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ORIGINAL RESEARCH

Spatiotemporal analysis of African swine fever outbreaks on South African smallholder farms, 1993–2018

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African swine fever (ASF) is a contagious viral disease of swine worldwide. ASF in South Africa has for many years been confined to a controlled area in the northeast of the country that was proclaimed in 1935. Since 2012, outbreaks are more likely to occur in the historically ASF-free area. This study aimed to analyse the spatial and spatiotemporal structure of ASF outbreaks in South Africa between 1993 and 2018. Global space-time clustering of ASF outbreaks was investigated by the Diggle space-time K-function while Kulldorff's spatial scan statistic was applied to detect local cluster of ASF outbreaks. Globally, ASF outbreaks exhibit statistically significant spatial clustering. They have shown a significant negative space-time interaction at month scale (p = 0.003) but no significant space-time interaction at year scale (p = 0.577), revealing strong evidence that ASF cases that are close in space occur in months which are close and vice versa. In studying local area space-time clustering at both month and year scale, three significant local clusters associated with high-rate were detected. These clusters are localised in both the ASF-controlled area and outside the controlled area with radius varying from 60.84 km up to 271.43 km and risk ratio varying from 6.61 up to 17.70. At month scale, clusters with more outbreaks were observed between June 2017 and August 2017 and involved 22 outbreaks followed by the cluster that involved 13 outbreaks in January 2012. These results show the need to maintain high biosecurity standards on pig farms in both inside and outside the ASF-controlled areas.

Keywords: space-time, distribution, ASF, space-time K function, Kulldorff's spatial scan statistic, South Africa

Introduction

African swine fever (ASF) is a contagious disease of pigs caused by the African swine fever virus (ASFV), a large double-stranded DNA arbovirus that replicates predominantly in the cytoplasm. Its mortality rates can be up to 100% in affected herds (Hess 1971; Penrith et al. 2004). ASFV belongs to the genus *Asfivirus*, family *Asfarviridae*, only affecting members of the family Suidae (Alonso et al. 2018). Due to the economic impact in affected countries, ASF is one of the main threats to the development of pork production in Africa (Penrith et al. 2013). In addition, the lack of vaccine aggravates its impact (Chang et al. 2006).

In Africa, South Africa has one of the three largest pig populations, following Nigeria and Uganda. In May 2017, statistics indicated 1.49 million pigs in South Africa. Most of the pig population is in Limpopo, North West and the Western Cape Province with 359 138, 315 566 and 162 859 pigs, respectively (Department of Agriculture, Forestry and Fisheries 2017). However, most of households farming pigs (91.3%) have fewer than 10 pigs (Statistics South Africa 2016), often kept under conditions of poor management (free-range system) and low biosecurity (Mokoele et al. 2014). In 2011, there were approximately 400 commercial producers and 19 stud breeders in South Africa (Department of Agriculture, Forestry and Fisheries 2012).

In South Africa, ASF has for many years been confined to a controlled area in the northeast of the country that was determined and proclaimed in 1935, based on the assumed distribution of infected warthogs. Subsequently, this area was confirmed by the presence of both infected warthogs and ticks (Magadla et al. 2016; Thomson 1985). However, since 2012 more outbreaks have been reported outside the controlled area. Considering its demonstrated ability to spread over distances (Beltrán-Alcrudo et al. 2017; Sánchez-Cordón et al. 2018), there is an urgent need for an effective approach to prevent and control ASF in the absence of preventive and curative treatment. ASF outbreaks occurred sporadically in the historically ASF-free areas of South Africa since 2012 and clustered in the controlled area, but there are no previous quantitative studies on space-time patterns of this disease in South Africa to confirm this qualitative statement. Thus, new clustering of significant areas indicating high risk should be estimated for better management of the disease and the pork production sector.

To achieve identification of patterns of ASF outbreaks, and devise more robust prevention and control programmes, knowledge of history, epidemiology and the identification of risk factors for disease occurrence is essential (Mott et al. 1995; Vergne et al. 2016). Once the disease is present in a region, control measures must be focused on early detection associated with rapid laboratory diagnosis reducing the potential transmission of the virus to uninfected herds, strict movement control of pork and associated products and strict enforcement of sanitary measures (Aguero et al. 2003; Sanchez-Vizcaino 2006).

