UNIVERSITY OF NAIROBI

FACULTY OF HEALTH SCIENCES

DEPARTMENT OF PUBLIC AND GLOBAL HEALTH

MODELLING POST EXPOSURE PROPHYLAXIS VACCINE COMPLETION AND ACCESSIBILITY TO SUPPORT HUMAN RABIES ELIMINATION IN MAKUENI COUNTY, KENYA

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W62/10948/2018

A report submitted to the Dept. of Public & Global Health in partial fulfilment of the requirements for the award of the degree of Master of Science in Medical Statistics of the University of Nairobi

Declaration of originality form

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Title of the work: Determinants of post exposure prophylaxis vaccine completion and modelling accessibility to support human rabies elimination in Makueni county, Kenya

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Dedication

I dedicate this project to my late father Dr. Mutunga who had an interest in this field, “Dad I did it!”.

I also dedicate this project to all the ladies out there who dare to dream and venture in uncharted paths. It is possible and it can be done.

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List of abbreviations

ABTC	Animal Bite Treatment Centre
ArcGIS	Aeronautical Reconnaissance Coverage Geographic Information System
DA	Department of Agriculture
DALYs	Disability Adjusted Life Years
DEM	Digital Elevation Model
DHIS2	District Health Information Systems version 2
DOH	Department of Health
EB	Epidemiology Bureau
FAO	Food and Agriculture Organization
GARC	Global Alliance for Rabies Control
GAVI	Global Alliance for Vaccines and Immunizations
HARSP	Haiti Animal Rabies Surveillance Program
IBCM	Integrated Bite Case Management
ID	Intradermal
IM	Intramuscular
KEMRI	Kenya Medical Research Institute
KNBS	Kenya National Bureau of Statistics
KNH	Kenyatta National Hospital
OIE	World Organization for Animal Health
OSM	OpenStreetMap
PEP	Post-Exposure Prophylaxis
PrEP	Pre-Exposure Prophylaxis
QGIS	Quantum Geographic Information System
R_0	Basic Reproductive Number
RCMRD	Regional Centre for Mapping of resources for Development
REDIPRA	Rabies Program Directors of the Americas
RIG	Rabies Immunoglobulin
SAR	Synthetic Aperture Radar
SARE	Stepwise Approach to Rabies Elimination
SRTM	Shuttle Radar Topography Mission
UHC	Universal Health Coverage
UNITID	University of Nairobi Institute of Tropical and Infectious Diseases

UON	The University of Nairobi
UTM	Universal Transverse Mercator
WHO	World Health Organization
WSU	Washington State University
WVS	Worldwide Veterinary Service

Abstract

Background: Rabies, primarily transmitted to humans through dog bites, is a neglected zoonotic disease that kills an estimated 59,000 people annually. To prevent human deaths following exposure, immediate administration of post-exposure prophylaxis (PEP) vaccines is required. However, availability and accessibility PEP is limited especially in rural settings where the vaccine is frequently out of stock or only available in select health facilities. Additionally, PEP vaccines are expensive, and the regimen is multi-course requiring up to 5 visits to the health facility over the course of one month, increasing the risk of non-compliance to recommended PEP doses. In this thesis research, I have a) determined the factors influencing PEP completion and b) determined the optimal placement of PEP within the health facility network in Makueni County.

Methods: The study was conducted in Makueni county, a rabies endemic region selected as a pilot county for rabies elimination in Kenya. Data collection was conducted between February 2021 to December 2021 for all dog bite patients visiting the Makueni County Referral Hospital for the period. Each case was included in the study and contact tracing in the community to confirm the status of the biting animal and identify additional bite cases completed. Contact tracing also conducted for cases reported from the community through a toll-free number that was availed to support rabies surveillance. The main variables collected during this study included age and sex of the bite patient, bite site, biting animal, ownership of the biting animal, bite category and vaccination status of biting animal. Logistic regression models were used to determine the factors associated with PEP completion. To determine the optimal placement of PEP within health facilities, accessibility analysis using the current health facilities administering PEP, and all the health facility network was carried out.

Results: A total of 241 bite patients were recruited. Most of them (86 %) were patients who reported to the health facility, and the rest (14 %) were reported through the toll-free number. More than half (57 %) of the patients were female, and majority of the bites were inflicted on the leg region (59 %) and mainly by dogs (84 % of the bites). The clinicians attending the bite patients at the health facility categorized 45 % of the bites as category III and 34 % of the bites as category II. Only 15 % of the patients completed the 5-dose regimen. At univariable analysis, age and severity of bite (bites on the head/face or multiple bite injuries) were associated with likelihood of PEP completion. At multivariable analysis age and patients with multiple bites were more likely to complete PEP dosage compared to those with bites on other body site.

Under the current scenario of only 12 health facilities in Makueni County stocking PEP, accessibility analysis showed only 17% of the population was within 2-hours of travel to these life-saving vaccines. The optimized scale up analysis showed that a 40% increase in the number of facilities stocking PEP by seventeen facilities optimally placed within the health facility network would increase accessibility to the vaccine by >3 times (from 17% to 57%) in the population within 2 hours of travel to a PEP stocking facility.

Conclusion: This study demonstrates that only a small proportion of the bite patients complete the recommended PEP doses. This shows that there is need for more studies to understand the social, economic and cultural factors that could be contributing to this and how to address them to increase accessibility. A large proportion of the population at risk of rabies are outside of the 2-hour travel time to a PEP stocking facility. This challenge could be addressed by a small increase in the number of PEP stocking facilities, optimally placed within the health facility network, and result in several fold increase in accessibility to vaccines for the population at risk of rabies in the study region.

Chapter 1

Introduction

1.1 Background

Rabies is an acute zoonotic disease caused by Lyssavirus whose main reservoir is the dog, and transmitted to humans through bites and scratches from rabid animals (World Health Organization 2018). It is estimated to kill around 59,000 people per year globally, with majority of the cases emanating from Africa and Asia (Hampson et al. 2015). Despite the availability of effective anti-rabies vaccines for both human and dogs, the disease remains a public health concern with significant mortality, economic losses and Disability-Adjusted Life-Years (DALYs) for rabies which are estimated to be over 3.7 million in this region (Hampson et al. 2015).

Routine data submitted to the World Health Organization (WHO) from Africa points to gross under-estimation of the true burden of the disease in many endemic countries. This is attributed to inadequate reporting systems, delayed health seeking behavior among the bite victims, misdiagnosis and poor community knowledge, attitude and practices towards rabies (Lembo et al. 2010). Patients in rural areas may cover longer distances to access healthcare, without certainty of receiving the services required in the health facilities (Lechenne et al. 2017). Unfortunately, once the clinical signs of rabies manifest, the outcome is almost always fatal. Many of these cases are misdiagnosed as other neurological encephalitis, such as cerebral malaria, further masking the true global burden of rabies (Mallewa et al. 2007).

Currently, there is no known cure for rabies once the patient gets clinical signs. However, rabies is preventable through vaccination using either the pre-exposure prophylaxis (PrEP) which is mostly administered to people considered to be at an increased risk of infection, or the post-exposure prophylaxis (PEP) which is administered following exposure through bites to neutralize the virus before it embeds in neurons (Fooks et al. 2014). If an individual is bitten by a suspected rabid dog, the prevention of progression to clinical disease entails thoroughly cleaning the wound with soap and running water for at least 15 minutes, and seeking immediate medical attention to receive PEP vaccinations. In cases of multiple bites or bites on the upper trunk of the body, infiltration of rabies immunoglobulin (RIG) into and around the bite wound(s) is required in addition to PEP vaccinations (Warrell 2012; World Health Organization 2018).

In rabies endemic areas, poor PEP access leads to preventable human deaths (Hampson et al. 2019). The decision to give PEP treatment depends on the risk of infection which is determined through assessment of multiple factors including rabies epidemiological status of the geographical location, severity and site of the bite, vaccination status and behaviour of the biting animal (Warrell 2012). Most PEP treatments in countries where rabies is endemic are given as a precaution without a confirmation of the true rabies status of the biting animal (Lavan et al. 2017). Although human vaccines are vital and important in preventing human rabies, these vaccines are expensive and often unavailable in many rabies endemic areas where they are needed, highlighting importance of rabies prevention, control and elimination programs without which costs associated with PEP are likely to keep escalating (Meslin and Briggs 2013).

The indiscriminate administration of PEP coupled with the high cost of PEP has been associated with PEP stock-outs in the health facilities (Shim et al. 2009). To reduce this unnecessary use of PEP, the WHO recommends PEP for patients with category II (persons with minor scratches or abrasions without bleeding) and category III (single or multiple transdermal bites or scratches or multiple wounds) (World Health Organization 2018). PEP is not recommended for patients with category I bites (persons who have come into contact with a suspect rabid animal through feeding, touching animals or licking on intact skin) not administered with PEP). In addition, a risk assessment through sharing of information between the human and animal health sector on the status of the biting animal can improve decision making on provision of PEP thus averting human deaths, and reducing stock-outs of PEP (Id et al. 2019; Lechenne et al. 2017).

Kenya is implementing a rabies elimination strategy that aims to end rabies human deaths by 2030 (Bitek 2018). The main elimination activities include annual mass dog vaccination achieving at least 70% in each region, timely provision of PEP to bite patients, increase in public awareness on rabies, and a functionally effective surveillance and outbreak response system (Bitek et al. 2018; Zoonotic Disease Unit 2014). Previous studies have highlighted the need to address the challenges of PEP availability, accessibility and the cost of the treatment in the health facilities (Wambura et al. 2019).

This study focused on the improvement of PEP access in a rural community in Makueni County, a rabies endemic area and a pilot region for the rabies elimination program in Kenya. Specifically, factors associated with seeking, completing and accessing post-exposure treatment among bite patients, and accessibility of PEP stocking facilities within the health-care facility network in Makueni County by the Makueni residents was studied.

1.2 Problem statement

Rabies is identified as one of the top five priority zoonotic diseases in Kenya (Munyua et al. 2016). To prevent clinical disease and death in humans following exposure to the virus, immediate administration of PEP and in severe cases, PEP and rabies immunoglobulins are required. Kenya follows the five-dose 'Essen' regimen (1-1-1-1-1) of PEP administration: consisting of one dose (1ml) of intramuscular (IM) each administered on day 0, 3, 7, 14 and 28 following bite exposures (WHO Position Paper on Rabies 2018).

PEP is an on-demand vaccine that is both expensive to the healthcare system and to bite patients when not offered for free or at a subsidized cost. As a result, PEP is only stocked in a subset of health facilities in each region. Additionally, the availability and accessibility of the vaccine is limited by frequent stockouts associated with limited budgets secured for procurement of PEP, and inability of patients to afford the cost of these life-saving doses. The disconnect between the health sector where the bite patients are treated and the veterinary sector that can determine the rabies status of the biting dogs means that appropriate risk assessments are rarely completed, resulting in indiscriminate use of PEP.

In addition to availability and affordability as factors affecting PEP uptake, accessibility which entails quality of care sought and geographical distance that potential bite patients cover to reach a health facility that stocks PEP further limits PEP uptake. With only a few PEP stocking facilities within the county, patients may require covering long distances to reach a health facility stocking the rabies vaccine. Frequent stockouts of the vaccine in these facilities result in patients seeking alternative vaccine sources such as pharmacies, which result to some patients not completing the full vaccine regimen.

This study sought to address the problems that affect PEP completion among patients and geographical accessibility of PEP vaccines for bite patients in a rabies-endemic region in rural Kenya. It aimed to investigate strategies that may be implemented in order to increase accessibility of PEP to those living in disadvantaged settings and are most at risk of contracting rabies.

Conceptual framework

If one is bitten by a suspected dog, risk assessment is important to establish the level of risk and ensure that the necessary cautionary measures are followed. There are several scenarios that come to play, the first is establishing if there was exposure or no exposure. If there was no exposure, then this is category I bite if there was exposure then it is either category II or III. The next step is to establish the status of the biting animal which is either known or unknown. If known, there should be proof of vaccination which if it exists the patient would be advised to thoroughly wash the wound and get a tetanus shot. In the case where the biting animal is unknown or there is no proof of vaccination (no vaccination card) the patient is advised to thoroughly wash the wound with soap and water for 15 minutes and promptly visit the health facility. Upon visiting the facility, the healthcare providers identify the category of wound depending on the severity of bite and administer RIG (if available) and the first dose of PEP after which they are supposed to inform the patients of the subsequent doses of PEP that should follow. The patients that adhere to the treatment avert death while those that do not eventually develop the clinical signs of rabies and die. Kenya currently uses the WHO-recommended 5-dose intramuscular vaccination schedule, "Essen" regimen where doses are administered on day 0, 3, 7, 14 and 28. The patients are expected to follow through with the treatment which is not always as straight forward. PEP treatment is often faced by various challenges especially in poor settings such as accessibility challenges given that PEP is an expensive on-demand vaccine that cannot possibly be placed in all the health facilities. Most of the times the health facilities stocking PEP are faced by stockouts which means that patients have to outsource the vaccine from other vendors outside the facility which is often quite expensive for the patients. This bring out three issues accessibility, affordability and availability which is what was addressed in this study. *Figure 1* shows the conceptual framework of this study.

