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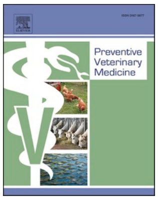

A comparison of risk factor investigation and experts' opinion elicitation analysis for identifying foot-and-mouth disease (FMD) high-risk areas within the FMD protection zone of South Africa (2007–2016)☆

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ABSTRACT

Foot-and-mouth disease is a controlled disease in accordance with the South African Animal Diseases Act (Act 35 of 1984). The country was classified by the World Organisation for Animal Health (WOAH) as having a FMD free zone without vaccination in 1996. However, this status was suspended in 2019 due to a FMD outbreak outside the controlled zones. FMD control in South Africa includes animal movement restrictions placed on cloven-hoofed species and products, prophylactic vaccination of cattle, clinical surveillance of susceptible species, and disease control fencing to separate livestock from wildlife reservoirs. The objectives of this study were to evaluate differences in identifying high-risk areas for FMD using risk factor and expert opinion elicitation analysis. Differences in risk between FMD introduction and FMD spread within the FMD protection zone with vaccination (PZV) of South Africa (2007–2016) were also investigated.

The study was conducted in the communal farming area of the FMD PZV, which is adjacent to wildlife reserves and characterised by individual faming units. Eleven risk factors that were considered important for FMD occurrence and spread were used to build a weighted linear combination (WLC) score based on risk factor data and expert opinion elicitation. A multivariable conditional logistic regression model was also used to calculate predicted probabilities of a FMD outbreak for all dip-tanks within the study area. Smoothed Bayesian kriged maps were generated for 11 individual risk factors, overall WLC scores for FMD occurrence and spread and for predicted probabilities of a FMD outbreak based on the conditional logistic regression model. Descriptively, vaccine matching was believed to have a great influence on both FMD occurrence and spread. Expert opinion suggested that FMD occurrence was influenced predominantly by proximity to game reserves and cattle density. Cattle populations and vaccination practices were considered most important for FMD spread. Highly effective cattle inspections were observed within areas that previously reported FMD outbreaks, indicating the importance of cattle inspection (surveillance) as a necessary element of FMD outbreak detection.

The multivariable conditional logistic regression analysis, which was consistent with expert opinion elicitation; identified three factors including cattle population density (OR 3.87, 95% CI 1.47–10.21) and proximities to game reserve fences (OR 0.82, 95% CI 0.73–0.92) and rivers (OR 1.04, 95% CI 1.01–1.07) as significant factors for reported FMD outbreaks. Regaining and maintaining an FMD-free status without vaccination requires frequent monitoring of high-risk areas and designing targeted surveillance.

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1. Introduction

Foot-and-mouth-disease (FMD) is a contagious transboundary animal disease that is considered to be one of the most important animal diseases globally, including within the southern African region (Sinkala et al., 2014). This importance is due to its effects on regional trade in livestock, wildlife and other agricultural products (Grubman and Baxt, 2004). The disease 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 (SAT) 1, 2 and 3 (Larska et al., 2009; Tully and Fares, 2008; Yoon et al., 2011).

South Africa controls FMD by separating wildlife from livestock with veterinary cordon fencing, vaccinating cattle, movement control of cloven-hoofed animals and products and surveillance (DAFF, 2014). FMD control areas are divided into three primary FMD control zones: infected, protection and free zones. The majority of the infected zone is comprised of the Kruger National Park (KNP) and adjacent wildlife conservation areas. The KNP is a national game reserve in the north-eastern part of South Africa that is approximately 480 km long and 60–80 km wide. The KNP and adjacent wildlife reserves are separated from communal farming areas by a 2.45-meter fence. The protection zone (approximately 480 km long and 10–20 km wide) is situated adjacent to the infected zone and falls within the three provinces of Mpumalanga, Limpopo, and Kwazulu Natal. The FMD protection zone is subdivided into two areas: the protection zone with vaccination and the protection zone without vaccination, where the latter is situated to the west and south of the protection zone with vaccination (Ferguson et al., 2012). In 1996, the International Committee on FMD of the World Organisation for Animal Health (WOAH) endorsed South Africa's FMD free zone status without vaccination Brückner et al. (2002). Prior to 1996, the most recent FMD outbreak in the free areas was during 1957, while post 1996 the free zone status was suspended in 2000, 2011 and 2019. The 2019 FMD free zone status suspension was due to a SAT2 FMD outbreak that occurred outside the protection zone of Limpopo Province (DAFF, 2019) and at the time of this writing, the free zone has yet to be reinstated.

FMD endemic countries often lack the resources necessary to maintain FMD control and access lucrative export markets. The alternative is to develop risk-based surveillance and targeted controls through a complete understanding of risk factors and their spatio-temporal distributions (van Schalkwyk et al., 2011). This approach maximizes the use of limited human resources by applying control measures efficiently in high-risk areas.

In southern Africa including South Africa, the risk of FMD detection is influenced by the presence of African buffalo (*Syncerus caffer*), the wildlife reservoir for the SAT serotypes (Thomson et al., 2003). Contacts between African buffalo and cattle are often close to water points including rivers (Miguel et al., 2017) and fence damage increases the risk of this contact (Mogotsi et al., 2016). Sirdar et al. (2021) reported four high-risk clusters for FMD in the protection zone with vaccination of South Africa and the spatial distribution of outbreaks in cattle were closer to game reserve fences and consistent with wildlife contacts as a main contributor of FMD occurrence.

Herd immunity of cattle in the protection zone, human population and fence maintenance, permeability of the KNP fence, river crossings, elephant density, African buffalo density, flooding events and landscape characteristics are important predictors of FMDV transmission from wildlife to livestock (Jori et al., 2009; Dion et al., 2011; Dion and Lambin, 2012; Jori and Etter, 2016; van Schalkwyk et al., 2016).

Many studies concerning factors associated with FMD outbreaks apply multivariable regression models (Bronsvoort et al., 2004; Ilbeigi et al., 2018; Sansamur et al., 2020). In an endemic FMD setting, it has been reported that contact or proximity to African buffalo, uncontrolled animal movements, production system, intermingling of cattle at grazing areas and water sources, movement of infected animals, high herd mobility, presence of a major livestock market, adjacency to a national park, density of small ruminants, drought, cross border movements, density of cattle herds and close proximity to slaughterhouses are risk factors for FMD occurrence and infection in pastoral systems (Cleland et al., 1996; 2004; Lindholm et al., 2007; Megersa et al., 2009; Dukpa et al., 2011; Jemberu et al., 2016; Nyaguthii et al., 2019).

Roads and proximity to borders play a major role in the endemic and epidemic phases of FMD outbreaks (Allepuz et al., 2015). FMD outbreaks reported in Tanzania were mainly aggregated in the border area with a neighboring country and railway networks indicating that FMDV spread was primarily related to human activity (Picado et al., 2011).

The use of a shared bull, the number of animals sourced from other farms, cattle purchases from livestock markets, use of communal dipping and multiple species sharing the same farm are factors associated with FMD introduction (Nyaguthii et al., 2019).

FMD risk estimation can be studied using several methods including expert opinion elicitation and risk factor analysis using regression models analysing reported outbreaks. The use of expert opinion elicitation is well documented and the weighted linear combination (WLC) method is one of the common approaches (Pfeiffer et al., 2008). Risk factors can be weighted using a pairwise comparison method, where each factor is rated against all other factors and weights are calculated from these pairwise ratings (Saaty, 1980). The analytical hierarchy process (AHP) is then used to obtain ratio scales from both discrete and continuous paired comparisons using a process of relative comparisons based on human judgment (Saaty, 1987; Saito et al., 2015). AHP and by extension WLC has been used to evaluate the control of infectious bursal disease virus in California (Saito et al., 2015). Similarly, WLC has been used by integrating GIS and fuzzy logic to generate hazard zones for hand-foot-and-mouth disease in Thailand (Samphutthanon et al., 2014). A modified AHP approach has also been used to estimate FMD occurrence and evaluate FMD surveillance performance in Rio Grande do Sul state, Brazil (Santos et al., 2017). Validation of produced spatial risk maps using this method is limited to the visual comparison with existing data or actual outbreak locations (Craig et al., 1999). The accuracy of expert-opinion data has not been investigated or compared formally with other methods of disease reporting and surveillance data (Garabed et al., 2009).

Regression models can be used to quantify the association between a set of explanatory variables and the presence/absence of an FMD outbreak at a given location (Souley et al., 2018). The objectives of this study were to evaluate differences in identifying high-risk areas for FMD using risk factor and expert opinion elicitation analysis. In addition, utilising expert opinion results to spatially describe the differences in risk between FMD introduction and spread within the FMD protection zone with vaccination of South Africa. Finally, this study compared FMD control measures between the two study provinces (Limpopo and Mpumalanga).

2. Material and methods

2.1. Study area

In 1996, the International Committee on FMD of the World Organisation for Animal Health (WOAH) endorsed South Africa's FMD free zone status without vaccination. According to the WOAH status, the areas excluded from the free zone were the endemically infected Kruger National Park (KNP) and the FMD protection areas (Bruckner et al., 2002).

FMD control areas are divided into three primary FMD zones: infected, protection and free. The majority of the infected zone is the KNP and adjacent wildlife conservation areas. The KNP and adjacent wildlife reserves are separated from communal farming areas by a fence 1.80–2.45 m in height (Ferguson et al., 2012). The Ndumo Nature Reserve and the Tembe Elephant Park in KwaZulu-Natal Province have also been considered infected since 2011 (DAFF, 2011).

