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Literature Review

CHALLENGES IN THE PREVENTION AND CONTROL OF RABIES DISEASE

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INFORMASI ARTIKEL

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Rabies; Disease: Rabies Disease: Literature Review

KORESPONDENSI

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A B S T R A K

Background: The death rate due to Rabies in Indonesia is still quite high at 100-156 deaths per year, with a Case Fatality Rate of almost 100 percent. This illustrates that rabies is still a threat to public health. Statistically 98% of rabies is transmitted through dog bites, and 2% of the disease is transmitted by cats and monkeys.
Purpose: make a literature review on rabies
Method: using the literature review method by looking for articles related to the rabies theme on Pubmed, so that 30 articles were obtained according to the theme and extracted
Result: Recognizing the disease's intricacy and manner of transmission might help to inform prevention and control approaches. The development and implementation of effective rabies elimination programs should involve veterinarians, public health professionals, physicians, ecologists, and vaccine manufacturers. Synchronization of operations through a multidisciplinary approach increases the likelihood of overcoming technical and infrastructural impediments to regional forces that drive disease management under the One Health concept.

INTRODUCTION

Rabies is a zoonotic illness that can infect all warm-blooded animals as well as humans. Rabies virus is transmitted through the saliva of rabies-infected animals and generally enters the body through initiation of rabid animal saliva containing the virus into a wound (e.g., a scratch) or direct exposure to the salivary mucosal surface of an infected animal (e.g. a bite). The rabies virus cannot penetrate or pass through the skin intact (without wounds). The rabies virus can proliferate further in the brain, resulting in clinical manifestations in individuals.

Rabies is present in 92 countries and is endemic in 72, according to the World Health Organization (WHO). It is estimated that 55,000 people die from rabies each year in the world, and according to WHO, more than 99 percent of cases of rabies in humans come as a result of a dog bite. Why do 50,000–55,000 people die from rabies each year around the world, with 25,000–30,000 deaths in India alone, and over 3 billion people still at danger of rabies virus infection in over 100 nations in the twenty-first century? These are staggering figures, especially given that they reflect people, many of whom are youngsters, who have been bitten or are expected to be attacked by rabid dogs, the primary source of rabies virus infection in many regions of the world that has yet to be eradicated. [32]

Rabies is still a major animal illness in Indonesia, and it is one of the infectious animal diseases that are strategic priorities due to the impact on socioeconomic and public health. Rabies in animals and people almost invariably results in death (case fatality rate 100 percent), hence this disease produces fear and anxiety in the population. Furthermore, rabies causes severe economic losses in the affected area, including high investigation expenses, high control costs, and high post-exposure treatment costs. And, as of yet, there is no effective rabies therapy medicine. [1] We analyze

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the existing control strategies, policies, programs, and actions aimed at minimizing canine-transmitted rabies in this review.

METHODS

The method used is literature review, literature review is a synthetic review and summary of what is known and unknown about the topic of a collection of scientific papers, including the current workplace in the existing knowledge [3]. The literature review uses the Pubmed database (https://pubmed.ncbi.nlm.nih.gov/) as a source of article searches. The articles used are articles from the last 10 years with a total of 30 articles reviewed. The article search strategy on Pubmed uses 3 keywords, namely: "rabies", "disease", "rabies disease". The working procedure of this literature review can be seen in Figure 1 below:

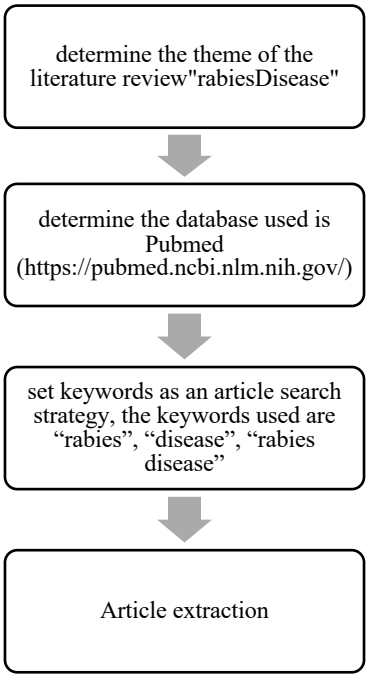

Figure 1: Literature Review Work Procedure

RESULT AND DISCUSSION

After obtaining 30 articles, then extraction of the articles was carried out, the results of the extraction from these articles were as follows:

No	Title/Years	Language	Objective of Research	Type of Research	Method of Collecting Data	Population and sample	Result
1	Estimation of the incidence of animal rabies in Punjab, India/ 2019	English	-	From August 15, 2016 to August 14, 2017, we studied canine and cattle populations in four sub-districts of Punjab, India.	From suspected rabies cases, demographic, clinical, and rabies diagnostic laboratory (RDL) data were collected. For each species, the yearly incidence rate / 10,000 animal years at risk (95 percent CI) was calculated in each sub-district.	-	During 2016–2017, a total of 41 suspected rabies cases were detected in four Punjab sub-districts. The incidence of laboratory confirmed rabies (LCR) in stray and pet dogs was 2.03/10,000 dog years (0.69, 5.96) and 2.71/10,000 dog years (1.14, 6.43), respectively. The incidence of LCR in farmed buffalo and cattle was 0.19/10,000 buffalo years (0.07, 0.57) and 0.23/10,000 cattle years (0.06, 0.88), respectively. The equine LCR incidence was 4.28/10,000 equine years (0.48, 38.10). The incidence of stray cow rabies in the selected sub-districts was 9.49/10,000 livestock years (3.51, 25.67). We predict that 98 (34–294) buffalo, 18 (2–156) horse, 56 (15–214)

							farmed cattle, 96 (35–259) stray cattle, 128 (54–303) pet dogs, and 62 (21–182) stray dogs would be confirmed with rabies in Punjab each year if similar enhanced surveillance for rabies was conducted state-wide. [2]
2	Knowledge, attitudes and practices regarding rabies and its control among dog owners in Kigali city, Rwanda/2018	English	The current study sought to better understand dog owners' knowledge, attitudes, and practices (KAP) on rabies and its control in Kigali, Rwanda.	cross-sectional survey	questionnaire	137	Of all the respondents, 58% had their dogs vaccinated at home by veterinarians while 86% indicated their veterinarians kept rabies vaccines on ice in a cool box. Multivariable logistic regression analyses indicated that none of the respondents' sex, educational level, and the length of dog ownership were statistically associated with their knowledge, attitudes and practices of rabies.[3]
3	Knowledge, attitudes and practices towards rabies: A survey of the general population residing in the Harare Metropolitan Province of Zimbabwe/2021	English	determine the province's rabies knowledge, attitudes, and practices	A cross-sectional survey	questionnaire	798	According to the findings of our study, the vast majority of respondents (92 percent) had heard of rabies. However, just 36% of respondents rated their rabies knowledge as "sufficient." According to the multivariate logistic regression analysis, pet ownership and occupation type were significantly associated with a greater grasp and awareness of the disease. 49 percent of the respondents owned at least one dog or cat, and suburb density and occupation were statistically associated with keeping a pet. 57 percent of pet owners saw an animal health practitioner at least once a year, and 75 percent were aware of a rabies vaccine for their pets. Age, education, and gender were statistically associated with pet owners taking their pets to an animal clinic, according to the multivariate logistic regression study. [4]
4	Challenges to the fight against rabies—the landscape of policy and prevention strategies in Africa/2021	English	In this analysis, we analyze the scope of canine-transmitted human rabies surveillance, prevention, and control initiatives in African countries	Review	MEDLINE, Global Index Medicus, BIOSIS, Science Citation Index, and EMBASE were used to search for literature published between 2014 and 2018.	-	Some level of rabies control and prevention strategy was available in forty nations, whereas no specific national control and prevention strategy for human rabies could be obtained in fourteen countries. Thirty-four countries used the Stepwise Approach to Rabies Elimination (SARE) tool to track national rabies control efforts; five of these countries were in the lowest tier of the SARE rating system, with no country achieving the highest score.