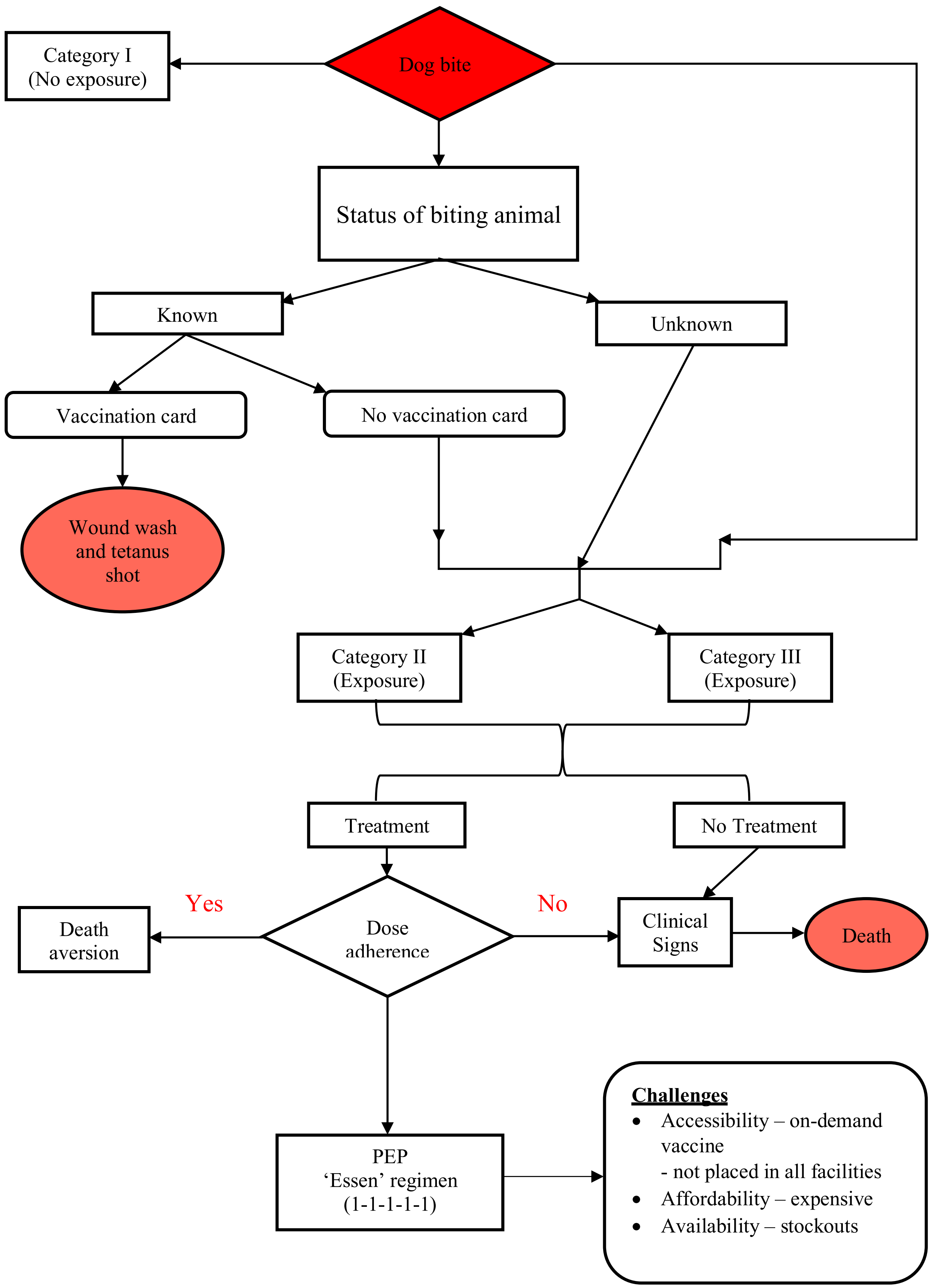

Figure 1: Problem statement conceptual framework

1.3 Justification

To reduce rabies deaths and support the 2030 target of eliminating human deaths from rabies in Kenya, PEP should be promptly -accessible to all bite patients at potential risk of contracting rabies. In 2018, the vaccine alliance (GAVI), made a commitment to invest in human rabies vaccine to improve their access across endemic countries that qualify for GAVI support (GAVI 2018). This investment aligns with the tripartite global goal to eliminate dog mediated human rabies by 2030. Reduced PEP costs would translate to reduced stock-outs within the health facility network, and affordability of the vaccine to exposed patients, leading to increased vaccine coverage for bite patients and improvement in accessibility.

PEP is an on-demand vaccine with expensive purchase costs, making it uneconomical and not feasible to stock PEP in all health facilities. Consequently, optimal placement of PEP within health facilities guided by the population at risk, rabies incidence and the vaccine demand would improve access and reduce preventable rabies deaths. Such facilities can be supported to constantly stock the vaccine minimising stockouts. Additionally, these facilities can be the target for continuous trainings on judicious use of PEP including in the switch from intramuscular (IM) administration of PEP to intradermal (ID) which is dose-sparing (Hampson et al. 2019). ID vaccination route uses smaller vaccine volumes to achieve an equivalent immune response as the IM vaccination route, enabling vaccine sharing and curbing vaccine shortages and affordability to the most vulnerable communities (Hampson, Cleaveland, and Briggs 2011). The facilities could also act as a trigger point for risk assessment to ensure that patients truly at risk of contracting rabies complete the recommended doses.

As part of the GAVI investment, risk assessment is a key and vital component for the vaccine alliance to make a commitment. Rabies risk assessment is a vital diagnostic component to ensure a bite patient at risk of rabies gets the appropriate post-exposure treatment. However, risk assessment is rare in many rabies endemic areas where all the bite cases are considered to be at risk, leading to an unnecessary cost burden to the bite victims and shortages of the vaccine supply (Ma et al. 2020). In countries making progress towards rabies elimination, risk assessment has been used to guide PEP administration while similar techniques have been successfully applied in rabies endemic settings (Rysava et al. 2019). This risk assessment could ensure that only patients at risk complete the dose and there is minimal to no vaccine wastage.

1.4 Study questions

My thesis research focused on two study questions:

a) What factors are associated with uptake and completion of rabies vaccine among bite patients in Makueni?
b) What is the optimal placement of PEP stocking facilities for dog bite patients within the health facility network?

1.5 Objectives

The main objective of this study was to understand factors associated with PEP uptake and dose completion and determine the optimal placement of PEP based on the least cost path, incorporating time and distance within the health facility network.

1.5.1 Specific objective

a) To determine the factors associated with PEP dose completion for exposed bite patients within Makueni county.
b) To identify optimal placement of rabies vaccine PEP within the public health facility network in Makueni County.

Chapter 2

Literature Review

2.1 Rabies background

Rabies is a neglected zoonotic disease that can be fatal once the clinical signs start to manifest in the human body. The predominant transmitter of human rabies is through bites and scratches from rabid domesticated dogs which act as the main reservoir of the virus (Lembo et al. 2010; Morters et al. 2013). Although rabies elimination is possible as evidenced in South and Central America, similar results have not been observed in Africa and Asia where continual rabies cases are reported even in areas where no cases previously existed like Bali in Indonesia (Lembo et al. 2010).

An estimated 59,000 human deaths are associated with rabies annually with 36% and 60% which are reported in Asia and Africa respectively (Hampson et al. 2015). Lack of good mortality data on rabies and gross underreporting of the burden and impact of the disease has resulted to low prioritization and under-estimation of rabies in the regions where the disease is still prevalent (Lembo et al. 2010).

Effective vaccines for both humans and dogs exist, making rabies a preventable disease when dogs are vaccinated and humans receive timely post-exposure prophylaxis once exposed. A lot of research on rabies has focused on vast areas including transmission dynamics of rabies (Asamoah et al. 2017), burden of rabies (Hampson et al. 2015; Sambo et al. 2013), efficacy of rabies vaccines, interventions that are paramount to eliminate the virus, mitigation strategies which advocate for 70% dog vaccination coverage (Davlin and VonVille 2012; Lembo et al. 2010) and cost effectiveness of the various interventions that have been developed. However, there is limited research on the spatial accessibility of PEP which entails investigating if the PEP stocking facilities are optimally placed and are accessible to the population at risk. This should be a major consideration accompanied by risk assessment to ensure that the vaccine is consumed by patients who are found to be truly at risk of developing rabies.

For rabies to be eliminated, significant barriers on development and implementation of vaccination programs to enable mass dog vaccinations over a short period of time should be attended to. Use of innovation and technology can enhance vaccination of a high proportion of dogs. Applications that enhance facial recognition of dogs during the vaccination process can be used to identify the vaccination status of a dog. The pilot phase of such an app is ongoing in the mara region of Tanzania . Similarly, mobile phone applications such as the World Veterinary Service (WVS) app have been developed to help in data collection and team management during mass dog vaccination and provides a huge potential for coordination and monitoring multiple vaccination teams from a central location, ensuring that all the geographical areas within a particular region are covered (Gibson et al. 2018).

2.2 Burden of rabies

The burden of rabies is not evenly distributed, it is influenced by socio-economic factors which highly favour patients with the financial capacity to pay for the treatment that entails five – doses of the vaccine spread out across a month (Darryn L Knobel et al. 2005). The annual global burden of rabies accounts for 59,000 deaths, 3.7 million (95% CI: 1.6 – 10.4 million) disability-adjusted life years (DALYs) and an economic burden of around 8.6 billion USD (95% CI: 2.9–21.5 billion) (Hampson et al. 2015). In Kenya the exact figures of mortality and morbidity remain unknown but estimates indicate about 523 annual deaths (95% CI 134, 1,100) (Hampson et al. 2015) with the Zoonotic Disease Unit (ZDU) estimating up to 2,000 annual human deaths (Zoonotic Disease Unit 2014).

Despite the inaccuracies of the existing data, the importance of estimating the true burden and impact of rabies should be prioritized by annihilating the perception of rabies being an insignificant disease, which has hampered development of prevention initiatives in developing countries (Coleman, Fèvre, and Cleaveland 2004). Public sensitization of rabies, its transmissibility, preventive measures once exposed and the adverse outcomes of non-compliance to treatment is paramount in endemic areas. This has the potential to change the perception of rabies emanating from witchcraft, starvation, thirst, prolonged exposure to sun/heat and thus preventing use of traditional remedies for rabies exposure (Jemberu et al. 2013; Lembo et al. 2010).

Passive surveillance is limited in assessing the true disease burden, mainly due to incompleteness and under-reporting (Taylor et al., 2017). Similarly, rabies burden is not evenly distributed across all societal sectors, varying by age and socioeconomic factors, both of which are important in estimating the burden of this disease in humans, and the economic losses associated with it (Darryn L Knobel et al. 2005).

The economic costs include direct PEP costs, indirect costs associated with seeking treatment, surveillance costs both on the human side and animal side, livestock losses and the prevention measures that include dog vaccination (Hampson et al. 2015; Darryn L Knobel et al. 2005). Indirect costs of suspected human rabies exposure contribute to a third of the total costs incurred by patients seeking treatment, which exert economic burden on both the patients and governments in rabies endemic regions (Shwiff et al. 2007). The implications of rabies burden are especially evident in poverty stricken areas which are dominated by resource shortages and limited access to public health facilities, which are deterrence to data collection and analysis (Fooks et al. 2014).

Epidemiological modelling of canine rabies has provided estimates of the disease burden in Africa and Asia, with standardized active surveillance data from various regional countries required to authenticate and validate the model estimates (Taylor et al. 2017). Rabies is a multi-sectoral burden between human medical practitioners and the veterinary sector, where coordination from both stakeholders is required to recognize the true burden of the disease (Hampson et al. 2008).

Rabies remains a significant economic problem, especially in the impoverished rural areas in endemic regions where victims have to incur the high costs of accessing PEP treatment and are less likely to receive the vaccine as compared to the patients living in urban areas (Sambo et al. 2013).

2.3 Control and prevention of rabies

Dog vaccination has been demonstrated as the most effective and efficient way of reducing human mediated rabies (Hampson et al. 2015). Once a person is bitten by a suspected dog, the first prevention measure should be to thoroughly clean the wound with soap and water, then seek medical attention where depending on severity, one is given an injection of rabies immunoglobulin (RIG) if the bites are severe which is thereafter accompanied by vaccination (Warrell 2012). PEP prevents manifestation of clinical disease but its access remains a challenge especially in rural areas leading to rabies risk increment of the larger population (Hampson et al. 2019).

Breaking dog-dog and dog-human transmission through 70% coverage of mass dog vaccination would reduce the need for the costly PEP (Hampson et al. 2015; Lembo et al. 2010). Kenya adopted the Stepwise Approach to Rabies Elimination (SARE) and developed a strategic plan to gradually reduce the risk of dog-mediated rabies in humans by 2030 (Bitek et al). The strategies proposed in the elimination plan include; elimination of rabies in dogs through an annual mass dog vaccination with a coverage of 70% and above for three consecutive years, prevention of human rabies through prompt provision of post-exposure prophylaxis to those at risk of exposure, strengthening of existing surveillance systems and timely response by engaging all the involved stakeholders, conduct and promote operational research which will guide practices and solutions in cases where challenges are experienced during program implementation, social mobilization, communication and advocacy to raise public awareness, resource mobilization and multi-sectoral coordination and enhancement of partnerships (Bitek et al. 2018).

There are significant barriers to control and prevention of rabies which include difficulty in developing and implementing vaccination programmes that target mass dog vaccination within a short period of time (vaccination timelines) and a high proportion of dogs enough to break the transmission cycle (Gibson et al. 2016). Distance to be covered, remoteness of the area, PEP shortages in health facilities and time spent raising money to cover hospital expenses, increases the risk of developing this fatal disease (Sambo et al. 2013).