The protection zone (approximately 480 km long and 10–20 km wide) is situated adjacent to the infected zone and falls within the three provinces of Mpumalanga, Limpopo, and KwaZulu Natal (DAFF, 2014). The FMD protection zone is subdivided into two areas: the protection zone with vaccination (PZV) and the protection zone without vaccination.

The majority of the FMD PZV are communal rangelands that accommodate communal farmers who are mainly involved in livestock rearing. Farmers are settled in villages that are in close proximity to each other along the PZV. The main agricultural activity in the area is livestock farming with cattle (indigenous breeds) as the most important species (Dovie, et al., 2002). Communal grazing areas are characterised by individual faming units, where in day-time cattle are herded around the village for grazing and water, while returned in the evening and kept in "kraals" ("kraal" is a livestock enclosure located within a village) in separate groups at night. Husbandry facilities (dip-tanks) and areas for grazing are shared during the day between several owners (Kaszta et al., 2017). Dip-tanks (animal assembly points) are used for routine inspection and disease control. A dip-tank serves at least one village within an average area of five km^2.

Cattle within the PZV are inspected for FMD at designated dip-tanks every 7 days and small stock (i.e. goats, sheep and pigs) are inspected every 28 days. In this zone, cattle are routinely vaccinated every four months using a commercial trivalent vaccine containing SAT serotypes 1, 2 & 3 (DAFF, 2014). The protection zone without vaccination is situated to the west and south of the protection zone with vaccination and all cattle in this area are inspected every 14 days. Routine FMD vaccination is not permitted in the protection zone without vaccination or the

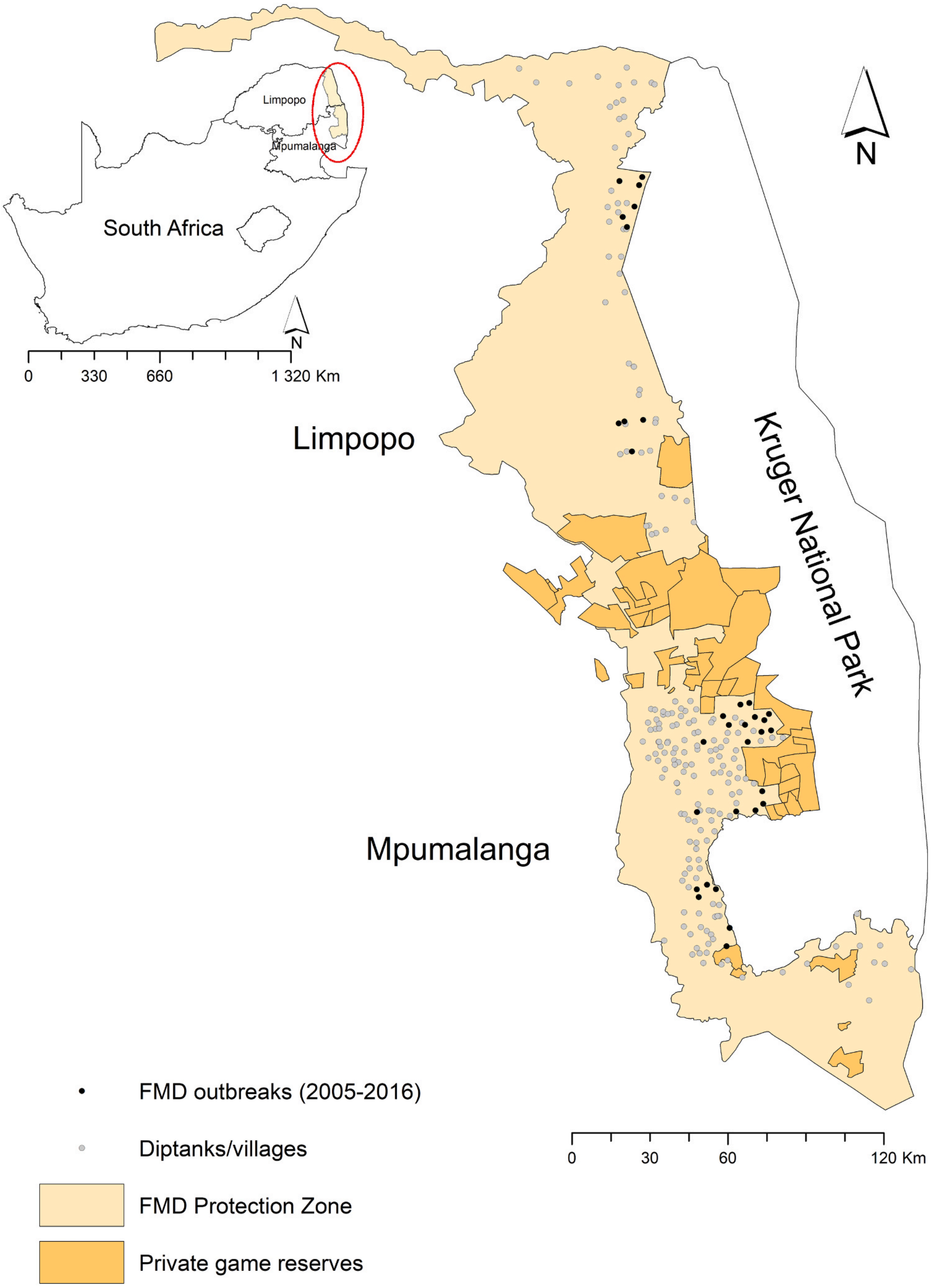

Fig. 1. South Africa's Limpopo and Mpumalanga Provinces' FMD control zones (infected and protection), livestock dip-tanks and FMD outbreaks 2007–2016 (Black dots are villages/dip tanks that experienced an outbreak during the study whereas the lighter dots did not experience a FMD outbreak).

free zone.

The study was performed in the FMD PZV in the South African provinces of Mpumalanga and Limpopo (Fig. 1). The FMD PZV of Mpumalanga and Limpopo Provinces includes four (Ehlanzeni North, Ehlanzeni South, Nkomazi and Mbombela) and six local municipalities (Musina, Thulamela, Greater Giyani, Ba-Phalaborwa, Maruleng and Collins Chabane), respectively. These study areas are regarded as the KNP human/wildlife/livestock interface adjacent to the FMD infected zone. The study excluded the KwaZulu-Natal Province since this protection area was designated in 2014 and FMD outbreaks had not been recorded during the study period (2007–2016).

2.2. Data collection and management

The statistical unit of analysis was livestock dip-tanks. The Department of Agriculture and Rural Development, Veterinary Services of both Mpumalanga and Limpopo Provinces provided information on all registered dip-tanks including georeferenced locations, total susceptible animals and animal-specific demographics. Animal demographics were extracted from the state veterinarian monthly disease reports. These reports included information on the total number of cattle per dip-tank at the beginning of each month as well as increases (births and in-movement) and decreases (death, out-movement and slaughter) of the population. The reports also provided information on the date and total number of FMD vaccinations administered to cattle. The disease inspection and dipping report had the weekly cattle inspection information including the total number of cattle inspected every week. The animal movement permit register was examined to extract data on animal movement in and out of all dip-tank locations. Data were collected between April 2007 and March 2016 and both provincial and national departments granted approval to use the collected data for the study analysis. Vaccination data were extracted for the entire study period (2007–2016), while only 2009 data were used to estimate the cattle population, inspection efficiency and permitted movements. For spatial modelling, missing data were imputed by calculating the mean of available data for each risk factor variable independently by province.

All reported FMD cases in domestic cattle for the same period in the PZV communal farming areas for both Limpopo and Mpumalanga Provinces of South Africa were identified from the WOAH database (WAHIS) (WOAH. 2016).

Coordinates for dip-tanks were converted to the Universal Transverse Mercator (UTM) zone 36 S World Geodetic System (WGS) 1984 format and plotted using ArcGIS version 10.4 (ESRI, Redlands, California, USA).

2.3. Study context and design

The context of this study was to perform a semi-quantitative risk assessment of FMD introduction (occurrence) based on confirmed reported cases and the risk of FMD spread following the initial reported FMD cases.

The study was performed using two approaches including a regression analysis of confirmed FMD outbreaks as a dependent variable. This analysis was considered a mixture of FMD introduction and spread because all outbreaks were included in the analysis due to the limited number of reports and uncertainty surrounding whether or not the first confirmed case represented the initial introduction. Expert opinion elicitation was also employed through questionnaire administration (not using Sheffield, Cooke's or Delphi methodologies) and performing a pairwise comparison method to generate risk factor weights in combination with spatial mapping of each risk pathway for FMD occurrence/introduction and spread.

2.4. FMD risk factors

A total of 11 potential risk factors for FMD introduction and spread in the PZV of South Africa were evaluated based on literature review and availability of data: i) cattle population, ii) proximity to a game reserve, iii) human population (density), iv) proximity to a road network, v) proximity to rivers, vi) SAT1 vaccine matching, vii) SAT2 vaccine matching, viii) dip-tanks weighted average for a combined SAT1 and SAT2 FMD vaccine matching, xi) vaccination coverage (vaccination proportion), x) vaccination interval, xi) cattle inspection (proportion), xii) permitted cattle movement into a village/location and xiii) permitted cattle movement outside a village/location (Table 1). Vaccine matching was analysed as three variables for SAT1, SAT2 and a combined variable for both serotypes. Data concerning cattle population, cattle vaccination numbers, cattle vaccination intervals, cattle inspections, cattle movement into a dip-tank (or village) and cattle movement outside to another dip-tank (or village) were extracted from the veterinary services reports.