Thus, reviewing of ASF outbreak history and evaluating the distribution of space-time clustering are urgent priorities, because the effectiveness of prevention programmes varies over time and space (Ayebazibwe et al. 2010; Dukpa et al. 2011; Ochwo et al. 2018). To our knowledge, no study has been conducted in South Africa in order to assess statistically and quantitatively, the clustering of ASF outbreaks over space and time. This study aimed to examine the spatiotemporal structure of ASF in South African domestic pigs using historic data in order to support the development of an accurate control strategy.

Methodology

Study area

South Africa is located at the southern tip of the African continent, occupying around 1 219 090 km^2, with 3 100 km length of coastline. Due to the oceanic effect and topographic variations, the climate varies from one region to another; it is mostly semiarid, but is subtropical along the East coast, where nights are cool and days are sunny. Observed high temperatures in some areas favour the development and maintenance of vectors and water-borne diseases (Wepener & Degger 2019).

Data collection

Retrospective data on ASF outbreaks were obtained from the OIE disease database, veterinary services annual reports available on the South African Department of Agriculture, Land Reform and Rural Development (DALRRD) website, formerly Department of Agriculture, Forestry and Fisheries (DAFF), published articles (Web of Science, PubMed, Scopus and Google Scholar). The OIE diseases database comprised the year and month of outbreaks, the province, the state veterinary area, the district, the species, and the number of outbreaks, cases, dead and killed animals. For each outbreak, an individual manual correction was applied to control for possible double or multiple entries of the same information from multiple sources.

Data analysis

Descriptive analysis was performed on ASF outbreaks in order to describe their spatial and temporal (annual and monthly) distribution. At the month and year levels, temporal aggregation was performed. The month is the precision utilised by the source that is the least precise. Because certain epidemics can last for several months, the year level was taken into account. This distinction allowed also to distinguish between seasonal patterns, available with the monthly aggregation, versus annual patterns, available at annual aggregation. The chi-square goodness-of-fit test for one sample known as the chi-squared test for given probabilities was used to compare proportions of outbreaks in the different months. Fisher's exact test was used to test the relationship between months and areas of occurrence (controlled or outside controlled areas). In addition, pairwise comparisons using exact binomial tests considering the *p*-value correction (Benjamin & Hochberg 1995) was used to identify months with more outbreaks.

To assess the spatial distribution of reported outbreaks, a spatial K-function of Ripley was calculated (Basáñez et al. 2009; Ripley 1976; Ripley 1977). $D_0(s,t)$ function (space-time K-function) was used to investigate global space-time interactions of ASF outbreaks in South Africa (Diggle et al. 1995). The $D_0(s,t)$ function analyses possible dependence between the spatial and temporal components of ASF outbreaks. This function detects if observed density of outbreaks in a region at a given time and scale is above or below the expected number; giving information on the scale and nature of the dependence between the spatial and temporal components (Ceyhan et al. 2013; Ruiz-Moreno et al. 2010; Wang et al. 2020). For a given distance and time separations, $D_0(s,t)$ given the proportional increase in cases attributable to the interaction space-time (Basáñez et al. 2009; Diggle et al. 1995). $D_0(s,t)$ is:

$$D_0(s,t) = \frac{D(s,t)}{K_S(s)K_t(t)}$$

Where: - $K_S(s)$ defines the K-function in space

- $K_t(t)$ defines the K-function in time and

- $D(s,t)$ is the K-function difference defined as: $D(s,t)=K(s,t)-K_S(s)K_t(t)$

The splancs package (Rowlingson & Diggle 1993) adapted for use in R software was used to estimate the global space-time interaction. The confidence envelope was obtained through Monte Carlo simulation (number of simulations = 999) to perform hypothesis testing. The outbreak that occurred in Modimolle in October 1993 was the landmark for the spatial distribution. It is the local municipality where the first outbreak recorded in the OIE database occurred.

The retrospective space-time analysis scanning for clusters with high rates using the discrete Poisson model in SaTScan 9.4.6 was used to detect local clusters. The detection of high rates clusters of ASF consist of comparing cases from previous space-time window with a user-defined baseline. The temporal window is limited to one month and one year selected based on the size and length of outbreaks. The spatial window was based on default input parameters. The statistical significance of clusters was determined using Monte Carlo testing set at 999 replications (Kulldorff et al. 2005; Mathes et al. 2017).

