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RESEARCH ARTICLE

REVISED A hundred years of rabies in Kenya and the strategy for eliminating dog-mediated rabies by 2030 [version 2; peer review: 4 approved]

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Abstract

Background: Rabies causes an estimated 59,000 human deaths annually. In Kenya, rabies was first reported in a dog in 1912, with the first human case reported in 1928. Here we examine retrospective rabies data in Kenya for the period 1912 – 2017 and describe the spatial and temporal patterns of rabies occurrence in the country. Additionally, we detail Kenya's strategy for the elimination of dog-mediated human rabies by 2030.
Methods: Data on submitted samples and confirmed cases in humans, domestic animals and wildlife were obtained from Kenya's Directorate of Veterinary Services. These data were associated with the geographical regions where the samples originated, and temporal and spatial trends examined.
Results: Between 1912 and the mid 1970's, rabies spread across Kenya gradually, with fewer than 50 cases reported per year and less than half of the 47 counties affected. Following an outbreak in the mid 1970's, rabies spread rapidly to more than 85% of counties, with a 4 fold increase in the percent positivity of samples submitted and number of confirmed rabies cases. Since 1958, 7,584 samples from domestic animals (93%), wildlife (5%), and humans (2%) were tested. Over two-thirds of all rabies cases came from six counties, all in close

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	Invited Reviewers			
	1	**2**	**3**	**4**
version 2 (revision) 15 Feb 2019	✓ report			
version 1 30 Jul 2018	? report	✓ report	✓ report	✓ report

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proximity to veterinary diagnostic laboratories, highlighting a limitation of passive surveillance.

Conclusions: Compulsory annual dog vaccinations between 1950's and the early 1970's slowed rabies spread. The rapid spread with peak rabies cases in the 1980's coincided with implementation of structural adjustment programs privatizing the veterinary sector leading to breakdown of rabies control programs. To eliminate human deaths from rabies by 2030, Kenya is implementing a 15-year step-wise strategy based on three pillars: a) mass dog vaccination, b) provision of post-exposure prophylaxis and public awareness and c) improved surveillance for rabies in dogs and humans with prompt responses to rabies outbreaks.

Keywords
rabies, elimination, Kenya, epidemiology

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Any reports and responses or comments on the article can be found at the end of the article.

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REVISED **Amendments from Version 1**

The updated version addresses the comments from the four reviewers. The main changes include greater detail in the methods section on data collection, cleaning and analysis, and on the process of developing the rabies elimination strategy for Kenya. Figure 5 has been modified to highlight the location of the rabies diagnostic laboratories in Kenya. Datasets used in the study, and the R codes used in the analysis have been provided - see the "Data availability" section. Direct responses to the reviewer's reports are provided as comments under each reviewer's report.

See referee reports

Introduction

Every year rabies is estimated to kill around 59,000 (95% CI: 25-159,000) people globally, with the vast majority of rabies deaths occurring in rural Africa and Asia[1,2]. Additionally, the disease is estimated to cause over 3.7 million (95% CI: 1.6–10.4 million) disability-adjusted life years (DALYs) and 8.6 billion USD (95% CI: 2.9–21.5 billion) in economic losses annually[1]. These human and economic losses occur despite the existence of effective anti-rabies vaccines for humans and animals and data that supports the feasibility of dog-rabies elimination[3,4]. In areas with high canine rabies burden, human rabies remains largely underreported owing to poor surveillance and misdiagnosis with other common diseases manifesting with nervous disorders such as cerebral malaria[1,3,5–7]. Consequently, this has led to a perceived lack of importance for human rabies, driving a cycle of neglect for this endemic disease[4].

In Kenya, rabies has been a public health problem since the first case was reported in a dog in the outskirts of Nairobi in 1912, and in a woman from the Lake Victoria basin in 1928[8]. The exact number of human deaths due to rabies in Kenya is unknown, although estimates have been made for some regions of the country and as part of the global burden of rabies estimates[1,9,10]. A recent review of research on human and animal rabies in Kenya revealed 12 published manuscripts and four theses on rabies covering mainly knowledge attitudes and practices on rabies, dog ecology and demographics and bite exposures[11]. A formal assessment of zoonotic diseases in Kenya has placed rabies among the top five priority zoonotic diseases[12]. As a result, Kenya developed a strategic plan for the prevention and elimination of dog-mediated human rabies. The strategy, adopted for implementation in 2014, provides the country with a framework for progressive reduction and eventual elimination of human deaths from rabies by 2030[13], in line with set target for the global elimination of dog-mediated rabies[14].

Here we review the historical data on human and animal rabies in Kenya from 1912 to 2017 and examine the patterns of rabies spread across the country, and the trends over time. Additionally, we detail the strategy adopted by Kenya towards elimination of dog-mediated human rabies by the year 2030.

Methods
Data collection
Rabies is a notifiable disease in Kenya, and the data are obtained through a passive surveillance system. Suspected cases of animal rabies are notified immediately to the local veterinary officers who are required to fill a standardised form with epidemiologically relevant information on the cases. The forms are sent to the Director of Veterinary Services (DVS), and the samples from the suspected rabid animals are sent to either the Central Veterinary Laboratory (CVL) located in Nairobi County or to any of six Regional Veterinary Investigation Laboratories (RVIL). The RVILs are placed across the country in Nakuru, Eldoret, Kericho, Garissa, Nyeri and Kilifi Counties. After initial testing, all samples were further submitted to one of three laboratories: the Central Veterinary Laboratory (CVL), the Regional Veterinary Investigation Laboratories (RVIL) in Kericho in Western Kenya, or RVIL in Kilifi at the Coast. These three laboratories carry out the Fluorescent Antibody Test (FAT), which is the confirmatory rabies diagnostic test recommended by the World Organisation for Animal Health (OIE)[15]. The test results were reported against the sample's source species and county of origin.

We obtained surveillance records on human and animal samples submitted and tested for rabies by the Central Veterinary Laboratory (CVL) in Kabete and the Regional Veterinary Investigation Laboratories (RVILs) in Kenya. Historically, human rabies diagnosis in Kenya has been conducted at the veterinary laboratories as public health laboratories have lacked diagnostic capacity for rabies. We obtained records for the years 1912 – 2017 from the Kenya Directorate of Veterinary Services and extracted data on the number of samples submitted for rabies testing, dates of sample submission, animal species and humans, administrative units (counties/districts) where the samples came from, and test results. As the administrative units in Kenya have changed over time, each unit reported in the raw data was matched to a current county. The analyses were conducted per existing counties to allow for consistency in reporting. Similar data were extracted from a published book containing historical data recorded by the Directorate of Veterinary Services for the years 1912 and 1981[8]. These data were reviewed, cleaned and merged to provide a database with complete records on rabies in Kenya for the years 1912 – 2017. Periods where data were missing have been highlighted in the relevant results. Retrospective data analyzed in this study were from routine national surveillance for rabies. Demographic and personal identifiable data were not collected together with the samples and individual consent was not obtained. The laboratory results of analysis of human samples were analysed as monthly aggregates.

For the period prior 1958, data on the number of samples submitted for testing and the species of animals they were obtained from were not available. Only aggregate numbers of positive cases of rabies per year per county were available for analyses.

Data analysis
We computed the proportions of human and animal samples submitted that tested positive for rabies by year, number of cases by species and administrative counties and examined spatial and temporal trends in rabies occurrence. We determined the proportion of samples submitted that were positive for rabies by year and for each county. Linear mixed-effect models with year as the fixed effect, and the county as a random effect (to account for proximity to testing laboratories) were used to

test if the proportion of submitted samples that were positive for rabies changed over time. The analysis was carried out using R platform (version 3.4.0) for statistical computing[16].

Strategic plan for the elimination of human rabies in Kenya

This manuscript discusses the strategies put in place for the elimination of human rabies in Kenya by the year 2030. The strategic plan was developed through an elaborate consultative process that involved government departments in health and livestock, research and academic institutions, non-governmental organizations and international partners in Kenya working on public and animal health. The detailed strategy is available online[13].