The distance from each dip-tank to the nearest fence of a wildlife reserve, road network and river were estimated using the measuring tool in GIS software (ESRI, Redlands, CA, USA). Human population densities were extracted from the national Statistics South Africa database (2011). Vaccine matching results assigned to each dip-tank were interpolated using data from a previous study (Sirdar et al., 2019) and the zonal statistics tool in the GIS software. A weighted average vaccine match for a combined SAT1 and SAT2 FMD results was calculated by the formula (Grossman et al., 1980):

$$\frac{\dot{S}SAT1 + \dot{S}SAT2}{Total \quad number \quad of \quad affected \quad SAT1\&SAT2diptanks} \tag{1}$$

$$\dot{S}SAT1 = (SAT1 vaccine\ matching\ for\ each\ diptank)\ x\ (total\ number\ of\ SAT1 affected\ diptanks)$$

$$\dot{S}SAT2 = (SAT2 vaccine\ matching\ for\ each\ diptank)\ x\ (total\ number\ of\ SAT2 affected\ diptanks)$$

Data for each evaluated risk factor were described by calculating the mean, standard deviation, median and interquartile range. The averaged risk factor data were compared between Limpopo and Mpumalanga provinces using Mann-Whitney U tests. Statistical analysis was performed using SPSS 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and results were interpreted at $p < 0.05$.

2.5. Expert opinion elicitation

All evaluated risk factors were weighted ('*risk factor's weight*') using a pairwise comparison method, where each factor was rated according to its relationship to all other factors (Saaty, 1980). Weights were calculated for each factor based on their pairwise rating and assigned a score using the preference response; risk factor *y* could be considered equally (01:01) to extremely more (16:01) or (less) important (01:16) when compared to risk factor *z* in relation to occurrence (and spread) of FMD. Weighting was performed independently for FMD introduction/occurrence and FMD spread (supplemental materials - questionnaire).

Table 1
Risk factors associated with SAT1 and SAT2 foot-and-mouth disease (FMD) ***occurrence (or spread)**** in the protection zone with vaccination of South Africa.

Potential risk factor for SAT1 and SAT2 FMD occurrence	Associated hypothesis	Indicator measurement
Cattle population (Perez et al., 2004; Jemberu et al., 2016)	Increasing cattle density increases the likelihood of FMD outbreak occurrence (or spread).	Total number of cattle registered per dip-tank
Proximity to a game reserve (Jori and Etter, 2016; Jemberu et al., 2016; Miguel et al., 2017)	Shorter distance to a game reserve fence increases the likelihood of FMD outbreak occurrence (or spread).	Euclidian distance (Km) from each dip-tank to the nearest private or public game reserve
Human population (density) (Dion et al., 2011)	Higher human density increases the likelihood of FMD outbreak occurrence (or spread), since it is assumed that higher human density is associated with increased animal populations and their interactions.	Total number of people per Km^2
Proximity to a road network (Allepuz et al., 2015)	Closer proximity to a road network increases the likelihood of FMD outbreak occurrence (or spread).	Euclidian distance (Km) from each dip-tank to the nearest road
Proximity to rivers (van Schalkwyk et al., 2016)	Closer proximity to rivers increases the likelihood of FMD outbreak occurrence (or spread) due to direct contact with buffalo during the dry season.	Euclidian distance (Km) from each dip-tank to the nearest river
SAT1 vaccine matching	Poorer vaccine matching increases the likelihood of FMD outbreak occurrence (or spread).	SAT1 zonal statistic output for each dip-tank generated from 21 SAT1 isolates vaccine matching results
SAT2 vaccine matching	Poorer vaccine matching increases the likelihood of FMD outbreak occurrence (or spread).	SAT2 zonal statistic output for each dip-tank generated from 20 SAT2 isolates vaccine matching results
Dip-tanks weighted average for a combined SAT1 and SAT2 FMD vaccine matching	Poorer vaccine matching increases the likelihood of FMD outbreak occurrence (or spread).	((SAT1 vaccine matching for each dip-tank multiplied by (total number of SAT1 affected dip-tanks) + (SAT2 vaccine matching for each dip-tank multiplied by (total number of SAT2 affected dip-tanks)) ÷ total number of affected SAT1 & SAT2 dip-tanks))
Vaccination coverage (vaccination proportion) (Jori et al., 2009; Jori and Etter, 2016)	Lower vaccination coverage increases the likelihood of FMD outbreak occurrence (or spread).	Total number of cattle vaccinated at each dip-tank divided by the total number cattle registered per each dip-tank for every fourth months interval
Vaccination interval (Jori et al., 2009; Jori and Etter, 2016)	Longer vaccination intervals increase the likelihood of FMD outbreak occurrence (or spread).	Total average of months between each vaccination during the study period of 108 months
Cattle inspection (proportion)	Lower inspection effectiveness increases the likelihood of FMD outbreak occurrence (or spread).	Total monthly cattle inspected divided by (total weekly inspections per month multiplied by total number of cattle)
Permitted cattle movement into a village/location (Megersa et al., 2009)	Higher number of cattle movements into a village increases the likelihood of FMD outbreak occurrence "or spread" (from the receiving village to a new village)*.	Average monthly permitted movement of cattle into a village/location
Permitted cattle movement outside a village/location (Megersa et al., 2009)	Higher number of cattle movements leaving a village increases the likelihood of FMD outbreak occurrence (within the village sending the cattle out). Higher number of cattle movements leaving a village increases the likelihood of FMD outbreak spread (to a new village)*. Movement outside a village was considered important for FMD spread, if an undetected outbreak is circulating in the herd. It is therefore not a risk factor for the affected dip tank but a risk factor for expansion of an outbreak	Average monthly permitted movement of cattle outside to another village/location

The weightings for each risk factor formed a '*comparison matrix*' using single values derived from the distributions of pairwise comparisons. The resulting matrix was reciprocal, so that the pairwise-comparison for risk factor y and risk factor z was ($a_{yz} = a_{yz}^{-1}$) and all its diagonal elements were similar ($a_{yz} = 1$ *when* $y = z$). The means from the pairwise '*comparison matrix*' were calculated to assign each risk factor its relative importance ('*risk factor weight*') (Boroushaki and Malczewski, 2008; de Glanville et al., 2014).

Pairwise comparisons were conducted by five co-authors (MMS, GTF, BB, LH, and DDL) based on their own assessment of the evidence available in the literature and personal experience (de Glanville et al., 2014). A second independent panel of five FMD experts (Joseph Hyera, Frank Banda, Misheck Mulumba, Mokganedi Mokopasetso & Zacarias Elias Massicame) were recruited to also perform the pairwise weighting. The correlation between the "co-author panel" and the "independent FMD expert panel" was assessed using Pearson's correlation coefficient. The method used to interpret correlations was based on four categories where ≤ 0.35 low or weak correlation, 0.36–0.67 modest or moderate correlation, 0.68–0.89 strong correlation and ≥ 0.9 very strong correlation (Tylor, 1990). All assessors had previously authored peer-reviewed articles related to FMD epidemiology in southern Africa.

Consistency of the pairwise '*risk factor's weight*' of the expert's responses was assessed using Pearson's correlation coefficient for both the individual expert responses as well as the overall combined responses (simple average). Analyses were performed for FMD occurrence and spread independently.

2.6. *Conditional logistic regression analysis*

Ten unaffected dip-tanks those that did not experience an outbreak during each particular year were randomly selected as controls for each FMD affected dip-tank (case) using incidence density sampling matching by year to increase the statistical power over 1:1 matching. Potential risk factors were evaluated using conditional logistic regression with the matching factor being outbreak year. Potential risk factors were categorized into four groups using percentiles, dichotomized at the median, and evaluated as continuous variables when approximately linear in the log odds (assessed using results from the categorized variable). Univariate models were used to screen each potential risk factor and Spearman's rho was used to assess collinearity among predictors. Variables with a Spearman's rho > 0.7 or < -0.7 were considered collinear and only the variable with the strongest apparent association with detected FMD outbreaks was considered for multivariable modelling. All non-collinear variables with significant Wald statistics at the $P < 0.2$ level were added into a multivariable conditional logistic regression model. Variables were removed one-by-one based on the largest Wald P value in a manual stepwise process until all remaining variables were $P < 0.05$. All pairwise interaction terms between variables in the final main effects only model were introduced one-by-one and retained if $P < 0.05$. Interaction terms and removed main effects were not assessed for confounding due to the exploratory nature of the analysis. Statistical modelling was performed using commercial software (IBM SPSS Statistics Version 27, International Business Machines Corp., Armonk, NY, USA). The coefficients from the final multivariable model were used to calculate the predicted probability of a FMD outbreak for all dip tanks within the study area.

