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Spatio-temporal patterns and risk factors of foot-and-mouth disease in Malawi between 1957 and 2019

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Corresponding Author:	Elizabeth Thandiwe Chimera, Msc University of Pretoria Faculty of Veterinary Science Pretoria, Non-US/Non-Canadian SOUTH AFRICA
First Author:	Elizabeth Thandiwe Chimera, Msc
Order of Authors:	Elizabeth Thandiwe Chimera, Msc
	Geoffrey T. Fosgate, PhD
	Eric M.C Etter, PhD
	Wudu.T. Jemberu, PhD
	Gladson Kamwendo, Msc
	Poya Njoka, MSc
Abstract:	Foot-and-mouth disease (FMD) is an important livestock disease causing short-term and long-term production losses and hindering local and international trade. To gain access to lucrative foreign markets and also improve local trade, there is a need to employ effective preventive and control strategies. Although FMD has been present in Malawi for over 60 years, little knowledge is available concerning the dynamics and drivers of FMD in the country. A modeling study based on retrospective data was conducted to establish the spatio-temporal distribution and determine the risk factors associated with FMD in Malawi. A retrospective space-time analysis was performed and a matched case-control study was carried out to investigate risk factors. The number of reported FMD outbreaks has descriptively increased after 2000 and the disease has spread to previously unaffected areas. Two significant spatio-temporal clusters of FMD were identified; one in the southern region and the other in the northern region. An analysis of only index cases (first detected locations) also detected two clusters with one in the northern region and the other in the southern region. Higher beef cattle density (p= 0.023), higher pig density (p= 0.043) and increased distance to wildlife protected areas (p= 0.036) were positively associated with the risk of FMD while increased distances to international borders (p=0.008) and roads (p= 0.034) were associated with reduced risk of FMD. High FMD risk areas were observed in the southern and northern regions but not in the central region during the early years (1957-1981). The more recent increase in FMD risk at the end of the study period (2019) in the central region might be attributed to increases in livestock density in this region. These findings provide insight into the pattern of FMD occurrence that will promote informed decisions for the progressive control of FMD in the region.
Suggested Reviewers:	Wassie Molla mollawassie@yahoo.com2
	Belinda Blignaut bohmerbelinda@gmail.com
	Kimberly VanderWaal, PhD kvw@umn.edu She has done some spatial research on FMD
	Abraham Sangula aksangula@kilimo.go.ke Published some work on FMD
	Laure Guerrini

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	laure.guerrini@cirad.fr Has done some work on FMD
Response to Reviewers:	

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Title

Spatio-temporal patterns and risk factors of foot-and-mouth disease in Malawi between 1957 and 2019

Authors

Elizabeth T. Chimera[a], Geoffrey T. Fosgate[a], Eric M.C Etter[a, b, c], Wudu.T. Jemberu[d], Gladson Kamwendo[e], Poya Njoka[e]

Author affiliations

[a]Epidemiology Section, Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, 0110, South Africa

[b]CIRAD, UMR Animal, Santé, Territoires, Risque et Ecosystèmes (ASTRE), Petit-Bourg, Guadeloupe, France

[c]ASTRE, Univ Montpellier, CIRAD, INRA, Montpellier, France

[d]International Livestock Research Institute, PO Box 5689, Addis Ababa, Ethiopia

[e]Department of Animal Health and Livestock Development, P.O Box 2096, Lilongwe, Malawi

Corresponding author

Elizabeth Thandiwe Chimera, BSc, MSc

Epidemiology Section, Department of Production Animal Studies, Faculty of Veterinary Sciences, University of Pretoria, Onderstepoort, 0110, South Africa

E-mail: chimeraelizabeth@gmail.com

Abstract

Foot-and-mouth disease (FMD) is an important livestock disease causing short-term and long-term production losses and hindering local and international trade. To gain access to lucrative foreign markets and also improve local trade, there is a need to employ effective preventive and control strategies. Although FMD has been present in Malawi for over 60 years, little knowledge is available concerning the dynamics and drivers of FMD in the country. A modelling study based on retrospective data was conducted to establish the spatio-temporal distribution and determine the risk factors associated with FMD in Malawi. A retrospective space-time analysis was performed and a matched case-control study was carried out to investigate risk factors. The number of reported FMD outbreaks has descriptively increased after 2000 and the disease has spread to previously unaffected areas. Two significant spatio-temporal clusters of FMD were identified; one in the southern region and the other in the northern region. An analysis of only index cases (first detected locations) also detected two clusters with one in the northern region and the other in the southern region. Higher beef cattle density (p= 0.023), higher pig density (p= 0.043) and increased distance to wildlife protected areas (p= 0.036) were positively associated with the risk of FMD while increased distances to international borders (p=0.008) and roads (p= 0.034) were associated with reduced risk of FMD. High FMD risk areas were observed in the southern and northern regions but not in the central region during the early years (1957-1981). The more recent increase in FMD risk at the end of the study period (2019) in the central region might be attributed to increases in livestock density in this region. These findings provide insight into the pattern of FMD occurrence that will promote informed decisions for the progressive control of FMD in the region.

Keywords

Conditional logistic regression

FMD virus

Kriging

Risk maps

Spatio-temporal analysis

Introduction

Foot-and-mouth disease (FMD) is a contagious disease of cloven-hoofed animals (Jamal and Belsham, 2013) that has a devastating impact on the economies of affected countries (Knowles and Samuel, 2003). FMD is caused by infection with FMD virus (FMDV), which belongs to the genus Aphthovirus within the family Picornaviridae (Kitching et al., 2005). There are seven serotypes of FMDV: O, A, C, Asia 1, and Southern African Territories 1-3 (SAT1-3) (Kitching et al., 2005). Serotypes A, O, C and Asia1 are also known as Euro-Asiatic serotypes that circulate mainly in Europe, Asia and South America while the SAT serotypes mainly occur in Africa (Davies, 2002; Aiewsakun et al., 2020; Rweyemamu et al., 2008). There are different epidemiological situations concerning FMD in southern Africa (Rweyemamu et al., 2008; Thomson, G.R., Vosloo, 2004; Vosloo et al., 2002). SAT serotypes are mainly maintained and spread by African buffalo (*Syncerus caffer*) to susceptible cattle (Thomson, G.R., Vosloo, 2004) while Eurasian or South American serotypes O, A and C are maintained and spread by cattle (Thomson et al., 2003; Vosloo et al., 1996). FMD has adverse effects on food security and economic growth of many developing countries due to the ban of infected countries from lucrative international trade (OIE and FAO, 2012). The disease has been detected sporadically in Malawi and impacts negatively on the livelihoods of the people (Edelsten 1993, Sinkala et al. 2014).