Results

Analysis of temporal distribution of ASF outbreaks in South Africa

The maximum number of outbreaks for a single year was observed in 2012 outside the controlled area, when 15 outbreaks were reported: nine in Mpumalanga and six in Gauteng (Figure 1).

Chi-squared test for given probabilities has shown that outbreaks are significantly not homogeneously distributed within months in South Africa ($p < 0.001$). January was the month that has reported significantly ($p < 0.05$) more outbreaks than any other month, followed by June, July, February, August and May. There was a significant relationship between month and occurrence area ($p < 0.05$). In the ASF-controlled area, outbreaks have been

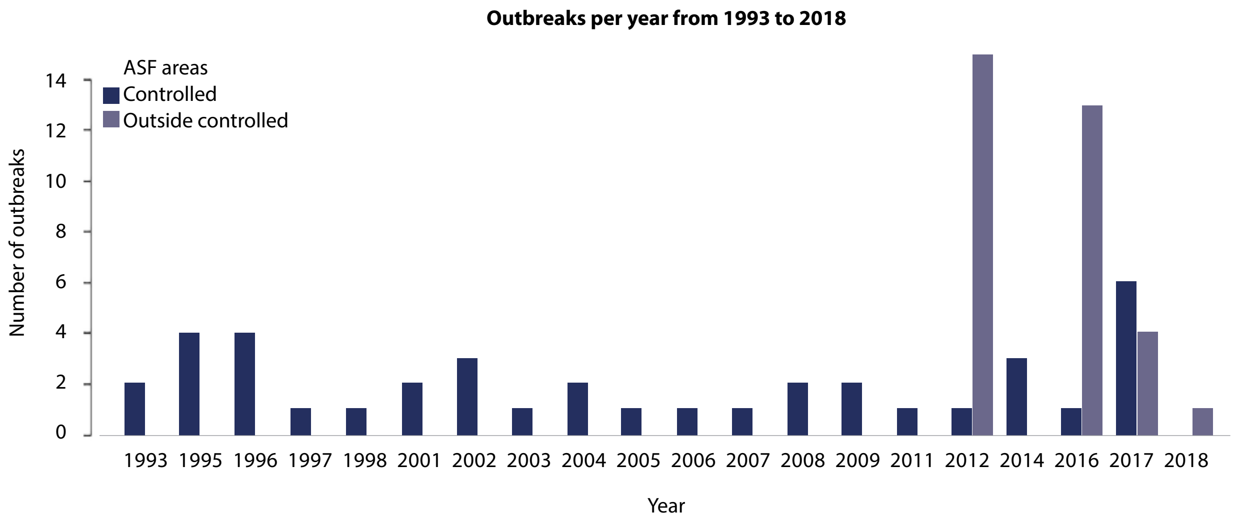


Figure 1: Temporal distribution of ASF in South Africa from 1993 to 2018; only the years in which outbreaks occurred are represented in Figure 1

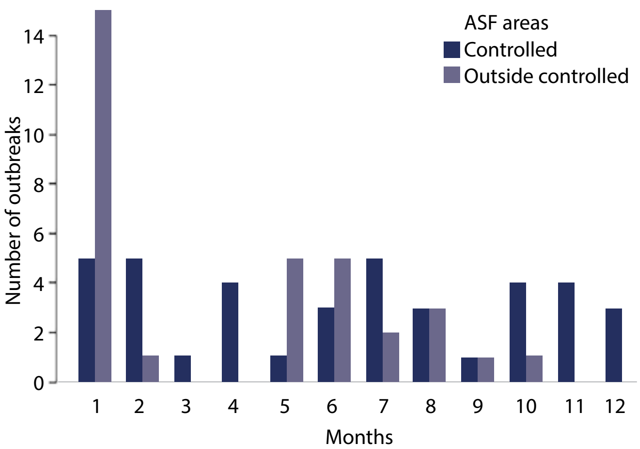


Figure 2: Monthly distribution of ASF outbreaks in South Africa from 1993 to 2018

reported in all months of the year (from January to December). In this area, they were more frequent in January, February and July with five outbreaks reported in each of them, followed by April, October and November with four outbreaks. During the period of this study (1993 to May 2018), outbreaks outside the ASF-controlled area had never been reported in March, April, November, and December. Most outbreaks in this area had been reported in January (15 outbreaks), followed by May and June with five outbreaks for each (Figure 2).