2.4 PEP provision

In Kenya, PEP is currently provided indiscriminately to bite patients presenting to the health facilities. While prompt PEP provision is advocated for, actual risk should be investigated to reduce false-positive and false negative cases that lead to cost implications and death respectively (Id et al. 2019). Prompt PEP provision still remains a serious challenge in rabies endemic countries due to the high socioeconomic costs that are incurred to access the costly PEP vaccine (Hampson et al. 2008).

To achieve the 2030 elimination goal of dog-mediated human rabies in rabies endemic regions, the capabilities approach which gives a framework of factors affecting individual's ability to access PEP should be investigated incorporating structural factors like socioeconomics factors (Wentworth et al. 2019). This framework highlights some of the key issues that prevent access to the PEP vaccine therefore revealing issues of inequity and injustice. For social justice to be achieved, market shaping is key to ensure that structural barriers are overcome through which there would be improved health seeking behavior and PEP dose adherence resulting to death aversion (World Health Organization 2018). A study by (Wambura et al. 2019) highlights the variability of rabies vaccines and immunoglobulins and the inadequacy that the supply chain faces from the procurement to the delivery of the vaccines in the health facilities in Kenya. These issues consequently lead to stockouts in health facilities which end up affecting PEP provision therefore requiring improvement in the current system of stock monitoring and forecasting. This can be achieved through public awareness, continuous training of health care workers and free provision of PEP across the country as has been adopted in Thailand which has resulted in reduction of human deaths from rabies to below ten cases annually (Wilde et al., 2017).

2.5 PEP accessibility

Accessibility Modelling entails combining ideas of distance, cost distance, time and geographical locations to measure the easiness or difficulty of an individual in accessing a facility, resource or service. Health facility placement should depend on the number of people it is meant to serve and there should be ease in accessibility to seek medical care. For patients in rural endemic settings, factors that influence healthcare seeking include geographical accessibility, availability of the right type of care to those in need, financial accessibility that entails value for money and acceptability (Peters et al. 2008). Geographical factors have been reported as a significant hinderance to accessing medical services in developing countries, with rural areas being more disadvantaged (Habibov, 2011; Hosseinpoor et al., 2011; Peters et al., 2008).

To measure accessibility of PEP vaccine by potential patients, there is need to quantify the cost implications due to movement of the patients from the place /village of bite occurrence to the health facility, hence need to do an accessibility model that will enable us to estimate the cost, distance and time taken to reach a particular health facility given a geographical location. This mostly entails the geographical accessibility which results in having an effect on the cost incurred and distance travelled while seeking medical attention. To reduce implications of rabies on human PEP, there is need for governments and especially those in the veterinary sector to invest in mass dog vaccinations (Sambo et al. 2013).

Distance or travel time have been reported as notable barriers towards effective treatment. This is paramount in time-bound emergencies which, if delayed, may lead to adverse effects. In cases of emergency; medical, obstetric, and surgical care like child bearing accessibility is very crucial and can lead to death if action is not taken immediately. In the case of rabies once a patient is exposed there should be urgency in receiving treatment therefore making rabies a medical urgency rather than emergency which is always critical and almost always fatal on the onset of clinical signs if timely medication / vaccination is not received.

A study by (Ouma et al. 2018) highlights the importance health facilities and the services that they provide which provide the core backbone of surveillance of diseases and how important it is to ensure that the majority of the population is covered by these facilities. Health facility placement in any region should ensure that the populations in geographically marginalised regions are reached by ensuring that there are improved transport systems, innovations that ensure standard emergency and ambulatory services or by increasing the number of health facilities within a specific geographical location.

In Kenya about 53% of child deliveries take place outside a health facility, 88% of mothers live less than five kilometres of a health facility with majority of the women indicating the reason for not delivering in a health facility was the physical difficulty in accessing health facilities (Kitui, Lewis, and Davey 2013). Physical access plays a key role on whether one reaches a health facility in time which affects the timeliness of receiving treatment. The most important feature of accessibility is not only being able to travel and access a health facility but also a function of community response to infectious diseases (Hulland et al. 2019).

Various studies have been conducted to analyze the effect that physical access to a health facility has on the probability of seeking care for children with febrile episodes (Alegana et al. 2018), time travel estimates to health facilities among populations at risk of viral haemorrhagic fevers (Hulland et al. 2019) and physical access to major hospitals in sub-Saharan Africa for essential surgeries (Broer et al. 2018).

2.6 Elimination of rabies

Rabies mostly affects the marginalized communities because of the delays in accessing PEP or its inaccessibility, sometimes due to unaffordability (Hampson et al. 2008). The most persistent challenge for global rabies elimination has been very low mass dog vaccination coverage, lack of PEP, poor access to PEP, and a lack of concerted elimination efforts. Collaborative efforts between countries provides a good avenue for purchase and distribution of rabies vaccines as has been evidenced by the Rabies Program Directors of the Americas (REDIPRA) network and incorporating control programs such as the KwaZulu-Natal, South Africa, that have resulted in initiatives and transboundary networks in neighbouring countries (Lankester et al., 2014).

Canine rabies elimination is logistically and epidemiologically possible given sufficient resources and effort dedication as has been evidenced in Western Europe where the disease was successfully eliminated in both dog and terrestrial wildlife populations (Fooks et al. 2014; Lankester et al. 2014). Albeit a shortfall in most endemic countries, elimination of canine rabies requires coordination, financial and political commitment to enable scale up of pilot projects to fully functional programs of disease prevention and control (Lankester et al. 2014).

Three themes that focus on dog-mediated rabies elimination in endemic regions have been identified; practicality of achieving and maintaining mass dog vaccination enough to interrupt the transmissibility of the virus thus achieving elimination, the role played by dog populations towards achieving management, control and elimination of rabies and the role of wildlife reservoirs of the rabies virus (Cleaveland et al. 2018).

The optimal cost-effective way of reducing the global burden of dog-mediated rabies in humans is to eliminate dog rabies through public awareness and educating the public health professionals on the basic understanding of rabies prevention (Hampson et al. 2019; Meslin and Briggs 2013). Most often, zoonotic diseases are neglected due to lack of collaboration between the human and animal health sectors. There is need for one-health approach to be implemented if rabies is to be eliminated as it is a shared public health problem that affects both sectors in different ways (Hampson et al. 2008). This one-health approach could provide important information triggering investigations that identify patients who have come into contact with rabid animals with a possibility of contracting rabies, leading to improved PEP administration (Rysava et al. 2019).

A blueprint approach on rabies elimination, which acts as a guide to authorities spelling out the standard operating procedures that will govern how to create country specific programs to prevent dog mediated rabies in humans is available (Lembo 2012). This toolkit advocates for multi-disciplinary efforts that are focused on working together and encouraging inter-sectoral collaborations through effective communication and planning to develop feasible programs geared towards rabies elimination. There is also a rabies economic model that gives a mathematical model used to estimate transmissibility of the virus estimating the rate of dog-to-dog and dog-to-human transmissions as well as the interventions necessary to break the transmission dynamics (Kunkel et al. 2021). Additionally, rabies is among the 20 diseases targeted for elimination in the WHO's road map for neglected tropical diseases 2021 – 2030 through three critical actions; first by improving forecast for rabies vaccine, timely delivery of PEP and ensuring dog vaccinations. Second building national capacity of health workers and dog management and third to improve compliance by strengthening rabies surveillance and reporting therefore ensuring data availability (WHO 2020a).

2.7 Cost effectiveness of PEP

Most PEP treatments in rabies endemic countries are given as a precaution rather than a confirmation of the true rabies status of the biting animal, either through suspicion or actual clinical diagnosis (Lavan et al. 2017). Rabies is totally preventable through vaccination using either the pre-exposure prophylaxis (PrEP) which is mostly administered to people considered to be at an increased risk of infection or PEP which is administered after exposure (Fooks et al. 2014).

If PEP was available free of charge, and administered judiciously, at least 30% of the current human deaths could be averted cost effectively in most rabies endemic regions (Shim et al., 2009). Despite this, PEP still remains a highly cost-effective intervention with regards to saving human lives and averting quality-adjusted life years (QALYs) when administered to bite victims of suspected rabid animals (Shim et al. 2009). According to Hampson *et al*, the cost-effectiveness of PEP depends on the national strategies and policies in place for provision of the vaccine (Hampson et al. 2019).

Currently, in most countries, individuals bear the PEP vaccination costs if they are not covered by an insurance fund. From 2021, GAVI, the vaccine alliance, is willing to invest in PEP costs through co-financing with national governments thus reducing monetary burden experienced in majority of the rabies endemic countries (Hampson et al. 2019). The investment by GAVI is likely to save lives by increased availability of PEP vaccine to bite victims at the point of care at no cost (Wambura et al. 2019). However, for the investment to take effect, individual countries must show readiness for GAVI support through reinforcement and strengthening of pre-existing rabies programs (GAVI 2018).

Chapter 3
Methodology

3.1 Study area

The study area was Makueni County, a rabies endemic region identified as one of the pilot counties for the rabies elimination programme in Kenya (Bitek et al. 2018). Makueni County was selected based on high number of reported cases of rabies in dogs and humans. According to the 2019 Kenyan census, the county had a population of about 987,653 people with a population density of 121 people per square kilometre (Kenya National Bureau of Statistics 2019). It has nine administrative units: Kathonzweni, Kibwezi, Kilungu, Makindu, Makueni, Mbooni East, Mbooni West, Mukaa and Nzaui sub counties (Kenya National Bureau of Statistics 2019).

Makueni County is the pioneer of subsidized healthcare in Kenya through the universal health coverage (UHC) program (Njeru et al., 2019). Residents of the County register for the program by paying an annual registration fee of Kes 500 (USD 4.87), which allows them to access cost-free inpatient, outpatient, ambulance services, maternity care, vaccines (including anti-rabies PEP) and medication dispensed at the health facilities within the county (Murira, F. 2019).

Makueni has 349 facilities with 239 (68%), 27 (8%), 4 (1%) and 79 (23%) owned by Ministry of Health, Faith-Based Organizations, Non-Governmental Organizations and Private Practice respectively (Kenya Ministry of Health 2022). Of these, only 12 public health facilities stocked PEP vaccine within the county. Out of this, data from the Kenya Medical Research Institute (KEMRI)–Wellcome Trust Research Programme was used for mapping and only 198 geocoded facilities were used (Maina et al. 2019). There being no catchment area data that would enable estimation of the population served by a healthcare facility, an average of the number of patients that visited the various health facilities in Makueni county was recorded in the District Health Information Systems version 2 (DHIS2) from 2016 – 2019 and extrapolated data for the facilities with missing values. 2020 – 2022 was excluded
when doing the average patient calculations due to the covid-19 pandemic that affected patient turnout at the health facilities (WHO 2020b).

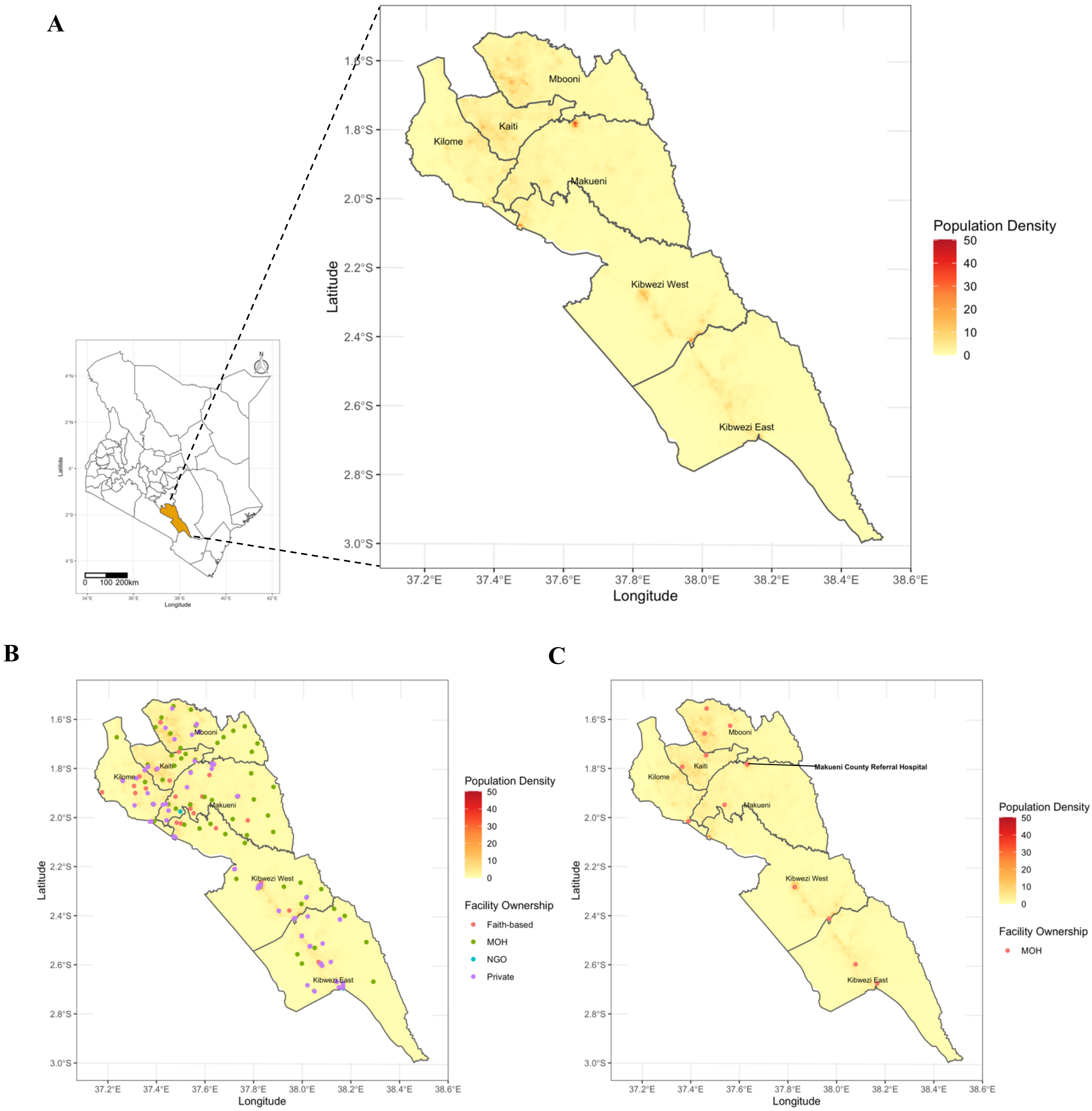

Figure 2:Map showing study area, the population density, distribution of geocoded health facilities and PEP stocking facilities within Makueni county

3.2 Study design

This was a prospective cohort study conducted for 11 months from February 2021 to December 2021. Patients with bites from suspect rabid dogs were recruited into the study and followed up through contact tracing. The cases of bite injuries investigated were identified through one of four ways i) presenting at Makueni County Referral hospital with bite injuries, ii) reported through a toll-free number from the community, iii) case of suspect rabid animal reported to the veterinary department, and iv) secondary cases identified through contact tracing.