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							Countries with a high rabies burden must accelerate the implementation of context-specific national rabies control, prevention, and monitoring measures. Rabies control and elimination, as a zoonosis, necessitate collaboration between human and veterinary health sectors under the "One Health" banner, and with national master plans for the prevention and control of neglected tropical diseases expiring in 2020, the time to act is now. [5]
5	Rabies vaccination compliance and reasons for incompletion/2020	English	The goal of this study was to figure out why patients in the United States don't finish their rabies treatment.	retrospective study	medical chart review	198	During the inclusion period, 198 patients underwent rabies post-exposure treatment, according to the findings. The rabies vaccine regimen was completed by 145 of these patients. 29 patients had reasons for therapy discontinuation, and 24 were lost to follow-up. Of the 29 patients evaluated for discontinuation, 23 (79.3 percent) discontinued therapy for valid reasons - either the animal implicated proved negative for the rabies virus or the patient had prior rabies treatment and only required two booster doses. The patient's decision not to return for treatment, a lack of awareness of the whole vaccination protocol, and the patient's refusal to begin rabies vaccine were all reasons for not finishing the series when medically required.[6]
6	Rabies post-exposure prophylaxis in Germany-what are the challenges?/ 2021	English	The purpose of this study was to assess the demographic characteristics of R-PEP patients, the chosen regimen, adherence to this regimen, and documentation of wound care and tetanus prophylaxis at a German University Hospital.	retrospectively analysed	We documented the patients' demo-graphic and clinical information in an electronic database, focusing on the animal exposed to, classification according to RKI exposure category, and country of exposure.	90	During the trial period, R-PEP was administered to 90 patients at the University Hospital Bonn, with R-PEP not being indicated in 10 cases. In total, we discovered 51 percent (n = 41/80) departures from R-PEP norms. RIG infiltration was missed in 12 patients, and it was administered inappropriately in 24 others. In addition, 11 patients had the wrong immunization schedule. Correct wound care and documentation of tetanus status were absent in 14% and 63% of patients, respectively. Despite the fact that rabies has been eradicated in Germany, patients routinely seek R-PEP counseling, the majority of whom have

							returned from foreign vacation. [7]
7	Public health responses to reemergence of animal rabies, Taiwan, July 16-December 28, 2013/ 2015	English	The report describes the surveillance actions and the rapid public health reaction to the reemergence of rabies in Taiwan.	descriptive study reports	-	-	After evaluating 205 preserved CSF specimens taken between January 2010 and July 2013, researchers discovered no occurrences of human rabies. We received 8,241 rabies PEP applications from July 16 to December 28, 2013, and 6,634 (80.5 percent) were consistent with recommendations. Among the 6,501 people who received at least one dose of rabies vaccine after being bitten by a dog, 4,953 (76.2 percent) were bitten by dogs, whereas just 59 (0.9 percent) were bitten by ferret-badgers. Preexposure prophylaxis was given to 6,247 people during the research period. There were 23 cases of AEFI, but no anaphylaxis, Guillain-Barré syndrome, or acute disseminated encephalomyelitis were observed. During the study period, there were 40,312 contacts to the Taiwan Centers for Disease Control hotline, of which 8,692 (22 percent) were connected to rabies. The recent discovery of rabies in ferret-badgers in a previously rabies-free nation spurred a quick response. To date, no cases of human rabies have been identified. Continued multidimensional surveillance and intermenstrual collaboration are critical for Taiwan to achieve rabies-free status.[8]
8	Rabies Virus Infection in Eptesicus fuscus Bats Born in Captivity (Naïve Bats)/	English	-	-	-	-	To date, all rabies virus (RABV) studies in bats have been performed in wild caught animals. To determine the host response to a heterologous RABV, a separate group of naı̈ve bats were inoculated with a Lasionycteris noctivagans RABV (LnV1).[9]
9	Analysis of rabies in China: transmission dynamics and control./2011	English	Our research shows that I reducing dog birth rates and boosting dog vaccine coverage rates are the most effective means of limiting human rabies infection in China; and (ii) dog culling can be substituted	This study takes into account both canines and people.	-	-	The model simulations agree with the Chinese Ministry of Health's human rabies data. We estimate the basic reproduction number R02 for rabies transmission in China and anticipate that the number of human rabies is declining but may peak again around 2030. We also do some R0 sensitivity analysis in terms of model parameters and compare the effects of dog culling and

