

# Infectious Diseases of Poverty

## Molecular characterisation of human rabies in East Africa - a case series report and phylogenetic investigation.

--Manuscript Draft--

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<b>Full Title:</b>	Molecular characterisation of human rabies in East Africa - a case series report and phylogenetic investigation.
<b>Article Type:</b>	Case Report
<b>Abstract:</b>	<p><b>SUMMARY</b></p> <p>Background</p> <p>Rabies remains a major public health problem in low- and middle-income countries. However, human rabies deaths are rarely laboratory-confirmed, especially in Africa. Here, we use rabies virus sequence data to enhance investigations for a series of 5 human rabies deaths in East Africa and discuss the implications of these at individual, healthcare, and societal-level.</p> <p>Case presentation</p> <p>The epidemiological context and care of these cases is contrasting: three of the bite victims did not receive any post-exposure vaccinations to prevent the fatal onset of disease, despite one attending a health facility on the day of exposure; one received only their first post-exposure vaccination; while the last received timely post-exposure vaccination but following a vaccination timeline that is not recommended by WHO. These differences raise concerns about health-seeking behaviour, competency of healthcare professionals in handling rabies exposures and accessibility and effectiveness of post-exposure prophylaxis as it is administered in these settings.</p> <p>Result and conclusion</p> <p>Our investigation confirms dog-mediated rabies as the cause of each of these deaths. The viral genomic data highlight the transboundary circulation of rabies within domestic dog populations across the region. We conclude that urgent action is needed to improve awareness around the need for emergency post-exposure prophylaxis that should be accessible in local communities and administered appropriately, as well as investment in coordinated dog vaccination to control dog-mediated rabies, the underlying cause of these deaths.</p>

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6**TITLE: Molecular characterisation of human rabies in East Africa - a case series report and phylogenetic investigation.**

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4 \*Joint contributions  
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9 **Key words:** Lyssavirus, One Health, Nanopore, next-generation sequencing, whole genome sequences,  
10 genomic surveillance  
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4 **SUMMARY (For IDP case report, 228 words)**  
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7 **Background:** Rabies remains a major public health problem in low- and middle-income countries.  
8 However, human rabies deaths are rarely laboratory-confirmed, especially in Africa. Here, we use rabies  
9 virus sequence data to enhance investigations for a series of 5 human rabies deaths in East Africa and  
10 discuss the implications of these at individual, healthcare, and societal-level.  
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13 **Case presentation:** The epidemiological context and care of these cases is contrasting: three of the bite  
14 victims did not receive any post-exposure vaccinations to prevent the fatal onset of disease, despite one  
15 attending a health facility on the day of exposure; one received only their first post-exposure vaccination;  
16 while the last received timely post-exposure vaccination but following a vaccination timeline that is not  
17 recommended by WHO. These differences raise concerns about health-seeking behaviour, competency  
18 of healthcare professionals in handling rabies exposures and accessibility and effectiveness of post-  
19 exposure prophylaxis as it is administered in these settings.  
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22 **Result and conclusion:** Our investigation confirms dog-mediated rabies as the cause of each of these  
23 deaths. The viral genomic data highlight the transboundary circulation of rabies within domestic dog  
24 populations across the region. We conclude that urgent action is needed to improve awareness around  
25 the need for emergency post-exposure prophylaxis that should be accessible in local communities and  
26 administered appropriately, as well as investment in coordinated dog vaccination to control dog-mediated  
27 rabies, the underlying cause of these deaths.  
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4 **BACKGROUND**  
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7 Domestic dogs are the source of almost all of the 59,000 human rabies deaths that occur every year  
8 globally [1,2]. In East Africa between 1500-2000 human deaths from dog-mediated rabies are estimated  
9 to occur annually [1,3,4]. Yet human rabies deaths are rarely ever confirmed from any country in East  
10 Africa [5]. The lack of verified statistics documenting the extent of the burden from this notifiable  
11 disease contributes to its continued neglect [6]. Unlike in high-income countries, where dog vaccination  
12 has been used to eliminate rabies and the resulting risk to humans [4,7], dog vaccination campaigns are  
13 still not conducted routinely or at scale across East Africa.  
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16 Post-exposure prophylaxis (PEP) is needed as an emergency measure for rabid bite victims to prevent  
17 the onset of this rapidly progressive fatal neurologic disease [8]. The rabies virus is highly neurotropic,  
18 moving along peripheral nerves from the virus inoculation site to the central nervous system, where it  
19 replicates and causes rabies [4]. In the absence of timely PEP, around one in five rabid bite victims will  
20 progress to rabies, depending on the site and severity of the bite(s) [3]. The World Health Organization  
21 (WHO) recommendations for PEP comprise thorough wound washing followed by a course of post-  
22 exposure vaccinations and, in the case of severe exposure, administration of rabies immunoglobulins  
23 (RIG) [6]. However, access to PEP and its timely use is far from universal. High costs and limited  
24 availability of rabies post-exposure vaccines, as well as a lack of awareness about the need for  
25 appropriate PEP leads to thousands of otherwise preventable deaths [6,9,10].  
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28 New approaches for rabies diagnosis such as sensitive molecular methods and sequencing can improve  
29 the confirmation of human rabies and be used to characterise pathogen spread [11]. Sequencing  
30 approaches have potential to enhance routine rabies surveillance and provide actionable information to  
31 inform elimination programmes, for example, to distinguish whether cases are due to continuous  
32 undetected local circulation or from new incursions and to identify the sources of such incursions  
33 [12,13]. More generally, sequencing could provide key insights into how rabies circulates within  
34 different populations and the processes responsible for its maintenance in specific geographic localities  
35 [14]. In-country genome sequencing of rabies viruses from human rabies cases on the African continent  
36 has so far only been carried out in South Africa [5,15–17], although partial genome sequences are  
37 available from one human rabies case from Senegal [18] and one human rabies case from Nigeria [19].  
38 In this case series we report rabies virus whole genomes sequenced from five human rabies cases in East  
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Africa, investigating the factors leading to each death and how such deaths might be prevented in future.

## CASE PRESENTATION

All five deaths described in this report resulted from exposures by domestic dogs and a lack of, or inappropriate, PEP administration (Table 1). Four of the five patients were children that were ten years old or younger. Three of the children were bitten on the head or neck, sites that are at highest risk for progression to rabies in the absence of PEP [20].

Case 1 was vaccinated against tetanus, but not advised rabies post-exposure vaccination despite attending a health facility the same day as being bitten multiple times by an unknown dog, including one bite to the forehead. Twenty-eight days after being bitten, case 1 started to show rabies symptoms. From symptoms onset the patient was treated for malaria, initially at home, then at a local hospital. The patient's condition deteriorated rapidly, leading to their transfer to a major referral hospital where they died upon arrival. Although Case 2 had no bite history, the patient had killed his two dogs after they manifested signs of rabies one month prior to his own death. After presenting to a nearby health facility with rabies symptoms the patient was transferred to a major referral hospital and pronounced dead 6 days later. Case 3 reported to a local hospital with bites to the lips from an unknown dog, and was vaccinated against rabies following an off-label intramuscular regimen (1mL on days 0, 7 and 18) that is not recommended by WHO. Rabies symptoms began 19 days later, i.e. one day after the third vaccination; and the patient died four days later following transfer to a major referral hospital. Case 4 started post-exposure vaccination, via the intramuscular route, one day after being bitten multiple times on the head and arm by an unknown dog, but did not receive further vaccinations as they were reportedly not advised to do so. After symptoms onset (69 days later) the patient was taken back to the health facility where they were initially vaccinated, then transferred to a major referral hospital where they died shortly thereafter. Case 5 was referred to a major hospital from a health facility where he presented with symptoms of rabies 19 days after exposure. The patient received traditional medicine after being bitten on the leg by his own dog, but otherwise did not receive health care after the bite. Palliative care was given until death 7 days after hospital admission. RIG was not administered to any of these patients, despite the site and severity of bites (multiple bites on the forehead and lips) for cases 1, 3 and 4. Details about each case are as follows:

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9      **Case 1:** On 23rd February 2018, a 10-year-old boy presented with fever, headache, and general body  
10 weakness from Nyawara village, Gem sub-county, Siaya county, Kenya. Suspecting malaria infection, the  
11 boy was initially treated at home with a single dose of the antimalarial Coartem and observed. However,  
12 his condition worsened, and the next day he complained of headache, dizziness, body weakness and  
13 restlessness, vomiting several times and reportedly talking excessively and at times incoherently. The  
14 family took the boy to the local health facility where a rapid diagnostic test was positive for malaria. He  
15 was started on an intramuscular dose of the antimalarial Artesunate, with a repeat dose after four hours.  
16 The nurse observed the boy to be restless, aggressive to touch and having abnormal vocalisation. Upon  
17 inquiry, the nurse learnt that he had been bitten (three times on his left forearm and forehead) on his way  
18 from school by an unknown dog one month earlier, but had not received PEP. The boy's parents described  
19 attending a local health facility on the day the boy was bitten where he was given painkillers  
20 (paracetamol), tetanus vaccination and his wound was cleaned with paraffin, but no advice or treatment  
21 was given to address the rabies risk. With rabies symptoms evident, the boy was referred to the nearest  
22 hospital, where he was given painkillers (Diclofenac). That night he was extremely restless, complaining  
23 of difficulty swallowing the oral medication, salivating uncontrollably, and extremely agitated at the sight  
24 of liquid. The next day, 25<sup>th</sup> February, his condition deteriorated and he was referred to the better  
25 equipped Siaya County Referral Hospital for palliative care where he was declared dead on arrival.  
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9      **Case 2:** On 8th July 2018, a 37-year-old man, from Rarieda village, Gem sub-county, Siaya county, Kenya,  
10 was reported dead due to suspected rabies. Family members were not aware of the man having been  
11 bitten by rabid animals prior to his death. However, his own two dogs had both manifested signs of rabies  
12 and the deceased had killed the animals after they changed their behaviour (one month and three weeks  
13 prior to his own death respectively). Details of whether the dogs were vaccinated during the mass  
14 vaccination campaign conducted in Siaya in 2018 were not disclosed. On 3rd July 2018 the patient visited  
15 a local health facility, presenting with paralysis, abnormal vocalisation, and difficulty breathing. He was  
16 given paracetamol. His condition worsened on 4th July, whereupon he was taken to Siaya County Referral  
17 Hospital for further treatment. The exact treatment he received is unclear, and on 8th July 2018, he was  
18 pronounced dead.