3.3 Study population

3.3.1 Case definition

Patients with bites and scratches from a suspect rabid animal presenting to the study health facility, or cases of bites or suspect rabies in humans or animals reported from the community through a toll-free number or to the veterinary department. Any of these reports prompted contact tracing.

3.3.2 Inclusion criteria

Patients with category II (nibbling of uncovered skin, minor scratches, or abrasions without bleeding (exposure)) and III bites (single or multiple transdermal bites or scratches, contamination of broken skin with saliva from animal licks, exposures due to direct contact with rabid animals (severe exposure) from suspected rabid animals) and whose details were captured in the anti-rabies vaccine register at the health facility, or in the community reported through the toll-free number, or to the veterinary department. Verbal consent was sort from the all the patients above 18 years while those below 18 years, the guardian's consent was sort and information captured and this was assumed to be the person who brought the patient to the hospital. These were the details that were used for contact tracing.

3.3.3 Exclusion criteria

Patients whose details were not captured by the anti-rabies vaccine register at the study health facility. Bite patients who were non-residents of Makueni county and those that declined to verbally consent to be included in the study.

3.4 Sample size determination

The study targeted to include all the patients that visited the health facility within the 11-month study period and whose records were captured on the anti-rabies vaccine register. The anti-rabies vaccine register is found at the Makueni county Referral health facility where the uptake of subsequent PEP doses to suspected rabies cases are recorded. All the cases that were triggered through the toll-free lines, veterinary department and secondary cases would always be advised to visit the health facility and followed up to ensure that they did hence the sample would include these persons.

Sample size calculation used the historical bite case data from previous records in the anti-rabies vaccine register, where the Makueni County referral hospital received an average of 31 patients per month (range: 12 – 50 bite patients). For the 11-month study period, an average number of 341 patients were estimated to visit the health facility with animal bites from suspected rabid animals.

Given the study period between February 2021 to December 2021 and the covid-19 pandemic that had hit the country, healthcare services were interrupted consequently affecting the number of patient-health facility turnout (WHO 2020b). Given the polices and restrictions that had been put in place during the study period disruptions were expected. Given that rabies is nearly fatal always and critical it was reported that 48% disruptions were encountered across non-communicable disease services (WHO 2020b) which would translate to an average of 164 patients. Despite the covid-19 situation the study included all the patients that visited the facility and met the inclusion criteria during the study period.

3.5 Sampling procedure and screening

We included all the individuals that met the inclusion criteria. At the time of this study, all patients vising the facility with suspected rabies cases were recorded in the Makueni County anti-rabies vaccine register located in Makueni County Referral hospital.

3.6 Recruitment and consenting procedures

Information for identifying the patients' during follow-up was retrieved from the toll-free line and the anti-rabies vaccine register which had information about the bite victims' phone number and village that they came from. All the participants that met the inclusion criteria were enrolled in the study and a verbal consent was always sought during the contract tracing exercise and before the questionnaire was administered. The questionnaire was useful in collecting human demographic data, the profile of the biting animal and the geographical coordinates of the village that the bite patient came from.

3.7 Data management

3.7.1 Data collection and storage

Data was collected using smartphones and the questionnaires structured and administered using CommCareâ platform and Worldwide Veterinary Service (WVS) application that have been used in different studies. The veterinarians were trained on how to carry out bite tracing and dissemination of information to the clinicians. Statistical data analysis was conducted using the R statistical software (RStudio Team 2020). Geographical accessibility of facilities offering PEP was conducted using AccessMod (OMS 2021) and QGIS (QGIS Development Team 2016).

3.7.2 Data access and confidentiality

The secondary data was extracted from the anti-rabies vaccine register showing daily records of patients that visited the health facility with suspected bites from 2017 to 2021. The bite tracing data was collected using the CommCareâ apps hosted on smartphones that ensured privacy and confidentiality of the patients' information. This data was password protected, encrypted and safely stored on the cloud. Only authorized personnel were able to access this data.

3.8 Data analysis

3.8.1 Factors influencing PEP completion

PEP is recommended for only patients who are at risk (bite category II and III). Investigations were conducted to find out whether the medical staff administering PEP had prior training on identification of bite wound category and if any follow up was done to determine the vaccination status of the biting animal. There was need to determine the basis the healthcare providers used to administer PEP (whether it was guided or given indiscriminatory), whether this affected whether the patients completed PEP or not.

Knowledge on the clinical management of bites from rabid animal and identification of the category of bites is very crucial for completion of PEP schedule. They should have prior knowledge on PEP and the schedule of doses and also ensure that they do not withhold vaccines to any potential patient rabies, even if the exposure took place in the distant past.

The primary analysis of this objective was to investigate the factors that influenced PEP completion among the bite patients. The source of data for this particular hypothesis was the anti-rabies vaccine register where most of the patient details were recorded. The bite risk assessment component of this objective was solely dependent on the accurate recording of the patients' telephone number in the anti-rabies vaccine register.

To determine the factors influencing PEP treatment recommendations at health facilities and how these relate to bite risk assessment, data that had been captured and extracted from anti-rabies vaccine register that were located within Makueni County referral hospital was collected. Bio-data of the patient and category of bite is included based on the knowledge of the clinician. This was important to measure the knowledge that the medical personnel had on WHO PEP recommendations and their ability to correctly identify the category of a patient's bite. The assessment was based on whether the healthcare providers identified any bites as category I and gave PEP for it.

The general formula that was adopted was a logistic regression model;

$$\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k$$

Where; $\beta_{1,}\ \beta_2, \ldots \beta_k$ are the partial regression coefficients of the model

$X_1, X_2 \ldots X_k$ are the variables

p – probability of event occurring (completing PEP doses)

$1\text{-}p$ – probability of event not occurring (not completing PEP doses)

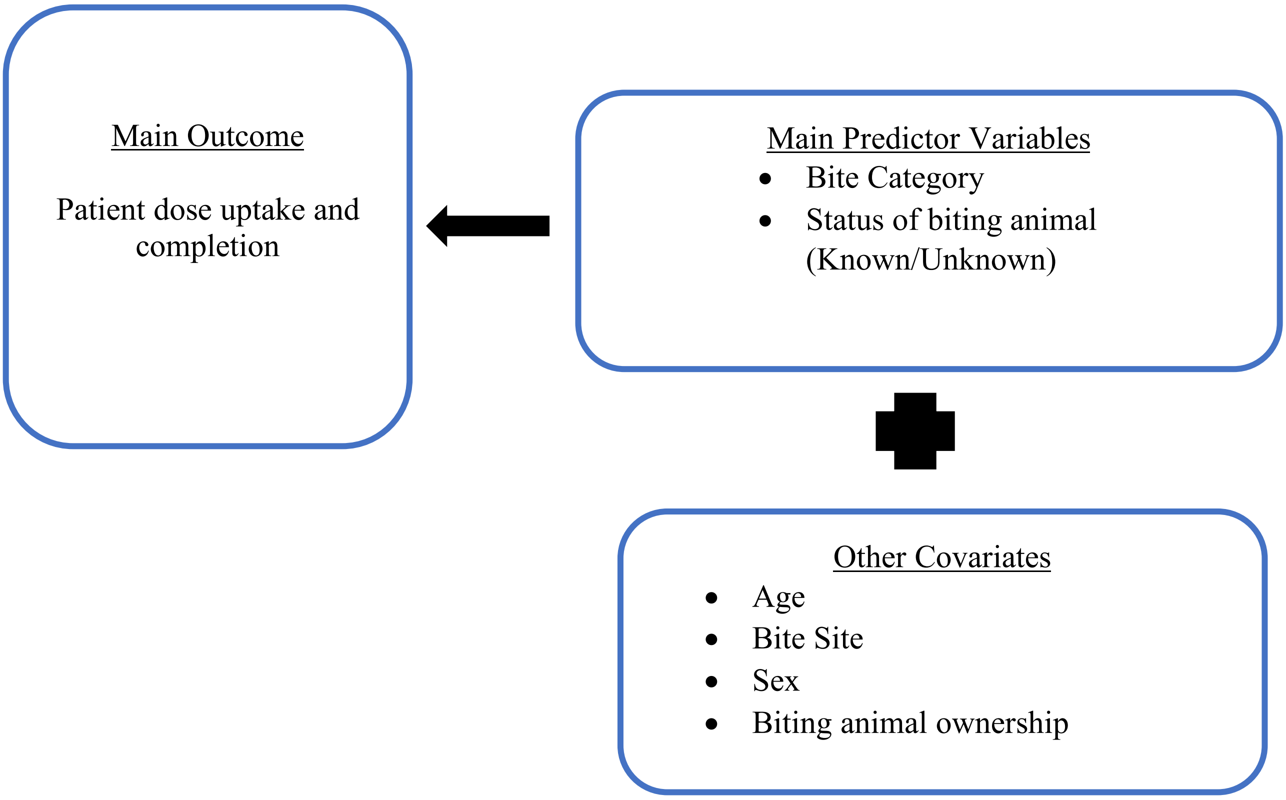

Figure 3: Analysis plan for PEP recommendation, dose adherence and completion in health facilities

To determine the factors associated with PEP completion among bite patients, a logistic regression model was fitted with the outcome variable being completion of PEP which was a binary outcome. A univariable analysis was performed for each variable to see if there was any influence on the PEP completion rates of patients. Variables with a P value of < 0.2 were included in the multivariable analysis.

3.8.2 Objective 2: To determine the optimal placement of health facilities offering PEP for dog bite patients in Makueni County

Geographical accessibility modelling entails combining ideas of distance and time to measure the ease or difficulty of an individual in accessing a facility, resource or service. Health facility placement should incorporate capacity and ease in accessibility, while seeking medical care. A health facility offering PEP should be easily accessible to the population at risk and have a constant supply of the rabies vaccine.

Rabies hotspots (areas with most cases of rabies) should be considered and put as a priority when establishing potential PEP facilities, and the population at a higher risk of exposure. The distance and time used to access a facility should also be a determining factor when recruiting facilities to serve as PEP providing centres.

The primary analysis was to determine the optimal placement of the anti-rabies vaccine within the health facility network in Makueni County. This included assessing the geographical accessibility of the population to all the health facilities in the county and comparing this to the facilities currently approved to stock PEP. The World Health Organization AccessMod tool was used to assess the geographical accessibility by using datasets given in Table 1;

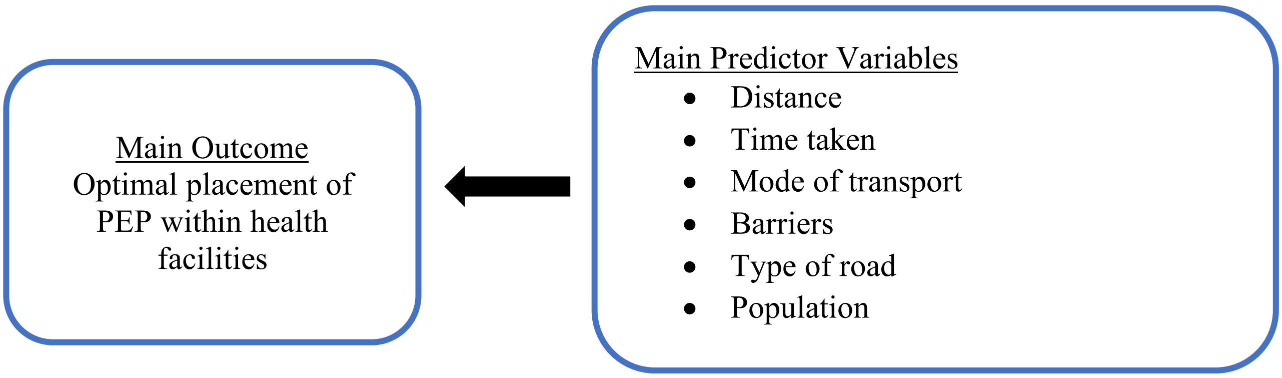

Figure 4: Analysis plan for the optimal placement of PEP stocking facilities within the healthcare network

To understand the accessibility of health facilities in Makueni County, several datasets were obtained including: spatial data on the Digital Elevation Model at 30m by 30m grid from Shuttle Radar Topography Mission (SRTM)(RCMRD GeoPortal 2015), data at 30m by 30m grid from Regional Centre for Mapping of resources for Development (RCMRD), population data at 100m by 100m grid from WorldPop (Lloyd et al. 2019), hydrographic and road network from for OpenStreetMap that is publicly available (GeoFabrik 2020). The geocoded list of health facilities within the county were obtained from the Kenya Medical Research Institute (KEMRI)–Wellcome Trust Research Programme (Maina et al. 2019).