FMD was first identified in southern Africa in 1931 (as reviewed by Guerrini et al., 2019) with the first outbreak reported in Malawi in 1957 (Dawe, 1978). The first outbreak in Malawi was due to cattle infected with a serotype O virus and it occurred in Karonga District, which is situated in the northern region of the country (Daborn 1982). Following this outbreak, more outbreaks have been reported in the northern region (Karonga and Chitipa Districts), southern region (Blantyre District, Shire Valley of Nsanje and Chikwawa Districts) (Edelsten 1993) and recently within the central region, previously considered an FMD-free area. The country was previously divided into three zones; the southern zone (high risk), the central zone (nationally self-proclaimed as FMD-free without vaccination) and the northern part of the country bordering Tanzania (low-risk area). Different FMD serotypes have been identified during these outbreaks: serotypes O, A, SAT1 and 2 in the northern region and O, A, SAT1, 2 and 3 in the southern region (Edelsten 1993). Clinical signs of FMD have been observed in cattle but pigs were only reported to have clinical disease during the 1988/89 outbreak (Edelsten, 1993). Sheep and goats in contact with cattle have not developed any clinical signs; however, sheep and goats have previously seroconverted against FMDV serotype A (Edelsten, 1993).

FMD has typically occurred in the south in the Shire Valley where there is potential contact between cattle and African buffaloes. In the southern region, wildlife from Lengwe National Park are the known reservoirs of FMDV with high antibody titres against SAT1, 2 and 3 being reported for buffalo from the park (DAHLD, 2017). FMD outbreaks in the northern region traditionally followed outbreaks from across the border in neighbouring Tanzania (Daborn 1982). It is assumed that susceptible livestock from Malawi are infected during grazing and when sharing water sources with infected livestock during the dry season (Daborn, 1982). To our current knowledge, no studies have been conducted to determine the space-time clusters of FMD and risk factors in Malawi. To better understand disease dynamics, our study aimed to determine the spatio-temporal distribution and risk factors associated with reported FMD outbreaks in Malawi from 1957 to 2019.

Materials and methods

Study area

Malawi is a land locked country in sub-Saharan Africa that is bordered to the north and northeast by Tanzania; to the east, south and southwest by Mozambique; and to the west and northwest by Zambia. Malawi is administratively divided into three regions and subdivided into 28 districts. The three regions are the northern, central and southern regions (Office NS. Government of Malawi, 2018).

The agriculture sector in Malawi contributes 28% of the total gross domestic product (GDP) of which 37% is derived from livestock (USAID, 2019). Livestock production has been increasing over the years but diseases including FMD limit productivity (Picado et al., 2011).

Data collection

The study analysed retrospective data for the years 1957 to 2019 with the period of the study based on data availability of the FMD status of dip tanks/village units from primary and secondary data sources. These data sources were: the Department of Animal Health and Livestock Development (DAHLD), the World Animal Health Information Systems (WAHIS) database and peer-reviewed journal articles. DAHLD is the main authority responsible for investigation of FMD outbreaks in Malawi and was therefore the primary source of information. The department mainly investigates and reports FMD outbreaks in cattle rather than other species including sheep and goats. Surveillance by DAHLD acts as an early warning system for reporting suspected cases. If suspected cases are not ruled out through epidemiological and clinical investigations then diagnostic specimens are collected and submitted to the Central Veterinary Laboratory. Surveillance involves regular clinical inspection and serological testing at high-risk areas and routine serological and clinical surveillance in the central region. In years with missing data, supplementary information was obtained from WAHIS and peer-reviewed journal articles. An FMD case was defined as cattle with clinical presentation of FMD-like lesions that was subsequently confirmed using liquid-phase blocking enzyme-linked immunosorbent assay (ELISA), reverse transcriptase real-time polymerase chain reaction (RT-PCR) or virus isolation. An outbreak was considered when one or more dip tanks (livestock inspection points) had confirmed FMD cases within the same month. Information that was collected included all FMD affected dip tanks, dip tanks/village units without outbreaks, year of outbreak, dip tank/village global positioning system (GPS) coordinates, number of affected dip tanks, number of susceptible livestock, serotype and animal demographics. Dip tank locations were projected to world geodetic system (WGS) 84 in ArcGIS version 10.7 (ESRI Corp., Version 10.4, Redlands, CA, USA). Outbreak locations were reported as dip tanks with all village units traced to the nearest dip tank.

Risk factor data were collected from DAHLD and downloaded from the Malawi data portal. These data included district/agriculture development division (ADD) level statistics of total cattle, beef cattle, dairy cattle, goats, pigs and sheep. Data were also collected concerning proximity to geographical features (potential risk factors) including distances to the nearest main road, river, lake, international border and wildlife protected area (Department of Forestry, 2019). Livestock densities were calculated as the number of animals per 100 square kilometres in the ADD. Due to the coarse scale and missing data, ordinary kriging was performed for the ADD livestock density data and from these kriged surfaces, livestock density values for all dip tanks/village units were extracted using the extraction tool in ArcGIS. The Near analysis geoprocessing tool was used to calculate the distance between dip tank locations and the geographical features of interest.

Data analysis

An epidemic curve was plotted for the period of study and proportions of outbreaks caused by each FMDV serotype were calculated for the three regions of Malawi. A retrospective space-time analysis was performed using SaTscan software http://www.satscan.org/) based on a Bernoulli probability model to detect clusters of higher probability of outbreaks (Kulldorff, 1999, 1997). Spatial and temporal window sizes were set to a maximum extent of 50% of the total area and time. The test statistic of the identified clusters was calculated by a maximum likelihood ratio function and *p*-values were obtained by Monte Carlo simulation with 999 replications of the dataset. A *p*-value of less than 0.05 was considered statistically significant. Spatio-temporal clusters and outbreak locations were visualised using ArcGIS.

A matched case-control study was conducted to investigate risk factors associated with FMD detection between 1957 and 2019. Cases were defined as dip tanks that were reported and confirmed to have FMD affected cattle within the period of study. Controls were matched to cases by year of outbreak and 10 controls were randomly selected from dip tanks unaffected by FMD during each year of case detection.

Conditional logistic regression was used to calculate odds ratios (OR) as an estimate of the association between potential risk factors and cases of FMD. Variables associated on univariate screening analysis with a *p-value* less than 0.2 were selected for multivariable model fitting. Statistically correlated predictors (for example, total cattle population is the sum of beef and dairy populations) and predictors with Spearman's rho correlations greater than 0.7 were considered collinear. When collinearity was detected, only the variable with the strongest univariate association was selected for multivariable modelling. Final multivariable models were constructed using a backward-stepwise approach through the removal of variables with the largest Wald *p-value*. Variables were excluded one-by-one until all remaining variables in the model had *p*-values less than 0.05. The primary purpose of model building was to define epidemiological associations and measures of overall model fit such as the AIC or BIC were not used to select the final model. The final model equation was used to estimate FMD risk at each study location based on observed predictor values. Statistical analysis was performed with a commercially available statistical software (IBM SPSS Statistics Version 26, International Business Machines Corp., Armonk, New York, USA).

Risk maps were created within ArcGIS (ESRI Corp., Version 10.7, Redlands, CA, USA) by interpolation of standardised risk values (standardised for each year by subtracting the mean of the predicted risk and dividing by the standard deviation for each year) calculated for each study location. Foot-and-mouth disease risk maps were plotted for selected years (1957, 1981, 2000, and 2019) to establish the trend of risk over time. Interpolated risk maps were created using ordinary kriging of the standardised FMD risk obtained from the multivariable conditional logistic regression analysis.

