



BMJ Open Rabies mortality and morbidity associated with animal bites in Africa: a case for integrated rabies disease surveillance, prevention and control: a scoping review

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ABSTRACT

Objective The objective of this scoping review was to map the current situation and available evidence and gaps on rabies morbidity, mortality, integrated rabies surveillance programmes, and existing prevention and control strategies in Africa.

Methods We conducted a systematic scoping review following the Joanna Briggs methodology and Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews checklist. Medline, Embase, CINAHL (EBSCOHost), Scopus, Web of Science and rabies web conferences were used to search for peer-reviewed publications between January 1946 and May 2020. Two researchers reviewed the studies and extracted data based on author (year) and region, study design and data collection duration, participants/comparators, interventions, control conditions/exposures and outcomes (rabies mortality and morbidity) and key findings/gaps/challenges. The results were reported narratively using Arksey and O'Malley's methodological framework.

Results Electronic search yielded 2775 records, of which 43 studies were included. A total of 543 714 bite victims were censored through the included studies. Most of the victims were less than 15 years of age. The studies included rabies morbidity (21) and mortality (15) fluctuating in space and time across Africa depending on countries' rabies prevention and control practices (16). Others were surveillance (nine studies); surveillance and prevention (five studies); management and control (seven studies); and surveillance, prevention and control (six studies). We found challenges in rabies reporting, existing dog vaccination programmes and post-exposure prophylaxis availability or compliance.

Conclusion This study found challenges for dog rabies control and elimination in Africa and the need for a policy to drive the goal of zero dog-transmitted rabies to humans by 2030.

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Strengths and limitations of this study

- We conducted an extensive search of published and grey literature to identify studies to include in the scoping review.
- Pulling together data from both published and grey literature from the Ministries of Health gave us an opportunity to understand the breadth of rabies epidemiology and how surveillance, prevention and control would be a critical tool in implementing effective control of rabies across Africa.
- We conducted screening of identified articles and extraction of data in duplicate.
- We reported the results narratively as it was not possible to combine data from different studies conducted using different study designs and different population groups.

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BACKGROUND

The natural history of rabies disease in Africa is not well known, but it is well accepted that the disease must have been present in northern Africa for hundreds of years, particularly as an urban dog disease and was also associated with cycles in the Middle East.¹ European colonisation influenced the spread of dog rabies in Western and Central Africa.² In many sub-Saharan African countries, rabies has become enzootic only in the 19th and

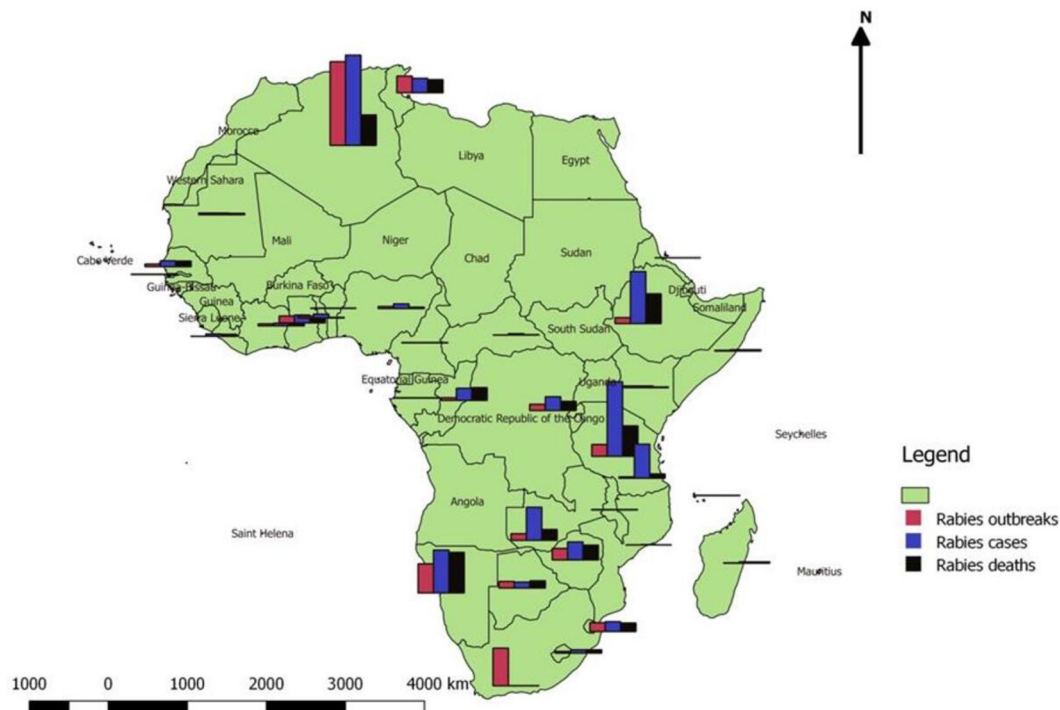


Figure 1 Human rabies distribution in 32 African countries (2011).

20th centuries involving domestic dogs and free-ranging wildlife species.^{1–3}

More than 59 000 people die of rabies worldwide every year,⁴⁵ 99% of them in African and Asian countries where dog rabies is endemic.^{4 6–10} Due to the lack of laboratory confirmation, sporadic epidemiological surveillance and unreported clinical cases in developing countries, current mortality estimates almost certainly under-represent the true incidence of human rabies deaths.^{4 8–10} Rabies is responsible for an estimated 21 000–25 000 deaths annually in Africa.^{4 11 12} Figure 1 shows a map illustrating rabies distribution in 32 African countries considering rabies outbreaks in animals, cases and deaths in humans.¹³ In 2011, a total of 33 African countries reported 1607 outbreaks of rabies, 2779 cases and 1524 deaths.¹³ Data show that rabies accounts for 7.2% of all animal disease outbreaks reported, making it the disease with the highest number of outbreak reports in Africa in 2011.¹³ Algeria, Namibia, Eswatini (former Swaziland), Tunisia, Uganda, Zambia and Zimbabwe reported high morbidity and mortality with 563 cases (33.9% deaths), 269 cases (94% deaths), 62 cases (88.7% deaths), 91 cases (90% deaths), 466 cases (40.9%), 207 cases (32.8% deaths) and 114 cases (80.7% deaths), respectively.¹³

Dog rabies predominates throughout most of Africa; the domestic dog is the principal reservoir host as well as the most important source of infection for people.¹⁴ In addition, there are many other lyssaviruses (also referred to as rabies-related viruses) reported from African countries. Most of these rabies-related viruses have been associated with obscure hosts including specific bat species and shrews, partly attributable to the difficulty in biosurveillance of these viruses. RABV, however, spreads in terrestrial

mammalian hosts in Africa and has not been associated with bat infections as it is the case in the Americas. While all mammals (domestic and wild) are susceptible to RABV infection, some are able to retain those virus variants adapted to their species while others are only reported as dead-end hosts.¹⁵ Rabies has been reported in both domesticated species and wildlife. These are sometimes diagnosed with rabies virus infection in Zambia, South Africa, Ethiopia, Kenya, Tanzania, Zimbabwe and Egypt.^{15–21}

Most reported cases of rabies in wild carnivorous species included yellow mongoose (*Cynictis penicillata*) and bat-eared fox (*Otocyon megalotis*)²² as well as critically endangered wild dogs (*Lycan pictus*).^{19 23–25} In Ethiopia, rabies outbreaks were described in the endangered Ethiopian wolf (*Canis simensis*) population.^{26 27} In 2014 and 2015, RABV infection was also observed in two wild dogs and a spotted hyaena (*Crocuta crocuta*) in the Madikwe Game Reserve, North West Province of South Africa, in Ethiopia and in Nigeria,^{21 25 28} monkeys and jackals (*C. adustus* and *C. mesomelas*).^{16 17 20 21} The review of 20 studies across Africa has revealed that bite victims account for 91.9% (48 092 dog bites), cat bite for 2.9%, jackal bite for 0.8% and 4.41% for others (monkey, donkey, horse, rat, pig, rabbit, Honey badger, kudu, goat, cattle, eland and hyaena).^{29–48}

