. doi:10.1016/j.jtbi.2010.10.011
30. Dürr S, Ward MP. Roaming behaviour and home range estimation of domestic dogs in Aboriginal and Torres Strait Islander communities in northern Australia using four different methods. *Prev Vet Med* (2014) 117(2):340–57. doi:10.1016/j.prevetmed.2014.07.008
31. Kitala PM, McDermott JJ, Coleman PG, Dye C. Comparison of vaccination strategies for the control of dog rabies in Machakos District, Kenya. *Epidemiol Infect* (2002) 129:215–22. doi:10.1017/S0950268802006957
32. Morters MK, Restif O, Hampson K, Cleaveland S, Wood JLN, Conlan AJK. Evidence-based control of canine rabies: a critical review of population density reduction. *J Anim Ecol* (2013) 82:6–14. doi:10.1111/j.1365-2656.2012.02033.x

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Corrigendum: Determinants of Vaccination Coverage and Consequences for Rabies Control in Bali, Indonesia

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Comparing Methods of Assessing Dog Rabies Vaccination Coverage in Rural and Urban Communities in Tanzania

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Rabies can be eliminated by achieving comprehensive coverage of 70% of domestic dogs during annual mass vaccination campaigns. Estimates of vaccination coverage are, therefore, required to evaluate and manage mass dog vaccination programs; however, there is no specific guidance for the most accurate and efficient methods for estimating coverage in different settings. Here, we compare post-vaccination transects, school-based surveys, and household surveys across 28 districts in southeast Tanzania and Pemba island covering rural, urban, coastal and inland settings, and a range of different livelihoods and religious backgrounds. These approaches were explored in detail in a single district in northwest Tanzania (Serengeti), where their performance was compared with a complete dog population census that also recorded dog vaccination status. Post-vaccination transects involved counting marked (vaccinated) and unmarked (unvaccinated) dogs immediately after campaigns in 2,155 villages (24,721 dogs counted). School-based surveys were administered to 8,587 primary school pupils each representing a unique household, in 119 randomly selected schools approximately 2 months after campaigns. Household surveys were conducted in 160 randomly selected villages (4,488 households) in July/August 2011. Costs to implement these coverage assessments were $12.01, $66.12, and $155.70 per village for post-vaccination transects, school-based, and household surveys, respectively. Simulations were performed to assess the effect of sampling on the precision of coverage estimation. The sampling effort required to obtain reasonably precise estimates of coverage from household surveys is generally very high and probably prohibitively expensive for routine monitoring across large areas, particularly in communities with high human to dog ratios. School-based surveys partially overcame sampling constraints, however, were also costly to obtain reasonably precise estimates of coverage. Post-vaccination transects provided precise and timely estimates of community-level coverage that could be used to troubleshoot the performance of campaigns across large areas. However, transects typically overestimated coverage by around 10%, which therefore needs consideration when evaluating the impacts of campaigns. We discuss the advantages and disadvantages of these different methods and make recommendations for how vaccination campaigns can be better monitored and managed at different stages of rabies control and elimination programs.

Keywords: rabies, rabies control, accuracy, dog vaccination, rabies elimination, dog rabies

INTRODUCTION

Rabies is a fatal viral disease transmitted to humans by animal bites, usually from domestic dogs. Although under control in most industrialized countries, rabies continues to kill an estimated 59,000 people each year in low- and middle-income countries (LMICs) (1). Reliable estimates of the proportion of dogs vaccinated against rabies are crucial to determine the performance of vaccination programs and their impact on disease transmission. Empirical and theoretical evidence shows that mass dog vaccination campaigns that reach at least 70% of the dog population can control rabies (2, 3). While achieving this coverage in all communities can lead to elimination, even small gaps in coverage can delay the time to elimination (4). As progress is made toward reaching global targets of zero human rabies deaths from dog-mediated rabies through the implementation of mass dog vaccinations (5), there is a clear need to identify reliable, cost-effective, and feasible approaches that can be used, at scale, to assess community-level vaccination coverage.

Limited population data on owned and free-roaming dogs in most LMICs make estimation of vaccination coverage challenging. Several methods have been used to estimate coverage including (i) the use of pre-campaign estimates of dog population size through human to dog ratios (HDRs) as the denominator, and the number of dogs vaccinated during the campaign as the numerator (6); (ii) post-vaccination household surveys to estimate the proportion of vaccinated dogs (7–11); and (iii) post-vaccination transects to estimate the proportion of marked (vaccinated) dogs (4, 12–14). However, these methods all have limitations.

If dog populations are estimated from data on HDRs, inaccuracies in estimates of the human population will invariably affect the accuracy of dog population estimates. This may occur, for example, through errors in extrapolating current human population sizes from census data (for example, using average population growth rates) or from administrative/boundary changes that affect village demarcations across different time periods. Furthermore, published data on HDRs usually reflect a sample from surveys across several communities (15), and even a small degree of variation in HDRs can have a major effect on dog population estimates at the community level.

Household surveys are restricted to capturing estimates of vaccination coverage in owned dog populations and are relatively intensive to complete. Moreover, there is known to be wide variability in patterns of dog ownership within communities—for example, in Tanzania, a much smaller proportion of Muslim and urban households own dogs in comparison with rural, livestock-keeping communities (15). This variability and the highly skewed pattern of dog ownership in some communities make household surveys prone to selection and measurement biases (16). Additional uncertainty from household surveys arises in relation to validation of dog vaccination status. In Tunisia, for example, about 14% of dog owners who claimed their dogs were vaccinated were unable to provide certificates (17).

Post-vaccination transects are limited to observations of free-roaming dogs and will, therefore, be biased toward dogs that are more likely to be observed from transects. For example, young puppies are likely to be less visible and are known to represent an age group that typically has a low vaccination coverage (9, 18, 19), thus resulting in the potential for overestimating coverage. In a recent study from Tanzania, post-vaccination transects were shown to overestimate coverage by approximately 7% in comparison with household surveys, although it was unclear in this study which of the approaches was most accurate (19).

Here, we present a detailed assessment of three methods to estimate dog vaccination coverage across settings in Tanzania. We use a complete household census as reference data for a simulation experiment to determine the impacts of sampling on the precision of coverage estimates. Specifically, we aim to answer the following questions: (i) What are the resources (personnel, time, and money) required to implement these methods? (ii) Which methods provide the most precise estimates of coverage? and finally (iii) Which approaches, therefore, generate acceptable coverage estimates to provide operational guidance to improve the performance of current or future campaigns?

MATERIALS AND METHODS

Study Sites

The study was conducted in 29 districts across Tanzania: 24 districts from southeast Tanzania, 4 districts from Pemba island, and 1 district (Serengeti district) from northwest Tanzania (**Figure 1**). These areas are inhabited by an estimated 9.1 million people (20% of the Tanzanian population) according to the 2012 national census (20) and represent districts that span a wide range of settings, comprising rural, urban, coastal and inland areas, and a range of livelihoods and religious backgrounds. Mass dog vaccination campaigns were conducted in all these districts by local government teams, with support of WHO and collaborating institutions. Various methods of estimating vaccination coverages achieved during campaigns were compared. **Table 1** summarizes the methods used in different locations and the rationale for data collection.

Post-Vaccination Transects

To generate rapid estimates of village-level vaccination coverage, post-vaccination transects were conducted on the same day as

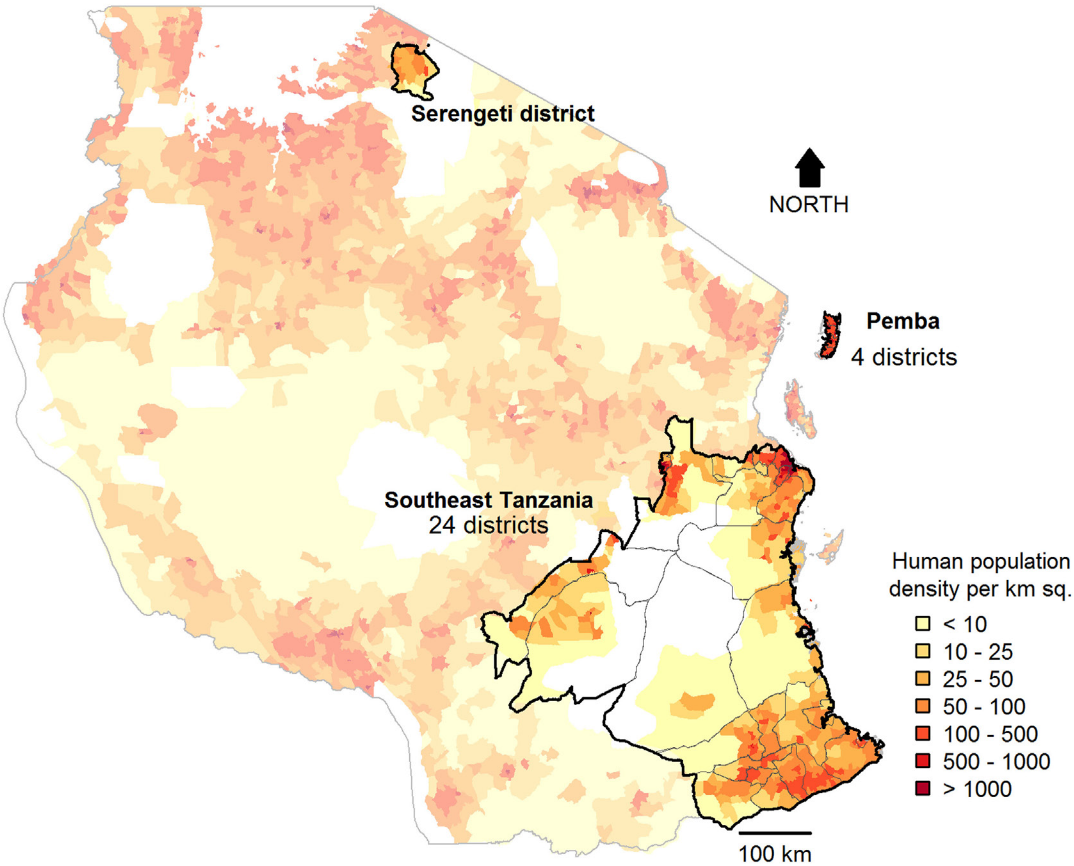

FIGURE 1 | Study sites in Tanzania. Post-vaccination transects (2 sub-villages/village in 2,070 villages), school-based surveys (6 schools/district), and household surveys (30 households/village in 6 villages/district) were conducted in southeast Tanzania and Pemba. In Serengeti district, transects were conducted in all sub-villages in almost all villages (85/88), and four school-based surveys and a complete census of dogs (surveys of 35,867 households) were undertaken. Km sq, Square Kilometres.

vaccination campaigns in each village from 4 p.m. to 6 p.m. when dogs were active and visible. Transects involved recording all dogs observed while walking (or occasionally cycling) a route through villages counting marked (vaccinated) and unmarked (unvaccinated) dogs. In rural communities, transects were conducted in two randomly selected sub-villages from each village (villages ranged in size from 2 to 10 sub-villages, with a median of 4 sub-villages/village), aiming to representatively sample coverage within each village. In the first sub-village, enumerators were instructed to start transects at the center of the sub-village heading to the outskirts, while in the other sub-village, transects started from the edge of the sub-village and headed toward the center. Each transect was conducted by one enumerator for 1 h, therefore, taking a total of 2 h to complete each village. In urban areas, enumerators were required to cover the jurisdiction of a street (a geographical area defined from the National Census, which covers a neighborhood with several roads). One day of training was held for enumerators prior to data collection and printed protocols, and data collection.

Printed protocols and data collection forms were provided to enumerators during this training. Enumerators selected the direction at the start of transects, at the border of sub-villages/streets and at road junctions by spinning a pen. In Serengeti district, transects were conducted in every sub-village of vaccinated villages.

School-Based Surveys

School-based surveys were conducted within 2 months of vaccination campaigns in southeast Tanzania, Pemba, and Serengeti district (**Table 1**). In each district in southeast Tanzania and Pemba, six primary schools (one school per village, as most villages in Tanzania have a primary school) were randomly selected, and in Serengeti district, four primary schools were selected. Logistic and financial limitations meant that school surveys were not conducted in some districts or were conducted in less than six schools per district as initially planned. Between 50 and 100 pupils (one per household) from Standard IV–VII (aged 11–15 years) were asked to complete a questionnaire to collect data from their household. We used total population purposive sampling with a target to interview 100 pupils per school. This resulted in all Standard VII pupils being selected to fill the questionnaire. If there was more than one pupil from one household recruited, the oldest was selected. If the school had fewer than 100 standard VII pupils, pupils were recruited

TABLE 1 | Study design and data collection including purpose of each dataset.

Method	Areas (number of villages)	Sampling design	Data collection period	Interval between village-level campaign and coverage survey	Purpose
Post-vaccination transects	Serengeti (85)	1 transect in every sub-village (357 total) in all villages	May–October 2015	2–3 h	Coverage estimates at village and district level. Data used for simulations to explore how the number of transects/village affect precision of district-level estimates
	Southeast Tanzania and Pemba (2,070)	1 transect in 2 sub-villages (4,140 total) in every village/district	November 2014–January 2015	2–3 h	Setup and implementation costs
School-based surveys	Serengeti (4)	100 pupils/school in 4 schools/district (333 pupils)	July 2015	1 month	Coverage estimates at district level. Precision of estimates compared with census data and simulation experiments.
	Southeast Tanzania and Pemba (115)	100 pupils/school in 6 schools/district (8,254 pupils)	November 2014 and February 2015	1–2 months	Setup and implementation costs
Household survey	Southeast Tanzania and Pemba (160)	30 households/village in 6 villages/district (4,488 households)	July–August 2011	2–6 months	Setup and implementation costs. Data used to parameterize simulations for settings with high: human dog ratios to explore precision of household surveys
Complete human and dog census	Serengeti (88)	All households in district (35,867)	From 2008 to 2015	Vaccination campaigns ~May–July each year. Census at different times of year for each village	Census does not provide a point estimate of coverage relative to a specific campaign. Data used for simulation experiment to determine how sampling (e.g., household and school-based surveys) affects precision of coverage estimates

from lower classes (Standard IV–VI). Written consent from the district executive officer and verbal consent of teachers and pupils were obtained at each primary school prior to the study. To introduce the project to schools, researchers were accompanied by the district veterinary officer, district health officer, and district education officer. Questionnaires were administered to pupils by the lead author and his research team. The questionnaire included questions on the number of adults and children (<18 years of age) living in the household, the number of dogs and puppies (<3 months of age) kept at the household, and the age of dogs and their vaccination status.

Household Surveys

Household surveys were conducted in all districts in southeast Tanzania and Pemba with the aim of obtaining an initial assessment of coverage from the first phase of vaccination campaigns. Six villages were randomly selected from all villages in each district, and the survey was conducted by surveying 30 households in each of the selected villages. In every randomly selected village, a landmark was identified (preferably a school, otherwise a dispensary, church, or mosque). From this starting point, interviewers randomly chose a direction for selecting households for interview by spinning a pen. Every third household was sampled, and interviews conducted until 30 households were completed in each village. Surveys were conducted in July and August 2011, around 4 months after dog vaccination campaigns conducted in March and April 2011. Interviewers were accompanied by local village officers to identify household heads and provide introductions. Prior to the administration of the questionnaire, permission was sought from the household head or other household members of at least 18 years of age in the absence of the household head. Interviewers explained the study background to each respondent and obtained verbal consent to carry out the questionnaire. For households that owned dogs, the questionnaire captured details of dogs owned (adults and puppies <3 months) and their vaccination status on the basis of owner recall.

Serengeti District Dog Population Census

In Serengeti district, a complete census was conducted to collect the same household questionnaire data as described above, for every household in the district. The census began in 2008 and was completed in 2015 (**Table 1**), as enumerators were only able to conduct the census in between other activities. Because the census was conducted over an extended period, it was not used to generate point estimates of vaccination coverage in relation to specific vaccination campaigns, which in Serengeti have been conducted annually over the last decade. Instead these data were used for a simulation experiment, whereby the data were sampled to simulate a household survey, thereby enabling a comparison of methods and how they affect the precision of coverage estimates (see Data Analysis).

Resources for Estimating Vaccination Coverage

The number of people involved in each survey method, the time required to complete data collection and associated costs to set up and implement each assessment across southeast Tanzania were recorded. Costs per surveyed village were calculated as total costs incurred in all districts divided by the number of villages surveyed. Costs per district were calculated as the overall costs for conducting the surveys across surveyed districts, divided by the number of surveyed districts. The costs incurred included per diems to government officials such as District Veterinary Officers, District Health Officers, District Education Officers, and researchers and allowances to enumerators who conducted transects. Communication costs covered phone calls to coordinate with enumerators and data collectors. Fares covered travel to districts to facilitate training, supervision, and to collect records. For school-based and household surveys, travel covered fuel for vehicle use. All costs were calculated for evaluation of a single mass dog vaccination campaign in Tanzanian shillings (TZS) and converted to US dollars (US$) using the average exchange rate in 2011 [1 TZS to US$ 0.000632 (21)].

Data Analysis

The census data from Serengeti district together with the transects and school-based surveys conducted in Serengeti in 2015 were used to determine the impacts of sampling on the precision of vaccination coverage estimation. We define accuracy as lack of bias. Repeated estimates using an accurate method will converge on the true coverage value as sample size increases. Precision is the absence of random sampling error from the measured value. Repeated estimates using a precise method will be close to their mean, although not necessarily close to the true coverage. Clearly, for an estimation method to be informative about the true coverage, it must be both accurate and precise. Across Tanzania there is considerable variation in dog ownership, from largely Muslim communities with very few dogs per household to pastoralists with many dogs in most households. This variation in dog ownership patterns among communities means that sampling designs should aim to deal with these variations and give accurate and precise estimates.

To examine the precision of different methods in estimating vaccination coverage, we estimated the district-wide mean coverage and 95% confidence intervals in Serengeti from the complete census (all households in all 88 villages) and from subsamples of households and villages from the census equivalent to a household survey. We also compared these to the precision of district-wide coverage estimates from the school-based surveys (in 4 villages) and post-vaccination transects (in 85 villages) in Serengeti district. To facilitate comparison, the four villages selected for the household survey during the simulation in **Figure 2** were the same ones sampled by the school-based survey. We fitted binomial generalized linear mixed models (GLMMs), with a random intercept to account for variation in mean coverage between villages.

To assess the impact of sampling on district-wide coverage estimates, we conducted simulations where we subsampled from the complete census (88 villages) different numbers of households per village (10, 20, 30, 40, and 50) and villages (5, 10, 20, 30, 40, 50, 60, 70, 80, and 88). Each of the 50 combinations of these two sampling choices was simulated 500 times, and mean coverage for the district was estimated from each simulated data set as the total number of vaccinated dogs divided by the total number of dogs. Although generally this simple method is inferior to fitting a GLMM as above (22), this was not feasible for sampling designs with low total dog numbers. The precision achieved using each sampling design was assessed by plotting coverage estimates against the numbers of villages and households sampled.

To assess the impact of variability in dog ownership or HDR on the precision of coverage estimates, we repeated the simulation described above. However, instead of subsampling from the Serengeti census dataset, we used a simulated dataset with the same structure but with fewer dogs per household. The number of dogs in each household was simulated from a negative binomial distribution with mean $\mu = 0.2$ and dispersion parameter $k = 0.06$ [calculated from the mean and variance of the household survey data in southeast Tanzania using the parameterization of the negative binomial with variance $\mu + (\mu^2/k)$]. The number of vaccinated dogs was simulated with mean coverage and random effect variances between villages, sub-villages, and households estimated from a binomial GLMM fitted to the Serengeti census dataset. As a result, the "low dog ownership" dataset was as similar as possible to (and therefore comparable to) the Serengeti dataset, but with dog numbers similar to the mean dogs/household in southeast Tanzania (**Table 1**). As the results presented here come from a single simulated "low dog ownership" dataset, we checked for sensitivity to random variation by comparing across several (>5) simulated data sets. We also assessed the impact of sampling using transect surveys. We examined the scenario of sampling 1, 2, 4 and 8 (or all if <8) sub-villages in a village and determined which sampling effort (sampling design) provided reasonable estimates of village-level coverage.

All statistical analyses were conducted using R version 3.3.1 (23). GLMMs were fitted using the *lme4* package (24), and the "low dog ownership" data set was simulated using the *sim.glmm* function (25).

Ethical Considerations

We obtained ethics approval from the Medical Research Coordinating Committee of the National Institute for Medical Research of Tanzania (NIMR/HQ/R.8a/Vol.IX/2109) and Tanzania Commission for Science and Technology (COSTECH). Before administering any questionnaires, participants were informed about the background and purpose of the study, highlighting that their participation was voluntary, and that their answers would be kept confidential. Only participants who verbally agreed were interviewed.

RESULTS

Across southeast Tanzania, Pemba Island and Serengeti district, we conducted (i) post-vaccination transects following vaccination campaigns in 2,155 villages and counted 24,721 dogs, (ii) questionnaires with 8,587 primary school pupil respondents, each representing a unique household, in 119 randomly selected schools (3,090 dogs recorded), and (iii) 4,488 household surveys in 160 randomly selected villages (731 dogs recorded—excluding Serengeti district). In addition, a complete census was conducted in Serengeti district covering 35,867 households, which

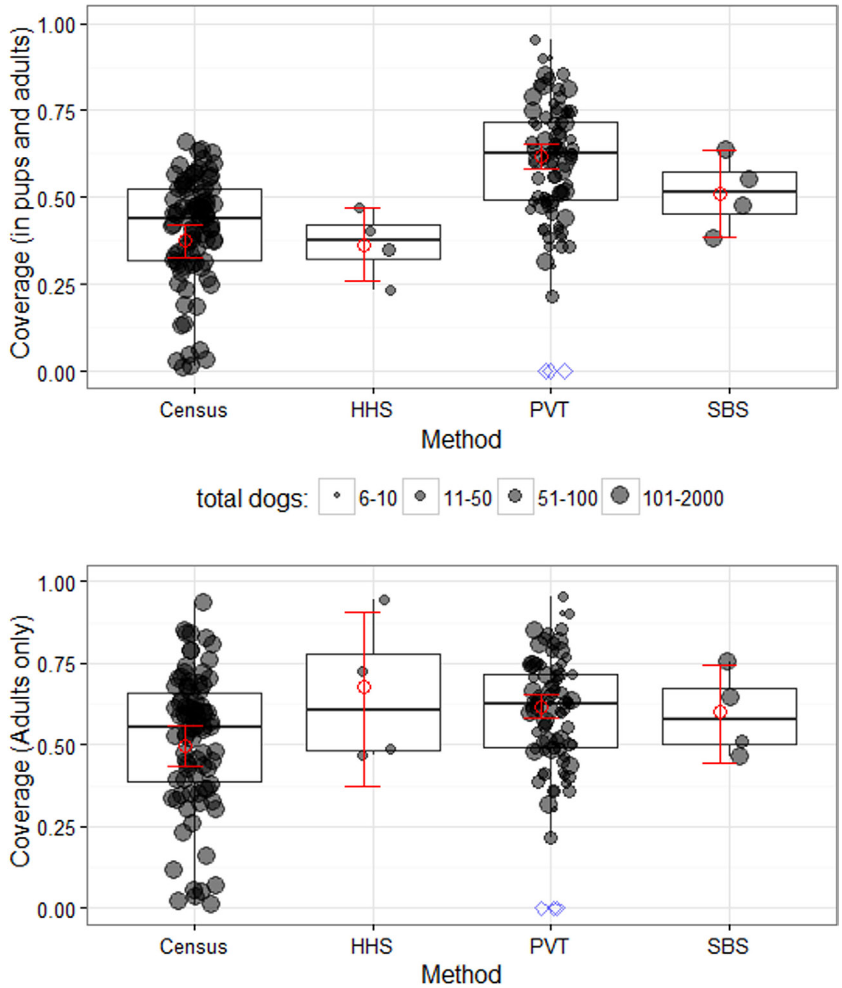

FIGURE 2 | **District and village-level vaccination coverage estimates and precision in Serengeti District**. Coverage estimates are shown for all dogs (including puppies, top) and adult dogs only (bottom) in surveyed villages (dots); the dots also represent the village-level coverage. Red squares and error bars show mean district-level coverage ±95% CI, estimated using generalized linear mixed models (see main text for details). The coverage distribution is plotted for individual villages (shaded circles) and summarized by box-and-whisker plots, where the thick line shows the median, the box covers the interquartile range and the whiskers extend to the range. Blue diamonds represent villages with no vaccination campaign where vaccination coverage was assumed to be zero (not included in calculation of mean ± 95% CI or boxplots). PVT, post-vaccination transects; SBS, school-based surveys; HHS, household surveys.

collectively owned 62,771 dogs (**Table 1**). **Table 2** summarizes the attributes of each study district and dogs recorded by each method. Many more dogs were observed on transects than were recorded in either household or school-based surveys, even in districts with low dog ownership i.e., high HDR (**Table 2**).

Logistics and Costs for Coverage Assessments

Post-vaccination transects usually took around 2 h to complete. Collars were fitted to dogs during vaccination campaigns with very few cases where this was not possible. As transects were conducted the same day as campaigns, collar loss was assumed to be negligible. School-based surveys involved two research scientists with the help of teachers. The questionnaire was administered in one classroom, and all pupils normally took approximately 40 min to complete questionnaires. Household surveys involved a research team comprised of two drivers, eight interviewers, and one supervisor split between two vehicles. Each vehicle covered four villages per day (an average of one village per interviewer/day), and the village leader accompanied each interviewer in every village. The census in Serengeti district was the most time-consuming method, with locally trained interviewers spending an average of 14 (8 h/day) days to complete a census of one village.

Costs of estimating coverage varied depending upon the method. The costs per village were $12.01, $66.12, and $155.70 for transects, school-based, and household surveys, respectively, and these costs scaled up with the sampling for each method (**Table 3**). Specifically, the average cost for assessing district-level coverage was around $1,300 with transects completed in every village, approximately $300 based on 6 school-based surveys per district and $900 based on sampling 30 households per village in six villages per district.

TABLE 2 | Descriptive characteristics of the study districts.

District	Setting (Urban/Rural, Coastal/inland, island)	Total villages (or wards)	Post-vaccination transects			Household survey				School-based survey			
			Villages/streets surveyed	Dogs sighted (Village mean)	Villages with no dogs seen	Villages surveyed	Households (HH) surveyed	Dogs recorded (mean dogs/HH)	Households without dogs	Schools surveyed	Pupil respondants	Dogs recorded (mean dogs/family)	Families without dogs
Chake Chake	Island	29	29	182 (6.28)	0	6	178	7 (0.04)	176	3	152	3 (0.02)	151
Ilala	Urban coastal	26	NA	NA	NA	6	133	34 (0.26.)	119	NA	NA	NA	NA
Kibaha Rural	Rural inland	55	55	759 (13.80)	0	2	93	30 (0.32)	82	6	412	199 (0.50)	355
Kibaha Urban	Urban inland	50	50	526 (7.21)	0	6	151	66 (0.44)	117	6	407	237 (0.51)	341
Kilombero	Rural inland	80	77	1,989 (25.83)	0	6	147	32 (0.22)	132	6	548	218 (0.40)	470
Kilwa	Rural coastal	102	78	606 (7.77)	4	6	158	26 (0.16)	144	NA	NA	NA	NA
Kinondoni	Urban coastal	34	83	349 (4.20)	19	6	183	59 (0.32)	154	6	471	163 (0.35)	430
Kisarawe	Rural inland	77	77	578 (7.41)	1	6	170	9 (0.05)	163	6	283	109 (0.39)	230
Lindi Rural	Rural coastal	134	134	1,754 (10.83)	8	6	177	15 (0.08)	168	5	254	60 (0.24)	242
Lindi Urban	Urban coastal	30	60	588 (9.80)	2	6	177	17 (0.10)	168	4	343	70 (0.20)	316
Liwale	Rural inland	76	73	531 (7.27)	6	6	175	19 (0.11)	169	NA	NA	NA	NA
Masasi	Rural inland	159	97	554 (6.16)	5	6	180	27 (0.15)	162	3	161	32 (0.20)	147
Micheweni	Island	27	27	178 (6.59)	0	6	173	25 (0.14)	164	3	156	4 (0.03)	155
Mkoani	Island	33	33	303 (9.18)	4	6	154	9 (0.06)	151	3	177	8 (0.05)	175
Mkuranga	Rural coastal	116	90	262 (2.91)	30	6	174	4 (0.02)	171	6	328	58 (0.18)	306
Morogoro Rural	Rural inland	144	93	1,056 (12.00)	15	6	168	41 (0.24)	145	5	393	103 (0.25)	356
Morogoro Urban	Urban inland	19	163	572 (3.51)	1	6	169	49 (0.29)	146	6	557	225 (0.40)	489
Mtwara Rural	Rural inland	156	85	427 (5.02)	16	5	140	16 (0.11)	138	5	334	31 (0.09)	328
Mtwara Urban	Urban coastal	86	15	148 (9.87)	1	6	150	14 (0.09)	130	3	288	69 (0.24)	266
Nachingwea	Rural inland	118	115	1,576 (13.70)	4	6	170	37 (0.22)	160	6	342	84 (0.25)	307
Nanyumbu	Rural inland	89	58	415 (7.16)	10	6	176	1 (0.01)	175	6	475	28 (0.06)	466
Newala	Rural inland	153	83	626 (7.54)	1	6	180	4 (0.02)	178	6	645	55 (0.09)	623
Ruangwa	Rural inland	89	79	758 (9.59)	1	6	179	37 (0.21)	164	4	168	24 (0.14)	156
Rufiji	Rural coastal	115	78	470 (6.03)	16	6	172	2 (0.01)	171	5	459	61 (0.14)	427
Tandahimba	Rural inland	156	130	360 (2.77)	42	3	79	2 (0.03)	78	3	175	24 (0.14)	170
Temeke	Urban coastal	30	106	276 (2.60)	19	6	159	8 (0.05)	155	NA	NA	NA	NA
Ulanga	Rural inland	70	70	2,381 (28.35)	0	6	177	85 (0.48)	146	6	560	326 (0.58)	464
Wete	Island	32	32	213 (6.63)	2	6	146	56 (0.38)	124	3	166	7 (0.04)	162
Serengeti	Rural	88	85	6,285 (35.21)	0	4[a]	120[a]	179 (0.37)[a]	0[a]	4	333	892 (2.68)	51

In urban areas the numbers of wards are listed per district rather than villages.
[a]*In Serengeti district a simulated household survey dataset was generated from a subsample of 120 households from four villages (30 households per village) of the complete census data.*
NA, not available.

TABLE 3 | Cost comparison between methods of evaluating dog vaccination campaigns in Southeast Tanzania and Pemba island.

	Cost item	Transects (n = 2,070)		School-based surveys (n = 115)		Household surveys (n = 160)	
Setup		**Total cost ($)**	**Cost/village ($)**	**Total cost ($)**	**Cost/village ($)**	**Total cost ($)**	**Cost/village ($)**
	Communication costs	606.08	0.29	20.01	0.17		
	Fare	613.02	0.3				
	Training/supervision	2,256.28	1.09	4,203.06	36.55		
Subtotal (setup costs)			**$1.68**		**$36.72**		
Implementation	Per diems/allowances	6,541.2	3.16	624.45	5.43	21,345.30	133.41
	Data collection	176.80	0.09			659.5	4.12
	Collars	13,858.09	6.69				
	Questionnaire	806.16	0.39	1,200.88	10.44		
	Fuel			1,555.64	13.53	2,992.92	18.17
Subtotal (implementation costs)			**$10.33**		**$29.40**		**$155.70**
Cost per village			**$12.01**		**$66.12**		**$155.70**
Cost per district		**$1,307.37**		**$310.60**		**$889.05**	

The numbers of villages and districts which these calculations were based on are shown in ***Table 1****. All costs are in USD. Per diems for household surveys covered supervisors, drivers, village leaders, and researchers. Allowances for enumerators conducting transects were $3.16/village. Household survey costs were based on interviewing 30 households per village. Data collection for household surveys also included the cost of mobile phones used by researchers for submitting data (six phones at $94.8/phone).*

Comparison of Coverage Estimates and Their Precision between Methods

Vaccination coverage in Serengeti district was estimated using each method and from the complete census to assess precision in coverage estimates. **Figure 2** illustrates village-level coverage estimates and the district-wide mean estimates. Transects in Serengeti were conducted in 85 out of 88 villages, with 6,285 dogs counted and school-based surveys were conducted in four schools, with interviewed pupils representing 333 households and collective ownership of 892 dogs. We observed that excluding puppies resulted in higher estimates of coverage (from 37.5% as estimated from the census including puppies and adults to 49.7% including only dogs >3 months of age), with similar increases for both the household and school-based surveys. However, we were unable to analyse the post-vaccination transect data according to age class of observed dogs as this information was not recorded during transects.

Our GLMM estimate of district-level coverage of all dogs (puppies and adults) from the census was 37.5% with relatively narrow 95% confidence intervals (32.8–42.3%). The coverage estimate from the census data subsampled to represent a household survey fell outside of these confidence intervals at 44.5% and had wider 95% CI (37.1–52.0%). Although the district-wide coverage for the school-based survey (51.2%) was not directly comparable to the census data, the span of the 95%CI can be compared and was found to be much wider (38.7–63.4%). The transect coverage estimate (61.7%) was higher than the school-based survey but had narrow 95% CI (58.2–65.2%) similar in span to the census.

In comparison to the census, only the post-vaccination transects method provided similar precision in coverage estimates (**Figure 2**) but these appeared to overestimate district-level vaccination coverage in comparison to the school-based survey. This is likely due to few puppies being observed during the transects. Transects generated coverage estimates for every village in a district, although village-level estimates were not very precise. Nonetheless, these village-level estimates were sufficient for identifying villages with low coverage, for example, less than 70% coverage.

Impact of Sampling on District-Level Coverage Estimates

Estimates of coverage from the school-based and household surveys were sensitive to the sampling design (**Figure 3**). As the sample size increases, in terms of the numbers of households sampled per village, coverage estimates became increasingly precise (**Figure 3A**). In Serengeti district, where there is high dog ownership, once at least 30 households within each of 20 villages were sampled, estimates were very close (±10% with high probability) to the true mean from the census data. In scenarios with low dog ownership (i.e., higher HDR), approximately three times the sampling effort (30 households × 60 villages) is required to achieve an equivalent degree of precision (**Figure 3B**). It was possible to sample more households more rapidly through school-based surveys than household surveys because it is easier to recruit pupils at school than visiting individual households.

For the transects, sampling two or more sub-villages per village gave coverage estimates that were within 10% of the true village-level coverage, although coverage estimates were more precise if transects were completed in all villages in all wards rather than just a sample of villages per ward (**Figure 3C**).