Results

Between 1958 and 2017, 7,584 samples from suspect human and animals rabies cases were submitted for laboratory testing. Samples from domestic animals (cattle, dogs, sheep, goats, pigs and equine) accounted for 93% (7,013/7,584), wildlife (jackal, fox, mongoose, lions, squirrels, bats, and civet) for 5% (407/7,584) and those from humans for 2% (164/7,584) of the total samples (Table 1).

Table 1. Number of samples submitted, tested for rabies and percent positivity by species, Kenya 1958 – 2017.

Species	Number of samples submitted	Number positive	% Positive
Domestic			
Dogs	4527	2796	62
Cattle	1461	1192	82
Cats	479	198	41
Goats/Sheep	361	280	78
Equine	167	113	68
Pigs	12	7	58
Camel	6	1	17
Sub-total	7013	4587	65
Wildlife			
Jackal	89	56	63
Fox	26	17	65
Honey badger	39	23	59
Hyena	15	7	47
Civet	9	3	33
Mongoose	61	38	62
Other wildlife	168	12	7
Sub-total	407	156	38
Human	164	120	73
Total	**7584**	**4863**	**64**

The most frequently submitted samples from domestic animals for rabies diagnosis were from dogs, comprising nearly two-thirds (4527/7,013) while those from domestic ruminants (cattle, sheep and goats) made up 26% of the samples (1822/7,013). Among samples obtained from domestic animals the overall percent positivity was 65%, while the percent positivity from wildlife was 38% and from humans was 73%. Samples from cattle, goats, sheep, and horses returned a higher percent positivity compared to those from dogs and cats (Table 1). We could not find records for the number of samples submitted and the species they we prior to 1958.

Temporal distribution of rabies cases by species, 1958 – 2017

Analysis of the number of human and animal samples submitted and confirmed for rabies shows three periods with distinct patterns of rabies occurrence. First is the period from 1958 to the early 1970s where a relatively low number of cases were reported (<50 cases/year). The second is the period covering the 1980's and the early 1990's where more than >200cases were reported per year. The third period covers the mid 1990s to 2017 with approximately 100 confirmed cases reported per year (Figure 1). Analyses of the percent positivity data show a general increase over time in the proportion of samples submitted that were positive for rabies (Figure 2). The model estimates were 0.38 (95% CI 0.17, 0.59) increase in percent positivity per year. Over time, most positive cases were consistently confirmed in domestic animals, with the majority being domestic dogs (Figure 3).

Spatial distribution of rabies in Kenya, 1912 – 2017

Historical records show the first case of rabies was in a dog reported in the outskirts of Nairobi in 1912, and the first human case in a woman from the Lake Victoria region in 1928. Our data shows the reported cases were relatively low in numbers and confined to less than 10% of the counties until outbreaks that occurred in the 1940s and 1950s (Figure 4). Up until 1970, less than half of the counties were reporting rabies cases, and the proportion of samples found positive for rabies was low. The high number of confirmed cases observed in the 1980's (Figure 1) was accompanied by increased geographical spread of the disease affecting more than half the counties. Since the 1980's over 85% of counties in Kenya have consistently reported confirmed cases of rabies (Figure 4). Cumulatively, 6 of 47 counties (Nairobi, Machakos, Nakuru, Kiambu, Nyeri and Kericho) accounted for nearly two-thirds of all samples submitted and those found positive for rabies (Figure 5). Each of the six counties has either a veterinary laboratory that carries out FAT or is adjacent to a county with A laboratory with capacity for rabies testing.

Discussion

Here we have examined data from passive surveillance for rabies in humans and animals in Kenya for the period 1912 – 2017. Although the first official records of the disease date back to 1912, a decade after the establishment of the veterinary department in Kenya, rabies was likely present earlier as local communities in South Nyanza already used the name "swao" to refer to rabies in dogs and jackals[17]. We were unable to find any literature on the historical emergence of rabies in Kenya,
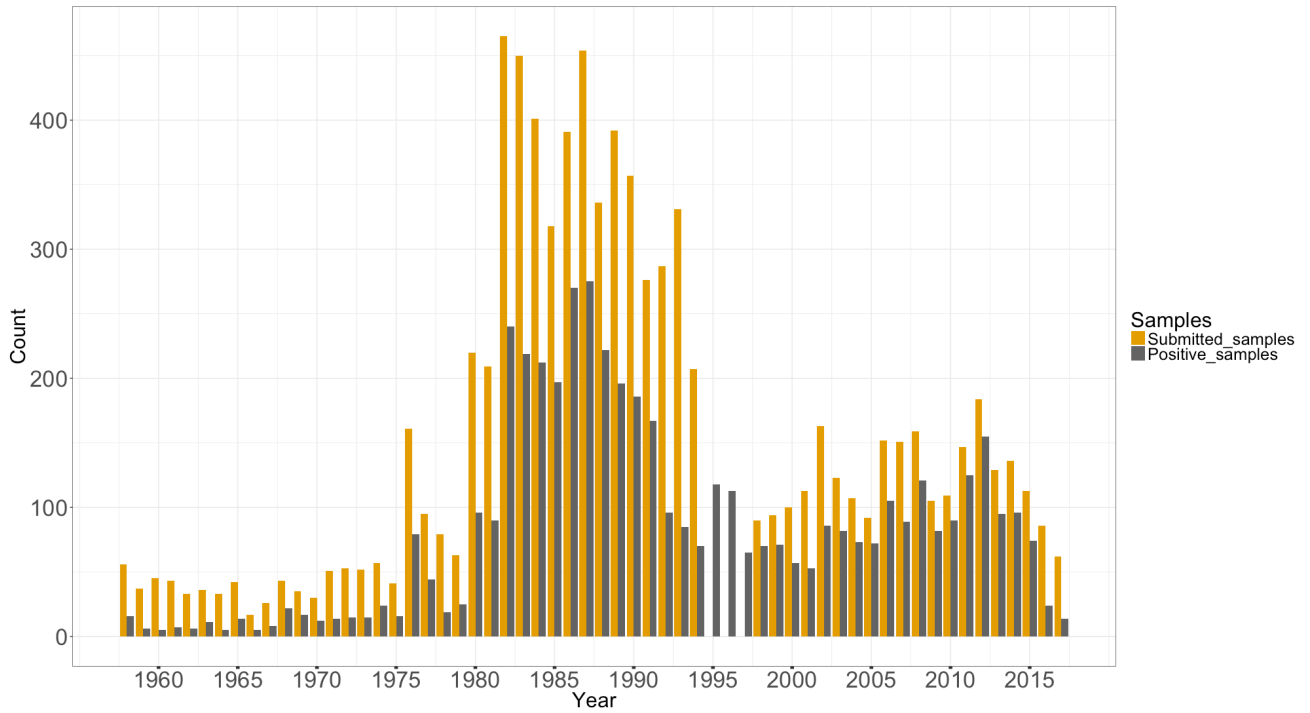
Figure 1. Trends in total submitted human and animal samples and confirmed rabies cases in Kenya from 1958 until 2017.
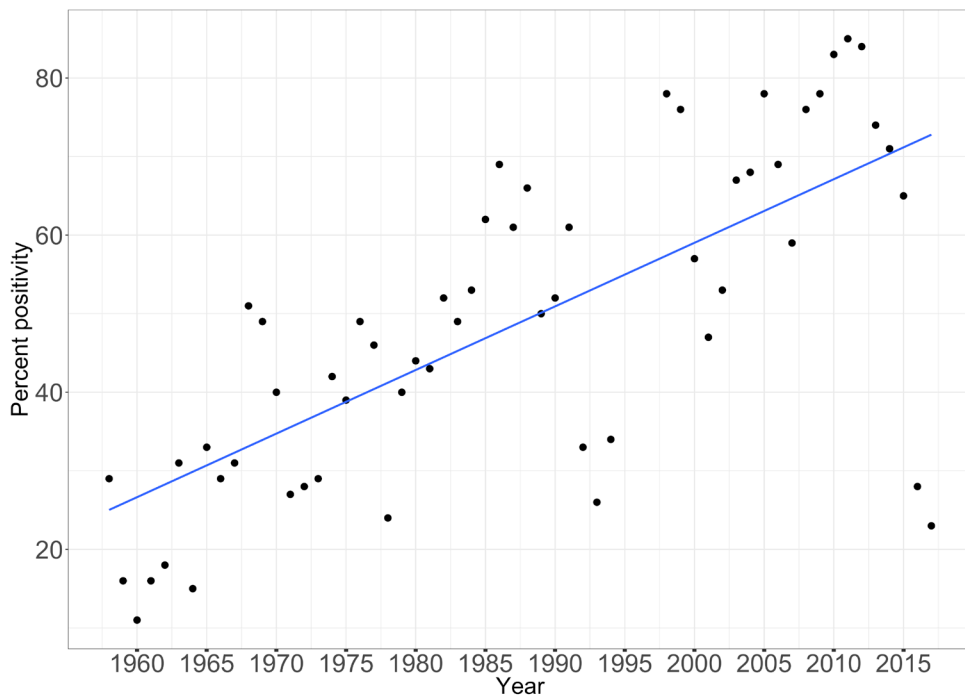
Figure 2. Figure showing the proportion of human and animal samples (%) submitted for rabies testing that were positive for each year 1958–2017. The proportion has steadily increased over time as shown by the regression line (blue). No records of samples submitted were available for the years 1995, 1996 or 1997.
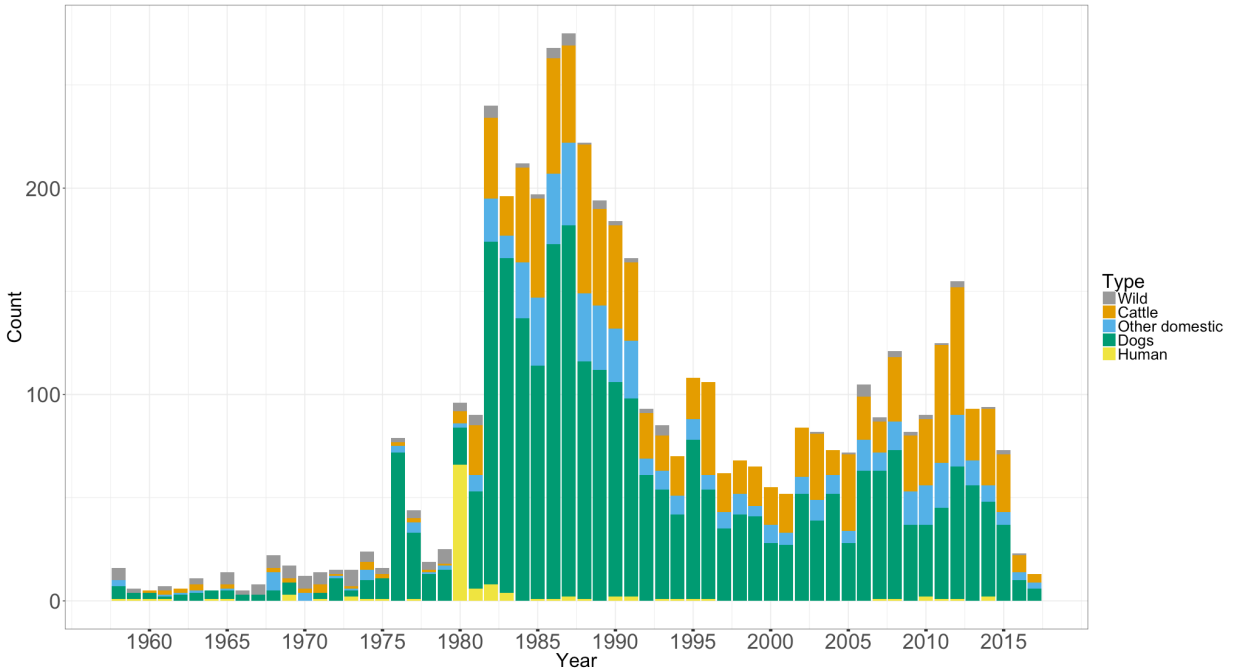
Figure 3. Trends of confirmed rabies cases by species for the period 1958 to 2017.