Results

There were 34 confirmed FMD outbreaks in cattle within Malawi between 1957 and 2019 that affected a total of 56 dip tanks or villages. Identified serotypes included SAT1, SAT2, SAT3, O and A (Figure 1). The first reported FMD outbreak in the country occurred in 1957 and was caused by serotype O. This serotype was also associated with other outbreaks between 1981 and 1998 and was last reported in 2010. SAT1 primarily occurred along the northern and southern borders while SAT2 was detected along the western boundary with Zambia (Figure 2). Out of the 34 FMD outbreaks, 2 (6%) were reported as serotype SAT1, 15 (44%) as serotype SAT2, 1 (3%) as serotype SAT3, 2 (6%) as serotype A, 9 as serotype O (26%) and 5 (15%) were untyped (Table 1). Descriptively, a higher proportion of outbreaks occurred in the northern (16/34 outbreaks; 47%) and southern regions (15/34; 44%) with the least number reported in the central region (3/34; 9%).

There were two significant space-time clusters during the study period (Figure 3). The first cluster was in Mzimba District located in the northern region (n=9 affected dip tanks, RR=132) with a radius of 33 km between 1st January 2000 and 31st January 2000. The second cluster was located in Chikwawa and Nsanje Districts within the southern region (n=16 affected dip tanks, RR= 26) with a radius of 50 km between January 2003 and December 2017. The analysis of only index dip tanks (first dip tank affected per outbreak) also identified two significant clusters (Figure 4). The first cluster was detected in Karonga District in the northern region (n=7 affected dip tanks, RR=89) with a radius of 11 km between January 1957 and December 1981. The second cluster was in Chikwawa District within the southern region (n=10 dip tanks, RR=33) with a radius of 45 km between January 2003 and December 2017.

An increase in cattle and pig density was observed over time (1957-2019) in all regions of the country (supplementary material). Univariate conditional logistic regression identified region and distances to an international border, road and a wildlife protected area as significant predictors of FMD affected locations (Table 2). In the final multivariable model, six variables were significantly associated with FMD affected locations (Table 3). Based on the risk mapping using the final multivariable model, high-risk areas were present in the southern and northern regions for the years 1957-2000, while in 2019, high FMD risk included all three regions of Malawi (Figure 5; supplementary material).

Discussion

The study identified serotypes SAT1, SAT2, SAT3, A and O as the circulating serotypes in Malawi, which is consistent with the epidemiological pattern for southern Africa

(Rweyemamu et al., 2008; Vosloo et al., 2002). Early outbreaks due to infections with serotypes SAT1, SAT2, A and O in the northern region were believed to be caused by the introduction of FMDV from neighbouring Tanzania (Daborn, 1982; Rweyemamu et al., 2008). The most prevalent serotype during the study period was SAT2. The SAT2 serotype was mainly reported at locations close to wildlife protected areas (Lengwe National Park, Majete and Mwabvi Game Reserve) in the southern region and international borders (Zambia and Tanzania) in the northern region. Cattle might have been infected at the domestic livestock-wildlife interface during grazing or from illegal movement of cattle across these international borders.

Two significant FMD clusters were identified with one in the northern region (Mzimba District) and the other in the southern region (Chikwawa District) during the study period. The cluster in Mzimba District was associated with serotype SAT1 infections from 1st January 2000 to 31st January 2000. This cluster was located on the western border with Zambia and possibly due to the spread of infection from Zambia. It has been previously reported that outbreaks in northern Zambia and northern Malawi are a consequence of outbreaks in southern Tanzania (Rweyemamu et al., 2008; Sinkala et al., 2014). The cluster in Chikwawa District (between 2003 and 2017) was due to SAT2 infections and the outbreaks occurred close to Majete Wildlife Reserve, Lengwe National Park and borders with Mozambique. This suggests that domestic livestock might have become infected from interactions with African buffalo, a known reservoir of FMDV (Hargreaves et al., 2004). African buffalo are capable of maintaining silent infection of serotypes SAT1, SAT2 and SAT3 for a long time (Hargreaves et al., 2004; Sutmoller et al., 2000). However, it was also possible that the SAT2 virus was being maintained and spread by domestic livestock since these viruses can also become established in cattle populations (Rweyemamu et al., 2008; Sinkala et al., 2014). Furthermore, these outbreaks could be related to outbreaks within neighbouring Mozambique because previous outbreaks that occurred in the southern region preceded reported outbreaks in Mozambique (Edelsten, 1993).

Two significant clusters of FMD were identified after analysing only index cases during the period of study. One cluster was in the northern region, from 1957 to 1981 (Karonga District) and another in southern region (Chikwawa District and Nsanje District) from 2003 to 2017. The first cluster from 1957 to 1981 in the northern region was due to infection with serotypes SAT1, SAT2, A and O. This cluster was located on the northern border with Tanzania and possibly due to the spread of infection from Tanzania and Zambia. The second cluster located in southern region was related to infections with serotype SAT2 viruses located close to Majete Wildlife Reserve, Lengwe National Park and along the boundary with Mozambique. There have been no recent reports of interaction of cattle with buffaloes from the wildlife protected areas, and therefore it is possible that illegal movement of cattle across the Malawi-Mozambique border is responsible for the transmission and spread of FMDV in the southern region. Movement of cattle across international borders has been previously reported to be a risk factor for FMDV transmission (Allepuz et al., 2015; Daborn, 1982; Rweyemamu et al., 2008).

Beef cattle density was positively associated with the risk of FMD detection and reporting. As beef cattle density increased, the likelihood of an FMD outbreak also increased. This is consistent with previous reports that FMD risk increases as the herd size/cattle population increases (Beyene et al., 2015).

The association between pig density and FMD detection is consistent with other studies that suggested that areas with high densities of cattle and pigs pose a higher risk of causing a large-scale outbreak after introduction (Hayama, 2011). In addition, pigs are considered to be the most infectious species regarding FMDV transmission (Hagenaars et al., 2011). However, during the period of study, pigs were only reported to have had clinical signs in 1989 and no outbreaks were reported to have been initiated by pigs. This might be due to under-reporting of clinical signs observed in pigs or due to the fact that most FMD control efforts in the country only consider cattle. The production systems in Malawi could also contribute to under-reporting of cases in pigs since they are not kept in close proximity with cattle. The role of the pig population within the epidemiology of FMD in Malawi needs to be investigated further.

In the current study, distance to wildlife protected areas was positively associated with the risk of FMD; as the distance from the wildlife protected areas increased, the corresponding risk of FMD detection also increased. This is in contrast with the descriptive findings discussed earlier as well as other studies that reported proximity to wildlife protected areas being a risk factor in endemic African countries (Allepuz et al., 2015; Ayebazibwe et al., 2010; Bronsvoort et al., 2004; Molla et al., 2010). We expected that proximity to wildlife protected areas would increase the risk of FMD as reported for other southern African countries (Blignaut et al., 2020; Hamoonga et al., 2014.,Sirdar et al., 2021); however, the risk of FMD was estimated to be lower in areas close to wildlife protected areas. The measured association might have also been affected by the wildlife protected areas spatial layer that was utilised in the study. For example, all designated wildlife protected areas might not have contained FMDV infected wildlife reservoirs. However, this finding might also suggest that wildlife do not play as great a role in the epidemiology of FMD in Malawi as other southern African countries and this is further supported by the wide range of serotypes reported during the study period. Further investigation is therefore required to determine the relative importance of wildlife areas in the epidemiology of FMD in the country.