To calculate the digital elevation models, SRTM uses elevation data of the earth's surface using a single-pass space-borne interferometric Synthetic Aperture Radar (SAR) system that is operated by transmission frequencies denoted by letters. These frequencies include C-band which is satellite space that operates at a wavelength of 3.8–7.5 cm and is responsible for global mapping, change detection among others, and X-band which is satellite space that operates at a wavelength of 2.4-3.8 cm responsible for high resolution SAR for urban monitoring, fast coherence decay in vegetated areas (Farr et al. 2007).

To create the land use datasets, RCMRD collects data from satellite images which are either captured using passive or active sensor technology in remote sensing while vector data is obtained through digitizing process which involves conversion of geographic data through tracing images or maps using coordinates either in point, line or polygon format (RCMRD GeoPortal 2015).

To calculate population data, WorldPop dataset is built using a Random Forest algorithm which is used to determine population density weighting, and is flexible to handle multiple covariates of different natures to produce semi-automated, dasymetric models that are used to produce human population distribution maps (Stevens et al. 2015). This data contains the most recent census data and the distribution correlated with the land cover types which are used to determine if a given area is populated or not.

To calculate hydrographic and road network, data from OpenStreetMap (OSM) (GeoFabrik 2020) was used. OSM is a collaborative mapping project that mostly relies on openly licensed satellite imagery to digitize objects which include buildings, roads and rivers. Users are able to add and edit layers within a map by use of rich attributes and key-value pairs agreed and governed by a set of Contributor Terms for factual mapping information. Data is presented in shapefiles which contain data in form of points (latitude and longitude coordinates), lines (sequence of OSM points with tags and a unique identifier) and polygons (identical to lines but enclose an area) (Lawal and Anyiam 2019).

Table 1: A summary of the data collected from the different data sources listed.

Data layer	Variables	Resolution	Year	Source	Reference
Digital elevation model	Spatial altitude	30m x 30m	2015	Shuttle Radar Topography Mission	(Farr et al. 2007)

Land use grid	Spatial distribution of land influencing travel speed	30m x 30m		Regional Centre for Mapping of resources for Development	(RCMRD GeoPortal 2015)
Population grid	Spatial population distribution within our study area	100m x 100m	2019	WorldPop	(Lloyd et al. 2019)
Hydrographic network	Hydrographic layers which act as barriers to movement		2021	OpenStreetMap	(GeoFabrik 2020)
Road network	Road types		2021	OpenStreetMap	(GeoFabrik 2020)

The initial approach of this study was to determine how accessible PEP stocking facilities are to potential bite patients and what were some of the barriers that hindered the accessibility and what were the necessary steps that were required to optimally place the PEP stocking facilities within the health facility network in Makueni county. All the health facilities within the county were considered regardless of the facility level of care, or ownership i.e. private or government operated. After administering first aid, most facilities that do not stock the anti-rabies vaccine or were experiencing stockouts, would refer the patient to a PEP-stocking facility (Chuchu et al. 2022). To conduct accessibility analysis, a merged land cover which incorporated road and hydrographic networks (rivers and lakes) was obtained by projecting data in AccessMod Universal Transverse Mercator (UTM) zone 36S which is the geographical zone for Makueni County (Ray and Ebener 2008).

AccessMod performs iterations during analysis which identifies the population that belongs to a computed health facility catchment which is subtracted from the overall population. It uses the Pearson correlation coefficient between travel times and is used to compute the corresponding population within the given time step. Through-out this spatial analysis, the anisotropic analysis was used to include slopes detected by the digital elevation raster file. This would in turn be used to modify the speed at which one would travel at and the time taken given the mode of transportation used to reach a given health facility.

Mode of transport to health facilities (walking and motorized form of transport) and landscape constraints (slope, rivers, lakes, military and airport zones and industrial complexes) were factored in when computing travel time to and from the nearest health facility. Anisotropic analysis corrections (used to account for the impact of slope and other barriers on the speed and mode of travel) were applied to travel speeds. Estimated walking speeds of 1km/hr and 2.5 km/hr on herbaceous land and other land types, respectively (Chen et al. 2017; Kim et al. 2020) and motorized transport speeds of 100 km/hr for trunk and primary roads, 80 km/hr for secondary roads, 50km/hr for tertiary and service roads and 20 km/hr for unclassified roads (Chen et al. 2017; Stewart et al. 2016; Toriola 2017) were used. Two scenarios were set where one; a 2-hour travel threshold in accessing the health facilities was adopted based on a previous study by (Ouma et al. 2018) that shows the importance of having health facilities located within reach of the population especially where universal health coverage is to be achieved. The second scenario there was no time limit set so as to observe the maximum time taken to reach the various health facilities and the PEP stocking facilities.

To conduct geographical coverage analysis, the initial focus was on all health facilities in Makueni County that were currently administering anti-rabies PEP. This analysis demonstrates the potential gaps that exists within the facilities reachability to cover the demand of potential bite victims within a 2-hour travel time and a no time limit scenario. The geographical analysis generated sets of data in vector, raster and table form where health facilities with the potential of covering a larger population within the set travel time were identified. To identify the catchment area of each facility, AccessMod combines health facility capacity, travel time and constrains present and population distribution.

All these parameters were considered together with physical constraints present to define the catchment area associated with each of these facilities. Anisotropic analysis was used and movement from each hospital towards the PEP stocking health facilities selected, this was done to see movement if a patient sort prior medical attention before being referred to any of the twelve facilities. Analysis on the ability of facilities to serve a larger population was conducted by layering the barriers present and incorporating health facility data inclusive of the patient capacity and the population within the set travel time to assess the need for resource redistribution in the event of underutilization.

Referral analysis was computed to show the least inexpensive path (i.e., least travel time) from all the other facilities towards PEP stocking facilities and amongst PEP facilities in scenarios where patients would be referred to the nearest PEP facility from a PEP facility. This involved looking at each of these health facilities with reference to movement, barriers, modes of transport and travel speed. This analysis would determine the health facilities closest to the PEP facilities by distance and time.

Lastly, AccessMod does an analysis to identify the most appropriate locations (away from the already existing facilities) was done to set up additional health facilities that could potentially be considered as PEP facilities considering population density and time. This analysis employed Euclidean distance to/from features (health facilities) and time travel to/from features; all the health facilities within Makueni County were used to view the best facilities for PEP placement reaching most of the population. To do so, a physical accessibility analysis on the raster cells was conducted and the site that covered the largest population was selected. This was repeated until the number of new heath facilities or population covered initially set by the user was located or reached respectively. The analysis used was set to cover 99% of the population within Makueni county.

3.9 Ethical consideration

This study received ethical approval from Kenyatta National Hospital – University of Nairobi Ethics and Research Committee (KNH/UoN - ERC) (P537/09/2020).

Chapter 4

Results

4.1 Determinants of PEP completion among bite patients

4.1.1 Demographic characteristics of bite patients

A total of 241 patients were enrolled in the study with female patients accounting for 136 (57%) reported bites. The median age of the patients was 22 years (range 1 - 90 years), with 42% of the bite patients being 15 years and below, age group 5–14 years old were 65 (27%) and 37 (15%) were children under five years. Only a small proportion of the patients (2 %) visiting these facilities referred from another facility.

Majority of the bite patients had bites on the leg region 141 (59%) closely followed by the arm/hand region 62 (26%) while the least number of patients reported bites on the face 3 (1%). Most of the patients , 80 (45%) exhibited category III bites, followed by category II in 61 (34%) patients and category I in 36 (20%) patients. (Table 2).

Table 2: Table showing the patient demographic information, type of visit, bite characteristics, and category of bite for the bite patients enrolled in the study.

Table 2: Characteristics of bite patients visiting Makueni County Referral.

Parameter	**Makueni County Referral Hospital**
Average number of patients per year	
Sex of patients	
- Male	104 (43 %)
- Female	136 (57 %)
Mean age of patients	
- < 5 years	37 (15 %)
- 5 - 14 years	65 (27 %)
- 15 - 24 years	31 (13 %)
- 25 - 34 years	28 (12 %)
- 35 - 44 years	16 (7 %)

- 45 – 54 years	25 (10 %)
- 55 + years	38 (16 %)
Type of visit	
- Initial	180 (98 %)
- Referral	4 (2 %)
Site of Patient's Bite	
- Arms/Hand	62 (26 %)
- Leg	141 (59%)
- Face/Head	3 (1 %)
- Multiple parts	4 (2 %)
- Trunk	17 (7 %)
- Other	14 (6 %)
Category of bite	
- Category I	36 (20 %)
- Category II	61 (34 %)
- Category III	80 (45 %)

The dog was the predominant biting animal in 203 (84 %) of the cases. Majority of the biting animals were identified to be domesticated 195 (84 %), while only 36 (15 %) were stray animals and the least identified biting animal were wild animals 2 (1 %). Investigations on the ownership status of the biting animal revealed that 186 (80 %) animals were owned by someone known to the patient while 46 (20 %) were not known to them and were classified as stray animals (Table 3).

Table 3: Table showing the species, known status and ownership of the biting animal as described by the patients enrolled in the study

Table 3: Characteristics of biting animals in Makueni county.

Parameter	**Makueni County Referral Hospital**
Species of biting animal	
- Dog	203 (84 %)

- Livestock	12 (5 %)
- Cat	14 (6 %)
- Wildlife	1 (0 %)
- Unidentified	11 (5 %)
Known status of biting animal	
- Domesticated	195 (84 %)
- Stray	36 (15 %)
- Wild	2 (1 %)
Ownership status of biting animal	
- Owned	186 (80 %)
- Stray	46 (20 %)

In addition to bite category identification, healthcare providers are encouraged to advice the patients on the anti-rabies vaccine by following the WHO guided PEP schedule. Dog bite care management training among healthcare providers is very important and critical for the elimination of rabies (Chuchu et al. 2022). Prior to this study, the healthcare providers were last trained in 2018/19 when the rabies surveillance was being rolled out in the county.

Visualization of the PEP uptake among exposed patients spread through the five doses and whether the patients complied to the scheduled WHO dose recommendations where dose 1, 2, 3, 4 and 5 should be taken on day 0, 3, 7, 14 and 28 respectively. About 11% of the bite patients received their first dose on the same day that the bite occurred, while about 8% received their first dose a day to two days post bite day. The dose compliance for dose two improved with about 20% receiving the dose on the third day while there was observed consistency with the third, fourth and fifth doses being received on day seven, fourteen and twenty-eight post bite respectively. There was a significant bite patient drop-out between vaccinations especially dose 3 (day 7), dose 4 (day 14) and dose 5 (day 28) as the proportions of patients who received those subsequent doses dropped (Figure 5).

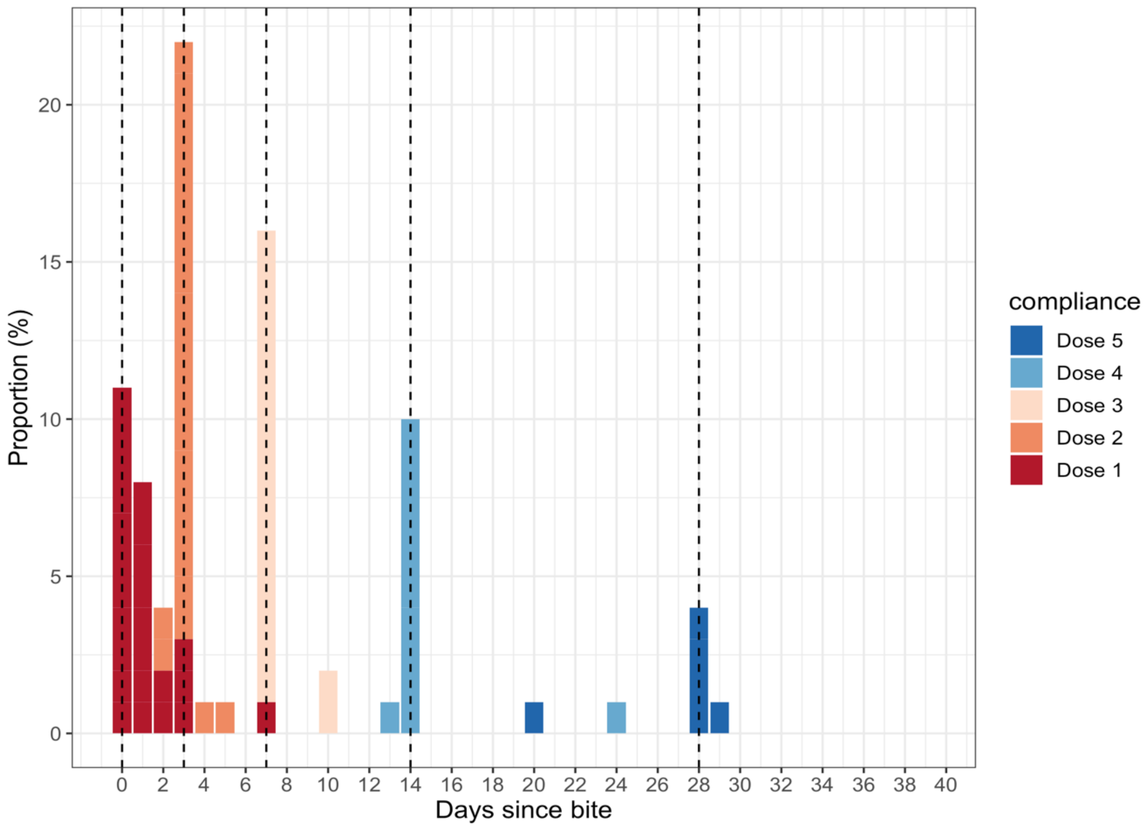

Figure 5: Figure showing uptake of the five PEP vaccine doses after bite. The dashed lines highlight the WHO recommended PEP- five dose schedule (WHO Position Paper on Rabies 2018).