Figure 4. Spatial and temporal occurrence of human and animal rabies in Kenya, 1912 – 2017.
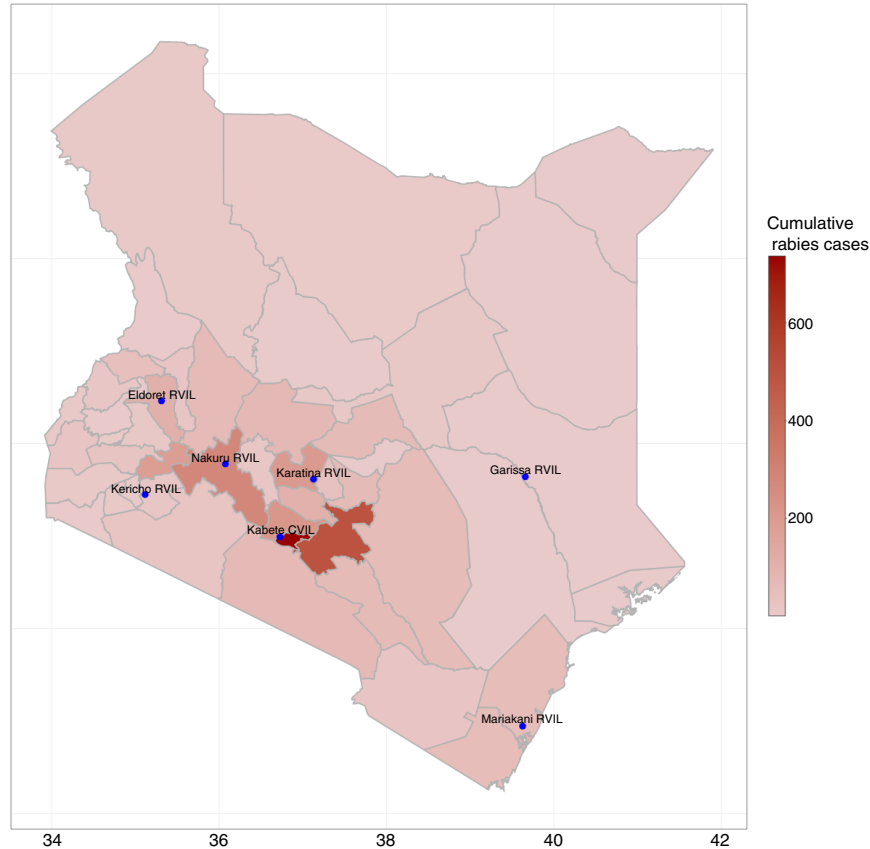
Figure 5. Distribution of confirmed human and animal rabies cases by counties, 1958 – 2017. The blue dots indicate the location of the seven veterinary laboratories (one central Veterinary laboratory and six regional investigative laboratories) in the country. The online version of this figure is interactive.

but phylogenetic analysis of rabies viruses in Tanzania show the circulation of two major genetic lineages one of which is thought to have originated from Kenya[18].

In the 20 years that followed detection of the first case in Kenya, only sporadic rabies outbreaks were reported in the central and north eastern parts of the country (Figure 4). By 1950 rabies was present in all counties in the present Western Kenya and was spreading eastwards. The data showed an increase in the number of samples submitted and those confirmed positive upon testing. These increases may be partly explained by changes in surveillance over time (i.e. rates of reporting over time with sample submission), increase in dog population or changes in the incidence of disease associated with rabies control efforts. The regional veterinary investigative laboratories were established within a period of 15 years starting with the laboratory in Nakuru in 1973 followed by Eldoret, Kericho, Garissa, Karatina and Mariakani in 1976, 1979, 1984, 1985 and 1987 respectively. The observed higher burden of rabies in 6 of 47 counties may represent a biased high incidence of rabies associated with close proximity to the regional veterinary investigative laboratories with diagnostic capacity for rabies.

The first systematic attempts to control rabies started with the introduction of a locally produced dog rabies vaccine in the 1950s.