2.7. *Spatial interpolation*

Data for all risk factors were standardised (‘*standardized score*’) by subtracting the mean and dividing by the standard deviation. A similar standardisation was performed on the weights elicited from experts (‘*standardized weight*’). The ‘*standardised score*’ for each risk factor was multiplied by the ‘*risk factor’s weight*’ forming a ‘*weighted score*’. A weighted linear combination (WLC) (Eq. 2) model was built using the calculated sum of ‘*weighted score*’ for each dip-tank incorporating vaccine matching results for SAT1 and SAT2 and subsequently used to generate risk maps using empirical Bayesian kriging (EBK) (Malczewski, 2000; Krivoruchko, 2012; Samsonova et al., 2017; ESRI, 2019).

$$V(x_i) = \sum_j w_j \quad v_j(x_i) = \sum_j w_j \quad r_{ij} \tag{2}$$

w_j is a normalised weight (standardised weight) such that $\sum w_j = 1$
$v_j(x_i)$ is the value function for the j-th attribute.

$$x_i = (x_{i1}, x_{x2}, \ldots\ldots., x_{in})$$

r_{ij} is the attribute transformed into comparable scale.

An additional risk map was created using EBK and based on the final multivariable conditional logistic regression model predicted probability of a FMD outbreak for all dip tanks within the study area. Spatial clusters of FMD outbreaks in the PZV were added to the map utilising the results of a previous study (Sirdar et al., 2021).

The average number of cattle for January and December 2009 (year corresponding to the mid-point of the study period) was used to describe the spatial distribution of the cattle population. The spatial distribution of cattle population was then modeled using a point density approach, which calculates a magnitude-per-unit area from point features that fall within a neighborhood around each cell.

All maps were produced in ArcGIS software version 10.4 (ESRI, Redlands, CA, USA). Spatial risk maps were descriptively (informally) validated by projecting the locations of FMD outbreaks during the study period in relationship to the maps (Craig et al., 1999).

3. Results

3.1. *Descriptive analysis*

There were a total of 223 dip-tanks within the PZV during the study period (2007–2016). Mpumalanga Province had 168 dip-tanks and Limpopo had 55 dip-tanks. A total of 998 cattle FMD cases were reported during the study period. These cases occurred within six outbreaks and all outbreaks were due to infection with SAT serotypes (Supplemental

Table 2
Descriptive statistics for potential risk factors[a] for FMD ***occurrence*** and ***spread*** in the FMD protection zone with vaccination of South Africa (2007–2016).

Potential risk factors (FMD occurrence and spread)							
	Combined study area		**Limpopo Province**		**Mpumalanga Province**		**Mann-Whitney Between provinces**
	Mean (SD)	**Median (IQR)[b]**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**p-value**
Vaccination interval (months)[c]	9.99 (10.59)	5.46 (2.86; 16.00)	20.99 (8.51)	18.35 (15.37; 33.01)	7.39 (9.30)	3.88 (2.57; 6.90)	< 0.001
Vaccination coverage (months)[d]	0.10 (0.07)	0.10 (0.03; 0.16)	0.02 (0.03)	0.02 (0.01; 0.03)	0.13 (0.06)	0.13 (0.07; 0.18)	< 0.001
SAT1 vaccine matching[e]	0.38 (0.06)	0.35 (0.33; 0.37)	0.46 (0.05)	0.47 (0.39; 0.50)	0.36 (0.02)	0.33 (0.32; 0.35)	< 0.001
SAT2 vaccine matching	0.06 (0.03)	0.05 (0.04; 0.08)	0.09 (0.03)	0.09 (0.07; 0.11)	0.05 (0.02)	0.04 (0.03; 0.06)	< 0.001
Dip-tanks weighted average (SAT1 & SAT2 vaccine matching)	0.12 (0.04)	0.11 (0.10; 0.14)	0.17 (0.03)	0.17 (0.13; 0.19)	0.1 (0.03)	0.1 (0.09; 0.12)	< 0.001
Cattle population[f]	647 (383)	592 (366; 871)	869 (488)	939 (367; 1287)	589 (328)	590 (363; 758)	0.002
Cattle inspection (%)	0.43 (0.27)	0.45 (0.28; 0.57)	0.29 (0.48)	0.20 (0.01; 0.30)	0.47 (0.16)	0.48 (0.34; 0.58)	< 0.001
Permitted cattle movement into a village/location[g]	3.59 (8.16)	1.67 (0.83; 3.46)	4.41 (13.50)	1.54 (0.46; 3.01)	3.37 (6.10)	1.67 (0.83; 3.67)	0.222
Permitted cattle movement outside a village/location[h]	5.37 (9.59)	2.25 (0.96; 5.38)	10.56 (13.40)	7.70 (3.80; 11.80)	3.78 (7.48)	1.67 (0.79; 3.08)	0.014
Human population (density)[i]	1300 (1116)	1026 (468; 1866)	1055 (735)	1000 (389; 1506)	1371 (1196)	1033 (491; 1911)	0.275
Proximity to a game reserve (km)	8.60 (7.20)	7.08 (3.55; 11.26)	8.80 (8.90)	6.80 (3.70; 10.40)	8.53 (6.58)	7.17 (3.2; 11.83)	0.795
Proximity to a road network (km)	9.65 (10.27)	5.6 (2.25; 13.51)	14 (14.21)	6.98 (3.19; 23.58)	8.22 (8.16)	5.12 (2.03; 12.15)	0.013
Proximity to rivers (km)	16.18 (11.49)	13.88 (5.47; 26.08)	7.27 (5.76)	6.17 (2.40; 10.79)	19.1 (11.4)	20.14(8.17; 28.6)	< 0.001

[a] Mean and median values of the absolute numbers of the potential risk factors for FMD occurrence and spread
[b] IQR: Interquartile Range (25th and 75th percentile)
[c] The total length in months between two vaccinations
[d] The proportion of vaccinated animals per month for each dip-tank cattle population
[e] The r1-value
[f] Average cattle population per month for the year 2009
[g] Average human population per month for the year 2009
[h] Average cattle population per month for the year 2009
[i] Average cattle population per month for the year 2009

Table 1). In total, twenty-nine dip-tanks were affected in both provinces. Four outbreaks and almost 79% (23/29) of the affected dip-tanks were in Mpumalanga Province (Sirdar et al., 2021).

Collected data concerning risk factors varied between Limpopo and Mpumalanga Provinces ($p < 0.05$) for all factors except human population density, proximity to a game reserve fence and cattle movement into a village or dip-tank. There was a remarkable variation between the two provinces for some risk factors including vaccination practices, cattle inspection and proximity to rivers (Table 2; Supplemental Table 2). Affected dip-tanks had a similar distribution to non-affected dip-tanks (controls) for SAT1 vaccine matching, cattle inspection proportion, permitted cattle movement into and outside a village/location, human population density and proximity to rivers. The other risk factors varied ($p < 0.05$) between cases and controls (Table 3).

Table 3

Descriptive statistics for FMD risk factors for affected and non-affected dip-tanks in the FMD protection zone with vaccination of South Africa (2007–2016).

	Cases (affected dip-tanks) (*n*=*29*)		Controls (no outbreak reported) (*n* =*194*)		Mann-Whitney
	Mean (SD)	Median[a] (IQR[b])	Mean (SD)	Median (IQR)	p-value
Vaccination interval (months)[c]	6.50 (7.12)	2.94 (2.03; 6.10)	11.83 (10.71)	6.54 (3.52; 16.53)	0.002
Vaccination coverage (months)[d]	0.16 (0.07)	0.15 (0.12; 0.17)	0.08 (0.07)	0.07 (0.02; 0.14)	< 0.001
SAT1 vaccine matching[e]	0.37 (0.07)	0.35 (0.33; 0.36)	0.36 (0.06)	0.34 (0.33; 0.36)	0.746
SAT2 vaccine matching	0.07 (0.03)	0.08 (0.05; 0.10)	0.06 (0.04)	0.04 (0.03; 0.08)	0.003
Dip-tanks weighted average (SAT1 & SAT2 vaccine matching)	0.14 (0.03)	0.13 (0.11; 0.15)	0.12 (0.04)	0.10 (0.09; 0.13)	0.006
Cattle population[f]	806 (218)	851 (720; 916)	708 (402)	601 (498; 992)	0.001
Cattle inspection (%)	0.46 (0.19)	0.51 (0.29; 0.62)	0.41 (0.21)	0.47 (0.24; 0.53)	0.138
Permitted cattle movement into a village/ location[g]	3.10 (3.10)	2.17 (2.17; 3.47)	4.08 (6.17)	2.83 (1.42; 3.47)	0.284
Permitted cattle movement outside a village/ location[h]	5.97 (5.57)	3.84 (2.00; 9.36)	6.89 (8.63)	3.84 (2.92; 7.20)	0.160
Human population (density)[i]	1201 (626)	1097 (666; 1753)	1280 (707)	1300 (678; 1911)	1.000
Proximity to a game reserve (km)	4.01 (3.04)	2.88 (1.86; 5.76)	10.69 (7.97)	7.89 (5.10; 14.00)	< 0.001
Proximity to a road network (km)	14.32 (11.34)	10.54 (4.02; 24.34)	9.73 (12.55)	4.77 (1.78; 12.04)	0.012
Proximity to rivers (km)	20.53 (14.66)	21.45 (7.03; 34.48)	16.26 (11.69)	12.81 (5.32; 28.13)	0.085

[a] Mean and median values of the absolute numbers of the potential risk factors for affected and non-affected dip-tanks

[b] IQR: Interquartile Range (25th and 75th percentile)

[c] The total length in months between two vaccinations

[d] The proportion of vaccinated animals per month for each dip-tank cattle population

[e] The r1-value

[f] Average cattle population per month for the year 2009

[g] Average human population per month for the year 2009

[h] Average cattle population per month for the year 2009

[i] Average cattle population per month for the year 2009

3.2. *Expert opinion analysis*

There was a very strong and strong positive correlation between the “co-author” and “independent FMD expert” panels for FMD occurrence and FMD spread respectively (Spearman’s rho = 0.93 & 0.74) (Supplemental Figs. 1a and 1b). Inverse ‘*risk factor’s weight*’ responses within experts were strongly correlated for all participants except one confirming internal consistency of the experts’ pairwise (inverse) risk factor weighting responses for FMD occurrence and spread. Experts participating in this study, ranked proximity to game reserves followed by cattle population density as the most important risk factors for FMD occurrence, while cattle population density followed by vaccination activities (vaccine matching and vaccination coverage and interval) were on the top of the list for FMD spread. In contrast, cattle inspection proportion, movement out, proximity to rivers and road networks were ranked by expert opinion as the lowest for the risk of FMD occurrence and spread (Table 4).