4.1.2 Factors associated with PEP completion

Table 4 shows the relationship between completion of PEP and the characteristics of bite patients within Makueni county. A patient was 2% less likely to complete the PEP dose for every additional year lived; however, this was statistically significant (OR = 0.98; 95% CI = 0.96–0.99; *P* = 0.047) therefore giving evidence of an association with PEP completion. Patients with bites on the face/head and on multiple parts increased the odds of completing PEP compared to others and was statistically significant (OR 20.5; 95% CI = 1.63 – 505.77; *P* = 0.023 and OR = 20.5; 95% CI =1.63 – 505.77; *P* = 20.5 respectively). Similarly, there was no significant association between PEP completion and sex, bite site (Leg and Trunk regions), category of bite and known status of the biting animal.

Table 4: Results of logistic regression analysis of factors associated with PEP completion; univariable analysis.

univariable analysis			
Parameter	**Odds ratio**	**95% CI**	***P* value**
Age	0.98	(0.96 – 0.99)	**0.047***
Sex			
- Male	0.85	(0.38 – 1.87)	0.698
- Female	Reference		
Bite Site			
- Head/Face	20.5	(1.63 – 505.77)	**0.023***
- Leg	1.74	(0.61 – 6.30)	0.341
- Multiple Parts	20.5	(1.63 – 505.77)	**0.023***
- Trunk	3.15	(0.66 – 15.14)	0.138
- Arm/Hand	Reference		
Biting Animal Ownership			
- Wild	5.68	(0.22 – 146.43)	0.224
- Domesticated	Reference		
Category of Bite			
- Category III	2.25	(0.85 – 6.68)	0.119
- Category II	Reference		
Known status of biting animal			
- Unknown	1.38	(0.60 – 3.74)	0.331
- Known	Reference		

* Significant variable

Univariate logistic regression analysis was applied to identify the variables independently associated with PEP completion among bite patients in Makueni. Only age, bite site and category of bite had an outcome of 0.2 level of significance and therefore were considered in the multivariable model. Table 5 shows the relationship between completion of PEP and age, bite site and bite category. A patient was 3% less likely to complete the PEP dose for every additional year lived; however, this remained statistically significant (OR = 0.97; 95% CI = 0.92–0.98; *P* = 0.043) therefore giving evidence of an association with PEP completion. Patients with bites on multiple parts increased the odds of completing PEP compared to others and was statistically significant (OR 15.2; 95% CI = 1.45 – 429.87; *P* = 0.019). There was no significant association between PEP completion and category of bite among the patients.

Table 5: Results of logistic regression analysis of factors associated with PEP completion; multivariable analysis.

multivariable analysis			
Parameter	**Odds ratio**	**95% CI**	***P* value**
Age	0.97	(0.92 – 0.98)	**0.043***
Bite Site			
- Head/Face	0.00	(0.00 – undefined)	0.992
- Leg	1.27	(0.38 – 5.12)	0.712
- Multiple Parts	15.2	(1.45 – 429.87)	**0.019***
- Trunk	1.28	(0.21 – 7.13)	0.778
- Arm/Hand	Reference		
Category of Bite			
- Category III	2.25	(0.91 – 8.24)	0.085
- Category II	Reference		

* Significant variable

4.2 Accessibility and availability of PEP in health facilities

AccessMod allows one to calculate referral analysis which computes the travel times and/or distance along least cost paths which maximise the total travel time taking into account the landscape modes and travel speeds between to health facilities (Ray and Ebener 2008). This analysis was calculated to determine the distance and time taken by patients to move from one

PEP stocking facility to another PEP stocking facility; this was of interest because a study by (Chuchu et al. 2022) demonstrated that healthcare providers would likely refer patients to other facilities that stocked PEP. On average the maximum distance that patients would cover from one PEP stocking facility to another was 30.64 kilometres and a time of 63 minutes (approximately 1 hour 3 minutes). On the other hand, the minimum distance that patients would cover from one PEP stocking facility to another was 15.75 kilometres and a time of 16 minutes (Table 6).

Table 6: Distance and time taken from PEP stocking facilities to other PEP stocking facilities.

From Facility	Movement from facility	Movement towards facility	Distance (Kilometres)	Time (Minutes)
1	Kibwezi Sub County Hospital	Makindu Sub County Hospital	25.00	16
2	Kilungu Sub County Hospital	Mukuyuni Sub County Hospital	29.08	39
3	Kisau Sub County Hospital	Mbooni Sub County Hospital	21.22	29
4	Makindu Sub County Hospital	Kibwezi Sub County Hospital	25.01	16
5	Makueni County Referral Hospital	Mukuyuni Sub County Hospital	24.64	22
6	Matiliku Sub County Hospital	Sultan Hamud Sub County Hospital	30.56	63
7	Mbooni Sub County Hospital	Mukuyuni Sub County Hospital	15.76	20
8	Mtito andei Sub County Hospital	Kambu Sub County Hospital	16.42	19
9	Mukuyuni Sub County Hospital	Mbooni Sub County Hospital	15.75	20
10	Sultan Hamud Sub County Hospital	Matiliku Sub County Hospital	30.64	63
11	Kambu Sub County Hospital	Mtito andei Sub County Hospital	16.31	19
12	Tawa Sub County Hospital	Mbooni Sub County Hospital	16.94	21

4.3 Mapping of health facility accessibility

An analysis to investigate the population in relation to the health facilities within the county was conducted. To determine the population proportion that accessed the different types of health facilities in Makueni within a specific target. Time / distance, was broken down in the analysis to investigate the population per sub-county given number of different health facility categorization in the sub-county. The highest populated sub-county was Makueni sub-county (193,802) and it also had the highest number of health facilities (91). The least populated sub-county was Kaiti (120,116) while the sub-counties with the least number of hospitals (39) were Kaiti and Kilome. The county with the highest number of health care facilities per 100 000 population was Makueni (47/100,000) while the county with the least number per 100 000 population was Kilome (21/100,000) Table 7.

Table 7: Population density and number of health facilities per sub-county in Makueni county.

	Sub-county	Population per subcounty	Ministry of Health	Number of MOH facilities per 100 000 population	Faith-Based organizations	Number of Faith-Based organization facilities per 100 000 population	Non-Governmental Organizations	Number of NGO facilities per 100 000 population	Private Practice	Number of Private Practice facilities per 100 000 population	Total no facilities per sub-county	Number of health-care facilities per 100 000 population
1	Kaiti	120116	35	29.1385	1	0.8325	0	0	3	2.4976	39	32.4686
2	Kibwezi East	132199	27	20.4238	5	3.7822	0	0	17	12.8594	49	37.0653
3	Kibwezi West	165933	43	25.9141	3	1.8080	4	2.4106	24	14.4637	74	44.5963
4	Makueni	193802	64	33.0234	5	2.5800	0	0	22	11.3518	91	46.9551
5	Mbooni	190979	46	24.0864	5	2.6181	0	0	6	3.14171	57	29.8462
6	Kilome	184624	24	12.9994	8	4.3331	0	0	7	3.7915	39	21.1240
	Total Population	987653	239	24.1988	27	2.7338	4	0.4050	79	7.9988	349	35.3363

Population densities varied per sub-county and ownership of health facility per 100 000 population. The number of health facilities per population ranged from 21.1240 per 100 000 in Kilome sub-county to 46.9551 per 100 000 in Makueni sub-county *Table 7*. The number of health facilities owned by ministry of Health per population ranged from 12.9994 per 100 000 in Kilome sub-county to 33.0234 per 100 000 in Makueni sub-county. The number of health facilities owned by faith-based organizations per population ranged from 0.8325 per 100 000 in Kaiti sub-county to 4.3331 per 100 000 in Kilome sub-county. Only Kibwezi West had the presence of Non-Governmental Organizations health facilities which covered a population density of 2.4106 per 100,000. The number of private practice facilities ranged from 2.4976 per 100 000 in Kaiti sub-county to 14.4637 per 100 000 in Kibwezi West sub-county.

Table 8 summarises the results of the 12 PEP stocking facilities within Makueni county, average outpatient capacity, population served by the facility and the population densities of each of the facility

Table 8: Patient capacity analysis of PEP stocking facilities within Makueni County.

		Sub-county	**Average outpatient capacity**	**Population per sub-county**	**Population per county**	**Total Population per 100 000**
1	Mukuyuni Sub County Hospital	Kaiti	2891	0.0241	0.002927141	292.7141
2	Kilungu Sub County Hospital	Kaiti	4766	0.0397	0.004825581	482.5581
3	Kambu Sub County Hospital	Kibwezi East	1954	0.0148	0.001978428	197.8428
4	Mtito andei Sub County Hospital	Kibwezi East	1950	0.0148	0.001974378	197.4378
5	Makindu Sub County Hospital	Kibwezi West	8677	0.0523	0.008785474	878.5474
6	Kibwezi Sub County Hospital	Kibwezi West	4603	0.0277	0.004660544	466.0544
7	Sultan Hamud Sub County Hospital	Kilome	5073	0.0275	0.005136419	513.6419
8	Matiliku Sub County Hospital	Makueni	2848	0.0147	0.002883604	288.3604

9	Makueni County Referral Hospital	Makueni	27982	0.1444	0.028331813	2833.1813
10	Tawa Sub County Hospital	Mbooni	4133	0.0213	0.004184668	418.4668
11	Kisau Sub County Hospital	Mbooni	2202	0.0115	0.002229528	222.9528
12	Mbooni Sub County Hospital	Mbooni	6041	0.0327	0.006116521	611.6521

To identify the catchment area of each health facility in Makueni county it was important to first assess the health facility capacity per 100 000. The population per sub-county was used to so as to identify the maximum number of potential patients that the health facility would be able to serve Table 8. The population per subcounty ranged from 0.0115 in Kisau sub county hospital, Mbooni subcounty to 0.1444 in Makueni county referral hospital in Makueni subcounty. The total outpatient capacity per total county population ranged from 197.4378 per 100 000 in Mtito Andei sub county hospital to 2833.1813 per 100 000 in Makueni county referral hospital in Makueni subcounty.

There was a marked change in the population that was able to access health facilities authorised to stock anti-rabies vaccine PEP in Makueni County from other health facilities within half an hour time step, up until 2 hours. In half an hour, only 7% of the total population was able to access health facilities authorised to stock PEP whereas this proportion increased by 10% to 17% within two hours travel time (*Table 9*). On the other hand, 46% of the population was able to access all the other health facilities and this proportion increased to 71% within two hours travel time. A significant difference in the population able to access the two types of health facilities was persistently observed over the time period (*Table 9*).

From the visualisation of the population able to access PEP stocking facilities only 7 % of the population and those closest to the facilities were able to reach the facilities within 30 minutes travel time while 46% of the population was able to reach any health facility within the same time. The peripheries were constantly underserved by these health facilities. On the other hand, when considering all the health facilities, the population had a relatively better coverage of the peripheries with almost the whole population being able to access the health facilities within a 2-hour time period (Table 9).

Table 9: Accessibility analysis of health facilities authorized to administer PEP and all the other health facilities in Makueni County.

	Facilities authorized to stock PEP		All facilities in Makueni County	
Travel Time (walking and motorized)	**Population**	**Percentage Covered (~ 987,700)**	**Population**	**Percentage Covered (~ 987,700)**
≦ 0.5 hour	70,417	7%	456,998	46%
≦ 1 hour	118,198	12%	640,512	65%
≦ 1.5 hours	148,801	15%	692,890	70%
≦ 2 hours	167,008	17%	705,039	71%

A visualization of the population able to access the health facilities given a time travel of more than 2 hours. Considering all the geo-coded facilities within Makueni county, majority of the population was within a health facility (*Figure 6A*). Given the PEP stocking facilities within the county and a time travel of more than two hours the population was able to access these facilities but at an increased time travel (*Figure 6B)*. Considering all the facilities in Makueni County the peripheries were able to access healthcare within a travel time of two hours including the populations that were in the peripheries (*Figure 6C*). On the other hand, upon adjusting the time travel to a maximum of two hours the population living around the PEP stocking facilities was able to access PEP but peripheries were constantly underserved by these health facilities (*Figure 6D)*.