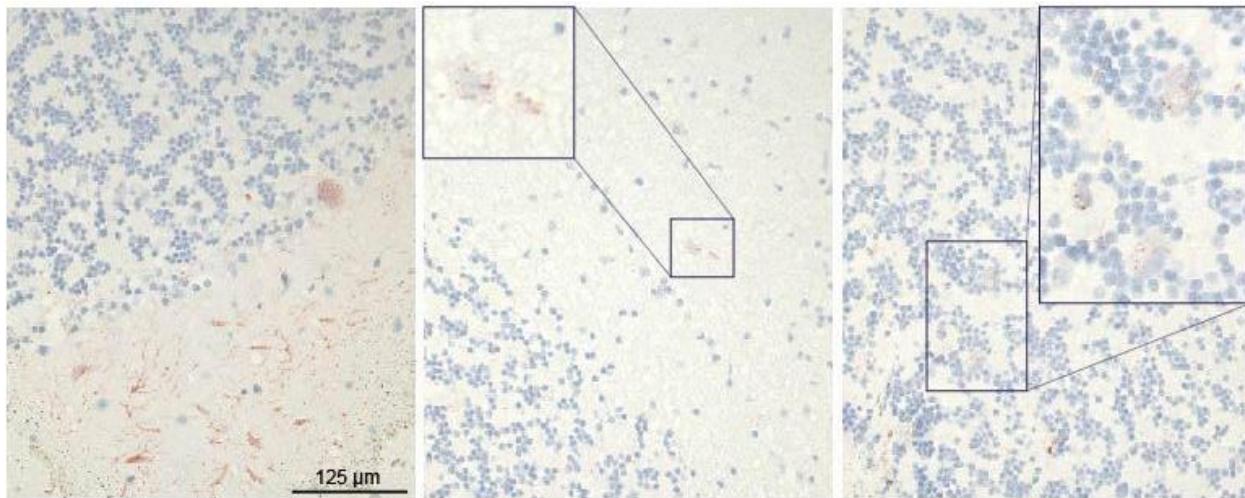
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4     **Case 3:** On 26th August 2019, a six-year-old girl from Tarakea-Rombo village, Moshi district, Kilimanjaro  
5 region, Tanzania, was bitten multiple times on the upper lip by an unknown dog that ran away after the  
6 bite. The patient reported immediately to her local health facility, received proper wound cleaning, and  
7 was administered a first dose of rabies vaccine on day 0 (26<sup>th</sup> August 2019) via the intramuscular route as  
8 well as an anti-tetanus injection. The girl returned for her second rabies vaccine dose on day 7 (2<sup>nd</sup>  
9 September 2019), followed by her third dose on day 18 (12<sup>th</sup> September). The family reported paying  
10 30,000 Tanzania Shillings (Tsh) per vaccination, excluding transportation fees to get the health facility with  
11 the vaccine (16 km away). The day after her third dose (13<sup>th</sup> September 2019), she was taken back to the  
12 same facility with a headache, was given painkillers (paracetamol) and discharged the same day. By the  
13 15th of September her condition had worsened with high fever, headache and hallucinations whereupon  
14 she was referred to Huruma district hospital and then on to Kilimanjaro Christian Medical Centre (KCMC)  
15 referral hospital in Moshi town the same day. She died the following day (16<sup>th</sup> September 2019, 22 days  
16 after the bite).

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20     **Case 4:** On 22nd June 2022, a six-year-old boy from Alara village, South West Sakwa ward, Bondo sub-  
21 county, Siaya county, Kenya, was bitten and scratched multiple times on the head and arm by an unknown  
22 dog while walking home. The dog was chased away by villagers. The boy received first aid at home, where  
23 his wound was washed with soap and water, and he was then rushed to the traditional herbalist where  
24 he received a concoction of herbs. On hearing this news, the community health worker advised the family  
25 to take the child to hospital for PEP. The family took the boy to a local health facility, in West Sakwa,  
26 Bondo sub-county where he received the first dose of rabies vaccine on 23rd June 2022 via the  
27 intramuscular route. The family reported paying 1,000 Kenya shillings (Ksh) for the vaccine, excluding  
28 transportation to the health facility (15 km away). They were given no further advice on the follow up  
29 course of vaccination nor the severity of rabies. On 29th August 2022, the boy was taken to the same  
30 health facility complaining of fever, insomnia, abnormal vocalisation, difficulty breathing and swallowing,  
31 hallucinations and restlessness. He was given normal saline IV and transferred to the referral hospital in  
32 Bondo after his condition worsened, where he was given palliative care and died four hours later.

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36     **Case 5:** On 27th September 2022, a thirteen-year-old boy from Bulati village, Ngorongoro district, Arusha  
37 region, Tanzania, was admitted to Fame hospital after being referred from Bulati health facility on the  
38 same day. The boy was showing signs of rabies including excessive salivation, paralysis, abnormal  
39 vocalisation and restlessness. The boy had apparently been bitten by his own dog on the left leg on 8th  
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September 2022 and did not report or receive any treatment from the health facility / hospital despite regularly attending the hospital for other medical treatment. The wound was washed by milk and a traditional practice for treatment was initiated (placing a coin on the wound to suck the poison). Upon reporting to the health facility, the medical staff inquiry found that the boy was bitten by the dog 20 days prior. He was referred to the major hospital on the same day where he received palliative care until he died on 3rd October 2022 (26 days after the bite).

The rabies incubation period varies; symptoms typically develop days to weeks after infection, but can take months depending on factors such as the bite location and severity [1]. Three of the patients in this case series progressed to rabies within one month of exposure (the date of exposure was not possible to confirm for Case 2, although was recalled to be around one month prior to death), whereas the fifth patient developed symptoms more than two months later. Each patient displayed common clinical signs of rabies: fever, abnormal vocalisation, difficulty breathing and swallowing, hallucinations, paralysis, hydrophobia, aggressiveness, excessive salivation and restlessness. All patients except case 2 had a clear history of a dog bite making the clinical diagnosis straightforward. A history of close contact with two suspect rabid dogs assisted in reaching a diagnosis for case 2. Samples from four of the five cases were positive by rapid diagnostic test. Case 3 had a negative test result; however the presence of rabies virus antigen was confirmed by immunohistochemistry, using the Streptavidin-biotin complex staining method (Fig 1).



**Figure 1. Positive immunohistochemistry staining of case 3, at 40x magnification.** The red stain zoomed in with higher resolution magnification indicates the presence of rabies virus antigen detected with specific labelled antibodies (RABV-N, antibody 5DF12) and Streptavidin-biotin complex staining.

	Case 1	Case 2	Case 3	Case 4	Case 5
<b>Sex/Age (y)</b>	M/10	M/37	F/6	M/6	M/13
<b>Case location</b>	Nyawara village, Central Gem ward, Gem sub-county, Siaya county, Kenya	Rarieda village, Central Gem ward, Gem sub-county, Siaya county, Kenya	Tarakea-Rombo village, Moshi district, Tanzania	Alara village, South West Sakwa ward, Bondo sub-county, Siaya county, Kenya	Bulati village, Ngorongoro district, Tanzania
<b>Bite history</b>	Bites to left arm & forehead by unknown dog	No bite history - but killed his 2 dogs with suspect rabies	Multiple bites to upper lip by unknown dog	Multiple bites to head and arm by unknown dog	Single bite to the left leg by own dog
<b>Exposure date</b>	23 Jan 2018	Unknown	26 Aug 2019	22 June 2022	8 Sep 2022
<b>Delay to attend health facility</b>	0 days	After symptoms onset (8 Jul 2018)	0 days	1 day	After symptoms onset (19 days)
<b>PEP received</b>	Wound cleaning only	None	Wound cleaning; IM vaccine: d0, 7, 18, no RIG	Wound cleaning, IM vaccine: d0 only, no RIG	Wound cleaning only
<b>Other treatment at health facility</b>	Paracetamol, anti-tetanus inj	None	Paracetamol and anti-tetanus inj	None	None
<b>Why no/ inadequate PEP?</b>	Not advised	Reported after symptom onset	Received regimen that is not recommended	Not advised	Reported after symptom onset
<b>Incubation period till symptom onset</b>	28 days	Approximately 1 month (family recall)	19 days	69 days	19 days
<b>Days of illness (symptomatic)</b>	3 days	6 days	4 days	1 day	7 days
<b>Diagnostic results</b>	RDT+ frozen brain	RDT+ frozen brain	RDT- frozen brain; IHT+ formalin-fixed brain tissue	RDT+ fresh brain	RDT+ fresh brain
<b>Viral lineages</b>	AF1b_A2	AF1a_A1.1	AF1b_A1.1	AF1a_C1	AF1b_A1.1
<b>Genome coverage (excluding masked sites)</b>	76.75	51.12	97.49	94.24	97.63
<b>Accession ID</b>	OR045959	OR045960	OR920212	OR045927	OR045947

**Table 1. Summary of human rabies case histories, diagnostic results and viral genome characterization.** All the viruses belong to the Cosmopolitan major clade, and are classified here by minor clade and lineage. RDT = rapid diagnostic test. IHT = Immunohistochemical test.