The spatial distribution of the cattle population was not uniform with higher cattle numbers in the central and northern areas of Limpopo Province. On the other hand, the northern part of Mpumalanga had more cattle numbers compared to the rest of the province (Fig. 2; Supplemental Fig. 2). Almost all dip-tanks were in close proximity to game reserves and major road networks, except for an area in central Limpopo (Supplemental Fig. 3 & 4). Distance to rivers was descriptively higher in northern Mpumalanga compared to the rest of the study area (Supplemental Fig. 5). Mpumalanga had a slightly poorer SAT1 vaccine match compared to Limpopo (Supplemental Figure 6). The SAT2 vaccine match was inadequate (< 0.3) over the entire study area (Supplemental Figure 7) and a similar trend was observed for the weighted vaccine match results (Supplemental Figure 8). Limpopo Province had a lower

Table 4

Standardized “co-author” and “independent FMD expert” panels’ opinion ranking for FMD risk factors associated with occurrence and spread.

Risk factor	FMD occurrence		FMD spread	
	Co-authors panel (ranking)	Independ FMD expert panel (ranking)	Co-authors panel (ranking)	Independ FMD expert panel (ranking)
Cattle population	0.75 (2)	0.17 (5)	1.10 (1)	0.33 (6)
Proximity to a game reserve	1.21 (1)	1.24 (1)	0.28 (5)	0.53 (4)
Human population (density)	-0.51 (8)	-1.26 (10)	-0.04 (7)	-1.54 (11)
Proximity to a road network	-0.61 (10)	-0.58 (9)	-0.17 (8)	-0.74 (9)
Proximity to rivers	-0.60 (9)	-0.14 (7)	-0.55 (9)	-0.38 (7)
Vaccine matching	0.74 (3)	1.17 (2)	0.63 (4)	1.46 (1)
Vaccination coverage (vaccination proportion)	0.70 (5)	0.88 (3)	0.70 (3)	1.09 (2)
Vaccination interval	0.73 (4)	0.72 (4)	0.99 (2)	0.88 (3)
Cattle inspection (proportion)	-0.28 (7)	-0.33 (8)	-0.72 (10)	-0.63 (8)
Permitted cattle movement into a village/ location	0.16 (6)	0.06 (6)	0.21 (6)	0.38 (5)
Permitted cattle movement outside a village/location	-2.30 (11)	-1.93 (11)	-2.44 (11)	-1.38 (10)

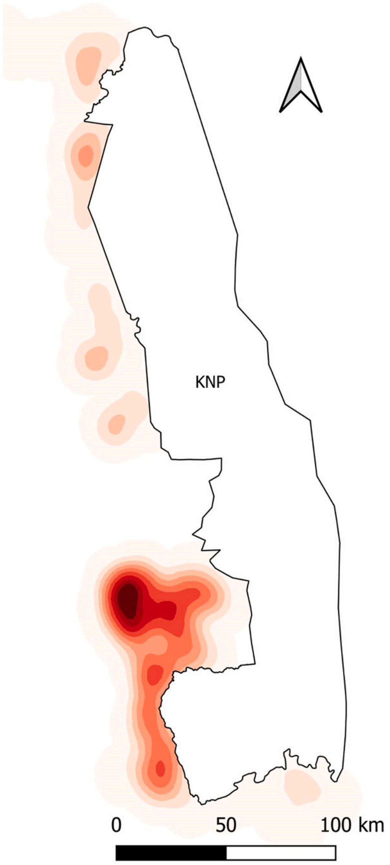

Fig. 2. Point density estimation of 2009 cattle population in the protection zone with vaccination of South Africa.

FMD vaccination proportion with longer vaccination intervals compared to Mpumalanga Province (Supplemental Figure 9 & 10). Fewer cattle inspections were performed in the northern areas of Limpopo Province and scattered areas of Mpumalanga (Supplemental Figure 11). Permitted cattle movement into villages appeared uniformly distributed across the study area with an exception of central Mpumalanga that had higher *in* movements (Supplemental Figure 12). There was also a high number of *out* movements in an area of southern Mpumalanga (Supplemental Figure 13). Human density was high in the south western areas of Mpumalanga (Supplemental Figure 14).

The majority of reported outbreaks occurred in areas with relatively low predicted risk for FMD occurrence and spread (Figs. 3 and 4). The far north of Limpopo Province and the central areas of Mpumalanga were at higher predicted risk of SAT1 and SAT2 FMD outbreak occurrence (Fig. 3). In contrast, the central areas of Limpopo and the southern parts of Mpumalanga were at higher predicted risk for FMDV spread (Fig. 4).

3.3. Conditional logistic regression analysis

Risk factors associated with FMD occurrence and spread were initially assessed using univariate conditional logistic regression analyses (Supplemental Table 3). Eight of these risk factors were selected for multivariable analysis including FMD vaccine match, cattle population, monthly cattle inspections, *in* movement, *out* movement, human population density, distance to game reserve fences, distance to roads and distance to rivers. The final multivariable model identified three risk factors significantly associated with FMD detection (Table 5). These factors included cattle population (OR=3.87; 95% confidence interval (CI)=1.47–10.21), distance to game reserve fences (OR=0.82; 95% CI=0.73–0.92) and distance to rivers (OR=1.04; 95% CI=1.01–1.07). No pairwise interaction terms significantly improved the fit of the final model.

The north central areas of Limpopo and northern Mpumalanga had the highest probability of FMD outbreaks that increased when in close

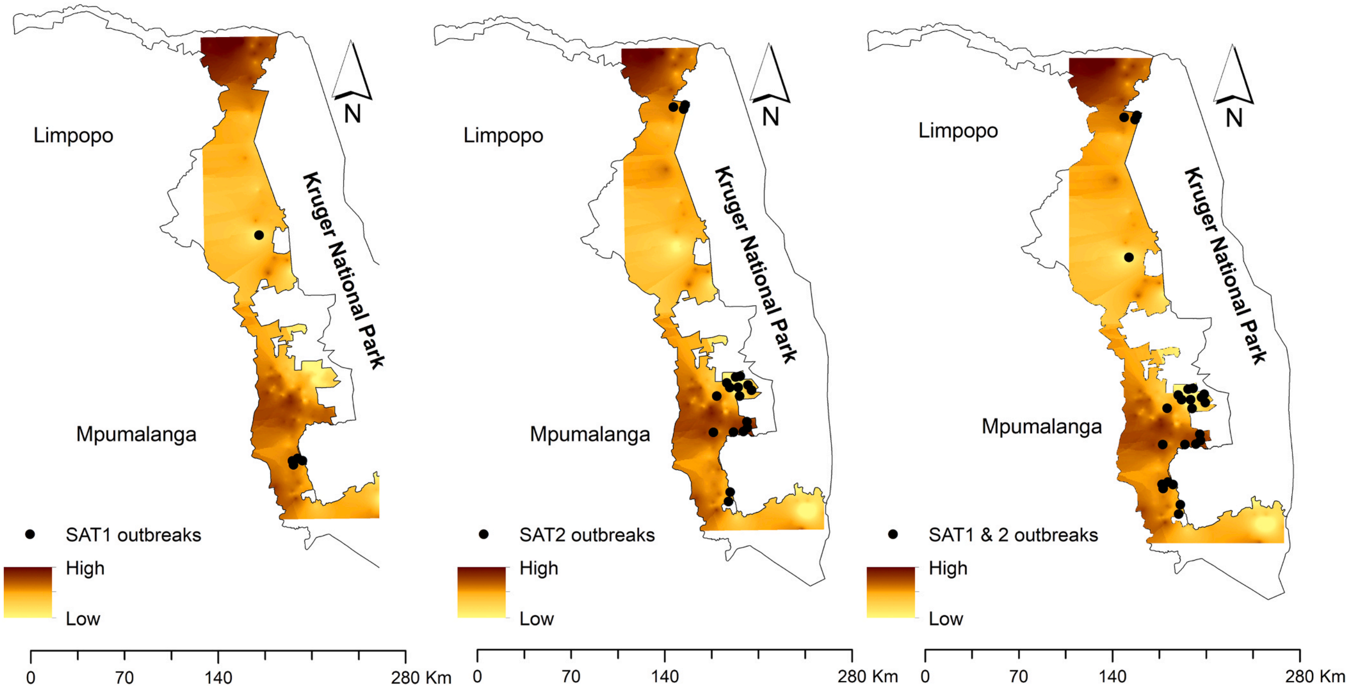

Fig. 3. Expert opinion elicitation (*left*) Southern African Territories (SAT)1 risk map for FMD ***occurrence*** in the protection zone with vaccination (PZV) of South Africa; (*middle*) SAT2 risk map for FMD occurrence in the PZV of South Africa; (*right*) combined SAT1 and SAT2 risk map for FMD occurrence in the PZV of South Africa.