Mass vaccination of dogs as a key component of national rabies elimination programmes has been successful in eliminating dog-transmitted rabies in Europe, North and Latin America, and Japan.^{49–51} By far, the most significant public health threat comes from RABV, and over 99% of all globally reported human cases are caused by exposure to unvaccinated dogs infected with canine RABV variant, mostly in Asia and Africa.⁵²

In most of Africa, and specifically Western and Central African countries, notification of rabies disease is not mandatory, so epidemiological data are scarce.⁵³ Human rabies could be prevented by the immediate administration of post-exposure prophylaxis (PEP) following exposure to rabid animals.^{5 45} However, people in low-income countries often do not receive these life-saving treatments because either PEP treatment is costly and not readily available, or because of lack of rabies awareness, people might not go to hospital for treatment.^{5 9 54} The lack of effective educational outreach at community level had led to gaps in knowledge as to the best way to avoid animal bites and administer first aid following bites or other potential rabies exposures.⁵⁵ A recent study has shown considerable in-country variability in the availability of rabies vaccines and immunoglobulin vaccine supply system, administration route (intramuscular (IM) vs subcutaneous (SC), cost of vaccine and rabies immunoglobulin (RIG). In a global survey conducted in rabies-endemic countries, 49 of the 54 African countries were rated as moderate to high risk for human rabies, while 16 of the 23 countries that responded to the survey had inadequate surveillance systems.^{12 56}

One major barrier is the difficulty of consistently achieving the required coverage of 70% of the dog population across the hard-to-reach landscapes that characterise much of sub-Saharan Africa.⁵⁷⁻⁵⁹ Reviewing dog vaccination coverage in African countries, only South Africa, Tanzania, Algeria, Morocco and Egypt had the dog vaccination coverage of 63%, 37.24%, 23.7%, 25% and 23.7%, respectively.^{60 61} In all other African countries, dog vaccination coverage was below 18% with further below 5% in some cases.⁶⁰ The analysis of the above data and the consideration of the framework for the elimination of dog rabies suggested by Wallace *et al* and others stipulated the existing coverage of dog rabies vaccination, that was directly associated with the number of years it would take to achieve rabies elimination.⁶² Theoretically, Global Dog Rabies Elimination Route consisting of a 13-year time frame would be an ample time for even the least developed rabies prevention systems to achieve elimination by 2030 if completely committed to this achievement.⁶² This system divided countries into three categories: (1) phase I—preparation (dog vaccination >18%), (2) phase II—vaccination of dogs (dog vaccination: <18% and >70%) and (3) phase III—70% continued vaccination of dogs. African countries have been categorised into phase I, II and III but with no data on dog vaccination.⁶³ The available data indicate that most African countries were still at the preparation phase since ‘zero rabies by 2020’ was initiated 5 years ago. Although the feasibility of reaching 70% dog vaccination coverage has been shown through pilot projects in a wide range of settings, African countries still struggle to achieve a 70% yearly dog vaccination rate.^{10 14} In Africa, dog mass vaccination systems have demonstrated some effectiveness as a proof of principle in countries such as South Africa,⁴⁹⁻⁶⁴ Tanzania,^{49 65-67} Malawi^{49 68} and Chad.^{54 69-71}

Inadequate education for veterinarians and physicians, insufficient resources for proper confirmatory diagnosis and risk assessment, and the lack of effective communication channels between Ministries of Health and Agriculture frequently have led to failures of prophylactic intervention, even in regions where vaccines and immunoglobulins were available.⁵⁵ A recent study conducted in Africa and Asia revealed that RIGs were found to be less available than the vaccine, with access restricted in almost two-thirds of the countries surveyed.⁷² Eleven (11) African countries had comprehensive access to RIG. Of the seven countries with broad access to vaccines, six of them had a national rabies prevention programme or policy. Two of the countries had only a monitoring programme/strategy in place.⁷² This is worrisome as it exposes a huge absence of surveillance and prevention policies in most African countries. The absence of a robust monitoring process is mostly attributed to the lack of rabies in national communicable disease plans and reporting systems at national level in Africa.⁷³ Therefore, widespread under-reporting is likely to occur in many affected countries due to lack of health information, civil registration and vital statistical systems, and inaccessibility of clinical care and diagnostic confirmation⁷³ as symptoms of the disease may be non-specific and similar to other encephalitic infections. Even where data exist in Africa, the lack of communication and exchange of data between the animal and human health sectors also hinders the collection, storage and reporting of coherent data to international databases.⁷³ The WHO meeting in Geneva in 2018 on ‘Moving Progress towards Rabies Elimination’ pointed out that political engagement is a key factor with governments providing leadership role in the coordination of elimination strategies.¹² The global collection of data on deaths from any neglected disease is a huge challenge, and early attempts to collate data for human deaths from canine rabies were no exception.⁷⁴ Due to the lack of regular reporting of rabies cases to the WHO from many member states, the RabNet Database was closed down in 2011.⁷⁵ Therefore, rabies is not reportable in many African countries, which restricts data collection by structured surveillance systems.⁷³ One Health evolved from the recognition that an interdisciplinary approach is required to understand complex health problems, and that the health of humans and animals is inextricably linked.⁷⁶ Rabies requires a comprehensive, strategic, and targeted control and prevention approach with collaboration from human, animal, and environmental health disciplines at local, national, and global levels to achieve more effective control.⁷⁷ In fact, most of African countries lack a One Health approach to prevent human rabies deaths.⁷⁸

The WHO, the World Organization for Animal Health (OIE), the Food and Agriculture Organization and the Global Alliance for Rabies Control (GARC) have developed a strategic global plan to end canine-mediated rabies by 2030.^{7 12 79} This initiative provides a concerted approach to the prevention of rabies, combined with the strengthening of human and veterinary health systems.

These would enable reaching out to the most underserved communities in the world by engaging, encouraging and supporting all countries to lead and improve elimination efforts.⁷³ This scoping review was therefore designed to map the evidence on rabies morbidity, mortality, integrated rabies surveillance, prevention and control in African countries. Its objectives were: (1) to assess the extent of available research on the morbidity and mortality of rabies due to animal bites conducted in Africa; (2) to identify research gaps in the literature on the impact of rabies in Africa so as to effectively plan public health intervention; (3) to ascertain the current level of rabies disease surveillance, prevention and control that exists in African countries; (4) to assess the published adverse events and complications associated with human rabies vaccination in African countries; (5) to assess the different types of vaccines used and the effectiveness of locally produced and imported vaccines in treating rabies in different parts of Africa; and (6) to assess rabies morbidity and mortality associated with dogs and contact with a suspect animal in humans.

METHODOLOGY

Study design

This paper used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews checklist⁸⁰ and the Joanna Briggs Institute guidelines⁸¹ as a norm for reporting scoping reviews. The analysis was conducted in accordance with the structure suggested by Arksey and O'Malley,⁸² further developed by Tricco *et al.*⁸³

Eligibility criteria

The search was conducted from 1 January 1946 until 30 May 2020. A PICO (Population/Interventions/Comparisons/Outcomes) search framework was set, where P (humans infected with rabies in African countries), I (integrated rabies disease surveillance, prevention and control), C (little or no integrated rabies disease surveillance, prevention and control) and O (reduced human morbidity and mortality of rabies associated with animal bites) were chosen. The included studies are described in online supplemental table 1.

Electronic search

We conducted a systematic search of the electronic databases Medline (OVID), Embase (OVID), CINAHL (EBSCOHost), Scopus (Elsevier), Web of Science and web conferences (rabiesalliance.org, www.who-rabies-bulletin.org and <https://www.oie.int/>). The search techniques were limited to English. The main search strategy was listed in online supplemental material 1. EndNote V.X9 reference manager was used to remove duplicates. JLT reviewed all the papers identified by title in order to pick those that were potentially appropriate, with a clear bias towards retention. The abstracts of all the studies chosen on the basis of their titles were independently reviewed by two

reviewers (PN and JLT) and any variations were preserved in the study.

Data charting process

For all studies selected at the abstract level, data were extracted and plotted in the table, covering author (year) and region, study design and data collection duration, participants/comparators, interventions and control conditions/exposures, outcomes (rabies mortality and morbidity), and key findings/gaps/challenges. The final decision to include studies was taken on the basis of this data extraction and whether it met the inclusion/exclusion requirements, based on an independent review by two authors (PN and JLT) and a discussion of any differences; the third author (RT) was available for consultation if consensus could not be reached. Our inclusion criteria were the following: rabies occurrence or mortality rates, all ages included, only studies performed in Africa, studies in which at least one intervention included monitoring, prevention and control of rabies, and only quantitative studies.