DISCUSSION

The feasibility of global canine rabies elimination has been recognized by major international health agencies, including the WHO, the World Animal Health Organization (OIE), and the Food and Agriculture Organization of the United Nations (FAO) (5). Implementation of mass dog vaccination programs to meet the 2030 target of zero human deaths are now underway in several countries in Asia and Africa. To guide the progress of these programs, it is important to evaluate the performance of mass dog vaccination campaigns. Specifically, monitoring is useful to

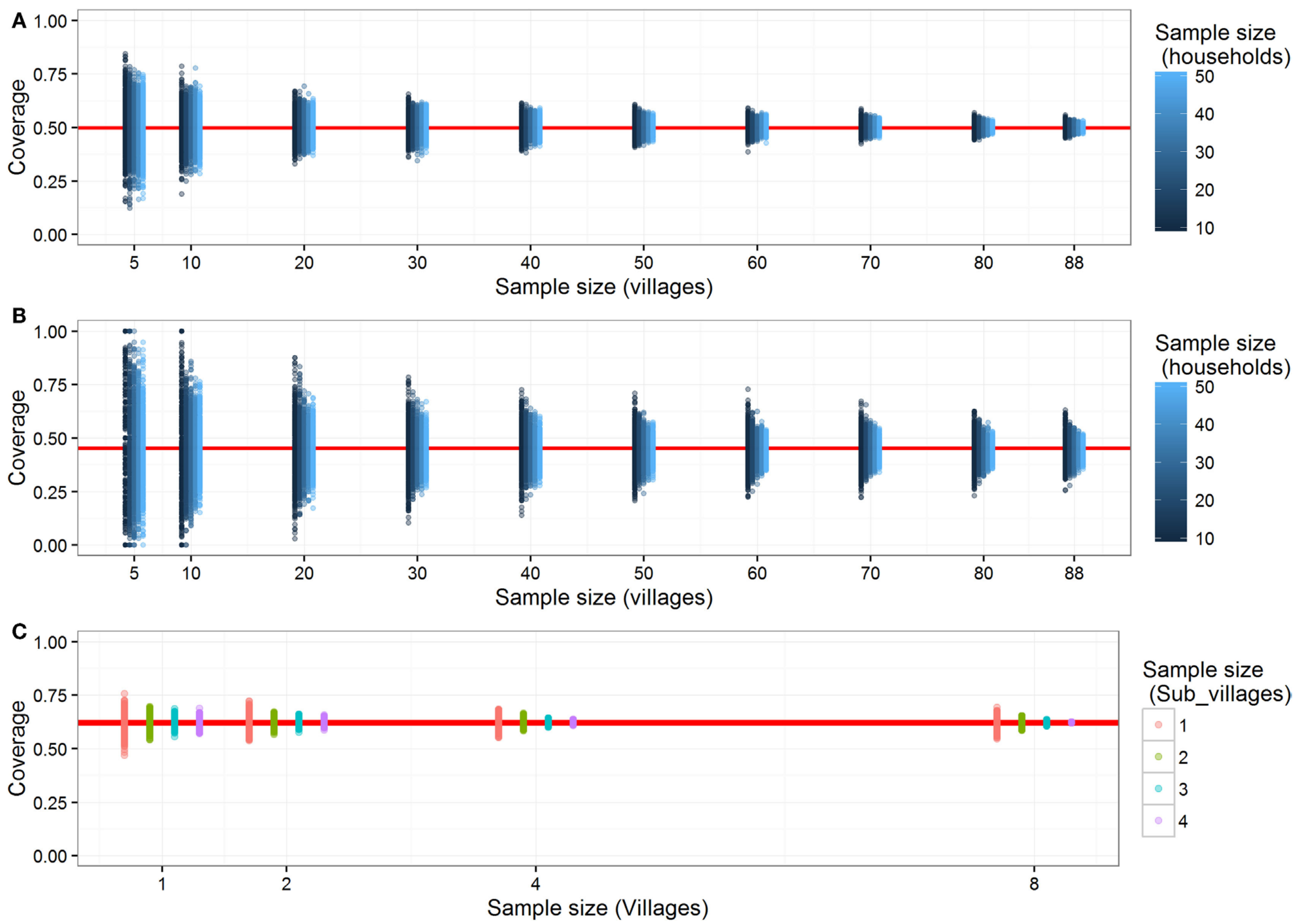

FIGURE 3 | The impact of sampling on precision of coverage estimates derived from household surveys in communities with (A) low human:dog ratios and, (B) high human:dog ratios, and from (C) post-vaccination transects. Estimated mean district-level vaccination coverage (red line) for different numbers of villages and households sampled from **(A)** actual Serengeti district dataset and **(B)** a dataset from Serengeti District but simulated with lower dog ownership (0.2 dogs per household). For each sampling design [i.e., the number of villages and households sampled in panels **(A,B)**], coverage estimates from 500 subsampled data sets are plotted (blue dots), with shading indicating the number of sampled households, and the mean of these estimates is shown by red line. Similar to panels **(A,B)**, each column of points shows sampling variation among 500 subsampled data sets for each sampling design using transects **(C)**. Coloured dots represent the number of subvillages sampled per village for estimating coverage from transects.

determine whether campaigns have reached the required vaccination coverage, to identify problematic areas with low coverage, and target communities that have been missed with intensified vaccination effort. Dog rabies control programs typically operate under financial constraints that affect both implementation and evaluation. While several studies have evaluated vaccination coverage as part of small-scale research/pilot vaccination campaigns (26), here we evaluate different approaches in the context of comparison of setup and implementation costs for generating precise and accurate coverage estimates at scale.

In this study, we demonstrated that transects were the simplest method that generated precise estimates of vaccination coverage and were also not cost prohibitive. A limitation of transects is that they tend to overestimate coverage. It was previously reported that post-vaccination coverage estimates in Tanzania from transects overestimate coverage by 10–15% (19). We saw a similar difference in our coverage estimates from the complete census when puppies were excluded. This suggests that puppies are rarely observed on transects and that puppies are less likely to be vaccinated, which could explain why coverage is overestimated from transects (19). Estimates of vaccination coverage from transects should therefore be reduced by around 10% when assessing whether coverage is sufficient or if remedial vaccination is required, and for determining the impacts of vaccination programs.

Household surveys generate useful data on vaccination coverage of owned dogs and provide opportunities for collection of additional demographic data (15, 18, 19). However, we found that household surveys were time consuming and costly at ~$150 per village. Because of these costs, we restricted out household (and school-based) surveys to a set number (6) per district, which meant that larger districts were sampled less. However, we found that approximately 30 villages would need to be surveyed to generate district-level estimates of coverage precise to within

10% of the true coverage. We conclude from our simulations that the sampling required to reach an adequate level of precision (say within 5%) would likely be cost prohibitive in most settings, particularly where HDRs are high and even larger sample sizes would be needed. The effort required to conduct these surveys would be difficult to justify, given the more urgent priority of vaccinating dogs.

School-based surveys can generate data from more households at lower cost, as pupils are easily recruited. Moreover, school pupils typically take their dogs to vaccination stations and, therefore, know the vaccination status of their dogs (18). The main costs of school-based surveys are at the setup stage, which requires considerable government support, although this cost is not incurred on successive campaigns. School-based surveys are, therefore, simple to implement and can capture a range of socioeconomic and religious backgrounds. However, estimates may be less accurate because of a biased subsample of children attend school and less precise in areas with low numbers of pupils attending schools, such as pastoralist communities. Critically, this method may, therefore, fail to capture coverage in the most vulnerable populations with the highest dog ownership (lowest HDR) but lowest school attendance (27). In communities with few dogs, school-based surveys are also sensitive to sampling, as very few pupils (<10 pupils per 100 households) reported to own dogs at their households (see also simulation experiments in **Figure 3B**). In these areas, large numbers of schools would need to be surveyed to obtain sufficient sample sizes for adequately precise coverage estimates.

Among the limitations of our household and school-based surveys was their timeliness; we also used the vaccination status of dogs reported by owners, which could be biased. More logistic effort was involved in setting up these surveys than for transects, therefore rapid assessments of vaccination performance (and remedial action if required) are more difficult with these methods, which also do not provide estimates of coverage for every village unless completed in every village which would be very costly. By contrast, transects were very efficient and generated immediate operational guidance at the village-level (**Figure 4**).

On the whole, many more dogs were recorded by transects than other methods. For example, fewer than 10 dogs were counted during household surveys in Chake Chake district on Pemba, while 182 dogs were counted during transects. Transects surveys are therefore more likely to generate more precise estimates of coverage than the other methods even in areas with fewer dogs. However, at the village-level dog counts even from transects were often very low and therefore village-level coverage estimates would be expected to be imprecise. Although transects could be carried out for longer periods of time, this might also result in recounting of dogs, and would make them more expensive to conduct. Overall, transects were affordable and generated more precise estimates of district-level coverage than questionnaire-based surveys that were affected by sampling. But costs of transects accrue as more villages are surveyed, so in very large populations (with lots of villages) the costs of transects increase.

Priorities in terms of vaccination campaign evaluation typically change over time (28). During initial stages of national control programs, the priority, for example, is likely to be planning for dog vaccine procurement, with estimates needed of the dog population size. Human census data are almost universally available and can be used with HDRs to provide a baseline for vaccine procurement (29). HDRs for a range of settings in Africa and Asia are a useful starting point (7, 15, 26). However, these data should not be considered sufficiently reliable to provide a denominator for generating vaccination coverage estimates. Indeed, our experience in southeast Tanzania was that dog population estimates derived from HDRs substantially overestimated dog populations and reassessment of vaccine procurement was required in subsequent years. But, in general, it was better to overestimate the dog population at this stage than underestimate it.

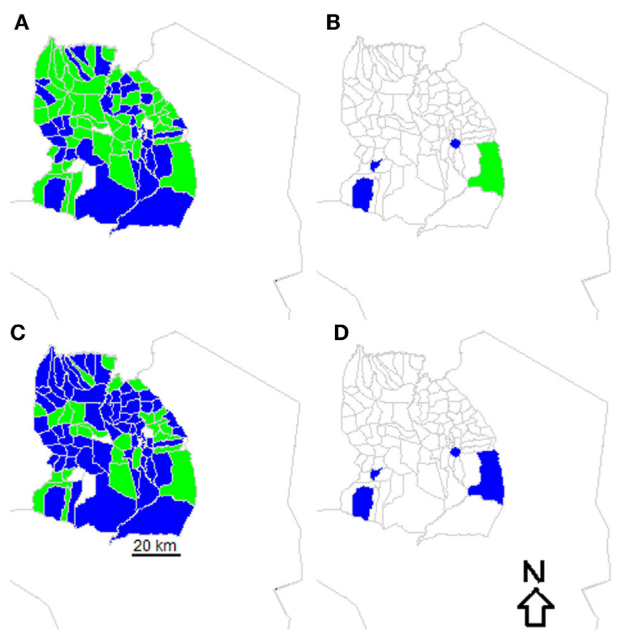

FIGURE 4 | **Vaccination performance in villages in Serengeti District**. Villages where surveys were conducted are colored based on whether village-level coverage exceeded 60% (green) or were less than 60% (blue) based on **(A)** post-vaccination transects and **(B)** school-based surveys versus whether coverage exceeded 70% (green) or were less than 70% (blue) based on **(C)** post-vaccination transects and **(D)** school-based surveys.

Consecutive vaccination campaigns should generate data on vaccine doses delivered at the village level. We therefore recommend post-vaccination transects be used in conjunction with monitoring vaccine doses delivered during campaigns to guide vaccine procurement for future campaigns. This approach may mean that once baseline levels of coverage have been established through accurate records of dogs vaccinated in each village/vaccination station, post-vaccination transects may not be required every year, but could be completed less frequently. In our experience, local government authorities in Tanzania do not have resources or incentives to invest in monitoring and evaluation, and their priority, understandably, is on vaccinating dogs. A further advantage of post-vaccination transects is that local paravets, community-based health officers, local community members, and volunteers can be rapidly trained to conduct transects and therefore provide relatively independent coverage data.

A major obstacle when approaching elimination is the need to address difficulties in program implementation in hard-to-reach populations (30). Post-vaccination transects could be used to troubleshoot the performance of vaccination coverage in stubborn foci. For example, vaccination programs across Latin America have achieved tremendous success in controlling dog rabies with average levels of coverage estimated to exceed 70% based on HDRs (31). However, in localized areas canine rabies persists, likely due to gaps in coverage or overestimation of routine coverage achieved (32). Transects could be used to identify areas in need of improved vaccination, where delivery was poor (for example in **Figure 4**). More generally, transects have proven to be effective in measuring the immediate success of vaccination campaigns in settings in both Asia and Africa (12–14, 29, 33). One concern is that transect routes are not pre-defined, which could result in recounting of dogs. But efforts can be taken to avoid recounting dogs, as we did by aiming to go from the outskirts to the center of sub-villages and vice versa. In our study, some enumerators cycled rather than walked transects, but enumerators were trained to cover routes slowly for 1 h, so we expect that any differences due to this would have been negligible. Simple tools are available to evaluate the performance of vaccination programs, capturing the spatial variation that transects provide, which could also address these concerns (29).

Patterns of dog ownership in Tanzania are very heterogeneous. As such, district-level coverage estimates from household or school-based surveys tend to be more imprecise than estimates from transects. To obtain estimates with comparable precision would require considerable increased sampling and costs. Moreover, from transects we were able to estimate village-level coverages. This can be useful when aiming to eliminate rabies as gaps in coverage can be detected, and therefore campaigns can be strengthened to effectively interrupt transmission. With the wide availability of mobile phones, real-time data on vaccinated dogs and coverage estimates from transects can easily be submitted by enumerators (29, 34). We therefore recommend transects as a relatively cheap method to estimate village-level coverage that can be conducted at scale, in comparison to other methods where high levels of sampling are required that are cost prohibitive.

AUTHOR CONTRIBUTIONS

Conceived and designed experiments: MS, JC, SC, TL, KL, ZM, MM, LS, and KH; performed experiments: MS, JC, AL, KL, MM, EM, ZM, LS, and KH; developed analytical tools: MS, PJ, and KH; and wrote the paper: MS, PJ, KHo, JC, TL, AL, KL, MM, EM, ZM, LS, and KH.

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REFERENCES

1. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9:e0003709. doi:10.1371/journal.pntd.0003709
2. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14:185–6. doi:10.1016/0264-410X(95)00197-9
3. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine Rabies. *PLoS Biol* (2009) 7:e53. doi:10.1371/journal.pbio.1000053
4. Townsend SE, Sumantra IP, Pudjiatmoko, Bagus GN, Brum E, Cleaveland S, et al. Designing programs for eliminating canine rabies from islands: Bali, Indonesia as a case study. *PLoS Negl Trop Dis* (2013) 7(8):e2372. doi:10.1371/journal.pntd.0002372
5. World Health Organisation. *Global Elimination of Dog-Mediated Human Rabies. The Time Is Now. Report of the Rabies Global Conference*. Geneva (2015). Available from: http://www.oie.int/for-the-media/press-releases/detail/article/global-strategic-framework-for-the-elimination-of-dog-mediated-human-rabies/
6. Cleaveland S, Kaare M, Tiringa P, Mlengeya T, Barrat J. A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* (2003) 16(21):1965–73. doi:10.1016/S0264-410X(02)00778-8
7. Gsell AS, Knobel DL, Kazwala RR, Vounatsou P, Zinsstag J. Domestic dog demographic structure and dynamics relevant to rabies control planning in urban areas in Africa: the case of Iringa, Tanzania. *BMC Vet Res* (2012) 8:236. doi:10.1186/1746-6148-8-236
8. Kayali U, Mindekem R, Yemadji N, Vounatsou P, Kaninga Y, Ndoutamia AG, et al. Coverage of pilot parenteral vaccination campaign against canine rabies in N'Djamena, Chad. *Bull World Health Organ* (2003) 81:739–44.
9. Kongkaew W, Coleman P, Pfeiffer DU, Antarasena C, Thiptara A. Vaccination coverage and epidemiological parameters of the owned-dog population in Thungsong District, Thailand. *Prev Vet Med* (2004) 65:105–15. doi:10.1016/j.prevetmed.2004.05.009
10. Kayali U, Mindekem R, Hutton G, Ndoutamia AG, Zinsstag J. Cost-description of a pilot parenteral vaccination campaign against rabies in dogs in N'Djaména, Chad. *Trop Med Int Health* (2006) 11:1058–65. doi:10.1111/j.1365-3156.2006.01663.x

11. Suzuki K, Pereira JAC, López R, Morales G, Rojas L, Mutinelli LE, et al. Descriptive spatial and spatio-temporal analysis of the 2000–2005 canine rabies endemic in Santa Cruz de la Sierra, Bolivia. *Acta Trop* (2007) 103:157–62. doi:10.1016/j.actatropica.2007.06.003
12. Muthiani Y, Traoré A, Mauti S, Zinsstag J, Hattendorf J. Low coverage of central point vaccination against dog rabies in Bamako, Mali. *Prev Vet Med* (2015) 120:203–9. doi:10.1016/j.prevetmed.2015.04.007
13. Tenzin T, McKenzie JS, Vanderstichel R, Rai BD, Rinzin K, Tshering Y, et al. Comparison of mark-resight methods to estimate abundance and rabies vaccination coverage of free-roaming dogs in two urban areas of south Bhutan. *Prev Vet Med* (2015) 118:436–48. doi:10.1016/j.prevetmed.2015.01.008
14. Léchenne M, Oussiguere A, Naissengar K, Mindekem R, Mosimann L, Rives G, et al. Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* (2016) 34(4):571–7. doi:10.1016/j.vaccine.2015.11.033
15. Knobel DL, Laurenson MK, Kazwala RR, Boden LA, Cleaveland S. A cross-sectional study of factors associated with dog ownership in Tanzania. *BMC Vet Res* (2008) 4:5. doi:10.1186/1746-6148-4-5
16. Jibat T, Hogeveen H, Mourits MCM. Review on dog rabies vaccination coverage in Africa: a question of dog accessibility or cost recovery? *PLoS Negl Trop Dis* (2015) 9:e0003447. doi:10.1371/journal.pntd.0003447
17. Touihri L, Zaouia I, Elhili K, Dellagi K, Bahloul C. Evaluation of mass vaccination campaign coverage against rabies in dogs in Tunisia. *Zoonoses Public Health* (2011) 2:110–8. doi:10.1111/j.1863-2378.2009.01306.x
18. Kaare M, Lembo T, Hampson K, Ernest E, Estes A, Mentzel C, et al. Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* (2009) 27:152–60. doi:10.1016/j.vaccine.2008.09.054
19. Minyoo A, Steinmetz M, Czupryna A, Bigambo M, Mzimbiri I, Powell G, et al. Incentives increase participation in mass dog rabies vaccination clinics and methods of coverage estimation are assessed to be accurate. *PLoS Negl Trop Dis* (2015) 9(12):e0004221. doi:10.1371/journal.pntd.0004221
20. National Bureau of Statistics. *The 2012 Housing and Population Census*. Dar Es Salaam; Tanzania (2015).
21. Bank of Tanzania. *Annual Financial Review*. Dar Es Salaam; Tanzania (2012).
22. Bolker BM, Brooks ME, Clark CJ, Geange SW, Poulsen JR, Stevens MH, et al. Generalized linear mixed models: a practical guide for ecology and evolution. *Trends Ecol Evol* (2009) 24(3):127–35. doi:10.1016/j.tree.2008.10.008
23. R Development Core Team. *A Language and Environment for Statistical Computing. R Foundation for Statistical Computing*. Vienna, Austria (2009). Available from: http://www.R-project.org
24. Bates D, Maechler M, Bolker B, Walker S. lme4: linear mixed-effects models using Eigen and S4. *R Package Version* (2014) 1(7).
25. Johnson PCD, Barry SJE, Ferguson HM, Müller P. Power analysis for generalized linear mixed models in ecology and evolution. *Methods Ecol Evol* (2015) 6:133–42. doi:10.1111/2041-210X.12306
26. Davlin SL, Vonville HM. Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* (2012) 30:3492–502. doi:10.1016/j.vaccine.2012.03.069
27. Bardosh K, Sambo M, Sikana L, Hampson K, Welburn SC. Eliminating rabies in Tanzania? Local understandings and responses to mass dog vaccination in Kilombero and Ulanga districts. *PLoS Negl Trop Dis* (2014) 8:e2935. doi:10.1371/journal.pntd.0002935
28. Lembo T, Partners for Rabies Prevention. The blueprint for rabies prevention and control: a novel operational toolkit for rabies elimination. *PLoS Negl Trop Dis* (2012) 6(2):e1388. doi:10.1371/journal.pntd.0001388
29. Gibson A, Handel I, Shervell K, Roux T, Mayer D, Muyila S, et al. The vaccination of 35,000 dogs in 20 working days using combined static point and door-to-door methods in Blantyre, Malawi. *PLoS Negl Trop* (2016) 10(7):e0004824. doi:10.1371/journal.pntd.0004824
30. Klepac P, Funk S, Hollingsworth T, Metcalf C, Hampson K. Six challenges in the eradication of infectious diseases. *Epidemics* (2014) 10:97–101. doi:10.1016/j.epidem.2014.12.001
31. Schneider MC, Belotte A, Adé M, Hendrickx S, Leanes LF, Rodrigues MJDF, et al. Current status of human rabies transmitted by dogs in Latin America. *Cad Saúde Pública* (2007) 23(9):2049–63. doi:10.1590/S0102-311X2007000900013
32. Ferguson EA, Hampson K, Cleaveland S, Consunji R, Deray R, Friar J, et al. Heterogeneity in the spread and control of infectious disease: consequences for the elimination of canine rabies. *Sci Rep* (2015) 5:18232. doi:10.1038/srep18232
33. Putra AAG, Hampson K, Girardi J, Hiby E, Knobel D, Mardiana IW, et al. Response to a rabies epidemic, Bali, Indonesia, 2008-2011. *Emerg Infect Dis* (2013) 19:648–51. doi:10.3201/eid1904.120380
34. Mtema Z, Changalucha J, Cleaveland S, Elias M, Ferguson HM, Halliday JE, et al. Mobile phones as surveillance tools: implementing and evaluating a large-scale intersectoral surveillance system for rabies in Tanzania. *PLoS Med* (2016) 13:e1002002. doi:10.1371/journal.pmed.1002002

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REVIEW
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The Role of Dog Population Management in Rabies Elimination—A Review of Current Approaches and Future Opportunities

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Free-roaming dogs and rabies transmission are integrally linked across many low-income countries, and large unmanaged dog populations can be daunting to rabies control program planners. Dog population management (DPM) is a multifaceted concept that aims to improve the health and well-being of free-roaming dogs, reduce problems they may cause, and may also aim to reduce dog population size. In theory, DPM can facilitate more effective rabies control. Community engagement focused on promoting responsible dog ownership and better veterinary care could improve the health of individual animals and dog vaccination coverage, thus reducing rabies transmission. Humane DPM tools, such as sterilization, could theoretically reduce dog population turnover and size, allowing rabies vaccination coverage to be maintained more easily. However, it is important to understand local dog populations and community attitudes toward them in order to determine whether and how DPM might contribute to rabies control and which DPM tools would be most successful. In practice, there is very limited evidence of DPM tools achieving reductions in the size or turnover of dog populations in canine rabies-endemic areas. Different DPM tools are frequently used together and combined with rabies vaccinations, but full impact assessments of DPM programs are not usually available, and therefore, evaluation of tools is difficult. Surgical sterilization is the most frequently documented tool and has successfully reduced dog population size and turnover in a few low-income settings. However, DPM programs are mostly conducted in urban settings and are usually not government funded, raising concerns about their applicability in rural settings and sustainability over time. Technical demands, costs, and the time necessary to achieve population-level impacts are major barriers. Given their potential value, we urgently need more evidence of the effectiveness of DPM tools in the context of canine rabies control. Cheaper, less labor-intensive tools for dog sterilization will be extremely valuable in realizing the potential benefits of reduced population turnover and size. No one DPM tool will fit all situations, but if DPM objectives are achieved dog populations may be stabilized or even reduced, facilitating higher dog vaccination coverages that will benefit rabies elimination efforts.

Keywords: canine rabies, dog population management, dog population control, free-roaming dogs, stray dogs, responsible dog ownership, sterilization

INTRODUCTION

Domestic dogs (*Canis lupus familiaris*) are responsible for over 99% of human deaths due to rabies (1). The key objective of a successful canine rabies elimination program is to maintain a high enough level of rabies vaccination coverage to interrupt rabies transmission within a defined dog population. This in turn reduces the incidence of rabies among human populations (1).

Stable dog populations with relatively low turnover rates make continuous vaccination coverage highly feasible. However, in many countries in which canine rabies persists, economic barriers and cultural attitudes toward dogs enable the maintenance of large free-roaming dog populations (2). Where the size of the free-roaming dog population is large and turnover is high, regularly vaccinating a large enough proportion of the population to achieve rabies elimination is a huge challenge. The stabilization of dog populations, and, in some cases, the humane reduction of the population over time to a manageable size, would be valuable adjuncts to long-term canine rabies control strategies.

Dog population management (DPM) is a multifaceted concept which aims to improve the health and well-being of free-roaming dogs, reduce problems they may cause, and may also set goals to reduce the size or turnover of the population (3). DPM may be enacted for numerous animal welfare, public health and safety, and economic reasons. These reasons include reducing the incidence of human bite injuries, secondary infections, and death; reducing or eliminating the transmission of rabies and other zoonotic diseases; reducing the level of noise and the amount of fecal contamination of the environment; reducing the incidence of traffic accidents; limiting the amount of negative publicity directed at governments; and minimizing the impact of reductions in tourism associated with free-roaming dog populations (2–5). Therefore, DPM programs can have one or more goals, depending upon specific situations, and these may or may not include permanently reducing the size of a dog population. Tools to achieve DPM objectives are humane and intended to produce a long-term positive impact on free-roaming dog populations, in contrast to dog culling (6).

Whether and how to manage dog populations effectively within rabies control programs has become the subject of debate (7, 8). However, because of the potential implications of DPM measures for the sustainability of rabies control programs, the World Organisation for Animal Health (OIE) recommends DPM as an integral part of such programs (9). Incorporating a DPM program with potential to improve animal, human, and environmental health into a rabies control program may increase motivation to tackle the issues and bring on board more stakeholders to support efforts.

Assuming that a rabies vaccination program is in place or being planned, this review aims to assess how different DPM tools might benefit rabies control programs and how to choose the most appropriate tools. We also consider available evidence for the impact of DPM measures on the health, stability, and size of dog populations. Finally, we review the feasibility and costs of implementing these interventions. This review does not aim to give prescriptive advice, but presents the available evidence, and allows program designers to assess, for their particular situations, whether it may be beneficial to integrate DPM into their rabies control planning.

DOMESTIC DOGS AND RESPONSIBLE DOG OWNERSHIP (RDO)

Domestic dog populations are dependent on people for food, either directly or indirectly (e.g., through open garbage dumps), and their presence and movements are linked tightly to human actions (10–12). Thus, dog population size is heavily dependent on human behavior, and dog-related problems are consequences of human behavior.

In most settings where this has been studied, the majority of dogs (even if free-roaming) have identifiable owners, which may be either individuals or community groups (12, 13 and see Section "Which DPM Approaches Might Be Suitable in a Particular Setting?"). RDO involves owners accepting their duties to provide the resources (e.g., food, water, shelter, health care, social interaction, exercise, and opportunity for natural behaviors) necessary for dogs to maintain an acceptable level of health and well-being in their environments; to act in accordance with the legislation in place (including vaccination); and to minimize any risks (aggression, disease transmission or injuries) that dogs may pose to communities, other animals, or the environment (3, 4). Dogs may have a single owner or be cared for collectively by a family or a group of individuals (3).

Widespread practice of RDO at a community level will be the most effective way to achieve DPM objectives, as long as veterinary services (such as vaccination and sterilization) are accessible and affordable to owners. Empowerment of communities with the knowledge to actively participate in DPM programs that are suited to the setting will be critical to ensuring DPM programs' success and sustainability. However, the intended impacts of RDO may be severely compromised where access to veterinary services is poor and in settings where a large proportion of dogs do not have responsible owners. For unowned dogs and those without responsible owners, the responsibility for providing veterinary care often falls upon government entities and non-govermental organizations (NGOs).

WHAT ARE THE THEORETICAL BENEFITS OF DPM PROGRAMS FOR RABIES CONTROL?

The primary focus of a rabies control program in dogs is vaccination (1). Mass dog vaccination programs generally aim for a 70% vaccination coverage so that between campaigns, levels of protection stay above the threshold necessary to prevent ongoing transmission (14, 15). High enough levels of canine vaccination will break the enzootic cycle of transmission between dogs, protecting them and their communities from rabies and leading to elimination of the disease. There is now much evidence that achieving 70% vaccination coverage, even where dog population turnover is high, is feasible (16–18), but it can be challenging.

Rapid population turnover (due to high death rates) of both owned and unowned dogs can present a significant challenge for the maintenance of high vaccination coverage (6, 17). Puppies comprise large proportions of dog populations in many rabies-endemic areas, even where almost all dogs are owned (12, 19, 20). A longitudinal study in West Bengal, India, found that 67% of new puppies died within 4 months and 82% within their first year (21). A survey in Nepal estimated 60% puppy mortality (13), and studies in Latin America and Africa have reported population-wide death rates as high as 30% per year (17, 20, 22, 23). All dogs, including puppies, can transmit rabies and should be vaccinated during mass vaccination campaigns. High population turnover means that vaccinated dogs often die and annual campaigns are generally required to vaccinate their replacements (24, 25).

There are several ways in which effective DPM programs could theoretically benefit rabies control activities.

Maintaining Vaccination Coverage

There is unlikely to be a clear impact of reduced dog population density on rabies transmission rates between dogs [measured as R_o (26)]. However, DPM programs that reduce the dog population size will make reaching 70% vaccination coverage of dogs much easier and less costly. This is particularly true of free-roaming dogs that are difficult to handle or unowned dogs which are often the most time consuming to vaccinate. DPM that improves the health and longevity of vaccinated dogs will, by reducing the population death rate, also reduce population turnover and allow vaccination coverage to be maintained more easily, even if the population size remains unchanged (17, 18).

Reducing Bite Incidents

In practice, in rabies-endemic areas any dog bite should be considered a possible exposure to rabies, and demand for human post exposure prophylaxis (PEP) is one of the major costs associated with canine rabies (27). Until canine rabies can be eliminated, DPM that reduces the incidence of dog-bite injuries will reduce the demand for PEP and, therefore, increase cost effectiveness of control programs.

Canine aggression that results in dog bites can have many different causes, including fear, resource guarding, pain, territorial behavior, maternal guarding of puppies, play aggression, and predatory behavior (28, 29), with fear the most common trigger of aggression (30). Some forms of aggression, such as inter-male aggression and female puppy-guarding aggression, are hormonally related and sterilization may reduce them (29, 31). However, the impact of different DPM methods on bite incidence may not be easily predicted. An analysis of free-roaming male dog behavior changes following castration in Chile showed no reduction in overall aggression as a result of surgical sterilization, and a significant increase in dog-to-dog aggression as a result of chemical castration (32).

Dog bites may be provoked by people, and high dog-bite incidences can feed a cycle of intolerance toward free-roaming dogs that makes the dogs more aggressive in return (2). Temporary marking of recently vaccinated dogs and permanent marking of sterilized animals can play a role in improving community acceptance of dogs and reducing cruelty toward them. Education and RDO programs aimed at changing community attitudes and behaviors toward dogs as part of a DPM program may result in reduced dog-bite incidence.

Increasing Support for Interventions

A combined program of DPM and rabies control (for example, one that seeks to reduce nuisance dog behavior, dog-bite incidence, and rabies transmission), may have much broader appeal to the public and health authorities or other stakeholders than a single program. For this reason, introducing DPM measures that improve animal welfare into rabies control programs may bring on board additional partners with expertise and funding. Evidence of this is provided by animal welfare NGOs which implement rabies control programs using DPM measures as their main strategy, where there might otherwise be no program at all (33–36).

Increasing Program Sustainability

Appropriate, acceptable DPM programs can allow communities to live in better balance with the free-roaming dogs in their environments. It is easier to maintain high vaccination coverage in populations of dogs that are healthier, live longer, and are more familiar with their environments (17, 18). Healthier, better managed dog populations may elicit more positive public attitudes toward those dogs (2), and increase the likelihood that communities seek rabies vaccinations for their dogs (17). Anecdotal reports from one community suggest that where DPM has achieved a reduction in dog population size, the remaining dogs are better cared for (37). Dogs that are well fed and cared for may in turn also mount a better immune response after vaccination (25).

MASS DOG CULLING IS NOT AN EFFECTIVE DPM TOOL

Mass dog culling is still used as a misguided emergency response to rabies outbreaks, based on the mistaken belief that reducing the size of dog populations will reduce rabies transmission (38). In fact, mass dog culling has been shown to have no long-term impact on the control of rabies within cities (36, 39, 40) or across countries such as Ecuador, Indonesia and Bangladesh (19, 41–43). When modeled in realistic scenarios, culling is not as effective as sterilization programs at reducing population size in the long term (44). This is because culling does not address the source of new or replacement animals, and has only a temporary effect on population size. Furthermore, rapid dog replacement rates have been documented in some areas following culling, leading to a younger population of generally rabies-susceptible dogs (45, 46).

Indiscriminate culling of dogs in communities where rabies vaccination programs are operating is likely to remove vaccinated dogs from communities, resulting in lower vaccination coverage and a counter-productive increase in rabies transmission as populations recover (7). Culling often meets with public resistance both within the local area and outside, especially as the methods employed are often inhumane (47). The result can be withholding of dogs from rabies vaccination efforts during current and future campaigns. People may even move dogs away from culling zones, a measure which has been documented to spread rabies (15). Some methods of culling, such as poisoning, may pose threats to public health. Culling operations can also be expensive (19, 42, 48) and harmful to tourism (49). For these reasons, the indiscriminate culling of dogs is now universally condemned as a means to control rabies (1).

WHAT ARE THE BENEFITS AND DRAWBACKS OF HUMANE DPM TOOLS?

The culling of dogs has now been replaced in some settings by a variety of humane DPM approaches that aim to exert sustainable, positive impacts on dog populations and the communities in which they live (6). DPM tools such as vaccination and other disease control methods, control of access to food (habitat control), the promotion of RDO, prevention and control of reproduction, identification and registration of individual dogs, the availability of shelters, rehoming centers and holding facilities, and the passage of legislation can interlink with each other to create effective DPM programs. Much of the motivation for DPM in rabies control efforts comes from the desire to reduce the size or the turnover of the free-roaming dog population to make effective vaccination more feasible. For this reason, reproductive control is usually a primary objective, but other efforts that increase longevity and reduce population turnover will also support rabies control efforts.

Tools for Reproductive Control

Both permanent and temporary methods of reproductive control are available (summarized in **Table 1**). Permanent sterilization is preferable in most settings where rabies control is the objective, but temporary contraceptive methods will be more appropriate where owners may wish to breed dogs in the future (50).

Surgical sterilization is currently the most widely used option. Surgical procedures to remove reproductive organs must be carried out by qualified veterinarians using good aseptic techniques and pain management throughout and after the procedures (3). In settings where the majority of dogs are family-owned, fixed point sterilization campaigns may have great success. In settings where there are large numbers of community-owned or unowned dogs, programs that capture, sterilize, vaccinate and return free-roaming dogs to their communities may be more effective. As dogs are territorial animals, it is assumed that returning sterilized dogs to their original locations helps to prevent new, fertile, and unvaccinated dogs from occupying these areas. Standard operating procedures generally recommend this practice (59). In some instances programs are referred to as "dog managed zones," where the aim is to establish stable populations of sterilized, vaccinated dogs within defined areas (35). Whether territories are effectively guarded or not, this process means that more of the ecological niches available to dogs in a particular area will be occupied by sterilized, vaccinated dogs, reducing the proportion of niches available to young, unvaccinated dogs. Ecological models have demonstrated that this leads to a reduction in the number of young, unvaccinated dogs in those areas (44).

Surgical sterilization provides lifelong reproductive control and may also reduce problematic behaviors such as some forms of aggression or the propensity for specific dogs to roam (28, 31). It could improve animal welfare by reducing the dumping and killing of unwanted puppies and the stress experienced by female dogs that produce litters repeatedly. Surgical sterilization has been documented to reduce the lifelong probability of cancers and other diseases in both male and female dogs and can also increase life expectancy (6, 31). On the other hand, if there are not enough skilled veterinarians with access to recommended drugs and equipment, the procedures could fail to achieve sterilization and, combined with post-operative complications, could increase animal suffering.

Population simulation models predict that the effect of sterilizing females is far more significant than that of sterilizing males in terms of reducing population sizes (60, 61). Dog population sizes can be reduced where enough female dogs are sterilized, but this is a long-term goal for which very high throughput surgery is often required. It is important that if only females are targeted for sterilization, male dogs should still be vaccinated to prevent rabies.

A variety of non-surgical methods can be used to prevent reproduction. These include physical restraint of females and males, as well as injectable, implantable and oral contraceptives. The methods are summarized in **Table 1** and their use for the management of free-roaming dogs is reviewed in more detail elsewhere (50, 62).

With the exception of physical restraint and dosing of oral contraceptives, all reproductive control methods should be implemented by trained individuals (e.g., veterinarians). Many of the newer tools are not widely licensed, experience and training in their use are limited and costs can be prohibitively high (50). Female dogs treated with hormone-based non-surgical methods must be monitored daily for evidence of pyometra (uterine infection) and other potentially life-threatening complications, and veterinary medical care must be accessible in the event that these occur (62). The administration of products with short-term contraceptive effects needs to be closely managed by responsible owners to be effective, and this method is not practical in most rabies-endemic countries. For unowned dogs, permanent sterilization will usually be required, and the costs and the feasibility of reaching enough dogs to achieve population-level effects must be carefully considered.

TABLE 1 | Reproductive Control tools currently available that can be incorporated into dog population management.