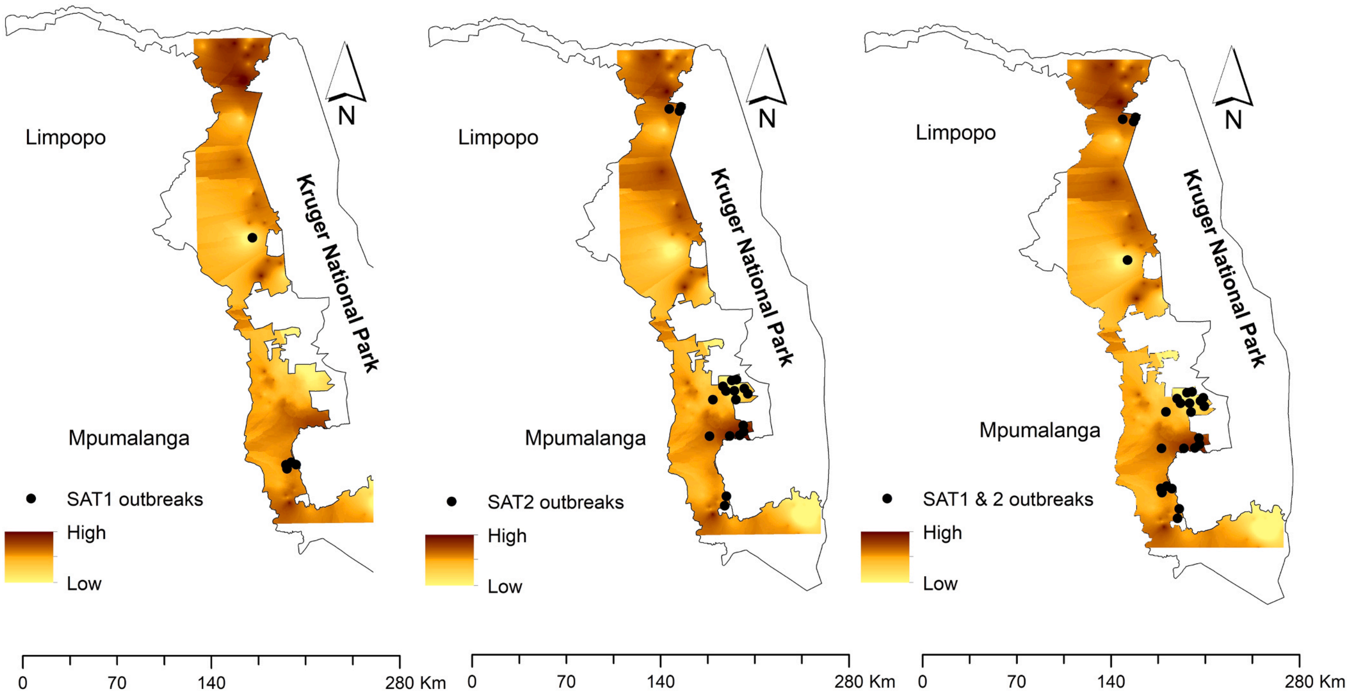

Fig. 4. Expert opinion elicitation (*left*) Southern African Territories (SAT)1 risk map for FMD ***spread*** in the protection zone with vaccination (PZV) of South Africa; (*middle*) SAT2 risk map for FMD spread in the PZV of South Africa; (*right*) combined SAT1 and SAT2 risk map for FMD spread in the PZV of South Africa.

Table 5

Multivariable associations for potential risk factors for FMD outbreak reporting in the FMD protection zone with vaccination of South Africa (2007–2016).

Variable	Level	Parameter estimate ($\widehat{\beta}$)	Odds ratio (95% CI)	P value
Cattle population	≤ 595 head	Referent		
	≥ 596 head	1.354	3.87 (1.47, 10.21)	0.006
Distance to game reserve				
	Continuous (km)	-0.201	0.82 (0.73, 0.92)	<0.001
Distance to rivers				
	Continuous (km)	0.038	1.04 (1.01, 1.07)	0.010

CI = confidence interval.’

proximity to the KNP fence across the whole study area (Fig. 5). Areas with high probability of a FMD outbreak were also adjacent to the previously identified FMD high-risk clusters (Sirdar et al., 2021).

4. Discussion

This study incorporated risk factor information for FMD occurrence and spread in the protection zone with vaccination (PZV) of South Africa to determine areas where FMD is more likely to occur and subsequently spread to other locations. The study generated smoothed risk maps with the aim of identifying high-risk areas for applying improved control measures.

Data for included risk factors often differed significantly between the two study provinces (Table 2). However, proximity of dip-tanks to game reserves was not different (Limpopo $M = 8.80$; $SD = 8.90$; Mpumalanga $M = 8.53$, $SD = 6.58$; $p = 0.795$). This was expected as the PZV was formed as a first line buffer to protect the rest of the country from FMD outbreaks introduced by contact between wildlife and livestock. There was also no difference between the two provinces regarding cattle movement *into* a village suggesting similar human activities and demand for consumption (Limpopo $M = 4.41$; $SD = 13.5$; Mpumalanga $M = 3.37$, $SD = 6.10$; $p = 0.222$). The significant differences between the provinces suggests that different approaches and implementation of FMD control is conducted in each province. FMD risk factors differed significantly between affected and non-affected dip-tanks (Table 3). However, SAT1 vaccine matching was not different between the two groups. Few SAT1 compared to SAT2 outbreaks were reported during the study period, which might explain the similarity between affected and non-affected groups.

Risk factor standardized weightings by participating FMD experts, ranked proximity to game reserves as the most important factor for FMD *occurrence* followed by the total cattle population. Results from the conditional logistic regression analysis were also in agreement with participating FMD experts’ opinion. The southern Africa literature supports this opinion as well, where reported buffalo sighting and by virtue proximity to national parks or wildlife reserves has been reported to be significantly associated with the risk of FMD outbreaks (Guerrini et al., 2019). However, in other parts of Africa the epidemiology of the disease is different, and wildlife often plays a minimal role in the risk of FMD outbreaks including distance to protected areas and sighting of susceptible wildlife species (Bronsvoort et al., 2004; Allepuz et al., 2015; Jemberu et al., 2016; Casey-Bryars et al., 2018). Cattle-African buffalo contact is a well-established cause of FMD occurrence in southern Africa (Vosloo et al., 2002; Thomson et al., 2003; Thomson, 2008; Jori and Etter, 2016). However, a recent manuscript from Malawi (Chimera et al., 2022), reported an opposite association, so this effect might differ depending upon the predominant serotypes in the country. These findings from Malawi are consistent with studies conducted in eastern Africa, where wildlife do not play a significant role in the epidemiology of the disease within susceptible domestic animals. This was attributed to the significant difference in circulating serotypes in African buffalos and cattle populations, in addition to the dominance of serotypes O and A in livestock compared to southern Africa (Casey-Bryars et al., 2018; Duchatel et al., 2019).