A data extraction sheet has been developed and used to extract data from included papers. The data collection sheet included: author, region, year, study design, level of evidence, sample size description, interventions or exposures, results, and key findings/gaps/challenges. Two reviewers (PN and JLT) worked separately at all levels of the study. The results were then compared and any variations were addressed and resolved by PN and JLT. The third author (RT), who also summarised the findings, was consulted when a discrepancy could not be resolved. The evaluation of the probability of bias, the methodological standard of the included studies, was not assessed due to the scoping review of the study.⁸²

Data items

Seven items were listed in the data collection chart table. We included the first author, the year of publication of the study and the country (item 1), study design and period of data collection (item 2), the sample size, mean or median age, and gender (item 3). The intervention and control conditions/exposures included surveillance, prevention and control of rabies and any other form of intervention used in human rabies (item 4). The number or rate of human rabies morbidity included annually or during the study period (item 5). Human rabies mortality recorded the death or mortality rate annually or during the study period (item 6). Main findings/gaps/challenges included other outcomes such as data gaps found, available research evidence as well as PEP or vaccine adverse events (item 7).

Critical appraisal of individual sources of evidence

The methodological quality of included studies was not evaluated due to the scoping nature of the review.⁸³

Synthesis of results

Studies were summarised based on author (year) and country, study designs, participants and comparator,

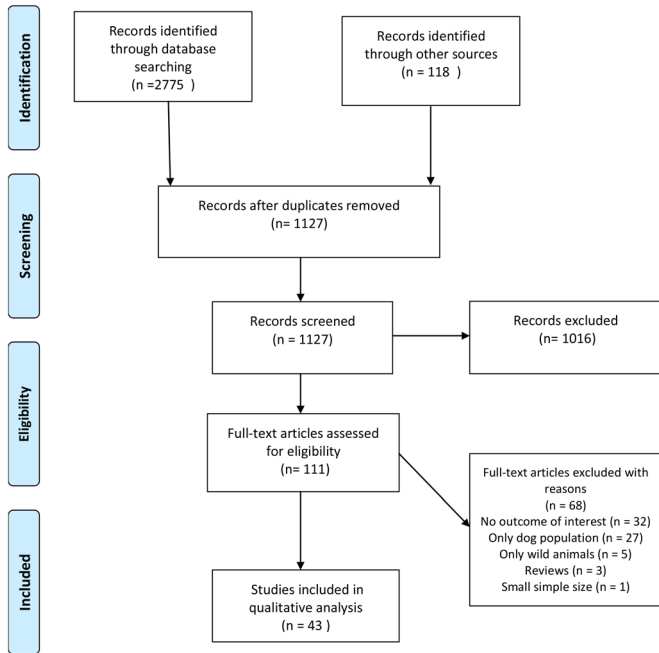


Figure 2 Flow diagram of human rabies mortality and morbidity associated with animal bites in Africa.

interventions and control conditions/exposures, key outcomes, gaps, findings and challenges. Interventions were subdivided into rabies prevention, surveillance, control and management. Where data were not clearly provided to compute morbidity and mortality rates, we reported the results narratively, as recommended in scoping reviews methodological framework.⁸²

RESULTS

Study selection

The searches from the five electronic databases hit a total of 2775 records (Medline: 696, Embase: 952, CINAHL: 289, Scopus: 431 and Web of Science: 407) that led to a total of 1127 titles and abstracts that were screened after the removal of duplicates. We retained 111 of these based on their title and abstract screening. The full-text screening's stage led to 43 potential articles relevant to our scoping review. The scoping review flow chart was described in figure 2.

Study characteristics

The review reported only quantitative studies on rabies surveillance, prevention and control. Thirty-two quantitative studies were retrospective cohort with 8 months to 14 years of study duration,^{21 29–31 33 34 36 38–46 48 84–98} three studies were mixed designs (retrospective and cross-sectional study),^{47 99 100} three were prospective cohort studies,^{32 35 101} two were cross-sectional studies,^{102 103} one was case-control,³⁷ one was clinical trial¹⁰⁴ and a randomised control trial.¹⁰⁵

We grouped the included studies into five categories based on rabies interventions, namely (1) prevention and control, (2) surveillance, (3) surveillance and prevention, (4) treatment and control, and (5) surveillance, prevention and control. Figure 3 shows the distribution of studies according to the intervention in 19 African countries. We also summarised all studies included in the final analyses in online supplemental table 1 which included seven parts in line with the specified framework for data synthesis: (1) rabies morbidity, (2) rabies

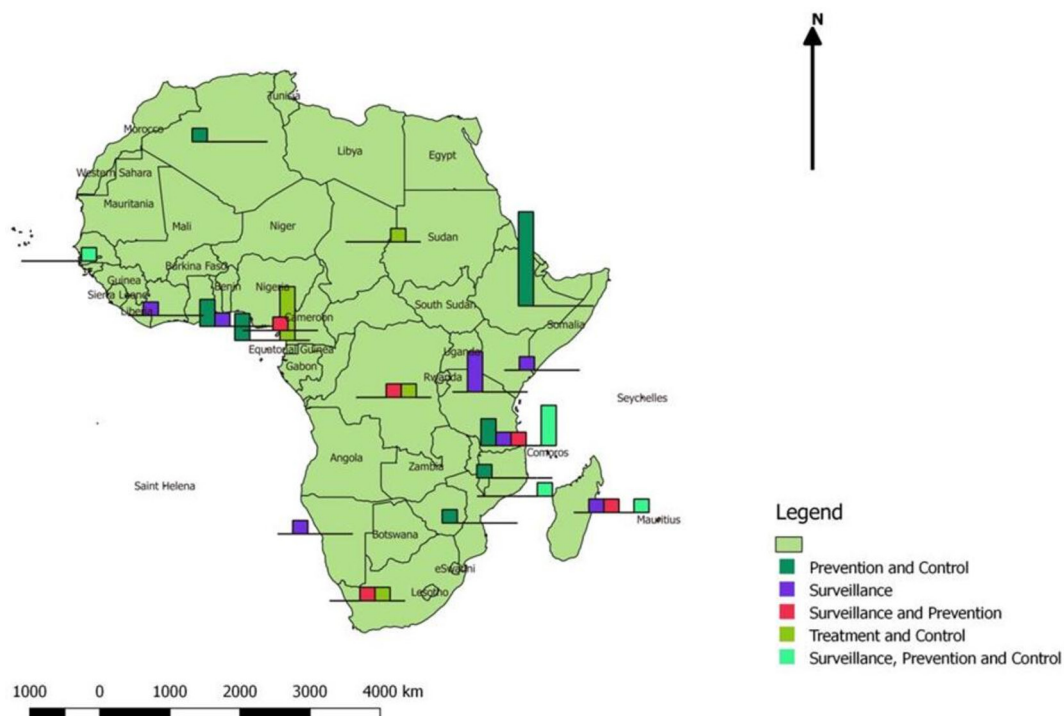


Figure 3 Distribution of 43 studies in African countries.

mortality, (3) interventions for rabies control, (4) rabies disease surveillance, prevention and control, (5) available research evidence, (6) research gaps identified, and (7) adverse events and complications associated with rabies vaccination.