Reproduction control tool	Required resources	Targeted population	Product	Targeted sex	Duration of infertility	Potential negative consequences	Cost	Reference
Surgical sterilization	– Veterinary personnel – Aseptic techniques – Suitable operating and recovery facilities – Medications	Unowned or owned dogs, depending on program structure	NA	Male and female	Permanent	– Surgical complications – Post-surgical complications	$6–$100+ (see **Table 4**) Cost	(33, 40, 51–54)
Injectable contraceptives	– Veterinary or trained/certified personnel for delivery and monitoring – Commercial product – Accessible veterinary service in event of complications	Unowned or owned dogs, depending on program structure	Zinc gluconate (*Zeuterin™/Esterilsol™/Neutersol™*)	Male	Permanent	– Abscess at injection site – Temporary swelling of testicles	$15	(50, 55)
			Progestins [melengestrol acetate (MGA)]	Female	6 months	– Need for regular monitoring – Uterine infections, cancer, endometrial disease, depression, death		(50)
			Calcium chloride	Male	Permanent	– Temporary swelling of testicles, scrotal abscesses and necrosis necessitating surgical intervention – Risks associated with inaccurate or non-sterile compounding – Still considered experimental	Pennies	(50, 56–58)
Implantable contraceptives	– Veterinary personnel for delivery and monitoring – Commercial product – Accessible veterinary service in event of complications	Unowned or owned dogs, depending on program structure	Progestins (MGA)	Female and male	Up to 2 years	Females: – Induces estrus – 4 to 6 weeks to take effect – Need for regular monitoring – Uterine infections, cancer, endometrial disease, depression, death	$25–$75	(50)
			GnRH agonists (*Suprelorin™*)	Female and male	Up to 27 months	– Initially causes estrus and ovulation	$100	(50)
Oral contraceptives	– Responsible owner – Daily treatments – Accessible veterinary service in event of complications	Owned dogs	Megestrol acetate	Female	Daily	– Requires daily treatments at specific times of cycle – Need for regular monitoring – Uterine infections, cancers, and depression		(50)
Physical confinement	– Trained, responsible owner – Suitable place for dog confinement	Owned dogs	NA	Female and male	Not applicable	– If confinement fails, pregnancy may result – Welfare and safety concerns as females in season still attract males – Welfare concerns if not correctly confined	Free	

Surgical sterilization remains the most widely used technique as it produces a permanent solution and is available for both sexes. If population reduction or stabilization is the desired outcome, then high throughput sterilization focused on female dogs is necessary, together with some method of clearly identifying dogs that have already been sterilized. Sterilization of at least 70% of females is often mentioned as a target to achieve for population reduction, but this has no theoretical or practical basis. The coverage level necessary to achieve an impact on population size instead depends on the turnover characteristics of the local dog population. A study on the island of New Providence in the Bahamas estimated that for the population to reach equilibrium, 83% of females would need to be prevented from breeding (63).

The length of time required to achieve a desired outcome will also vary according to population turnover and sterilization efforts. Studies of sterilization programs in different settings have suggested that their full impact on reducing population size would not be achieved for over 30 years [for a shelter based spay/neuter campaign in the US (64)], up to 10 years [for sterilization of free-roaming dogs in Brazil (54)] and between 13 and 18 years [for sterilization of free-roaming dogs in India (34)]. Therefore, sterilization may be useful in reducing dog populations over a relatively long time period, but its impact will also need to be considered within the scope and timeframe of a rabies control program.

Vaccination and Parasite Control

Reducing the incidence of canine diseases other than rabies such as canine distemper, and the prevalence of parasitic worms, may improve dog health and life expectancy and, therefore, reduce population turnover rates. Reducing the incidence of canine zoonoses also benefits public health. Many DPM programs routinely treat dogs with ivermectin to reduce parasitic infections and suffering due to itchy skin conditions (36, 51, 59, 65, 66). Anecdotal reports indicate that improving the body condition of dogs led to significant improvements in RDO and community acceptance of dogs in some settings (2).

Controlling Access to Food

Based on the availability of resources (food, water, shelter) and human acceptance, there is an upper limit on the dog population size that can be supported by any environment (10). The dependence of the dog population on environmental resources such as waste food around markets and garbage dumps has been suggested to be high in some settings (19, 36, 67, 68) but very low in others (12, 69), depending on the quality of the waste food sources. There is some evidence that the percentage of ownerless dogs is higher around garbage dumps than elsewhere (10, 67). Free-roaming dogs may be frequently observed scavenging in waste, leading to claims that waste removal will help reduce the population (70, 71). However, without studies of the nutritional quality of waste food sources needed to sustain a population, it is unclear if these interventions will help. In Cameroon, residents associated open garbage dumps with an increase in stray dogs and, therefore, an increased risk in rabies transmission, although this was not confirmed empirically (68).

In one general dog population dynamics model, changing the parameter value of the upper limit of dog population size was identified as the most effective way to modify dog population dynamics of both owned and unowned dogs (72). While the owned dog population is unlikely to be reduced easily, reducing environmental food sources and shelters was expected to have a strong influence on reducing population size among ownerless dogs. However, if abandonment rates or other factors are not simultaneously changed, population size reduction will only be achieved by high death rates due to starvation (72).

Reducing access to food waste such as garbage in the streets, waste around abattoirs, butcher shops, and market areas, and protecting garbage dumps from scavengers have been suggested as practical, cheap, and sustainable ways to reduce free-roaming dog population sizes (73). There is a need to determine first whether food waste does in fact limit the size of a population, and any reduction of this food source must be gradual to avoid increased aggression between dogs over fewer resources, and to prevent starvation of existing animals or their migration to neighboring areas (3). This approach will also require public education (possibly supported by legislation) and may not work where dogs feed on other animals such as rats (74) or where dog populations are regularly fed by people. If free-roaming dogs are regularly fed by the community (75), changing attitudes and practices toward this activity may be extremely difficult, particularly in cultural settings such as Buddhist communities where feeding stray animals is perceived as a selfless act of kindness and generosity (76).

Community Education, Engagement, and Empowerment

Dog ecology is integrally linked with human activities. The promotion of RDO coupled with the availability of vaccination and sterilization services could significantly reduce abandonment, the numbers of free-roaming dogs and the incidence of dog bites and zoonotic diseases (3, 4, 77). In the long term, RDO is key to the changes in human behavior that will allow DPM achievements to be sustained.

Where problems related to the dog population have been identified in or by a community, its involvement in developing a program and increasing access to information can help the community to identify the best options to deal with those issues. Supplying information about the benefits and practicalities of sterilization and vaccination, and how it will affect their dogs' behavior, can help to change community attitudes, dispel myths that may be circulating and encourage owners to have their dogs sterilized and vaccinated. Awareness of solutions to dog-related problems may in itself empower communities to demand better access to veterinary services.

Community engagement initiatives are long-term investments, as the benefits of healthier and possibly smaller dog populations may not be seen for several years. Nevertheless, they still require resources. Educational materials need to be tailored to the community, taking into account cultural differences and literacy levels and utilizing appropriate networks for information dissemination. It takes time and resources to work out how to convey messages to different audiences, and the development of culturally appropriate materials across numerous languages can be a significant challenge. Helping communities to assume ownership of the DPM program enables them to become engaged and empowered. This maximizes the chances of creating and maintaining a successful, sustainable program.

Again, accessible and affordable veterinary services will be critical if programs are to achieve DPM goals.

Identification and Registration

Registration and identification can be emphasized as part of RDO and are often linked to animal health programs such as mandatory rabies vaccination and traceability.

Registration of animals in a centralized database can be used to support the enforcement of legislation on vaccination, the reuniting of lost animals with owners, prevention of theft and illegal breeding and trade, and identification of owners of biting dogs (3, 4). The control of dog reproduction by sterilization can be encouraged through reduced registration fees for sterilized dogs.

In practice, dog registration systems require extensive and centralized data management systems and consistent input and maintenance if they are to be kept updated and effective. In settings with a high proportion of family-owned dogs this method may be effective even if many are free roaming, but unowned dogs and those more loosely owned by the community are very unlikely to be counted by registration programs. In most resource-poor settings and where turnover in the dog population is very high, registration systems may be impractical (20). Registration mandates may be viewed with great suspicion by the public and could be undermined. Thus, registration or identification strategies must be designed considering their context and implemented using good communication strategies and incentives to encourage participation and alleviate community mistrust. High registration fees may deter dog owners from complying with the scheme (78).

Legislation

The creation and enforcement of RDO and dog breeding legislation can strongly support community-level efforts to tackle dog population-related problems (4). DPM legislation is a necessary element of the government's engagement and is important for the effective management and sustainability of DPM programs. Legislation can be used to ensure DPM is carried out humanely, that culling is not used, that indiscriminate breeding and sale are prevented, that owners of biting dogs are held accountable, and that importation/exportation of dogs is controlled. Relevant laws may be divided across different statutes, laws or acts covering rabies or other diseases, dog ownership, stray animal management, waste management, and other features of DPM. Ideally, legal codes are designed with incentives for complying and punishments for non-compliance and are enforced by authorities working together with the program; fines levied are used to support the maintenance of the enforcement program.

However, legislative change can be a long and bureaucratic process. Enforcement of legal codes is frequently very challenging, especially where the personnel needed to enforce codes are in short supply. In addition, such mechanisms may fail if enforcement is not seen as a priority, corrupt officials are an issue, or the community members' ability to pay fines is low.

Shelters/Rehoming Centers

Many high-income country models of DPM rely on a model where free-roaming dogs are collected from the streets by authorities and taken to shelters or pounds, from where they are ideally collected by their owners or rehomed. Dogs whose owners no longer want them can also be surrendered to shelters. Both these methods reduce the free-roaming dog population. In shelters, there is the opportunity to sterilize and vaccinate animals before they are rehomed and to educate new owners in RDO.

In practice, however, the number of dogs admitted to shelters usually far outpaces the community's capacity to rehome them (54). Shelters are expensive and time consuming to run, and once facilities are overwhelmed with animals, animal welfare standards can fall dramatically (3).

In areas where rehoming rates are low due to cultural practices or limitations in local resources, euthanasia in shelters will remain necessary in order to prevent animal welfare violations that are inherent to overcrowded, under-funded shelters. Even in high-income countries with well-established shelter adoption schemes the proportion of dogs euthanized can be significant. Limited data point to 10.4% of shelter dogs euthanized in the UK (79), over 30% in Australia (80), over 40% in Brazil (81), and 40–50% in the US (82).

The cost of running shelters can also be prohibitively expensive. The Humane Society of the US estimates that each year $2.5 billion is spent by humane organizations and $800 million to $1 billion is spent by animal control organizations on managing the pet overpopulation problem (82). An OIE survey of DPM strategies found that shelters were prohibitively costly for most low-income countries (38).

Finally, the availability of dog shelters that absorb unwanted dogs can counterproductively increase animal abandonment (3). This may be because people surrender dogs to the shelter, or instead abandon dogs to the street thinking that shelters will pick them up and take care of them. Shelters do not address the source of dogs, and dogs taken from the streets are quickly replaced by new puppies if enough breeding females remain or if dog abandonment rates are high.

Thus, for practical, economic, and welfare reasons, in most rabies-endemic settings alternatives to shelters must be explored fully prior to any commitment to build one (3, 54).

Holding Facilities

Holding facilities aim to safely, but temporarily, house dogs that will generally be returned to owners or to the streets. Such facilities can be beneficial for safely assessing aggressive or sick animals, including those suspected of rabies which might otherwise transmit the disease. These types of facilities can also be centers for safe and humane euthanasia of animals that are a threat to people, or have no chance of healthy lives in their communities. They can also serve as centers where street dogs are sterilized and vaccinated before being returned to the streets.

Euthanasia

Ideally, euthanasia should be reserved for animals who are incurably ill, or whose suffering due to behavioral problems or lack of guardianship cannot be alleviated with available resources. Unfortunately, many dogs are euthanized as a means of population control as well. When the decision for euthanasia is made, it must be carried out by qualified veterinary staff with access to the necessary drugs and training in humane handling and euthanasia. Robust euthanasia policies and legislation can prevent the indiscriminate culling of dogs by defining clearly the only circumstances when euthanasia is acceptable, and this can build public trust in DPM programs (3). However, euthanasia deals only with the symptoms and not the causes of dog population problems and will not solve the underlying causes of overpopulation. Euthanasia can also be distasteful and stressful to professional animal caretakers (83, 84) and this can be a strong driving force for more acceptable DPM tools to be used.

WHICH DPM APPROACHES MIGHT BE SUITABLE IN A PARTICULAR SETTING?

There can be many different relationships between people and domestic dogs within a community. Dogs may be owned for a variety of reasons, such as for companionship, for guarding the home or livestock, for hunting, or as a source of food. These relationships may affect the degree to which they are cared for and whether veterinary services or reproductive control may be sought by the owner [reviewed in Ref. (2, 6, 47)]. Where community ownership of dogs occurs, there may be some joint acceptance of responsibility for feeding these animals, but frequently this does not extend to full RDO (2, 13, 76). Understanding the ownership patterns and roles of dogs in a community is integral to choosing an appropriate DPM tool that will be acceptable to the community, thereby ensuring that it is as effective as possible.

Terminology around dog populations is varied and often misused. Dogs may be referred to as owned, unowned, semi-owned, free-roaming, unwanted, pet, feral, stray, community, village or neighborhood dogs. Local terminology may also apply. These terms are often not informative for the purposes of planning an effective DPM program. The often-used term, "stray" dog, is not consistently defined, sometimes being used interchangeably with free-roaming [which can include unowned, free-roaming owned, and owned lost dogs (4)] and elsewhere referring specifically to dogs with no owners.

Only two characteristics of dog guardianship are highly relevant to disease control and DPM: "confinement status" and "ownership status" [(3) and **Box 1**], and these are not mutually exclusive. Unowned dogs are never confined, but a free-roaming dog may be owned, community owned, unowned, or feral. In many countries, dogs are allowed to roam freely, but many of these dogs have owners [(10, 12–13, 24, 85, 86) and reviewed in Ref. (6)].

Community-owned and family-owned roaming dogs can enjoy high standards of welfare when their needs are fulfilled. However, regardless of ownership status, free-roaming dogs are at higher risk for contracting diseases, injuries such as those caused by road-traffic accidents or acts of cruelty, and culling by governments or local communities, compared to owned confined dogs. This can lead, in turn, to owners failing to invest in their care (17), creating a vicious cycle of neglect and poor health.

Dog populations can vary across countries (6, 70, 78) and at more local scales (85). Understanding the composition of the dog population (such as the numbers of owned and unowned dogs in each category of confinement) and identifying which of these categories are the causes of the dog-related problems, will help to decide which DPM approaches should be considered (**Table 2**). Characterizing a dog population with terms like "stray" is of little use. The source of those dogs must also be

BOX 1 | Key characteristics of dog guardianship for DPM purposes.

CONFINEMENT STATUS

- A *confined dog* remains under owner control at all times, often within a home or walled compound, and is walked on a leash or maintained under control when outside those confines.
- A *partially free-roaming dog* spends part of its time confined to a home or a walled property, but is also allowed to freely roam in the community.
- A *fully free-roaming dog* is never confined to a home or walled property.

OWNERSHIP STATUS

- A *family (or individual)-owned dog* is a dog that a family or individual states is their property or claims a right over.
- A *community-owned dog* is a dog that more than one individual or family state is their property or claim a right over.
- An *unowned dog* is not claimed by anyone in the community. It may be accepted, tolerated or despised by the community.

TABLE 2 | Different sub-populations of dogs and factors relevant to dog population management.

Ownership status	Confinement status	Dependency on humans	Acceptance by community	Risk for rabies transmission (if unvaccinated)	Target for population reduction	Target for responsible dog ownership programs	Target for central-point sterilization	Target for capture–sterilize–release programs
Family owned	Confined	Fully dependent	High	Low	No	Yes	Maybe	No
Family owned	Partially free roaming	Fully or Semi-dependent	High	Moderate	No	Yes	Maybe	Maybe[a]
Family owned	Free roaming	Semi-dependent	High	High	No	Yes	Maybe	Maybe[a]
Community owned	Free roaming	Semi-dependent	High	High	Maybe	Maybe	Maybe	Maybe[a]
No owner	Free roaming	Independent	Variable, but lower	High	Usually yes	No (unless abandonment rates are high)	No	Yes

[a]*The suitability of this program will depend on obtaining owner consent where needed.*

considered to enable the design of a DPM program that will address the problem in a sustainable manner. Ownerless puppies may be abandoned (by owners, breeders or pet shops) or be born on the streets, and each cause may require a different management strategy. Finally, potential strategies need to be assessed for a number of features, including their acceptability to the community, their potential impact, the accessibility of dogs, animal welfare considerations, veterinary infrastructure needs and cost implications (50).

No one DPM strategy should be expected to solve all problems or fit all situations (78). Knowledge, Attitude and Practices surveys of the community can be particularly helpful in elucidating what would be the most acceptable and therefore successful DPM components to apply in a particular setting (23, 75, 87). For example, if the unowned dog population is sustained mostly by owners dumping unwanted puppies, then legislative and educational efforts to increase RDO and central-point sterilization programs may improve the health and longevity of family-owned dogs and reduce the number of unwanted litters. If breeders are dumping unwanted animals, then better regulation of such establishments will be needed. However, if the unowned dog population is sustained by puppies born on the streets, then sterilization and release programs may be considered. Where there are plentiful food resources on the streets, tackling this issue may need to be prioritized in order for other DPM tools to have their anticipated impact.

Finally, it is important to understand that DPM strategies will not have the desired impact without community buy in. The whole community may not have a uniform attitude toward dogs, which can cause tension (2). It is important to assess exactly what the views are within a local community toward potential interventions. If members of a community want to own more dogs, more (generally unvaccinated) dogs will likely be bred or imported, even if DPM programs are being implemented. Assessing the dog population and understanding community attitudes are integral to development of a successful DPM program.

DO DPM TOOLS HAVE A MEASURABLE IMPACT IN CANINE RABIES-ENDEMIC COUNTRIES?

Community surveys in rabies-endemic countries often identify the need for improved DPM to help reduce the risk of rabies (6, 9, 17, 77), and small- and large-scale DPM interventions on free-roaming dogs are carried out in many places. However, before adding DPM interventions to an existing rabies control program, there is a need for solid evidence that DPM tools can have the desired impact on reducing dog population size or turnover, which will benefit rabies control objectives.

Although the impact of DPM programs is often assumed and sometimes informally reported (39, 51), it is often not critically assessed and even more rarely published following peer-review. A review of the literature on DPM recently compiled by the International Fund for Animal Welfare found very little information on the effectiveness of specific approaches to DPM, and found that the most comprehensive programs were generally not making their outcome data available (88).

The use of mixed DPM interventions, though often advisable, makes it very difficult to determine which of the individual interventions is responsible for success. For example, the successful impact of sterilization and release programs on reductions in rabies cases (39) is most likely due to the impact of dog vaccination and community engagement, not sterilization. While the establishment of a shelter in Erzurum City in Turkey has been credited with a 30% reduction in the number of bites from rabies suspect dogs (89), this shelter was primarily sterilizing, vaccinating, and then releasing free-roaming dogs, and the impact on rabies could be due to the vaccination component. A pilot program using Esterilsol™ on male dogs in Raipura Island, Bangladesh was found to be flawed as it also involved extensive use of culling (90). Reported benefits of adequate waste removal practices on free-roaming dog populations could instead be explained by the ongoing collection of free-roaming dogs from the streets in that particular setting (70).

Available data on the effectiveness of DPM programs are summarized below, but their interpretation is still fundamentally limited by the lack of control areas.

Injectable Sterilants

The injectable sterilant Esterilsol™ has been used successfully in small scale safety and immunogenicity trials for male dogs in Todo Santos, Guatemala (91), and in Chile (55). However, no attempt has been made to assess its effect on longevity, population turnover, or individual dog behavior and aggression. The sterilization of male dogs is not expected to produce a reduction in population size, which is much more critically impacted by reductions in the reproductive capacity of female dogs (60, 61).

Removal of Waste Food Sources

Food waste in garbage has been suggested as an important factor in maintaining dog populations (10, 68, 92), and better waste management has been implemented as part of some documented DPM programs (39). However, there is a lack of evidence of the impact of removal of food sources in garbage dumps and marketplaces on dog population size or rabies control.

Leashing and Confinement

There is some evidence that in low-income countries, leashing or confinement of dogs can be both effective at reducing contact between dogs and well-tolerated during rabies outbreak situations, but after an outbreak is over it is less likely to be tolerated, as communities prefer dogs to roam freely (19, 93). Thus the value of confinement as a means to reduce dog populations is unlikely to be high in most settings, and there can be welfare implications for dogs depending on the method and duration of confinement.

Awareness and Legislation

The purpose of legislation and awareness measures is generally to support other DPM measures and their individual impact is hard to assess. However, without legal enforcement and the awareness needed to build community participation, large-scale sustainable DPM programs will be very challenging. Poor results from DPM programs have been suggested to be the result of a lack of public awareness about the program (94). Public awareness and enforcement of dog ownership laws in the Philippines helped to increase the proportion of households that registered their dogs and stopped them from roaming freely. Concurrently, the demand for sterilization services from the community increased (95).

Among high-income OIE member countries surveyed, enforcement of dog registration laws was the chief tool used to support DPM tools, but use of laws was much less common in low-income countries (38). Most countries have legislation related to stray dog control, but there is huge variation, often incompliant with OIE animal welfare guidance and generally inadequately enforced [summarized in Ref. (96)]. The fact that legislation frequently still permits culling in the event of rabies outbreaks may well contribute to the lack of application of more effective means of DPM and rabies control. In the OIE member country survey mentioned above, 46 out of 76 countries stated that it is official policy to kill free-roaming dogs (38).

One notable example of comprehensive humane legislation on DPM is India's Animal Birth Control (Dogs) Rules, which became law in 2001 (97). These laws stipulate that owners are required to control the breeding of their dogs, while municipalities and local authorities are required to sterilize and vaccinate street dogs, with the participation of animal welfare organizations, private individuals and the local authority. Appeals to local authorities relying on this legislation have been responsible for the proliferation of DPM programs in Indian cities (39).

Surgical Sterilization

Most of the available data on DPM programs aimed at benefiting rabies control come from sterilization, vaccination and release programs, and there is evidence of some success (**Table 3**). However, these campaigns frequently do not report an impact on population size or dog characteristics such as longevity which could impact population turnover (**Table 3**). There is limited evidence of population size reduction, primarily from India (33, 34), but effects have not always been achieved (94) or maintained (98). Sterilization rates need to be maintained for many years to reach their maximum impact (34). Very few programs have reached out beyond cities, and very few have sustainable government support for their implementation.

COST CONSIDERATIONS

The primary tool of rabies control remains canine vaccination. While DPM can in theory benefit vaccination efforts, it also incurs considerable additional costs and requires additional technical skills. DPM programs require long-term commitment, and implementing two project aims can be logistically difficult. When limited budgets and personnel are stretched too far there is a risk that trying to tackle more than one goal detracts from the achievement of either. If expensive and time consuming DPM approaches detract from vaccination goals, or draw funding away from vaccinating a sufficient proportion of dogs, then rabies control efforts will be hindered. However, if overlapping interests draw in additional partners (such as animal welfare NGOs) or additional budgets (perhaps from different government sectors such as public safety) to strategically integrate DPM tools into a rabies control program, then this could be a very positive outcome.

Data on programmatic field costs of many DPM tools are uncommon, but some estimates of DPM by sterilization (which may include rabies vaccination even if not specified), are shown

TABLE 3 | Available information on impacts of surgical sterilization programs on dog population characteristics.

Location and assessment dates	Coverage achieved	Reported impacts	Reference
Not peer reviewed			
Bali, Indonesia, 1998–2005	51%	None	(6)
Bangkok, Thailand, 2002–2005	Less than 30%	None	(99)
Sri Lanka, 2005	70–90%	None	(6)
Rosebud Reservation, USA, 2003–2010	Not measured	(Unmeasured) reduction in population size, 50% reduction in bite incidents, 75% reduction in complaints of cruelty to dogs, and increased demand for veterinary services	(51)
Kathmandu, Nepal, 2006–2012	47% of females	Overall population size reduction from 2006–2010 but no further impact to 2012, within zones mixed results found	(98)
Peer reviewed			
Gelephu and Phuentsholing towns, South Bhutan, 2012	56–58%	Majority of free-roaming dogs had healthy body and skin conditions	(100)
Dhaka, Bangladesh, 2012–2013	19.2–79.3% across 29 of 92 city wards	Neutered dogs tended to be healthier than intact dogs	(36)
Bangalore, India, 2000–2001	10.4%	None	(94)
Colombo, Sri Lanka, 2007–2010	Not measured	% Lactating females reduced from 8 to 1.1%. Slight increase in population size (possibly a rebound effect from ceasing of culling). Dog bites dropped by 33%, public perceptions of free-roaming dogs improved	(35, 40)
Pink city area, Jaipur, India, 1994–2002	65% of females	28% reduction in population size	(33)
Pink city area, Jaipur, India, 2003–2011	70–80% of females	Around 50% reduction in dog bites, associated with reduction in breeding females	(101)
Jodhpur, India, 2005–2007	61.8–86.5% across 6 areas	Dog population declines of 51%*, 40%, 39%*, 28%*, 3% (*significant)	(34)
Jodhpur, India, 2006	Not measured	Sterilized dogs had higher body condition scores, but worse skin conditions	(65)

TABLE 4 | Published data on sterilization costs for high throughput programs.

Intervention	Location	Reported cost/dog	US$ cost/dog	Reference
Surgical sterilization + vaccination	Tamil Nadu, India	Rs. 1,164	$22	(53)
Surgical sterilization + vaccination	Jaipur, India	GBP 4.80	$8.83[a]	(33)
Surgical sterilization	Bhutan	Nu 288	$6.36	(52)
Surgical sterilization	Campinas, Brazil	Real 105	$33.34[b]	(54)
Surgical sterilization	Indian reservation, USA		$23–28	(51)
Surgical sterilization (including staff and infrastructure)	Several WSPA sites		$10.30–$52.00 (average $25)	(40)
Surgical sterilization	Costa Rica		$8–$12	(62)
	India		$15–$20	
	Quezon City, Philippines	P 1,000–1,500	$24–$36	
	Phuket, Thailand		$30	
	Palawan, Philippines		$11.02 (excl. boarding)	
	Bangkok, Thailand		$23.25	
	Beijing, China		$43.69–$203.89	
	Chennai, India		$14.11	
	Shanghai, China	800–1,000 yuan	$128–$160	
	Shanghai, China	800–1,200 yuan	$128–$192	
Pinhole castration	Uganda		$2.12	(102)

Costs in US$ are as reported in the sources, except [a]1GBP = US$ 1.84 (average for 2006); [b]1 Real = US$ 0.30 (average for 2015); exchange rates from http://www.x-rates.com.

in **Table 4**. Although these costs of sterilization may not seem very large for an individual dog, given the scale necessary, full program costs can be high. For the four years of an intervention in Colombo City, Sri Lanka, costs within the animal sector were over $1 million, compared to $190,875 for the four preceding years (35).

Higher throughput programs can reduce costs per dog (33) (**Table 4**) but overall, there are insufficient data available on costs in different settings. Sterilization and release programs are usually focused on urban areas, where dog and human population densities likely make economies of scale more feasible and travel costs more reasonable. A rabies control intervention that involved sterilization as well as vaccination in selected cities in Tamil Nadu, India was not considered economically viable at the scale of the entire state (53).

Programs targeting only female dogs for sterilization (with vaccination of both sexes) will be a much more cost-effective way to reduce population size and turnover (44, 59–61) although this is uncommon in the studies listed in **Table 3**. In areas where the community keeps more male than female dogs (34, 61) this strategy will be even more effective at impacting population-wide demographics.

The source of funding will also need to be considered as well as the cost of interventions, in planning DPM interventions. As some canine rabies-endemic countries are considered to be middle income countries, there may be at least a proportion of dog owners who can pay for sterilization of their dogs through private veterinary services. Increased training of private and non-profit veterinarians in high throughput sterilization coupled with community engagement on RDO could benefit the wider goals of DPM by increasing access to these services. However, in the poorest countries, even a very low cost of sterilization is likely to be beyond the means of dog owners. In these settings governments and non-governmental organizations will need to fund any services to owned as well as unowned dogs. In many settings, the provision of free sterilization services could be used as a way to establish a model for more RDO, and once their value is established, owners could perhaps be asked to pay some contribution toward costs.

The scarcity of data on the costs of different DPM strategies and of their effectiveness in canine rabies-endemic settings severely limits assessment of their cost effectiveness (78), and where different tools are combined in a program the cost effectiveness of different components becomes even harder to disentangle.

Given the current high costs of sterilizing sufficient numbers of dogs to impact population turnover and size, it is likely that for most settings, sterilization is not a cost-effective additional technique to support a rabies control program. An exploratory model for rabies control in India concluded that canine vaccination alone was more cost effective than combined vaccination and sterilization (61). However, further exploration of the additional costs and indirect benefits of sterilization, improvements in waste management, treatment for skin and parasitic conditions, educational interventions and legislative interventions to support rabies control would be very valuable.

DPM AND RABIES CONTROL NOW AND IN THE FUTURE

Humane DPM tools offer the theoretical possibility of better integration of dogs into communities and a stabilization, or even reduction in size of dog populations where it is easier to maintain vaccination coverage.

Unfortunately, the main DPM methods successfully employed in most high-income countries (well-enforced breeding and RDO laws, encouragement of sterilization and removal of free-roaming dogs from the streets into shelters, supported by dog identification and registration) do not transfer easily to low-income settings (19, 38, 77). Laws may not exist, are not enforced, or have meager consequences; sterilization services are not always readily available or affordable; shelters quickly get overwhelmed where rates of adoption are low; and high turnover makes registration impractical. While the tools and lessons developed for rabies control in high-income countries may provide some insight, more cost effective and culturally appropriate methods must be considered for rabies control in low-income countries.

Where population reduction of free-roaming dogs is wanted by owners and communities, veterinary services are abundant, and political will and funding are sufficient to address the issue, there is evidence that high throughput sterilization and release programs can achieve population reduction (33, 34). However, where sterilization, vaccination and release programs do not reach 70% of dogs, additional vaccination must be encouraged to ensure that vaccination levels are sufficient to halt rabies transmission as quickly as possible (36, 94, 100). Combined sterilization and vaccination programs that are enacted as a rabies control strategy but fail to reach sufficient dogs will be very ineffective at achieving goals of reducing rabies transmission (94).

Where veterinary services and funding to pay for DPM programs are insufficient, theoretical arguments would suggest that waste management programs to reduce food resources for free-roaming dogs should be encouraged. Along with promotion of RDO to reduce free-roaming dog population sizes, waste management could be the best option to reduce dog populations and the spread of diseases in resource limited settings (3), but evidence of this method's effectiveness is currently lacking.

It is possible that large-scale DPM success in most low-income countries will require the development of a cost-effective (non-surgical) safe and permanent sterilizing agent for female dogs. Such research is being actively pursued and progress is being made (50, 62, 103).

Currently, the most promising option for permanent sterilization of female free-roaming dogs is GonaCon, a single-dose GnRH-based vaccine, but issues over side effects require further work on its formulation (50). Small scale safety trials of GonaCon given along with rabies vaccinations have been completed in female dogs in Mexico (104) and on an American Indian reservation in the US (105), but there are as yet no data on its effects on fertility.

The availability of a safe and effective single-dose injectable sterilant for both sexes would enable provision of reproductive control as an additional service to owners during mass dog vaccination campaigns. Such a sterilant could also be delivered to ownerless dogs under a capture, sterilize, vaccinate and release model that did not require transportation to surgical centers. Such a tool could revolutionize DPM programs and, in some settings, rabies control as well. However, until such a permanent sterilizing agent becomes available, a safe and effective sterilant that lasted even 2–4 years could still be very beneficial to animal welfare and rabies control.

CONCLUSION

Integrating DPM programs into rabies elimination programs could supplement the goal of breaking the rabies transmission cycle with the goal of stabilizing dog populations. In theory this is the most sustainable way to eliminate canine rabies, but three factors critically limit its wider implementation in practice. First, the clear lack of systematic data collection and the paucity of DPM program evaluation need to be addressed. Organizations currently conducting DPM programs in rabies-endemic countries should strive to improve their methods of evaluating impact (78) using available guidelines (106) and publish their findings in peer-reviewed journals. Second, there needs to be an improved understanding of the costs of current DPM tools and their benefits to rabies control in order that full cost effectiveness analyses can be conducted. Third, a single-dose, permanent, non-surgical sterilant that is safe and effective in female dogs would dramatically increase the possibilities for DPM to cost-effectively improve rabies control and elimination efforts. Armed with this knowledge, integrating DPM into rabies control programs in low-income countries could move the world closer to freedom from canine-mediated human rabies deaths.

AUTHOR CONTRIBUTIONS

LT drafted the initial manuscript. All authors revised it critically for important intellectual content and approved the version to be published.