Spatial distribution of ASF outbreaks in South Africa

In South Africa, from 1993 to 2018, ASF outbreaks had mainly been reported in Limpopo province with 35 outbreaks (48.6%) and other northern South African provinces such as Gauteng, Mpumalanga, North West and Free State provinces reporting respectively six, nine, six and 11 outbreaks (Figure 3).

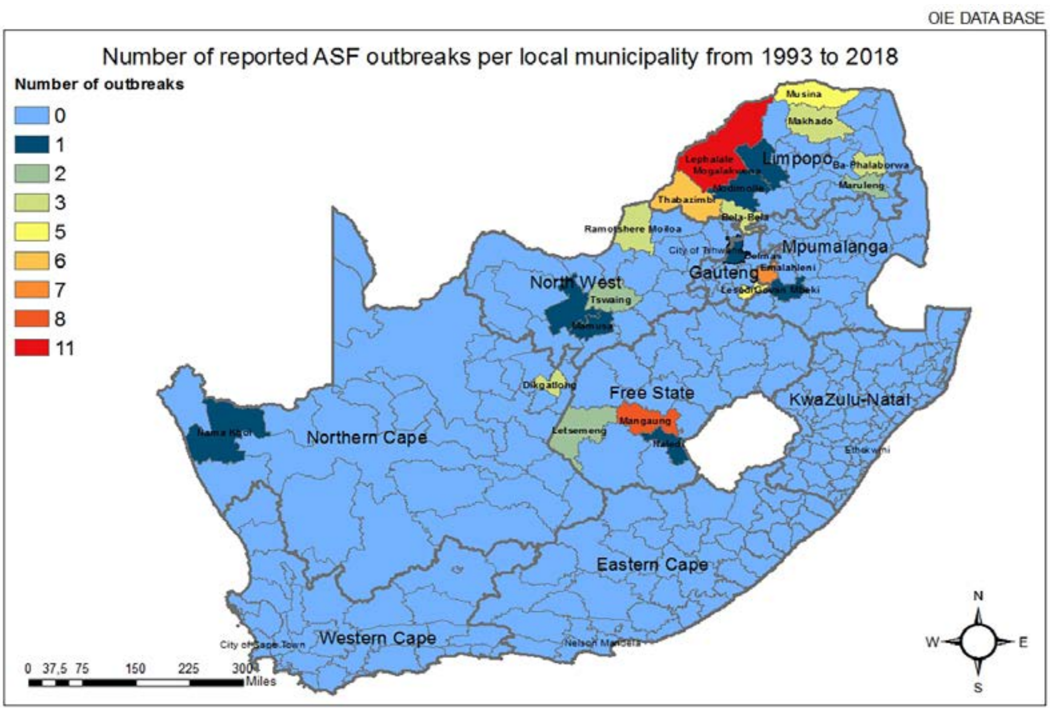


Figure 3: Number of ASF outbreaks per local municipality from 1993 to 2018

The spatial K-function has shown that ASF outbreaks are not uniformly distributed across South Africa (Figure 4), meaning that outbreaks tend to cluster in space (short distances). Thus, between 0 and index 40, the distribution was more of clustered than random distribution as observed K values were larger than expected K values in that interval, while it became more dispersed than a random distribution from index 40 as observed K values were smaller than expected K values (Figure 1).

Spatiotemporal clustering of ASF outbreaks in South Africa

Global clustering

The D-function was used to analyse possible dependence between the spatial and temporal components of ASF outbreaks. For both month and year scales, $D_0(s,t)$ decreased in distance 's' and time 't'. The decrease was faster in the interval between the first confirmed reported outbreaks between 1993 (t = 0) and 2002 (t = 9) and the distance less than four degrees around the centroid of Modimolle (first outbreak reported to OIE) considered as landmark (s = 0).