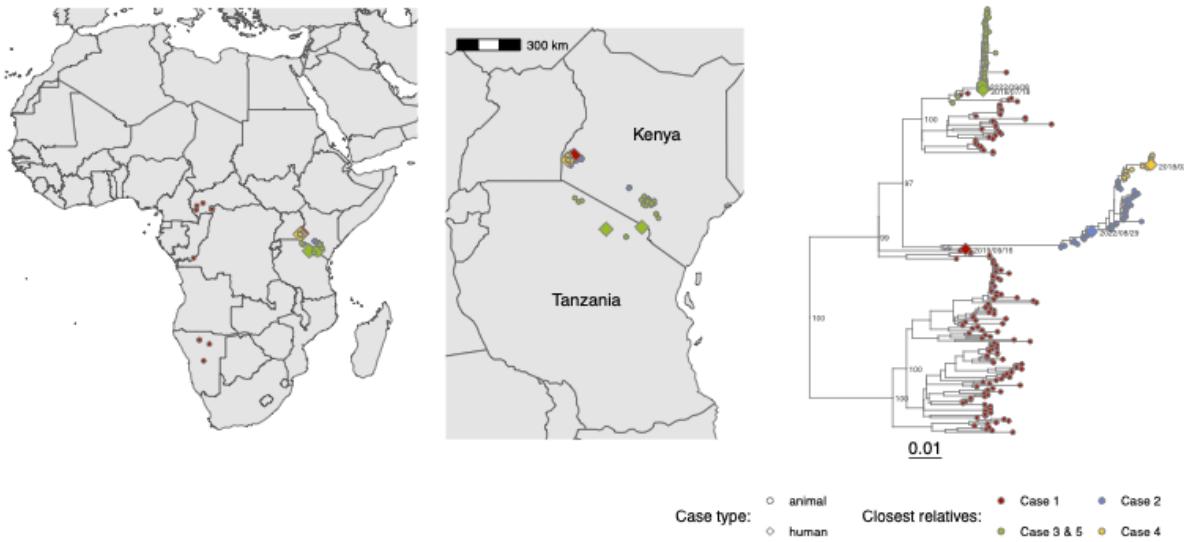
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4 ***Phylogenetic Investigation***  
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6 Amplicon-based sequencing was carried out to compare rabies viruses (RABVs) from the five human  
7 cases to those from recent animal rabies cases in the region. Details of the laboratory procedure are  
8 found in Supplementary File 1. Due to the poor sample conditions and primer mismatches related to the  
9 early primer set used (i.e., targeting RABV diversity in Tanzania from 2019-2020), a few of the sequences  
10 generated (14/98) had less than 90% genome coverage. Sequences from cases 1 and 2 from Kenya both  
11 had less than 90% genome coverage (Supplementary Table 1).  
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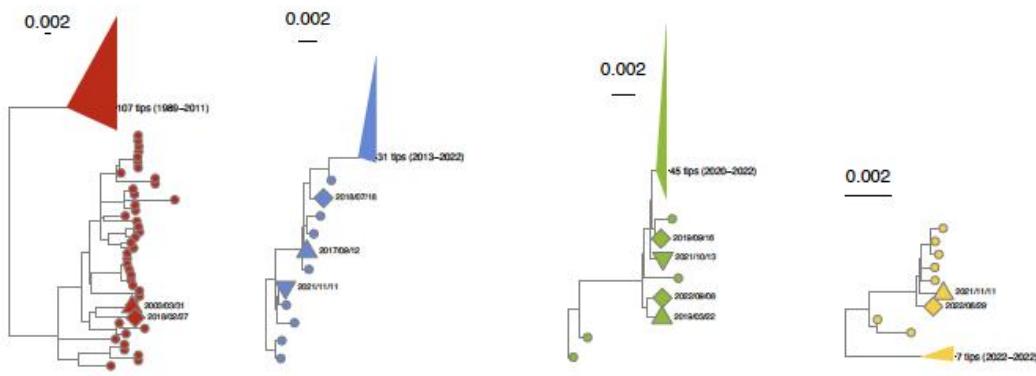
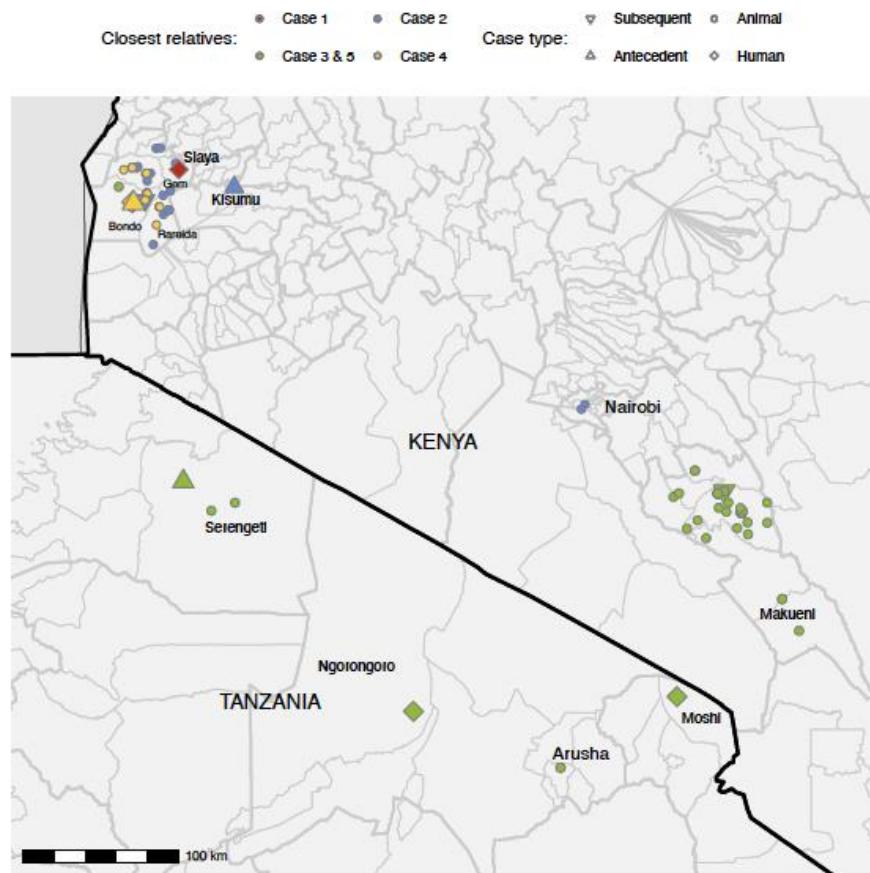
14 All the sequenced viruses were from the Cosmopolitan clade; cases 2 and 4 belonged to minor clade  
15 AF1a (both from Kenya), and cases 1, 3 and 5 belonged to minor clade AF1b (from Kenya, Tanzania and  
16 Tanzania respectively) (Fig 2). Cases 1, 2, 3 and 5 were from previously reported circulating lineages,  
17 with cases 3 and 5 from the same lineage (AF1b\_A1.1), while case 4 was from a newly designated  
18 lineage (AF1a\_C1). The most closely related antecedent and subsequent sequences to all the human  
19 cases were from domestic dogs, except for the subsequent sequence to case 2 which was from a cow,  
20 indicating likely spill over from lineages circulating in domestic dogs.  
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23 All cases except case 4 represent cross-border lineages, with lineage AF1b\_A2, widespread across Africa  
24 but only reported from East Africa in 2018 with this human death (case 1) in Kenya (Fig 3). The most  
25 closely related antecedent sequence to case 1 is from Bangui, CAR, where over 85% of cases in this  
26 lineage were also from (Fig 2A). The geographic distance and phylogenetic divergence between these  
27 cases indicate limited wider sampling of the lineage, which likely originated decades ago (supplementary  
28 Table 2) and is now widespread, though largely undetected, across Africa. In contrast, lineage  
29 AF1b\_A1.1 (cases 3 and 5) has been seen exclusively in East Africa; first in Burundi in 1990, Rwanda in  
30 1994, Kenya in 2001, then Uganda in 2009 followed by Tanzania in 2011. After initial detection, the  
31 lineage was not detected in Kenya again until 2020, since when there has been ongoing circulation and  
32 frequent detection, predominantly in Makueni county. Conversely, detection in Tanzania, has been  
33 sporadic and in close proximity to the Kenyan border (Fig 3A), suggestive of cross-border spread. The  
34 closest antecedent sequence is the same for both cases 3 and 5 - a rabid dog from Serengeti District in  
35 Tanzania sampled in 2019 (Fig 3A). Lineage AF1a\_A1.1 (case 2), was originally detected in Ethiopia in  
36 1987, then in Morocco from 1989 where it was seen frequently until 2008. There have also been  
37 infrequent detections of AF1a\_A1.1 in Algeria since 2000. Virus infections from this lineage were first  
38 detected in Kenya in 2013 with human cases in both Nairobi and Siaya (fig 3B). Lineage AF1a\_C1 (case 4)  
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is newly designated and highly localised, found exclusively in Siaya County, Kenya since 2021. The detection of three lineages (corresponding to cases 1, 2 and 4) all within years or months of each other within Siaya County (Fig 3) highlight the apparent localised co-circulation of lineages.



**Figure 2. Phylogeny of Rabies virus sequences from human cases in the context of relevant circulating lineages.**  
Maximum likelihood tree of lineages relevant to each case and map showing locations for each sequence (n=262). Sequences from the Arctic AL1a clade (GenBank accession AB699220, AY956319, EF437215, HE802675, HE802676, KF154996, KY775603, KY775604, LT909539, LT909541 and MG099711) were used as an outgroup (not shown) to root the tree. Tips and points are coloured by lineage, with diamonds denoting the human cases (OR045959, OR045960, OR920212, OR045927, OR045947). Scale in substitutions/site. Ultrafast bootstrap values of lineage-defining nodes shown.



**Figure 3. Subtrees showing phylogenetic relationships between sequences from human and animal cases.** The map shows the locations of the sequenced human and animal cases from East Africa coloured by lineage. Phylogenetic subtrees shown for case 1 from lineage AF1b\_A2 ( $n = 151$ ) in red; case 2 from lineage AF1a\_A1.1 ( $n = 42$ ) in blue; cases 3 and 5 from lineage AF1b\_A1.1 ( $n = 53$ ) in green and case 4 from lineage AF1a\_C1 ( $n = 16$ ) in yellow. Human cases denoted by diamonds (OR045959, OR045960, HB002 & OR045947, OR045927), and most closely related animal cases (antecedent and subsequent) as determined by minimum patristic distance by triangles (ID = KT119642 (Case 1), OR920307 & OR920256 (Case 2), OR045943 & OR920240 (Case 3 and 5), OR920236 (Case 4)). Relevant locations labelled. Scale in substitutions/site, and outgroup rooted with ordered nodes.

## Discussion

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4 Human rabies deaths occur when rabies-exposed victims fail to receive timely or appropriate PEP. This  
5 case series highlights multiple challenges that bite victims face in obtaining PEP, including inappropriate  
6 advice from medical staff not fully aware of the dangers of rabies (case 1, 4 and 5) or not trained in  
7 correct PEP administration (case 3 and 4); high costs that act as obstacles to initiating (case 1) and  
8 completing PEP courses (case 4) as well as more general lack of understanding about rabies risks. We  
9 report how traditional yet ineffective healing practices are still commonplace (case 4 and 5), with two  
10 cases (2 and 5) only visiting hospitals after symptoms onset, when death is inevitable. Human rabies  
11 deaths in East Africa are typically not confirmed or reported and as a result rabies receives negligible  
12 investment for prevention and control. The clinical history of these five human cases together with use  
13 of rapid diagnostic tests and immunohistochemistry enabled their confirmation, while sequencing  
14 provided further epidemiological context as to their source of origin. This report demonstrates the  
15 feasibility of improving human rabies surveillance in East Africa (all 5 cases were identified via  
16 surveillance networks initiated by research projects), but also only begins to reveal the scale of the  
17 rabies burden. Most human rabies deaths within these communities are not confirmed, while the rabies  
18 virus sequences we report indicate that circulating viral lineages remain largely uncharacterized.  
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### 31           **Improving rabies diagnosis and surveillance**

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33 Human rabies diagnosis remains a challenge in Low- and Middle-Income Countries (LMICs) and cases are  
34 often misdiagnosed, for example, case 1 was considered malaria. If a history of rabies exposure is  
35 elicited, as for all five cases that we report (although atypical for case 2), clinical presentation of furious  
36 rabies is diagnostic, but paralytic rabies can be more difficult to identify[7]. Ante-mortem diagnostic  
37 tests include antigen detection, antibody assays and virus isolation, but all have limited success [8]. Post-  
38 mortem tests are rarely performed due to lack of personnel trained to collect samples, lack of  
39 accredited laboratories (Biosafety Level 2 or 3) for diagnosis and because many clinical cases return  
40 home in the absence of palliative care options and are subsequently not reported within surveillance  
41 networks which might allow the possibility of sample collection [15]. The direct fluorescent antibody  
42 test (DFA) is the recommended “gold standard” for post-mortem diagnosis [21], but requires  
43 fluorescence microscopy which is expensive and limited in availability. The Direct Rapid  
44 Immunohistochemical Test which has similar sensitivity and specificity to the DFA and only requires light  
45 microscopy [22] is based on a simplified version of the immunohistochemistry diagnostic assay [23].  
46 Immunohistochemistry was performed on one of the five cases reported here (case 3) at an overseas  
47 laboratory (Netherlands) through ongoing research, but is not carried out in East Africa. Rapid diagnostic  
48

tests show promise, being successfully used here to diagnose 4 cases *in situ*. The negative result for case 3 was likely due to sample storage (in formalin). More generally freeze-thaw cycles compromise the sensitivity of these tests which are recommended for use only on fresh brain samples. Though rapid diagnostic tests may increase human rabies diagnosis, they are not yet recommended by international organisations. Concerns remain about test sensitivity and quality control [21,23], particularly with respect to PEP decision-making. Laboratory comparisons of rapid test brands under different protocols have been inconsistent, with batch variability presenting an issue [24,25]. Nonetheless, the best performing test has been found to have high sensitivity on fresh samples [26,27]. In our situation, we found rapid tests provided a valuable diagnostic that was possible to quickly and easily perform in the absence of alternatives, and where the risk of rabies was already apparent.