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REFERENCES

1. WHO. WHO expert consultation on rabies, second report. *WHO Technical Report Series 982*. (2013). Available from: http://apps.who.int/iris/bitstream/10665/85346/1/9789240690943_eng.pdf
2. Arluke A, Atema K. Roaming dogs. In: Kalof L, editor. *The Oxford Handbook of Animal Studies (Online)*. Oxford Handbooks Online (2015). Available from: http://www.oxfordhandbooks.com/view/10.1093/oxfordhb/9780199927142.001.0001/oxfordhb-9780199927142-e-9

3. International Companion Animal Management Coalition. *Humane Dog Population Management Guidance*. (2007). Available from: http://www.icam-coalition.org/downloads/Humane_Dog_Population_Management_Guidance_English.pdf
4. OIE. Stray dog population control. *Terrestrial Animal Health Code*. (Chap. 7.7), OIE (2015). Available from: http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_aw_stray_dog.htm
5. World Animal Protection. *Humane Dog Management: Better Lives for Dogs* (2015). Available from: http://www.worldanimalprotection.org/sites/default/files/int_files/humane-dog-management.pdf
6. Jackman J, Rowan AN. Free-roaming dogs in developing countries: the benefits of capture, neuter, and return programs. In: Salem DJ, Rowan AN, editors. *The State of the Animals IV: 2007*. Humane Society Press (2007). Available from: http://www.fao.org/fileadmin/user_upload/animalwelfare/1_CNVR%20Jackman%20and%20Rowan%20(2).pdf
7. Cleaveland S, Lankester F, Townsend S, Lembo T, Hampson K. Rabies control and elimination: a test case for one health. *Vet Rec* (2014) 175(8):188–93. doi:10.1136/vr.g4996
8. Rowan AN, Lindenmayer JM, Reece JF. Role of dog sterilisation and vaccination in rabies control programmes. *Vet Rec* (2014) 175(16), 409. doi:10.1136/vr.g6351
9. OIE. Infection with rabies virus. *Terrestrial Animal Health Code*. (Chap. 8.13), OIE (2015). Available from: http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_rabies.htm
10. Wandeler AI, Matter HC, Kappeler A, Budde A. The ecology of dogs and canine rabies: a selective review. *Rev Sci Tech* (1993) 12(1):51–71. doi:10.20506/rst.12.1.663
11. Fournier AK, Geller ES. Behavior analysis of companion-animal overpopulation: a conceptualization of the problem and suggestions for intervention. *Behav Soc Issues* (2004) 13:51–68. doi:10.5210/bsi.v13i1.35
12. Morters MK, McKinley TJ, Restif O, Conlan AJ, Cleaveland S, Hampson K, et al. The demography of free-roaming dog populations and applications to disease and population control. *J Appl Ecol* (2014) 51(4):1096–106. doi:10.1111/1365-2664.12279
13. Massei G, Fooks AR, Horton DL, Callaby R, Sharma K, Dhakal IP, et al. Free-roaming dogs in Nepal: demographics, health and public knowledge, attitudes and practices. *Zoonoses Public Health* (2016) 64(1):29–40. doi:10.1111/zph.12280
14. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14(3):185–6. doi:10.1016/0264-410X(95)00197-9
15. Townsend SE, Sumantra IP, Pudjiatmoko, Bagus GN, Brum E, Cleaveland S, et al. Designing programs for eliminating canine rabies from islands: Bali, Indonesia as a case study. *PLoS Negl Trop Dis* (2013) 7(8):e2372. doi:10.1371/journal.pntd.0002372
16. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
17. Davlin SL, Vonville HM. Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* (2012) 30(24):3492–502. doi:10.1016/j.vaccine.2012.03.069
18. Conan A, Akerele O, Simpson G, Reininghaus B, van Rooyen J, Knobel D. Population dynamics of owned, free-roaming dogs: implications for rabies control. *PLoS Negl Trop Dis* (2015) 9(11):e0004177. doi:10.1371/journal.pntd.0004177
19. Beran GW, Frith M. Domestic animal rabies control: an overview. *Rev Infect Dis* (1988) 10(Suppl 4):S672–7. doi:10.1093/clinids/10.Supplement_4.S672
20. Kitala P, McDermott J, Kyule M, Gathuma J, Perry B, Wandeler A. Dog ecology and demography information to support the planning of rabies control in Machakos District, Kenya. *Acta Trop* (2001) 78(3):217–30. doi:10.1016/S0001-706X(01)00082-1
21. Pal SK. Population ecology of free-ranging urban dogs in West Bengal, India. *Acta Theriol* (2001) 46:69–78. doi:10.1007/BF03192418
22. Acosta-Jamett G, Cleaveland S, Cunningham AA, Bronsvoort BM. Demography of domestic dogs in rural and urban areas of the Coquimbo region of Chile and implications for disease transmission. *Prev Vet Med* (2010) 94(3–4):272–81. doi:10.1016/j.prevetmed.2010.01.002
23. Schildecker S, Millien M, Blanton JD, Boone J, Emery A, Ludder F, et al. Dog ecology and barriers to canine rabies control in the Republic of Haiti, 2014–2015. *Transbound Emerg Dis* (2016). doi:10.1111/tbed.12531
24. Gsell AS, Knobel DL, Kazwala RR, Vounatsou P, Zinsstag J. Domestic dog demographic structure and dynamics relevant to rabies control planning in urban areas in Africa: the case of Iringa, Tanzania. *BMC Vet Res* (2012) 8:236. doi:10.1186/1746-6148-8-236
25. Morters MK, McKinley TJ, Horton DL, Cleaveland S, Schoeman JP, Restif O, et al. Achieving population-level immunity to rabies in free-roaming dogs in Africa and Asia. *PLoS Negl Trop Dis* (2014) 8(11):e3160. doi:10.1371/journal.pntd.0003160
26. Morters MK, Restif O, Hampson K, Cleaveland S, Wood JL, Conlan AJ. Evidence-based control of canine rabies: a critical review of population density reduction. *J Anim Ecol* (2013) 82(1):6–14. doi:10.1111/j.1365-2656.2012.02033.x
27. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4), e0003709. doi:10.1371/journal.pntd.0003709
28. Lockwood R. The ethology and epidemiology of canine aggression. In: Serpell J, editor. *The Domestic Dog: Its Evolution, Behavior, and Interactions with People*. New York: Cambridge University Press (1995). p. 131–8.
29. Landsberg GM, Denenberg S. Behavioral problems of dogs. *Merck Veterinary Manual*. Merck Sharp & Dohme Corp (2014). Available from: http://www.merckvetmanual.com/mvm/behavior/normal_social_behavior_and_behavioral_problems_of_domestic_animals/behavioral_problems_of_dogs.html
30. King T, Hemsworth PH, Coleman GJ. Fear of novel and startling stimuli in domestic dogs. *Appl Anim Behav Sci* (2003) 82:45–64. doi:10.1016/S0168-1591(03)00040-6
31. Root Kustritz MV. Effects of surgical sterilization on canine and feline health and on society. *Reprod Domest Anim* (2012) 47(Suppl 4):214–22. doi:10.1111/j.1439-0531.2012.02078.x
32. Garde E, Perez GE, Vanderstichel R, Dalla Villa PF, Serpell JA. Effects of surgical and chemical sterilization on the behavior of free-roaming male dogs in Puerto Natales, Chile. *Prev Vet Med* (2016) 123:106–20. doi:10.1016/j.prevetmed.2015.11.011
33. Reece JF, Chawla SK. Control of rabies in Jaipur, India, by the sterilisation and vaccination of neighbourhood dogs. *Vet Rec* (2006) 159(12):379–83. doi:10.1136/vr.159.12.379
34. Totton SC, Wandeler AI, Zinsstag J, Bauch CT, Ribble CS, Rosatte RC, et al. Stray dog population demographics in Jodhpur, India following a population control/rabies vaccination program. *Prev Vet Med* (2010) 97(1):51–7. doi:10.1016/j.prevetmed.2010.07.009
35. Hasler B, Hiby E, Gilbert W, Obeyesekere N, Bennani H, Rushton J. A one health framework for the evaluation of rabies control programmes: a case study from Colombo City, Sri Lanka. *PLoS Negl Trop Dis* (2014) 8(10):e3270. doi:10.1371/journal.pntd.0003270
36. Tenzin T, Ahmed R, Debnath NC, Ahmed G, Yamage M. Free-roaming dog population estimation and status of the dog population management and rabies control program in Dhaka City, Bangladesh. *PLoS Negl Trop Dis* (2015) 9(5):e0003784. doi:10.1371/journal.pntd.0003784
37. Nolen RS. *High Volume Neuter Clinic a Ray of Hope on American Indian Reservation JAVMA News*. (2013). Available from: https://www.avma.org/News/JAVMANews/Pages/131215a.aspx
38. Dalla Villa P, Kahn S, Stuardo L, Iannetti L, Di Nardo A, Serpell JA. Free-roaming dog control among OIE-member countries. *Prev Vet Med* (2010) 97(1):58–63. doi:10.1016/j.prevetmed.2010.07.001
39. Krishna CS. *The Success of the ABC-AR Programme in India*. (2010). Available from: http://www.fao.org/fileadmin/user_upload/animalwelfare/S.%20Chinny%20%20Krishna_ABC_August_2010.doc
40. Hiby E. Dog population management. 2nd ed. In: Macpherson CLM, Meslin F-X, Wandeler AI, editors. *Dogs, Zoonoses and Public Health*. Wallingford, UK and Boston, USA: CAB International (2013). p. 177–204.
41. Windiyaningsih C, Wilde H, Meslin FX, Suroso T, Widarso HS. The rabies epidemic on Flores Island, Indonesia (1998–2003). *J Med Assoc Thai* (2004) 87(11):1389–93.
42. Hossain M, Bulbul T, Ahmed K, Ahmed Z, Salimuzzaman M, Haque MS, et al. Five-year (January 2004–December 2008) surveillance on animal bite

and rabies vaccine utilization in the Infectious Disease Hospital, Dhaka, Bangladesh. *Vaccine* (2011) 29(5):1036–40. doi:10.1016/j.vaccine.2010.11.052

43. Putra AA, Hampson K, Girardi J, Hiby E, Knobel D, Mardiana IW, et al. Response to a rabies epidemic, Bali, Indonesia, 2008–2011. *Emerg Infect Dis* (2013) 19(4):648–51. doi:10.3201/eid1904.120380
44. Yoak AJ, Reece JF, Gehrtc SD, Hamilton IM. Optimizing free-roaming dog control programs using agent-based models. *Ecol Model* (2016) 341:53–61. doi:10.1016/j.ecolmodel.2016.09.018
45. Moreira ED, de Souza VMM, Sreenivasan M, Nascimento EG, de Carvalho LP. Assessment of an optimized dog-culling program in the dynamics of canine *Leishmania* transmission. *Vet Parasitol* (2004) 122:245–52. doi:10.1016/j.vetpar.2004.05.019
46. Nunes CM, Lima VM, Paula HB, Perri SH, Andrade AM, Dias FE, et al. Dog culling and replacement in an area endemic for visceral leishmaniasis in Brazil. *Vet Parasitol* (2008) 153(1–2):19–23. doi:10.1016/j.vetpar.2008.01.005
47. Reece JF. Dogs and dog control in developing countries. In: Salem DJ, Rowan AN, editors. *The State of the Animals III*. Washington, DC: Humane Society Press (2005). p. 55–64.
48. Wera E, Velthuis AG, Geong M, Hogeveen H. Costs of rabies control: an economic calculation method applied to Flores Island. *PLoS One* (2013) 8(12):e83654. doi:10.1371/journal.pone.0083654
49. Cochrane J. *Beach Dogs, a Bitten Girl and a Roiling Debate in Bali*. The New York Times March 15th. (2015). Available from: http://www.nytimes.com/2015/03/05/world/beach-dogs-a-bitten-girl-and-a-roiling-debate-in-bali.html
50. Massei G, Miller LA. Nonsurgical fertility control for managing free-roaming dog populations: a review of products and criteria for field applications. *Theriogenology* (2013) 80(8):829–38. doi:10.1016/j.theriogenology.2013.07.016
51. Soldier DW, Steinberger R. *Report on the Rosebud Sioux Indian Reservation Spay/Neuter Project, 2010*. (2010). Available from: http://www.spayfirst.org/wp-content/uploads/2016/12/2010-RST-report.pdf
52. Tenzin, Wangdi K, Ward MP. Human and animal rabies prevention and control cost in Bhutan, 2001–2008: the cost-benefit of dog rabies elimination. *Vaccine* (2012) 31(1):260–70. doi:10.1016/j.vaccine.2012.05.023
53. Abbas SS, Kakkar M, Rogawski ET; Roadmap to Combat Zoonoses in India (RCZI) Initiative. Costs analysis of a population level rabies control programme in Tamil Nadu, India. *PLoS Negl Trop Dis* (2014) 8(2):e2721. doi:10.1371/journal.pntd.0002721
54. Dias RA, Baquero OS, Guilloux AG, Moretti CF, de Lucca T, Rodrigues RC, et al. Dog and cat management through sterilization: implications for population dynamics and veterinary public policies. *Prev Vet Med* (2015) 122(1–2):154–63. doi:10.1016/j.prevetmed.2015.10.004
55. Vanderstichel R, Forzan MJ, Perez GE, Serpell JA, Garde E. Changes in blood testosterone concentrations after surgical and chemical sterilization of male free-roaming dogs in southern Chile. *Theriogenology* (2015) 83(6):1021–7. doi:10.1016/j.theriogenology.2014.12.001
56. Jana K, Samanta PK. Sterilization of male stray dogs with a single intratesticular injection of calcium chloride: a dose-dependent study. *Contraception* (2007) 75(5):390–400. doi:10.1016/j.contraception.2007.01.022
57. Leoci R, Aiudi G, Silvestre F, Lissner EA, Lacalandra GM. Alcohol diluent provides the optimal formulation for calcium chloride non-surgical sterilization in dogs. *Acta Vet Scand* (2014) 56:62. doi:10.1186/s13028-014-0062-2
58. Alliance for Contraception in Cats and Dogs. *ACC&D Statement and Recommendations Regarding Calcium Chloride-Ethyl Alcohol Injection for Chemical Castration [Online]*. (2015). Available from: https://www.acc-d.org/docs/default-source/Research-and-Innovation/accdstatementandrecommendationsoncacl2-web-rev2015.pdf?sfvrsn=2
59. Animal Welfare Board of India. *Standard Operating Procedures for Sterilization of Stray Dogs under the Animal Birth Control Programme*. (2009). Available from: http://awbi.org/awbi-pdf/SOP.pdf
60. Barlow ND, Kean JM, Briggs CJ. Modelling the relative efficacy of culling and sterilisation for controlling populations. *Wildlife Res* (1997) 24:129–41. doi:10.1071/WR95027
61. Fitzpatrick MC, Shah HA, Pandey A, Bilinski AM, Kakkar M, Clark AD, et al. One Health approach to cost-effective rabies control in India. *Proc Natl Acad Sci U S A* (2016) 113(51):14574–81. doi:10.1073/pnas.1604975113
62. Alliance for Contraception in Cats and Dogs. *Contraception and Fertility Control in Dogs and Cats*. (2013). Available from: https://www.acc-d.org/docs/default-source/Resource-Library-Docs/accd-e-book.pdf?sfvrsn=0
63. Fielding WJ, Plumridge SJ. Characteristics of owned dogs on the island of New Providence, The Bahamas. *J Appl Anim Welf Sci* (2005) 8(4):245–60. doi:10.1207/s15327604jaws0804_2
64. Frank J. An interactive model of human and companion animal dynamics: the ecology and economics of dog overpopulation and the human costs of addressing the problem. *Hum Ecol* (2004) 32(1):107–30. doi:10.1023/B:HUEC.0000015213.66094.06
65. Totton SC, Wandeler AI, Ribble CS, Rosatte RC, McEwen SA. Stray dog population health in Jodhpur, India in the wake of an animal birth control (ABC) program. *Prev Vet Med* (2011) 98(2–3):215–20. doi:10.1016/j.prevetmed.2010.11.011
66. Graham HG. *Dog Field Care Manual*. (2015). Available from: http://www.calciumchloridecastration.com/dog-field-care-manual-revised-oct-2015/
67. Dias RA, Guilloux AG, Borba MR, Guarnieri MC, Prist R, Ferreira F, et al. Size and spatial distribution of stray dog population in the University of Sao Paulo campus, Brazil. *Prev Vet Med* (2013) 110(2):263–73. doi:10.1016/j.prevetmed.2012.12.002
68. Raymond TN, Roland ME, Francoise KM, Francis Z, Livo EF, Clovis ST. Do open garbage dumps play a role in canine rabies transmission in Biyem-Assi health district in Cameroon? *Infect Ecol Epidemiol* (2015) 5:26055. doi:10.3402/iee.v5.26055
69. Morters MK, Bharadwaj S, Whay HR, Cleaveland S, Damriyasa IM, Wood JL. Participatory methods for the assessment of the ownership status of free-roaming dogs in Bali, Indonesia, for disease control and animal welfare. *Prev Vet Med* (2014) 116(1–2):203–8. doi:10.1016/j.prevetmed.2014.04.012
70. Kato M, Yamamoto H, Inuka Y, Kira S. Survey of the stray dog population and the health education program on the prevention of dog bites and dog-acquired infections: a comparative study in Nepal and Okayama Prefecture, Japan. *Acta Med Okayama* (2003) 57(5):261–6.
71. Manor R, Saltz D. The impact of free-roaming dogs on gazelle kid/female ratio in a fragmented area. *Biol Conserv* (2004) 119:231–6. doi:10.1016/j.biocon.2003.11.005
72. Santos Baquero O, Akamine LA, Amaku M, Ferreira F. Defining priorities for dog population management through mathematical modeling. *Prev Vet Med* (2015) 123:121–7. doi:10.1016/j.prevetmed.2015.11.009
73. Wandeler AI. Ecological and epidemiological data requirements for the planning of dog rabies control. In: Kuwert EM, Koprowski CH, Bögel K, editors. *Rabies in the Tropics*. Berlin, Heidelberg: Springer-Verlag (1985). p. 657–61.
74. Kachani M, Heath D. Dog population management for the control of human echinococcosis. *Acta Trop* (2014) 139:99–108. doi:10.1016/j.actatropica.2014.05.011
75. Fielding WJ, Gall M, Green D, Eller WS. Care of dogs and attitudes of dog owners in Port-au-Prince, the Republic of Haiti. *J Appl Anim Welf Sci* (2012) 15(3):236–53. doi:10.1080/10888705.2012.683760
76. Toukhsati SR, Phillips CJ, Podberscek AL, Coleman GJ. Semi-ownership and sterilisation of cats and dogs in Thailand. *Animals (Basel)* (2012) 2(4):611–27. doi:10.3390/ani2040611
77. Arechiga Ceballos N, Karunaratna D, Aguilar Setien A. Control of canine rabies in developing countries: key features and animal welfare implications. *Rev Sci Tech* (2014) 33(1):311–21. doi:10.20506/rst.33.1.2278
78. FAO/WSPA/IZSAM. Dog population management. FAO/WSPA/IZSAM expert meeting – Banna, Italy, 14–19 March 2011. *FAO Animal Production and Health*. (2014). Available from: http://www.fao.org/3/a-i4081e.pdf
79. Stavisky J, Brennan ML, Downes M, Dean R. Demographics and economic burden of un-owned cats and dogs in the UK: results of a 2010 census. *BMC Vet Res* (2012) 8:163. doi:10.1186/1746-6148-8-163
80. Marston LC, Bennett PC, Coleman GJ. What happens to shelter dogs? Part 2. Comparing three Melbourne welfare shelters for nonhuman animals. *J Appl Anim Welf Sci* (2005) 8(1):25–45. doi:10.1207/s15327604jaws0801_3
81. Ardila Galvis JO, Santos Baquero O, Dias RA, Ferreira F, Nestori Chiozzotto E, Grisi-Filho JH. Monitoring techniques in the capture and adoption of dogs and cats. *Geospat Health* (2015) 10(2):339. doi:10.4081/gh.2015.339

82. HSUS. *Pets by the Numbers [Online]*. (2015). Available from: http://www.humanesociety.org/issues/pet_overpopulation/facts/pet_ownership_statistics.html
83. Arluke A. Coping with euthanasia: a case study of shelter culture. *J Am Vet Med Assoc* (1991) 198(7):1176–80.
84. Scotney RL, McLaughlin D, Keates HL. A systematic review of the effects of euthanasia and occupational stress in personnel working with animals in animal shelters, veterinary clinics, and biomedical research facilities. *J Am Vet Med Assoc* (2015) 247(10):1121–30. doi:10.2460/javma.247.10.1121
85. Kayali U, Mindekem R, Yemadji N, Vounatsou P, Kaninga Y, Ndoutamia AG, et al. Coverage of pilot parenteral vaccination campaign against canine rabies in N'Djamena, Chad. *Bull World Health Organ* (2003) 81(10):739–44.
86. Kayali U, Mindekem R, Hutton G, Ndoutamia AG, Zinsstag J. Cost-description of a pilot parenteral vaccination campaign against rabies in dogs in N'Djamena, Chad. *Trop Med Int Health* (2006) 11(7):1058–65. doi:10.1111/j.1365-3156.2006.01663.x
87. Rinzin K, Tenzin T, Robertson I. Size and demography pattern of the domestic dog population in Bhutan: implications for dog population management and disease control. *Prev Vet Med* (2016) 126:39–47. doi:10.1016/j.prevetmed.2016.01.030
88. Eckman H. Monitoring comprehensive approaches to dog population management: how are we doing? *Presented at: Second International Conference on Dog Population Management*. Istanbul, Turkey (2015). Available from: https://www.youtube.com/watch?v=-NT52kZL1DQ
89. Vancelik S, Set T, Akturk Z, Calikoglu O, Kosan Z. The changing rate of suspected rabies bites after begin to act animal shelter in Erzurum city. *Eurasian J Med* (2014) 46(3):151–5. doi:10.5152/eajm.2014.49
90. Bangladesh Anti Rabies Alliance. *A Pilot Study on Prevention and Control of Rabies by Animal Birth Control (ABC) in Raipura, Narsingdi, Bangladesh*. (2010). Available from: http://www.fao.org/fileadmin/user_upload/animalwelfare/Rabies_ABC_Study_Bangladesh[1].pdf
91. Alliance for Contraception in Cats and Dogs. *ACC&D-Sponsored Field Studies [Online]*. (2014). Available from: http://www.acc-d.org/available-products/sponsored-field-studies
92. Devleesschauwer B, Aryal A, Sharma BK, Ale A, Declercq A, Depraz S, et al. Epidemiology, impact and control of rabies in Nepal: a systematic review. *PLoS Negl Trop Dis* (2016) 10(2):e0004461. doi:10.1371/journal.pntd.0004461
93. Widyastuti MD, Bardosh KL, Sunandar, Basri C, Basuno E, Jatikusumah A, et al. On dogs, people, and a rabies epidemic: results from a sociocultural study in Bali, Indonesia. *Infect Dis Poverty* (2015) 4:30. doi:10.1186/s40249-015-0061-1
94. Sudarshan MK, Mahendra BJ, Narayan DH. A community survey of dog bites, anti-rabies treatment, rabies and dog population management in Bangalore city. *J Commun Dis* (2001) 33(4):245–51.
95. Lapiz S, Miranda M, Garcia R, Daguro L, Paman M, Madrinan F, et al. Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol rabies prevention and elimination project. *PLoS Negl Trop Dis* (2012) 6(12):e1891. doi:10.1371/journal.pntd.0001891
96. World Animal Net. *Report on the OIE's International Standard on Stray Dog Population Control*. (2015). Available from: http://worldanimal.net/images/stories/documents/Stray_control_report_FINAL.pdf
97. Government of India. *Animal Birth Control (Dogs) Rules [Online]*. (2015). Available from: http://envfor.nic.in/legis/awbi/awbi13.pdf
98. Kakati K. *Street Dog Population Survey, Kathmandu 2012, Final Report to WSPA*. (2012). Available from: https://animalnepal.files.wordpress.com/2013/09/dog-survey-kathmandu-valley-2012.pdf
99. Hemachudha T. Rabies and dog population control in Thailand: success or failure? *J Med Assoc Thai* (2005) 88(1):120–3.
100. Tenzin T, McKenzie JS, Vanderstichel R, Rai BD, Rinzin K, Tshering Y, et al. Comparison of mark-resight methods to estimate abundance and rabies vaccination coverage of free-roaming dogs in two urban areas of south Bhutan. *Prev Vet Med* (2015) 118(4):436–48. doi:10.1016/j.prevetmed.2015.01.008
101. Reece JF, Chawla SK, Hiby AR. Decline in human dog-bite cases during a street dog sterilisation programme in Jaipur, India. *Vet Rec* (2013) 172(18):473. doi:10.1136/vr.101079
102. Okwee-Acai J, Omara R, Onyait JS, Agwai B, Okullo P, Acon J. An evaluation of pinhole castration as an alternative technique for dog population control in resource-poor communities. *Bull Anim Health Prod Afr* (2013) 61. Available from: https://www.ajol.info/index.php/bahpa/article/view/105267
103. Found Animals Foundation. *Michelson Grants Research Findings [Online]*. (2016). Available from: http://www.michelsonprizeandgrants.org/michelson-grants/research-findings
104. Vargas-Pino F, Gutierrez-Cedillo V, Canales-Vargas EJ, Gress-Ortega LR, Miller LA, Rupprecht CE, et al. Concomitant administration of GonaCon and rabies vaccine in female dogs (*Canis familiaris*) in Mexico. *Vaccine* (2013) 31(40):4442–7. doi:10.1016/j.vaccine.2013.06.061
105. Bender SC, Bergman DL, Wenning KM, Miller LA, Slate D, Jackson FR, et al. No adverse effects of simultaneous vaccination with the immunocontraceptive GonaCon and a commercial rabies vaccine on rabies virus neutralizing antibody production in dogs. *Vaccine* (2009) 27(51):7210–3. doi:10.1016/j.vaccine.2009.09.026
106. International Companion Animal Management Coalition. *Are We Making a Difference? A Guide to Monitoring and Evaluating Dog Population Management Interventions*. (2015). Available from: http://www.icam-coalition.org/downloads/ICAM_Guidance_Document.pdf

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Cost Description and Comparative Cost Efficiency of Post-Exposure Prophylaxis and Canine Mass Vaccination against Rabies in N'Djamena, Chad

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Rabies claims approximately 59,000 human lives annually and is a potential risk to 3.3 billion people in over 100 countries worldwide. Despite being fatal in almost 100% of cases, human rabies can be prevented by vaccinating dogs, the most common vector, and the timely administration of post-exposure prophylaxis (PEP) to exposed victims. For the control and prevention of human rabies in N'Djamena, the capital city of Chad, a free mass vaccination campaign for dogs was organized in 2012 and 2013. The campaigns were monitored by parallel studies on the incidence of canine rabies based on diagnostic testing of suspect animals and the incidence of human bite exposure recorded at selected health facilities. Based on the cost description of the campaign and the need for PEP registered in health centers, three cost scenarios were compared: cumulative cost-efficiency of (1) PEP alone, (2) dog mass vaccination and PEP, (3) dog mass vaccination, PEP, and maximal communication between human health and veterinary workers (One Health communication). Assuming ideal One Health communication, the cumulative prospective cost of dog vaccination and PEP break even with the cumulative prospective cost of PEP alone in the 10th year from the start of the calculation (2012). The cost efficiency expressed in cost per human exposure averted is much higher with canine vaccination and One Health communication than with PEP alone. As shown in other studies, our cost-effectiveness analysis highlights that canine vaccination is financially the best option for animal rabies control and rabies prevention in humans. This study also provides evidence of the beneficial effect of One Health communication. Only with close communication between the human and animal health sectors will the decrease in animal rabies incidence be translated into a decline for PEP. An efficiently applied One Health concept would largely reduce the cost of PEP in resource poor countries and should be implemented for zoonosis control in general.

Keywords: cost efficiency, One Health, Chad, rabies control and prevention, post-exposure prophylaxis

INTRODUCTION

Rabies is a viral zoonotic disease first described in Mesopotamia in 3000 B.C. Humans are infected mainly through the domestic dog (1). Once clinical signs of rabies become apparent, the outcome is nearly 100% fatal (2). Annual human deaths due to rabies are estimated at 59,000 cases worldwide, and over 29 million people are exposed and need post-exposure prophylaxis (PEP) (3). Approximately 99% of these cases occur in Africa and Asia (1, 3). Animal rabies can be controlled through immunization and population management of the reservoir species (4). Vaccination of domestic dogs, their confinement, and application of quarantine measures following importation are key prevention strategies (5). With effective control measures in place, human exposure to rabies can be drastically reduced leading to elimination of dog-mediated rabies (6).

In the United States, dog-mediated rabies was eliminated through vaccination of dogs (7), as vividly described by Tierkel et al. (8). This success story has been replicated in Latin America, where rabies transmitted by domestic dogs has been significantly reduced (9), and the same approach shows positive effect in Tanzania and Bali (10, 11). Despite ample proof of value for public health, control of rabies in the animal reservoir remains very limited in many endemic countries to date and, in the absence of dog vaccination, human rabies cases are only prevented through administration of PEP (1, 12).

The biggest challenges in Africa and Asia are free roaming dog populations, limited available resources for dog owners, limited veterinary and human health infrastructure, low disease awareness, and absence of efficient communication between the veterinary and the human health sectors (13, 14).

The absence of efficient control at the source is excessively costly in terms of disability-adjusted life years (DALY) lost due to premature death and the cost of PEP to the public and private sectors (14, 15). Economic losses also occur in the agricultural sector due to loss of livestock.

The cost of animal rabies vaccination depends on the respective context and varies from country to country (16). Cost for PEP also fluctuates greatly between countries and vaccination scheme applied (17, 18). The highest cost accrues from rabies immunoglobulin (RIG) which, according to WHO guidelines, must be injected on day 0 together with a first active vaccination dose for category 3 exposures (single or multiple transdermal bites or scratches) (1). However, in most endemic countries, RIG is not available or not affordable for victims, and PEP is limited to wound treatment and administration of anti-rabies vaccine.

In N'Djamena, Chad, rabies research studies began in 2000 and continue to date. In 2001, a pilot dog vaccination campaign showed that the societal cost for vaccination was 1,610 FCFA (2.6 USD, current exchange rate) per vaccinated animal (19).

In 2008, the incidence of human rabies was estimated at 0.7 persons per 100,000 inhabitants, using a decision tree model (20). The same study showed that over 99% of reported animal bites were inflicted by owned, but free roaming, dogs. Based on these data, a model was established, forecasting transmission of rabies within the dog population and between dogs and humans. This model proposed that the cumulative cost of a dog mass vaccination campaign combined with PEP would be less than the cumulative costs of PEP, reaching a break-even point 6 years after the start of the intervention (21). The cost effectiveness of dog vaccination combined with PEP was proposed to be higher than for an exclusive PEP approach from the fifth year onward.

The present study aims to validate and update the model predictions, through the detailed cost analysis of a citywide mass vaccination campaign carried out in 2012 and 2013 in N'Djamena. Together with data from the continuous reporting of animal rabies cases diagnosed at the rabies laboratory of the Institut de Recherche en Elevage pour le Developpement (IRED) and human bite exposures reported from selected health centers, a prospective cost effectiveness analysis between PEP alone (scenario 1) and dog vaccination with PEP (scenario 2) was done.

Following an animal bite, communication between human and animal health facilities potentially contribute to a high cost reduction for PEP, financial gains from prevented exposures, and overall number of DALY averted. To estimate the potential extent of the added value through maximal communication between veterinarians and human health workers, a third scenario was included envisioning ideal One Health communication (scenario 3).

The costs described in this article provide the basis for the planning and organization of a national mass vaccination campaign (22) and a proposed approach to lower expenses due to rabies in view of elimination of dog-mediated human rabies by 2030, as jointly outlined by WHO, FAO, OIE, the Global Alliance for Rabies Control, and the international community (23).

MATERIALS AND METHODS

Study Site

The study took place in N'Djamena, the capital city of Chad, with a rapidly increasing population (3.3% growth rate) of approximately 1 million inhabitants in 2012 in an area of 520 km^2. The town is divided into 10 districts and 56 quarters (24). The vaccination intervention and data collection on animal rabies incidence and incidence of human bite exposure covered the entire administrative area of the city.

Planning and Cost Description of the Mass Vaccination Campaign

The vaccination intervention was organized by a tripartite partnership comprised of the Swiss Tropical and Public Health (Swiss TPH) Institute, the Centre de Support en Santé Internationale (CSSI), and the Institut de Recherches en Elevage pour le Développement (IRED). Selected members of these three institutions formed the supervisory and technical committees. District and quarter chiefs were invited to an information workshop prior to the campaign and were actively involved in notifying the public and planning the progression. The campaign was launched in both years by the minister of livestock at the World Rabies Day celebrations on 28th September. Vaccinators were recruited among local animal health workers and veterinarians and were trained on animal handling, vaccination, and registration techniques. The campaign was advertised prior to the start through posters distributed by the responsible administrative officers. During the campaign, radio and loud speaker announcements informed the public on the progression and location of the vaccination posts. Loudspeakers were also used to inform the populations close to the respective posts on the vaccination days. Both years, the vaccination campaign lasted 13 weeks, progressing from district to district. Vaccination days were held Friday to Sunday. Each Monday and Tuesday after vaccination in a given zone, data on the coverage level were collected through a household study and counting of dogs in the street on random transects. The data sets where combined in a Bayesian model that estimated total dog population, percent of ownerless dogs, and overall coverage level. A real-time preliminary analysis done in the field guided the campaign progression. A detailed coverage analysis was done after the campaign period each year. The detailed methodology of this analysis is published elsewhere (25).

Wednesday and Thursdays were used for planning and meeting with authorities in the upcoming vaccination zone. Locations of vaccination posts were defined in agreement with the community authorities and were usually close to the house of a block chief, who provided tables and chairs. GPS data on the location of each vaccination post were collected.

The campaign was funded in equal parts by the UBS Optimus Foundation (material, vaccine, and research cost) and the ministry of livestock in Chad (logistics and salary). Based on the dog to human ratio estimated during a dog demographic survey in 2001 and extrapolated to 2012, the required vaccination doses were estimated at 50,000. The Rabisin® vaccine doses were provided by Merial at a cost of 143 FCFA (0.28 USD, exchange rate 2012) per dose. In addition, Merial provided collars to mark vaccinated animals for 150 FCFA (0.29 USD, exchange rate 2012) each and vaccination certificates free of cost. The cold chain was ensured using storage boxes with cooling elements that were delivered together with the vaccine doses. Syringes and needles were procured locally.

The 30 vaccinators were split into 10 teams of 3 people: one responsible for vaccination and collaring and two for registering the animal and completing the vaccination certificate. Three trucks with drivers transported the 10 teams. Each vehicle was attributed to a supervisor responsible for three to four teams. The teams were each equipped with a cooler box for the vaccine and a box containing all necessary material (syringes, needles, registration forms, muzzle, gloves, first aid kit). Every day the material was checked by the supervisor against a control sheet and the performance of the post (number of vaccinated animal by species, working time, vials used) was reported for each team on a data sheet. Supervisors were responsible to replenish posts under their supervision and provide lunch and water. Each supervisor had additional cooler boxes for vaccine and water bottles. Supervisors decided in consultation with the block chiefs and members of the coordination team on the relocation of posts when owner attendance was low. A detailed list of the costs is listed in **Table 1** for both years. Material cost is depicted by unit whereas cost for personnel and transport is calculated per day. Each campaign lasted for 37 working days, from October to December 2012 and 2013, respectively. Because the campaign period included two public holidays, vaccinators were paid for 39 days in total in both years. Car rental and fuel cost are calculated for a total of 50 days, including 37 working days and 13 days of sensitization. In 2013, the information campaign was considerably strengthened, which is reflected in the difference between the respective budget lines in 2012 and 2013.

The overall public cost of the vaccination campaign includes material cost, the cost for personnel and transport, as well as cost for the sensitization campaign. In addition to these public costs, the cost of the private sector is considered. These include dog owner expenditures for transportation to the vaccination post and loss of work time. The average waiting time at a post was assumed to be 1 h, valued at 327 FCFA (0.6 USD, exchange rate 2012) based on monthly per capita income in Chad of 52,325 FCFA (104 USD, exchange rate 2012) (26). For transport, the mean cost of 650 FCFA (1.3 USD, exchange rate 2012) was assumed, which corresponds to the price of one liter of fuel. The sum of public and private cost forms the societal costs.

Epidemiological Monitoring

To assess effectiveness of the intervention, the vaccination campaign was accompanied by an epidemiological study on the incidence of human exposure to animal bites and a study on the incidence of dog rabies cases in N'Djamena.

Data on bite exposure was collected in collaboration with selected health facilities, including public health centers, hospitals, pharmacies, private medical clinics, and a few veterinary practices. Overall 91 facilities were contacted, with 61 completing at least one questionnaire during the study period, from June 2012 to December 2014. The facilities were visited by study members at least once a week to collect completed questionnaires. Collected data included basic information about the bite victim (sex, age, address), the status of the animal (species, vaccination history, alive/deceased), bite history, severity of the wound(s) inflicted, and the treatment recommendation. Data were double entered into Access® databases by the data management team at CSSI. The analysis was done with Stata/IC™ 14. During the data analysis, it was observed that recommendation for PEP made by health personnel was based on the severity of the bite wound rather than on the status of the biting animal. This meant that reported numbers of PEP could not be used as a proxy for human rabies exposure for the DALY calculation nor to estimate the actual number of PEP needed. Therefore, a dummy variable was assigned to each reported case defining victim rabies exposure risk according to fate and vaccination status of the biting animal: (1) high risk exposure (PEP definitely needed for the bite victim) was defined when the animal had been killed, had died, or was missing following the attack, regardless of reported vaccination status; (2) moderate exposure risk (PEP need depending on the observation result) was attributed to bites inflicted by animals with unknown, outdated, or no vaccination history which were alive and could be placed under observation; (3) bites inflicted by a confirmed vaccinated animal which was alive and under observation were not considered as an exposure to rabies (no PEP needed).

These exposure risk categories were used for DALY calculations and to estimate actual number of PEP needed (as opposed to reported number of PEP). In addition to bite cases, information on the cost of human anti rabies vaccine and the vaccination

TABLE 1 | List of costs and expenses of dog mass vaccination campaigns in 2012 and 2013.

Cost item	2012			2013		
	Number of units	Price per unit	Total cost	Number of units	Price per unit	Total cost
Public sector						
Material cost						
Animal vaccine	18,182	143	2,600,026	22,306	143	3,189,758
Human vaccine	100	21,703	2,170,340	40	21,337	853,480
Collars	18,182	150	2,727,300	22,306	150	3,345,900
Vaccination certificate	Included in vaccine cost					
Syringes and needles	18,182	40	727,280	22,306	40	892,240
Tables and chairs	Provided by block chiefs					
Material transport box	10	20,300	203,000	1	20,300	20,300
Muzzle	14	6,400	89,600	3	6,400	19,200
Rope	10	8,100	81,000	2	1,350	2,700
Registry	10	8,000	80,000		Reused	
Other writing and documentation material (e.g., pen, stamp, paper)	NA	NA	329,750	NA	NA	126,850
Work protection (face mask, coat, first aid kit)	NA	NA	495,348	NA	NA	617,200
Consumables (e.g., garbage bags, gloves)	NA	NA	45,300	NA	NA	8,800
Cooler boxes	17	20,441	347,500		Reused	
Cost for personnel						
Training of vaccinators	NA	NA	250,000	NA	NA	314,750
Daily wages vaccinators	39	151,923	5,925,000	39	151,923	5,925,000
Daily wages supervisors	39	10,000	390,000	3	390,000	1,170,000
Daily wages driver (vaccination and sensitization)	50	11,700	585,000	50	13,860	693,000
Fees for local responsibles (district chiefs and block chiefs)	37	51,216	1,895,000	37	47,108	1,743,000
Lunch provisions (per day)	37	42,791	1,583,250	37	50,372	1,863,750
Transport cost						
Transport (car rental and maintenance)	50	9,900	495,000	50	8,308	415,383
Daily fuel cost	50	36,532	1,826,576	50	40,896	2,044,824
Sensitization						
Information workshop for town authorities	NA	NA	1,172,000	NA	NA	1,296,000
T-shirts, hats, and banners	315	6,746	2,125,000		Reused	
Posters	1,000	719	719,000	1,000	1,114	1,114,000
Leaflets	5,000	204	1,020,000	5,000	163	815,000
Radio announcements	39	25,000	975,000	39	47,821	1,865,000
Loudspeaker	3	20,000	60,000		Reused	
Poster distribution and cost for loudspeaker campaign (per day)	20	12,040	240,800	52	15,731	818,000
Admin and communication cost						
Coordination cost	NA	NA	1,365,000	NA	NA	1,215,000
Administrative cost	NA	NA	200,000	NA	NA	100,000
Communication supervisor (per person)	3	190,000	570,000	3	195,000	585,000
Communication coordination (per person)	3	131,667	395,000	3	130,000	390,000
Other cost	1	353,750	353,750	1	5,000	5,000
Total public sector			32,041,820			31,449,135
Mean public cost per dog vaccinated	18,182		1,762	22,306		1,410
Private sector						
Lost working time (60 min, 327 CFA)	18,182	327	5,945,514	22,306	327	7,294,062
Transport to vaccination post	18,182	650	11,818,300	22,306	650	14,498,900
Total private sector			17,763,814			21,792,962
Societal cost of the vaccination campaign			49,805,634			53,242,097
Overall cost in USD[a]			98,715			110,747
Cost per dog vaccinated in FCFA			2,739.28			2,387
Cost per dog vaccinated in USD			5.43			4.96

[a]1 USD = 504.54 FCFA (October 2012); 480.75 FCFA (October 2013).

schedule prescribed for PEP was collected during the health facility based study.