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			by dog immunization.				immunization. Our findings show that I reducing dog birth rates and boosting dog vaccine coverage rates are the most effective ways to manage rabies in China; and (ii) large-scale culling of susceptible dogs can be replaced by immunization.[10]
10	Rabies as a public health concern in India⇔a historical perspective/ 2020	English	-	review	-	-	As a result of these measures, rabies no longer constituted a substantial threat to the British, and it fell out of administrative and public health priority in India near the end of colonial rule—a fall that has yet to be reversed in modern-day India. The assessment also highlights aspects of British India's administrative, scientific, and sociological approaches to dealing with this disease that are still in place today. [11]
11	Role of oral rabies vaccines in the elimination of dog-mediated human rabies deaths/2020	English	-	-	-	-	ORV of dogs is one of the most underutilized methods in the battle against rabies. ORV is a critical instrument in the global elimination of dog-mediated human rabies mortality, and particular recommended efforts should be followed quickly to promote safe and cost-effective adoption of ORV. [12]
12	Incidence and Mortality from a Neglected Tropical Disease (Rabies) in 28 African Countries/ 2020	English	The objective of this study was to present the incidence and mortality rates from ra- bies in 28 African countries from 2005 to 2018	-	Second- ary data were obtained from the World Organization for Animal Health Database.	-	In the time period (2005—2018), the greatest combined rabies incidence and fatality was 1601 in 2006, while the lowest was 157 in 2005. Only five countries (Angola, Central African Republic, Kenya, Mozambique, and Senegal) accounted for 65 percent of rabies cases and deaths. Notably, the numbers on incidence and mortality were exactly the same. [13]
13	Challenges of rabies serology: Defining context of interpretation./2021	English	-	-	-	-	The high fatality rate of rabies, the virus's unusual pathogenesis, which allows for vaccination both before and after exposure to effectively protect, and laboratory testing capabilities all have an impact on the interpretation of rabies serology. The cut-off level chosen for a laboratory is determined by the laboratory method, the objective of testing, and the sample under research.[14]
14	Function of host protein staufen1 in rabies virus replication/2021	English	-	-	-	-	This study reveals that the host protein STAU1 was recruited to the NBs in RABV-

							infected cells and may play a role in host antagonism against rabies virus proliferation.[15]
15	Rabies epidemiology, prevention and control in nigeria: Scoping progress towards elimination/2021	English	-	scoping review	-	-	Studies conducted in areas distant from rabies diagnostic facilities accounted for more human rabies cases and fewer dog rabies cases. [16]
16	Public health implication towards rabies elimination in Sri Lanka: A systematic review/2021	English	conducted a systematic review of scientific literatures and data to assess current human and animal rabies control and prevention strategies in Sri Lanka.	Systematic review	-	-	Despite the nationwide standard of dog to human ratio of 1:8, there are huge disparities or unknown of dog ecology in regions. Awareness raising including has been enhancing for both general public and school children. Surveillance system is poorly operated so that simultaneous data analysis for decision-making is impractical [17]
17	Limited brain metabolism changes differentiate between the progression and clearance of rabies virus/ 2014	English	-	-	-	-	We believe that the increase in corticosterone is part of RABV's attempt to prevent the development of immunological responses that would otherwise impede its spread. In support of this idea, we show that in the absence of vaccination administration, pharmaceutical intervention to suppress corticosterone production greatly reduces RABV pathogenicity. [18]
18	On the use of phylogeographic inference to infer the dispersal history of rabies virus: A review study/2021	English	-	Review Study	-	-	a comparative meta-analysis of RABV lineage dispersal dynamics, re-analyzing data sets including diverse host species (raccoons, skunks, bats, and domestic dogs).. [19]
19	carrageenan P32 is a potent inhibitor of rabies virus infection/ 2015	English	-	-	-	-	The findings suggest that -CG P32 is a promising agent that can reduce RABV infection primarily by inhibiting viral internalization and glycoprotein-mediated cell fusion, and that it can be exploited to build innovative anti-RABV medicines. [20]
20	Evaluating the role of surgical sterilisation in canine rabies control: A systematic review of impact and outcomes/2020	English	-	A systematic review	-	-	The studies were contextually diverse, the programs being implemented were complex, and there was heterogeneity in key indicator measurement and reporting. As a result, given this evidence, it was difficult to compare the two methods of intervention and hard to assess the role of sterilizing.[21]
21	Human rabies: Neuropathogenesis, diagnosis, and management/2013	English		Review			Rabies is unique in that it has the greatest death rate of any viral encephalitide. Prospective treatment approaches include