Increased distances to an international border and roads decreased the risk of FMD detection and reporting. This is consistent with previous studies, where early FMD outbreaks in Malawi were observed in locations that were close to international boundaries. FMD outbreaks in the northern region of Malawi have been associated with outbreaks in Tanzania while those in the southern region were related to outbreaks in Mozambique (Daborn, 1982; Edelsten, 1993). The introduction of FMDV in these areas might be attributed to the movement of livestock across international borders while roads contribute to animal movement and disease spread within the country. Illegal smuggling and uncontrolled transboundary movement of cattle can lead to the introduction of FMDV infected animals (Allepuz et al., 2015; Picado et al., 2011; Kivaria, 2003). The observation that distances to individual countries was not significantly associated with the risk of FMD might have been due to low statistical power and a potential distance threshold effect that was not addressed within the study.

In 2019, all regions of the country had areas of higher FMD risk as compared to the period between 1957 and 2000 and this can be attributed to increases in cattle and pig populations (the only time varying predictors in the logistic regression model) in the central region. The central region was previously a self-declared FMD-free zone (Edelsten, 1993) until recently when the number of outbreaks in the region had increased. Higher ruminant density/livestock density is associated with increased likelihood of FMDV contact (Dos Santos et al., 2017; Fèvre et al., 2006). This increase in the animal densities might be concomitant with an increase in trade within Malawi and therefore increases in animal movements that lead to spread of FMD.

The findings of the study are limited to the data set that was available and cannot account for possible under-reporting of FMD outbreaks. Under reporting of FMD outbreaks across space and time can lead to inaccurate estimates of incidence changes and spatial patterns, which might lead to in inaccurate conclusions. Analyses were based on reported outbreaks at the village/dip tank level and errors in reporting locations are another possibility. The FMDV serotype distributions might also have been affected by untyped outbreaks. Data represented only reported cases of FMD in cattle because FMD control efforts in the country are mainly directed towards this species. Livestock density interpolations were also based on small numbers of locations and this fact might have biased spatial distributions.

It is possible that the measured association was confounded by other factors including distance to cattle markets, increased commercial production or increased FMD control efforts around wildlife protected areas, which were not considered in our study. To avoid potential bias as a result of confounders in future studies, collection of data on all possible risk factors associated with FMD in Malawi should be considered.

Despite these limitations, the current findings could be used to inform risk-based surveillance and a national FMD control programme aimed at reducing FMDV circulation in the country. Understanding the epidemiological situation in endemic countries is one of the important aspects of the Foot and Mouth Disease Progressive Control Pathway (FMD-PCP) (FAO et al., 2018), which provides a basis for implementing an effective national FMD control programme. Progression along the FMD-PCP pathway could lead to Malawi and other FMD endemic countries gaining internationally recognised FMD-free zone status with or without vaccination allowing for access to lucrative international livestock markets.

Conclusions

The results of the current study provide useful information for policymakers on the identification of high-risk locations and predictors of FMD in endemic countries in the region. Foot-and-mouth disease control efforts should first aim at addressing the endemic transmission of FMDV and employ a surveillance programme involving all regional countries. Identification of clusters in this study have been associated with international borders, wildlife areas and a possible maintenance of virus in domestic livestock, which are very important findings as they guide investigation of the possible source of infection during outbreaks as well as guides the possible areas of control to prevent further spread of infection. The FMD control efforts should be directed towards areas with high livestock density and it appears inappropriate to focus control efforts predominantly on the assumption of wildlife reservoir introductions with cattle as the only epidemiologically important transmission route. Another locally important finding is that the central region of Malawi is no longer FMD free potentially due to increases in livestock production and changing livestock movement patterns. This study was limited to the data that was available during the period of study from the different sources. In order to ensure quality and reliable data in future studies, collection of field data should be improved and a formal evaluation of laboratory diagnostic data could be considered.

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References

Aiewsakun, P., Pamornchainavakul, N., Inchaisri, C., 2020. Early origin and global colonisation of foot-and-mouth disease virus. Nat.Res.1,1-9.

Allepuz, A., Stevenson, M., Kivaria, F., Berkvens, D., Casal, J., Picado, A., 2015. Risk factors for foot-and-mouth disease in Tanzania, 2001-2006. Transbound. Emerg. Dis. 62, 127–136.

Ayebazibwe, C., Tjørnehøj, K., Mwiine, F.N., Muwanika, V.B., Ademun Okurut, A.R., Siegismund, H.R., Alexandersen, S., 2010. Patterns, risk factors and characteristics of reported and perceived foot-and-mouth disease (FMD) in Uganda. Trop. Anim. Health Prod. 42, 1547–1559.

Beyene, B., Tolosa, T., Rufael, T., Hailu, B., Teklue, T., 2015. Foot and mouth disease in selected districts of western Ethiopia: Seroprevalence and associated risk factors. OIE Rev. Sci. Tech. 34, 939–952.

Blignaut, B., van Heerden, J., Reininghaus, B., Fosgate, G.T., Heath, L., 2020. Characterization of SAT2 foot-and-mouth disease 2013/2014 outbreak viruses at the wildlife–livestock interface in South Africa. Transbound. Emerg. Dis. 67, 1595–1606.

Bronsvoort, B.M.D.C., Nfon, C., Hamman, S.M., Tanya, V.N., Kitching, R.P., Morgan, K.L., 2004. Risk factors for herdsman-reported foot-and-mouth disease in the Adamawa Province of Cameroon. Prev. Vet. Med. 66, 127–139.

Cleaveland, S., Sharp, J., Abela-Ridder, B., Allan, K.J., Buza, J., Crump, J.A., Davis, A., Del Rio Vilas, V.J., De Glanville, W.A., Kazwala, R.R., Kibona, T., Lankester, F.J., Lugelo, A., Mmbaga, B.T., Rubach, M.P., Swai, E.S., Waldman, L., Haydon, D.T., Hampson, K., Halliday, J.E.B., 2017. One health contributions towards more effective and equitable approaches to health in low- and middle-income countries. Philos. Trans. R. Soc. B Biol. Sci. 372.

Davies , G., 2002. Foot and mouth disease. Res. Vet. Sci. 73, 195–199.

Daborn, C.J., 1982. Foot-and-mouth disease control in the Songwe Valley, Malawi-A review. Trop. Anim. Health Prod. 14, 185–188.

DAHLD, 2017. Foot-and-mouth disease country status-Malawi.

Dawe, B.P.S., 1978. Seasonal foot-and-mouth disease. Br. Vet. J. 134, 249–257.

Dos Santos, D.V., Sousa e Silva, G., Weber, E.J., Hasenack, H., Groff, F.H.S., Todeschini, B., Borba, M.R., Medeiros, A.A.R., Leotti, V.B., Canal, C.W., Corbellini, L.G., 2017. Identification of foot and mouth disease risk areas using a multi-criteria analysis approach. PLoS One 12, 1–19.