Molecular techniques for diagnosis such as PCR and sequencing are promising and further help in understanding rabies virus biology, molecular epidemiology, pathogenesis and sources of transmission [11]. The viral genomic data associated with the cases presented here highlights the role of domestic dogs in maintaining rabies circulation and resultant risk to humans. These deaths could be avoided if the disease was eliminated from source populations of domestic dogs through mass vaccination, which remains the most cost-effective measure for rabies prevention in endemic regions. Furthermore, the genomic data uncover population connectivity and frequent transboundary viral spread (cases 1, 3 and 5) indicating the need for regional planning and coordinated dog vaccination, as well as for much improved surveillance. Further interpretation is limited by the availability of sequences, though lineage assignment begins to reveal the extent to which under sampling is a problem. Our recent sequencing identified the lineage AF1b\_A2 for the first time in Kenya, and a new lineage, AF1a\_C1 only seen in Kenya. The new lineage designation and considerable divergence of the most closely related sequences to case 1 within lineage AF1b\_A2 (Table S1) illustrate the negligible sampling of circulating rabies viruses.

#### Improving access to post-exposure prophylaxis

WHO now recommends an intradermal post-exposure vaccination regimen that can be completed in one week, requiring visits only on day 0, day 3 and day 7 respectively [1]. This highly effective abridged regimen is both dose-sparing and more economical for patients and health providers [28]. Yet, rabies endemic countries have been slow to adopt the updated WHO position. In parts of Tanzania a post-exposure vaccination regimen is used that is not recommended (case 3). Moreover, while advised for

WHO category III exposures such as cases 1, 3 and 4, RIG has rarely been available in East Africa. Concern has been raised regarding recent human deaths in Tanzania attributed to confusion in post-exposure management, with RIG speculated to have been given and not vaccination. Hence there is an urgent need to update national guidelines to follow WHO guidance and ensure healthcare practitioners are trained and competent to manage rabies exposures appropriately. The high cost of vaccines remains a barrier for bite victims (typically costing around \$10 per vaccination in East Africa, for example, case 3 paid 30,000 Tanzania shillings per dose, equivalent to \$13 while case 4 paid 1000 Kenya shillings per dose, equivalent to \$8) as well as for health providers, translating into inadequate supply and chronic stockouts. Meanwhile, indirect costs to patients (travel, lost income) also can be prohibitively high. The promise of investment in human rabies vaccines by Gavi, the Vaccine Alliance, offers a chance to address PEP access issues and radically redress inequalities underlying human rabies deaths [29,30]. Estimates from modelling studies suggest improved PEP access would prevent over 1.3 million human rabies deaths by 2035 [31]. But with global health priorities disrupted by the pandemic, Gavi support for human rabies vaccines has yet to begin and these deaths continue.

### **Recommendations to address rabies from a One Health perspective**

Through this case series we highlight critical steps needed to combat the problem of rabies in East Africa. Thousands of people every year in the region still face challenges in accessing life-saving PEP. Medical practitioners urgently need training about the risk of rabies and to ensure effective post-exposure management [32]. However, the high cost of PEP remains the most immediate obstacle for rabies-exposed patients[3], compounded by structural factors leading to poor supply and frequent shortages in East Africa. If Gavi delivers on its proposed investment, it can address the market failure in access to lifesaving rabies vaccines [31], catalysing progress on this One Health pathway. Unfortunately, human rabies cases are still rarely diagnosed. To improve the rate at which cases are diagnosed, we suggest rapid tests can be carefully deployed to confirm human cases, given the absence of decentralised laboratory capacity and highly trained personnel. We further present the first whole genome sequences from human rabies cases generated in the region. Viral genomic data support the role of domestic dogs in maintaining rabies circulation and resultant risk to humans. Research across large parts of Tanzania demonstrates that domestic dogs maintain rabies virus circulation [33–35], in settings with abundant wildlife and even where wildlife cases are common [36]. However, misperceptions of wildlife being responsible for rabies persistence, still act as a barrier to implementing rabies control in domestic dog populations [37]. A One Health approach is necessary to reduce the

burden of rabies, comprising the scaling up of mass dog vaccination to interrupt transmission in reservoir populations, improving access to PEP while rabies continues to circulate, and public education to ensure participation in dog vaccination campaigns and improve health seeking for PEP. As countries pursue the global ‘Zero by 30’ goal to eliminate human deaths from dog-mediated rabies [38], genomic approaches have potential to enhance rabies surveillance and provide actionable information, for example, distinguishing undetected local circulation from introductions that often set back progress towards elimination. We urge regional coordinated action towards this goal to prevent these tragic deaths.

## **List of abbreviations**

DFA	Direct Fluorescent Antibody
dRIT	Direct Rapid Immunohistochemically Test
IHT	Immunohistochemistry
KCRI	Kilimanjaro Clinical Research Institute
LMICs	Low- and middle-income countries
PCR	Polymerase chain reaction
PEP	Pre-Exposure Prophylaxis
RABV	Rabies virus
RDT	Rapid diagnostic tests
RIG	Rabies Immunoglobulin
UNITID	University of Nairobi Institute of Tropical and Infectious Diseases
WHO	World Health Organisation

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10 **DECLARATIONS**  
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13 **Ethics approval**  
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15 The study was approved by the Medical Research Coordinating Committee of the National Institute for  
16 Medical Research (NIMR/HQ/R.8a/vol.IX/2788), the Ministry of Regional Administration and Local  
17 Government (AB.81/288/01), and Ifakara Health Institute Institutional Review Board (IHI/IRB/No:22-  
18 2014) in Tanzania; and the University of Nairobi Institute of Tropical and Infectious Diseases  
19 (P947/11/2019) and the Kenya Medical Research Institute (KEMRI-SERU protocol No. 3268) in Kenya.  
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25 **Patient and Public Involvement**  
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27 Carers of family members were consulted to request permission for post-mortem sample collection and  
28 to describe diagnostic and investigative procedures. Following confirmation of results from investigations  
29 the families of these patients and their communities were visited to discuss the meaning of the  
30 investigation results and how findings can be used to advocate for improved rabies prevention and  
31 control, documenting discussions for sharing with practitioners and policymakers.  
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37 **Patient consent**  
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39 Attached SP2  
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43 **Data source and availability**  
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45 Data and code to reproduce the analyses and figures are available from our public repository  
46 [https://github.com/Gurdeepjaswant/EA\\_human\\_rabies\\_case\\_series](https://github.com/Gurdeepjaswant/EA_human_rabies_case_series)  
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50 **Conflicts of interest**  
51

52 There are no conflicts of interest.  
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56

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### **Author's Contributions**

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Literature research: Jaswant G, Campbell K.

Data analysis: Jaswant G, Campbell K, Hampson K, Brunker K, Mutunga M, Czupryna A, Mwatondo A, Ogoti B, Embregts CWE, GeurtsvanKessel CH, Kayuki C, Kuchaka D, Wambura G, Oigo J, Changalucha J, Lushasi K, Sikana L, Zwetselaar Mv, Dekker MCJ, Muturi M, Maritim M, Durrant R, Abala T, Chuchu V.

Manuscript writing: Jaswant G, Campbell K, Mutunga M,

Manuscript editing: Hampson K, Brunker K

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### **Copyright**

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Figure 1

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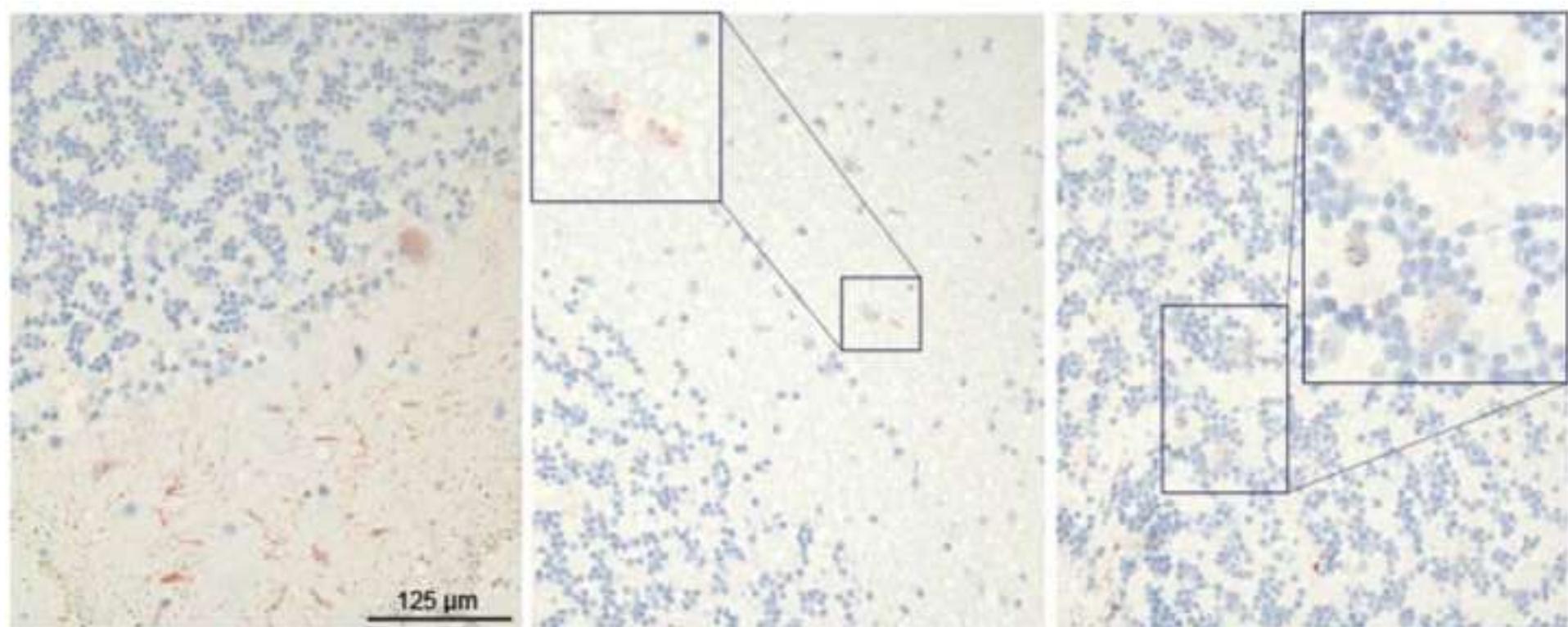
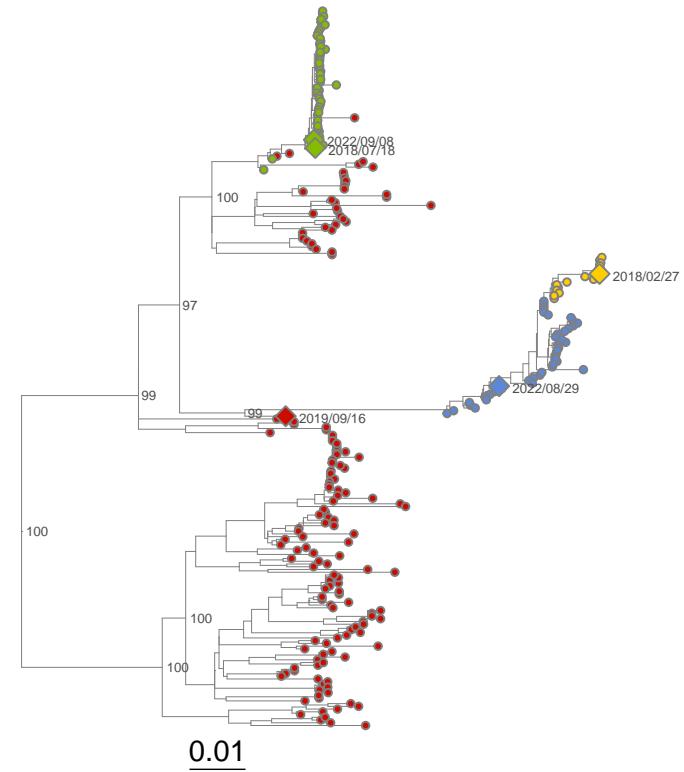
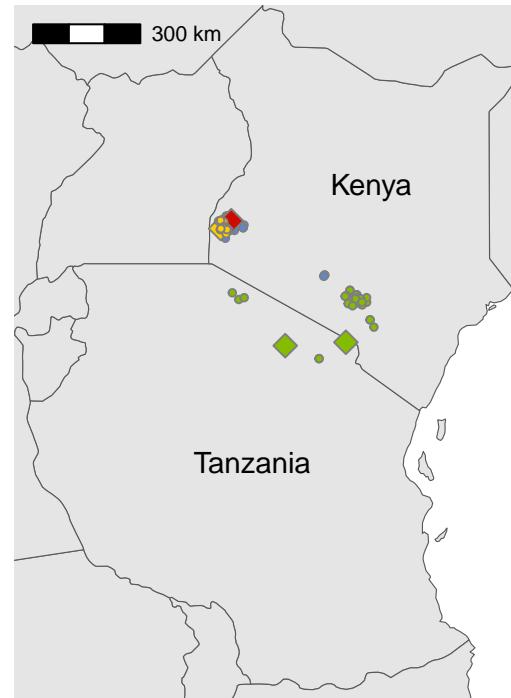