Vaccines were delivered through compulsory annual vaccinations, with prosecution of dog owners who did not present their dogs for vaccination. This strategy is reported to have effectively controlled rabies incidence and spread observed until the early 1970s[8].

The rapid increase in the number of rabies cases detected and regions affected (from the mid 1970s to the mid 1980s) coincided with the implementation of the Structural Adjustment Policies (SAPs) that privatized veterinary services in Kenya[19]. The SAPs resulted in marked reduction in the provision of crucial public goods including decreased public funding for veterinary services. The veterinary sector was privatized with government employing fewer veterinary officers and providing reduced public financing for disease control and animal production. The result was a collapse of veterinary services including of the mass dog vaccination campaigns, which may have contributed to the spread of rabies across the country and resulting endemic status.

Data used in this manuscript comes from a passive surveillance system, and are likely a gross underestimate of the total human and animal rabies cases[1,20]. Previous studies in East Africa have identified poor surveillance systems and diagnostic capacity leading to underreporting as drivers of the cycle of neglect

for rabies[9,21,22]. The incidence of canine rabies estimated from passive surveillance has been estimated to be between one and two orders of magnitude less than estimates from active surveillance in Kenya and Tanzania[9,21].

In the last century, vaccination of dogs has led to the elimination of dog rabies in the U.S.A, Western Europe and elsewhere in the world (see Table 1 in [23]) and more recently in some developing countries[24,25]. The feasibility of dog rabies elimination in much of Africa is supported by findings that domestic dogs are the reservoirs of the rabies virus and not wildlife, and that most dogs can be reached for parenteral vaccination[3,26,27].

Although there is evidence rabies that can be eliminated, common misconceptions about rabies epidemiology and transmission among governments in endemic countries may be contributing to the inaction against rabies. These misconceptions that include that rabies is a low priority public health problem, that stray dogs play significant roles in the transmission of rabies, and that wildlife are important reservoir hosts have largely been dispelled through scientific data[4,28,29]. Given the evidence on the feasibility of rabies elimination, and the ranking of rabies as a top priority zoonotic disease in Kenya, the national government developed a 15-year joint human and veterinary sector strategic plan to progressively reduce the burden of rabies in the country with the goal of achieving elimination of dog-mediated human rabies in Kenya by 2030[13].

Strategic plan for elimination of dog-mediated human rabies in Kenya

The strategy is based on the Stepwise Approach to Rabies Elimination (SARE), a comprehensive risk-based framework that proposes a progressive reduction of disease risk, allowing for coordination of regional activities to achieve disease elimination[30]. Kenya's SARE consists of six stages, stage 0 to 5, with a set of activities at each stage building on the previous stage to continuously reduce the risk of disease, until the country is declared free of dog-mediated human rabies at stage 5 (Figure 6). The initial implementation of the strategy is being carried out in select pilot areas (five counties) to demonstrate success before scaling up to the rest of the country. The pilot areas (Figure 7, Zone A) were selected to include areas with a high burden of disease (see Figure 5 with the cumulative number of positive rabies samples by county), and areas with and without natural barriers e.g. water bodies and mountains to test the importance of natural barriers in restricting transmission within specific geographical areas. Kisumu and Siaya counties which have natural barriers (Lake Victoria region to the West and Nandi escarpment to the East) and Machakos, Kitui and Makueni Counties which have no defined natural barriers but have reported high numbers of dog and human rabies cases were selected. Experiences and lessons learnt from the pilot regions are being documented and will be used to inform subsequent program scale up to the rest of the country. Scaling up will begin with counties immediately bordering the pilot areas (Zone B) and moving to Zone C (Figure 7).
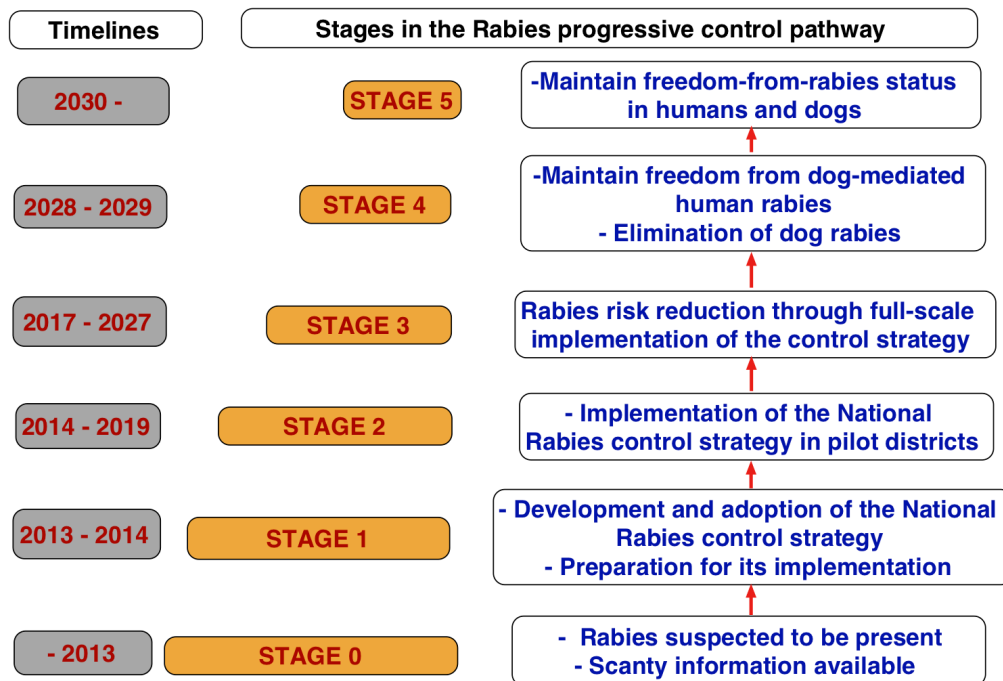

Figure 6. Stepwise Approach to Rabies Elimination (SARE) in Kenya, showing the six stages of the control strategy, associated activities and timelines.
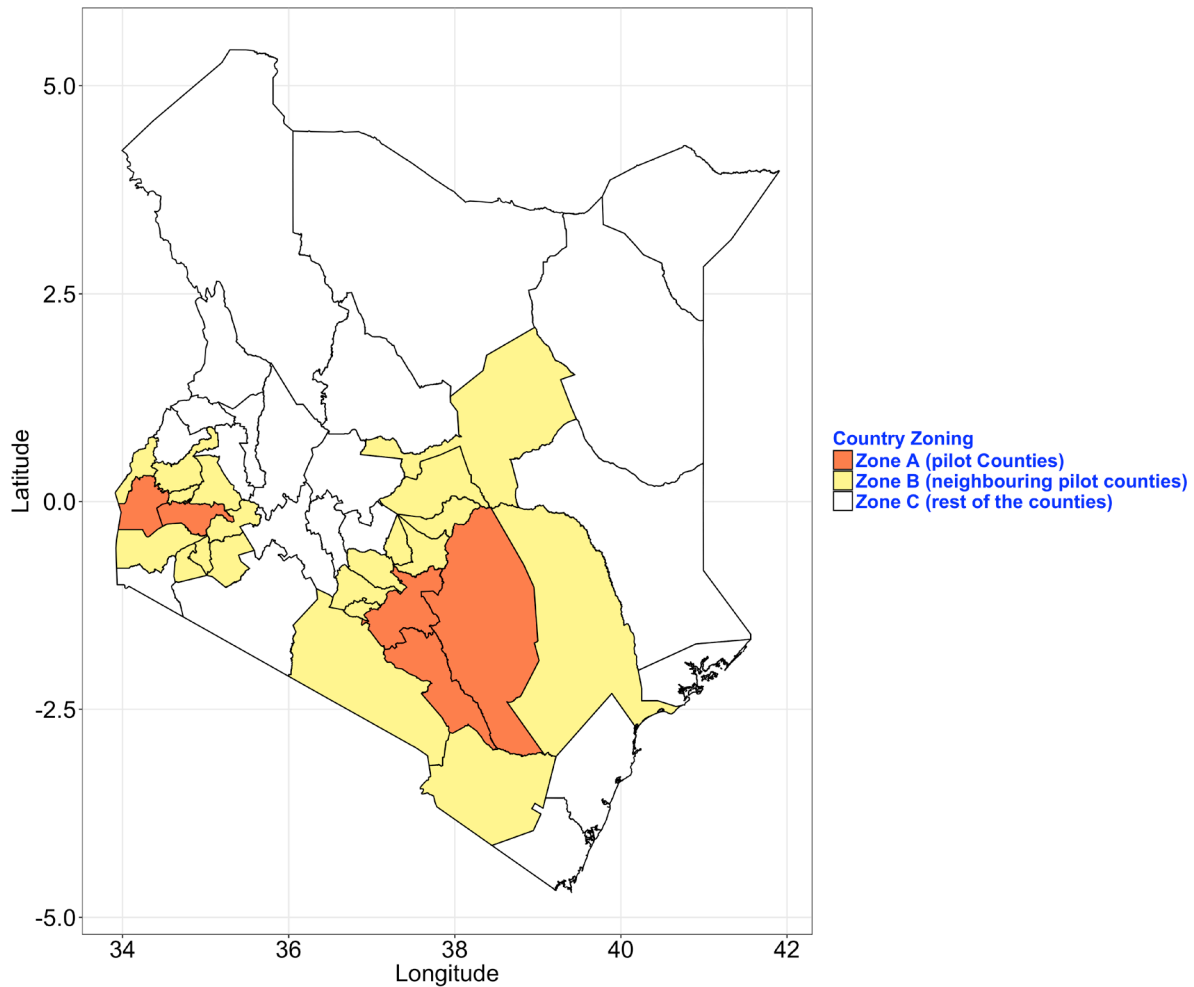
Figure 7. Map of Kenya showing the three zones for the implementation of rabies elimination program. Elimination starts in pilot counties (Zone A), followed by counties neighbouring them (Zone B) and later rolled out in the rest of the counties (Zone C).