Edelsten, R.., 1993. Foot and mouth disease in Malawi. A review of epidemiology and control.

FAO, OIE, GF-TADs, EU-FMD, 2018. The Progressive Control Pathway for Foot and Mouth Disease control (PCP-FMD).

http://www.fao.org/3/CA1331EN/ca1331en.pdf (accessed 5.11.21).

Fèvre, E.M., Bronsvoort, B.M.D.C., Hamilton, K.A., Cleaveland, S., 2006. Animal movements and the spread of infectious diseases. Trends Microbiol. 14, 125–131.

Guerrini, L., Pfukenyi, D.M., Etter, E., Bouyer, J., Njagu, C., Ndhlovu, F., Bourgarel, M., De Garine-Wichatitsky, M., Foggin, C., Grosbois, V., Caron, A., 2019. Spatial and seasonal patterns of FMD primary outbreaks in cattle in Zimbabwe between 1931 and 2016. Vet. Res. 50, 1–12.

Hamoonga, R., Stevenson, M.A., Allepuz, A., Carpenter, T.E., Sinkala, Y., 2014. Risk factors for foot-and-mouth disease in Zambia, 1981-2012. Prev. Vet. Med. 114, 64–71.

Hargreaves, S.K., Foggin, C.M., Anderson, E.C., Bastos, A.D.S., 2004. An Investigation Into the Source and Spread of Fmd Virus From a Wildlife Conservancy in Zimbabwe. 23, 783–790.

Hagenaars, T.H.J., Dekker, A., de Jong, M.C. and Eblé, P.L., 2011. Estimation of foot and mouth disease transmission parameters, using outbreak data and transmission experiments. Revue scientifique et technique/Office International des Epizooties. 30, 467-481.

Hayama, Y., 2011. Potential impact of species and livestock density on the epidemic size and effectiveness of control measures for foot-and-mouth disease in Japan. J. Vet. Med. Sci.

Jamal, S.M., Belsham, G.J., 2013. Foot-and-mouth disease : past , present and future. Vet Res.44, 1-14.

Kivaria, F.M., 2003. Foot and mouth disease in Tanzania: An overview of its national status. Vet. Q. 25, 72–78.

Kitching, R.P., Hutber, A.M., Thrusfield, M. V., 2005. A review of foot-and-mouth disease with special consideration for the clinical and epidemiological factors relevant to predictive modelling of the disease. Vet. J. 169, 197–209.

Knowles, N.J., Samuel, A.R., 2003. Molecular epidemiology of foot-and-mouth disease virus. Virus Res. 91, 65–80.

Kulldorff, M., 1999. Scan Statistics and Applications. Scan Stat. Appl. https://doi.org/10.1007/978-1-4612-1578-3

Kulldorff, M., 1997. A spatial scan statistic. Commun. Stat. - Theory Methods 26, 1481–1496.

Molla, B., Ayelet, G., Asfaw, Y., Jibril, Y., Ganga, G., Gelaye, E., 2010. Epidemiological study on foot-and-mouth disease in cattle: Seroprevalence and risk factor assessment in south omo zone, south-western Ethiopia. Transbound. Emerg. Dis. 57, 340–347.

Offiice NS. Government of Malawi, 2018. Malawi in Figures 2018 Edition. http://www.nsomalawi.mw/images/stories/data_on_line/general/malawi_in_figures/2018 Malawi in Figures.pdf (accessed 6.28.19).

OIE, FAO, 2012. The Global Foot and Mouth Disease Control Strategy: Strengthening animal health sysyems through improved control of major diseases. http://www.fao.org/docrep/015/an390e/an390e.pdf (accessed 4.16.21).

Picado, A., Speybroeck, N., Kivaria, F., Mosha, R.M., Sumaye, R.D., Casal, J., Berkvens, D., 2011. Foot-and-mouth disease in Tanzania from 2001 to 2006. Transbound. Emerg. Dis. 58, 44–52.

Rweyemamu, M., Roeder, P., MacKay, D., Sumption, K., Brownlie, J., Leforban, Y., Valarcher, J.F., Knowles, N.J., Saraiva, V., 2008. Epidemiological patterns of foot-and-mouth disease worldwide. Transbound. Emerg. Dis. 55, 57–72.

Sinkala, Y., Simuunza, M., Muma, J.B., Pfeiffer, D.U., Kasanga, C.J., Mweene, A., 2014. Foot and mouth disease in Zambia: Spatial and temporal distributions of outbreaks, assessment of clusters and implications for control. Onderstepoort J. Vet. Res. 81, 1–6.

Sirdar, M., Fosgate, G., Blignaut, B., 2021. Spatial distribution of foot-and-mouth disease (FMD) outbreaks in South Africa (2005-2016). Trop. Anim. Health Prod.

Sutmoller, P., Thomson, G.R., Hargreaves, S.K., Foggin, C.M., Anderson, E.C., 2000. The foot-and-mouth disease risk posed by African buffalo within wildlife conservancies to the cattle industry of Zimbabwe. Prev. Vet. Med. 44, 43–60.

Thomson, G.R., Vosloo, W., Bastos, A.D.S., 2003. Foot and mouth disease in wildlife. Vir.

Res. 1, 145-161.

USAID, 2019. Green Investment Opportunities for Malawi Livestock Sector. https://www.climatelinks.org/resources/green-investment-opportunities-malawis-livestock-sector (accessed 4.7.21).

Vosloo, W., Bastos, A.D., Kirkbride, E., Esterhuysen, J.J., Janse Van Rensburg, D., Bengis, R.G., Keet, D.W., Thomson, G.R., 1996. Persistent infection of African buffalo (Syncerus caffer) with SAT-type foot-and-mouth disease viruses: Rate of fixation of mutations, antigenic change and interspecies transmission. J. Gen. Virol. 77, 1457–1467.

Vosloo, W., Bastos, A.D.S., Sangare, O., Hargreaves, S.K., Thomson, G.R., 2002. Review of the status and control of foot and mouth disease in sub-Saharan Africa. OIE Rev. Sci. Tech. 21, 437–449.

Vosloo, W., and G. R. Thomson, 2004: Natural habitats in which foot- and- mouth disease viruses are maintained. in: Sobrino, Francisco and Domingo, E. (Ed.), Foot and Mouth Disease: Current Perspectives. CRC Press, 384–410.