Patient characteristics

A total of 543 714 bite victims were recorded in included studies. Age-specific and sex-specific distribution revealed that the most fatal cases belonged to age groups 0–14 years.^{29 33 35 38 43 45 46 48 84 91 92 94 96 100 102} Other studies identified rabies victims of 15 years and above.^{30 38 39 42 46 84 95 96 100 103} The median age was 18 years in most of the studies and ranged from 1 to 95 years. Most of the children were males.^{45 46 94 96} However, another study has indicated that females have more animal-related bites than males.²⁹ Young children are at higher risk of contracting rabies in the absence of PEP and wound care due to the location of the bites they incur.¹⁰² Based on the extent and depth of injury, 1567 victims were recorded. Extent and depth of injury was classified as broken skin (11.1%), scratch (9.25%), superficial (loss of epidermis only) (36.38%), deep (27.31%) and simple (affect only one tissue) (12.38%).^{29 31 101 103} Further, 10 006 bites were described in regard to the site of exposure among which included the head/neck/face (5.08%), leg/feet (61.06%), arm/hand (23.23%), buttocks/trunk (10.32%) or multiple (0.31%).^{29–33 42 47 93 95 99 102}

Individuals suspected to have rabies were clinically managed by the chief doctor paediatricians and nurses.^{32 36 37 40 84 94 99 103} The main treatments were wound management, antibiotics, and prophylaxis against tetanus and rabies. Nine studies reported wound management as part of PEP.^{32 37 40 47 93–96} Reports were collected in hospitals, treatment and health centres, health clinics and pharmacies.¹⁰³

Study outcomes

Rabies morbidity

Twenty-one studies reported human rabies morbidity in Africa (table 1).^{30 34–39 41 43 46 48 84 86 88–92 97 99–101 103} Among them, five studies were undertaken in Tanzania, the first study estimated an average annual incidence per 100 000 bites of 37.1, 11.3 and 33.5 in the human population districts of Ulanga (193 280 inhabitants), Kilombero (321 611 inhabitants) and Serengeti (176 057 inhabitants), respectively.⁸⁹ The second study found that the incidence of bite patients seeking PEP declined substantially (>50%) from 2011 to 2015.⁹⁰ The third study estimated an annual incidence of ~58 cases per 100 000,⁴¹ the fourth study reported a mean incidence of 74 bites considered at risk of rabies transmission per 100 000 persons per year,⁹⁷ and the last study conducted in Tanzania revealed an average of 75.6 and 19.3 probable rabies exposures per 100 000 persons per year.⁹⁹ Three studies conducted in Ghana reported 54 dog bite victims bitten by rabies-positive dogs within 3 years,⁸⁴ 13 cases of human rabies in a 6-year retrospective records review³⁸ and an annual

incidence of rabies cases of 172 per 100 000 people.⁴⁸ Four studies reported rabies morbidity in Ethiopia. Yizengaw *et al* reported a high incidence rate of rabies exposure during spring (360, 39%) and summer (244, 26.4%) seasons and a total of 924 human rabies exposure cases received the anti-rabies PEP from September 2015 to August 2017.¹⁰⁰ The incidence of human rabies exposure was reported to be 40 per 100 000 persons in Ethiopia,³³ annual estimated rabies incidence of 2.33 cases per 100 000 in humans,¹⁰¹ and the incidence of human rabies exposure cases calculated per 100 000 persons was 35.8, 63.0, 89.8 and 73.1 in 2012, 2013, 2014 and 2015, respectively.⁹³ A study conducted in Zimbabwe found among rabies suspect, 42 (73.7%) were positive.³⁹ In Madagascar, 9 of the 11 suspected human cases tested from 2005 to 2010 with a laboratory-confirmed rabies.⁸⁶ In Uganda, a total of 208 720 patients with animal bite injuries were treated at health facilities across the country.⁸⁸ Ivory Coast reported 50 cases of human rabies with annual incidence of 0.06–0.08 per 100 000.³⁵ The incidence of human injuries caused by animal bites was 289 per 100 000 persons with the highest incidence reported at 302 per 100 000 and lowest at 121 per 100 000 persons in Kenya.³⁸ Another study undertaken in Malawi reported 14 paediatric rabies cases during the study period.⁹² A 6-year retrospective study revealed 31 positive cases of human rabies in Madagascar.⁴⁶ In Democratic Republic of Congo (DRC), a 5-year retrospective study found 29 positive to rabies in a total of 5053 dog bites recorded in the veterinary clinics,³⁴ and Frey *et al* estimated an annual incidence of bites from suspected rabid animals of 12.9/100 000 and an incidence of 0.7 human rabies deaths/100 000 in Chad.¹⁰³ Namibia reported above 16 cases per year from 2011 until 2015 with a maximum of 23 cases observed in 2015 with an incidence of 1.0 and 2.4 per 100 000 inhabitants and per year on average.⁴³

Rabies mortality

Sixteen studies reported rabies-related mortality in Africa (table 2).^{21 31 37 40 42 44 45 85 87–89 98 99 101–103} Ethiopia reported three studies among which 320 people, diagnosed clinically, died of rabies in a 5-year retrospective study conducted in the national level,²¹ 386 human rabies fatalities were reported in an 8-year retrospective study with an annual range of 35–58 deaths in Addis Ababa and outside of Addis Ababa.⁴⁵ There were also 32 cases of human rabies recorded from which 3 people ended with fatality in North Gondar administrative zone.¹⁰¹ Four studies assessed rabies mortality in Tanzania from which Ulanga, Kilombero and Serengeti districts reported human rabies mortality rates of 2.4, 0.8 and 1.4/100 000 per year, respectively.⁸⁹ Sixteen human deaths (1291 bite victims) due to rabies were reported within the Integrated Bite Case Management Study across 20 districts in 4 regions in Southern, Central and Northern Tanzania.⁹⁸ Other studies reported 28 deaths from suspected rabies cases during the 5-year period in the two districts, an average of 1.5/100 000 per year in

Table 1 Mapping human rabies morbidity rate

Country (region, district and town)	Human rabies morbidity rate	Study duration
Chad (N'Djamena)	An annual incidence of bites from suspected rabid animals of 12.9/100 000 ¹⁰³	7 months, September 2008–April 2009 ¹⁰³
Democratic Republic of Congo (Kinshasa)	29 positive to rabies in 5053 dog bites recorded in the veterinary clinics ³⁴	5 years, 2009–2013 ³⁴
Ethiopia (national level; Ababa and outside of Addis Ababa; North Gondar administrative zone)	A total of 924 human rabies reported. ¹⁰¹ The incidence of human rabies exposure was reported to be 40 per 100 000 people in Ethiopia ³³ ; annual estimated rabies incidence of 2.33 cases per 100 000 in humans ¹⁰¹ ; the incidence of human rabies exposure cases calculated per 100 000 people was 35.8, 63.0, 89.8 and 73.1 every year ⁹¹	1 year, January 2016–31 December 2016; 2 years, 2015–2017; 3 years, 2012–2015; 11 months, April 2009–March 2010 ^{33 91 100 101}
Ghana (Techiman municipality; eastern region of Ghana)	54 dog bite victims bitten by rabies-positive dogs ³⁴ ; 13 cases of human ³⁵ ; an annual incidence of rabies cases of 172 per a population of 100 000 ⁴⁸	4 years, 2009–2012; 6 years, 2011–2016; 2 years, 2013–2015 ^{38 48 84}
Ivory Coast (national level)	Annual incidence of 0.06–0.08 per 100 000 ³⁵	3 years, 2014–2016 ³⁵
Kenya (Machakos and Kitui counties in lower eastern region; Kisumu county in Lake Victoria basin; Nandi county in Central Rift Valley and Kilifi coastal region)	Human injuries caused by animal bites, incidence of 289 per 100 000 persons ³⁰	6 years, 2011–2016 ³⁰
Madagascar (national level)	9 of the 11 suspected human cases tested with a laboratory-confirmed rabies ⁸⁶ 31 positive cases of human rabies reported ⁴⁶	6 years, 2006–2011; 6 years, 2005–2010 ^{46 86}
Malawi (Blantyre)	14 paediatric rabies cases reported ⁹²	6 years, 2012–2017 ⁹²
Namibia (Kavango)	An incidence of 1.0 and 2.4 per 100 000 inhabitants and per year on average ⁴³	7 years, 2011–2017 ⁴³
Tanzania (Mwanza region; Tabora; Shinyanga; Mara; Ulanga; Kilombero; Serengeti; Dodoma region; Ngorongoro districts in northern Tanzania and in the 11 districts in southern Tanzania)	Average annual incidence per 100 000 bites of 37.1, 11.3 and 33.5 in human population ⁸⁹ An incidence of bite patients seeking PEP declined substantially (>50%) ⁹⁵ An annual incidence of 58 cases per 100 000 ⁴¹ Mean incidence of 74 bites considered at risk of rabies transmission per 100 000 persons per year ⁹⁷ An average of 75.6 and 19.3 probable rabies exposures per 100 000 persons per year ⁹⁹	5 years, 2002–2006; 4 years, 2002–2006; January 2011–January 2013; 7 years, 2008–2014; 2002–2017; 2011–2017; 2011–2016 ^{41 89 90 97 99}
Uganda (national level)	208 720 patients with animal bite injuries treated across the country ⁸⁸	14 years, 2001–2015 ⁸⁸
Zimbabwe (national level)	Among rabies suspect, 42 (73.7%) were positive ³⁹	11 years, 1992–2003 ³⁹

PEP, post-exposure prophylaxis.