The most commonly used protocol was the Essen 5 dose scheme. Other protocols, applied rarely, were the Essen 4 dose scheme and the Zagreb protocol. The details of the protocols are described in **Table 2**.

In parallel to the health facility study, the results of rabies diagnostic tests routinely performed at the IRED laboratory on suspect animals were collected. The observed percentage of rabies positive dogs among all dogs tested was used as a baseline for the probability of an exposure being inflicted by a rabid dog.

TABLE 2 | The three different post-exposure prophylaxis protocols used in N'Djamena [table adapted from Hampson et al. (17)].

Protocol	Number of clinical visits	Days of injection after exposure	Number of injections per day	Overall vaccine quantity needed (ml)	Administration pathway	Approved by
Essen 5 doses	5	0,3,7,14,28	1,1,1,1,1	5[a]	IM	WHO (1992)
Essen 4 doses	4	0,3,7,14	1,1,1,1	4[a]	IM	ACIP[b] (2009)
Zagreb	3	0,7,21	2,1,1	2[a]	IM	WHO (1992)

[a]*Calculated on the basis of 0.5 ml per dose.*
[b]*Advisory Committee on Immunization Practices.*

Cost Comparison

The evidence collected on cost of dog vaccination and PEP, together with the epidemiological background information, allowed for evaluation of different control scenarios in regard to their comparative cost effectiveness. The three different scenarios compared were (1) cost of PEP alone, (2) cost of PEP and dog mass vaccination intervention, without communication between the human health and veterinary sector, and (3) cost of PEP and dog mass vaccination, with maximal communication between human and animal health workers (One Health paradigm). Measures for improvement of communication were not part of the study, so scenario 3 is uniquely hypothetical. Under ideal One Health communication conditions, a veterinarian would automatically be contacted for each bite case reported and cases of unknown vaccination status would become negligible, provided that the dog was owned and an effective registration system was in place.

The overall cost of PEP was calculated following examples from other resource limited countries (17, 27) and included medical and non-medical expenditures. Medical fees were comprised of cost of vaccine multiplied by the doses needed for a given schedule, the cost for syringes and needles (here included in the vaccine cost), and institutional costs (salaries, administration). Non-medical costs were costs accrued by victims, including transport and lost working time similar to private costs for vaccination of dogs.

For the calculation of PEP cost alone (scenario 1), the monthly number of PEP recommended by the health personnel within the first 6 months of the study period was used as a basis.

Yearly cost for canine vaccination was derived from the cost description of the vaccination campaigns in 2012 and 2013. From 2014 onward, it was assumed that the two campaigns would lead to interruption of transmission, assuming no reintroduction from outside the vaccinated area, and therefore, only a baseline cost for control of reintroduction and emergency vaccination was included. Cost of PEP for scenario 2 was calculated based on the number of PEP recommended by health personnel observed during the study period. From 2015 onward, the mean number of registered PEP in 2013 and 2014 was used as the calculation basis.

Cost for the hypothetical scenario 3 was calculated by summing the dog vaccination cost as used in scenario 2 and the yearly actual number of PEP needed based on the exposure risk variable defined described above. It was assumed that maximal One Health communication would lead to better decision-making in regard to need of PEP and that there would be fewer animals with unknown vaccination status. Based on the coverage rate achieved during the vaccination campaign (25), 70% of the registered bites from dogs with unknown or unconfirmed vaccination were considered as vaccinated and further excluded from the number of exposures in the scenario. In addition it was assumed that in case of a bite inflicted by an unvaccinated dog, victims would initially start treatment, but discontinue if the animal was still alive after the 10-day observation period.

The age distribution of victims exposed to rabies used for the calculation of averted DALY was based on a previous study on animal rabies cases in N'Djamena (28) reporting proportion of age groups among victims of rabies positive dogs as follows: age 0–5 years 19%; age 5–15 years 36%, and age above 15 years 45%.

For the estimation of averted life years lost by a given scenario, it was assumed that in the absence of PEP, rabies exposure would lead to death in 19% of cases (29). It was further assumed that 66% of suspect exposures are inflicted by a rabid animal. This assumption is based on the proportion of animals tested positive among all animals sent for rabies diagnosis to IRED during the study period.

Because clinical rabies inevitably leads to death within days, only averted life years lost were considered without any adjustment for disability (30). We used the standard formula described by Murray within the model life-table West Level 26 (31).

The discount rate used was 4%. The parameter for the age weight function (b) utilized was 0.04 and the constant (C) was set at 0.1658. The disability weight function was defined as 1.

Cost efficiency of PEP alone was calculated as discounted cumulative cost of baseline PEP number before the start of the mass vaccination campaigns divided by the cumulative number of DALY averted. Cost efficiency of the mass vaccination campaign and PEP together was calculated from the cumulative discounted cost of canine vaccination and number of PEP registered during the intervention period divided by the difference between the cumulative number of DALY averted by PEP alone and the cumulative number of DALY averted by vaccination of dogs.

Ethical Consideration

This study was authorized by the ministry for higher education and scientific research (Ministère de l'Enseignement Supérieur et de la Recherche Scientifique) under the document number N°012/PR/PM/MES/SG/DGESRSFP/DRST/012 on May 31, 2012.

The Mayoral office of N'Djamena was informed about the study and gave consent. All personnel involved in immunization of dogs were vaccinated against rabies before participating.

RESULTS

During the vaccination campaign, a total of 18,182 dogs were vaccinated in 2012 and 22,306 in 2013. The analysis revealed an overall coverage of 71% in both years. On the district level, observed coverage varied widely ranging from 33 to 86% depending on the cultural and socioeconomic background of the area. The dog population of N'Djamena was estimated to be around 30,000 of which only 14% are ownerless (data from 2013). The intervention led to a considerable drop in dog rabies incidence from 0.7/1,000 in 2012 to 0.07/1,000 in 2014. Detailed coverage analysis and epidemiological data are presented elsewhere (25).

The total cost for the 2012 campaign was 98,715 USD (49,805,634 FCFA), and in 2013 the cost was 110,747 USD (53,242,097 FCFA). Expressed in cost per dog vaccinated, 5.43 USD were spent in 2012 and 4.96 USD in 2013 (cats and primates were excluded). The difference between the 2 years was due to higher expenses for sensitization to boost the vaccination coverage. The success of this intensified information campaign is reflected in the higher number of dogs vaccinated in 2013, which increased the overall cost but lowered the cost per animal vaccinated. In both years, the public cost represented roughly 2/3 of the societal cost (64% in 2012 and 59% in 2013).

Over the 2½-year study period, 1,203 questionnaires on bite victims were collected, of which 1,143 matched the inclusion criteria (victim was from N'Djamena, bite inflicted by a mammal species). All recorded incidences were category III exposure, with 902 (79%) inflicted by a dog, 56 (5%) by a cat, and 15 (1%) by a primate, while in 170 (15%) the species was not specified.

Figure 1 shows the distribution of bite cases by district in N'Djamena. The distribution reflects the difference in dog to human ratio observed during the vaccination campaign (25).

The highest proportion of bite exposure (42%) was reported in the age group of children younger than 13 years. Overall, 46% of biting animals had a confirmed vaccination status. The vaccination campaign only slightly (10%) increased the number of confirmed vaccinated animals over the period of the mass vaccination intervention (**Figure 2**).

In 99% of PEP recommendations, the scheme applied was the Essen 5 dose regimen, while the remaining PEP treatments followed the Essen 4 dose or Zhagreb regimen. As the study did not include a follow up of the victims, information on completeness and success of the treatment was not collected. Details on the three different treatment schemes are presented in **Table 2**. Because the number of Essen 4 dose and Zagreb regimens recommended was negligible, only the cost of the Essen 5 dose regimen was considered for the cost calculation. It was assumed that all victims underwent wound cleaning as recommended by WHO (washing with soap and water for 15 min) (1) and that 40% of victims were accompanied by a parent. One completed course of PEP, therefore, incurred a cost to society of 198 USD (97,512 FCFA) (**Table 3**).

In total, 455 (38%) victims were recommended to follow PEP treatment over the study period. In 202 of these cases, no rabies risk was identified according to the animal status. Conversely, PEP was not recommended in 36 cases where the animal status was defined as high risk and in 289 cases defined as moderate risk during the analysis phase. This indicated that in many cases the recommendation of health personnel was not appropriate. Contact with a veterinary structure was reported in only one-third of overall bite cases ($n = 349$, 30%), and this number might be even lower due to misrepresentation. Using the example of reporting to IRED, it was mentioned in 144 cases (15%) that the animal was brought to the rabies laboratory. However, this number did not reflect the actual registered diagnostic requests at the rabies diagnostic facility over the same period of time. Reflecting this lack of communication between the veterinary and the human health sector, the drop in animal rabies cases induced by the mass vaccination campaign did not lead to a parallel reduction of PEP use.

The amount of PEP used compared to the number of cases within the different risk exposure groups is shown in **Figure 3**. Stratified by intervention year, a total of 284 PEP

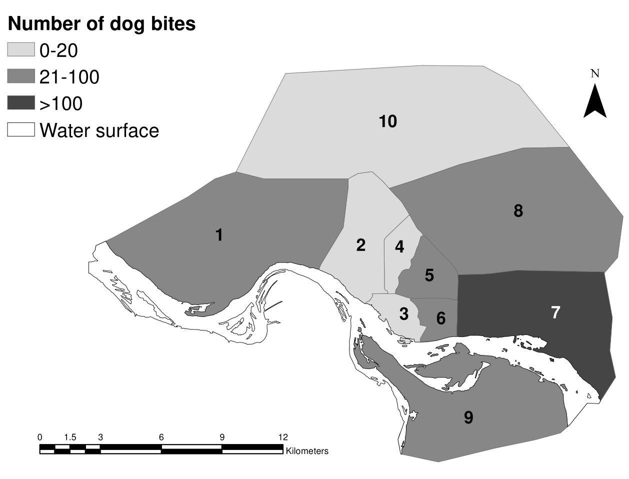

FIGURE 1 | **Distribution of total number of bite cases reported for the 10 different districts of N'Djamena over the whole study period**.

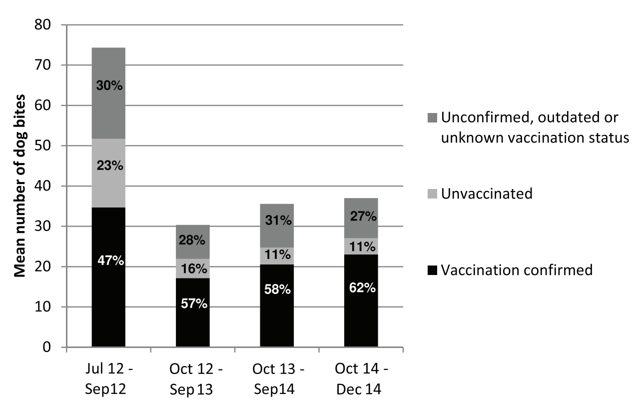

FIGURE 2 | **Mean number of dog bites inflicted per time period and proportion of vaccination status categories**. July to September 2012 corresponds to the pre-vaccination campaign period. June 2012 was excluded due to very low overall number of cases reported.

recommendations were estimated in 2012, while 164 were observed in 2013 and 149 were registered in 2014. It was assumed that without dog mass vaccination, the demand would have remained at the same level as in 2012, and therefore, PEP numbers from 2012 were used as a baseline for the extrapolation of PEP cases hypothetically occurring from 2013 onward in scenario 1 (**Table 4**). For scenario 2, the actual reported numbers of PEP recommendations were applied to the respective year of the study period. As no data were available from 2015 onward, the mean number of PEP observed after the vaccination campaign (2013 and 2014) was applied to the following years (2015–2030) (**Table 4**). For the extrapolations, uncertainty was not accounted for in our recorded data for the sake of clarity.

Because PEP recommendations and exposure risk did not correspond, the real number of PEP needed to prevent 100% of human deaths from rabies would be much higher than actual reported PEP use. In 2012, 374 bite cases of high and moderate exposure risk occurred. In 176 of these cases, PEP was not recommended and assumed to not be administered. Based on the exposure risk cases observed from the health facility data, the cost of effective rabies prevention in humans by use of PEP alone would require an investment of 36,469,488 FCFA each year as opposed to the observed yearly investment of 27,693,408 FCFA.

As a result of the vaccination campaign, the observed exposure (assuming 70% vaccination coverage) declined in 2013 to 102 cases and in 2014 a total of 135 exposure cases were observed. This corresponds to a yearly mean of 119 exposures for which a rabies infection in the biting animal could not be excluded and which would, therefore, require PEP, despite the mass dog vaccination, to ensure that 100% of human rabies cases are prevented. Compared to the mean of 156 PEP recommendations which still occurred after the vaccination campaign, the number of PEP would at least be reduced by 24% ($n = 37$) with better One Health communication.

The background for the cost analysis and the results of the cost comparison of the three different scenarios are presented in **Table 4** and **Figure 4**.

Intervention in the animal reservoir shows a clear advantage over prevention measures solely on the human medical side. The break-even point of dog vaccination and PEP with sole use of PEP is forecast about 15 years after the start of intervention. If maximum One Health communication was achieved in addition to dog vaccination, the cost even point is reached only 10 years after the start of the intervention. This is due to reduction in inappropriate use of PEP (dog confirmed vaccinated and in good health during the observation period), which leads to lower human vaccine cost for scenario 3 compared to scenario 2.

The advantage of investment into the veterinary sector for the control of rabies in humans became even more striking when cost

TABLE 3 | Cost calculation for post-exposure prophylaxis treatment.

Cost item for a complete five doses Essen protocol	Cost in FCFA	Cost in USD[a]	Unit basis
Vaccine cost (5 doses)	55,000	111.79	Per person
Cost for technician	3,307	6.72	Per person
Cost for syringes and needle	987	2.01	Per treatment
Tetanus vaccine (1 dose)	4,000	8.13	Per person
Antibiotics and anti-inflammatories	11,385	23.14	Per treatment
Water	36	0.07	Per person
Antiseptic	197	0.40	Per person
Lost work time[b]	10,000	20.33	Per treatment
Transport cost[c]	12,600	25.61	Per treatment
Total	97,512	198.20	Per treatment

Rabies immunoglobulin is not included because of unavailability in Chad.
[a]Exchange rate 1 USD = 492 FCFA.
[b]40% of exposed victims are accompanied.
[c]Expenses for accommodation not included.

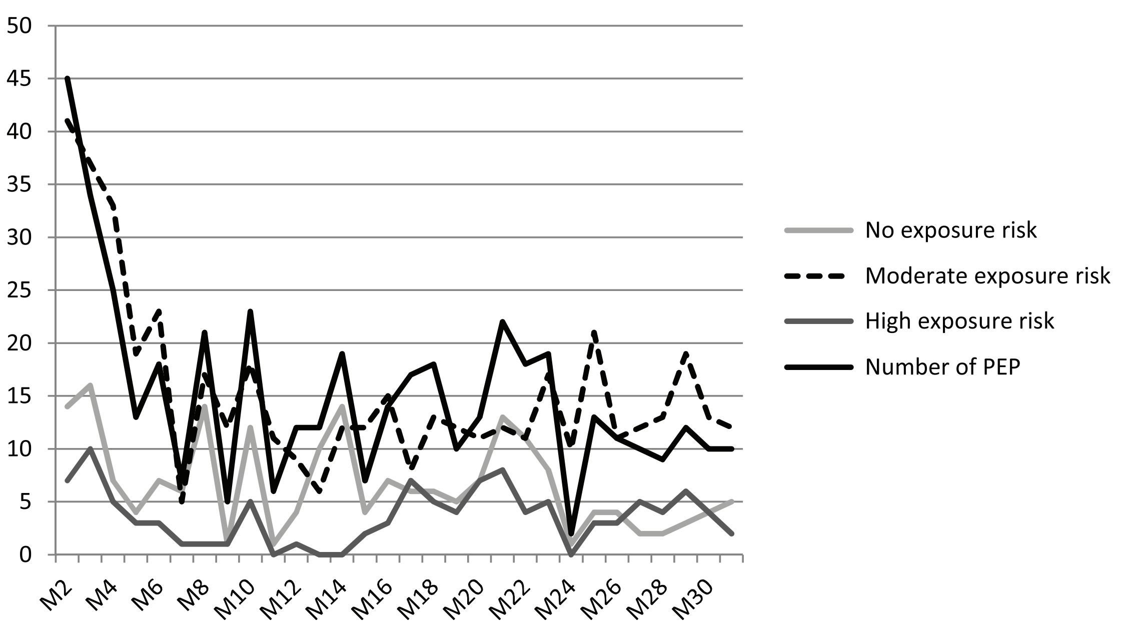

FIGURE 3 | **Number of post-exposure prophylaxis (PEP) recommended per month compared to the number of monthly cases per exposure risk group**.

TABLE 4 | Description of the principle background for the calculation of crude cost and cost-efficiency by scenario.

Cost calculation

Scenario	Cost composition	Calculation basis 2012	Calculation basis 2013	Calculation basis 2014	Calculation 2015 onward
1	Post-exposure prophylaxis (PEP)	Number of recommended PEP registered June to December 12, extrapolated to 12 months	Number of recommended PEP registered June to December 2012, extrapolated to 12 months	Number of recommended PEP registered June to December 2012, extrapolated to 12 months	Number of recommended PEP registered June to December 2012, extrapolated to 12 months
2	PEP and vaccination	number of recommended PEP registered in 2012	number of recommended PEP registered in 2013	number of recommended PEP in 2014	mean number of recommended PEP registered in 2013 and 2014
		Cost of vaccination campaign in 2012	Cost of vaccination campaign in 2013	Estimated yearly flat rate for reintroduction control and small scale emergency vaccination	Estimated yearly flat rate for reintroduction control and small scale emergency vaccination
3	PEP and vaccination	Sum of high risk exposures and 30% of moderate risk exposures registered June to December 2012, extrapolated to 12 months	Full cost for Essen 5 doses PEP for sum of high risk exposures and cost of three doses for 30% of moderate risk exposures registered in 2013	Full cost for Essen 5 doses PEP for sum of high risk exposures and cost of three doses for 30% of moderate risk exposures registered in 2014	Full cost of PEP for mean number of high risk exposures and cost for three doses for 30% of moderate risk exposures registered in 2013 and 2014
		Cost of vaccination campaign in 2012	Cost of vaccination campaign in 2013	Estimated yearly flat rate for reintroduction control and small scale emergency vaccination	Estimated yearly flat rate for reintroduction control and small scale emergency vaccination

Cost-effectiveness calculation

Scenario	Calculation of exposures averted	Calculation of disability-adjusted life years (DALY) averted	Cumulative cost after 20 years	DALY averted after 20 years	Cost per DALY averted over 20 years
1	Number of recommended PEP with high and moderate exposure risk background registered in 2012 and extrapolated to the following years	19% of number of exposures averted multiplied with years of life lost (YLL) according to different age classes	388,515,250 FCFA/ 770,038 USD	6,372	60,971 FCFA/121 USD
2	Difference of extrapolated number of high and moderate risk exposure cases registered in 2012 and effective exposures (100% of high risk and 70% of moderate risk) registered in 2013 and 2014	19% of number of exposures averted multiplied with YLL according to different age classes	349,001,170 FCFA/ 691,721 USD	9,055	38,544 FCFA/76 USD
3	Difference of extrapolated number of high and moderate risk exposure cases registered in 2012 and effective exposures (only high risk) registered in 2013 and 2014	19% of number of exposures averted multiplied with YLL according to different age classes	287,226,252 FCFA/ 569,283 USD	9,055	31,721 FCFA/63 USD

For all costs, a discount rate of 4% was applied.
Exchange rate 2012 applied, 1 USD = 504.54 FCFA.

efficiency per DALY averted was compared. The yearly number of DALY averted with scenario 1 was 454, whereas dog vaccination led to a total of 659 DALY averted each year. This showed that PEP use as currently applied in N'Djamena is costly but does not prevent human rabies cases because the exposure of humans to rabid animals remains, and many bite victims who are in need do not get PEP due to failure to consider the status of the biting animal.

Vaccination of the animal vector was about 30% less costly over a period of 20 years and this cost efficiency would be

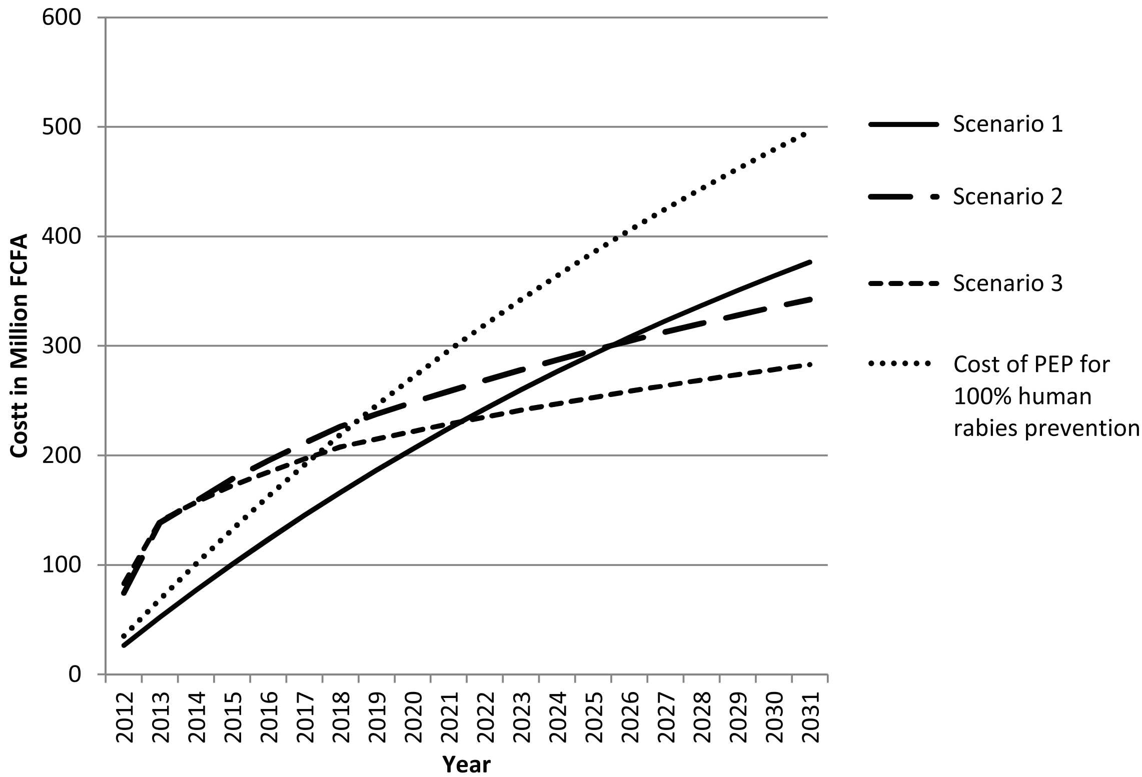

FIGURE 4 | **Display of the cost trend of the three different rabies control scenarios**.

improved by strengthening communication between animal and human health workers. Overall, yearly number of DALY averted with scenario 2 and 3 are the same, but One Health communication led to a significant reduction of PEP cost compared to dog vaccination alone. In the absence of such communication, the cumulative number of PEP prevented by the vaccination intervention after 20 years was only 2,423 as compared to 4,057 doses of PEP prevented with scenario 3. This difference led to a slightly higher cost effectiveness of scenario 3 compared to scenario 2 (**Table 4**; **Figure 4**).

Because the observed PEP recommendations in this study were not able to prevent human rabies deaths, we calculated the cost for optimal use of PEP in N'Djamena, defined as numbers of PEP correspond to the number of observed high and moderate exposure risk cases. Compared to these estimated costs for prevention of 100% of human rabies deaths by PEP only, scenario 3 would be advantageous after 6 years and scenario 2 after 8 years.

DISCUSSION

The cost analysis of the vaccination campaigns in 2012 and 2013 are based on a previous description of the cost of a pilot vaccination campaign in the same town (19). Compared to the former campaign in 2003, the costs per dog vaccinated almost doubled due to higher personnel cost, which reflects the economic development over the past 10 years in Chad.

Our costs observed were considerably higher than described by Shwiff et al. (18), where a mean of 1.55 USD was grossly estimated for Africa, Asia, and Latin America. As the success of a rabies vaccination campaign depends on the coverage achieved, the goal is to maximize the number of animals vaccinated per dollar invested. Lower cost at the expense of lower coverage might lead to lower cost effectiveness because of ineffective control of the disease. This was illustrated in Tanzania where a study compared cost effectiveness for different coverage levels (16). As coverage depends heavily on accessibility of dogs and accessibility is in turn defined by the socio-demographic, cultural, and economic background of the human population, costs vary greatly between different regions (32). Even across a limited area, such as the town of N'Djamena, costs vary significantly between different contexts (25).

Although the total number of vaccination days remained the same in 2013 compared to 2012 and higher costs were observed in the second year due to reinforcement of sensitization, the cost per dog vaccinated was lower in 2013. This highlights that the number of dogs vaccinated per day is an important factor for cost effectiveness of a campaign and that investment to enhance accessibility is beneficial.

Ongoing surveillance showed a reduction of weekly animal rabies incidence. Animal rabies surveillance in our study was based on passive reporting of suspected cases. A study in Tanzania suggests that a passive surveillance system is only able to detect 1% of actual rabies cases (33), and Townsend et al. estimate that only a detection success of 10% can prove the absence of animal rabies within the time period of 2 years (34). In our study reporting was boosted by a sensitization campaign, and we also hypothesize that the urban context with high human density leads to a higher detection rate. Therefore, we are confident that we were able to detect at least 10% of dog rabies cases occurring within the city limits.

Despite the reported decline of animal rabies incidence after the vaccination campaigns, PEP demand did not decrease to an equal extent. During the analysis phase, it became evident that health personnel judged the rabies risk according to the severity of the wound inflicted and only rarely considered the animal background. In consequence, PEP was sometimes provided without real indication, causing an unnecessary burden for the public sector and for households with low income. Regardless of the investment into animal rabies, the cost effectiveness of PEP could be increased through better communication between veterinarians and human health workers and also through changing from the intramuscular Essen regime to an intradermal protocol (17).

Overall, the predicted break-even point between dog mass vaccination with PEP and PEP alone in the earlier simulation (21) matches the observed time period under a scenario of no reintroduction from outside of town. The main difference to the earlier work is that two campaigns were needed instead of one. Given the suggested interruption of rabies transmission in N'Djamena by the high coverage achieved in both years and the subsequent drop in need for PEP, dog vaccination would have a higher cost effectiveness after 15 years, despite the high investment. This is due in part to the equally high cost for PEP observed in Chad. Even without inclusion of RIG, an entire course of PEP equals the cost of PEP with RIG in South Africa (35) and is considerably higher than in Tanzania (29). This means that if the WHO recommended inclusion of RIG for Category 3 exposures was applied in Chad, canine vaccination would have a much higher cost effectiveness than described in this study. For rural areas where accessibility is geographically very limited, the cost for travel and accommodation would also be higher than that presented here for an urban setting.

However, on the veterinary side, costs could also be higher because some were not included within the calculation presented, for example, costs related to animal observation, surveillance, and diagnostics. Finally, with regard to the DALY, we only considered cost in regard to years of life lost. Rabies also leads to a psychological burden in families of victims and in exposed people who fear contracting the disease (3, 36). This psychological aspect of disability has not been described empirically to date but potentially leads to a productivity loss and higher burden of disease.

Our results show that One Health communication is crucial to get a maximum return on the investment and prevent prevailing unnecessary high PEP cost. The overall number of DALY averted in scenario 2 was equal to scenario 3, but scenario 3 had higher cost-efficiency due to lower investment into PEP. This highlights that dog vaccination together with One Health communication allows for maximal translation of effect on rabies control in the animal sector to cost saving for the public health sector.

One health communication also incurs cost, for example, meeting fees, transport costs, and telephone credit. These costs were not included in the calculation due to absence of reliable data. Also, PEP cost calculation for scenario 3 was based on the assumption that, if the biting animal is not vaccinated, an observation period of 10 days applies, during which PEP in all victims is already initiated. This means that for the duration of the observation period 3 doses of vaccine would be needed. Currently, the observation period applied in Chad is 14 days, which requires 4 doses before discontinuing the unnecessary treatment.

The cost efficiency calculation was based on the assumption that canine rabies transmission can be interrupted in N'Djamena by two vaccination rounds. Thus after 2 years, only the costs for prevention of reintroduction are incurred. Disease modeling and phylodynamic analysis of the epidemiological and molecular data collected during the study period suggest that interruption was achieved but that rabies was re-introduced from outside the relatively small (254 km^2) vaccination area (37).

Data from ongoing routine diagnostics at IRED also show that without control at the town border, rapid reintroduction into the city occurs. The epidemiological pressure from the rural to urban areas is also described for Bangui and its surroundings (38). Therefore, sustainable control can only be achieved with either stringent reintroduction control for rabies free areas requiring movement restrictions on dogs or large scale national campaigns. A preliminary budget estimate for a Chadian national dog rabies vaccination campaign suggests costs between 1.9 and 4.7 million Euros, depending on the number of dogs vaccinated per day per vaccination post and the overall duration (22). Despite several limitations and assumptions, our study proves the financial advantage of investment into dog mass vaccination for prevention of human rabies, identifies the need for better communication between the human and animal health sectors to improve cost effectiveness of interventions in the animal reservoir, and highlights the urgency for large scale control of animal rabies in Chad.

CONCLUSION

Despite the high initial cost for mass vaccination, the advantage of investment into rabies control in the host species is evident. Our results clearly show that canine mass vaccination has a higher cost effectiveness per DALY averted than PEP alone and is less costly over a period of 15–20 years. The study successfully demonstrates the added value of a One Health approach in zoonotic disease control. PEP remains the main prevention strategy to avert rabies deaths but compared to animal vaccination, it is not cost effective and does not lead to reduction and elimination of human rabies cases.

AUTHOR CONTRIBUTIONS

RM: data collection, analysis, and writing of the paper. ML: data collection, analysis, and writing of the paper. AO: data collection and analysis. KN: data collection. BK: data collection. LO: analysis and writing of the paper. SS: analysis and writing of the paper. IA: veterinary supervision of the study. DM: medical supervision of the study. JZ: study design, analysis, and paper writing.

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REFERENCES

1. World Health Organization. *WHO Expert Consultation on Rabies. Second Report. World Health Organization Technical Report Series*. Geneva: WHO (2013). p. 1–139.
2. Jackson AC. Current and future approaches to the therapy of human rabies. *Antiviral Res* (2013) 99(1):61–7. doi:10.1016/j.antiviral.2013.01.003
3. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
4. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7(3):e53. doi:10.1371/journal.pbio.1000053
5. Rupprecht CE, Hanlon CA, Slate D. Control and prevention of rabies in animals: paradigm shifts. *Dev Biol (Basel)* (2006) 125:103–11.
6. Cleaveland S, Lankester F, Townsend S, Lembo T, Hampson K. Rabies control and elimination: a test case for one health. *Vet Rec* (2014) 175(8):188–93. doi:10.1136/vr.g4996
7. Velasco-Villa A, Reeder SA, Orciari LA, Yager PA, Franka R, Blanton JD, et al. Enzootic rabies elimination from dogs and reemergence in wild terrestrial carnivores, United States. *Emerg Infect Dis* (2008) 14(12):1849. doi:10.3201/eid1412.080876
8. Tierkel ES, Graves LM, Tuggle H, Wadley SL. Effective control of an outbreak of rabies in Memphis and Shelby county, Tennessee*. *Am J Public Health Nations Health* (1950) 40(9):1084–8. doi:10.2105/AJPH.40.9.1084
9. Vigilato MA, Clavijo A, Knobl T, Silva HM, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368(1623):20120143. doi:10.1098/rstb.2012.0143
10. Cleaveland S, Kaare M, Tiringa P, Mlengeya T, Barrat J. A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* (2003) 21(17–18):1965–73. doi:10.1016/S0264-410X(02)00778-8
11. Putra AA, Hampson K, Girardi J, Hiby E, Knobel D, Mardiana IW, et al. Response to a rabies epidemic, Bali, Indonesia, 2008-2011. *Emerg Infect Dis* (2013) 19(4):648–51. doi:10.3201/eid1904.120380
12. Wunner WH, Briggs DJ. Rabies in the 21st century. *PLoS Negl Trop Dis* (2010) 4(3):e591. doi:10.1371/journal.pntd.0000591
13. Knobel DL, Cleaveland S, Coleman PG, Fevre EM, Meltzer MI, Miranda ME, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83(5):360–8. doi:/S0042-96862005000500012
14. Meltzer MI, Rupprecht CE. A review of the economics of the prevention and control of rabies. Part 2: rabies in dogs, livestock and wildlife. *Pharmacoeconomics* (1998) 14(5):481–98. doi:10.2165/00019053-199814050-00003
15. Anderson A, Shwiff SA. The cost of canine rabies on four continents. *Transbound Emerg Dis* (2013) 62(4):446–52.
16. Fitzpatrick MC, Hampson K, Cleaveland S, Mzimbiri I, Lankester F, Lembo T, et al. Cost-effectiveness of canine vaccination to prevent human rabies in rural Tanzania. *Ann Intern Med* (2014) 160(2):91–100. doi:10.7326/M13-0542
17. Hampson K, Cleaveland S, Briggs D. Evaluation of cost-effective strategies for rabies post-exposure vaccination in low-income countries. *PLoS Negl Trop Dis* (2011) 5(3):e982. doi:10.1371/journal.pntd.0000982
18. Shwiff S, Hampson K, Anderson A. Potential economic benefits of eliminating canine rabies. *Antiviral Res* (2013) 98(2):352–6. doi:10.1016/j.antiviral.2013.03.004
19. Kayali U, Mindekem R, Hutton G, Ndoutamia AG, Zinsstag J. Cost-description of a pilot parenteral vaccination campaign against rabies in dogs in N'Djamena, Chad. *Trop Med Int Health* (2006) 11(7):1058–65. doi:10.1111/j.1365-3156.2006.01663.x
20. Frey J, Mindekem R, Kessely H, Doumagoum Moto D, Naïssengar S, Zinsstag J, et al. Survey of animal bite injuries and their management for an estimate of human rabies deaths in N'Djaména, Chad. *Trop Med Int Health* (2013) 18(12):1555–62. doi:10.1111/tmi.12202
21. Zinsstag J, Durr S, Penny MA, Mindekem R, Roth F, Menendez Gonzalez S, et al. Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc Natl Acad Sci U S A* (2009) 106(35):14996–5001. doi:10.1073/pnas.0904740106
22. Anyiam F, Lechenne M, Mindekem R, Oussigere A, Naissengar S, Alfaroukh IO, et al. Cost-estimate and proposal for a development impact bond for canine rabies elimination by mass vaccination in Chad. *Acta Trop* (2016). doi:10.1016/j.actatropica.2016.11.005
23. WHO. *Global Elimination of Dog-Mediated Human Rabies – The Time is Now!*. (2015). Available from: http://www.who.int/rabies/international_conference_dog_mediated_human_rabies/en/
24. Mindekem R, Kayali U, Yemadji N, Ndoutamia AG, Zinsstag J. [Impact of canine demography on rabies transmission in N'Djamena, Chad]. *Med Trop (Mars)* (2005) 65(1):53–8.
25. Lechenne M, Oussiguere A, Naissengar K, Mindekem R, Mosimann L, Rives G, et al. Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* (2016) 34(4):571–7. doi:10.1016/j.vaccine.2015.11.033
26. IBRD. *GDP Per Capita (Current US$)*. (2015). Available from: http://data.worldbank.org/indicator/NY.GDP.PCAP.CD
27. Wera E, Velthuis AG, Geong M, Hogeveen H. Costs of rabies control: an economic calculation method applied to Flores island. *PLoS One* (2013) 8(12):e83654. doi:10.1371/journal.pone.0083654
28. Kayali U, Mindekem R, Yemadji N, Oussiguere A, Naissengar S, Ndoutamia AG, et al. Incidence of canine rabies in N'Djamena, Chad. *Prev Vet Med* (2003) 61(3):227–33. doi:10.1016/j.prevetmed.2003.07.002
29. Shim E, Hampson K, Cleaveland S, Galvani AP. Evaluating the cost-effectiveness of rabies post-exposure prophylaxis: a case study in Tanzania. *Vaccine* (2009) 27(51):7167–72. doi:10.1016/j.vaccine.2009.09.027
30. Coleman PG, Fevre EM, Cleaveland S. Estimating the public health impact of rabies. *Emerg Infect Dis* (2004) 10(1):140–2. doi:10.3201/eid1001.020774
31. Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. *Bull World Health Organ* (1994) 72(3):429.
32. Kaare M, Lembo T, Hampson K, Ernest E, Estes A, Mentzel C, et al. Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* (2009) 27(1):152–60. doi:10.1016/j.vaccine.2008.09.054
33. Cleaveland S, Fevre EM, Kaare M, Coleman PG. Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries. *Bull World Health Organ* (2002) 80(4):304–10.
34. Townsend SE, Lembo T, Cleaveland S, Meslin FX, Miranda ME, Putra AAG, et al. Surveillance guidelines for disease elimination: a case study of canine rabies. *Comp Immunol Microbiol Infect Dis* (2013) 36(3):249–61. doi:10.1016/j.cimid.2012.10.008
35. Nel LH, Le Roux K, Atlas RM. Meeting the rabies control challenge in south africa. *Microbe* (2009) 4(2):61–5.
36. Jemberu WT, Molla W, Almaw G, Alemu S. Incidence of rabies in humans and domestic animals and people's awareness in North Gondar Zone, Ethiopia. *PLoS Negl Trop Dis* (2013) 7(5):e2216. doi:10.1371/journal.pntd.0002216
37. Zinsstag JLM, Laager M, Mindekem R, Naïssengar S, Oussigéré A, Bidjeh K, et al. Mass dog vaccination rapidly interrupts rabies transmission and human exposure in an African city. *Sci Trans Med* (2017) (in press).
38. Bourhy H, Nakoune E, Hall M, Nouvellet P, Lepelletier A, Talbi C, et al. Revealing the micro-scale signature of endemic zoonotic disease transmission in an African urban setting. *PLoS Pathog* (2016) 12(4):e1005525. doi:10.1371/journal.ppat.1005525

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Elimination of Dog-Mediated Human Rabies Deaths by 2030: Needs Assessment and Alternatives for Progress Based on Dog Vaccination

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Background: Rabies imposes a substantial burden to about half of the world population. The World Health Organization (WHO), World Organization for Animal Health, and the Food and Agriculture Organization have set the goal of eliminating dog-mediated human rabies deaths by 2030. This could be achieved largely by massive administration of post-exposure prophylaxis—in perpetuity—, through elimination of dog rabies, or combining both. Here, we focused on the resources needed for the elimination of dog rabies virus by 2030.