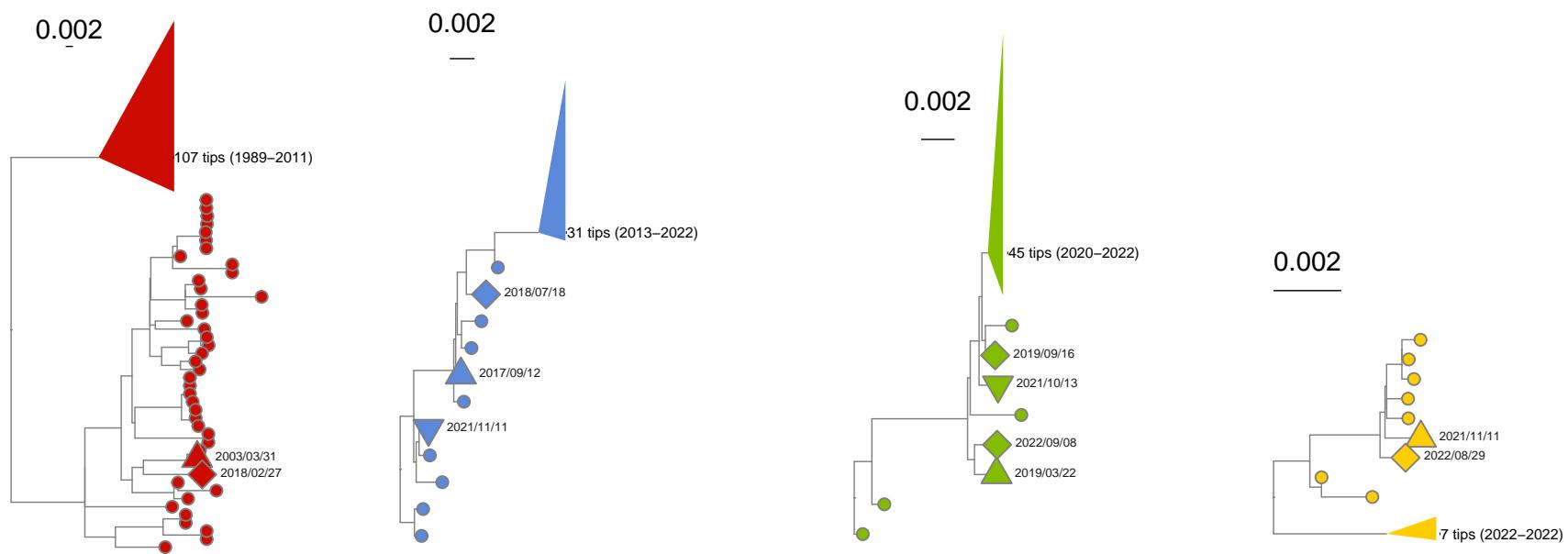
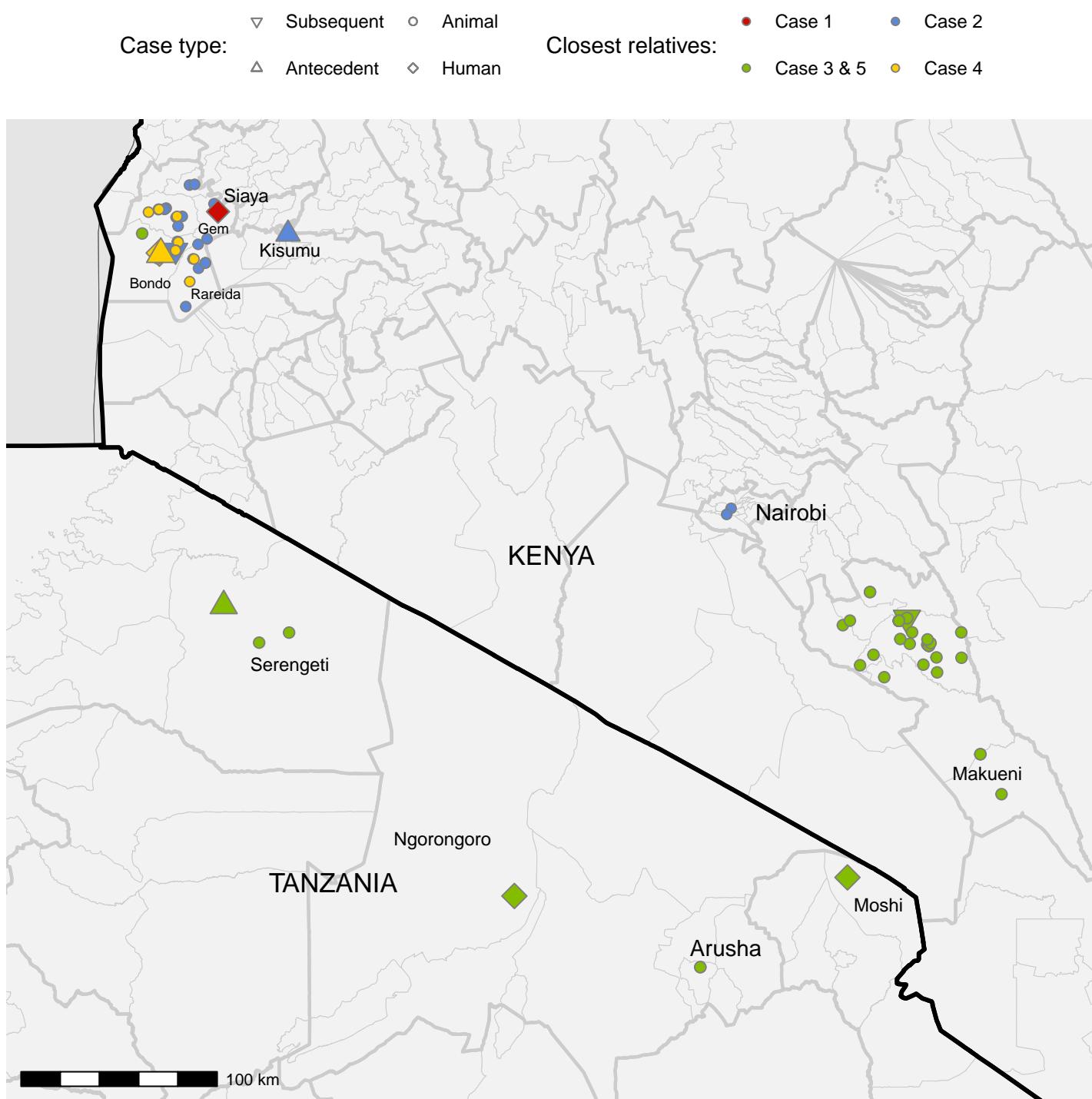
Figure 2

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Case type:  
○ animal  
◊ human

Closest relatives:  
● Case 1     ● Case 2  
● Case 3 & 5     ● Case 4

Figure 3

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University of Nairobi

24<sup>th</sup> June 2024

Editor in Chief  
*Infectious Diseases of Poverty*

Dear Xiao-Nong Zhou,

We hope that you will consider our manuscript entitled “Molecular characterization of human rabies in East Africa - a case series report and phylogenetic investigation” for publication in *Infectious Diseases of Poverty* as a case series report. We believe that our draft covers an important timely topic that has for too long been neglected: public health failings that lead to human rabies.

Many thousands of human rabies deaths are estimated to occur every year in LMICs, yet few are reported, including in East Africa, the focus of our study. Lack of diagnostic confirmation renders rabies invisible in official statistics and, perhaps, to the global health community. Since there is no treatment for this invariably fatal disease, rabies epitomizes the need for prevention. The proximate means to prevent rabies is emergency post-exposure vaccination of bite victims (which every rabies victim has failed to receive). Domestic dogs are the reservoir of rabies across Africa, but dog vaccination ultimately needed to control rabies has not been prioritized, even as rhetoric around One Health has become mainstream.