The strategy hinges on three main pillars: a) elimination of rabies in dogs through mass dog vaccination, b) prevention of rabies in humans through increased access to post-exposure prophylaxis and public awareness, and c) improved surveillance for rabies in dogs and humans and response to outbreaks.

Domestic dogs are the main source of infection to humans[3,6]. The principal method for control of dog rabies is mass vaccination, which has been carried out successfully in many countries including Malaysia, Philippines, Tunisia, and those in Western Europe and North America among others. The OIE and the World Health Organization (WHO) recommends that, to achieve control and eventual elimination of dog rabies, programs must ensure that mass dog vaccination campaigns achieve vaccination coverage of at least 70% of the population in a given area, and that such campaigns are conducted annually for at least three years. This coverage, achieved during a campaign of relatively short duration and using high quality World Organization

for Animal Health (OIE) approved dog vaccines that provide long-lasting immunity, is sufficient to maintain the population immunity above the critical threshold for at least 12 months, despite dog population turnover due to births, deaths and migrations during this period without need for a booster dose within the year. This target coverage is supported by validations worldwide investigating the relationship between vaccination coverage and reductions in rabies incidence[27,31–33].

Evidence from Serengeti ecosystem in Tanzania suggests that domestic dogs are the only population essential for rabies maintenance[32]. From experiences in Western Europe and North America, rabies elimination in dogs has been successful despite the presence of wildlife hosts capable of transmission where mass dog vaccinations have successfully eliminated the disease from domestic dog populations[34]. Kenya's target is to vaccinate at least 70% of dogs in each region annually for at least 3 years to achieve elimination, followed by a maintenance phase with

an effective surveillance and outbreak response system. In addition, the national strategy objectives are to provide timely access to post-exposure vaccines for bite patients from suspect rabid dogs, increased public awareness on rabies and establishment of an effective surveillance system for both dog rabies and human rabies.

There is a now growing momentum among countries with endemic dog-mediated rabies to work towards its elimination supported by the Pan Africa Rabies Control Network (PARACON), which assists the coordination of rabies control networks for the different regions in Africa to collaborate and share experiences towards rabies elimination[30]. Kenya's strategy is in line with that advocated by the international agencies and builds on a solid body of evidence supporting the 2030 target for countries to have eliminated dog-mediated human rabies[14]. Data from Kenya has shown that, prior to the Structural Adjustment Program, rabies was relatively better controlled than currently. A functioning veterinary health care system is critical towards achieving rabies elimination. Countries endemic with the disease require to invest in the provision of veterinary services to have effective mass dog vaccination and rabies surveillance systems. Scientific evidence provides strong support that the disease can still be controlled today, and that zero deaths from dog-mediated human rabies by 2030 is a feasible goal for Kenya.

Data availability

The data underlying this study is available from Open Science Framework http://doi.org/10.17605/OSF.IO/B6WKR[35]. It contains two datasets - dataset 1: "KenyaRabiesData1958to2017.csv" that produces Figure 1, Figure 2, Figure 3 and Figure 5 and dataset 2: "100YearsRabiesData.csv" that produces Figure 4.

The R codes used are provided in a file named "Rcodes_100yearsRabiesinKenya.R". These datasets are available under a CC0 1.0 Universal license. No records of samples submitted were available for the years 1995, 1996 or 1997.

Disclaimer

The findings and conclusions in this paper are by the authors and views expressed in this publication do not necessarily represent the decisions, policy, or views of their institutions.

References

1. Hampson K, Coudeville L, Lembo T, *et al.*: **Estimating the global burden of endemic canine rabies.** *PLoS Negl Trop Dis.* 2015; **9**(4): e0003709.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

2. World Health Organization: **WHO fact sheet on rabies [Internet]**. 2018.
   Reference Source

3. Lembo T, Hampson K, Kaare MT, *et al.*: **The feasibility of canine rabies elimination in Africa: dispelling doubts with data.** *PLoS Negl Trop Dis.* 2010; **4**(2): e626.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

4. Cleaveland S, Beyer H, Hampson K, *et al.*: **The changing landscape of rabies epidemiology and control.** *Onderstepoort J Vet Res.* 2014; **81**(2): E1–8.
   PubMed Abstract | **Publisher Full Text**

5. Mallewa M, Fooks AR, Banda D, *et al.*: **Rabies encephalitis in malaria-endemic area, Malawi, Africa.** *Emerg Infect Dis.* 2007; **13**(1): 136–9.
   PubMed Abstract | **Publisher Full Text** | **Free Full Text**

6. Knobel DL, Cleaveland S, Coleman PG, *et al.*: **Re-evaluating the burden of rabies in Africa and Asia.** *Bull World Health Organ.* 2005; **83**(5): 360–8.
   PubMed Abstract | **Free Full Text**

7. Fèvre EM, Kaboyo RW, Persson V, *et al.*: **The epidemiology of animal bite injuries in Uganda and projections of the burden of rabies.** *Trop Med Int Health.* 2005; **10**(8): 790–8.
   PubMed Abstract | **Publisher Full Text**

8. Kariuki DP, Ngulo WK: **Epidemiology of Animal Rabies in Kenya (1900–1983).** *Rabies Trop.* Heidelberg, Berlin: Springer Berlin; 1985; 451–64.
   Publisher Full Text

9. Kitala PM, McDermott JJ, Kyule MN, *et al.*: **Community-based active surveillance** for rabies in Machakos District, Kenya. *Prev Vet Med.* 2000; **44**(1–2): 73–85.
   PubMed Abstract | **Publisher Full Text**

10. Obonyo M, Akoko JM, Orinde AB, *et al.*: **Suspected Rabies in Humans and Animals, Laikipia County, Kenya.** *Emerg Infect Dis.* 2016; **22**(3): 551–3.
    PubMed Abstract | **Publisher Full Text** | **Free Full Text**

11. Kemunto N, Mogoa E, Osoro E, *et al.*: **Zoonotic Disease Research in East Africa.** *BMC Infect Dis.* 2018; **18**(1): 545.
    PubMed Abstract | **Publisher Full Text** | **Free Full Text**