Materials and methods: Drawing from multiple datasets, including national dog vaccination campaigns, rabies literature, and expert opinion, we developed a model considering country-specific current dog vaccination capacity to estimate the years and resources required to achieve dog rabies elimination by 2030. Resources were determined based on four factors: (a) country development status, (b) dog vaccination costs, (c) dog rabies vaccine availability, and (d) existing animal health workers. Our calculations were based on the WHO's estimate that vaccinating 70% of the dog population for seven consecutive years would eliminate rabies.

Findings: If dog rabies vaccine production remains at 2015 levels, we estimate that there will be a cumulative shortage of about 7.5 billion doses to meet expected demand to achieve dog rabies elimination. We estimated a present cost of $6,300 million to eliminate dog rabies in all endemic countries, equivalent to a $3,900 million gap compared to current spending. To eliminate dog rabies, the vaccination workforce may suffice if all public health veterinarians in endemic countries were to dedicate 3 months each year to dog rabies vaccination. We discuss implications of potential technology improvements, including population management, vaccine price reduction, and increases in dog-vaccinating capacities.

Conclusion: Our results highlight the resources needed to achieve elimination of

Abbreviations: DEC, dog rabies endemic country; FAO, Food and Agriculture Organization; HDI, human development index; GDREP, global dog rabies elimination pathway; NGO, non-governmental organization; OIE, World Organization for Animal Health; PEP, post-exposure prophylaxis; RIG, rabies immunoglobulin; WHO, World Health Organization.

dog-mediated human rabies deaths by 2030. As exemplified by multiple successful disease elimination efforts, one size does not fit all. We suggest pragmatic and feasible options toward global dog rabies elimination by 2030, while identifying several benefits and drawbacks of specific approaches. We hope that these results help stimulate and inform a necessary discussion on global and regional strategic planning, resource mobilization, and continuous execution of rabies virus elimination.

Keywords: infectious disease, rabies control and prevention, dog vaccination, population management, zoonotic diseases, one health, global health, rabies elimination

> …it is villainous that our pounds should be so little patronized and such swarms of dogs allowed to run unmuzzled….[Dogs] swarm in all the streets, obstruct the pavements, make night hideous with their howls…
> New York Daily Times (1)

INTRODUCTION

The control of dog rabies presents a unique and challenging undertaking. The One-Health nature of rabies—requiring the integration of medical and veterinary sectors—has challenged how animal control and rabies prevention efforts are designed and implemented. Animal control has posed a challenge for centuries (1, 2), as suggested by the epigraph, which continues to resemble many urban and peri-urban settings today. Rabies is a zoonotic disease that kills an estimated 59,000 people and hundreds of thousands of animals annually, with most of the burden falling in low- and middle-income countries, particularly among children and poor urban and rural communities (3, 4). About 99% of rabies human cases originate by rabid domestic dogs (4–7). Few other zoonotic diseases have provoked the same sense of terror in humans as rabies, and dog bites in general have been a focal issue in the control of dog populations (1, 8). Controlling dog rabies substantially reduces human exposures (9, 10) and can be accomplished through periodic campaigns of dog vaccination (9, 11, 12). World Health Organization (WHO) recommends recurrent vaccination campaigns covering at least 70% of the dog population to control and potentially eliminate dog rabies (7, 13, 14).

The One-Health character of rabies has for centuries illuminated inherent divisions of responsibilities between institutions focused on animal health and human health. This has often complicated and delayed the development of modern rabies control programs, as most early efforts to control rabies were relinquished to non-public health agencies (1). As public health agencies became more involved in rabies prevention, particularly after the introduction of post-exposure prophylaxis, they remained primarily reactive, providing care to humans after a potential rabies exposure (2). Even today, determining whether health or agriculture has responsibility for leading control efforts often impedes initiation of rabies control plans (7).

Despite these challenges, dog rabies has been successfully eliminated in most of the Western Hemisphere, western Europe, and some Asian countries. Effective control of dog rabies at the community level through dog control programs (e.g., confinement, stringent leash-law legislation, and destruction of stray animals) began in parts of Europe as early as the nineteenth century (2). However, mass vaccination programs starting in the 1920s and 1930s were largely responsible for the elimination of dog rabies in Canada, Europe, Japan, and the United States (2, 15–18). Similarly, regional rabies control efforts in Latin America, with support from the Pan American Health Organization, were initiated in the early 1980s and have been successful in reducing the number of reported cases of rabies in dogs by 98% (19–21). These success stories have resulted from a combined effort involving mass dog vaccination, dog population control, and coordination at national and community levels, all supported and promoted by national governments (2, 22, 23).

In 2016, the WHO, the World Organization for Animal Health (OIE), the Food and Agriculture Organization (FAO), and many non-governmental organizations agreed to mobilize their member states, portfolios, and resources to eliminate dog-mediated human rabies by 2030 (24, 25). Many dog-rabies endemic countries (DECs) are at the early stages of their control efforts and are still overcoming barriers related to limited understanding of the local epidemiology, logistic and operational challenges, lack of resources, and competing priorities of other diseases (3, 26, 27). Many of these barriers have been addressed and overcome by other nations, affording the opportunity for those countries still at early stages to benefit from prior experiences (4, 6, 26, 28).

This analysis intends to provide both a realistic assessment and feasible projections for a path toward global dog rabies elimination by 2030 through dog vaccination. Building on previous experience of dog vaccination programs (7, 19, 21, 29), we focused on four factors that are likely to affect a country's ability to eliminate dog rabies: country development, cost of vaccinating 70% of the dog population, dog rabies vaccine production, and availability of trained personnel for vaccine administration. We considered and evaluated several categories of plausible technological improvements and innovations as a sensitivity analysis, including increasing vaccination capacity, decreasing vaccine costs, and massive dog population management efforts. Our results quantitatively highlight some of the main challenges and provide overview of possible modifications, directions, and pathways to be considered. Our goal is to provide a realistic description of the *status quo* and present gaps hampering possible elimination. In particular, this manuscript highlights the urgent need to initiate action among public health officers, donors, academics, and the global rabies community if 2030 is to be maintained as a realistic target for elimination.

MATERIALS AND METHODS

Overview

We combined multiple data sources to derive quantitative estimates of the four factors that are likely to influence the feasibility of dog rabies elimination by means of dog vaccination: country development, cost of dog vaccination programs, potential demand for dog vaccine, and the current number of trained dog vaccination personnel (e.g., para-veterinarians). We included a total of 192 countries in our analysis. We classified countries as either DECs or dog rabies-free countries and used United Nations (UN) geographic regions to group them to summarize our main results (30). For the purposes of this study, we assumed constant human, dog, and health-care worker populations for the time period 2017–2030.

Framework for Eliminating Dog Rabies

We developed a theoretical global dog rabies elimination pathway (GDREP) consisting of a 13-year time frame; with the assumption that this would be enough time for even the least-developed rabies control programs to achieve elimination by 2030 if they fully committed to this achievement. A country's starting point within the GDREP timeframe was dependent upon their current (2015) estimated dog vaccination rate, and each country was assumed to progress through the program in annual increments. We assumed that all DECs would start the program at the same time (January 1, 2017), and that countries would progress through each annual stage of the program without regress.

Dog vaccination programs typically rely on robust logistical support, including infrastructure and human capital (31–34). Based on expert opinion from dog vaccine implementation strategies in Haiti, Ethiopia, United States, Vietnam, and Latin America, we assumed that the current dog rabies vaccination coverage was an indicator of a country's capabilities to conduct mass dog vaccination campaigns. We divided the GDREP into three phases (**Figure 1**), as a function of their current dog vaccination rates. In this framework, a countries would progressively move toward phase III, a threshold at which they would conduct a full-scale dog vaccination campaign.

Countries with current dog vaccination coverage below 18% (i.e., 25% of WHO's goal of 70% of the dog population vaccinated) were classified as Phase I. These countries entered the program at year 1, and we estimated that they would need the full 13 years to achieve elimination. Phase I countries were given 3 years to develop field studies, workforce training, adequate legislation, and other infrastructural improvements. We estimated the annual cost for each of the 3 years that these countries remained in Phase I as the country-specific cost of the 2015 dog vaccination efforts plus the cost for these infrastructural developments. Because we found no available evidence of the costs to scale-up a fledgling rabies vaccination program, and the exact amount is likely to vary from country to country based on available capabilities and dog population size, we defined the costs of infrastructural developments as approximately the cost to vaccinate 10% of the dog population that remained to be vaccinated. The 10% was estimated based on CDC's dog vaccination support activities in Haiti (27, 35, 36).

Countries with vaccination coverage above 18% and below 70% were classified as Phase II. Phase II was equally divided into three 1-year periods based on current dog vaccination: 18–35% coverage countries entered the program at year 4, 36–53% coverage countries entered at year 5, and 53–69% coverage countries entered the program at year 6. Phase II countries were charged an annual rabies elimination cost equal to their current dog vaccination efforts plus the cost to vaccinate an additional 10% of their dog population. These additional costs were estimated to be necessary to further develop their mass dog vaccination programs, focused on scale-up of services, logistical improvements, and pilot implementation of elimination programs. Depending on the estimated 2015 dog vaccination rates, countries entering the program in Phase II could take 8–10 years to achieve elimination.

Implementation Phase:	Phase I: Preparation			Phase II: Scale-up dog vaccination			Phase III: Sustained 70% dog vaccination						
Program year	1	2	3	4	5	6	7	8	9	10	11	12	13
Expected dog vax coverage:	<18% (current rate)			18% - 35%	35% - 53%	53% - 70%	≥70%						
Activities achieved	Field studies Workforce training Strengthening lab capacity			Pilot implementation Scaling-up vaccination coverage Logistical improvements Operational equipment			Mass vaccination of dog Surveillance to establish disease burden and assess progress						
Cost estimates:	Current vaccination coverage Infrastructure improvements*			Expected vaccination coverage Infrastructure improvements*			Vaccination of 70% of the dog population						

FIGURE 1 | Global Dog Rabies Elimination Pathway (GDREP): phases for a dog rabies elimination program based on 70% dog population vaccination coverage. Notes: there is variation between and within countries for the implementation and scaling-up of national dog vaccination campaigns. Based on expert opinion from dog vaccine implementation strategies in Haiti, Ethiopia, United States, Vietnam, and Latin America, we assumed that the current dog rabies vaccination coverage was directly correlated to the number of years it will take to achieve elimination, as illustrated by the three distinct phases shown in the figure. For countries in Phase II, we estimated dog vaccination as the median value in the corresponding year range (e.g., we used 26% vaccination coverage in the rage 18–35%), or the current country vaccination rate for those countries that were already vaccinating dogs at a rate equivalent to Phase II. *Infrastructural improvement costs were estimated to be equivalent to the cost of vaccination for 10% of the country's unvaccinated dog population.

Countries with vaccination coverage currently at or above 70% were classified as Phase III. Based on WHO recommendations, we estimated that countries would have to vaccinate 70% of the dog population for 7 years to eliminate dog rabies (7, 13, 14). All DECs currently vaccinating at 70% entered the program at year 7, and required 7 years to achieve elimination. Therefore, if all DECs committed to dog rabies elimination in 2017 and progressed through this program, the earliest a country could achieve elimination is 7 years and the longest it would take is 13 years.

Analysis and Input Data

Country-specific estimates for each of the four factors evaluated in this study (i.e., country development, cost of dog vaccination to achieve goal, expected number of dog vaccines required, and currently trained personnel) were derived and then aggregated by UN Regions and at the global level. **Table 1** shows the main parameters and sources of data used to obtain the estimates in this study. We obtained country populations and proportion residing in urban areas for the year 2015 from the World Bank (37).

We estimated country-specific dog populations by applying regional human-to-dog ratios to each country's human population based on previous literature (6, 19) (**Table 1**). We calculated dog populations for both urban and rural areas, and the total was represented as the summation of these two values. We obtained estimates of dog rabies vaccination coverage from Hampson et al. (4).

We estimated country-specific veterinary workforce using data from OIE (40), based on two optimistic scenarios: (A) all public health veterinary workforce is available to provide dog rabies vaccinations (including private and public practice) and (B) that all public health para-veterinarian workforce is available to provide dog rabies vaccinations. For each scenario, we calculated the potential gap or surplus in vaccinator capacity for programs that operate both 1- and 3-month vaccination campaign duration. We calculated the capacity by country and then aggregated it globally. Information on veterinary workforce is voluntarily provided by countries. We imputed the size of the animal health workforce, weighted by country cluster, for countries for which data were not available.

The cost to vaccinate a dog is variable and may differ from country to country. We estimated the cost to vaccinate a dog based on the average inflation-adjusted estimate from articles of dog vaccination costs to prevent rabies in three developing countries: Chad (41), Tanzania (42), and the Philippines (43). These costs included vaccine costs (e.g., syringes, certificates, vaccine), equipment, cold chain, dog vaccinators' salaries, transportation, awareness, and information, among others, but the specific items included varied by study. We used other published estimates to inform our sensitivity analysis on costs per vaccine (6, 44, 49). We focused solely on dog vaccination; we did not include other costs associated with rabies control, such as rabies surveillance, laboratory diagnostics, or training dog vaccination personnel, which despite being integral to an effective rabies control program cannot be readily quantified and are unlikely to change the overall conclusions of our analysis. We used a 3% discount rate in all our estimates (45), and adjusted all cost to 2015 US dollars using US gross domestic product implicit price deflators (48).

Dog rabies vaccine production is a potentially limiting factor in the effort to eliminate dog rabies globally. The 2015 estimated number of dog rabies vaccines used in 2015 was obtained from Hampson et al. (4). This current DEC dog rabies vaccine demand was assumed to approximate the supply, as there have been no reports of large-scale expiration of animal rabies vaccines. We compared the current supply of vaccine to DECs to the anticipated annual demand from 2017 to 2030 and calculated the gap in current supply to anticipated demand.

Last, we ranked the UN Regions in terms of likelihood of achieving dog rabies elimination based on aggregate indicators of the four factors used in our country-level analysis, plus two regional indicators. Criteria included: country development index, estimated funding gap for elimination, current dog vaccination coverage, gap in vaccinator capacity, proportion of the cluster that was considered rabies free, and expected years to

TABLE 1 | Main parameters and data sources to inform the estimates for Global Dog Rabies Elimination Pathway (GDREP), 2017–2030.

Parameter	Value	Source
Demographic and epidemiological data		
Human population	Country specific	(37)
Urban population (%)	Country specific	(37)
Human-to-dog ratios (humans per dog)	Mean: 10.8	Estimated
Asia and Oceania	Urban: 7.5; rural: 14.3	(6)
China	Urban: 48.3; rural: 48.3	(6)
Africa	Urban: 21.2; rural: 7.4	(6)
The Americas	Urban: 7.5; rural: 7.5	(19)
Europe	Urban: 6.5; rural: 6.5	Estimate
HDI	Country-specific	(38)
Dog vaccine administration		
Vaccination coverage needed	70%	(7, 13, 14)
Vaccinated dogs by country	Country specific	(4)
Daily vaccination capacity[a]	100 dogs/day/person	(39)
Animal health workers		
Public health veterinarians	Country specific	(40)
Public health para-veterinarians	Country specific	(40)
Cost to vaccinate[b]		
Cost per dog vaccinated (point estimate)	$2.18	(41–43)
Vaccine, syringes, and needles (%)	26.8	(41, 42, 44)
Personnel (%)	28.5	(41, 42, 44)
Overhead and other costs (%)	44.7	(41, 42, 44)
Discounting rate (%)	3	(45)
Dog population management[c]		
Share of female dogs sterilized in first round (%)	70	(46)
Maintenance sterilization (%)	30	(46, 47)
Reduction in dog population over 5 years (%)	40	(47, 49)
Cost per female dog sterilized	$8.00	(47, 49)

HDI, human development index; it is a composite measure of health, education, and income used by the United Nations Development Program (38).
[a]Dog vaccination capacity is consistent with unpublished data collected by the authors of this analysis in urban, semi-urban, and rural areas of Haiti.
[b]All costs were adjusted to 2015 US dollars using gross domestic product implicit price deflators (48).
[c]The dog population management scenario is based on the expected/plausible technological developments in coming years.

achieve elimination. Each of the six criteria was ordered from most optimal to least optimal value and received the corresponding numerical score. We summed the country cluster rank scores to obtain a cumulative rabies elimination rank score. Lower scores represent UN Regions that appear to be more favorably situated to achieve the rabies elimination goal.

Sensitivity Analysis, Main Assumptions, and Robustness Checks

To assess what future efforts might have the greatest impact on global dog rabies elimination, we developed four hypothetical scenarios assuming that a new technology would be developed which would impact the feasibility of dog vaccination. These illustrative scenarios included a 50% decrease in the price of dog rabies vaccine (including syringe and needle), 50% and 100% increases in the daily vaccination capacity of a vaccinator, and a global reduction in the dog population to a level that is presumed to be sustainable under currently available resources (a 40% reduction in population) (46, 47). We estimated the distribution of the aggregate costs of dog vaccination campaigns by component (vaccines, syringe and needles, personnel, and overhead and other costs) based on the average cost distribution accrued during dog vaccination campaigns in Chad and Tanzania (41, 42, 44).

Daily vaccination capacity is likely to vary depending, among other factors, on vaccinator experience, dog density, and dog owner reception to vaccination (39, 50–53). A large-scale campaign in an African city was able to vaccinate approximately 100 dogs per person, per day (39). This figure is consistent with unpublished data collected by the authors of this analysis in urban, semi-urban, and rural areas of Haiti and was used for vaccinator capacity calculations. Other estimates for daily dog vaccination capacity (median number of dogs vaccinated per person per day) include ~9 in Mali (54), ~21 in Chad (51), ~50 in a different area of Chad (53), ~25 in Guatemala, and ~100 in Haiti (unpublished data collected by CDC). A much higher estimate was obtained in Malawi (39) where ~200 dogs were vaccinated per person per day in each static point station. We used a 50% increase to 150 dogs per day and a 100% increase to 200 dogs per person per day for our sensitivity analysis, because we were interested in showing the results from the best plausible scenarios of dog vaccination.

Last, we assumed a new technology for relatively inexpensive, effective management of dog populations would be developed; it would be capable of effecting a 40% decrease in the total dog population over a 5-year period and would cost US$8, similar to the current cost of sterilizing a female dog (46, 47, 49). We assumed that dog population management activities would require reasonable country infrastructure and would therefore begin during Phase II of the GDREP. The scenario required a one-time 70% sterilization of the female dog population to achieve a 40% population reduction and maintenance of this population through continued sterilization of 30% of female dogs (45, 46).

The results from our model are based on several critical assumptions, informed by previous literature, dog vaccination campaigns, and expert opinion. For transparency and ease of understanding, we provide a list of the main assumptions of our model and their rationale in **Table 2**.

TABLE 2 | Main assumptions that inform our estimates.

Assumption	Rationale
70% of the dog population has to be vaccinated annually for 5–7 years to eliminate dog rabies	WHO recommendation; research suggests 70% threshold (7, 13, 14). Caveat: possibly varies by setting (55)
Dog vaccination coverage estimated by Hampson et al. (4) is reasonably accurate	Refereed review; provides country-specific estimates
Regional human-to-dog ratios estimated by Knobel et al. (6) are representative of countries in each region	We crossed-checked using human-to-dog ratio estimated from Davlin and VonVille (29) and found a ~3% aggregate difference
Countries where rabies has been eliminated from specific regions within the country (e.g., Brazil) still require national vaccination coverage	Our aim is not to explore detailed trends at the subnational level but to illustrate global trends
The time frames presented in the GDREP accurately reflect a country's progression toward elimination	However, we recognize that between and within country capabilities and willingness to conduct dog rabies elimination campaigns using vaccines will, in reality, vary
All countries commit to dog rabies elimination at year 1 of GDREP and move through the phases as predicted	While this assumption is unlikely to reflect reality, this analysis and supplementary table can be used to forecast needs on a country-specific level
After 7 years of vaccination of 70% of dog population, we consider the country rabies free and do not longer estimate dog vaccination maintenance costs	Countries completing the GDREP will likely continue to fund rabies prevention programs and maintain some level of dog rabies vaccination. However, these activities are no longer for the purpose of elimination, rather they are for the purpose of preventing re-incursion of the virus. Therefore, these costs are not considered
Vaccination capacity: all public health veterinary work force would be willing/able to do dog vaccinations, and veterinary workers can move within countries at ease. We assume the workforce reported by OIE (40) is reasonably accurate	Larger cities may have an unequal distribution of vaccination capacity. This is not accounted for under the vaccinator capacity assessment

WHO, World Health Organization; OIE, World Organization for Animal Health; GDREP, Global Dog Rabies Elimination Pathway.

We conducted a robustness check on two key parameters. First, we assessed whether our estimate of dog population was reasonable, by calculating the global dog population based on human-to-dog ratios obtained from Davlin and VonVille (29). Second, we checked the robustness of the assumption that the current dog rabies vaccination coverage was an indicator of a country's capability to conduct mass dog vaccination campaigns by comparing current dog vaccination rates to their UN-defined human development index (HDI). The HDI is an aggregate composite index of life expectancy at birth, mean of years of schooling, and gross national income per capita (38). The UN's HDI is a method of quantifying the development of a country in a more robust manner than economic growth alone.

We compared HDI to dog vaccination coverage among DECs, with mean, SD, and analysis of variance calculated to determine if significant differences were present. Development measures, such as HDI, have been used as benchmark for health system capabilities in other studies of disease burden (4, 56–59).

RESULTS

Dog Populations

Our estimates show that there are approximately 687 million dogs globally (an average global human-to-dog ratio of 11:1), of which 536 million resided in the 122 DECs (78.1%) in 2015. Based on the WHO's recommendation of 70% vaccination coverage during 7 years for elimination (7, 13, 14), a total of 375 million dogs would need to be immunized in DECs. An estimated ~130 million dog rabies vaccines were utilized in 2015, representing a gap of 246 million annual dog vaccinations to achieve the desired vaccination goal of 70% (country-specific estimates are shown in the Supplementary Material) (4). We compared these global estimates of dog population with estimates based on Davlin and VonVille's (29) human-to-dog ratios. While differences were noted between individual country estimates, estimates of the global mean were within 2.5% difference, not statistically different (paired t-test, p-value = 0.96).

Human Development Index

Seventy countries were determined to be dog rabies virus free; 122 were categorized as DECs. Countries free of dog rabies ($n = 70$) had a significantly higher mean HDI score of 0.78 compared to 0.60 for DECs ($p < 0.05$). Five mean HDI scores were calculated in accordance with the 13-year vaccination program phases and are displayed in **Table 3**. Only 5 DECs were estimated to be vaccinating more than 70% of dogs as of 2015 (Phase III); 56 (46%) were vaccinating less than 18% (Phase I). The remaining 61 DECs were defined as Phase II. The mean HDI score for DECs in Phase I was significantly lower than DECs in Phases II and III (mean 0.46 vs 0.71, $p = 0.004$). We interpreted this to suggest that significant structural improvements would be needed in these countries before sustained higher dog vaccination levels could be achieved, which validated our assumption that current dog vaccination coverage is a reasonable indicator of a country's capabilities to conduct mass dog vaccination campaigns (specific details are shown in the Supplementary Material).

Dog Vaccines Required

Figure 2 shows the number of dog vaccinations required annually for the 13-year dog rabies elimination program. The line shows the number of dog vaccinations estimated to have occurred in 2015 as a reference ($n \approx 130$ million). The results suggest that, if the current scenario does not change, by the second year of the GDREP, we would require additional production of at least 30 million doses. The largest gap in dog rabies vaccines is predicted to occur in year 7 of the program, with a potential gap of 245 million doses. However, this spike in dog vaccine needs is model dependent, as it corresponds to the point where we would expect the largest number of countries vaccinating at 70%, if all countries begin in year 1 and progress as expected. The cumulative dog rabies vaccine gap for the duration of the 13-year program is 7.5 billion doses, assuming vaccine production remains at the estimated 2015 level.

Vaccination Costs

Using an average cost per dog vaccinated of $2.18, based on estimates from vaccination campaigns in three developing countries (**Table 1**), we estimated a total present cost of $6,315 million to eliminate dog rabies in all DECs. Most DECs are currently vaccinating some proportion of their dog population, at an estimated value of $2,457 million over the course of the 13-year elimination program. Therefore, the additional present cost of dog vaccination to achieve elimination would be $3,858 million. An estimated $299 million is required to move all Phase I countries into Phase II; $1,386 million to move all Phase II countries to Phase III, and $4,631 million to move all countries through Phase III, elimination. Year 1 of the global elimination program is anticipated to have a funding gap of $60 million (**Figure 3**). The funding gap is anticipated to reach a peak in year 7 of the global campaign ($448 million).

The costs of vaccinating a dog vary substantially within and between countries (6, 41–44). **Figure 4** shows the aggregate cost of eliminating dog rabies for a range of estimates of unit costs per dog vaccinated derived from previous studies. If the mean cost to vaccinate a dog was as high as $8.60, then the gap for global elimination could be $13.5 billion. If the cost to vaccinate a dog could be reduced to approximately $0.30, there would be no

TABLE 3 | Association between Human Development Index (HDI) and dog rabies vaccine coverage and elimination.

	Dog rabies free	Dog rabies endemic	Current dog vaccination coverage, endemic countries				
			>70%	53–69%	35–53%	18–35%	<18%
Countries	70	122	5	9	24	28	56
Total HDI score[a]	54.30	73.04	3.49	6.38	18.18	18.91	26.09
HDI range	0.43–0.95	0.28–0.89	0.63–0.77	0.57–0.89	0.45–0.88	0.43–0.85	0.28–0.77
Mean HDI score	0.78	0.60	0.70	0.71	0.76	0.68	0.47
95% CI	0.76–0.80	0.58–0.62	0.57–0.83	0.63–0.79	0.71–0.81	0.64–0.72	0.44–0.50
SD	0.13	0.16	0.05	0.10	0.06	0.12	0.12

Test of significance; two-tailed t-test: $p < 0.05$; ANOVA: $p = < 0.05$.

CI, confidence interval.

[a]HDI is a composite measure of health, education, and income used by the United Nations Development Program to rank countries based on their human development (38).

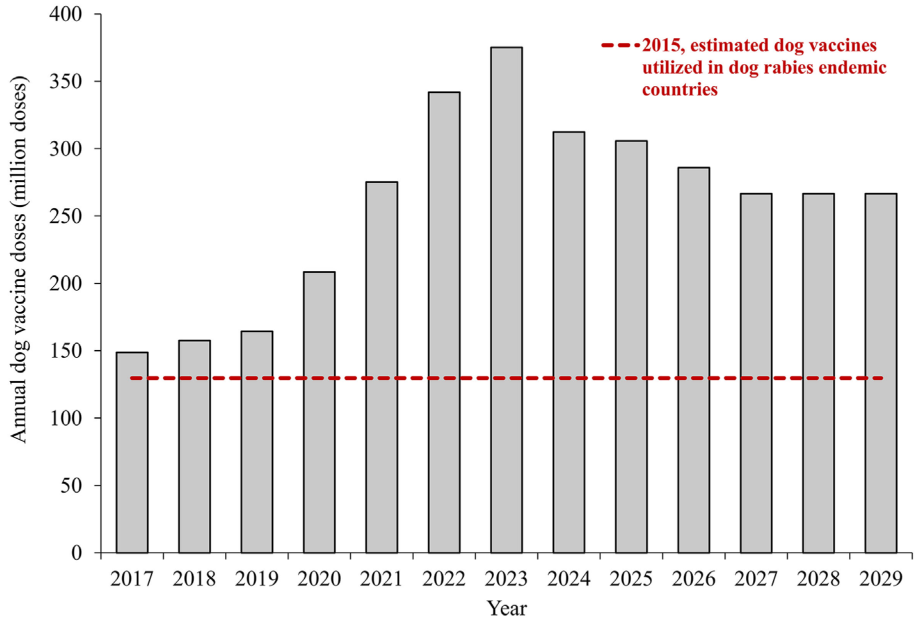

FIGURE 2 | Annual dog vaccinations required to achieve rabies elimination goal by 2030. Notes: the estimates show aggregate values of canine vaccination requirements for countries, assuming that all countries begin working toward rabies elimination in the first year. The estimates are based on current human and dog population and vaccine availability.

anticipated gap in funding to achieve global elimination. At $0.30 per dog vaccinated, this value is sevenfold lower than the current most likely cost ($2.18).

Animal Health Workers' Vaccination Capacity

Using data for animal health work force from OIE (40), we estimated each country's dog vaccination capacity. We estimated that each worker would be able to vaccinate 100 dogs per day (39), and compared animal workforce requirements for a single 1-month vaccination campaign (25 work days) compared to a 3-month campaign.

Figure 5 shows the aggregate results for annual dog vaccination capacity (total dogs potentially vaccinated by existing workforce) for (A) all public health veterinary workforce (n = 115,864) and (B) all public health para-veterinarian workforce (n = 39,635). Under scenario (A), our estimates show that there will be a global shortage of dog vaccinators in year 5 of the GDREP, assuming 1-month vaccination programs are utilized. Dog vaccinator shortages would reach their peak in year 10 of GDREP, at 91 million dogs unable to be reached for vaccination. The vaccinator workforce may be adequate if they were to dedicate 3-months each year to dog rabies vaccination.

Under scenario (B), utilizing only the para-veterinarian workforce for dog vaccination, we would expect an immediate workforce shortage in year 1 under GDREP when utilizing a 1-month vaccination program. Dog vaccinator shortages under this method would peak in year 7, at 276 million dogs unvaccinated. If this para-veterinary workforce were to dedicate 3-months toward dog rabies vaccination, a shortage in workforce would still be expected in year 5 of the GDREP and peak in year 7 (expected shortage of 132 million dogs) (further details about country capacity by year are shown in the Supplementary Material).

Sensitivity Analysis: Hypothetical Scenarios Based on Technological Improvements

The four scenarios based on hypothetical technological improvements to reasonably improve current dog vaccination practices included a 50% decrease in the price of dog rabies vaccine, a 50% and 100% increase in the daily vaccination capacity of a vaccinator and a 40% global reduction in the dog population (46, 47).

Figure 6 shows the annual costs of dog rabies elimination in endemic countries under each of the four hypothetical scenarios. The results suggest that, based on the limited existing evidence of dog population management, massive sterilization campaigns with current technology are the costliest path toward global rabies elimination. The spike in aggregate costs around the fourth year corresponds to our assumption that countries currently lagging in dog vaccination would be able to conduct massive sterilization only once they have achieved the capabilities of implementing massive vaccination campaigns.

Figure 7 compares the total costs of each of these hypothetical scenarios. Reduction of the cost of the rabies vaccine (including syringe and needle) by 50% would equate to an overall 13% reduction in the global cost to eliminate dog rabies ($5,471 million). Increasing daily capacity to vaccinate dogs from 100 dogs per person to 150 dogs per person would result in an expected ~10% reduction in total program costs, and increasing the daily capacity to 200 dogs per person/day would yield a net cost

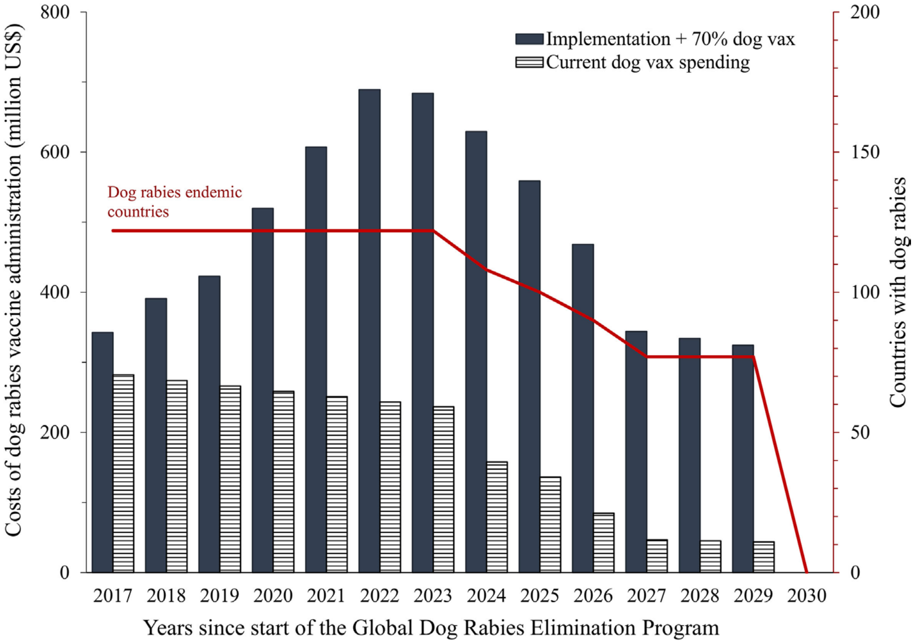

FIGURE 3 | Global annual costs of dog rabies vaccine administration to achieve dog rabies elimination in endemic countries, and number of countries with endemic rabies. Notes: costs are in 2015 US dollars; we used a 3% discount rate (45).