Serengeti and 2.3/100 000 in Ngorongoro.⁴⁴ Fourteen (14) among 1005 bite victims died showing clinical signs of rabies within 5 years.⁹⁹ Three (3) studies identified rabies mortality in Uganda. Among them, there were 592 (95% CI 345 to 920) deaths,¹⁰² where one dose of PEP was sufficient for protection following a rabid animal bite. Another research estimated a total of 371 deaths of rabies with a cumulative total of 117 085 rabies cases in 9 years⁸⁷ and a 14-year retrospective study revealed a total of 486 suspected human rabies deaths among 208 720 patients with animal bite injuries treated at health facilities across the country.⁸⁸ A study undertaken in Moramanga district (Madagascar) recorded an annual incidence of 42–110 rabies exposures and 1–3 deaths per 100 000 persons.³¹ An estimated seven rabies deaths (95% CI 4 to 10 deaths) per year was recorded in N'Djamena (Chad).¹⁰¹ A study conducted in Algeria excluding Sahara region found an annual average of 20.6 human rabies deaths.⁹⁰ A total of

14 cases of fatal rabies with 12 deaths were reported in Maputo city, which is the capital of Mozambique.³⁷ An average annualised rabies attack rate of 136 rabies cases per 100 000 dog bite injuries (7 of 5139) with 6 of 7 deaths were reported in South Africa.⁴² There were patients with serious rabies manifestations and the case fatality rate of 100% in a study conducted in Kinshasa (DRC).⁴⁰

Rabies disease surveillance, prevention and control

Rabies prevention and control

The review summarised rabies prevention and control based on rabies exposure status, PEP, dog vaccination and seasonality. Among 36 741 bite victims recorded in studies reporting PEP^{29 41 45 84 91 92 97} the PEP was initiated based on WHO grade of exposure.¹⁰⁶ We found 505 bites in grade 1 (8.78%), 2050 in grade 2 (35.63%) and 3199 in grade 3 (55.59%).^{32 33 42 95 96} The overall PEP course among bite victims varied between 24% and 99%.^{29 84}

Table 2 Mapping human rabies mortality rate

Country (region, district and town)	Morbidity rate	Study duration
Algeria (national level excluding Sahara region)	An annual average of 20.6 human rabies deaths ⁸⁵	13 years, 2006–2018 ⁸⁵
Chad (N'Djamena)	An estimated 7 rabies deaths (95% CI 4 to 10 deaths) per year ¹⁰³	8 months, September 2008–April 2009 ¹⁰³
Democratic Republic of Congo (Kinshasa)	Case fatality rate of 100% ⁴⁰	8 months, December 2008–July 2009 ⁴⁰
Ethiopia (national level, Ababa and outside of Addis Ababa, North Gondar administrative zone)	320 people died of rabies in 5 years ²¹ 386 human rabies fatalities were reported with annual range of 35–58 deaths ⁴⁵ 32 cases in human rabies recorded ¹⁰¹	5 years, 1997–2001, 8 years, 2001–2009; 11 months, April 2009–March 2010; 1 year, January 2016–31 December 2016; 2 years, 2015–2017; 3 years, 2012–2015; 11 months, April 2009–March 2010 ^{21 33 45 91 100 101}
Madagascar (Moramanga district)	An annual incidence of 42–110 rabies exposures and 1–3 deaths per 100 000 persons ³¹	1 year, 2016–2017 ³¹
Mozambique (Maputo city)	A total of 14 cases of fatal rabies with 12 deaths ³⁴	3 months, April–July 2014 ³⁴
South Africa (Uthungulu District of Kwazulu-Natal province)	An average annualised rabies attack rate of 136 rabies cases per 100 000 dog bite injuries (7 of 5139) with 6 of 7 ⁴²	3 years, 2008–2010 ⁴²
Tanzania (Ulanga, Kilombero and Serengeti districts; 20 districts in 4 regions in Southern, Central and Northern Tanzania; Serengeti and Ngorongoro)	Human rabies mortality rates of 2.4; 0.8 and 1.4/100 000 per year, respectively ⁸⁹ 16 human deaths (1291 bite victims) due to rabies were reported ⁹⁹ 28 deaths from suspected rabies cases during the 5-year period in the two districts, an average of 1.5/100 000 per year and 2.3/100 000 ⁴⁴ 14 among 1005 bite victims died showing clinical signs of rabies within 5 years ⁹⁹	5 years, 2002–2006; 3 years, 2006–2008; 2002–2017; 2011–2017; 2011–2016 ^{44 89 99}
Uganda (national level; 10 districts)	592 (95% CI 345 to 920) deaths ¹⁰² An estimated total of 371 deaths of rabies with a cumulative total of 117 085 rabies cases in 9 years ⁸⁷ A total of 486 suspected human rabies deaths among 208 720 patients in 14 years ⁸⁸	8 years, 2001–2009; 14 years, 2001–2015; 3 months ^{87 88 102}

We reported 2652 bites victims in studies reporting PEP and mass dog vaccination.^{33 38 39 85 100} Dog vaccination coverage varied from 14.1% to 68.78%.^{33 85} In Ethiopia and Zimbabwe, the dog vaccination decreased significantly across the study and also the health status of most dogs involved in biting was unknown.^{39 100} Rabies prevention and control also depended on the seasonality. In Ethiopia, two studies reported season-wise rabies exposure. The first study reported rabies exposure during spring (360 of 924, 39%) and summer (244 of 924, 26.4%) seasons.¹⁰⁰ The second study that found the highest human rabies exposures were reported in spring (April–June) followed by winter (January–March), while the lowest distribution of human rabies exposure was recorded in autumn (October–December).³³ In Nigeria, Osaghae reported the prevalence of dog bite was highest, 41 of 81 (50.6%), during the hot season (April–June) and low, 14 of 81 (17.3%), during the wet season (July–October).⁹³ Another study conducted in Nigeria recorded the highest number of dog bites with two peaks

in April and October 2008.⁴⁷ However, the number of dog bite cases was lowest. For all years, the numbers of dog bite cases recorded were lowest at the beginning of the year and dog bites increased during the last 3 months (October–December) of the year 2006.⁴⁷ Animal-to-human rabies transmission was highest during the dry months of July–November in Zimbabwe.³⁹ In DRC, a study found there was no seasonal difference observed for rabies occurrence either for clinical cases or confirmed cases throughout the study period.³⁴ In Tanzania, each year, the majority of rabies cases were recorded during the period June–October.⁴¹ In the dry season, significantly fewer rabies-positive cases were reported than in the rainy season in Namibia.⁴³ In Chad, more rabies records per month were collected during the hot, dry season months (March and April), than during the dry season months (September–February).¹⁰³ In Senegal, dog bite victims were higher in dry season (November–May) than rainy season (June–October).³² Besides, bite victims in rural areas took longer, on average, to receive PEP than those

in urban areas.^{89 97 100} Probable human rabies cases were higher in rural than urban areas.^{33 35}

Rabies surveillance, prevention and control

The findings revealed that 39802 bite victims were recorded in rabies surveillance and prevention interventions. The studies included laboratory, database and network surveillance.^{34 36 42 46 90} The rabies prevention included PEP and dog vaccination. Laboratory surveillance has improved rabies diagnosis,^{34 36 42 46 90} and database and network surveillance improved mortality and morbidity records^{35 42 90} and allowed better estimates of the true rabies burden.³⁶ Furthermore, compliance with PEP regimens was significantly higher, rating from 83.7% to 93% in two studies.^{42 90} In contrast, dog vaccination remained low (10%–12.6%).^{36 46}