Physical separation of wildlife and livestock is one of the most

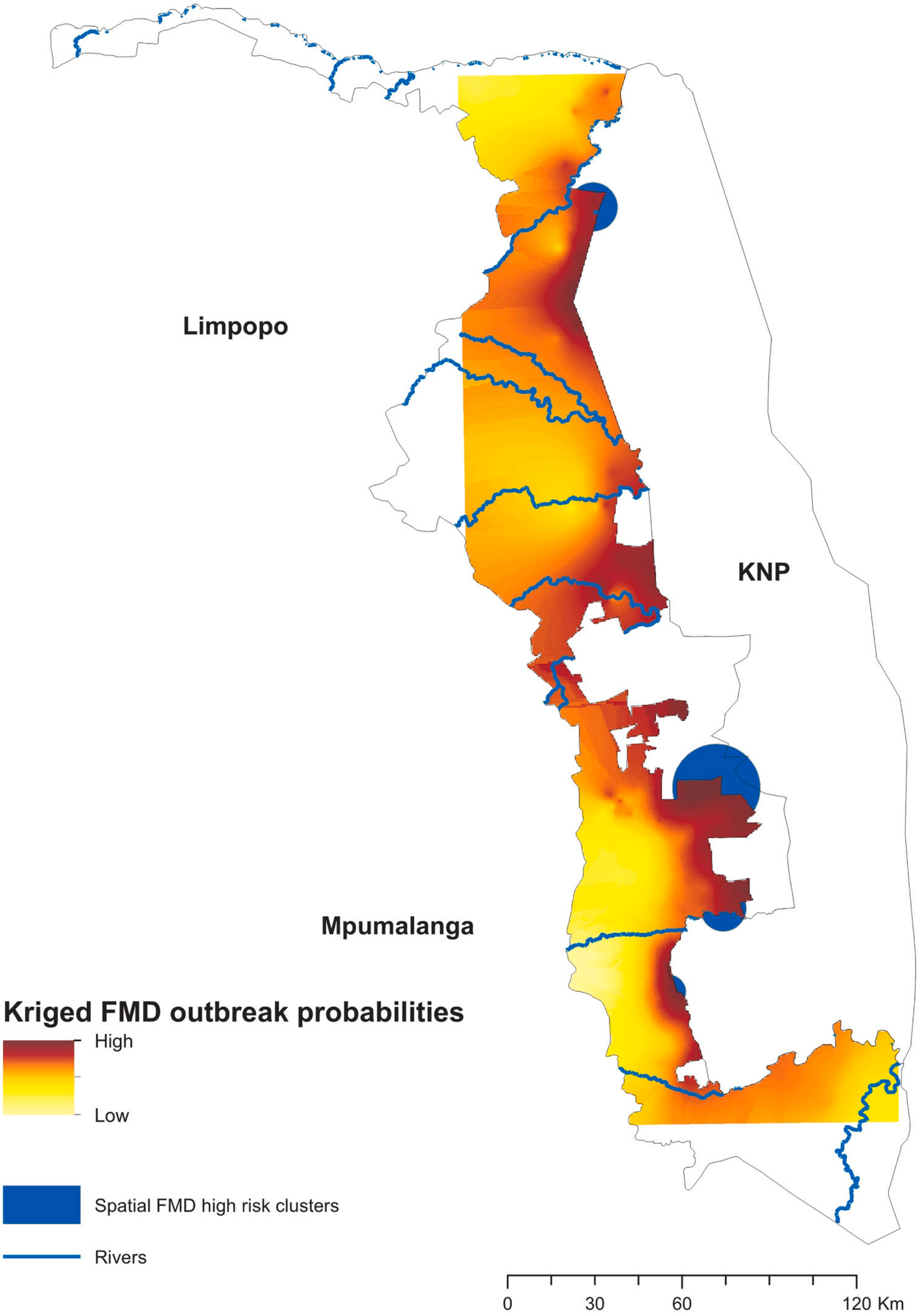

Fig. 5. FMD outbreak probabilities in relation to spatio-temporal high-risk areas of the protection zone with vaccination of South Africa (Conditional Logistic Regression model).

important factors of FMD control in southern Africa (Dion and Lambin, 2012). Although fences were erected to mitigate the contact risk, the efficiency of disease control fencing in the protection zone of South Africa is questionable due to several factors including increased elephant populations, increased human settlements near the fence and major flooding events (Jori et al., 2009; Scoones et al., 2010). Fences are difficult to maintain and are frequently damaged by animals, humans and floods allowing cattle-African buffalo contact (Kaszta et al., 2018), which is estimated at 30–120 contacts occurring annually and about 650 African buffaloes escaping KNP a year (Jori et al., 2009; van Schalkwyk et al., 2016). Dip-tanks that experienced FMD outbreaks were closer to KNP or private game reserve fences. Therefore, a cause of outbreaks was likely wildlife/cattle contacts due to fence permeability increasing the risk of FMD occurrence (Sirdar et al., 2021). However, cattle-to-cattle transmission is highly probable in the study area. In all the outbreaks that were recorded in this study, the first dip-tank to be infected was the closest dip-tank to the disease control fence; however, subsequently affected dip-tanks were always further away. This finding implies that subsequently infected dip-tanks were caused by cattle-to-cattle transmission. The fact that the majority of reported outbreaks occurred in areas with relatively low predicted risk for FMD occurrence (areas with relatively high inspection practices and vaccination) other areas might have undetected outbreaks. In the event of an outbreak, movement control is placed on all cloven-hooved animals and their products.

Surveillance is conducted using clinical inspection and serological sampling that is repeated according to WOAH standards. In communal areas, emergency vaccination is typically practiced but not stamping-out.

Based on the expert opinion in this study, cattle population density was the most important risk factor for FMD *spread* followed by vaccination activities (vaccine matching and vaccination coverage and interval). This was consistent with the conditional logistic regression results in which areas with higher cattle numbers had a higher risk of a FMD outbreak compared to areas with lower numbers (OR=3.93; 95% CI=1.49–10.34). Cattle density has been previously reported to be associated with the FMD dissemination pathway (Santos et al., 2017). Other studies also reported the positive association between cattle densities and high likelihood of FMD spread (Bessell et al., 2010b; Dukpa et al., 2011). This might be attributed to the high number of susceptible animals for disease spread following FMD introduction. However, a study conducted in Tanzania reported that cattle density had a lower effect on FMD transmission than expected possibly due to the confounding effect of animal movements (Allepuz et al., 2015). The contribution of cattle population to FMD occurrence might also be linked to cattle incursions into KNP or wildlife leaving the reserves and interacting with cattle (Jori et al., 2011; Brahmbhatt et al., 2012).

Availability of roads could contribute to legal and illegal movements of animals, increased likelihood of FMD detection and access to human activities such as markets. Cattle inspection proportion, movement *out*, proximity to rivers and road networks were ranked by expert opinion as the lowest for the risk of FMD occurrence and spread. This finding contradicts results from Tanzania where road network and proximity to international boarders were associated with FMD spread (Picado et al., 2011). It is expected that if susceptible animals are in close proximity to infrastructure like roads and railways, they might be subjected to intensive surveillance for FMD and hence increase FMD outbreak detections. In Ethiopia, it was reported that major livestock markets/-routes were associated with animal trade movements and were significant risk factors for FMD spread. (Jemberu et al., 2016). In Tanzania, proximity to road networks was identified as a risk factor and considered the main driver of FMD transmission compared to other factors studied in the country. For instance, increased distance to wildlife game reserves decreased the likelihood of FMD outbreaks in 2001, but this result was not the case in the following endemic years. These findings emphasize that the epidemiology of FMD differs among African regions due to the different circulating viruses and the minimal role of wildlife in the epidemiology of the disease in eastern Africa. Additionally, this might be attributed to selection bias since the reported study was based on passive surveillance and convenience sampling (Allepuz et al., 2015), in contrast to our study that analyzed active surveillance data within weekly inspection intervals.

Rivers and water points crossing the KNP fence might play a role in FMD occurrence and spread through cattle-African buffalo contacts. Cattle and buffalo move and aggregate around rivers during the dry season in search for water. It is assumed that direct contact between buffalo and cattle at river points increase the likelihood of FMD occurrence and spread. Contacts between cattle and African buffalo are 1.25 times more likely to occur inside the KNP around rivers and water sources compared to locations without water (Jori and Etter, 2016). However, our conditional logistic regression results suggested an opposite effect to the hypothesis that closer proximity to rivers increases the likelihood of FMD outbreak occurrence and spread. While this could be a modelling artefact, multicollinearity diagnosis for the two factors revealed non-collinearity (Spearman rho 0.21; CI 0.097 – 0.313; p <0.001). The tolerance and variance inflation factor were 0.96 and 1.036 respectively. This might be due to the modeling of the distance as a continuous variable and the relatively long distance between dip-tanks and the nearest river especially in Mpumalanga Province (Mean=19.1 Km; Median=20.14, IQR (8.17–28.6)). This effect could also be a proxy for other variables not investigated within the current study and requires further investigation. The inclusion of fence permeability and the number of buffalo escaping from the KNP as risk factors (not available in provincial veterinary records), might have influenced the results of the study regarding the occurrence of FMD outbreaks. In a previous study, it was reported that the predicted African buffalo distribution in KNP suggested moderately higher numbers of African buffalo in the southern part of KNP close to two high-rate spatiotemporal FMD clusters (Sirdar et al., 2021). These and other potential risk factors not included in the current study require further investigation.

The effectiveness of vaccination depends on the match of the vaccine strain to the circulating viruses (Robinson et al., 2016; Sirdar et al., 2019). Therefore, vaccine matching is an essential step to monitor the effectiveness of FMD vaccination as a control measure. The vaccine currently used in the PZV is not a good match for circulating strains in South Africa and this reduces the effectiveness of prophylactic vaccinations (Thomson et al., 2013; Sirdar et al., 2019). The SAT1 vaccine match was descriptively better than SAT2. However, the inadequate SAT2 vaccine match was even worse in Mpumalanga compared to Limpopo Province. A recent study conducted in Mpumalanga reported that SAT2 antibody responses were better than SAT1 (Lazarus et al., 2018) and a stronger response might be able to overcome some deficiencies in vaccine matching.

Vaccination coverage varied between the two study provinces with the FMD vaccination proportion being very poor in Limpopo Province (Median (IQR): 0.02 (0.01; 0.03)) relative to Mpumalanga (Median (IQR): 0.13 (0.07; 0.18)). The latter is known for excellent dipping attendance and facilities (Lazarus et al., 2017). Human and operational resources in addition to infrastructure deficiencies might have affected the vaccination practices in Limpopo Provinces. Mpumalanga had more dip-tanks compared to Limpopo and the dip-tanks were close to each other, whereas in Limpopo, the dip-tanks were distributed over a larger area. This might also contribute to the observed poorer vaccination practices due to increased travel costs. In Mpumalanga, the overall seropositivity was previously reported to be less than the recommended 75%, thus potentially increasing the risk of FMD outbreaks (Lazarus et al., 2017).

Cattle in the PZV are supposed to be vaccinated every four months (DAFF, 2014). Vaccination intervals in Limpopo Province were quite large (Median (IQR): 18.35 (15.37; 33.01)) in relation to the recommendations of the veterinary authorities and vaccine manufacturer while Mpumalanga Province had shorter intervals (Median (IQR): 3.88 (2.57; 6.90)). Isolated areas in northern Mpumalanga and far south also had relatively longer intervals. The latter is consistent with a reported prolonged vaccination interval in one area of Mpumalanga (Lazarus et al., 2017, 2018). Longer intervals and low percentage of vaccinated cattle has also been reported in Zimbabwe, where it had a negative effect on controlling the FMDV transmission cycle (Miguel et al., 2017).