Through investigation of five recent human rabies deaths in East Africa we illustrate systemic failures and recommend actions to address this entirely preventable disease. We uncover stark inequalities underlying these deaths that highlight the need to improve access to life-saving post-exposure vaccines and raise awareness about their appropriate use. We further show local capacity to confirm human rabies deaths, which we have frequently heard as a reason for not addressing rabies. Moreover, for the first time on the continent outside of South Africa, we sequence rabies viruses from human cases to investigate their origin and illustrate the value of applying genomic surveillance beyond SARS-CoV-2. The resulting viral genomes help to reveal the scale of the problem and highlight cross-border circulation that is maintained in domestic dog populations, necessitating large-scale and coordinated dog vaccination.

Gavi, the Vaccine Alliance, recently agreed to un-pause their 2018 promised investment in human rabies post-exposure vaccines that was put on hold in 2020. Gavi investment should be a game changer in improving access to life-saving human rabies vaccines and for catalysing action on the deeper structural failure to adopt a One Health approach, so communities can be spared from the trauma of rabies outbreaks. Our manuscript demonstrates how scientists and clinicians in East Africa are ready to improve rabies surveillance to support Gavi’s investment to prevent human rabies. *Infectious Diseases of Poverty* contributes significantly to medical knowledge and enhances educational value by highlighting the need for changes in clinical practice and diagnostic/prognostic approaches. We would therefore be honored to have our work published in the journal.

Sincerely,

Gurdeep Jaswant  
Corresponding Author



## Informed Consent Forms (English Version)

**Rabies Elimination Program in Kenya**

**Principal investigator Thumbi Mwangi**

**Name of interviewer** \_\_\_\_\_

**Date** \_\_\_\_\_

### **Introduction**

Kenya has recently adopted a strategic plan for the elimination of rabies in humans by 2030. As part of the plan, your county has been selected to participate in the pilot study as among the first counties where rabies will be eliminated. The rabies elimination strategy involves three main activities; vaccination of dogs, vaccination of persons that have been bitten by dogs, and surveillance for cases of human and dog rabies at the health facilities and at homes.

Here we would like to gather information about cases of dog-bites that have happened to you or your family members, information on how you managed these dog-bites, whether the bite victims accessed health care including vaccinations. We will use these data to understand the magnitude of the rabies problem in your community, and determine the best ways to prevent the disease in people and their dogs. The choice of you, or any member of your household including children participating in the study is completely voluntary, and you may refuse to join now or withdraw from the study anytime without any consequences on you or your child.

**What we would like to do:** If you agree for you, a family member or any child under your care to be part of the study, we would like to administer a questionnaire collecting the information I have just mentioned above. We will not require to collect any human sample from any of you. Additionally, if the biting dog belongs to you, we may collect samples from your dog to allow for health monitoring. We estimate these household visits and questionnaire administration will take about 20 minutes.

### **Benefit from being in this study:**

The data obtained from the study will aid in gaining more knowledge on the epidemiology of rabies in the country whose ultimate benefits are reducing its public health burden. As a participant, we will inform you on ways of reducing the risk of dog bites, and proper wound management if dog bites do occur to you or to your family members.

### **Risks from being in this study:**

Participation will entail answering questions about the history of dog bites and how these were managed, and the management of dogs within the household. None of these activities poses any danger to you or any member of your family. There will be minor inconveniences from the time required to administer the questionnaire at the household.

The facts about you and your family from this study will be kept private as much as allowed by law. No names will be used on any of the study reports. If you want to discuss this study with a doctor not involved in the study, contact Dr. Athman Mwatondo at the Ministry of Health, Zoonotic Disease Unit in Nairobi. His phone number is 0721-579-276. These include problems from the study that you may want a doctor to look at or any questions about your rights as a study member. Should any more questions arise, if you feel your child may have been harmed by being in the study, or if you want to quit the study, please contact Dr. Thumbi Mwangi using the office line in Kisian (2022983).

**Consent signing:**

The consent form has been explained to me and I agree to participate, or my child to take part in the study. I understand that I am free to choose not to take part in this study at any time and that saying “NO” will have no effect on me, my child or my family.

<b>Parent's name</b>	Name: .....	Signature:.....	date <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
<b>Witness*</b>	Name: .....	Signature:.....	date <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

- Subject may sign or provide verbal consent in the presence of a witness. The witness (by his/her signature) verifies that the consent form has been accurately translated to the subject and this is the subject's signature or that he/she has provided verbal consent.

## Appendix A1: Informed Consent Forms (Dholuo Version 2.0)

### Chenro mar tieko tuo mar Siwao

Jatend nonro: Thumbi Mwangi

Nying ja nonro \_\_\_\_\_

Tarik	□□□□□	Gweng/Dala, Ot	□□□□□, ,
Nying nyathi		..... .....	
Nying nyathi/jarit nyathi		..... .....	

### Motelo

E thuolo masani, piny Kenya chako kao chenro mar tieko tuo mar siwao e dhano kochopo higa mar 20130. Kuom chenro ni, county u oyier mondo otigo kaka ranyisi mar kuonde mibonyisgo kaka inya tiek tuoni. Chenro mar tieko tuo ni biro luwo ratiro adek; chanjo guogi, chanjo dhano ma guogi okayo ka achiel gi timo nonro mar manyo kecho mar guogi kuonde thieth gi delni.

Mondi magi tee otimre, wabiro timo chenro motenre ginono weche kaka kecho mar guogi kuomi kata anyuola ni, ratiro mane ika kane guok okai, ka ngat mane oka ne omanyo thieth machalo kaka chanjo. Komedre, wabiro manyo weche motenre gi pidho guogi, kit ngima gi, gi kaka irito guogi mipidho. Weche gi ibotigo e ng'eyo kit pek kata ting mabiro gi tuoni e dak u, kaka inyalo geng' tuo ni kuom dhano gi guogigi. Donjo e nonro ni en yiero mari kata mar jaodi moro amora kata nyithindo kendo oyiene nga'to ang'ata mondo otamre donjo kata wuok ma onge gimarach mibotimne obed in kata nyathina.

Chenro mar tich: Ka iyie ni idonjo e nonro, iyie ne jaodi moro amora donjo kata nyathi moro amora mani e buoyi donjo, wabiro penjo weche motenre gi tuo mar siwao gi guogi. Ok wabikao kit del moro amora kuomu. Ka oyier odi mondo obed e limbe mag nonro makinde kakinde mondo ong'e dak mar guogi kaka ngima gi kod pon margi, wabiro limi dwe ka dwe ka wakwai mondo idwok penjo . Komedre gi mano, wabokao kit del mag gwogi mondo wang'e go ngima ne. Ma ibotim dwe ka dwe kuom dweche 18. Limbe gi penjo gi bokao thuolo manyaloromo dakika 20.

### Ber bet e nonro:

Nonro ni bokonyo medo ng'eyo gi rieko e landruok mar tuo mar siwao e piny wa mar Kenya, ma biro konyo e dwoko chein hinyruok ma tuo ni kelo. Kaka ng'at moyie donjo e nonro, ibiro yudo

puonjruok kaka inyalo duoko chien kecho mag guogi kod kaka inyalo thiedho adhola ka guok okai kata jaodi moro amora.

Rach bedo e nonro:

Donjo e nonro biro keti e dwoko penjo mag kecho mag gwogi, ratiro mane okau bang' kecho gi kaka urito guogi. Onge gimoro amora mabiro inyi kata jaodi moro amora e nonro ni. Rach matin manyalo bet en thuolo ni ma ibiro kau seche limbe.

Weche kod dwoko ma ibiro chiwo kata joodi ibiro kan moondo maling' ling' kaka chik nonro dwarz. Onge nying ma ibiro tigo e ripot moro amora . In gi ratiro ma inyalo dwarz ng'eyo go hinyruok moro amora ma nonro ni nyalo keloni kata joodi kuom laktar kata penjo moro ma inyalo bet go. Ka inyalo bet gi penjo moro e thuolo ma nyime, ka ineno ni jaodi kata nyathini oyudo hinyruok ka owuok e nonro, ka idwa wuok e nonro, tudri gi jatelo maduong' mochung' ne ratiro mag nonro duto e KEMRI e mbuyi ka itiyo gi: [seru@kemri.org](mailto:seru@kemri.org) kata e namba simo: 0717719477.

Keto seyi:

Weche gi oselerna kendo aseyie mar donjo e nonro ni gi nyithinda. Awinjo ni an thuolo mar tamruok donjo e nonro ni sa asaya kendo tamruok ni ok biro kelo hinyruok moro amora ne an, nyathina kata jooda.

<b>Nying janyuol</b>	<b>Nying:</b> .....	<b>Seyi:</b> .....	<b>tarik</b> □□□□□
<b>Janeno*</b>	<b>Nying:</b> .....	<b>Seyi:</b> .....	<b>tarik</b> □□□□□

- Ng'at madonjo e nonro nyalo keto seyi kata yie gidhoge e nyim janeno. Keto seyi gi janeno en ranyisi ni weche mondiki gi oseler ni jadonjo e nonro kendo seyi ne kata yie ne en kamano.

Wuon ot	Nying:	Seyi/Luedo:	tarik□□/□□/□□
Janeno	Nying:	Seyi:	tarik□□/□□/□□
Janonro	Nying:	Seyi:	tarik□□/□□/□□



# Chenro mar tieko tuo mar Siwao

Jatend nonro: Thumbi Mwangi

Nying ja nonro ... TOK ABALA

Tarik.... 30/08/22

Gweng/Dala, Ot..... ALARAK

Nying wuon dala.... LILAK ATIENDA

Motelo thuolo masani, piny Kenya chako chenro mar tieko tuo mar siwao e dhano kochopo higa mar 2030. Kuom chenro ni, county ma siaya oyier mondo otigo kaka ranyisi mar kuonde mibonyisgo kaka inya tiek tuoni. Chenro mar tieko tuo ni biro luwo ratiro adek; chanjo guogi, chanjo dhano ma guogi okayo ka achiel gi timo nonro mar manyo kecho mar guogi kuonde thieth gi delni. Mondi magi tee optimre, wabiro timo chenro motenre ginono weche kaka kecho mar guogi kuomi kata anyuola ni, ratiro mane ika kane guok okai, ka ngat mane oka ne omanyo thieth machalo kaka chenjo. Komedre, wabiro manyo weche motenre gi pidho guogi, kit ngima gi, gi kaka irito guogi mipidho. Weche gi ibotigo e ng'eyo kit pek kata ting mabiro gi tuoni e dak u, kaka inyalo geng' tuo ni kuom dhano gi guogigi. Donjo e nonro ni en yiero mari kata mar jaodi moro amora kata nyithindo kendo oyiene nga'to ang'ata mondo otamre donjo kata wuok ma onge gimarach mibotimne obed in kata nyathina.

**Chenro mar tich:**

Ka iyie ni idonjo e nonro, iyie ne jaodi moro amora donjo kata nyathini moro amora mani e buoyi donjo, wabiro choko weche motenre gi kecho mar guok manotimre nein kata joodi, gima nitimo sama ne guok okayi, kata ka ngama nokano be nodhi e hospital moyudo chanjo ma siwawo. Kadipo ni nitie hinyruok moro kata tho kaluwore gi kecho mar guogno dewagomb penji kata joodi penjo moko kaluwore gi kaka guogno nokai. Ma biro konyowa ngeyo matut kuma guok ayie kendo fwenyo kata kabenyudo chanjo mar siwawo. Mano biro konyowa mar ngeyo matut kaka tuoni(siwawo) kelo chandruok nejogueng. Mno nyalo konyo mondo mi wane kaka wanyalo duoko tuoni chien kuom dhano kaachiel gi guogi magipidho.