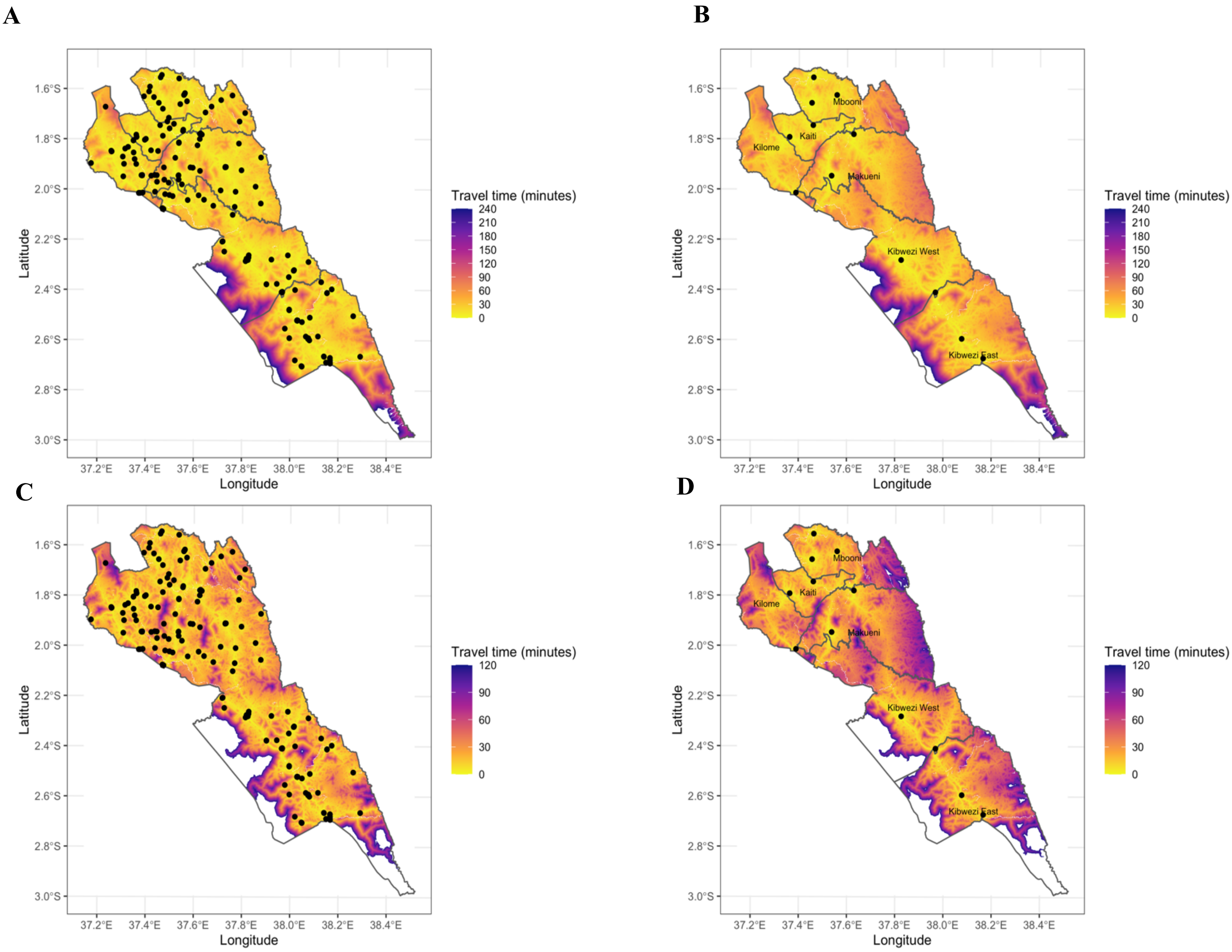

Figure 6: Maps showing travel time to the nearest health facility in Makueni county.

The distribution of time travel to the nearest health facility within Makueni varied greatly across the time distribution selected while conducting accessibility analysis. Given all the health facilities, most of the population was within a 1-hour travel time. This changed when we considered the PEP stocking facilities which showed that only the population living near to the health facilities were at a travel advantage with majority of the populating traveling for longer hours to access them.

The scaleup analysis identified seventeen potential locations for health facilities that would be able to stock PEP in order to achieve the minimum travel by the population therefore increasing access healthcare within a given travel time period (*Figure 7)*. These seventeen had a higher catchment area and their locations were evenly distributed across the county giving them the ability to cover a larger population. These new facilities would increase the population covered by health facilities stocking PEP from 17% to 57% within a 2-hour threshold. The grey area displayed on *Figure 7* showed the associated catchment area of the respective proposed PEP facilities, the red dots represent the current PEP stocking facilities in Makueni while the blue shapes represent the proposed optimally placed facilities.

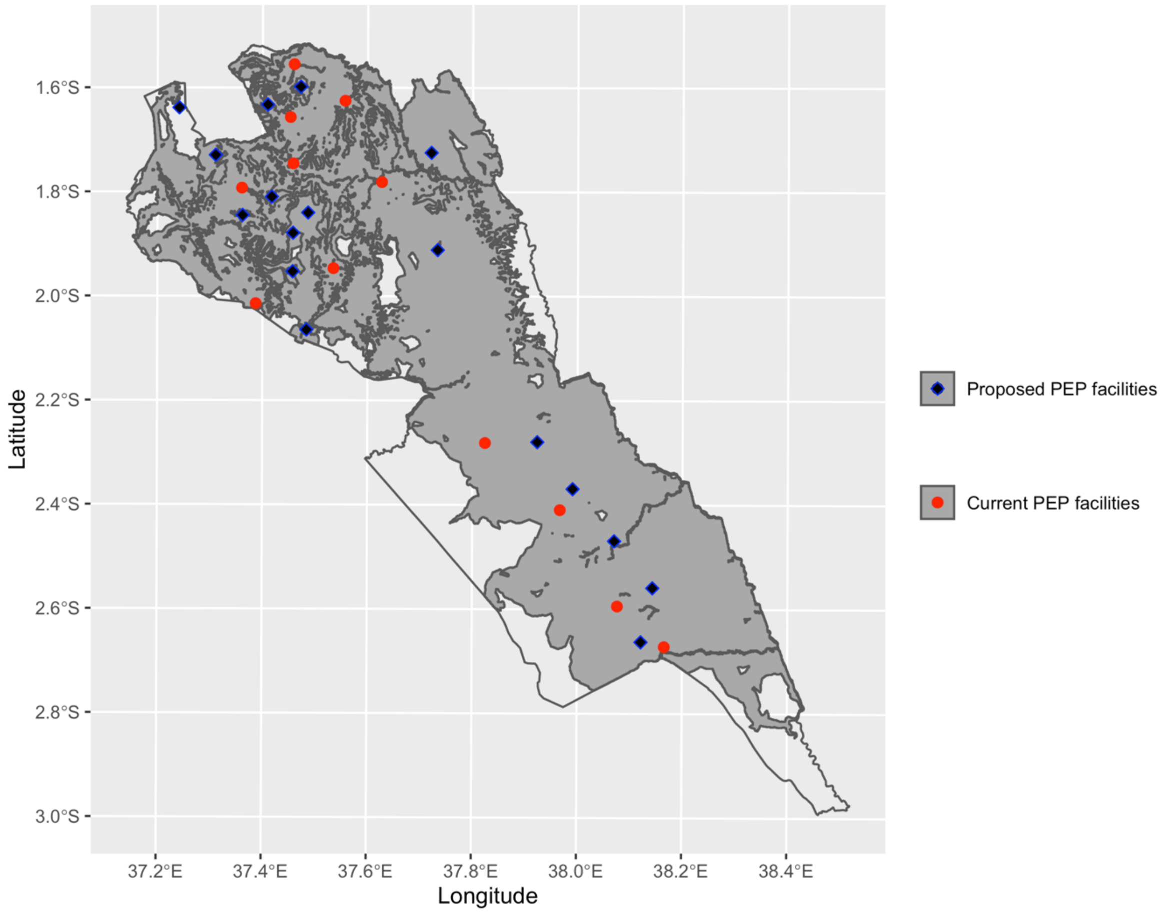

Figure 7: Proposed optimally placed PEP stocking facilities and their respective catchment area

Chapter 5

Discussion

The domesticated dog remains the most dominant animal that mainly causes morbidity in Makueni county. Most of the patients that reported at the health facility had category II and III bites but only 15% of the patients completed the recommended five-dose PEP regimen. Non-compliance increases the risk of contracting rabies and progression to clinical stages. Similar non-compliance to rabies vaccine regimen has been reported in Ethiopia (Beyene et al. 2018). PEP accessibility remains a challenge and in Makueni, despite there being dedicated PEP providing facilities within the health facility network, only 17% of the population is within a 2-hour travel of such a facility. This hinders the timely accessibility of PEP, coinciding with studies that have shown limited vaccine access in rural settings in Africa mostly characterized by high rabies incidence and poor residents living below the poverty line (Hampson et al. 2015; Darryn L. Knobel et al. 2005).

These results were consistent with other studies that showed that the dogs who are the principal reservoir of the lyssavirus were the main contributors of most of the reported bite incidents associated with rabies cases (Mnyone et al. 2010; Obonyo et al. 2016). Currently Kenya does not have any laws that govern ownership of dogs and therefore most of the dog owners allow dogs to roam freely for food consequently leading to ungoverned interaction with other dogs (Kitala et al. 2001) which increases risk of infection if unvaccinated and comes into contact with a rabid dog. Majority of the bite patients that visited the facility during this study were identified to be of category II and III which are always associated with exposure and are therefore always advised to complete PEP with the absence of risk assessment to indicate otherwise. One study conducted in Tanzania shows that a wound being small and lack of advice by the clinician were some of the factors that made a patient not start, complete or adhere to PEP treatment (Hampson et al. 2008). If this is closely linked to risk assessment of the biting animal, then it would help make the decision whether a patient should continue with PEP uptake. For this to happen two key players are required; the medical personnel trained to correctly identify the bite category and veterinary doctors to make a follow-up to ensure the health status of the biting animal.

Physical accessibility plays a major role on whether bite patients will be able to seek care especially in cases where not one but five vaccines have to be administered. This study precisely identified the population who reside at areas with a high estimated travel time to especially PEP stocking facilities which could be used to inform policy makers where to urgently focus on to increase physical accessibility to the healthcare facilities. It could also help the policy makers identify the most underserved populations and who are least likely to seek treatment once bitten by a rabid animal causing unnecessary death due to lack of access to the vaccine. Interventions that are necessary to bridge the time taken to access rabies treatment could include; placement of bite centres within the health facility network considering incidence of bites and coming up with transport programs that would see vaccines being placed in facilities that are closest to the patients and meet the cold-chain requirements such patients do not have to travel long distances to receive the subsequent vaccine doses.

The study maps also estimated the time travel to PEP stocking facilities which could also be used by the policy makers to guide them identify the most underserved populations that are least likely to visit the facilities when bitten by a suspected rabid animal because of low physical access to such facilities. This could be in turn used to monitor and gather data of bites from rabid animals that end up not being reported thereby increasing detection and treatment efforts consequently averting human deaths due to rabies. Distance or time travel have been reported as notable barriers towards effective treatment. A study by Ouma *et.al* shows that only 33.3% of the African countries have more than 80% of the population located within a 2-hour travel time of emergency care (Ouma et al. 2018). Another study showed that distance and driving time to a health facility was one of the factors that were consistently and significantly associated with severe malaria in Yemen (Al-Taiar et al. 2008). A study conducted by Mwaliko *et al*. reported that patients especially pregnant women were willing to only travel a distance of 2 kilometers while seeking health care otherwise they preferred a home delivery (Mwaliko et al. 2014). These studies cited physical distance, transport and financial constraints as some significant barriers to seeking treatment.

Increasing the PEP stocking facilities could bring majority of the population closer to the vaccine. From the scale-up, it is evident that adding the 17 facilities identified could bring 57% of the population within a 2-hour travel time of these facilities. This could translate to improved health seeking behaviors among bite patients. This could see many patients visit the hospital at the same time which could translate to arguing the case of switching from intramuscular (IM) vaccine administration to intradermal (ID) as recommended by WHO and one of the conditions for GAVI to invest in rabies PEP. This will be a huge boost for the rabies endemic regions since rabies is termed as the "poor man disease" which mostly affects the poor and marginalized communities living in the rural settings (Darryn L. Knobel et al. 2005). This switch could also mean judicious use of the vaccine; meaning that one vial would be shared among patients that visit the health facility at a time resulting to cost savings for the patients especially in counties and countries where they cater for the purchase of the vaccine. This would also result to lowered costs of vaccine purchase from GAVI by governments though the country's buy-in.

This study could also be used to justify budget allocations to ensure additional facilities stock PEP, are always equipped with the anti-rabies vaccine and train staff on how to identify bite categories, administer the vaccine and advice the patients accordingly. This study can be replicated and used by other counties and countries to strategically plan to have PEP stocking facilities within their healthcare system placed and accessible by the population within a significant travel time.

Currently Kenya is focused on rabies elimination by 2030 through annual vaccination of at least 70% of dogs in each region, increase in public awareness on rabies, setting up a functionally effective surveillance and outbreak response system and timely provision of PEP to bite patients (Bitek et al. 2019). This study could be used as a tool especially in the scale-up of rabies elimination through increased detection of the bites and contact tracing that could help control rabid animals by prompt removal from the community, significantly contributing to achievement of the goal of zero human deaths from dog-mediated rabies in Kenya.

Limitations

This study had several limitations. First, not having the actual health facility catchment area created an opportunity for bias when doing analysis, it is therefore important to ensure that the catchment areas for health facilities are provided for incorporation into the model. No publicly available data set that comprehensively gave the actual number of outpatient and inpatients served within health facilities in Makueni county was available. To account for cases reported in the health facilities I obtained outpatient data from the District Health Information Systems version 2 (DHIS2) which had information of number outpatient visits per month and year, populated them to obtain the catchment area of each hospital. For the facilities that did not have their data in DHIS2 it was extrapolated based on the information obtained from facilities of the same nature.