At the year scale, the residual plot in Figure 6b strongly suggests the absence of space-time interaction since the standardised residuals $R(s,t)$, fluctuated around 0 that seems closer to the expected value 0 and variance 1. Nevertheless, the larger $R(s,t)$ values at smaller $K(s,t)$ values suggest that there is an interaction at the smaller spatial and/or temporal scales. Furthermore, the residual plot does not suggest any grouping.

Considering the sum of residuals as statistic test, Monte-Carlo test of ASF outbreaks in South Africa at year scale found no significant space-time clustering (p = 0.577) which implies lack of significant space-time interaction at year level. It means that there is no spatiotemporal pattern of clustering when outbreaks data were compiled per year.

The trend in $\hat{D}(s,t)$ values at month level was similar to the trend in $\hat{D}(s,t)$ at year scale. Nevertheless, at month level, the standardised residuals $R(s,t)$ were almost all positive suggesting a probable presence of space-time interaction in ASF outbreaks

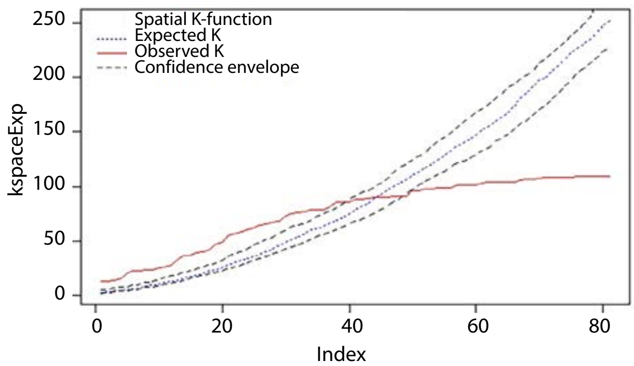
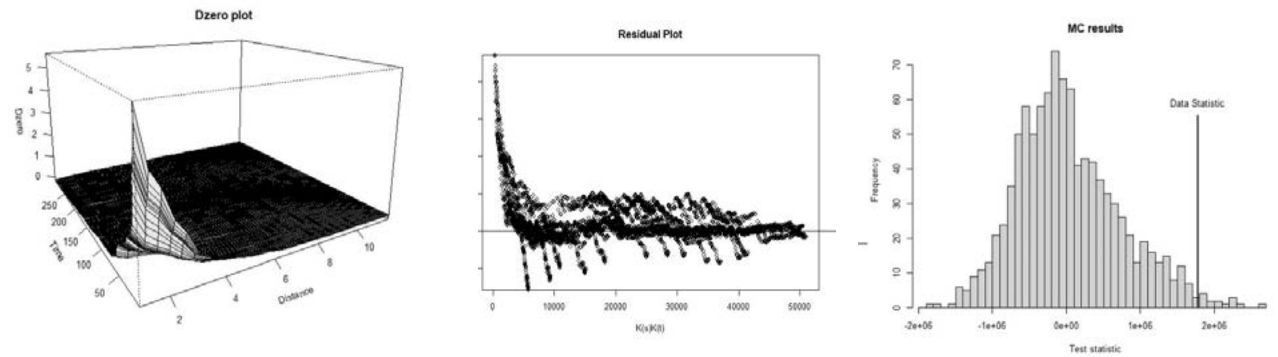


Figure 4: Spatial K-function analysis for uniformity of distribution of ASF outbreaks in South Africa



5a 5b 5c

Figure 5: Diagnostic plots for space-time clustering at month scale (a: the perspective plot of the difference between spatiotemporal K-function and the product of the spatial and temporal K-functions; b: the standardised residuals against the product of the spatial and temporal K-functions (middle) and c: histogram of the test statistics, where the statistic for the data is indicated with a vertical line)