Wakuayo bende ni weche ma ochok kuomu kata joodi ibiro tiyogo mondo ondik go ripot maluwore gi tuoni, ma nyalo konyo duoko chien tuoni epiny kenya kata gi pinje maoko. OK WABI TIYO GI NYING NGATO ANGATA E RIPODEWA. Donjo enonro en yiero mari, inyalo yie kata tamri kata inyalo yie tiwuok saa asaya midwaro, onge gimoro amora mibiro timni kata joodi.

**Ber bet e nonro:**

Nonro ni bokonyo medo ng'eyo gi rieko e landruok mar tuo mar siwao e piny wa mar Kenya, ma biro konyo e dwoko chien hinyruok ma tuo ni kelo. Kaka ng'at moyie donjo e nonro, ibiro yudo puonruok kaka inyalo duoko chien kecho mag guogi kod kaka inyalo thiedho adhola ka guok okai kata jaodi moro amora. Ratiro mar chenro tiyo gi sirikal mar gwenge ma siaya ekeklo chenjo mar nono mar guogi.

Kaponi ngato guok okayo, chenroni biro temo mondo chanjo mar tuo mar siwao obedie e kuonde thieth mag sirikal masiaya,to kanyalre to thiedh no biro bet manono.

**Rach bedo e nonro:**

Donjo e nonro biro keti e dwoko penjo mag kecho mag gwogi, ratiro mane okau bang' kecho gi kaka urito guogi, Onge gimoro amora mabiro inyi kata jaodi moro amora e nonro ni. Rach matin manyalo bet en thuolo ni ma ibiro kau seche limbe. Weche kod dwoko ma ibiro chiwo kata joodi ibiro kan mopondo maling' ling' kaka chik nonro dwarz. Onge nyng ma ibiro tigo e ripot moro amora . In gi ratiro ma inyalo dwarz ng'eyo go hinyruok moro amora ma nonro ni nyalo keloni kata joodi kuom laktar kata penjo moro ma inyalo bet go. Ka inyalo bet gi penjo moro e thuolo ma nyime, ka ineno ni jaodi kata nyathini oyudo hinyruok ka owuok e nonro, ka idwa wuok e nonro, tudri gi jatelo maduong' mochung' ne ratiro mag nonro duto e KEMRI e mbuyi ka itiyo gi: seru@kemri.org kata e namba simo: 0717719477.

Keto seyi

Weche gi oselerna kendo aseyie mar donjo e nonro ni gi nyithinda. Awinjo ni an thuolo mar tamruok donjo e nonro ni sa asaya kendo tamruok ni ok biro kelo hinyruok moro amora ne an, nyathina kata jooda.

Nying wuon ot: LILIAN ATIENO..... Seyi: .....  Tarik 30 / 08 / 2022

Janeno\*: Gabriel Owino..... Seyi: .....  Tarik 30 / 08 2022

- Ng'at madonjo e nonro nyalo keto seyi kata yie gidhoge e nyim janeno. Keto seyi gi janeno en ranyisi ni weche mondiki gi oseler ni jadonjo e nonro kendo seyi ne kata yie ne en kamano.

# Chenro mar tieko tuo mar Siwao

Jatend nonro: Thumbi Mwangi

Nying ja nonro ..... TOM ABALA

Tarik..... 12/07/2018

Gweng/Dala, Ot..... RARIETA

Nying wuon dala..... PAMELA AWINPO

Motelo thuolo masani, piny Kenya chako chenro mar tieko tuo mar siwao e dhano kochopo higa mar 2030. Kuom chenro ni, county ma siaya oyier mondo otigo kaka ranyisi mar kuonde mibonyisgo kaka inya tiek tuoni. Chenro mar tieko tuo ni biro luwo ratiro adek; chanjo guogi, chanjo dhano ma guogi okayo ka achiel gi timo nonro mar manyo kecho mar guogi kuonde thieth gi delni. Mondi magi tee optimre, wabiro timo chenro motenre ginono weche kaka kecho mar guogi kuomi kata anyuola ni, ratiro mane ika kane guok okai, ka ngat mane oka ne omanyo thieth machalo kaka chenjo. Komedre, wabiro manyo weche motenre gi pidho guogi, kit ngima gi, gi kaka irito guogi mipidho. Weche gi ibotigo e ng'eyo kit pek kata ting mabiro gi tuoni e dak u, kaka inyalo geng' tuo ni kuom dhano gi guogigi. Donjo e nonro ni en yiero mari kata mar jaodi moro amora kata nyithindo kendo oyiene nga'to ang'ata mondo otamre donjo kata wuok ma onge gimarach mibotimne obed in kata nyathina.

Chenro mar tich:

Ka iyie ni idonjo e nonro, iyie ne jaodi moro amora donjo kata nyathini moro amora mani e buoyi donjo, wabiro choko weche motenre gi kecho mar guok manotimre nein kata joodi, gima nitimo sama ne guok okayi, kata ka ngama nokano be nodhi e hospital moyudo chanjo ma siwawo. Kadipo ni nitie hinyruok moro kata tho kaluwore gi kecho mar guogno dewagomb penji kata joodi penjo moko kaluwore gi kaka guogno nokai. Ma biro konyowa ngeyo matut kuma guok ayie kendo fwenyo kata kabenyudo chanjo mar siwawo. Mano biro konyowa mar ngeyo matut kaka tuoni(siwawo) kelo chandruok nejogueng. Mno nyalo konyo mondo mi wane kaka wanyalo duoko tuoni chien kuom dhano kaachiel gi guogi magipidho.

Wakuayo bende ni weche ma ochok kuomu kata joodi ibiro tiyogo mondo ondik go ripot maluwore gi tuoni, ma nyalo konyo duoko chien tuoni epiny kenya kata gi pinje maoko. OK WABI TIYO GI NYING NGATO ANGATA E RIPODEWA. Donjo enonro en yiero mari, inyalo yie kata tamri kata inyalo yie tiwuok saa asaya midwaro, onge gimoro amora mibiro timni kata joodi.

Ber bet e nonro:

Nonro ni bakonyo medo ng'eyo gi rieko e landruok mar tuo mar siwao e piny wa mar Kenya, ma biro konyo e dwoko chien hinyruok ma tuo ni kelo. Kaka ng'at moyie donjo e nonro, ibiro yudo puonruok kaka inyalo duoko chien kecho mag guogi kod kaka inyalo thiedho adhola ka guok okai kata jaodi moro amora. Ratiro mar chenro tiyo gi sirikal mar gwenge ma siaya ekeklo chenjo mar nono mar guogi.

Kaponi ngato guok okayo, chenroni biro temo mondo chanjo mar tuo mar siwao obedie e kuonde thieth mag sirikal masiaya,to kanyalre to thiedh no biro bet manono.

**Rach bedo e nonro:**

Donjo e nonro biro keti e dwoko penjo mag kecho mag gwogi, ratiro mane okau bang' kecho gi kaka urito guogi, Onge gimoro amora mabiro inyi kata jaodi moro amora e nonro ni. Rach matin manyalo bet en thuolo ni ma ibiro kau seche limbe. Weche kod dwoko ma ibiro chiwo kata joodi ibiro kan mopondo maling' ling' kaka chik nonro dwarz. Onge nying ma ibiro tigo e ripot moro amora . In gi ratiro ma inyalo dwarz ng'eyo go hinyruok moro amora ma nonro ni nyalo keloni kata joodi kuom laktar kata penjo moro ma inyalo bet go. Ka inyalo bet gi penjo moro e thuolo ma nyime, ka ineno ni jaodi kata nyathini oyudo hinyruok ka owuok e nonro, ka idwa wuok e nonro, tudri gi jatelo maduong' mochung' ne ratiro mag nonro duto e KEMRI e mbuyi ka itiyo gi: seru@kemri.org kata e namba simo: 0717719477.

Keto seyi

Weche gi oselerna kendo aseyie mar donjo e nonro ni gi nyithinda. Awinjo ni an thuolo mar tamruok donjo e nonro ni sa asaya kendo tamruok ni ok biro kelo hinyruok moro amora ne an, nyathina kata jooda.

Nying wuon ot: PAMELA AWINO Seyi: ~~AA~~ Tarik 12/07/2018

Janeno\*: KEVIN OIENO Seyi: ~~KK~~ Tarik 12/07/2018

- Ng'at madonjo e nonro nyalo keto seyi kata yie gidhoge e nyim janeno. Keto seyi gi janeno en ranyisi ni weche mondiki gi oseler ni jadonjo e nonro kendo seyi ne kata yie ne en kamano.

# Chenro mar tieko tuo mar Siwao

Jatend nonro: Thumbi Mwangi

Nying ja nonro ..... TOM ABALA

Tarik..... 27 FEB 2018

Gweng/Dala, Ot..... N YAKARA

Nying wuon dala..... PHILIP OTI expo

Motelo thuolo masani, piny Kenya chako chenro mar tieko tuo mar siwao e dhano kochopo higa mar 2030. Kuom chenro ni, county ma siaya oyier mondo otigo kaka ranyisi mar kuonde mibonyisgo kaka inya tiek tuoni. Chenro mar tieko tuo ni biro luwo ratiro adek; chanjo guogi, chanjo dhano ma guogi okayo ka achiel gi timo nonro mar manyo kecho mar guogi kuonde thieth gi delni. Mondi magi tee optimre, wabiro timo chenro motenre ginono weche kaka kecho mar guogi kuomi kata anyuola ni, ratiro mane ikao kane guok okai, ka ngat mane oka ne omanyo thieth machalo kaka chenjo. Komedre, wabiro manyo weche motenre gi pidho guogi, kit ngima gi, gi kaka irito guogi mipidho. Weche gi ibotigo e ng'eyo kit pek kata ting mabiro gi tuoni e dak u, kaka inyalo geng' tuo ni kuom dhano gi guogigi. Donjo e nonro ni en yiero mari kata mar jaodi moro amora kata nyithindo kendo oyiene nga'to ang'ata mondo otamre donjo kata wuok ma onge gimarach mibotimne obed in kata nyathina.

**Chenro mar tich:**

Ka iyie ni idonjo e nonro, iyie ne jaodi moro amora donjo kata nyathini moro amora mani e buoyi donjo, wabiro choko weche motenre gi kecho mar guok manotimre nein kata joodi, gima nitimo sama ne guok okayi, kata ka ngama nokano be nodhi e hospital moyudo chanjo ma siwawo. Kadipo ni nitie hinyruok moro kata tho kaluwore gi kecho mar guogno dewagomb penji kata joodi penjo moko kaluwore gi kaka guogno nokai. Ma biro konyowa ngeyo matut kuma guok ayie kendo fwenyo kata kabenyudo chanjo mar siwawo. Mano biro konyowa mar ngeyo matut kaka tuoni(siwawo) kelo chandruok nejogueng. Mno nyalo konyo mondo mi wane kaka wanyalo duoko tuoni chien kuom dhano kaachiel gi guogi magipidho.