Inspection was descriptively good in Mpumalanga Province and moderate in the southern areas of Limpopo. However, the northern part of Limpopo had poor inspection proportions. The areas with the highest inspection proportion in Mpumalanga coincided with the areas that reported previous FMD outbreaks. This finding might indicate that surveillance is more likely linked to FMD detection rather than occurrence *per se*. This finding supports the objectives of the South African FMD Veterinary Procedural Notice (VPN). The VPN states that to prevent FMD occurrence and spread, clinical surveillance must be performed in the PZV by inspecting cattle every seven days and routinely mouthing at least 10 cattle randomly selected from the presented cattle on each inspection day (DAFF, 2014). However, clinical surveillance alone might not be sufficient and should be supported by a routine (not an ad-hoc) laboratory-based surveillance to account for undetected cases (Teifke et al., 2012). This is important because FMD SAT outbreaks might be underdiagnosed in the field due to frequently mild or subclinical infections. This has been previously documented in a study where no clinical signs were reported in the wildlife/livestock interface of the Great Limpopo Transfrontier Conservation Area during a one-year study, suggesting that clinical expression of SAT serotypes circulating in cattle was mild while the disease remained undetected (Jori et al., 2009, 2016). To our knowledge, no previous reports have analysed cattle inspection practices and their role in FMD outbreaks and spread. However, it is assumed that lower inspection effectiveness increases the likelihood of FMD spread due to FMDV infected animals going undetected. The cases reported during the study period therefore might not be an accurate reflection of the actual number of outbreaks that had occurred in the field due to inadequacies in surveillance efforts.

Expert opinions ranked "*movement into*" a village(s) as a moderate risk factor for FMD occurrence and spread, while "*movement out*" the lowest risk factor for both investigated outcomes. FMD outbreaks were not descriptively different between areas with high "*movement out*" and "*movement in*" to village(s). High animal "*movement into*" a village(s) was observed in some low-risk areas for FMD occurrence and spread that actually reported outbreaks during the study period. This finding suggests the possibility that animals are moved to these areas from locations with ineffective surveillance thus increasing the risk of outbreaks. Many communal farmers within the study area depend solely on livestock for their livelihood. Our results suggest that there are more permitted movements of cattle to other locations than cattle being introduced to dip-tanks within the PZV. This might represent the selling of cattle for income generation. The higher animal movement *outside* to other villages in the central and northern areas of Limpopo Province could be due to a relatively large cattle population in these areas. The higher movement (*into villages*) in the southern parts of Mpumalanga Province could be associated with higher human population densities and greater demands for consumption.

The expert opinion modelled predicted risk of FMD occurrence did not differ considerably from spread. This finding is influenced by the ranking of risk factors for occurrence and spread by co-author and independent experts in combination with available data. Despite the strong correlation between co-authors and independent FMD experts, formally analyzing results from the outside experts might have produced different maps for introduction and spread. The high-risk area for FMD occurrence in the far north is clearly influenced by the low vaccination proportion, longer intervals between vaccinations and poor inspection efficiency. In contrast, the northern part of Mpumalanga Province, despite being well inspected and with good vaccination coverage/interval, was also identified as a predicted high-risk area for FMD occurrence. A possible reason for this finding is the inadequate vaccine match for SAT2 and SAT1 isolates.

The overall expert opinion predicted risk for FMD spread identified the far north and central areas of Limpopo Province as being at relatively higher risk for FMD spread. This could be due to higher cattle densities, dip-tanks in close proximity to rivers and considerable movement of animals (*outside* to other locations). Similarly, the southern parts of Mpumalanga are at higher risk of FMD spread where there were larger human populations.

Comparing the overall expert opinion derived predicted risk model for FMD occurrence and spread (Fig. 3 & 4) to the model depicting the conditional logistic regression predicted probabilities of FMD outbreaks (Fig. 5), the latter mirrors similar trends to the risk map for FMD occurrence. This similarity is likely due to the agreement of FMD experts ranking proximity to game reserve fences as the most important risk factor for FMD occurrence and the calculated probability of a FMD outbreak being higher when moving closer to a game reserve. Furthermore, areas identified in both models as high-risk areas for FMD occurrence had reported previous FMD outbreaks during the study period. This finding is in agreement with a previous study where for all FMD outbreaks that were recorded, the first dip-tank to be infected was the closest dip-tank to the disease control fence; subsequently affected dip-tanks were always further away (Sirdar et al., 2021).

The majority of reported outbreaks occurred in areas with relatively low predicted risk for FMD occurrence and spread. This suggests possible bias in the study methods because these areas are characterized by efficient cattle inspection and vaccination practices. A possible explanation is that vaccination is preferentially applied in high-risk areas and that efficient cattle inspection is a major determinant whether or not an outbreak is detected and subsequently reported. Also, within these high-risk areas mostly SAT2 outbreaks were reported, which had low vaccine matching results. FMD outbreaks in other locations might have been missed because of inefficient cattle inspection. Although inspection was not significantly different between affected and non-affected dip-tanks (Table 3), this finding might be masked by other factors including the relatively small sample size and the variation of inspection practices between provinces. Previous studies at the KNP interface suggested the possibility of undetected FMD transmission in cattle after the initial wildlife introduction (van Schalkwyk et al., 2011). Also, the total number of reported outbreaks has increased 7-fold during the three years following the study period (2017–2019) and totaling 42 outbreaks (WOAH, 2020).

There was a large difference in data availability between the two provinces and this might have affected the calculated risk scores and the comparison between provinces. Availability of data, especially in Limpopo Province, was one of the challenges of the study. Informative risk assessment requires credible and complete data to provide an informed outcome (Wieland et al., 2015). Despite the differences between provinces, "province" was not evaluated as a potential risk factor in the conditional logistic regression model. It is likely that the effect of province is through the evaluated (and potentially unevaluated) risk factors and thus including it in the statistical modelling might have introduced confounding due to being on the causal pathway. The influence of province as an independent risk factor therefore requires further investigation and it is recommended that data storage and management are improved in the study area to improve data quality.

Although results from the expert opinion model were consistent with the conditional logistic regression results, the relatively small number of experts that participated in the study suggests that it might be beneficial to repeat the modeling with more quantitative data and a larger number of experts. This limitation could have been addressed by employing a more formal expert opinion elicitation such as the Delphi method where the group decision mechanism could have been based on consensus rather than an averaging approach. A complete dataset for the entire study period was obtained for vaccination coverage, vaccination interval, vaccine matching and time-invariant distance data. However, the other risk factors were based on 2009-year data (middle-point) that was selected due to the availability of a more complete dataset to limit the need to interpolate missing data. This approach might have biased model results, for instance human population demographics might have changed substantially between the beginning and the end of the study period and subsequently causing changes in the cattle population and related farming activities. Moreover, movement data only included permitted (legal) movement, which might have affected results as illegal movements are expected to be associated with higher FMDV transmission risks. FMD susceptible livestock have been reported to be moved within the study area without obtaining official permits (Lazarus et al., 2021). Another limitation was that data concerning proximity to rivers was generated by calculating the nearest river point to a dip-tank without considering an intersection between a river and game reserve fence.

The initial selection of risk factors was based on literature review, expertise of co-authors and availability of data. Formal elicitation of opinions from an independent panel of experts might have provided ideas of other risk factors that could have been investigated. Another limitation is the exclusion of certain risk factors due to the unavailability of data. Some of these factors include elephant population size due to their effect on fence permeability events (Jori and Etter, 2016) in addition to buffalo population size and the number of buffalo escaping from KNP (van Schalkwyk et al., 2016). Further work overcoming these limitations to compare and validate the findings of this study would be valuable for accurately quantifying the risk of FMD occurrence and spread in communal settings.

5. Conclusion

In communal farming areas there is the necessity to maintain efficient separation between wildlife and cattle, evaluate vaccination programmes (post-vaccination monitoring) and enhance animal health surveillance at areas identified as high risk for FMD outbreak occurrence and spread. Detecting actual FMD outbreaks and studying the disease trends will assist in designing effective control measures in endemic areas. Furthermore, it is imperative to introduce risk-based surveillance to investigate possible undetected outbreaks and perform periodic FMD risk assessments that account for the environmental, cultural and epidemiological dynamics of the disease. While this study was a retrospective semi-quantitative study, we propose developing a quantitative predictive model incorporating other risk factors to allow better insight into FMD risk factors associated with FMD occurrence and spread in communal farming areas that are complemented with risk mitigation, management and communication.

CRediT authorship contribution statement

Mohamed Mahmoud Sirdar: Conceptualization, Data curation, Formal analysis, Writing – original draft. **Geoffrey Theodore Fosgate:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Conceptualization. **Belinda Blignaut:** Validation, Supervision, Methodology. **Livio Heath:** Supervision. **David Dazhia Lazarus:** Data curation, Writing – review & editing. **Lucas R Mampane:** Conceptualization, Data curation, Investigation. **Oupa Boetie Rikhotso:** Data curation, Investigation. **Ben Du Plessis:** Investigation, Data curation. **Bruce Gummow:** Writing – review & editing, Supervision.

Declaration of Competing Interest

None of the authors has any financial or personal relationship that could inappropriately influence or bias the content of this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.prevetmed.2024.106192.

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