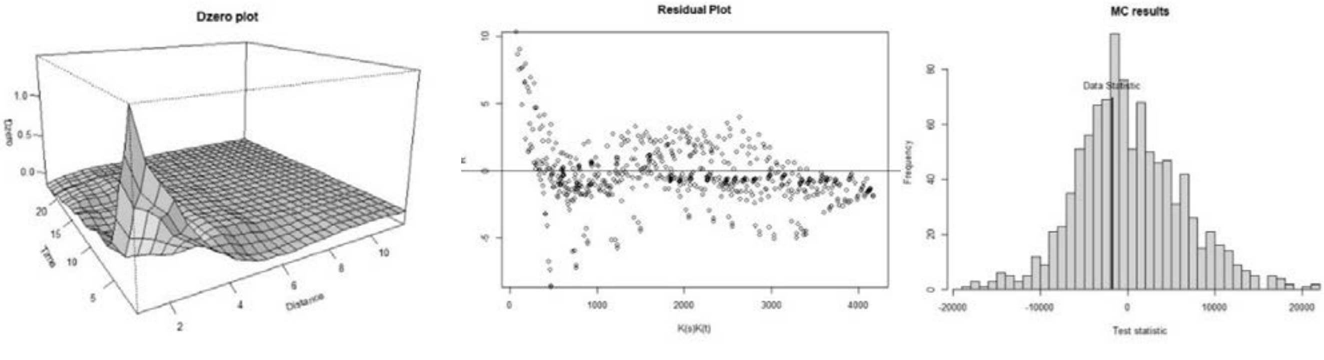


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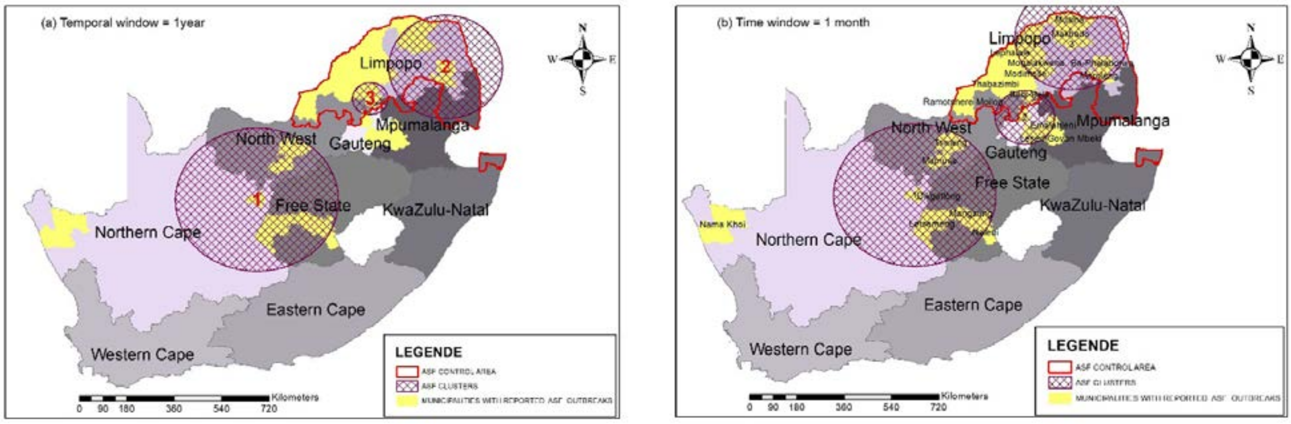
Figure 6: Diagnostic plots for space-time clustering at year scale (a: the perspective plot of the difference between spatiotemporal K-function and the product of the spatial and temporal K-functions; b: the standardised residuals against the product of the spatial and temporal K-functions (middle) and c: histogram of the test statistics, where the statistic for the data is indicated with a vertical line)



SOURCE: OIE DISEASE DATABASE

SOURCE: OIE DISEASE DATABASE

Figure 7: Local spatiotemporal clusters of ASF outbreaks in South Africa using SaTScan

Table I: Summary of spatiotemporal clusters analysis of ASF in South Africa

Time aggregation	Clusters	(Coordinates) / Radius	Time frame	Observed cases	Expected cases	RR (*p*-value)	Number of outbreaks
1 month	1	(28.403510 S, 24.414840 E) / 271.43 km	2016/5/1 to 2017/6/30	1 404	143.30	17.70 (< 0.001)	7
	2	(25.746111 S, 28.188056 E) / 101.96 km	2012/1/1 to 2012/1/31	250	25.75	10.51 (< 0.001)	13
	3	(23.018208 S, 29.783106 E) / 198.36 km	2017/6/1 to 2017/8/31	309	48.09	7.06 (< 0.001)	22
1 year	1	(28.403510S, 24.414840E) / 271.43 km	2015/6/1 to 2018/5/31	1 404	167.37	15.02 (< 0.001)	7
	2	(23.875992S, 30.842721E) / 196.65 km	2017/6/1 to 2018/5/31	216	28.84	8.00 (< 0.001)	13
	3	(24.956246 S, 28.273060 E) / 60.84 km	1993/10/1 to 1995/5/31	41	6.27	6.61 (< 0.001)	2