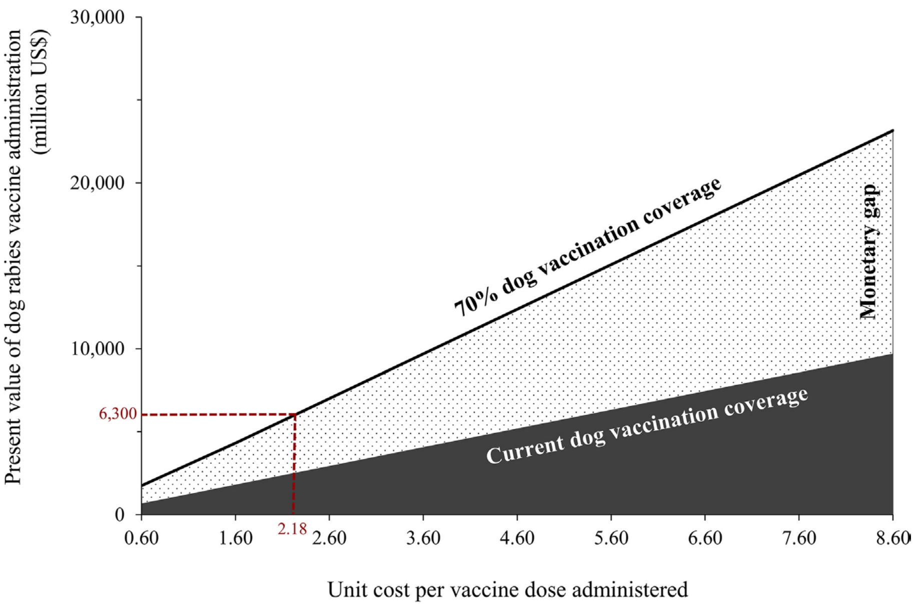

FIGURE 4 | Variability of the aggregate costs of GDREP based on the costs of administering rabies vaccines to 70% of the dog population, in rabies endemic countries, for a range of unit costs per dog vaccinated. Notes: costs are in 2015 US dollars; we used a 3% discount rate (45). Unit costs per dog vaccinated were informed by previous economic studies of dog vaccination (6, 41–44, 49). GDREP denotes Global Dog Rabies Elimination Pathway.

reduction of ~14%. Based on an estimated cost for spay surgery of $8, a 40% reduction in the global dog population would result in a ~29% reduction in rabies vaccination program costs. However, the cost necessary to achieve global dog population reduction was estimated at $4,331 million, and thus, the overall program cost was ~40% higher than the current estimate for elimination based solely on dog vaccination with no population management. The costs per female dog sterilized would need to be reduced to less

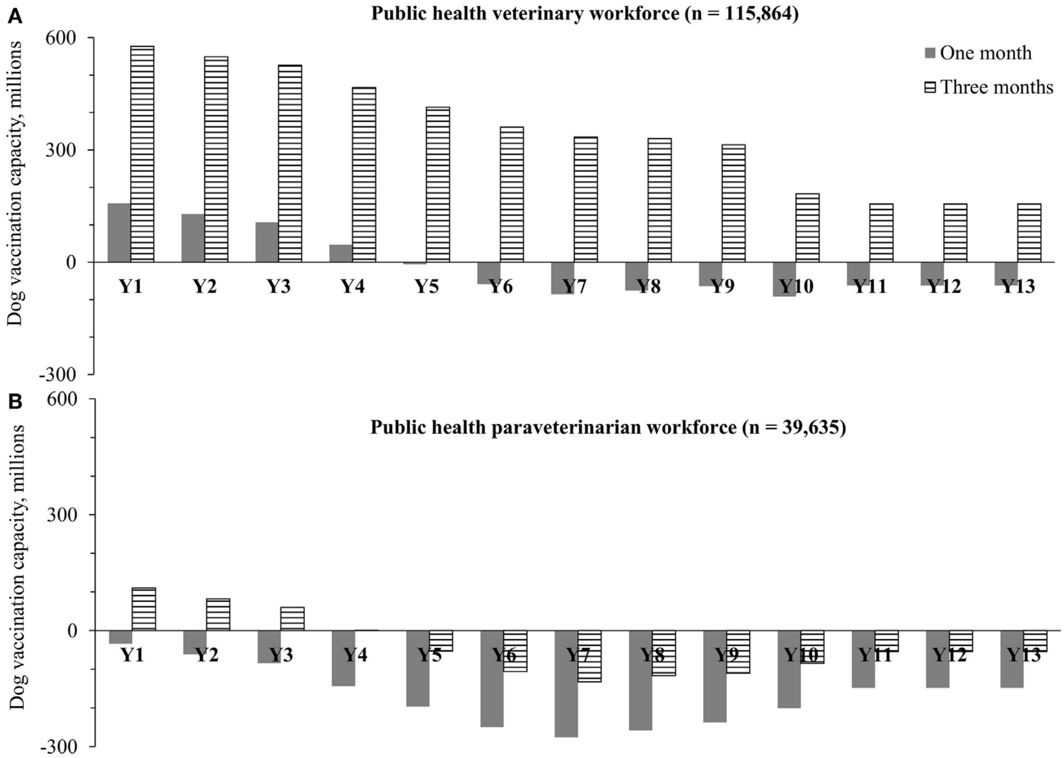

FIGURE 5 | Annual surplus or deficit of global dog vaccination capacity (total dogs potentially vaccinated by existing workforce) to achieve rabies elimination in dog rabies endemic countries based on (A) public health veterinary workforce and (B) public health para-veterinary workforce. Notes: workforce data were obtained from the World Organization for Animal Health (40); the vaccination capacity was estimated for each country with dog endemic rabies and then aggregated at the global level. The estimates are based on a dog vaccination capacity of 100 dogs per worker per day (39).

than half the price, about $3.50 per dog, to make the costs of dog population management plus dog vaccines comparable to that of only vaccinating dogs.

Prioritization for Global Dog Rabies Elimination

The UN define 22 clusters of countries. Of these clusters, six were free of dog rabies. Of the remaining 16 clusters in which dog rabies is currently endemic, our applied elimination scores ranged from 16 to 84 (**Table 4**). Clusters with the lowest elimination scores were primarily located in the Western Hemisphere and Europe (**Figure 8**). Countries with the highest scores were mainly located in Africa and Asia. The 16 ranked clusters were stratified into three groups. Group 1, consisting of seven countries, had a mean HDI of 0.77, compared to 0.65 and 0.47 for the second and third groups. Group 1, with the lowest elimination scores, had a mean elimination time of 5.4 years, compared to 10.1 and 11.7 years for Groups 1 and 2.

DISCUSSION

The goal set forth by WHO, OIE, FAO, and global experts for the elimination of dog-mediated human rabies deaths will undoubtedly be the impetus for numerous countries to improve their rabies control and elimination programs. Achieving this global target will take international coordination from governments, non-government entities, private industry, educational institutions, and many more partners. Establishing a framework that clearly describes the challenges that these partners will face is a critical first step in developing both regional and global strategies. There are several key approaches for how countries might achieve this goal; however, only mass vaccination of dogs has been effectively proven as a sustainable and cost-effective method. In this assessment, we have attempted to describe the scope of the resources that will be required to eliminate dog-mediated human rabies deaths through mass vaccination of dogs. In our attempt to conduct this global analysis, we made several critical assumptions to develop a model of an ideal scenario of dog rabies elimination. We focused on quantitative, measurable factors that affect a country's ability to eliminate dog rabies, but there are many qualitative aspects of rabies control that would need careful consideration when assessing individual country prospects for elimination. The capacity to eliminate dog rabies varies by country, with unique challenges and opportunities that cannot be readily quantified or generalized. These include, but are not limited to, political support, economic support, political stability, veterinary capacity, dog ownership characteristics, legislation, and dog ecology. We acknowledge that there is variation between and within countries for the implementation and scaling-up of national dog vaccination campaigns. However, the purpose of this analysis was not to provide a detailed roadmap for countries to follow toward rabies

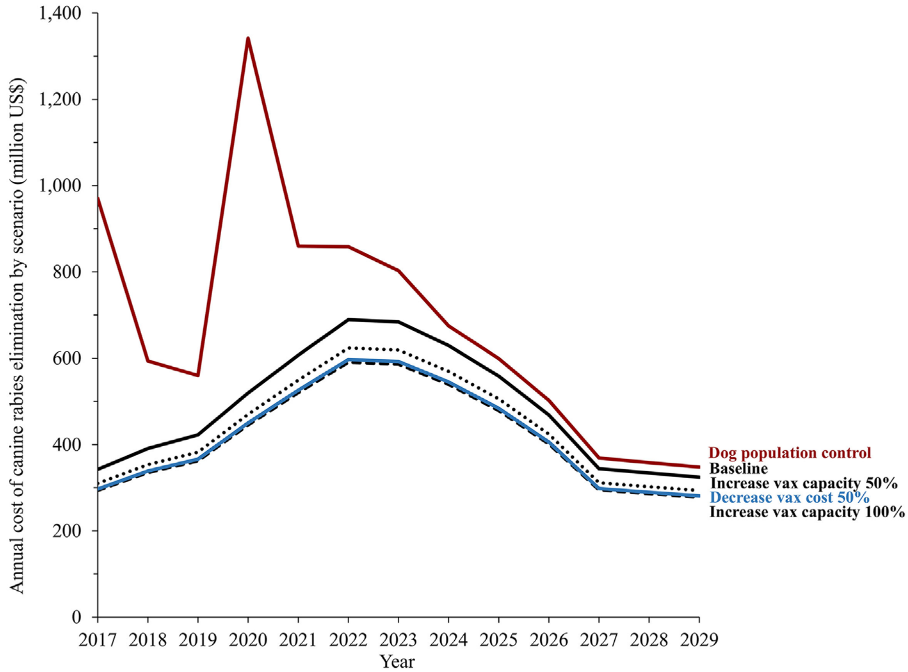

FIGURE 6 | Annual costs of dog rabies control under four hypothetical scenarios: decrease in the price of dog rabies vaccine, (including syringe and needle) increases in daily vaccination capacity of health workers, and effective dog population management and control. Notes: the four hypothetical scenarios assuming that a new technology impacted the feasibility of dog vaccination, reasonably improving current practices. The estimates are based on current human and dog population and vaccine availability. The distribution of aggregate costs components was estimated based on previous literature (41, 42, 44).

elimination, but rather to provide evidence for regional and global leaders to continue to advocate for resources, be they monetary, human, or material, to support global rabies elimination efforts.

At first glance, the feasibility of global dog-mediated human rabies elimination through mass dog vaccination is sobering. Of the four main factors assessed in this analysis, three are likely to represent substantial barriers to this goal: country capabilities (measured by HDI), vaccine demand, and funding. We have predicted gaps in the availability of dog rabies vaccines to the order of hundreds of millions. The cost of global elimination is likely to be billions of dollars. In a recent WHO expert consultation (7), scaling-up of animal rabies vaccines was determined to be possible, but the degree of expansion was not reported. However, with more countries developing the technology to produce local animal rabies vaccines (e.g., Ethiopia, India, and China), and growing demand for dog vaccines, the regional supply could be expanded. Clearly, local capacity building, regional approaches, and joint attempts for funding mobilization would be critical components of elimination efforts.

As a neglected disease, rabies control will always be susceptible to priority shifting based on new agendas or more urgent public health threats. New tools like the Stepwise Approach toward Rabies Elimination and the One-Health Prioritization tool may help nations to identify if rabies is a priority and make necessary steps to develop sustainable elimination plans. Development of regional consortiums to support national elimination planning, coordinate efforts between countries, share surveillance data and technical assistance, and leverage regional resources may be critical in achieving global elimination. The Rabies Program Directors of the Americas have followed this model and have been a critical component of the successful elimination efforts in Latin America.

To assess the importance of a country's overall human development and its relationship to public health programs, we adapted the HDI as an indicator of a country's capabilities to conduct effective mass vaccination campaigns. While rabies elimination successes are not limited to high-income countries, dog rabies-free countries had a significantly higher HDI compared to countries that have not yet achieved elimination. This finding has two main implications for the interpretation of this study. First, it supports several assumptions used to create the GDREP, particularly the assumption that countries with lower vaccination coverage will probably require more time and monetary inputs before effective mass vaccination campaigns are realized. Second, this finding suggests that the resources available today may not be adequate for dog rabies elimination in the resource-poor countries that remain endemic. High levels of international support (ranging from monetary to technical assistance) have been provided in Tanzania, Chad, Malawi, and Haiti to achieve adequate dog vaccination coverage. As the global community prepares to provide support for dog rabies elimination, considerations for supporting national infrastructure should be considered.

World Organization for Animal Health vaccine bank mechanisms for lower cost procurement of vaccines is one of the most recent developments, which may facilitate vaccine acquisition and distribution. However, with the likely increase in dog vaccine

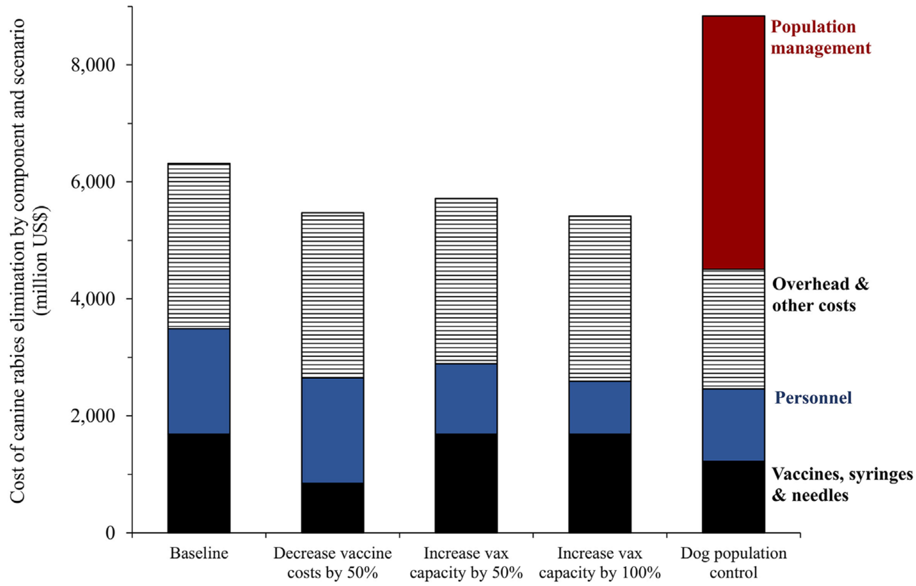

FIGURE 7 | **Aggregate costs of dog rabies control (2017–2030) under four hypothetical scenarios: decrease in the price of dog rabies vaccine (including syringes and needles), increases in daily vaccination capacity of health workers, and effective dog population management and control**. Notes: the four hypothetical scenarios assuming that a new technology impacted the feasibility of dog vaccination, reasonably improving current practices. The distribution of aggregate costs components was estimated based on previous literature (41, 42, 44).

demand, thorough analyses of global vaccine production capacity is needed. During rinderpest elimination AU-PANVAC was created to monitor quality of vaccine used in Africa (60). Similar approaches for vaccine capacity and quality monitoring should be adapted and implemented for GDREP.

This analysis shows that there may be an adequate veterinary workforce to vaccinate dogs to desired levels if this workforce can be utilized appropriately. This estimate has several potential limitations, including a lack of validation of the reported capacity in the OIE database and the assumption that the entire workforce would be able to dedicate time to vaccination of dogs. Each country is likely to address vaccination in a method that suits their specific capabilities. Vaccination of dogs has been carried out successfully by veterinarians, para-veterinarians, international organizations, and/or students, depending on the campaign design. Students were not considered a resource in this analysis, as they are unlikely to represent a reproducible and reliable resource in the majority of dog rabies endemic countries when considering mass vaccination on a national scale. While there may be scenarios in which there exists the capacity to vaccinate the required amount of dogs, diverting veterinary personnel to dog vaccination is likely to take them away from other disease control activities. Depending on the resources available, and the time commitment required, national vaccination programs would need to consider whether they have the current human capacity for rabies elimination or if more human capacity will need to be developed. The supplemental tables developed for this analysis could be used as a preliminary guide for national programs to determine what resources may be required.

While adequate resources for global rabies elimination appear to be lacking, it is not unrealistic to expect that new advances in control techniques and resources will be developed. We analyzed several hypothetical improvements to determine the potential impact they could have on rabies elimination. Dog rabies vaccines, including syringes and needles, account for approximately 27% of the cost to vaccinate a dog (41, 42, 44). While investments in cheaper vaccines are likely to have an impact toward the elimination goal, the costs of personnel and overhead and other costs represent a larger proportion of the cost to vaccinate a dog. There is vast documented variation in daily dog vaccination capacity (39, 50–53), which may be a relatively low-hanging fruit for cost reduction. By doubling a vaccinator's daily efficiency from 100 to 200 dogs, the total cost to eliminate dog rabies dropped by over 14%. Current technologies such as oral rabies vaccination and applications that improve logistical coordination may be key to improving vaccinator efficiency.

Perhaps the most debatable hypothetical scenario considered in this analysis is the global reduction of the dog population. Currently, only surgical sterilization is used for large-scale operations, and the capacity to sterilize the required number of dogs does not exist globally. Therefore, this scenario assumes that new methods of population management will be developed. One such method is an injectable sterilizing agent, of which several candidates have appeared on the market in recent years. However, their use in mass sterilization has not yet been realized nor evaluated, and the cost for these injectable sterilizing agents is still prohibitive for most countries. Our analysis suggests that if an effective sterilizing agent was available at the current cost of $8 per sterilized female dog (including personnel and overhead),

TABLE 4 | Elimination Rank Scores for the feasibility of dog rabies elimination.

	United Nations Cluster	Elimination Rank Score[a]	Dog-variant endemic countries	Human Development Index (HDI) (mean)	Gap in funding (US$)	Current dog vaccination coverage (%)	Gap in vaccinator capacity[b]	Average years for elimination
Dog rabies free	Micronesia	0	0 of 5	0.65	$0	70.0	6	0.0
	Australia and New Zealand	0	0 of 2	0.92	$0	70.0	795	0.0
	Western Europe	0	0 of 8	0.90	$0	70.0	−4,435	0.0
	Polynesia	0	0 of 5	0.76	$0	70.0	8	0.0
	Melanesia	0	0 of 4	0.57	$0	70.0	−193	0.0
	Northern America	0	0 of 2	0.91	$0	76.1	−973	0.0
Group 1	Northern Europe	16	3 of 10	0.87	$444,538	68.6	−1,213	2.7
	Southern Europe	22	6 of 13	0.82	$2,395,923	64.8	−158	4.5
	Caribbean	28	3 of 13	0.72	$2,694,433	43.4	2,663	2.9
	Central America	31	4 of 8	0.68	$0	72.4	−6,689	5.0
	Eastern Asia	37	3 of 5	0.78	$35,848,426	36.8	21,315	7.8
	Eastern Europe	39	10 of 10	0.78	$18,956,245	46.2	36,090	8.9
	South America	40	9 of 13	0.73	$12,631,906	58.7	−4,947	5.9
Group 2	Western Asia	51	16 of 17	0.73	$25,414,328	31.1	3,704	9.5
	Central Asia	52	5 of 5	0.66	$5,394,654	28.9	5,165	10.4
	Southern Africa	56	5 of 5	0.57	$1,726,750	53.1	−1,239	12.0
	Northern Africa	60	6 of 6	0.63	$22,562,725	17.3	9,302	10.8
	South-Eastern Asia	63	7 of 11	0.64	$56,600,142	25.3	−9,725	7.6
Grou 3	Middle Africa	74	8 of 9	0.46	$20,372,954	0.6	−3,894	12.2
	Eastern Africa	75	14 of 17	0.44	$56,414,022	4.1	−3,606	11.4
	Southern Asia	78	8 of 9	0.55	$190,629,398	13.2	−19,724	10.8
	Western Africa	84	15 of 16	0.41	$42,702,854	6.7	−7,205	12.6

[a]Country clusters were given a ranked score based on the following criteria: proportion of the cluster that was considered rabies free, HDI, estimated funding gap for elimination, current dog vaccination coverage, gap in vaccinator capacity, and expected years to achieve elimination. Each of the six criteria was ordered from most optimal to least optimal value and received the corresponding numerical score, we summed the country cluster rank scores to obtain a cumulative rabies elimination rank score. Lower scores represent UN Regions that appear to be more favorably situated to achieve the rabies elimination goal.

[b]Includes all vet professionals marked as "public health" and assumes they can vaccinate 100 dogs per day and they can work 25 days per year on rabies vaccination (1 month).

the estimated total cost for global elimination would still be substantially higher (~40%) than in the scenario with no population control. Only considering rabies control, to be comparable in terms of total costs an effective sterilizing agent would need to be produced at less than about $3.50 per dog (conditional on the assumptions in our model). Country-specific socio-cultural characteristics, legislation, and dog ownership, among other factors, would need close consideration in such scenario.

If we are to achieve the goal of dog-mediated human rabies elimination by 2030, we cannot wait for technological advances. It is also unlikely that, in the near-future, the global community will raise the total financial resources we predict are necessary to achieve this goal. Prioritization of countries or regional clusters for the finite available resources may be required. This study provides one possible method for considering resource prioritization through an elimination rank score. Three groupings of countries were identified, one group that appears to be nearing elimination, a group that is in the process of controlling dog rabies, and a group that appears to be at an early stage in their dog rabies control efforts. If prioritization of limited resources is a reality the rabies community must face, then international partners should address a global strategy where limited resources can be effectively distributed to begin making strategic regional progress toward the global target. Internationally sponsored vaccination

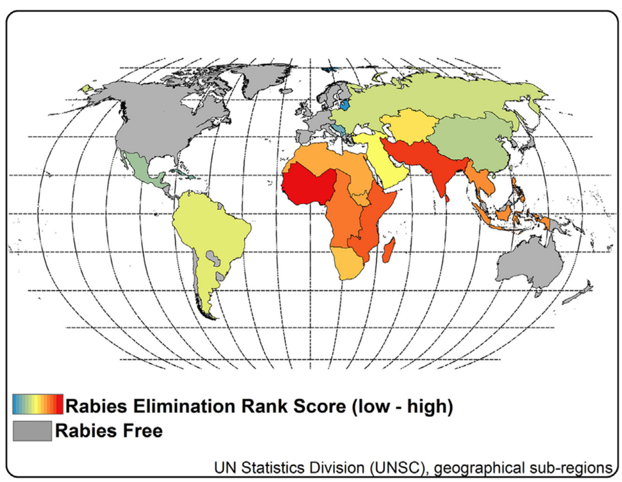

FIGURE 8 | Rabies elimination rank scores by rabies clusters. Notes: elimination rank scores were estimated for each rabies cluster (4) based on six criteria: proportion of the cluster considered rabies free, funding gap for elimination, dog vaccination coverage for 2015 estimates, gap in vaccination workforce, average years to achieve elimination, and average human development index. Rank scores ranged from 16 to 84. A low rank score represents a theoretically quicker pathway toward elimination.

programs of tens of thousands of dogs may benefit a community and assist with raising awareness or collect scientific data, but these small-scale vaccination efforts will not achieve elimination globally. If considering global elimination, there should be a discussion over whether resources are directed toward countries that are nearing elimination, to ensure they complete and thereby open up their resources and capacity to others sooner, or whether the focus should be directed toward countries with the highest rabies burden, where a larger reduction in human deaths from dog rabies would occur. In either case, if more resources are not allocated, and in a strategic manner, then global elimination of dog rabies by 2030 is unlikely to be achieved.

Achieving global dog rabies elimination will require unique regional and national strategies. Funding, vaccination methods, personnel, and technological advances will be utilized differently. Countries will progress at the pace set by their governments and with assistance by international supporters, not at the predicted pace of the 13-year elimination program utilized in this analysis. Natural disasters, human-made disasters, competing needs, political processes, economic stagnation, and other unpredictable events will undoubtedly derail rabies elimination efforts in some countries. But the information provided here can be used to discuss and advocate, in a quantifiable manner, the approximate resources that will be required, the technological advances that should be pursued, and the prioritization processes that may be necessary. We hope that these results help stimulate and inform a necessary discussion on global and regional strategic planning, resource mobilization, and continuous execution of rabies virus elimination.

AUTHOR CONTRIBUTIONS

All the authors have contributed substantially to the article and approve its contents. RW conceived the study. RW and EU collected and analyzed the data. RW, EU, JC, JB, and RF interpreted the data, wrote the article, and provided critical revision and interpretation of contents and implications.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at http://journal.frontiersin.org/article/10.3389/fvets.2017.00009/full#supplementary-material.

REFERENCES

1. Wang J. Dogs and the making of the American State: voluntary association, state power, and the politics of animal control in New York City, 1850–1920. *J Am Hist* (2012) 98(4):998–1024. doi:10.1093/jahist/jar566
2. Rupprecht CE, Hanlon CA, Hemachudha T. Rabies re-examined. *Lancet Infect Dis* (2002) 2(6):327–43. doi:10.1016/S1473-3099(02)00287-6
3. Dodet B, Adjogoua EV, Aguemon AR, Amadou OH, Atipo AL, Baba BA, et al. Fighting rabies in Africa: the Africa rabies expert bureau (AfroREB). *Vaccine* (2008) 26(50):6295–8. doi:10.1016/j.vaccine.2008.04.087
4. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9(4):e0003709. doi:10.1371/journal.pntd.0003709
5. Shwiff S, Hampson K, Anderson A. Potential economic benefits of eliminating canine rabies. *Antiviral Res* (2013) 98(2):352–6. doi:10.1016/j.antiviral.2013.03.004
6. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda MEG, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83(5):360–8. doi:S0042-96862005000500012
7. World Health Organization. *WHO Expert Consultation on Rabies. Second Report Geneva*. (2013). Available from: http://apps.who.int/iris/bitstream/10665/85346/1/9789240690943_eng.pdf
8. Teigen PM. Legislating fear and the public health in gilded age Massachusetts. *J Hist Med Allied Sci* (2007) 62(2):141–70. doi:10.1093/jhmas/jrl016
9. World Health Organization. Rabies vaccines: WHO position paper. *Wkly Epidemiol Rec* (2010) 85:309–20.
10. Pan American Health Organization. *Rabies. Epodemiological Alert*. Washington, DC: World Health Organization (2015).
11. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7(3):e1000053. doi:10.1371/journal.pbio.1000053
12. Belotto A, Leanes L, Schneider M, Tamayo H, Correa E. Overview of rabies in the Americas. *Virus Res* (2005) 111(1):5–12. doi:10.1016/j.virusres.2005.03.006
13. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14(3):185–6. doi:10.1016/0264-410X(95)00197-9
14. Cleaveland S, Kaare M, Tiringa P, Mlengeya T, Barrat J. A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* (2003) 21(17):1965–73. doi:10.1016/S0264-410X(02)00778-8
15. Tierkel ES, Graves LM, Tuggle H, Wadley SL. Effective control of an outbreak of rabies in Memphis and Shelby County, Tennessee*. *Am J Public Health Nations Health* (1950) 40(9):1084–8. doi:10.2105/AJPH.40.9.1084
16. Shimada K. The last rabies outbreak in Japan. In: Nagano Y, Davenport FM, editors. *Rabies*. Baltimore: University Park (1971). p. 11–28.
17. Nicholls E, Davies J. Rabies control and management. *Can Med Assoc J* (1982) 126(11):1286.
18. Velasco-Villa A, Orciari LA, Juárez-Islas V, Gómez-Sierra M, Padilla-Medina I, Flisser A, et al. Molecular diversity of rabies viruses associated with bats in Mexico and other countries of the Americas. *J Clin Microbiol* (2006) 44(5):1697–710. doi:10.1128/JCM.44.5.1697-1710.2006
19. Vigilato MAN, Clavijo A, Knobl T, Silva HMT, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368(1623):20120143. doi:10.1098/rstb.2012.0143
20. Clavijo A, Vilas VJDR, Mayen FL, Yadon ZE, Beloto AJ, Vigilato MAN, et al. Gains and future road map for the elimination of dog-transmitted rabies in the Americas. *Am J Trop Med Hyg* (2013) 89(6):1040–2. doi:10.4269/ajtmh.13-0229
21. Vigilato MAN, Cosivi O, Knobl T, Clavijo A, Silva HMT. Rabies update for Latin America and the Caribbean. *Emerg Infect Dis* (2012) 19(4):678–9. doi:10.3201/eid1904.121482
22. Bögel K. Chapter 13: Control of dog rabies. In: Jackson AC, Wunner WH, editors. *Rabies*. San Diego, USA: Elsevier Academic Press (2002). p. 429–43.
23. Steele JH. Rabies in the Americas and remarks on global aspects. *Rev Infect Dis* (1988) 10(Suppl 4):S585–97. doi:10.1093/clinids/10.Supplement_4.S585
24. Scott T, Coetzer A, de Balogh K, Wright N, Nel L. The Pan-African rabies control network (PARACON): a unified approach to eliminating canine rabies in Africa. *Antiviral Res* (2015) 124:93–100. doi:10.1016/j.antiviral.2015.10.002
25. Jarvis S. One Health. Aiming for elimination of dog-mediated human rabies cases by 2030. *Vet Rec* (2016) 178(4):86–7. doi:10.1136/vr.i51
26. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts

with data. *PLoS Negl Trop Dis* (2010) 4(2):e626. doi:10.1371/journal.pntd.0000626
27. Wallace RM, Reses H, Franka R, Dilius P, Fenelon N, Orciari L, et al. Establishment of a canine rabies burden in Haiti through the implementation of a novel surveillance program. *PLoS Negl Trop Dis* (2015) 9(11):e0004245. doi:10.1371/journal.pntd.0004245
28. Nel LH, Taylor LH, Balaram D, Doyle KAS. Global partnerships are critical to advance the control of neglected zoonotic diseases: the case of the global alliance for rabies control. *Acta Trop* (2017) 165:274–79. doi:10.1016/j.actatropica.2015.10.014
29. Davlin SL, VonVille HM. Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* (2012) 30(24):3492–502. doi:10.1016/j.vaccine.2012.03.069
30. United Nations Statistics Division. *Composition of Macro Geographical (Continental) Regions, Geographical Sub-Regions, and Selected Economic and Other Groupings*. New York: Department of Economic and Social Affairs (2014). Available from: http://unstats.un.org/unsd/methods/m49/m49regin.htm
31. Lankester F, Hampson K, Lembo T, Palmer G, Taylor L, Cleaveland S. Implementing Pasteur's vision for rabies elimination. *Science* (2014) 345(6204):1562–4. doi:10.1126/science.1256306
32. Jibat T, Hogeveen H, Mourits MCM. Review on dog rabies vaccination coverage in Africa: a question of dog accessibility or cost recovery? *PLoS Negl Trop Dis* (2015) 9(2):e0003447. doi:10.1371/journal.pntd.0003447
33. Cleaveland S, Lankester F, Townsend S, Lembo T, Hampson K. Rabies control and elimination: a test case for one health. *Vet Rec* (2014) 175(8):188–93. doi:10.1136/vr.g4996
34. Banyard AC, Horton DL, Freuling C, Müller T, Fooks AR. Control and prevention of canine rabies: the need for building laboratory-based surveillance capacity. *Antiviral Res* (2013) 98(3):357–64. doi:10.1016/j.antiviral.2013.04.004
35. Millien MF, Pierre-Louis JB, Wallace R, Caldas E, Rwangabgoba JM, Poncelet JL, et al. Control of dog mediated human rabies in Haiti: no time to spare. *PLoS Negl Trop Dis* (2015) 9(6):e0003806. doi:10.1371/journal.pntd.0003806
36. Undurraga EA, Meltzer MI, Tran CH, Atkins CY, Etheart MD, Millien MF, et al. Cost-effectiveness evaluation of a novel integrated bite case management program for the control of human rabies, Haiti 2014–2015. *Am J Trop Med Hyg* (in press). doi:10.4269/ajtmh.16-0785
37. World Bank. *World Bank Open Data*. (2016). Available from: http://data.worldbank.org/indicator/SP.URB.TOTL.IN.ZS
38. United Nations Development Programme. *Human Development Reports. Human Development Index*. (2016). Available from: http://hdr.undp.org/en/content/human-development-index-hdi
39. Gibson AD, Handel IG, Shervell K, Roux T, Mayer D, Muyila S, et al. The vaccination of 35,000 dogs in 20 working days using combined static point and door-to-door methods in Blantyre, Malawi. *PLoS Negl Trop Dis* (2016) 10(7):e0004824. doi:10.1371/journal.pntd.0004824
40. World Organization for Animal Health (OIE). *World Animal Health Information Database (WAHIS) Interface*. (2016). Available from: http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home
41. Kayali U, Mindekem R, Hutton G, Ndoutamia A, Zinsstag J. Cost-description of a pilot parenteral vaccination campaign against rabies in dogs in N'Djaména, Chad. *Trop Med Int Health* (2006) 11(7):1058–65. doi:10.1111/j.1365-3156.2006.01663.x
42. Kaare M, Lembo T, Hampson K, Ernest E, Estes A, Mentzel C, et al. Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* (2009) 27(1):152–60. doi:10.1016/j.vaccine.2008.09.054
43. Lapiz SMD, Miranda MEG, Garcia RG, Daguro LI, Paman MD, Madrinan FP, et al. Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol rabies prevention and elimination project. *PLoS Negl Trop Dis* (2012) 6(12):e1891. doi:10.1371/journal.pntd.0001891
44. Hatch B, Anderson A, Sambo M, Maziku M, Mchau G, Mbunda E, et al. Towards canine rabies elimination in South-Eastern Tanzania: assessment of health economic data. *Transbound Emerg Dis* (2016). doi:10.1111/tbed.12463
45. World Health Organization. *WHO-CHOICE. Choosing Interventions that Are Cost-Effective Geneva: WHO_CHOICE*. (2015). Available from: http://www.who.int/choice/en/
46. Totton SC, Wandeler AI, Zinsstag J, Bauch CT, Ribble CS, Rosatte RC, et al. Stray dog population demographics in Jodhpur, India following a population control/rabies vaccination program. *Prev Vet Med* (2010) 97(1):51–7. doi:10.1016/j.prevetmed.2010.07.009
47. Reece J, Chawla S. Control of rabies in Jaipur, India, by the sterilisation and vaccination of neighbourhood dogs. *Vet Rec* (2006) 159:379–83. doi:10.1136/vr.159.12.379
48. US Department of Commerce BoEA. *National Income and Product Account Tables. Table 1.1.9 Implicit Price Deflators for Gross Domestic Product*. (2015). Available from: http://www.bea.gov/iTable/iTable.cfm?reqid=9&step=3&isuri=1&903=13#reqid=9&step=3&isuri=1&904=2000&903=13&906=a&905=2015&910=x&911=0
49. Tenzin, Wangdi K, Ward MP. Human and animal rabies prevention and control cost in Bhutan, 2001–2008: the cost–benefit of dog rabies elimination. *Vaccine* (2012) 31(1):260–70. doi:10.1016/j.vaccine.2012.05.023
50. Dürr S, Meltzer MI, Mindekem R, Zinsstag J. Owner valuation of rabies vaccination of dogs, Chad. *Emerg Infect Dis* (2008) 14(10):1650. doi:10.3201/eid1410.071490
51. Léchenne M, Oussiguere A, Naissengar K, Mindekem R, Mosimann L, Rives G, et al. Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* (2016) 34(4):571–7. doi:10.1016/j.vaccine.2015.11.033
52. Polo G, Acosta CM, Dias RA. Spatial accessibility to vaccination sites in a campaign against rabies in São Paulo city, Brazil. *Prev Vet Med* (2013) 111(1):10–6. doi:10.1016/j.prevetmed.2013.03.010
53. Kayali U, Mindekem R, Yemadji N, Vounatsou P, Kaninga Y, Ndoutamia A, et al. Coverage of pilot parenteral vaccination campaign against canine rabies in N'Djamena, Chad. *Bull World Health Organ* (2003) 81(10):739–44. doi:10.1590/S0042-96862003001000009
54. Muthiani Y, Traoré A, Mauti S, Zinsstag J, Hattendorf J. Low coverage of central point vaccination against dog rabies in Bamako, Mali. *Prev Vet Med* (2015) 120(2):203–9. doi:10.1016/j.prevetmed.2015.04.007
55. Kitala P, McDermott J, Kyule M, Gathuma J, Perry B, Wandeler A. Dog ecology and demography information to support the planning of rabies control in Machakos District, Kenya. *Acta Trop* (2001) 78(3):217–30. doi:10.1016/S0001-706X(01)00082-1
56. Kassebaum NJ, Arora M, Barber RM, Bhutta ZA, Brown J, Carter A, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: a systematic analysis for the global burden of disease study 2015. *Lancet* (2016) 388(10053):1603–58. doi:10.1016/S0140-6736(16)31460-X
57. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the global burden of disease study 2015. *Lancet* (2016) 388(10053):1459–544. doi:10.1016/S0140-6736(16)31012-1
58. Lim SS, Allen K, Bhutta ZA, Dandona L, Forouzanfar MH, Fullman N, et al. Measuring the health-related sustainable development goals in 188 countries: a baseline analysis from the global burden of disease study 2015. *Lancet* (2016) 388(10053):1813–50. doi:10.1016/S0140-6736(16)31467-2
59. Undurraga EA, Halasa YA, Shepard DS. Use of expansion factors to estimate the burden of dengue in Southeast Asia: a systematic analysis. *PLoS Negl Trop Dis* (2013) 7(2):e2056. doi:10.1371/journal.pntd.0002056
60. Tounkara K, Nwankpa N, Bodjo C. The role of the African Union Pan African veterinary vaccine centre (AU-PANVAC) in rinderpest eradication. *Transbound Anim Dis Bull* (2011) 38:43–5.