12. Munyua P, Bitek A, Osoro E, *et al.*: **Prioritization of Zoonotic Diseases in Kenya, 2015.** *PLoS One.* 2016; **11**(8): e0161576.
    PubMed Abstract | **Publisher Full Text** | **Free Full Text**

13. Republic of Kenya - Zoonotic Disease Unit: **Strategic Plan for the Elimination of Human Rabies in Kenya 2014 – 2030**. Nairobi, Kenya; 2014.
    Reference Source

14. Abela-Ridder B, Knopf L, Martin S, *et al.*: **2016: the beginning of the end of rabies?** *Lancet Glob Health.* World Health Organization; 2016; **4**(11): e780–1.
    PubMed Abstract | **Publisher Full Text**

15. OIE: **Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2013.** Paris; 2013.
    Reference Source

16. R Core Team: **R: A language and environment for statistical computing.** R Foundation for Statistical Computing, Vienna, Austria. 2017.
    Reference Source

17. Hudson J: **A short note on the history of rabies in Kenya.** *East Afr Med J.* 1944; **21**: 322–7.

18. Brunker K, Marston DA, Horton DL, *et al.*: **Elucidating the phylodynamics of endemic rabies virus in eastern Africa using whole-genome sequencing.** *Virus Evol.* 2015; **1**(1): vev011.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

19. Oruko L, Ndungu L: **An analysis of animal healthcare service delivery in Kenya.** *Institutional Economics Perspectives on African Agricultural Development.* Washington DC; 2009.
Reference Source

20. Taylor LH, Hampson K, Fahrion A, *et al.*: **Difficulties in estimating the human burden of canine rabies.** *Acta Trop.* Elsevier B.V.; 2017; **165**: 133–40.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

21. Cleaveland S, Fèvre EM, Kaare M, *et al.*: **Estimating human rabies mortality in the United Republic of Tanzania from dog bite injuries.** *Bull World Health Organ.* 2002; **80**(4): 304–10.
PubMed Abstract | **Free Full Text**

22. Nel LH: **Discrepancies in data reporting for rabies, Africa.** *Emerg Infect Dis.* 2013; **19**(4): 529–33.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

23. Hampson K, Dushoff J, Bingham J, *et al.*: **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.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

24. Cleaveland S, Lankester F, Townsend S, *et al.*: **Rabies control and elimination: a test case for One Health.** *Vet Rec.* 2014; **175**(8): 188–93.
PubMed Abstract | **Publisher Full Text**

25. Townsend SE, Sumantra IP, Pudjiatmoko, *et al.*: **Designing Programs for Eliminating Canine Rabies from Islands: Bali, Indonesia as a Case Study.** *PLoS Negl Trop Dis.* 2013; **7**(8): e2372.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

26. Lembo T, Hampson K, Haydon DT, *et al.*: **Exploring reservoir dynamics: a case study of rabies in the Serengeti ecosystem.** *J Appl Ecol.* 2008; **45**(4): 1246–57.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

27. Zinsstag J, Lechenne M, Laager M, *et al.*: **Vaccination of dogs in an African city interrupts rabies transmission and reduces human exposure.** *Sci Transl Med.* 2017; **9**(421): pii: eaaf6984.
PubMed Abstract | **Publisher Full Text**

28. Lankester F, Hampson K, Lembo T, *et al.*: **Infectious Disease. Implementing Pasteur's vision for rabies elimination.** *Science.* 2014; **345**(6204): 1562–4.
PubMed Abstract | **Publisher Full Text**

29. Lembo T, Haydon DT, Velasco-Villa A, *et al.*: **Molecular epidemiology identifies only a single rabies virus variant circulating in complex carnivore communities of the Serengeti.** *Proc Biol Sci.* 2007; **274**(1622): 2123–30.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

30. Scott TP, Coetzer A, De Balogh K, *et al.*: **The Pan-African Rabies Control Network (PARACON): A unified approach to eliminating canine rabies in Africa.** *Antiviral Res.* Elsevier B.V; 2015; **124**: 93–100.
PubMed Abstract | **Publisher Full Text**

31. Coleman PG, Dye C: **Immunization coverage required to prevent outbreaks of dog rabies.** *Vaccine.* 1996; **14**(3): 185–6.
PubMed Abstract | **Publisher Full Text**

32. Fitzpatrick MC, Hampson K, Cleaveland S, *et al.*: **Potential for rabies control through dog vaccination in wildlife-abundant communities of Tanzania.** *PLoS Negl Trop Dis.* 2012; **6**(8): e1796.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

33. Zinsstag J, Dürr S, Penny MA, *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.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

34. Hampson K, Dushoff J, Cleaveland S, *et al.*: **Transmission dynamics and prospects for the elimination of canine rabies.** *PLoS Biol.* 2009; **7**(3): e53.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

35. Thumbi M: **Rabies in Kenya.** *Open Science Framework.* Web. 2018.
http://www.doi.org/10.17605/OSF.IO/B6WKR

Open Peer Review

Current Peer Review Status: ✓ ✓ ✓ ✓

Version 2

Reviewer Report 25 February 2019

https://doi.org/10.21956/aasopenres.14005.r26769

✓ **Tariku Jibat Beyene** (iD)

[1] College of Veterinary Medicine, Center for outcome research and Epidemiology, Kansas State University, Manhattan, KS, USA
[2] College of Veterinary Medicine, Addis Ababa University, Bishoftu, Ethiopia

I thank the authors for a detailed revision of the manuscript. They have addressed my concerns and have considered suggestions/comments. This paper is worth reading for experts working in the field of rabies prevention and control.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 04 September 2018

https://doi.org/10.21956/aasopenres.13938.r26556

✓ **Bassirou Bonfoh** (iD)

[1] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire (CSRS), Abidjan, Cote d'Ivoire
[2] Afrique One-ASPIRE, Abidjan, Cote d'Ivoire

This paper is an historical or retrospective study that provide valuable information on the trend of

rabies since 1912 and how to eliminate the disease by 2030. The form is good and well structured and provides useful and relevant scientific information. The method is innovative.

Explain more how the data quality was performed. Were there comments in the annual reports to be considered? We would like to see the explained link between the structural adjustment of 80s and how that has impacted the outbreak. This will strongly support the proposed strategy. The structural adjustment has dismantled the public services and if we have to reconsider the success of early 70s intervention, we need to compare the current strategy with what has been done before (compulsory vaccination, local vaccine production...). Recommendations should also consider other causes of rabies suspicion (negative samples). The conclusion must comprise the re-organisation of veterinary services as well as the importance of data storage and archives in our countries. This can provide valuable information. We advise the authors to add in their conclusion vet services as key factor for rabies control. The spread of rabies is also due to the neglected aspect of the disease.

The comment attached does not alter the content but considered as minors issues to improve the paper

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

> Author Response 27 Nov 2018
> **Thumbi Mwangi**, Kenya Medical Research Institute, Nairobi, Kenya
>
> Many thanks for the very useful review comments and suggestions. We have addressed them and please find below some specific responses.

Data used in the study came from national records maintained at the central veterinary laboratory and were obtained as a compiled dataset with information on the geographic location and species the samples were obtained from, and the test results. Individual annual reports were not accessed or used.

We have provided details (Methods - Data collection – Paragraph 2) of how the data were obtained, reviewed, cleaned and used to create the dataset analysed in this manuscript.

Paragraph 4 of the discussion section has addressed the structural adjustment programs and their consequence on the provision of veterinary services and disease control including for rabies.

"The rapid increase in the number of rabies cases detected and regions affected (from the mid 1970s to the mid 1980s) coincided with the implementation of the Structural Adjustment Policies (SAPs) that privatized veterinary services in Kenya [19]. The SAPs resulted in marked reduction in the provision of crucial public goods including decreased public funding for veterinary services. The veterinary sector was privatized with government employing fewer veterinary officers and providing reduced public financing for disease control and animal production. The result was a collapse of veterinary services including of the mass dog vaccination campaigns, which may have contributed to the spread of rabies across the country and resulting endemic status."