We found five studies including rabies disease surveillance, prevention and control.^{31 32 37 44 98 99} Among them, three studies^{32 37 44} have reported significantly improved rabies morbidity and mortality and also PEP uptake. The PEP uptake was 71% and it dramatically reduced the risk of developing rabies.³⁹ Another study did not report any death with high number of patients receiving PEP.³²

A combined strategy of mass dog vaccination, enhanced surveillance, and expanded access to PEP reduced the annual incidence of rabies exposures and deaths annually in Madagascar.³¹ Strict measures such as vaccination of dogs in the neighbourhoods where human rabies cases had occurred, mass vaccination campaign of dogs, participation of private veterinary clinics in animal vaccination, collection of stray dogs in selected neighbourhoods, and community education regarding prevention and control measures had drastically reduced rabies cases in humans to 14 during the study period in Mozambique.³⁷

Post-exposure management

We found seven studies on rabies management and control. Among them, six studies addressed wound management and PEP.^{40 47 93–95 103} Wound severity was graded as follows: 0=no apparent injury seen, 1=skin scratch with no bleeding, 2=minor wound with some bleeding, 3=deep or multiple injuries.⁹⁵ The reported severity of the wound was classified as deep wound, lacerated wound, superficial wound or scratch.¹⁰³ The severity of the injury was determined using the WHO dog bite injury grading system.¹⁰⁶ Soap, water, wound dressing, tetanus prophylaxis, anti-rabies vaccination, intravenous fluids, diazepam and antibiotics were also part of the management. The overall review reported 5754 bites managed according to the WHO dog bite injury grading system, 3199 (55.59%) were grade 3; 2050 (35.63%) were grade 2 and 505 (8.78%) were grade 1. In 52 cases (7%), the grade of the bite was not recorded.^{30 31 40 93 97}

Available research evidence on human rabies

Rabies cases in various committees emphasise the need for active surveillance by following up of people bitten by animals and mass dog vaccinations to alleviate the zoonotic

threat of the virus.⁸⁷ Strengthening rabies surveillance, controlling rabies in dogs, proper post-exposure management, increasing the awareness of the community and ensuring availability of PEP at lower health facilities are the best approaches of eliminating rabies.^{88 92 101} Other studies have demonstrated that reinforcement of rabies surveillance system can improve rabies reporting, which ultimately allows for better estimates of the true rabies burden in the countries.^{34 36 42 90} Compliance with PEP regimens was significantly higher for patients following the implementation of automated reminders in comparison with patients attending normal clinics.^{42 90} Other studies concluded that preventing dog bites would most effectively reduce bite injuries by improving public health education among children below 15 years.⁴² Public health education is also enhanced by encouraging early PEP initiation and completion, development and implementation of responsible dog ownership, animal behaviour educational programmes as well as improving human and veterinary health linkages.^{30 42} Evidence also showed that no rabies victim in Mozambique received full post-exposure vaccination and the factors significantly associated with human rabies were: age <15 years ($p=0.05$), bite by stray dog ($p=0.002$), deep wound ($p=0.02$), bite in the head ($p=0.001$), bite by unimmunised dog ($p=0.01$), no use of soap and water ($p=0.001$), and no PEP ($p=0.01$).³⁹ Studies have shown that all the rabies vaccines including suckling mouse brain virus (SMBV), fetal bovine kidney virus (FBKV), purified chicken embryo cell rabies vaccine, purified vero cell rabies vaccine, sheep brain anti-rabies vaccine, human diploid-cell vaccine and purified equine RIG were efficacious. However, the WHO and OIE contraindicated SMBV and FBKV in both animals and humans.^{29 31 32 36 45 46 102 104 105} Furthermore, a clinical trial with a purified chicken embryo cell rabies vaccine dose used intramuscularly every 2 years generated ineffective immune response to rabies virus¹⁰⁴ as the Zagreb protocol (two intradermal injections of 0.1 mL at two sites, deltoids and/or thighs, on days 0, 3, 7 and 28) was not applied. Even though a randomised control trial showed antibody response 26.7% of SMBV recipients and 28.6% of FBKV recipients within a week, both SMBV and FBKV were equally efficacious and well tolerated,¹⁰⁵ however those vaccines are contraindicated by the WHO because of its association with neurological adverse reactions (severe allergic encephalomyelitis). Furthermore, these vaccines are inferior to modern vaccine in terms of potency and immunogenicity.¹⁰⁷ **Table 3** describes the available research evidence on human rabies in Africa.

Adverse events and complications associated with rabies vaccination

Adverse events and complications associated with rabies vaccination were reported based on SMBV, FBKV, purified chicken embryo cell rabies vaccine, purified vero cell rabies vaccine, sheep brain anti-rabies vaccine, human diploid-cell vaccine and purified equine RIG. All the four-dose or Zagreb regimen was reported in all the RIGs.¹⁰⁸

Table 3 Mapping human rabies evidence identified in Africa

Evidence map	Studies	Impacts/outcomes
Strengthening rabies surveillance	35 36 42 87 88 90 92 101	Reinforcement of rabies surveillance system that can improve rabies reporting and increase the awareness of the community, and ensuring availability of PEP at lower health facilities are the best approaches of eliminating rabies.
Automated short message service (SMS) reminders and telephone contacts	42 44 90 98 99	Compliance with PEP regimens was significantly higher for patients following the implementation of automated SMS reminders and telephone contacts.
Public health education (PEP initiation and completion, responsible dog ownership, behaviour educational programmes and veterinary health linkages)	30 42 47 88 92 101	Lack of enforcement of regulations for licensing of dogs and rabies vaccination increased human rabies morbidity and mortality.
Accurate rabies diagnostic	31 35 36 38 39 46 86 99	The diagnosis of dog bite and rabies was clinical and laboratory based. This improved accurate rabies cases reporting.
Mass dog vaccination	39 85 92	Even though the 70% coverage was not achieved, there was an inverse relationship between dog vaccination coverage and dog rabies cases during the study period.
SMBV, FBKV, purified chicken embryo cell rabies vaccine, purified vero cell rabies vaccine, sheep brain anti-rabies vaccine, human diploid-cell vaccine and purified equine rabies immunoglobulin (RIG) (Zagreb protocol)	29 31 32 35 46 102 104 105	Studies have shown that all the rabies vaccines and RIG were efficacious and well tolerated. However, the WHO contraindicated SMBV and FBKV.
Effective rabies control and management	36 42 85 92	PEP, mass dog vaccination and WHO dog bite injury grading system
Integrated bites case management/rabies disease surveillance, prevention and control	31 32 37 44 98 99	Studies have shown the importance of coordinated surveillance, prevention and control in the eradication of rabies.

FBKV, fetal bovine kidney virus; PEP, post-exposure prophylaxis; SMBV, suckling mouse brain virus.

Among the studies reporting rabies vaccination, only one study using a purified vero cell rabies vaccine at day 0 (two doses), day 7 (one dose) and day 21 (one dose) study found that adverse events occurred in 6% of the patients with two doses and after the third dose, 3% developed adverse events. However, most of the adverse events were minor and associated with headache, fever and pain at the injection site that occurred simultaneously on the same day of the vaccine injection.³² Other studies did not report any adverse events and complications associated with rabies vaccination.^{29 31 36 45 46 102 104 105}

Research gaps identified

In this review, we identified 66.67% African countries reporting poor rabies diagnostic capacity, 50% reported the lack of coordinated surveillance, 50% showed the lack of PEP course completion, 22.22% had insufficient rabies control and 77.78% had low dog vaccination coverage. Insufficient knowledge and practice on rabies prevention was also identified as a gap. However, we did not find enough studies to evaluate this gap in Africa (table 4).