for smaller and greater $\hat{K}$■(s,t). The Monte-Carlo test for space-time interaction was highly significant ($p = 0.003$), which implied significant space-time interaction at the month level. That is, space-time interaction relied on cluster at month scale.

Local clustering using space-time scan statistic to detect ASF outbreak clusters

As ASF outbreaks were clustered, Figure 7 tried to identify significant local space-time clusters depending on the chosen aggregation time.

Details of the space-time analysis scanning for clusters illustrated in Figure 7 are summarised in Table I. For each cluster, the location (radius and centre's coordinates), period, number of outbreaks and the relative risk (RR) are given.

At month and year levels, we identified three significant high-rate spatiotemporal clusters of ASF outbreaks where hotspots could be associated with environmental, anthropogenic and other risk factors. Details on clusters' centre, radius, start date and end date, risk ratio and *p*-value are in the Table I.

Discussion

This study explored the spatiotemporal analysis of ASF using historic outbreak data in South Africa between 1993 and 2018. During the period of interest, South Africa reported 72 community outbreaks of ASF. The incidence of ASF outbreaks could not be accurately determined, and may have been underreported as data on ASF could not be collected systematically, especially in the subsistence sector represented by small-scale production mainly in rural areas. Pigs held in small-scale farms represent a significant part of the South African pig population (Mokoele et al. 2014). On such farms, outbreaks are most unlikely to have been detected, and if detected, may not be reported due to limited access to veterinary services, poor communication and lack of knowledge and sensitisation of the rural population on animal diseases. As a result, ASF outbreaks in this study include only those that were reported to the OIE and declared by DALRRD in their database, which may be an underestimation of the scale of the problem.

The detection of spatial and spatiotemporal clustering represents a preliminary step for an in-depth analysis of ASF outbreaks. A series of ASF outbreaks has been observed in South Africa, especially in the controlled area (Magadla et al. 2016). As spatial and temporal dimension to outbreaks interrelate, as well as with other risk factors, this study adds precision to this qualitative description. This type of analysis is well suited for working with historical data on outbreak incidence and allows a visual assessment of their development in time (Kulldorff et al. 2005). However, the degree of detail and completeness of reports and histories could have affected the quality of outputs.

Regarding ASF epidemiology, we found that ASF outbreaks are not uniformly distributed across South Africa. There was strong statistical evidence of space-time interaction between reported outbreaks at month scale. However, the space-time interaction appeared to be more spread out in time considering the year scale. Thus, when an outbreak occurs there is a clustering in the following months that can be interpreted as representing epidemiological links between outbreaks at a monthly scale. Vergne, Gogin and Pfeiffer (2017) found significant space-time clusters of ASF outbreaks in two regions (Krasnodar and Tver regions) of the Russian federation from 2007 to 2014. In these two regions, the spatial proximity to an infected farm was a strong risk factor for infection of a susceptible farm. In South Africa, outbreaks of ASF are mainly linked to the movements of pigs rather than to climatic and environmental factors. More pigs move and are slaughtered at Christmas, during the New Year festivities until January due to the need of money at the beginning of the school year (Penrith & Vosloo 2009).

For both month and year scales, $\hat{D}(s,t)$ decreased in distance and time implying an apparent clustering of outbreaks with a rapid spread observed at short distances over short periods of time (Basáñez et al. 2009; Diggle et al. 1995).