We have included a statement in the conclusion on the importance of vet services in achieving rabies elimination.

"A functioning veterinary health care system is critical towards achieving rabies elimination. Countries endemic with the disease require to invest in the adequate provision of veterinary services to have effective mass dog vaccination and rabies surveillance system."

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 August 2018

https://doi.org/10.21956/aasopenres.13938.r26554

✔️ **Deborah J Briggs**
College of Veterinary Medicine , Kansas State University, Manhattan, KS, USA

This is an excellent review article detailing the history of rabies across Kenya. The 59 year data set that has been used for the analysis was extracted from laboratory submitted samples in Kenya beginning in 1958 and continuing through 2017. The authors have conducted a thorough analysis

of the available data and have explained both the weaknesses and strengths of their analysis. The authors clearly explain some of the contributing factors as to why rabies increased in Kenya in the past and why this deadly disease has been neglected despite having such a high case fatality rate. The authors conclude by detailing the 6 logical steps that Kenya is taking to eliminate rabies throughout the country. Their 15 year strategic plan follows the proven strategies and published recommendations of the WHO, OIE and other international organizations including most importantly, mass vaccination of dogs, improving the access of rabies biologicals for exposed patients, and increasing educational awareness on all levels of society. The paper also details the importance of the final stage of maintenance that includes surveillance on a national level. This paper fills a gap in the history of rabies in Kenya that has been absent until now. It also provides an example for other countries in Africa and elsewhere that are in the fight to prevent human rabies. This paper is a must read for all public health experts working in the field of rabies prevention.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Rabies prevention

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 27 Nov 2018
Thumbi Mwangi, Kenya Medical Research Institute, Nairobi, Kenya

Many thanks for taking time to review the work we present in this manuscript and for the encouraging comments.

Competing Interests: No competing interests were disclosed.

Reviewer Report 14 August 2018

Darryn L Knobel [ID]
[1] Center for Conservation Medicine and Ecosystem Health, Ross University School of Veterinary Medicine (RUSVM), Basseterre, Saint Kitts and Nevis
[2] Department of Veterinary Tropical Diseases, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, South Africa

This article reviews historical data on human and animal rabies in Kenya from 1912 to 2017, and gives a broad description of the spatial and temporal trends over this period. The authors also detail the strategy adopted by Kenya towards elimination of dog-mediated human rabies by 2030.

This is a well-written article that provides a useful synopsis of the available national data on rabies, a notifiable disease in Kenya. While limited by the passive nature of the surveillance system, the data have value in showing historical trends as well as the current status, and the authors are careful to acknowledge the limitations of the data.

My main comments concern the reproducibility of the results. From what I can make out, the available source data[1] is useful to replicate Figure 5 only (Distribution of confirmed rabies cases by counties, 1958-2017). The source data underlying Figures 1-4 do not appear to be available. The authors should make these available or provide a statement if there are issues preventing this.

More detail, either in the article or as metadata to the source files, is also necessary to describe how the dataset was compiled. For example, I know the administrative units in Kenya have not remained constant over the period of the study. How was this handled in attributing location to specimens?

There is a lack of detail in the paper regarding the distribution of rabies diagnostic laboratories which should be addressed, given the authors' assertion that this affects surveillance effort and creates bias. The county locations of the CVL and RVIL should be given, to allow the reader to relate this information to Figure 5 and the results presented in the section on spatial distribution of rabies. (For example, the Central Veterinary Laboratory is described as 'in Kabete' but in which county is it [relating to Figure 5]? The second paragraph of the Methods section states that specimens should be submitted to only two other regional laboratories that carry out the FAT [n addition to the CVL], namely Kericho and Mariakani, but in what county are these?) Other regional laboratories are mentioned in the second paragraph of the discussion, implying that these have strengthened the surveillance system, but do these laboratories conduct the FAT? Or are they only mentioned as an indicator of the improvements in the general surveillance system (not specific to rabies)? Why is there no evidence of submission bias around the Mariakani RVIL?

Although the paper is generally very well written, it would benefit from a further editorial review

with a critical eye. For example: the use of a comma separator for 1,000s is inconsistent between the first and second paragraph of the Results; apostrophes should not be used to form plurals of numbers such as "the 1950's" etc. (at least not according to the APA Style); the second and third sentences of the first paragraph of the Discussion should be combined; "US" should be written as "U.S.A." or in full in the 6th paragraph of the Discussion, and the writing in the 7th paragraph of the Discussion needs to be reviewed (e.g. "there is evidence *that* rabies can be eliminated"; ""may be may be contributing"; These misconceptions <u>that</u> include that rabies").

References
1. Thumbi M: Rabies in Kenya. *Open Science Framework.Web*. 2018. Reference Source

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 27 Nov 2018

Thumbi Mwangi, Kenya Medical Research Institute, Nairobi, Kenya

We have provided the two datasets:
- "KenyaRabiesData1958to2017.csv" that is used to produce Figure 1, 2, 3 and 5, and
- "100YearsRabiesData.csv" that is used to produce Figure 4.
The R codes for the analysis are also provided named "Rcodes_100yearsRabiesInKenya.R".
These datasets and R codes are available under the "Data availability" section of the manuscript

through the Open Science Framework - http://doi.org/10.17605/OSF.IO/B6WKR

More detail, either in the article or as metadata to the source files, is also necessary to describe how the dataset was compiled. For example, I know the administrative units in Kenya have not remained constant over the period of the study. How was this handled in attributing location to specimens?

We have included the statement below under the "Data Collection" section to clarify how we attributed location to the specimens submitted.

"We obtained records for the years 1912 – 2017 from the Kenya Directorate of Veterinary Services and extracted data on the number of samples submitted for rabies testing, dates of sample submission, animal species and humans, administrative units (counties/districts) where the samples came from, and test results. As the administrative units in Kenya have changed over time, each unit reported in the raw data was matched a current county. The analyses were conducted per existing counties to allow for consistency in reporting."

There is a lack of detail in the paper regarding the distribution of rabies diagnostic laboratories which should be addressed, given the authors' assertion that this affects surveillance effort and creates bias. The county locations of the CVL and RVIL should be given, to allow the reader to relate this information to Figure 5 and the results presented in the section on spatial distribution of rabies. (For example, the Central Veterinary Laboratory is described as 'in Kabete' but in which county is it [relating to Figure 5]? The second paragraph of the Methods section states that specimens should be submitted to only two other regional laboratories that carry out the FAT [n addition to the CVL], namely Kericho and Mariakani, but in what county are these?) Other regional laboratories are mentioned in the second paragraph of the discussion, implying that these have strengthened the surveillance system, but do these laboratories conduct the FAT? Or are they only mentioned as an indicator of the improvements in the general surveillance system (not specific to rabies)? Why is there no evidence of submission bias around the Mariakani RVIL?

We have included the location of the CVL and RVILs within Figure 5. Under the section "Data collection", we have clarified on the locations of the central and regional veterinary laboratories and how they operate in regard to rabies diagnosis.

"The samples can be sent to the Central Veterinary Laboratory (CVL) located in Nairobi County or to any of six Regional Veterinary Investigation Laboratories (RVIL). The RVILs are across the country in Nakuru, Eldoret, Kericho, Garissa, Nyeri and Kilifi Counties. After initial testing, all samples were further submitted to one of three laboratories: the Central Veterinary Laboratory (CVL), the Regional Veterinary Investigation Laboratories (RVIL) in Kericho in Western Kenya, or RVIL in Kilifi on the Coast. These three laboratories carry out the Fluorescent Antibody Test (FAT), which is the confirmatory rabies diagnostic test recommended by the World Organisation for Animal Health (OIE)[15]. The test results were reported against the sample's source species and county of origin."

The Mariakani RVIL is located at the Coast, a region with less cultural practice of keeping dogs associated with the predominant religion and could possibly explain the observation.