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Rabies Control: Could Innovative Financing Break the Deadlock?

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The neglected zoonotic diseases (NZDs) have been all but eradicated in wealthier countries but remain major causes of ill-health and mortality in over 80 countries across Africa, Asia, and Latin America. The nature of neglect for the NZDs has been ascribed, in part, to underreporting resulting in an underestimation of their global burden that, together with a lack of advocacy, downgrades their relevance to policy-makers and funding agencies. While this may be the case for many NZDs, for rabies this is not the case. The global burden estimates for rabies (931,600 DALYs) more than justify prioritizing rabies control building on the strong advocacy platforms, functioning at local, regional, and global levels (including the Global Alliance for Rabies Control), and commitments from WHO, OIE, and FAO. Simple effective tools for rabies control exist together with blueprints for operationalizing control, yet, despite elimination targets being set, no global affirmative action has been taken. Rabies control demands activities both in the short term and over a long period of time to achieve the desired cumulative gains. Despite the availability of effective vaccines and messaging tools, rabies will not be sustainably controlled in the near future without long-term financial commitment, particularly as disease incidence decreases and other health priorities take hold. While rabies control is usually perceived as a public good, public private partnerships could prove equally effective in addressing endemic rabies through harnessing social investment and demonstrating the cost-effectiveness of control. It is acknowledged that greater attention to navigating local realities in planning and implementation is essential to ensuring that rabies, and other neglected diseases, are controlled sustainably. In the shadows of resource and institutional limitations in the veterinary sector in low- and middle-income countries, sufficient funding is required so that top-down interventions for rabies can more explicitly engage with local project organization capacity and affected communities in the long term. Development Impact Bonds have the potential to secure the financing required to deliver effective rabies control.

Keywords: rabies, development impact bonds, zoonotic, neglected tropical diseases, disease control, finance

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INTRODUCTION

More than a decade of advocacy has resulted in ambitious control and elimination targets for neglected tropical diseases (NTDs) set by WHO for 2020. Partnerships have been formed to raise funds and provide advocacy for NTD control, including the Global Programme to Eliminate

Lymphatic Filariasis[1] and the Global Network for NTDs.[2] Advocacy resulted in the 2012 London Declaration[3] and WHO Roadmap to accelerate the work to overcome the global impact of 17 NTDs,[4] followed by the World Health Assembly (WHA) Resolution WHA66.12 on NTDS in May 2013. However, for the neglected zoonotic diseases (NZDs) that were included in this Roadmap (rabies, echinococcosis hydatid disease, leishmaniasis, *Trypanosoma brucei rhodesiense* sleeping sickness, and *Taenia solium* cysticercosis), little progress has been made. Anthrax, brucellosis, and bovine TB were not included in the resolution.

Rabies is one of the most feared human diseases, estimated to cause some 55,000 deaths each year, predominately among children and the rural poor in Asia and Africa (1–3). The rabies virus has a simple route of transmission; *via* saliva from the bite of an infected animal, the rabies virus invades the central nervous system and, in the absence of postexposure prophylaxis (PEP), is fatal once clinical signs appear (4). Symptoms in dogs can be non-specific but often include "hydrophobia," hypersalivation, respiratory difficulties, biting, and aggression. Since the vast majority of human rabies cases are caused by domestic dogs (5) and an effective vaccine is available, dog vaccination is the most effective control strategy together with dog population management, movement regulations, and the promotion of responsible dog ownership (5–7). A number of initiatives have been undertaken (8–12), and a combination of intensive canine vaccination and surveillance efforts, implemented since the 1980s in Latin America, has shown dramatic progress (13).

Eliminating infection from dogs reduces the demand for costly PEP, although the relationship is not always as predicted and may vary considerably (14, 15). Despite all the evidence of the benefits of targeting the domestic canine reservoir, dog vaccination remains under-prioritized in most low- and middle-income countries (LMIC) with competing health issues and limited resources. Despite a number of successful initiatives having been implemented, erroneous perceptions of operational constraints among policy-makers (lack of knowledge about the dog population, inadequate resources, and wildlife transmission) are barriers to vaccination (5).

To successfully eliminate rabies, vaccination must reach at least 70% of a dog population over consecutive years, yet, despite the feasibility of elimination, programs in Africa struggle with reaching high levels of coverage (16); vaccination rates lower than 30% are considered a "waste of resources" (5). Despite good quality vaccines for dogs, a genuine science of rabies elimination is needed (17) to understand complex social–ecological determinants of vaccination effectiveness (18). Vaccination coverage declines rapidly in dog populations with high turnover rates (19). Most dogs in Africa are owned by a family but are free roaming and generally young; often half of dogs are less than 1 year of age (20–23). Dog bite data, used to infer numbers of human deaths, were used to calculate the threshold density for rabies persistence as 4.5 dogs/km^2 (1).

[1] http://www.filariasis.org/.
[2] http://globalnetwork.org/.
[3] http://unitingtocombatntds.org/resource/london-declaration.
[4] http://www.who.int/neglected_diseases/NTD_RoadMap_2012_Fullversion.pdf.

Validated estimates of dog populations are essential for planning successful mass dog vaccinations yet in most cases are lacking (12); for example, a study in Tanzania showed that the dog population was six times larger than the official estimate (23). Interventions are influenced by local dog ownership practices; attitudes toward dogs; the ability and willingness of owners to handle their dogs; the location of vaccination points, and the extent of information dissemination and knowledge of rabies, all of which influence compliance (8, 22, 24, 25). Despite higher costs, house-to-house strategies were necessary to achieve 70% coverage in pastoralist communities in Northern Tanzania (26). Capacity and working norms of implementing organizations are also key; most campaigns are planned nationally and delivered at district and subdistrict level. In many African LMIC, a legacy of structural adjustment in the veterinary sector had resulted in reduced capacity in the animal health sector. Large remote geographical areas together with low salaries, insufficient resources, and rigid bureaucratic norms can further inhibit such campaigns, which depend, to a large degree, on adapting strategies to fit community needs. However, even with cheap and effective dog vaccines available and with burdens and costs well understood, there is no guarantee that elimination will be easily achieved (27).

From a human health perspective, a dog bite wound requires cleaning and a postexposure treatment (PET) vaccination is essential, but expensive. As dog-to-dog transmission drives rabies epidemics, PET alone will not eliminate rabies. From an animal health perspective, rabies in cattle, and not dogs, is considered more important, because of the greater economic value of a cow relative to a dog, so national rabies vaccination programs are not prioritized.

THE PROBLEM WITH RABIES CONTROL

Neglected zoonotic diseases may be described as the neglected NTDs, beset by problems of underreporting that tends to underestimate their global burden and so diminishes their relevance to policy-makers and funding agencies. Interventions in the animal reservoir for NZDs (mass vaccination, drug treatment, and education) must be supported and operationalized across health and agriculture ministries. Long-term national and regional plans for elimination demand significant buy-in from both human and animal health sectors. When a full cross-sector analysis is undertaken and all stake-holder benefits (monetary/non-monetary) are taken into account, interventions for NZDs can become highly cost-effective, and among all neglected NZDs, dog rabies elimination is the lowest hanging fruit, with all the necessary tools for elimination already available (28, 29). However, for rabies, the cost benefits of vaccinating dogs may take many years to be realized and requires universal high coverage to be achieved annually. For example, mathematical models of rabies control in Ndjamena, Chad, suggest the cumulative cost of dog rabies mass vaccination and human PET was equal to the cumulative cost of PET alone after 6 years and only became more cost-effective after 7 years (15). Costs of rabies control are borne almost entirely by people in the developing world where >99% of all fatalities occur and dog owners have not been willing to

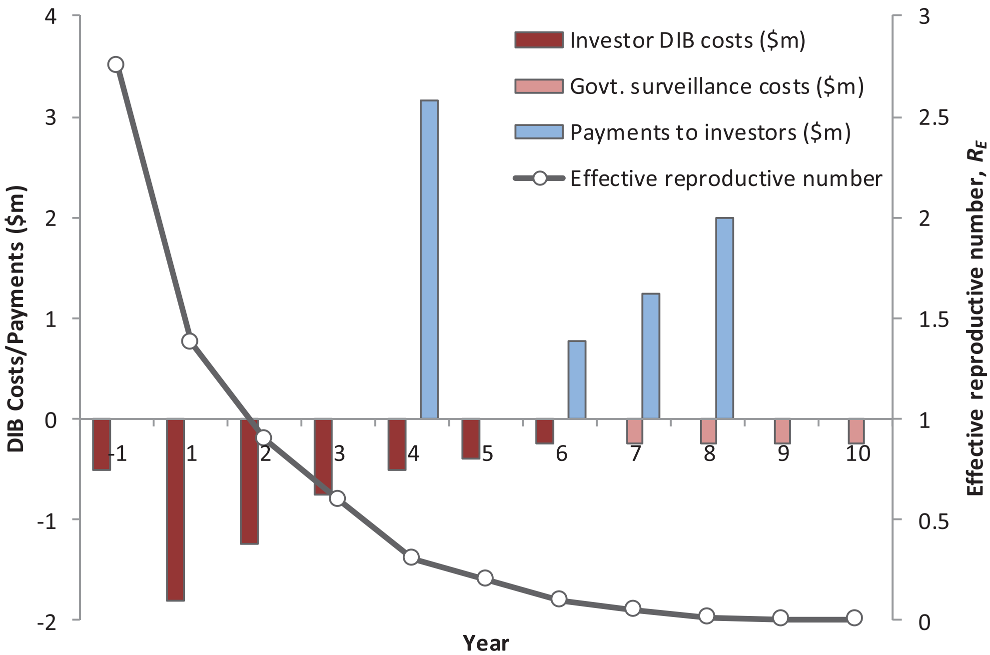

FIGURE 1 | The annual cash-flow requirements, the performance-related payments to investors, and impact on rabies transmission dynamics for a hypothetical Development Impact Bond (DIB). The total cost of the DIB is US$ 6.45 million, including Year 1 establishment costs, with US$ 5.45 million financed by investors (Years 1–6) and US$ 1 million by the Government (Years 7–10 in the post-elimination maintenance phase). This excludes the ongoing government spend providing the routine rabies surveillance platform independent of any specific strengthening or refinements needed to deliver the DIB. The model assumes mass vaccination of 70% of dogs in year 1 (US$ 1.8 million) and then a second round of 70% vaccination spread over 3 years (total cost $2.5 million). Costs for community messaging are included throughout the program. Based on achieving the vaccination targets, the investors receive a payment at the end of Year 4 equal to 66% of the DIB spend over the first 5 years. The remaining payments to the investors in Years 6–8 are linked to reduced rabies transmission and are back-loaded to incentivize a successful transition to embedding the maintenance phase under government spend. The surveillance system is embedded into national veterinary and public health services and assumes an annual cost of US$ 250,000, which includes provision for reactive ring vaccination following confirmed sporadic canine rabies cases and continued use of postexposure prophylaxis following confirmed exposure. The total return to investors is US$ 7.2 million, representing an internal rate of return of 8%.

pay the full costs of vaccination, indicating that rabies control should be considered a public good (30).

There are proven systems to identify those individuals exposed to the rabies virus, most often following a rabid dog bite, and ensure PET is administered promptly to avoid death from rabies, which is otherwise inevitable once the victim starts to display clinical symptoms. Any death due to dog-mediated rabies is a failure of the public and veterinary health systems, but the main constraint to widespread implementation is finance. Poor countries do not have access to the funds required to develop and deliver an appropriate control strategy tailored to their epidemiological conditions that can be implemented over sufficient time to unlock and sustain public health and economic benefits.

DEVELOPMENT IMPACT BONDS (DIBs)—A NEW APPROACH TO FUNDING RABIES CONTROL

The tools for effective control and the evidence that they work have been around for a long time; the constraining factor has been the financing to implement sustained efforts at scale. Traditional financing streams for NTD control in resource poor settings, particularly grant funding through international governmental donors, charitable organizations, or private institutions, have not been available at the levels required to combat the continued burden of rabies. The failure to secure the necessary financing is in part due to the inability to compete against other pressing infectious disease burdens, which have historically secured the majority of the resources going into NTD control. What can be done to break this deadlock and mobilize additional resources and unlock the benefits of achievable rabies control?

A new model of sustainable investment in rabies control is required, and DIBs is one approach that potentially could secure the financing required to deliver effective rabies control. We argue that financing structure of a DIB is particularly well suited to financing rabies control and so provides a highly compelling case to donors interested in controlling NTDs in a highly cost-effective manner (**Figure 1**).

Development Impact Bonds are a form of Social Impact Bonds (SIBs), which are themselves a form of payment for results (31). SIBs have been applied to address a variety of societal problems primarily across the developed world, and although the number and size of transaction is small, the market is growing rapidly

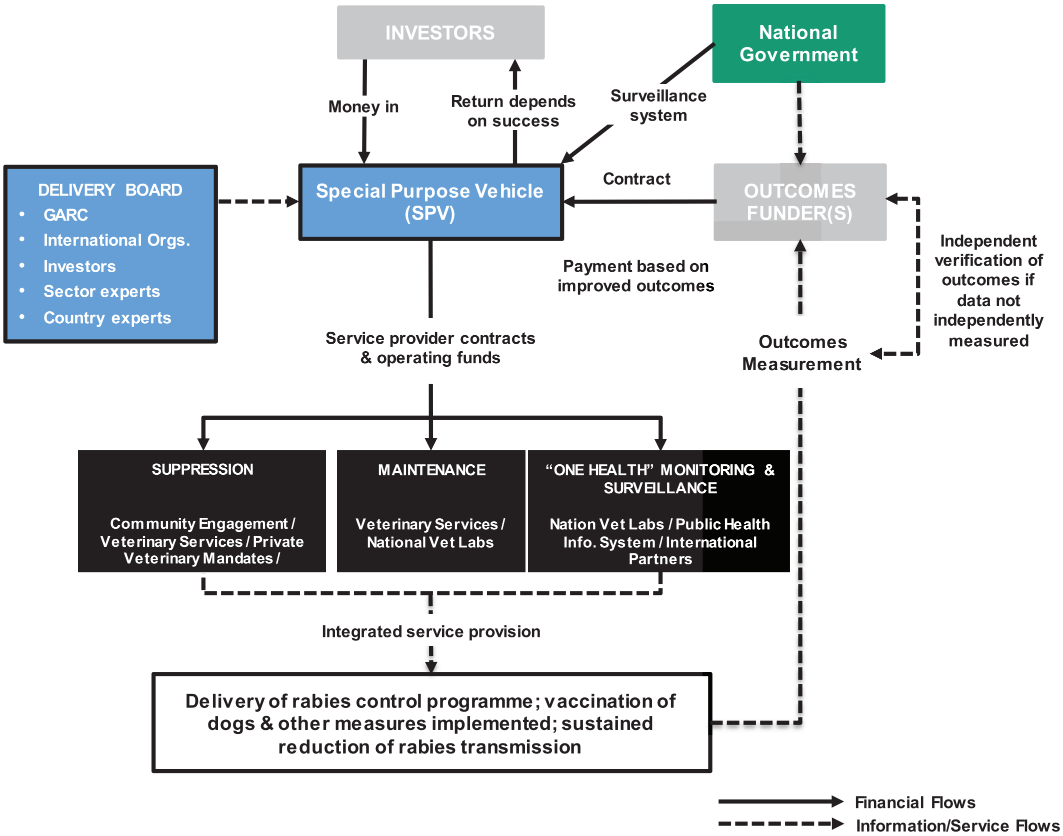

FIGURE 2 | **Plausible Development Impact Bond (DIB) structure for rabies control**. The flow of money from the National Government to embed rabies surveillance post-vaccination control into the veterinary and public health systems may be through the SPV established to deliver the DIB or may be independent of the DIB structure but counts toward the overall delivery costs. Note, the structure was developed based on the work conducted with Global Alliance for Rabies Control (GARC) and is applicable for rabies control in general with other advocacy agencies playing similar roles to GARC.

(31). In developing settings, DIBs, while far from being a panacea, have been advocated as potentially important in helping address a broad range of inequalities including improved public health provision (32), childhood development (33), and infectious disease control (34).

More broadly, DIBs are one example of a new form of social impact financing in which donor or government payments are structured around the delivery of specific outcomes. There is significant and growing interest among traditional development donors (such as DFID, USAID, and The World Bank), philanthropic institutions (such as UBS Optimus Foundation, Children's Investment Fund Foundation, Bill & Melinda Gates Foundation, and Rockefeller Foundation), and the emerging class of impact investors, in the use of DIBs to effectively deliver impact in developing countries.[5] One of the most advanced propositions currently in development is the area-wide control of zoonotic sleeping sickness in Uganda (34).

Development Impact Bonds use private investment to provide up-front risk capital for development programs, only calling on donor (or government) funding to repay capital, plus a potential return (i.e., premium), once clearly defined and measured development outcomes are achieved. DIBs have the potential to attract new capital from impact investors motivated by both social and financial returns. By transferring the risk of program failure to these investors, DIBs bring a greater focus on implementation and delivery of successful results. In this way, DIBs also satisfy the growing demands that public funding, be it internal or spent on overseas aid, should be paid on successful results and in a transparent manner (**Figure 2**).

There are characteristics of infectious disease control programs in general, and rabies control in particular, which map neatly onto a DIB including

(1) *Strong evidence base that successful program delivery is technically achievable.*
Development Impact Bonds are about scaling proven interventions and primarily look to shift implementation risk (not technical risk) from outcome payers to investors. The evidence base for effective rabies control has been

[5] https://www.gov.uk/government/news/uk-development-bonds-will-combat-global-poverty.

validated and is strong. The constraints to implementation are known to be financial and operational. A consensus has emerged in the international community about the basis for implementing control with detail guidelines, *The Blueprint for Rabies Prevention and Control* (2014) developed by the Partners for Rabies Prevention (10), which includes the *Stepwise Approach to Rabies Elimination* tool (developed by FAO, the Global Alliance for Rabies Control, and other partners) and the approach endorsed by the WHO–OIE–FAO tripartite.[6]

Models for designing and running effective rabies vaccination campaigns have been developed and trialed in a variety of developing country settings. For example, Tanzania, where rabies is endemic with an estimated 1,500 deaths each year (35), was among three countries selected by the WHO for large-scale rabies elimination demonstration trials between 2009 and 2013—funded by the Bill and Melinda Gates Foundation (BMGF) (see http://www.who.int/rabies/bmgf_who_project/en/index.html).

(2) *Substantial up-front investment is needed to unlock long-term net benefits*.
The ideal cash-flow profile of the DIB (front loaded investment followed by long-term lower cash needs) mirrors the high up-front effort needed to interrupt rabies transmission followed by reduced effort to maintaining disease control. In poor countries, the money is rarely available to cover these up-front costs while traditional donor funding does not advance large amounts of cash; in the DIB, private investors provide the capital needed up front, at risk.

(3) *Affordable and sustainable maintenance of long-term impact*.
Successful dog rabies mass vaccinations (providing sufficient coverage over sufficient time) will interrupt transmission allowing a shift to a disease-free maintenance phase based on surveillance, reactive vaccination, and appropriate human case management. Maintenance costs are significantly lower than the up-front costs of mass vaccination [e.g., Ref. (15, 36)], and there is the potential to embed the maintenance activities in routine public and veterinary health systems funded by the country government to ensure long-term sustainability beyond the end of the DIB.

(4) *Successful implementation requires coordination between multiple partners*.
Controlling rabies requires engagement from partners across ministries and the private and public sector and demands a "One Health" approach in which there is close coordination between the veterinary and public health sectors. The investment structure in the DIB ensure a common drive to deliver specific outcomes providing a unified focus for the veterinary and human health delivery partners.

(5) *Tractable and affordable measure of outcomes that are valid indicators of long-term impact*.
Tractable and affordable measure of outcomes will trigger payments from the outcome funders to the investors. For rabies, there exist established, validated, and robust diagnostic procedures to confirm positive rabies samples as well as case recording systems to monitor human rabies exposure. These measures provide a basis for quantifying the reduction in disease transmission relative to a pre-intervention baseline. The growing economic literature investigating the burden of rabies provides the evidence basis for understanding the impact unlocked by long-term reduction in rabies transmission.

[6] http://www.rabiesblueprint.com/.

STRUCTURING A DIB FOR RABIES INTERVENTION

The structure of a DIB applied to rabies would partition interventions into four phases:

(1) *Pre-implementation phase* in which the detailed delivery plan is developed; baseline incidence data collected; existing public and veterinary health surveillance systems are, where necessary, strengthened and refined to provide the basis for tracking success across all phases of the intervention; reporting systems developed and tested; DIB infrastructure (e.g., establishment of special purpose vehicle for DIB contracting) and recruitment/contracting of delivery partners secured; payment triggers agreed; and an independent outcome auditor appointed.
(2) *Suppression phase* in which the mass vaccination campaigns are implemented at national level; routine reporting implemented; and audit of vaccination coverage by the independent outcome measurement group is conducted.
(3) *Consolidation phase* in which there is a shift from mass vaccination to surveillance and reactive vaccination following confirmed canine cases; protection of borders; audit of canine rabies incidence and suspect rabid dog bites.
(4) *Post-elimination maintenance phase* in which the surveillance capacity is embedded in government services and fully financed by the government.

For rabies, ideally DIB payment triggers would be split between a partial return of capital based on delivery of mass vaccination coverage (measured against the 70% target threshold) and a series of outcome payments (back-loaded to incentivize long-term sustainability) linked to a reduction in disease incidence in the reservoir dog population and also exposure in humans.

CONCLUSION

The major constraint to progressing beyond a concept and launching a rabies-DIB is the lack of active engagement from a payer. Discussions with leading overseas development agencies, who have to act as the primary payers if DIBs are ever to be a significant source of financing in LMICs, have confirmed an interest among donors about DIBs in principle but in practice revealed a lack of internal expertise and capacity in engaging in the detailed planning of a DIB. This is not unexpected given the novelty of DIBs as a financing alternative to direct grant support.

Moreover, novel structures are perceived as risky and so avoided. Part of the risk is the perception issues that a successful DIB will cost the payer more than direct grant funding. Another aspect of the risk is the lack of any large-scale working examples of a DIB, which itself is a function of the lack of donor backing to test a DIB and develop the evidence. To break this catch 22 situation the evidence generated from SIBs from developed settings should start to emerge to help support, or not, the theory of the impact bond financing approach. Despite increased advocacy for rabies, it should be noted that rabies is not perceived as a priority disease, even among the NTDs, and donors are positioning other development issues in the pipeline for possible DIB financing ahead of rabies.

Several approaches may help progress the DIB concept for NTD in general, and rabies more specifically, to accelerate the involvement of traditional government aid agencies:

First, an emerging theme in DIB design is the central importance of identifying an appropriate outcome measure and that can be tractably, affordably, and verifiably measured to provide a robust quantitative basis for triggering payments. This is central to all DIBs. These issues are complex for the NTDs, which are characterized by a high degree of underreporting in affected human populations and a particular problem for NZDs, where the work on sleeping sickness (37) and rabies (1) points to using measures of transmission in the animal reservoir population as a proxy measure for human disease burden. Potential locations suitable for pilot DIB-financed interventions are characterized by having an active, well-respected academic research group with a track-record of peer-reviewed papers detailing a robust understanding of the disease epidemiology and empirical evidence of successful pilot interventions; engaged local veterinary and human public health agencies and relevant central government support.

Second, although a single international donor may be reluctant to finance a DIB in full, there may be potential to attract a co-payer, such as a foundation or a national government. This would catalyze the involvement of donor agencies and stimulate the broader DIB market. In the case of rabies, the blueprint for rabies control can be used as a starting point to divide the task of global rabies elimination into a series of DIBs investments, scaled to investors. A philanthropic foundation that has previous been funding rabies control (e.g., The BMGF) could consider switching spend to cover part of a DIB payment. Similarly, a country that has previously benefited from donor funding for rabies control (e.g., South Africa where The BMGF has funded rabies vaccination through WHO) could undertake to cover part of the outcome payments and attract additional donors to secure the balance of outcome payment. A general DIB structure and site-specific example for rabies elimination in Chad have been developed and are currently market tested with investors and donors (36). The framework exists to develop other site-specific DIB proposal for rabies control, which local governments and non-governmental advocacy agencies can market to potential payers.

Finally, consideration should be given to how rabies control could be integrated into other NTD/NZD intervention platforms. While any one NTD/NZD may not be prioritized by a donor, an integrated approach that delivers multiple impacts through a common delivery platform could be attractive and highly cost effective. With a burden of 931,600 DALYs (38), the burden for rabies is higher that Chagas, cutaneous Leishmaniasis, trypanosomiasis, cysticercosis, echinococcisis, trachoma, yellow fever, Ebola, trichuriasis and leprosy (39), and programs could be aligned so adding value. For example, strengthening veterinary public health surveillance systems to track rabies cases could be beneficial for tracking the impact of interventions against several diseases, while awareness messaging could be extended to deliver important health messages against multiple disease in which dogs are important reservoirs of disease (including cutaneous Leishmaniasis and echinococcisis) (40–44). If additional interventions can be delivered at marginal costs utilizing the same delivery teams and infrastructure, then cost-effectiveness of each intervention is improved and the likelihood of donor support potentially increased. The integration of rabies into other large-scale intervention programs was an emerging theme at the recent Partners for Rabies Prevention meeting (May 2015). This could form the basis of a more compelling DIB, which developing country governments could prioritize and potentially unlock donor support.

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All authors listed have made substantial, direct, and intellectual contribution to the work and approved it for publication.

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REFERENCES

1. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, Miranda ME, et al. Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* (2005) 83:360–8. doi:10.1590/S0042-96862005000500012
2. Sambo M, Cleaveland S, Ferguson H, Lembo T, Simon C, Urassa H, et al. The burden of rabies in Tanzania and its impact on local communities. *PLoS Negl Trop Dis* (2013) 7:e2510. doi:10.1371/journal.pntd.0002510
3. Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, et al. Estimating the global burden of endemic canine rabies. *PLoS Negl Trop Dis* (2015) 9:e0003786. doi:10.1371/journal.pntd.0003709
4. Hemachudha T, Laothamatas J, Rupprecht C. Human rabies: a disease of complex neuropathogenetic mechanisms and diagnostic challenges. *Lancet Neurol* (2002) 1:101–9. doi:10.1016/S1474-4422(02)00041-8
5. Lembo T, Hampson K, Kaare M, Ernest E, Knobel D, Kazwala RR, et al. The feasibility of canine rabies elimination in Africa: dispelling doubts

with data. *PLoS Negl Trop Dis* (2010) 4:e626. doi:10.1371/journal.pntd.0000626
6. Davlin S, Vonville H. Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* (2012) 30:3492–502. doi:10.1016/j.vaccine.2012.03.069
7. Morters MK, Restif O, Hampson K, Cleaveland S, Wood JL. Evidence-based control of canine rabies: a critical review of population density reduction. *J Anim Ecol* (2013) 82:6–14. doi:10.1111/j.1365-2656.2012.02033.x
8. Lapiz SM, Miranda ME, Garcia RG, Daguro LI, Paman MD, Madrinan FP, et al. Implementation of an intersectoral program to eliminate human and canine rabies: the Bohol Rabies Prevention and Elimination Project. *PLoS Negl Trop Dis* (2012) 6:e1891. doi:10.1371/journal.pntd.0001891
9. Lembo T, Attlan M, Bourhy H, Cleaveland S, Costa P, de Balogh K, et al. Renewed global partnerships and re-designed roadmaps for rabies prevention and control. *Vet Med Int* (2011) 2011:923149. doi:10.4061/2011/923149
10. Lembo T; Partners for Rabies Prevention. The blueprint for rabies prevention and control: a novel operational toolkit for rabies elimination. *PLoS Negl Trop Dis* (2012) 6:e1388. doi:10.1371/journal.pntd.0001388
11. Putra AA, Hampson K, Girardi J, Hiby E, Knobel D, Mardiana IW, et al. Response to a rabies epidemic, Bali, Indonesia, 2008–2011. *Emerg Infect Dis* (2013) 19:648–51. doi:10.3201/eid1904.120380
12. Lechenne M, Oussiguere A, Naissengar K, Mindekem R, Mosimann L, Rives G, et al. Operational performance and analysis of two rabies vaccination campaigns in N'Djamena, Chad. *Vaccine* (2016) 34:571–7. doi:10.1016/j.vaccine.2015.11.033
13. Vigilato M, Clavijo A, Knobl T, Silva H, Cosivi O, Schneider MC, et al. Progress towards eliminating canine rabies: policies and perspectives from Latin America and the Caribbean. *Philos Trans R Soc Lond B Biol Sci* (2013) 368:20120143. doi:10.1098/rstb.2012.0143
14. Cleaveland S, Kaare M, Tiringa P, Mlengeya T, Barrat J. A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* (2003) 21:1965–73. doi:10.1016/S0264-410X(02)00778-8
15. Zinsstag J, Dürr S, Penny MA, Mindekem R, Roth F, Menendez Gonzalez S, et al. Transmission dynamics and economics of rabies control in dogs and humans in an African city. *Proc Natl Acad Sci U S A* (2009) 106:14996–5001. doi:10.1073/pnas.0904740106
16. Muthiani Y, Traore A, Mauti S, Zinsstag J, Hattendorf J. Low coverage of central point vaccination against dog rabies in Bamako, Mali. *Prev Vet Med* (2015) 120:203–9. doi:10.1016/j.prevetmed.2015.04.007
17. Zinsstag J. Towards a science of rabies elimination. *Infect Dis Poverty* (2013) 2:22. doi:10.1186/2049-9957-2-22
18. Mosimann L, Traoré A, Mauti S, Léchenne M, Obrist B, Véron R, et al. A mixed methods approach to assess animal vaccination programmes: the case of rabies control in Bamako, Mali. *Acta Trop* (2016) 165:203–215. doi:10.1016/j.actatropica.2016.10.007
19. Hampson K, Dushoff J, Cleaveland S, Haydon DT, Kaare M, Packer C, et al. Transmission dynamics and prospects for the elimination of canine rabies. *PLoS Biol* (2009) 7:e1000053. doi:10.1371/journal.pbio.1000053
20. Butler JR, Bingham J. Demography and dog-human relationships of the dog population in Zimbabwean communal lands. *Vet Rec* (2000) 147:442–6. doi:10.1136/vr.147.16.442
21. Kitala P, McDermott J, Kyule M, Gathuma J, Perry B, Wandeler A. Dog ecology and demography information to support the planning of rabies control in Machakos District, Kenya. *Acta Trop* (2001) 78:217–30. doi:10.1016/S0001-706X(01)00082-1
22. Knobel DL, Laurenson MK, Kazwala RR, Boden LA, Cleaveland S. A cross-sectional study of factors associated with dog ownership in Tanzania. *BMC Vet Res* (2008) 4:5. doi:10.1186/1746-6148-4-5
23. Gsell AS, Knobel DL, Kazwala RR, Vounatsou P, Zinsstag J. Domestic dog demographic structure and dynamics relevant to rabies control planning in urban areas in Africa: the case of Iringa, Tanzania. *BMC Vet Res* (2012) 8:236. doi:10.1186/1746-6148-8-236
24. Durr S, Meltzer M, Mindekem R, Zinsstag J. Owner valuation of rabies vaccination of dogs, Chad. *Emerg Infect Dis* (2008) 14:1650–2. doi:10.3201/eid1410.071490
25. Kayali U, Mindekem R, Yémadji N, Vounatsou P, Kaninga Y, Ndoutamia AG, et al. Coverage of pilot parenteral vaccination campaign against canine rabies in N'Djamena Chad. *Bull World Health Organ* (2003) 81:739–44. doi:10.1590/S0042-96862003001000009
26. Kaare M, Lembo T, Hampson K, Ernest E, Estes A, Mentzel C, et al. Rabies control in rural Africa: evaluating strategies for effective domestic dog vaccination. *Vaccine* (2009) 27:152–60. doi:10.1016/j.vaccine.2008.09.054
27. Bardosh K, Sambo M, Sikana L, Hampson K, Welburn SC. Eliminating rabies in Tanzania? Local understandings and responses to mass dog vaccination in Kilombero and Ulanga districts. *PLoS Negl Trop Dis* (2014) 8:e2935. doi:10.1371/journal.pntd.0002935
28. Abela-Ridder B, Knopf L, Taylor L, Torres G, De Balogh K. 2016: the beginning of the end of rabies? *Lancet Glob Health* (2016) 4:e780–1. doi:10.1016/S2214-109X(16)30245-5
29. WHO World Organisation for Animal Health. *Global Elimination of Rabies: The Time is Now*. (2016). Available from: http://apps.who.int/iris/bitstream/10665/204621/1/WHO_HTM_NTD_NZD_2016.02_eng.pdf?ua=1
30. Durr S, Mindekem R, Kaninga Y, Doumagoum Moto D, Meltzer MI, Vounatsou P, et al. Effectiveness of dog rabies vaccination programmes: comparison of owner-charged and free vaccination campaigns. *Epidemiol Infect* (2009) 137:1558–67. doi:10.1017/S0950268809002386
31. Gustafsson-Wright E, Gardiner S, Putcha V. *The Potential and Limitations of Impact Bonds: Lessons from the First Five Years of Experience Worldwide*. (2015). Available from: https://www.brookings.edu/research/the-potential-and-limitations-of-impact-bonds-lessons-from-the-first-five-years-of-experience-worldwide/
32. Rowe R, Stephenson N. Speculating on health: public health meets finance in 'health impact bonds'. *Sociol Health Illn* (2016) 38:1203–16. doi:10.1111/1467-9566.12450
33. Gustafsson-Wright E, Gardiner S. *Using Impact Bonds to Achieve Early Childhood Development Outcomes in Low- and Middle-Income Countries*. (2016). Available from: http://www.brookings.edu/research/reports/2016/02/Impact-bonds-early-childhood-development-wright
34. Welburn SC, Bardosh K, Coleman PG. Novel financing model for neglected tropical diseases: development impact bonds applied to sleeping sickness and rabies control. *PLoS Negl Trop Dis* (2016) 10:e0005000. doi:10.1371/journal.pntd.0005000
35. Cleaveland S, Fevre EM, Kaare M, Coleman PG. Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries. *Bull World Health Organ* (2002) 80:304–10. doi:10.1590/S0042-96862002000400009
36. Anyiam F, Lechenne M, Mindekem R, Oussigéré A, Naissengar S, Alfaroukh IO, et al. Cost-estimate and proposal for a development impact bond for canine rabies elimination by parenteral mass vaccination in Chad. *Acta Trop* (2016) S0001–706X:30510–1. doi:10.1016/j.actatropica.2016.11.005
37. Maudlin I, Eisler MC, Welburn SC. Neglected and endemic zoonoses. *Philos Trans R Soc Lond B Biol Sci* (2009) 364:2777–87. doi:10.1098/rstb.2009.0067
38. GBD 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* (2016) 388:1603–58. doi:10.1016/S0140-6736(16)31460-X
39. Molyneux DH, Savioli L, Engels D. Neglected tropical diseases: progress towards addressing the chronic pandemic. *Lancet* (2017) 389(10066):312–25. doi:10.1016/S0140-6736(16)30171-4
40. Coleman PG, Dye C. Immunization coverage required to prevent outbreaks of dog rabies. *Vaccine* (1996) 14:185–6. doi:10.1016/0264-410X(95)00197-9
41. Investing in Social Outcomes: Development Impact Bonds Working Group Report. *Consultation Draft*. Centre for Global Development & Social Finance (2013). Available from: http://www.socialfinance.org.uk/wp-content/uploads/2014/03/cgd-sf-dibreport_online.pdf
42. Hampson K, Dobson A, Kaare M, Dushoff J, Magoto M, Sindoya E, et al. Rabies exposures, post-exposure prophylaxis and deaths in a region of endemic canine rabies. *PLoS Negl Trop Dis* (2008) 2:e339. doi:10.1371/journal.pntd.0000339
43. Mableson HE, Okello A, Picozzi K, Welburn SC. Neglected zoonotic diseases the long and winding road to advocacy. *PLoS Negl Trop Dis* (2014) 8:e2800. doi:10.1371/journal.pntd.0002800

44. Welburn SC, Beange I, Ducrotoy MJ, Okello AL. The neglected zoonoses – the case for integrated control and advocacy. *Clin Microbiol Infect* (2015) 21:433–43. doi:10.1016/j.cmi.2015.04.011

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