Second, the absence of geo-coordinates for some of the health facilities in Makueni limited this study making the analysis results not fully explain and portray all the accessibility aspects of the healthcare system within the county Similarly, the lack of well documented referral systems that are in place within the county from primary, secondary and tertiary care, any other facility to PEP stocking facilities which affects access to the rabies vaccine and uptake of all the subsequent doses. These factors are likely to vary within and across other counties in Kenya and rabid endemic countries.

Thirdly, the role of the private sector in PEP provision was not included in the analysis yet some private health facilities provide similar services as those provided by the public health facilities. Future analyses should ensure that the private sector is included as the services they provide are equally essential and play a major role especially for the on-demand vaccines. At the time of this study, data was accessed from the public health facilities that stock anti-rabies vaccine and it would be of great importance if future studies collect data on PEP consumption from private facilities.

Fourth, "costs" associated with travel were not put into consideration instead AccessMod uses movement and cost distance algorithm estimation. Monetary costs were not included because they greatly vary and are affected by various factors including fuel costs, seasonality and peaks. It is therefore not easy to quantify these factors and identify the degree to which they affect movement.

Finally, surveillance component of the study involved both hospital-based surveillance and community contact tracing to identify the vaccination status of the biting animal and human cases of people who did not seek medical care after bite. Contact tracing faced challenges in tracing persons who migrated, lacked sufficient information to contact bite patient, lacked information on biting animal due to lack of information or dog owners being unknown. There is a disconnect between clinicians and the veterinary personnel in terms of collaborations towards rabies elimination resulting to poor information flow between the two departments in the county.

The selected study design did not influence the limitations of the study and does not therefore create bias, instead it invites further investigations by gathering more data from other endemic setting to ensure comparability. Despite these limitations, this study shows the gaps that currently exists in a rabies endemic setting and provides possible and practical solutions to help bridge the gaps.

Chapter 6

Conclusion and Recommendations

This study has shown that the domesticated dog remained the most reported biting animal among the patients and therefore making rabies a major public health issue in Makueni county. Majority of the reported bites were inflicted on the Leg region (59%) and the arm / hand region (26%). Category II and III bites were the most recorded bites as identified by the clinicians translating to patients being at a high risk of developing rabies and therefore should ensure adherence to completing the rabies PEP vaccine.

The results also showered that out of all the patients that visited the health facility only 15% completed all the five doses of PEP. This shows the health seeking behaviors of the bite patients in Makueni county and could also be used to question the accessibility, availability or affordability of the vaccine to the patients. The multivariate and univariate logistic regression analysis that were fitted to determine the factors that affected PEP completion revealed that patients with multiple bites and bites on the head/face region were more likely to complete the rabies vaccine dosage. Prolonging the study time and increasing the sample size could possibly see completion of PEP being influenced by more variables.

The number of health facilities in the county could imply that the entire population is covered leading to a conclusion that majority of the population is within a health facility and have access to good healthcare. This study shows otherwise and highlights the importance of ensuring on-demand vaccines and specialised treatment should be carefully considered when placing health facilities in a population. This study highlights the role that barriers play in accessibility of health services and the need to prioritize on-demand vaccines such as the anti-rabies vaccine in endemic countries.

In the case of rabies in Makueni county, only 12 public health facilities offer the service making it even harder to access and without guarantee that they will receive services. This translated to only 7% of the population accessing the PEP stocking facilities and 17% within a 2-hour travel time. This leaves a majority of the population especially those in the peripheries not able to access the rabies PEP vaccine in the county. Having additional PEP stocking facilities that are optimally placed could improve the access of PEP ensuring that majority of the population at risk is able to receive the lifesaving rabies vaccine. This study could be used to guide policy makers on ideal placement of PEP within the health facility network by employing the population incorporated with the incidence of bites within an area. These PEP stocking facilities would be placed in such a way that potential patients would not have to travel longer distances to receive the vaccine thus saving time and costs.

Recommendations

- There is need to train healthcare providers on the bite categorization to ensure guided PEP administration. This will also help in the administration of PEP and counselling on the importance of completing PEP especially to patients with high-risk bites. This guidance is especially key because of the different days that a patient needs to subsequent visit the health facility for the five doses. Training also equips the healthcare providers with the skills that are necessary to inform patients on the first aid procedures once one has been bitten by a suspected rabid animal which have always proved to be crucial when exposed.
- Most rabies endemic countries contain highly populated areas where rabies poses a major life threat to the people living there, most especially those countries having little to no physical access to facilities that stock PEP. Maps in this study show there is need to consider on-demand vaccines especially in public health facilities which are always the most preferred by majority of people in rural settings where there is limited choice. These maps could also inform health system planning for other on-demand vaccines and services that are only found in specific health facilities due to their characteristics, such as expensive nature making them economically impossible to stock in all the health facilities.
- By the time of this study the different sectors were working independently and there was minimal to no communication concerning rabies. The data from the health facilities was being handled by the clinicians, while the veterinary department was conducting rabies surveillance on their own and each department kept their own records separate. While doing contact tracing during this study, my team of trained animal health technicians were tasked with identifying the bite category.
- This study could be used to gradually roll out integrated bite case management (IBCM) by continually training the clinicians on bite identification, veterinary doctors on conducting risk assessment and have the PEP stocking facilities as bite centres and ensure that information is transmitted and used to guide vaccine distribution. This strategic program aims to link the public health and veterinary sectors towards investigation of suspected rabies exposure and

provision of full vaccine doses to high-risk bite patients. This program is structured in a way that an alert from the public, health or veterinary department triggers an investigation of the animal that is suspected to have rabies. After the risk assessment is conducted, all the parties involved are then notified on the outcome of the suspected animal which in turn informs the decision whether to continue or terminate PEP uptake.

- This strategy has been successful in Haiti where unnecessary use of vaccines for cases where no exposure was experienced has been reduced (Etheart et al. 2017). It should be noted though that these strategic programs are not a substitute of mass dog vaccination but instead offer a complementary anti-human rabies preventive measure. In addition, the IBCM approach can be used to guide treatment recommendations saving many human lives within a short period of time (Lechenne et al. 2017).
- Data is the one most important piece of information that could provide freedom from rabies through a one-health strategy. Tanzania has applied this strategy by generating more accurate surveillance data which has resulted to guidance of policy formulation and decisions that guide public health measures as was evidenced by the outbreak containment experienced in Morogoro region Tanzania (Lushasi et al. 2020).
- There is need for more studies showing physical accessibility of health facilities to identify further variations from the reported results. There is also need for further studies that use this methodology and tool to map physical accessibility to identify further variations from the reported results Hospitals also need to declare their in-patient and out-patient capacity as this data is currently lacking in many Kenyan hospitals.
- There is need and importance of using other spatial analysis tools to analyse this data for comparative purposes despite inclination to AccessMod due to its freeware nature. Data types and their quality greatly impact the outcomes of the models that are produced from the analyses conducted and any slight mistake could cause one to make the wrong conclusions.

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Appendices

Appendix 1: Questionnaire

Human Data

1. Date of contact tracing(date)
2. Unique patient ID creation (automatically created by system)
3. County of the Patient

   i) Makueni County

   ii) Siaya County
4. Subcounty of the patient (list)
5. Ward of the patient (list)
6. Village coordinates (coordinates automatically picked by the system system)
7. Name of the patient (text)
8. Age of patient
9. Name of Next of kin (if less than 18 years or greater than 60 years) (list)
10. Sex of the Patient

    i) Male

    ii)Female
11. Can you provide a working phone number or the next of kin's phone number? (Number the patient can be traced with)

    i) Yes

    ii) No
12. If yes, phone number (phone number – restrict to 10 digits)
13. Body site of bite (List) (Tick all that apply)– have images

    i) Leg

    ii) Arm / Hand

    iii) Trunk

    iv) Private part

    v) Multiple Parts

    vi) Other (specify)
14. Category of bite (list according to WHO guidelines

    i) Category I

    ii) Category II

    iii) Category III

Profile of biting animal

1. What type of animal bit you?

   i) Dog

   ii) Cat

   iii) Goat

   iv) Donkey

   v) Cattle

   vi) Other (specify)

2. <u>What was the patient doing at the time of bite?</u>

   i) Nothing

   ii) Provoked/ attacked the animal

   iii) Stepped on animal

   iv) Playing with animal

   v) Don't know

   vi) Other (Specify)

3. Do you know the details of the animal?

   i) Yes

   ii) No

4. If yes in question 3 above,

   i) Less than 3 months

   ii) 3 – 12 months

   iii) more than 12 months

5. Sex of biting animal

   i) Female

   ii) Male

6. If female, is the animal nursing

   i) Yes

   ii) No

7. What is the ownership of the animal?

   i) Owned

   ii) Stray

   iii) Unknown

8. If known contact (telephone) details of the owner (if details of owner are unknown, please ask of the details of the reporting person) Treatment administered to the patient

9. Animal vaccination status
   i) Vaccinated
   ii) Not vaccinated
   iii) Unknown
10. If vaccinated, what evidence of vaccination do you have?
   i) Vaccination card
   ii) Verbal report from owner
   iii) Verbal report from veterinarian
   iv) Vaccination mark on the dog
   v) Other (specify)
11. Year of last vaccination
12. What is the name of the county where bite occurred?
   i) Makueni County
   ii) Siaya County
13. What is the name of the sub-county where bite occurred? (List)
14. Ward bite occurred? (list)
15. What is the name of the village where bite occurred?
16. Were other people exposed?
   i) Yes
   ii) No
17. If yes, number of animals exposed(number)
18. Is the animal currently alive?
   i) No
   ii) Yes
   iii) Unknown
19. Was the animal showing signs of illness or aggression?
   i) Yes
   ii) No
20. Was the animal owner contacted?
   i) Yes
   ii) No
21. Is the animal available for in-house quarantine?
   i) Yes
   ii) No

22. Do you feel the owner will comply with verbal instructions for quarantine?
    i) Yes
    ii) No

Contact Tracing

Here assume that the case being investigated was triggered from the either the toll-free line, health facility or the vet department.

1. Date of contact tracing (date)
2. Contact Tracing County
    i) Makueni County
    ii) Siaya County
3. Name of the subcounty (List)
4. Name of the ward? (list)
5. Type of tracing conducted
    i) Phone tracing
    ii) Physical/ in-person tracing
6. Current status of biting animal
    i) Alive
    ii) Dead
    iii) Not found
    iv) Unknown
7. Date of death (date)
8. If alive, has this animal had any of the following types of contact in the past 6 months?
    i) Bitten by a suspect rabid animal
    ii) Scratched by a suspect rabid animal
    iii) Eaten dead animal(s)
    iv) Other close contacts with suspect rabid animal
    v) Unexplained wounds
    vi) None of the above
9. What happened to the animal that bit this animal?
    i) Alive
    ii) Dead
    iii) Unknown
10. Has the biting animal been investigated?

i) Yes

ii) No

iii) Unknown

11. Is/ was the suspect animal showing any signs of illness or rabies?

i) Yes – showing signs

ii) No – healthy

iii) Unknown

12. What date did the first symptom appear?

i) Date

ii) Unknown

13. If dead, did this animal exhibit the following signs before dying?

i) Aggression

ii) Hypersalivation

iii) Biting

iv) Paralysis

v) Change in voice

vi) Loss/ lack of appetite

vii) Restlessness

viii) Unknown

ix) Other (specify)

14. How did the animal die?

i) Killed by owner

ii) Killed by public

iii) Killed by car

iv) Natural causes

v) Unknown

15. Were any people exposed?

i) Yes

ii) No

iii) Unknown

16. If yes, how many people were exposed? (number)

17. Did the exposed people visit a health facility?

i) Yes

ii) No

iii) Unknown

18. If yes, which health facility did they visit? (Text)
19. Were any animals exposed?

    i) Yes

    ii) No

    iii) Unknown
20. If yes, how many animals were exposed?
21. Did you report the case to any relevant authority?

    i) Yes

    ii) No
22. If yes, who did you report to?

    i) Health facility

    ii)Vet department

    iii) Public/ Community - Toll- free line

    iv) Other (specify)

Appendix 2: Turnitin report

Turnitin Originality Report

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IMPROVING ACCESSIBILITY OF POST EXPOSURE PROPHYLAXIS VACCINES TO SUPPORT HUMAN RABIES ELIMINATION IN MAKUENI COUNTY, KENYA By Lucy Mutunga

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Appendix 3: KNH-UON ethical approval letter

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Ref: KNH-ERC/A/42

5th February 2021

Lucy Mumbua Mutunga
Reg. No. W62/10948/2018
Institute of Tropical and Infectious Diseases (UNITID)
College of Health Sciences
University of Nairobi

Dear Lucy

RESEARCH PROPOSAL – IMPROVING ACCESSIBILITY OF RABIES POST-EXPOSURE PROPHYLAXIS THROUGH INTEGRATED BITE CASE MANAGEMENT(IBCM) IN KENYA – A CASE STUDY OF MAKUENI COUNTY (P537/09/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 5th February 2021 – 4th February 2022.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

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For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Director, Institute of Tropical and Infectious Diseases (UNITID), UoN
Supervisors: Prof. Thumbi Mwangi, Institute of Tropical and Infectious Disease (UNITID), UoN
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