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							temporary blood–brain barrier breach using ultrasound and microbubbles, therapeutic miRNAs or nanoengineered compounds, and generalised or localised brain cooling treatments. [22]
22	Rabies: A preventable but incurable disease/2017	English	-	-	-	-	In Japan, rabies has been eradicated for more than a half-century. However, rabies-free countries are extremely unusual. Traveling to Asian nations where many rabies victims still occur is simple and just takes a few hours by plane from Japan. Because Japanese tourists are rarely aware of rabies, they are at high risk of being bitten by a potentially rabid animal. Even if domestic human rabies cases are no longer reported in Japan, imported rabies cases are always possible. [23]
23	Quantifying the risk of rabies in biting dogs in Haiti/2020	English	-	-	-	-	The probability of rabies in a biting dog was greatly increased when the dog showed hypersalivation (OR = 34.6, 95 percent CI 11.3–106.5) or paralysis (OR = 19.0, 95 percent CI 4.8–74.8) and when the dog was dead at the time of the assessment (OR = 20.7, 95 percent CI 6.7–63.7). Lack of past rabies immunization, biting two or more persons, and being a puppy all raised the likelihood that a biting dog had rabies. When tested with validation data, the model demonstrated high sensitivity (100%) and specificity (97%). [24]
24	Human rabies a disease of complex/2002	English	-	Review	-	-	The treatment is strictly symptomatic, with the goal of reducing agitation and providing comfort to the patient and family. Fear of rabies is widespread among health-care workers, leading to subpar nursing care. Attending nurses and physicians who habitually care for rabies patients may require pre-exposure immunization, whereas other staff should only receive postexposure treatment if a true exposure occurs despite measures. Attempts to prevent fatal outcomes in the past have failed, with no spontaneous recoveries. A few survivors have been identified, all of whom were either pre-exposure or post-exposure

							therapy failures with severe consequences.[25]
25	Rabies elimination research: Juxtaposing optimism, pragmatism and realism/2017	English	-	Perspective	-	-	Recent rabies research has produced a solid body of evidence supporting the feasibility of eliminating canine rabies through widespread vaccination of household dogs. Global momentum is now rising toward the execution of large-scale programs to achieve, first, the abolition of human deaths caused by canine rabies, and, second, the interruption of trans- mission within the dog population and the abolition of canine rabies totally. However, time is running out to meet these worldwide targets. [26]
26	Postgenomics biomarkers for rabies - The next decade of proteomics/ 2015	English	-	Review	-	-	The growing results show that, in addition to the evident changes in proteins involved in synapse and neurotransmission, the majority of cytoskeletal proteins are also relevant, indicating neuronal degeneration. An intriguing finding is that certain molecules, such as KPNA4, may be possible rabies diagnostic indicators. Proteomic investigations involving body fluids such as cerebrospinal fluid, for example, bring fresh insights for antemortem diagnosis. To construct a comprehensive integrative biology picture, it is necessary to examine the entire CNS (regionally) and, in particular, the brain.[28]
27	Rabies in Asia: The Classical Zoonosis/2012	English	-	-	-	-	T The biggest challenge to controlling this costly endemic is a lack of motivation by authorities to address the issue, as well as a regional inability of public health and livestock (agricultural) officials to work together to address the issue. Rabies was one of the first known zoonoses, and it serves as a model for a real "One Health" management aim in which human, veterinary, and government officials must collaborate to battle this illness.[29]
28	Rabies. Relevance, Prevention, and Management in Travel Medicine/2012	English	-	-	-	-	Terrestrial rabies, often known as bat rabies, is found in practically every country on the planet. Travelers are at risk of being bitten in enzootic areas; the rabies infection risk for the particular traveler and the indication for preexposure

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						prophylaxis must be considered on an individual basis. Preexposure prophylaxis consists of one intramuscular or one intradermal injection on each of days 0, 7, and 21 (or 28). Postexposure prophylaxis must be administered as soon as feasible (within 24-48 hours) after interaction with a potentially rabid animal. Antirabies immunoglobulin is difficult to obtain in many parts of the world. 2/3 of all travelers[30]
29	Epidemiology, Impact and Control of Rabies in Nepal: A Systematic Review/2016	English	Systematic review	-	-	Different state and non-Over the years, governmental actors have undertaken rabies control measures, but these efforts have often been focalized, of limited duration, and uncoordinated. At the moment, communication and cooperation between veterinary and human health authorities is poor, hampering rabies control in Nepal. The reporting biases for both human and animal rabies, the ecology of stray dog populations, and the true role of the sylvatic cycle are all important study gaps.[31]