Although the paper is generally very well written, it would benefit from a further editorial review with a critical eye. For example: the use of a comma separator for 1,000s is inconsistent between the first and second paragraph of the Results; apostrophes should not be used to form plurals of numbers such as "the 1950's" etc. (at least not according to the APA Style); the second and third sentences of the first paragraph of the Discussion should be combined; "US" should be written as "U.S.A." or in full in the 6th paragraph of the Discussion, and the writing in the 7th paragraph of the Discussion needs to be reviewed (e.g. "there is evidence *that* rabies can be eliminated"; ""may be may be contributing"; These misconceptions <u>that</u> include that rabies").

Many thanks for highlighting these errors – these have been rectified.

Competing Interests: No competing interests were disclosed.

Reviewer Report 07 August 2018

https://doi.org/10.21956/aasopenres.13938.r26555

?

Tariku Jibat Beyene iD
[1] College of Veterinary Medicine, Center for outcome research and Epidemiology, Kansas State University, Manhattan, KS, USA
[2] College of Veterinary Medicine, Addis Ababa University, Bishoftu, Ethiopia

This study summarizes historical data on rabies in Kenya for 105 yrs and attempts to examine the patterns of rabies spread across the country, and the trends over time. A strategy adopted by Kenya towards the elimination of dog-mediated human rabies by the year 2030 was also discussed.

My compliments for such a great deal of work in gathering and summarizing a large dataset on rabies in Kenya.

Nevertheless, I have the following general and specific suggestion/comments.

General
- The study seems to be a mix of a research article (spatiotemporal part) and review (the Kenyan strategy) and lacks a rigorous method for both sections.
- The spatiotemporal part lacks detail on the method of data collection, analysis, and results. For example:
  The objective was to examine the pattern of rabies spread in the country from 1912-2017

but the data in Fig 1-3 shows only for 1958-2017. Thus I advise to clearly state that in the method section.
○ The Kenyan strategy aspect of the paper is not mentioned in the methods as well as results section. Was it based on personal opinion or systematic review/ literature search?
○ One of the evaluations guidelines of this manuscript asks if the authors provided the necessary data for others to replicate the study. I would recommend the authors to provide the data and R codes used in a usable format.
○ The fact that diagnostic labs were established at different times, comparing the number of samples submitted/tested positive could be tricky as the distance of countries forms labs, public awareness, lab capacities could have influenced it. For instance Figure 2 tells that the percent positive increased over time. Does it mean that the labs used improved methods over time?
○ As one of the objectives was to see the trend of rabies overtime, the method section does not explicitly show the method applied. The authors may consider statistical methods to explore the trend. However, a higher number of submitted/reported samples doesn't mean a high incidence of rabies. Thus, using mixed models where proximity to a lab, the age of the lab (which might have contributed to public awareness) should be included in the analysis to account for the clustering effect.

Specific
○ The statement "the first reported case in a dog in the outskirts of Nairobi in 1912, and in a woman from the Lake Victoria basin in 1928" was mentioned twice in the MS, one in the second paragraph of the introduction and second, under "spatial distribution of rabies in Kenya".
○ The last sentence of under the 'spatial distribution of rabies in Kenya" could move to discussions section.
○ I think it would be more explicit if table 1 contains info on the region from which the samples came and year.
○ Please make the distinction if numbers given on fig 1-3 are for dogs or all species? As dogs are major sources of rabies for human and others, a line graph or bar graph for all animal spp involved would show the contributions of each over time.
○ The third paragraph from the last, discuss " at least 70% of the population in a given area, and that such campaigns are conducted annually for at least three years. This coverage, achieved during a campaign of relatively short duration, is sufficient to maintain the population immunity above the critical threshold for at least 12 months". Could you add how often a booster dose should be provided with a cost-effective way to keep the incidence so low?
○ Figure 7, would be good if the names of zones/districts are labeled on the map.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Epidemiology of infectious diseases, the economics of disease control, food safety, antimicrobial resistance

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 27 Nov 2018
Thumbi Mwangi, Kenya Medical Research Institute, Nairobi, Kenya

The study seems to be a mix of a research article (spatiotemporal part) and review (the Kenyan strategy) and lacks a rigorous method for both sections. The spatiotemporal part lacks detail on the method of data collection, analysis, and results. For example: The objective was to examine the pattern of rabies spread in the country from 1912-2017 but the data in Fig 1-3 shows only for 1958-2017. Thus I advise to clearly state that in the method section.

We have provided a clarification for this correct observation under the data collection section (Methods).
For the period prior 1958, data on the number of samples submitted for testing and the species of animals they were obtained from were not available and only aggregate numbers of positive cases of rabies per year per county were available for analyses.

The Kenyan strategy aspect of the paper is not mentioned in the methods as well as results section. Was it based on personal opinion or systematic review/ literature search?

We have included a statement in the methods section on how the strategy was developed and provided a reference linking to the detailed strategy.

"This manuscript discusses the strategies put in place for the elimination of human rabies in Kenya by the year 2030. This strategic plan was developed through and elaborate consultative process that involved government departments in health and livestock, research and academic institutions, non-governmental organizations and international partners in Kenya working on public and animal health. The detailed strategy is available online13."

One of the evaluations guidelines of this manuscript asks if the authors provided the

necessary data for others to replicate the study. I would recommend the authors to provide the data and R codes used in a usable format.

We have provided the datasets and the R codes used for this manuscript under the "Data availability" section
"The data underlying this study is available from Open Science Framework
http://doi.org/10.17605/OSF.IO/B6WKR35. It contains two datasets - dataset 1:
"KenyaRabiesData1958to2017.csv" that produces Figure 1, 2, 3 and 5 and dataset 2:
"100YearsRabiesData.csv" that produces Figure 4. The R codes used are provided in a file named
"Rcodes_100yearsRabiesinKenya.R". These datasets are available under a CC0 1.0 Universal
license. No records of samples submitted were available for the years 1995, 1996 or 1997."

The fact that diagnostic labs were established at different times, comparing the number of samples submitted/tested positive could be tricky as the distance of countries forms labs, public awareness, lab capacities could have influenced it. For instance Figure 2 tells that the percent positive increased over time. Does it mean that the labs used improved methods over time? As one of the objectives was to see the trend of rabies overtime, the method section does not explicitly show the method applied. The authors may consider statistical methods to explore the trend. However, a higher number of submitted/reported samples doesn't mean a high incidence of rabies. Thus, using mixed models where proximity to a lab, the age of the lab (which might have contributed to public awareness) should be included in the analysis to account for the clustering effect.

We have carried out the analysis using mixed effect models to account for proximity to the testing
laboratories. We did not have any data on the changes in the sensitivies of the testing methods
or when the exact time when laboratories would have diagnostic methods. This is however
unlikely to have caused a major difference since rabies diagnostic methods using brain samples
have been known to have be fairly reliable. We tested models with and without the random effect
and the results were consistent – an increase in the proportion of samples submitted that were
positive for rabies.
We have provided details of the data analysis as below – within the methods section.
"We determined the proportion of samples submitted that were positive for rabies by year and for
each county. Linear mixed-effect models with year as the fixed effect, and the county as a random
effect (to account for proximity to testing laboratories) were used to test if the proportion of
submitted samples that were positive for rabies changed over time."

The statement "the first reported case in a dog in the outskirts of Nairobi in 1912, and in a woman from the Lake Victoria basin in 1928" was mentioned twice in the MS, one in the second paragraph of the introduction and second, under "spatial distribution of rabies in Kenya".
The statement under the "spatial distribution of rabies in Kenya" has been rephrased.

The last sentence of under the 'spatial distribution of rabies in Kenya" could move to discussions section.
We have moved the statement to the discussion section.

I think it would be more explicit if table 1 contains info on the region from which the samples came and year.

We have 47 regions in the country and including information on region, species and proportion of submitted samples would result in a long difficult to read table. We have however provided all the data as part of the supplementary files (see data availability section).

Please make the distinction if numbers given on fig 1-3 are for dogs or all species? As dogs are major sources of rabies for human and others, a line graph or bar graph for all animal spp involved would show the contributions of each over time.

We have amended the legend of Figures 1 and 2 to indicate these are from all human and animal samples available in our dataset.

Competing Interests: No competing interests were disclosed.