Wakuayo bende ni weche ma ochok kuomu kata joodi ibiro tiyogo mondo ondik go ripot maluwore gi tuoni, ma nyalo konyo duoko chien tuoni epiny kenya kata gi pinje maoko. OK WABI TIYO GI NYING NGATO ANGATA E RIPODEWA. Donjo enonro en yiero mari, inyalo yie kata tamri kata inyalo yie tiwuok saa asaya midwaro, onge gimoro amora mibiro timni kata joodi.

**Ber bet e nonro:**

Nonro ni bokonyo medo ng'eyo gi rieko e landruok mar tuo mar siwao e piny wa mar Kenya, ma biro konyo e dwoko chien hinyruok ma tuo ni kelo. Kaka ng'at moyie donjo e nonro, ibiro yudo puonruok kaka inyalo duoko chien kecho mag guogi kod kaka inyalo thiedho adhola ka guok okai kata jaodi moro amora. Ratiro mar chenro tiyo gi sirikal mar gwenge ma siaya ekeklo chenjo mar nono mar guogi.

Kaponi ngato guok okayo, chenroni biro temo mondo chanjo mar tuo mar siwao obedie e kuonde thieth mag sirikal masiaya,to kanyalre to thiedh no biro bet manono.

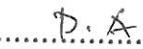
**Rach bedo e nonro:**

Donjo e nonro biro keti e dwoko penjo mag kecho mag gwogi, ratiro mane okau bang' kecho gi kaka urito guogi, Onge gimoro amora mabiro inyi kata jaodi moro amora e nonro ni. Rach matin manyalo bet en thuolo ni ma ibiro kau seche limbe. Weche kod dwoko ma ibiro chiwo kata joodi ibiro kan mopondoo maling' ling' kaka chik nonro dwaro. Onge nyung ma ibiro tigo e ripot moro amora . In gi ratiro ma inyalo dwaro ng'eyo go hinyruok moro amora ma nonro ni nyalo keloni kata joodi kuom laktar kata penjo moro ma inyalo bet go. Ka inyalo bet gi penjo moro e thuolo ma nyime, ka ineno ni jaodi kata nyathini oyudo hinyruok ka owuok e nonro, ka idwa wuok e nonro, tudri gi jatelo maduong' mochung' ne ratiro mag nonro duto e KEMRI e mbuyi ka itiyo gi: seru@kemri.org kata e namba simo: 0717719477.

Keto seyi

Weche gi oselerna kendo aseyie mar donjo e nonro ni gi nyithinda. Awinjo ni an thuolo mar tamruok donjo e nonro ni sa asaya kendo tamruok ni ok biro kelo hinyruok moro amora ne an, nyathina kata jooda.

Nying wuon ot: Philip Otieno Seyi:  Tarik 27/02/2018

Janeno\*:  Seyi:  Tarik 27/02/2018

- Ng'at madonjo e nonro nyalo keto seyi kata yie gidhoge e nyim janeno. Keto seyi gi janeno en ranyisi ni weche mondiki gi oseler ni jadonjo e nonro kendo seyi ne kata yie ne en kamano.



**Kilimanjaro Christian Medical College**  
An Institution of the Good Samaritan Foundation  
P. O. Box 3010, Moshi, Tanzania. Telephone: 255 27 2753477/83 Fax: 255 27 2753481  
Email [kcmcadm@kcmc.ac.tz](mailto:kcmcadm@kcmc.ac.tz) Website: <http://www.kcmc.ac.tz>

### Informed consent form

The undersigned,

Name: **Kimario Kavishe**

EHMS # 43525.

Gender: Male / Female (strike off what is not applicable)

Date of birth: 43 years

gives permission to doctors of the department of Paediatrics Child Health, Kilimanjaro Christian Medical Centre/Kilimanjaro Christian Medical University College in Moshi (strike off what is not applicable):

- To take photographs for medical education.
- To store sampled biologic material (e.g. blood, biopsy) and to analyse this material for diagnostic purposes where indicated.
- To use clinical data, unedited photographs and results of additional investigations for publication in a national or international medical journals.

*NB separate KCMC hospital autopsy/postmortem consent form was signed and is stored in patient file (paper)*

Name of disorder: Clinical rabies.

Sample Type: minimally invasive postmortem biopsy

Test to be performed on sample: tissue obtained in minimally invasive postmortem procedures (abdominal organs/mesentery; cerebellum; lymph nodes

I give permission as a parent / guardian (strike off what is not applicable), of the following patient:

Name of child: **Emiliana Kavishe**

Gender: Male/Female (strike off what is not applicable)

Date of birth: 6 years

I am aware of and allow KCMC/an external body to perform the above designated test(s) on the sample from me and my baby. My signature below encompasses my acknowledgment that the benefits, risks, consequences and limitations of this testing have been explained to my satisfaction by a qualified health professional.

- I was in the situation that I could consider my participation deliberately and I understand that, if I would decide not to participate, this will not have any influence on the treatment that I/my child will receive.
- I/my child will have the right to withdraw the consent at any moment without the obligation to give a reason and without further consequences in treatment.
- I have been informed about the content of this consent comprehensively and I was in the opportunity to ask questions.

An identical version of this form has been provided to me in Swahili and I have been able to read it.

Place: KCMC Moshi,

Date: 18 Sept 2019

Signature:

Dr: Dekker Marieke /Rego Garcia Iago

Department: Paediatrics

Mobile telephone: +255784669314

Signature:



Foundation for African Medicine & Education

P.O .BOX 351 KARATU TANZANIA

**AUTOPSY CONSENT**

Name of the patient/deceased : OLTOISTI OSIRINGETI MOLLEL (10 -45-

Date of death : 3/10/2022

Diagnosis at Time of death: Rabies

Reason why the autopsy is done : - Diagnosis Confirmation + Research of type of Rabies virus involved

The reason why the autopsy is to be done has been explained clearly and I as a patient/relative

LENGAKINI OSIRINGETI on the behalf of the patient permission /deaced ,I agree body organs to be used for research purpose and education purpose to help science development in the area of improving the care of other patient.

Patient/ close relative name LENGAKINI OSIRINGETI

OSIRINGETI  
3/10/2022

Patient/relative signature and date

2<sup>nd</sup> relative name SINDIMA MASAYA

Relative signature and date : 3/10/2022

Attending Doctors name THOMAS MUNYENO NCHIMBA

Signature and date 03/10/2022

DR GABRIEL PAUL KISSIMA

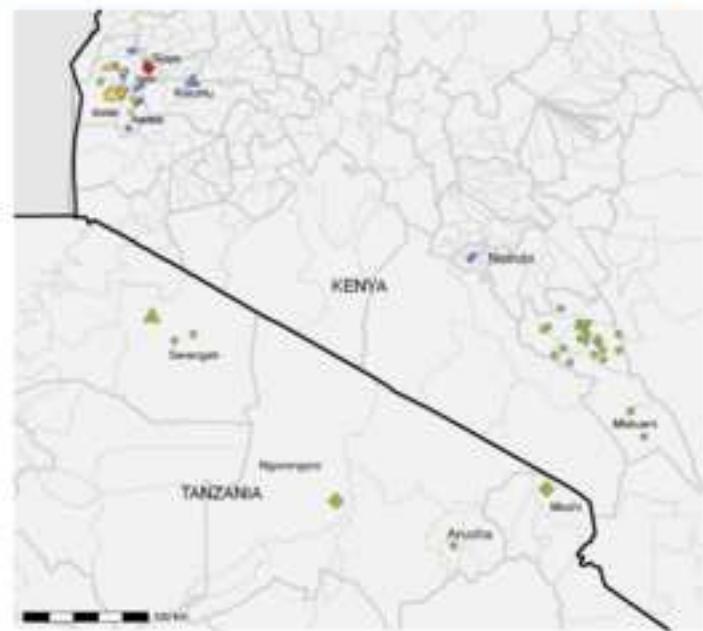
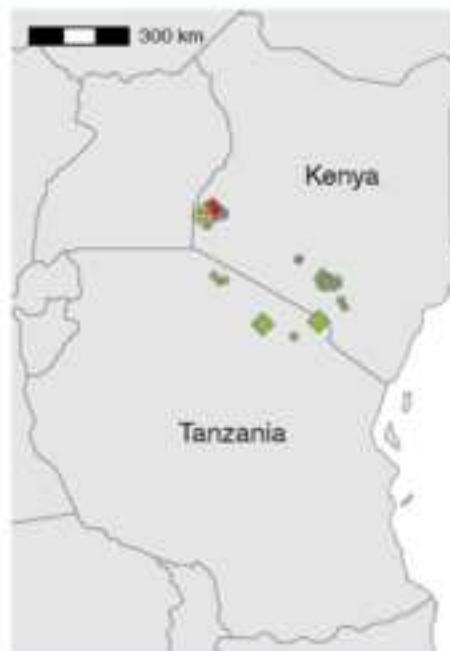
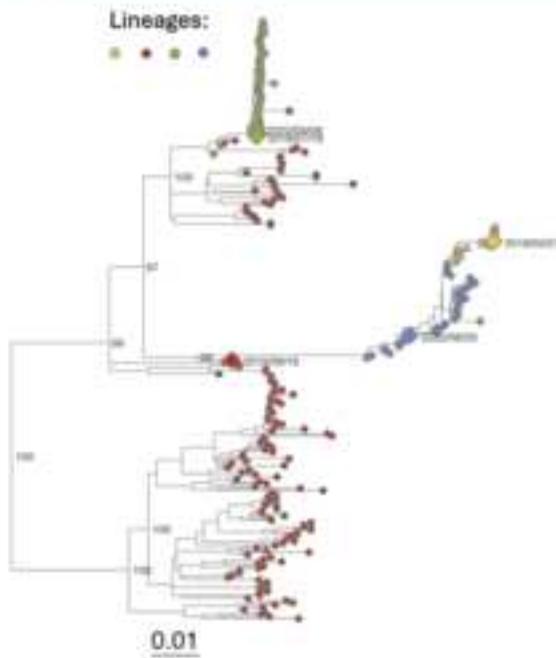
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## AIM: Investigate 5 human rabies deaths in East Africa 2018-2022



**PHYLOGENETIC INVESTIGATION**

- All cases due to dog-mediated rabies
- Transboundary circulation evident
- Multiple co-circulating lineages

**EPIDEMIOLOGICAL INVESTIGATION**

- 3 had no post-exposure vaccination
- 1 had only 1 vaccine dose only
- 1 had all doses but incorrect timeline

### CONCLUSIONS & RECOMMENDATIONS:

- ◆ Train medical staff on bite management
- ◆ Improve access to free PEP
- ◆ Increase rabies awareness
- ◆ Enhance diagnosis with rapid tests and genomics
- ◆ Coordinate regional efforts for the 'Zero by 30' goal through better PEP access and mass dog vaccination.