The equine LCR incidence was 4.28/10,000 equine years (0.48, 38.10). The incidence of stray cow rabies in the selected sub-districts was 9.49/10,000 livestock years (3.51, 25.67). According to the findings, 99.5 percent of those polled knew at least one host susceptible to rabies. According to multivariable logistic regression analysis, none of the respondents' sex, educational level, or length of dog ownership were statistically associated with their rabies knowledge, attitudes, and practices. [3].

According to the findings of our study, the vast majority of respondents (92 percent) had heard of rabies. There was some level of rabies control and prevention strategy available in forty countries (40/54), but no specific national control and prevention strategy for human rabies could be retrieved in fourteen (14/54) countries. Countries with a high rabies burden must accelerate the implementation of context-specific national rabies control, prevention, and monitoring measures. Of the 29 patients evaluated for discontinuation, 23 (79.3 percent) discontinued therapy for valid reasons - either the animal implicated tested negative for the rabies virus or the patient received prior rabies treatment[6].

During the trial period, R-PEP was administered to 90 patients at the University Hospital Bonn, with R-PEP not being indicated in 10 cases. Despite the fact that rabies has been eradicated in Germany, patients routinely seek R-PEP counseling, the majority of whom have returned from foreign vacation. We received 8,241 rabies PEP applications from July 16 to December 28, 2013, with 6,634 (80.5 percent) being compliant with recommendations. Preexposure prophylaxis was administered to 6,247 people during the research period. Previous research has shown that the presence of VNA after a natural or experimental inoculation is frequently transient[11].

Despite the fact that the objective of eliminating human deaths from dog-mediated rabies by 2030 was just recently defined, increased dog vaccination programs and access to human vaccines during the last century has resulted in a 98 percent reduction in global human rabies deaths (14). The remaining 2% constitute the traditional "final mile," and removal has proven more challenging due to a variety of infrastructural, financial, and sociodemographic concerns. In the time period (2005—2018), the greatest combined rabies incidence and fatality was 1601 in 2006, while the lowest

was 157 in 2005. As a result, additional efforts should be made to do research on rabies prevention and treatment [13].

The high fatality rate of rabies, the virus's unusual pathogenesis, which allows for vaccination both before and after exposure to effectively protect, and laboratory testing capabilities all have an impact on the interpretation of rabies serology. The cut-off level chosen for a laboratory is determined by the laboratory method, the objective of testing, and the sample under research. The prevalence of rabies virus antigen detection ranged from 3% to 28%, with more studies in the north. [5]

Similar to Talbi et al., they emphasized the role of human activities in the high diffusivity of RABV in domestic dogs. Given the enormous number of vaccination and sterilisation programs carried out over the world, the dearth of papers accessible for analysis reveals a deficit in data collecting or reporting, which is critical for impact assessment. There are significant knowledge gaps about the impact of sterilizing alone, as well as the subsequent consequences on rabies transmission and control [23].

The probability of rabies in a biting dog was greatly increased when the dog showed hypersalivation (OR = 34.6, 95 percent CI 11.3–106.5) or paralysis (OR = 19.0, 95 percent CI 4.8–74.8) and when the dog was dead at the time of the assessment (OR = 20.7, 95 percent CI 6.7–63.7). Lack of past rabies immunization, biting two or more persons, and being a puppy all raised the likelihood that a biting dog had rabies. Treatment is purely symptomatic, with the goal of reducing agitation and comforting the patient and family. Attempts to prevent fatal outcomes in the past have failed, with no spontaneous recoveries.[27]

CONCLUSION

Our findings are consistent with past analyses that have found a lack of capacity in Africa to prevent and control canine-mediated rabies. The very little attention paid to integrated rabies control and prevention makes the global goal of attaining rabies elimination by 2030 problematic. The bulk of NTD master plans or national plans will expire in 2020, therefore now is the time to act.

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