Table 1: Total number of foot-and-mouth disease outbreaks (n=34), and their corresponding serotypes reported from the three regions of Malawi between 1957-2019

Region	***SAT1**	**SAT2**	**SAT3**	**A**	**O**	**Untyped**	**Total**
North	2	5	0	1	7	1	16
Central	0	3	0	0	0	0	3
South	0	7	1	1	2	4	15
Total	**2**	**15**	**1**	**2**	**9**	**5**	**34**

*SAT: Southern African Territories

Table 2: Univariate conditional logistic regression results of risk factors associated with foot-and-mouth disease affected locations in Malawi between 1957 and 2019

Variables	**Slope parameter**	**Odds ratio**	**95% Confidence Interval**	**P-value**
Density* of cattle	0.020	1.020	0.827-1.258	0.848
Density of beef cattle	0.169	1.185	0.935-1.501	0.159
Density of dairy Cattle	0.046	1.047	0.950-1.155	0.356
Density of goats	0.007	1.007	0.982-1.033	0.572
Density of sheep	-0.144	0.866	0.617-1.217	0.572
Density of pigs	0.028	1.028	0.986-1.072	0.194

Distance** to lakes	0.638	1.893	0.555-6.457	0.307
Distance to railways	-0.069	0.934	0.436-1.997	0.86
Distance to rivers	0.738	0.739	0.182-2.983	0.671
Distance to roads	2.87E-08	0	0.000-0.105	0.024
Distance to protected areas	3.040	20.90	1.185-368.6	0.038
Distance to Mozambique	-0.077	0.926	0.193-4.434	0.923
Distance to Tanzania	0.141	1.152	0.384-3.454	0.801
Distance to Zambia	-0.08	0.812	0.306-2.152	0.675
Distance to any international border	-2.715	0.066	0.007-0.666	0.021
South region associated with occurrence of FMD compared to the Northern region	-0.178	0.836	0.328-2.129	0.709

Central region associated with occurrence of FMD compared to Northern region	-3.345	0.035	0.008-0.155	<0.001

* Density in heads/100sq.km, ** Measured in decimal degrees

Table 3: Multivariable conditional logistic regression results for risk factors associated with foot-and-mouth disease affected locations in Malawi between 1957 and 2019

Variable	**Slope parameter**	**Odd ratio**	**95% Confidence Interval**	**P-value**
Density of beef cattle*	0.125	1.133	1.017-1.261	0.023
Density of pigs*	0.026	1.026	1.001-1.053	0.043
Distance to roads**	-15.791	0	0.000-0.304	0.034
Distance to any international border**	-2.744	0.058	0.08-0.494	0.008
Distance to Protected Areas**	2.691	14.74	1.198-181.4	0.036
Central region associated with occurrence of FMD compared to the northern and southern regions	-2.84	0.058	0.019-0.177	<0.001

*Density in heads/100sq.km, ** Measured in decimal degrees

Figure legends

Figure 1: Total number of the foot-and-mouth disease affected dip tanks/ villages and serotypes in Malawi from 1957-2019 (SAT: Southern African Territories)

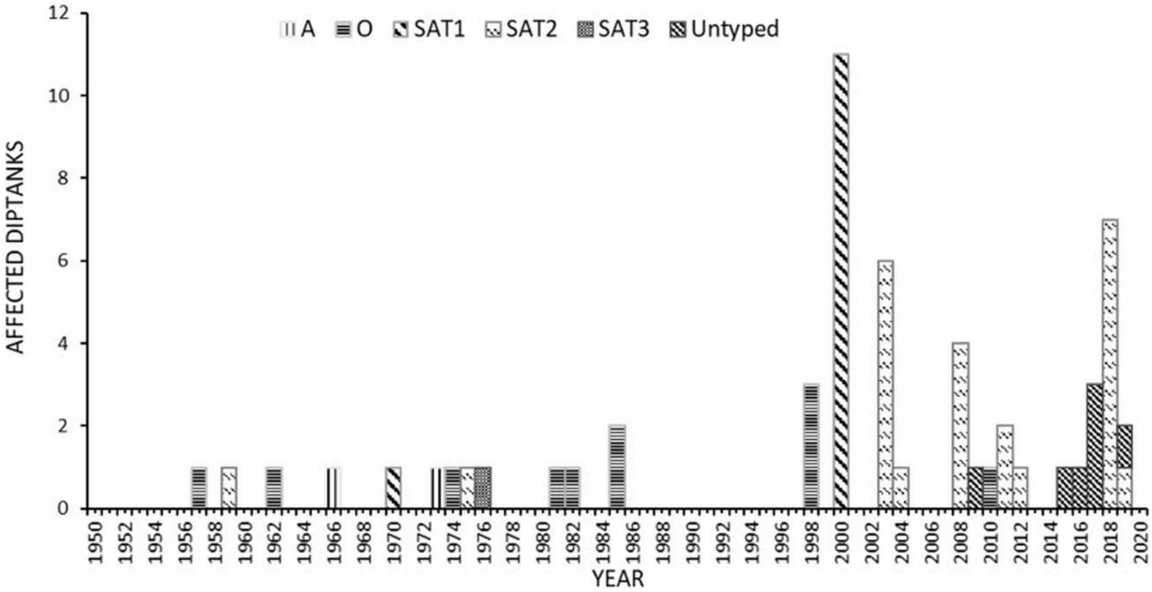
Figure 2: Spatial distribution of foot-and-mouth disease virus serotypes in all affected locations in Malawi from 1957-2019

Figure 3: Space-time analysis of foot-and-mouth disease high-rate clusters from 1957-2019 in Malawi

Figure 4: Space-time clusters of foot-and-mouth disease index cases from 1957-2019 in Malawi

Figure 5: Maps illustrating the trend of risk of foot-and-mouth disease in all regions of Malawi from 1957-2019

Figure 1


A
O
SAT1
SAT2
SAT3
Untyped
AFFECTED DIPTANKS
0
2
4
6
8
10
12
YEAR
1950
1952
1954
1956
1958
1960
1962
1964
1966
1968
1970
1972
1974
1976
1978
1980
1982
1984
1986
1988
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1992
1994
1996
1998
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2004
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2008
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2012
2014
2016
2018
2020