Considering cases and susceptible domestic pigs, different high-rate clusters were identified depending on aggregation time. However, aggregation per year was just overlapping the monthly aggregation, losing some precision in terms of time interval between outbreaks. For all aggregation times high rates areas were in both controlled and outside the controlled ASF areas. Small clusters (less than 100 km radius) were detected and could be related to local transmission and contacts due to local human transportation of animals. Regarding the area of occurrence, clusters in areas where the sylvatic cycle is constantly present should be related to local transmission through direct contact (free ranging pigs) or warthogs contact without being able to distinguish. Therefore local survey should be implemented in regions with high transmission rates. ASF clusters outside the ASF-controlled area have all been linked to smallholder, low biosecurity pig farming and pig movements. It would therefore be important to focus on addressing challenges in the smallholder pig farming sector to improve profitability and minimise the risk of disease introduction, thereby improving livelihoods and food security (Penrith & Vosloo 2009). Nevertheless genomic data would help to understand the cluster's diversities and the relatedness of ASFV involved and their origin. Considering the recent increase of outbreaks outside the ASF-controlled area, the prescribed control measures and areas should be reconsidered. Magadla et al. (2016) earlier confirmed that ASF-infected warthogs, warthog burrows and tampans that may be involved in ASF transmission in South Africa could be found beyond the ASF control line. Vergne et al. (2017) concluded that there was no statistically significant difference between two regions of the Russian federation for the risk of ASF infection in rural farms located close to wild boar and those located further away. This shows the minimal role that wild boar-to-domestic pig transmission played in the ASF outbreaks that occurred in those regions. However, European wild boars die as much as the domestic pigs but warthogs may be long-term carrier and disseminators, via *Ornithodoros* ticks, of infection.

According to Ceyhan et al. (2013), spatiotemporal analysis is essential in dealing with disease spread patterns because it helps decision makers to identify problematic regions in order to focus on these specific regions at specific times and develop policies and strategies for prevention and control of disease outbreaks, taking note of other spatial patterns. This study is, to our knowledge, one of the rare local scale studies characterising ASF outbreaks in South Africa through spatiotemporal perspectives, which encourages future geospatial research in animal disease epidemiology.

However, some limitations should be considered when interpreting the results of this study. The use of centroids of affected local municipalities by DALRDD instead of true geographic coordinates in order to keep the anonymity of affected farms. However, this should not affect the analysis too much taking into account the size of obtained clusters. The analysis is based mainly on OIE reports. OIE receives six-monthly updates from countries with an established endemic situation, such as within South Africa's ASF-controlled area. Due to reporting not being done via immediate notifications, for those outbreaks that are reported, the reporting is usually delayed. Furthermore, the fact that outbreaks in the controlled area occur because the regulations for keeping pigs have not been observed, we would suggest that under-reporting is highly likely. This has led us to consider only outbreaks that occurred before May 2018 (investigations completed). Given that different and independent genotypes of the ASF virus have been involved in the outbreaks in domestic pigs reported in the period of interest, the data analysed include a very heterogeneous mix (Boshoff et al. 2007; Janse van Rensburg et al. 2020). However, the aim of this study was not to analyse the spatiotemporal structure of the different genotypes in South Africa.

Based on the methodology proposed, further analysis can be conducted. This includes considering the same models used in this study but considering the different and independent ASFV genotypes involved in the outbreaks in domestic pigs reported in the period of interest. In addition, outbreaks from areas where the sylvatic cycle is constantly present can be analysed independently with outbreaks outside the controlled area, given that the two cycles most likely are driven by different factors. It also includes considering alternative models testing space-time clustering and more precise data (for example, primary data).

Conclusion

This study aimed to examine the spatiotemporal structure of ASF outbreaks in South African pig production systems. The spatial analysis has shown that ASF outbreaks are not uniformly distributed across South Africa while the interaction time and space found significant clustering at month level. Different spatial and temporal clusters associated with high-rate ASF outbreaks were detected both inside and outside the ASF-controlled areas. Thereby, investigations of ASF clustering added considerable information and provided a foundation on which to build causal hypotheses and implement prevention and control strategies.

The findings from this study can be used as a baseline for further epidemiological studies to identify risk factors involving socio-economic factors associated with high-rate regions, spread greater awareness and develop effective measures to prevent and control ASF in South Africa. For better prevention and control of ASF, strategies should at least consider the season and pig movements and involve all stakeholders, especially smallholder pig keepers. In South Africa prevention and control measures should be applied not only to the controlled area but in all areas identified as high-risk areas.

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Conflict of interest

None of the authors and collaborators had any competing interest that could negatively influence or bias the content of this paper.

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