The recorded data available so far have shown the underestimation of rabies diagnosis, PEP and fatal human cases, and could be attributed to poor diagnostic capacity and the absence of national rabies surveillance system. In African countries, rabies diagnostic is mostly clinical.^{21 30 32-34 37 40 42 43 45 48 87-89 92-94 97 102 103} Among 11

studies, including human rabies surveillance, only 4 reported adequate and successful surveillance,^{35 36 42 90} 12 studies reported lack of accurate data or non-existing surveillance data^{30 34 37 42 43 46 48 86-88 102 103} (table 4). Other studies reported that dog bite victims did not complete the post-exposure anti-human rabies vaccine course and were not likely to receive PEP^{31 32 35 41 42 44 84 89 94 97 99} (table 4). The exposure victims considered to be at risk of rabies either did not receive any PEP or did not receive all PEP vaccinations due to unavailability, shortage, cost barriers, insufficient knowledge about prompt PEP, category 1 exposure injury or misadvice.^{36 40 42 44 47 48 95 98 99} A study has reported that the lack of PEP was the cause of 100% fatality rate in DRC.⁴⁰ There was significant difference between rural and urban exposure cases in respect of the time of arrival to the hospital, and living in rural areas was statistically associated with loss to follow-up after the first dose.^{34 47 97 100} There was also high human rabies exposure rate in children and in the rural community.^{31 34 97 100} Insufficient knowledge about rabies' dangers and prevention, particularly prompt PEP, as well as wound management, was the main cause of rabies deaths.⁴⁴ A higher proportion of human rabies exposures was caused by unprovoked dogs and of these, the majority were unvaccinated.^{33 47} Dog vaccination remains an urgent intervention gap. Among 18 studies conducted

Table 4 Mapping research gaps and strengths in Africa

Mapping research gaps and strengths in Africa						
African countries	Diagnostic capacity	Coordinated surveillance	Lack of PEP course completion/PEP unavailable	Inefficient control	Insufficient knowledge and practice on rabies prevention	Low dog vaccination coverage (<70%)
Algeria	N/A	N/A	N/A	√ ⁹⁰	N/A	X ⁹⁰
Cameroon	√ ³⁶	√ ³⁶	X ³⁶	√ ³⁶	N/A	X ³⁶
Chad	X ¹⁰⁸	X ¹⁰⁸	X ¹⁰⁸	X ¹⁰⁸	N/A	X ¹⁰⁸
Democratic Republic of Congo	X ^{34 40}	X ³⁴	X ^{34 40}	X ^{34 42}	N/A	X ⁴²
Ethiopia	X ^{21 33 45}	N/A	X ⁹¹	X ^{33 91 101}	X ¹⁰¹	X ^{33 91 101}
Ghana	X ⁴⁸	X ⁴⁸	X ^{48 84}	X ^{38 48 84}	N/A	X ^{38 84}
Ivory Coast	√ ³⁵	√ ³⁵	X ³⁵	X ³⁵	N/A	X ³⁵
Kenya	X ³⁰	X ³⁰	X ³⁰	X ³⁰	N/A	N/A
Madagascar	√ ^{31 46 86}	X ^{46 86}	X ^{31 46}	X ^{31 46 86}	N/A	X ^{31 46}
Malawi	X ⁹²	√ ⁹²	√ ⁹²	√ ⁹²	N/A	N/A
Mozambique	X ³⁷	X ³⁷	X ³⁷	X ³⁷	N/A	X ³⁷
Namibia	X ⁴³	X ⁴³	N/A	X ⁴³	N/A	N/A
Nigeria	X ^{93 94}	N/A	X ^{47 93–95}	X ^{47 93–95}	N/A	X ⁴⁷
Senegal	X ³²	√ ³²	X ³²	X ³²	√ ³²	X ³²
Tanzania	X ^{90 97}	√ ^{89 97}	X ^{41 44 89 97 99}	X ^{41 44 89 97 99}	X ⁴⁴	N/A
Uganda	X ^{87 88 102}	X ^{87 88 102}	X ¹⁰²	X ^{87 88 102}	N/A	X ^{87 102}
South Africa	√ ⁴²	√ ⁴²	X ^{42 96}	√ ⁴²	N/A	N/A
Zimbabwe	√ ³⁹	√ ³⁹	N/A	X ³⁹	N/A	X ³⁹

PEP, post-exposure prophylaxis.

in 9 countries, none of them reported the target of 70% of dog vaccination (table 4). The highest dog vaccination rate was reported in Algeria (67.3%)⁸⁵ and the lowest in Madagascar (10%).⁴⁶

DISCUSSION

This is to our knowledge the first scoping review synthesising publicly available data on rabies in Africa and weighing such data in support of the global goal of ‘zero human rabies deaths by 2030’. The purpose of this scoping analysis was to provide a summary of evidence on rabies morbidity, mortality, integrated rabies surveillance, prevention and control in Africa. Overall, studies have shown that African countries face a range of problems based on rabies surveillance, prevention and control that have negative effects on rabies mortality and morbidity. Reviewing rabies morbidity and mortality rates across Africa, data obtained fluctuated largely over time and space in various countries, as well as in different regions or districts across the same area. While some countries may have shown significant improvement in rabies morbidity and mortality data, the morbidity and mortality rates in Africa generally remain high. Included studies showed no standardisation in reporting human rabies outcomes, human rabies morbidity and mortality rates were reported in terms of annual incidence and number

of infected human rabies and deaths related to rabies. Moreover, small-scale studies may not reflect the national or regional human rabies morbidity and mortality rates. Therefore, it was difficult to have an accurate picture per country and assess human rabies situation between African countries.

These are the consequences of a lack of laboratory rabies confirmation, epidemiological surveillance, inadequate mass dog vaccination and PEP policy, and unreported clinical cases in African countries. Lack of monitoring data on rabies or low data quality is problematic, resulting in rabies being poorly addressed in most African countries. Results have also shown that of the 11 countries in which rabies surveillance has been applied, only 4 studies reported that surveillance decreased rabies morbidity and mortality.^{35 36 42 90} Comparing old and new data (before and after the ‘zero rabies by 2030’ target), rabies diagnosis and surveillance have not improved in most of the African countries. As a result, well-structured rabies surveillance enhanced the reporting of morbidity and mortality and also has a visible impact on rabies elimination strategy in Africa. While strategies have been subdivided into surveillance, prevention, control and management of rabies (see table of included studies), only three studies have shown the efficacy of the combination of surveillance, prevention and control of rabies.^{32 37 44}

However, passive surveillance has shown its limitations in rabies elimination because cases are reported clinically with or without laboratory-based strategies, inducing inaccurate diagnostic tools, scarcity of laboratory confirmation and poor reporting system.^{30 43 46 87 88 102} This is why both passive and active surveillance are preferable to strengthen rabies monitoring and reporting in African countries.¹⁰⁹ Strengthening rabies surveillance is also the foundation of the provision of actionable data for efficient management of wildlife diseases.¹¹⁰ Besides, the review has shown that strengthening surveillance, prevention and management of rabies has shown good evidence in three separate studies.^{32 37 44} Coordination of surveillance, prevention and control of rabies can play an important role in the eradication of rabies in Africa. It is worth noting that specific awareness of when and where the disease occurs is essential to the formulation of prevention, control and elimination strategies.¹¹⁰

As seen above, the implementation of different rabies interventions at national level has never reached African countries. It is vital that African countries achieve the 2030 target of eliminating human rabies by providing readily accessible and affordable PEP in all countries in the continent where rabies infection is endemic. The exposed victims considered to be at risk of rabies either did not receive any PEP or did not receive complete PEP vaccinations due to unavailability, shortage, cost barriers, insufficient knowledge about prompt PEP or misadvice.^{36 40 44 48 95 98 99} This could be emulated from Thailand, which has significantly reduced human deaths from rabies to fewer than 10 cases per year by educating the public and health workers and delivering PEP free of charge across the country before mass dog vaccination achieved the minimum 70% coverage.^{111 112} When provided correctly and in a timely manner, rabies PEP is almost 100% effective in the prevention of the disease.^{72 113} The findings of the review revealed that the dog bite victims found to be at risk of rabies either did not receive PEP or did not receive all the PEP vaccines due to unavailability, shortages, cost barriers, long distance travel to the hospital or misadvice.^{31 32 35 36 40 41 44 48 84 89 94 95 97-99} It is important to remember that PEP, combined with other treatments such as soap, water, wound dressing, antibiotics, tetanus prophylaxis and anti-rabies vaccination, has been shown to be beneficial for dog bite victims. Two studies have shown that compliance with PEP regimens was substantially higher for patients who did not receive PEP after automated reminders.^{42 90} Taken together, our results point to a suboptimal system requiring specific improvements to achieve prompt provision of rabies PEP for persons exposed to rabies.¹¹²