Figure 2

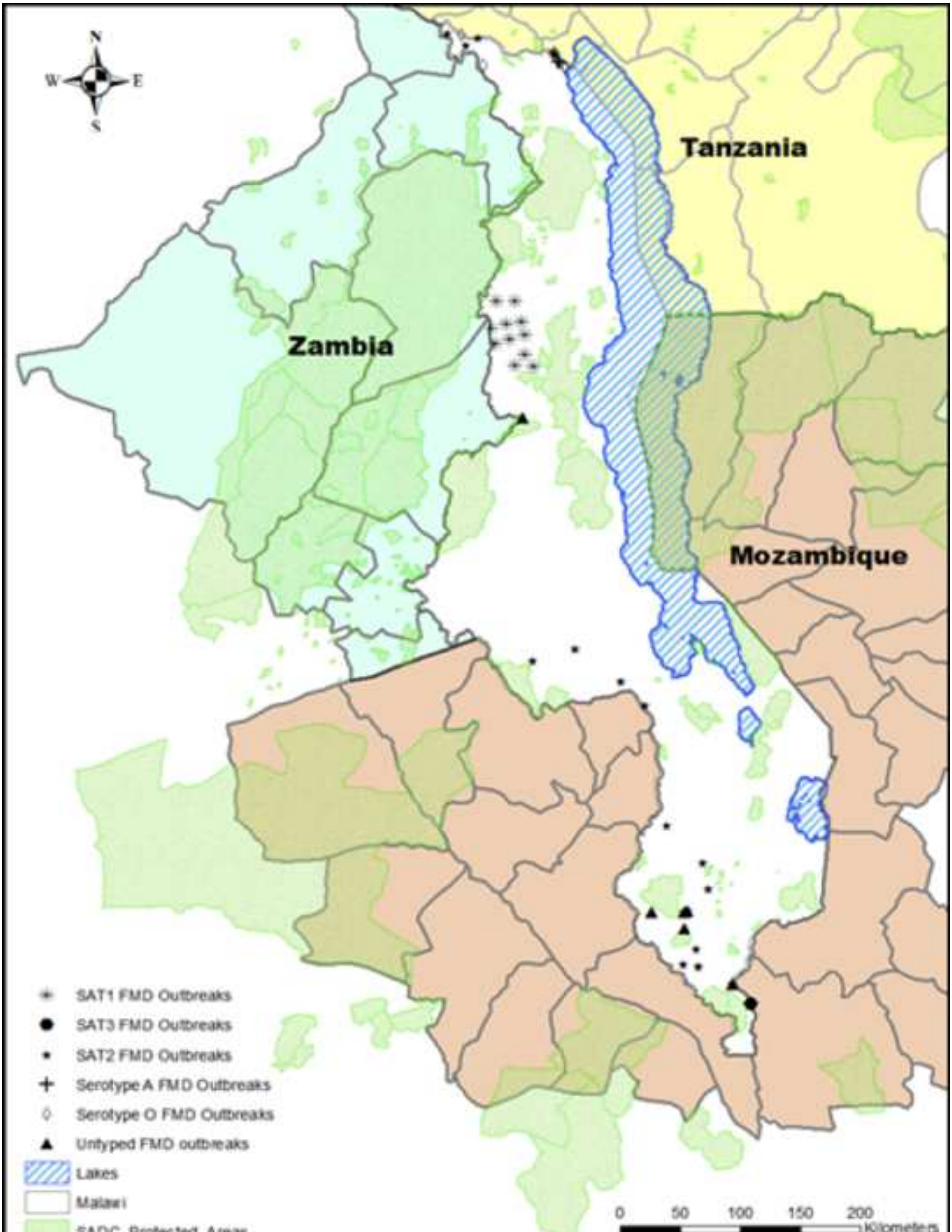

N
W
E
S
Tanzania
Zambia
Mozambique
SAT1 FMD Outbreaks
SAT3 FMD Outbreaks
SAT2 FMD Outbreaks
Serotype A FMD Outbreaks
Serotype O FMD Outbreaks
Untyped FMD outbreaks
Lakes
Malawi
SADC_Protected_Areas
0
50
100
150
200
Kilometers

Figure 3

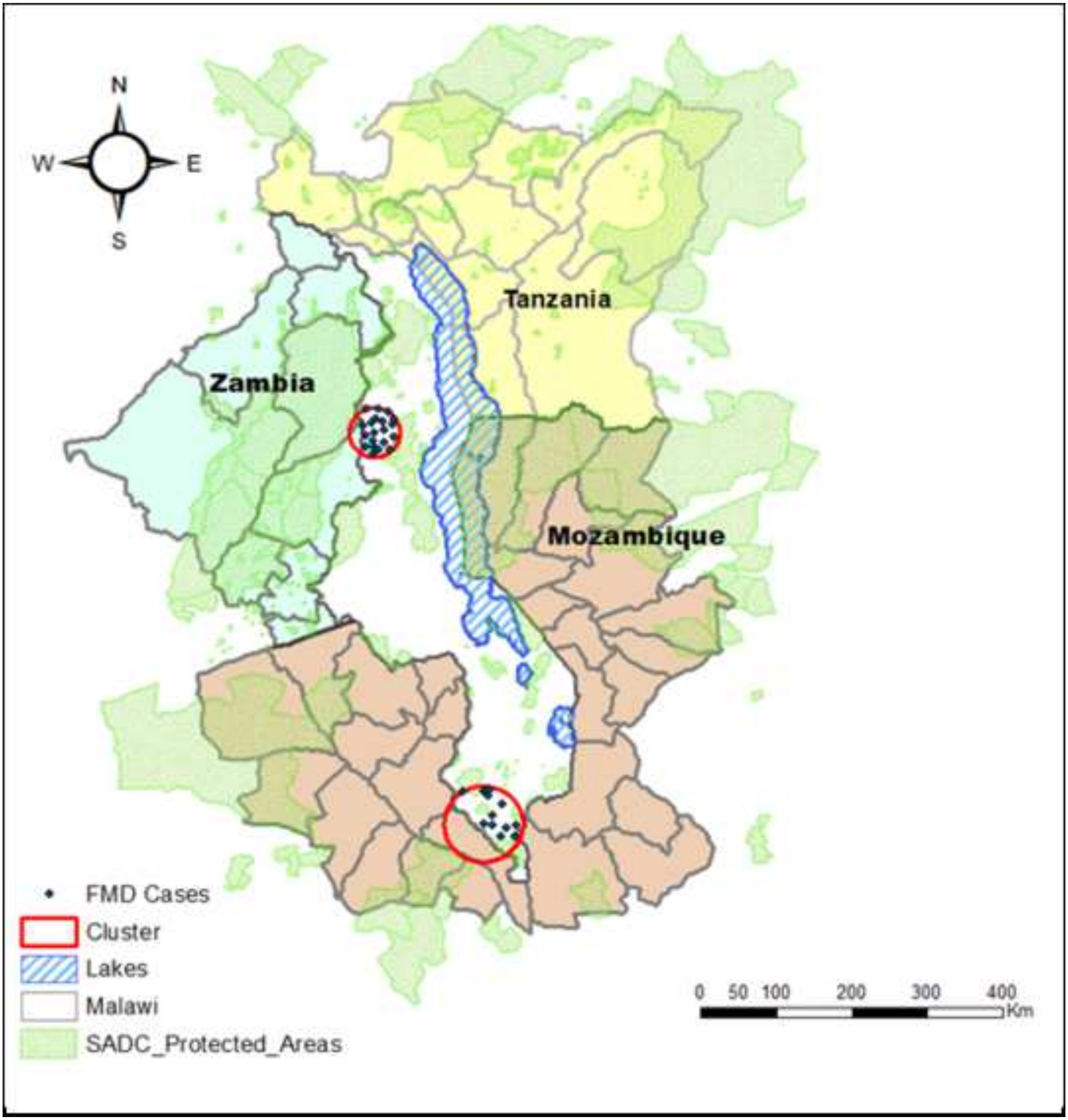

N
W
E
S
Tanzania
Zambia
Mozambique
FMD Cases
Cluster
Lakes
Malawi
SADC_Protected_Areas
0 50 100 200 300 400
Km

Figure 4

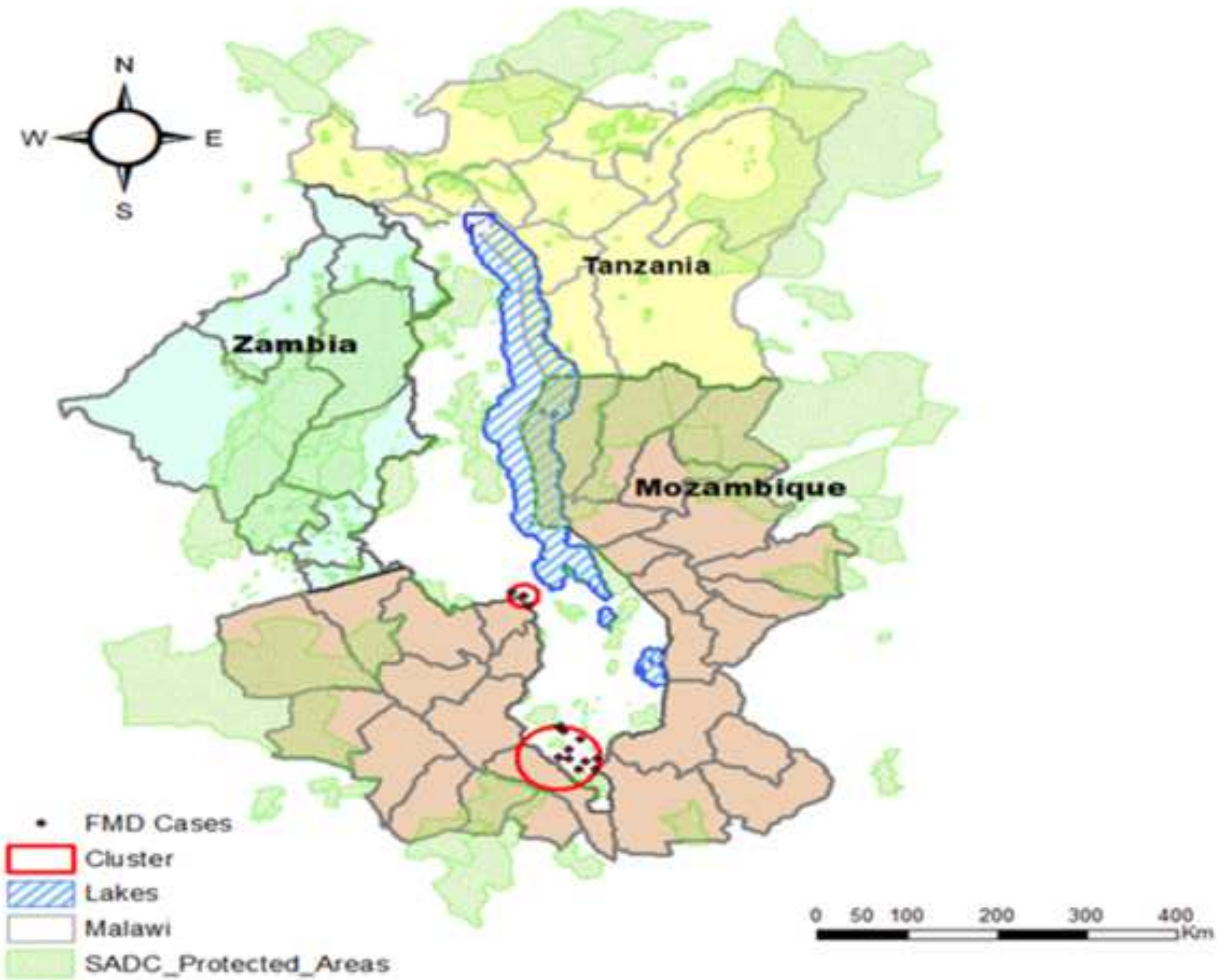
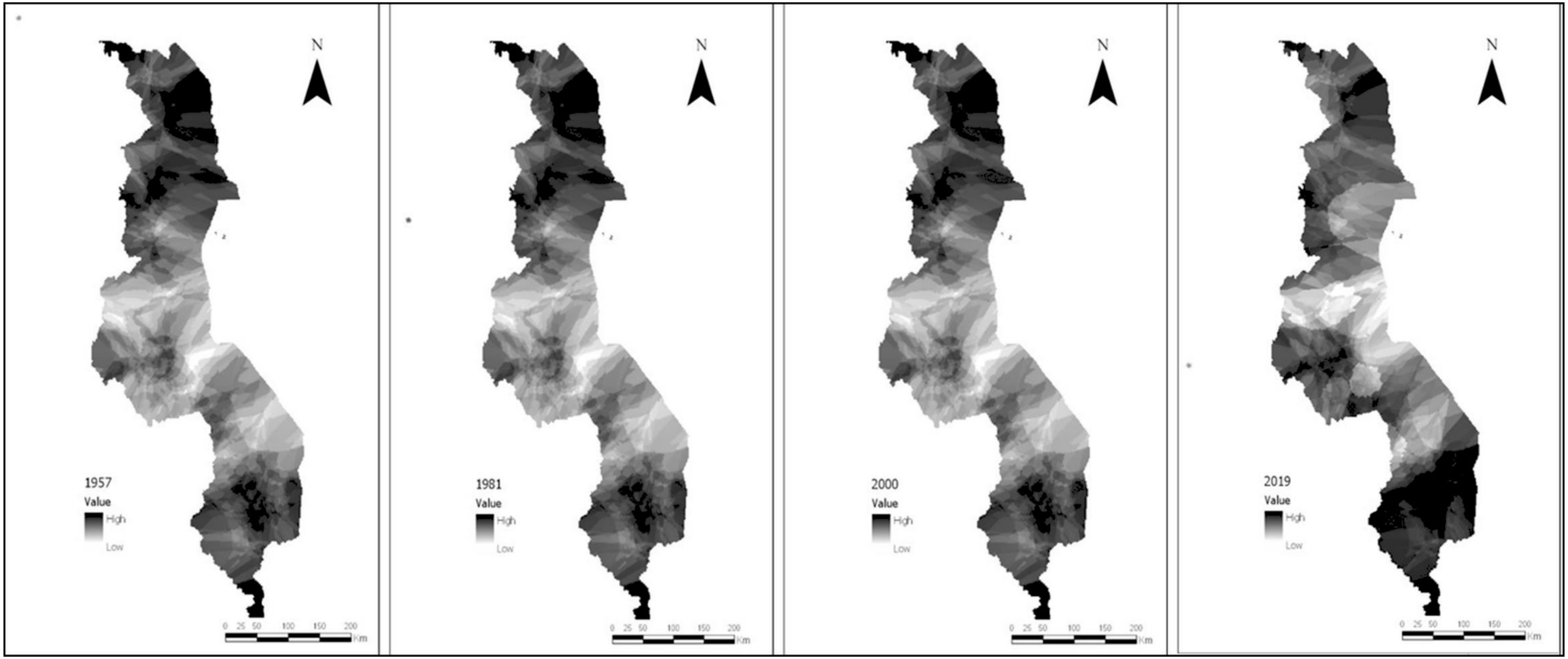

N
W
E
S
Tanzania
Zambia
Mozambique
FMD Cases
Cluster
Lakes
Malawi
SADC_Protected_Areas
0 50 100 200 300 400
Km

Figure 5



N
1957
Value
High
Low
0 25 50 100 150 200
Km
N
1981
Value
High
Low
0 25 50 100 150 200
Km
N
2000
Value
High
Low
0 25 50 100 150 200
Km
N
2019
Value
High
Low
0 25 50 100 150 200
Km