Statistical modelling studies show that the annual vaccination of 70% of the canine population would induce adequate herd immunity to effectively eradicate canine rabies and subsequent human exposure.^{10 44} The lowest and highest reviewed dog vaccination rates were 10% and 67.3%, respectively,^{10 46} and no reliable data on dog vaccination were reported in most of the studies. This is because

many campaigns, if conducted, struggle to achieve a 70% vaccination rate.^{10 14} This is due to husbandry practices, rabies knowledge, geographical area/location and the ages of dogs.¹¹⁴ Evidence has shown the dog mass vaccination systems have demonstrated some effectiveness in reducing human rabies morbidity and mortality in countries such as KwaZulu-Natal, South Africa,^{49 65} Serengeti, Tanzania,^{49 66 68} Malawi^{44 69} and Chad.^{70 71} However, the Tanzanian study has shown that, if vaccine coverage was not sustained, rabies infection would resurface extremely quickly.³⁴ Despite effective monitoring of rabies at the Tanzania study site from 1998 to 2001, vaccine coverage decreased from 2001 to 2003 resulting in a new rabies outbreak, with human exposures increasing by six times in 2003 relative to previous years.⁴⁴ Further, free mass dog vaccination intervention has proven to increase dog vaccination coverage. Government and stakeholders should work actively to provide a free sustainable dog vaccination.

Besides, the evidence has also illustrated the effectiveness of other strategies, such as mobile phone touch tracing strategies, new rabies vaccines, integrated bite case management and wound management, which were correlated with PEP and/or mass dog vaccination. Africa is yet to recognise rabies as an immediate public health problem; this may be due to a lack of awareness of the burden of disease and inadequate surveillance. Policies should be put in place to raise awareness of rabies at grassroots level and coordination between the appropriate agencies for improvements of the policies.^{47 54}

The World Animal Health Information System is a well-established global animal disease reporting system that reproduces the data submitted by countries to the OIE, but is also constrained by the under-reporting problems inherent in national reporting systems.^{115 116} The need for regional One Health-oriented reporting network has therefore become apparent.^{117 118} The development of rabies-specific regional bulletins has been extremely effective in the Pan-American Health Organization field.¹¹⁷ The database such as the New Latin American Rabies Surveillance System should be applicable in Africa.

Indeed, the elimination of rabies is not feasible without African cooperation. No single country will retain rabies-free status unless it is brought under control in neighbouring countries.¹¹³ Regionally organised efforts are required to eradicate human rabies, taking into account country-specific needs and sociocultural acceptability.¹¹³ Canine rabies-endemic regions have formed international rabies networks based on the successful Meeting of Rabies Program Directors of the Americas (REDIPRA) model which enables them to create a unified and directed approach towards elimination within their regions.¹¹⁹ REDIPRA meetings can be considered a model for coordination and governance in the world.^{7 118 119} In Africa, the Pan-African Rabies Control Network (PARACON) was formed under the secretariat of GARC, as an Africa-focused advisory and networking initiative.¹¹⁹ It was established in order to unify all sub-Saharan African countries and any related rabies networks in a One Health

approach towards rabies control and elimination.¹¹⁹ The PARACON facilitates the development and implementation of national rabies elimination strategies, with a focus on sustainability through governmental support.¹¹⁹ However, the probability of meeting the 2030 goal without African and international solidarity is low, as more than two-thirds of countries are in the low-level human development community.¹²⁰ Leading countries should serve as role models, sharing their knowledge and skills so that no nation is left behind. African unification with international support will enable the common goal of zero human rabies deaths to be achieved by 2030.¹²⁰ Therefore, regional network support, channel and pool efforts and support-monitoring platforms will help make much progress.¹²¹ Partnerships are important to the achievement of an objective and the last mile is going to be the most demanding.¹²¹ In addition, contact and collaboration between human health and veterinary systems is also critical for the follow-up of both human and animal cases.¹²² Data collected on alleged cases of human rabies, human exposures and rabid animals must be constantly reviewed and effectively disseminated.¹²² Communication between the various national levels of healthcare administration is a crucial means of disseminating outcomes.¹²² Finally, stakeholders need to be engaged in the long term to ensure that surveillance is effective.¹²² Knowing that the Global Strategic Plan is catalytic and not intended to replace the strategies and commitments of individual countries,¹²¹ African countries should emphasise gaps, challenges, barriers and evidence applicable to the various districts, countries and regions as indicated in this present study. One Health interventions are provided by approaches to the prevention of human rabies deaths.¹²³ In African countries, the Ministries of Health, Animal Resources, Natural Resources, Environment and Tourism are in charge of implementing the canine and human rabies programmes in accordance with local, national and international bodies.

Human rabies is 100% preventable through two complementary measures: first, PEP, which involves administration of RIG and a multidose course of rabies vaccination to people bitten by suspected rabid animals; second, mass vaccination of animal reservoirs (primarily domestic dogs, the reservoir in the vast majority of human cases), which reduces the risk of human exposure and can ultimately result in rabies virus elimination.¹²³

New rabies control tests and technologies that have been developed, such as oral rabies vaccine (ORV), may be considered as an additional tool for the canine rabies control and elimination. ORV is effective, for instance, in skunks, red foxes and raccoons.¹²⁴ ORV has been demonstrated to be effective for the oral immunisation of foxes, some of them being competitors for long baits year consumption. Switzerland eradicated wild rabies since 1985.¹²² However, strategies to eliminate human rabies in Africa should adapt the REDIPRA model in African context, which emphasises that people exposed to rabies have timely access to quality immunobiologicals,

that appropriate levels of vaccination coverage in dogs in highly enzootic areas are maintained, that national rabies plans are strengthened and that systematic implementation is ensured, that the surveillance system for human rabies transmitted by dogs is strengthened and that systematic implementation is ensured, and that training and the development of a laboratory quality control system, particularly in highly enzootic areas, strengthen education, communication and advocacy in enzootic areas, to ensure the continuous political support that is necessary, develop and adopt a guide that delineates the requirements for declaring countries or areas free of human rabies transmitted by dogs.¹¹⁹

CONCLUSION

This comprehensive scoping review is of crucial importance in assessing various pieces of evidence of human rabies morbidity, mortality, monitoring, prevention and management. Rabies control strategies and case effects and available studies established to address various gaps are also important in the management of rabies in Africa. The analysis included past, existing and future viewpoints that are important for African countries to achieve zero rabies transmitted by dogs to humans by 2030. The findings of 43 studies included 32 quantitative retrospective studies, 3 mixed designs (retrospective and cross-sectional studies), 3 prospective cohort studies, 2 cross-sectional studies, 1 case-control, 1 clinical trial and 1 randomised control study. Mapping the outcomes, the review included rabies morbidity (21 studies), mortality (15 studies), rabies prevention and control (16 studies), surveillance (9 studies), surveillance and prevention (5 studies), management and control (7 studies), surveillance, prevention and control (6 studies), strong research evidence (14 studies), rabies vaccination or PEP adverse events (4 studies), and research gaps (41 studies).

Evidence has shown that human rabies morbidity and mortality remain high compared with rabies globally, and human rabies morbidity and mortality fluctuate in time and space across different African countries. In order to better understand this, the review has shown that monitoring, prevention and control of rabies are inadequate and insufficient in most African countries. This is attributable to a variety of gaps and challenges across African countries. In addition, this study found insufficient and ineffective surveillance of rabies, unavailability of PEP, high cost, lack of information on prevention of rabies, and poor or non-existent data on dog vaccination. However, few studies have shown a thorough design of rabies measures such as enhanced surveillance of rabies, regulation of rabies in dogs, proper post-exposure treatment, improved community awareness and availability of PEP in all rural areas, use of cell phone intervention to enhance surveillance of rabies, prevention and control of enhanced rabies morbidity, and more. In addition, African countries can learn about different community-based obstacles that can interfere with surveillance, prevention



and control of rabies disease. This is important to point out that no single country will preserve rabies-free status unless it is brought under control in neighbouring countries.¹¹⁹ That is why African countries should build a forum for rabies that may be significant to exchange data and experience on rabies. Finally, African countries can also look at futuristic rabies innovations such as ORV.

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