Received: 29 September 2021 | Revised: 18 February 2022 | Accepted: 23 February 2022

DOI: 10.1111/tbed.14499

ORIGINAL ARTICLE

Transboundary and Emerging Diseases WILEY

Spatio-temporal cluster analysis and transmission drivers for Peste des Petits Ruminants in Uganda

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Funding information
German Federal Ministry of Economic Cooperation and Development; CGIAR Research Programs on Livestock and Agriculture for Nutrition and Health; CGIAR Fund Donors Research and Innovations Fund (RIF) of Makerere University, Grant/Award Number: MAK/DVCFA/481/19

Abstract

Peste des Petits Ruminants (PPR) is a transboundary, highly contagious, and fatal disease of small ruminants. PPR causes global annual economic losses of between USD 1.5 and 2.0 billion across more than 70 affected countries. Despite the commercial availability of effective PPR vaccines, lack of financial and technical commitment to PPR control coupled with a dearth of refined PPR risk profiling data in different endemic countries has perpetuated PPR virus transmission. In Uganda, over the past 5 years, PPR has extended from northeastern Uganda (Karamoja) with sporadic incursions in other districts /regions. To identify disease cluster hotspot trends that would facilitate the design and implementation of PPR risk-based control methods (including vaccination), we employed the space–time cube approach to identify trends in the clustering of outbreaks in neighbouring space–time cells using confirmed PPR outbreak report data (2007–2020). We also used negative binomial and logistic regression models and identified high small ruminant density, extended road length, low annual precipitation and high soil water index as the most important drivers of PPR in Uganda. The study identified (with 90–99% confidence) five PPR disease hotspot trend categories across subregions of Uganda. Diminishing hotspots were identified in the Karamoja region whereas consecutive, sporadic, new and emerging hotspots were identified in central and southwestern districts of Uganda. Inter-district and cross-border small ruminant movement facilitated by longer road stretches and animal comingling precipitate PPR outbreaks as well as PPR virus spread from its initial Karamoja focus to the central and southwestern Uganda. There is therefore urgent need to prioritize considerable vaccination coverage to obtain the required herd immunity among small ruminants in the new hotspot areas to block transmission to further emerging hotspots. Findings of this study provide a basis for more robust timing and prioritization of control measures including vaccination.

KEYWORDS
GIS, hotspots, Peste des Petits Ruminants, regression models, transmission drivers, Uganda

1 | INTRODUCTION

Peste des Petits Ruminants (PPR) is a distressing viral disease of domestic small ruminants (goats and sheep) in Africa, Asia and the middle East caused by Peste des Petits Ruminants virus (PPRV) (family *Paramyxoviridae*) (Amarasinghe et al., 2019; Banyard et al., 2010; Parida et al., 2015).

PPRV has one serotype with four distinct phylogenetic lineages. The PPRV lineages I, II and III are stable in Africa whereas lineage IV is predominant in Asia and the middle East. However, there has been recent geographical expansion of lineage coverage with lineage IV reported in many parts of Africa including Tanzania, Ethiopia and South Sudan, countries neighbouring or close to Uganda. PPRV lineage IV territorial expansion has been attributed to uncontrolled cross border animal movements (Alemu et al., 2019; Padhi & Ma, 2014; Tounkara et al., 2018). Three (I, II and III) of the four virus lineages have been confirmed to circulate in Uganda. During the past 7 years, most of the PPR occurrences in Uganda have been as a result of PPRV Lineage III (Dundon et al., 2020; Muniraju et al., 2014; Nkamwesiga et al., 2019).

PPR is endemic in most parts of Africa and Asia. Coincidentally, Africa and Asia are home to more than 80% of the global small ruminant population. The estimated PPR seroprevalence in Africa and Asia is about 40% (Ahaduzzaman, 2020). The disease presents with sudden increase in temperature (40—41.3°C). In the early days post infection, the animals look visibly weak, dull, restless with reduced appetite. This is usually followed by serous discharge from the eyes and nose that later becomes mucoid sometimes leading to matting of the eyelids and blockage of the nasal passage. Diarrhea usually follows leading into dehydration and emaciation. After 10–12 days, affected animals either die or recover to obtain immunity from subsequent PPR infections (Balamurugan et al., 2014; Diallo et al., 2007). The morbidity rate in naïve small ruminant populations can reach up to 100% whereas the mortality rate ranges between 23% and 100%, depending on the breed of the animals and the virulence of the PPRV lineage involved (Chowdhury et al., 2014). Even though PPR-induced small ruminant mortality and morbidity is much lower in PPR endemic areas, PPR still causes significant production losses through reduced milk yield, poor animal body condition and cost of treating secondary bacterial infections in unvaccinated flocks. The global annual losses as a result of PPR are estimated to be between USD 1.45–2.10 billion (Jones et al., 2016; OIE-FAO, 2015). This indicates that PPR significantly affects the livelihoods and wellbeing of smallholder livestock farmers in Africa and Asia. In recognition of its socioeconomic importance, the World Organisation for Animal Health (OIE) and the Food and Agriculture Organisation (FAO) launched the PPR Global Control and Eradication Strategy (PPR GCES) in 2015. It is anticipated that affected countries (or regions) will develop and implement the progressive control pathway for PPR (PCP-PPR) and eradicate the disease by the year 2030 (OIE-FAO, 2015). The strategy is built around four stages which are (i) assessment stage, (ii) control stage, (iii) eradication stage and (iv) post-eradication stage (OIE-FAO, 2015). Uganda is currently at stage 2 of this PPR-GCES and has drafted a PPR-GCES aligned PPR national control strategy that is pending approval and publication.

Effective PPR control requires deep understanding of the disease epidemiology in the affected countries (Mariner et al., 2016). The disease majorly spreads from infected to susceptible animals through human activities such as animal movements for purposes of breeding, social functions, livestock trade, returning unsold livestock to the flocks without observing quarantine measures and communal animal husbandry practices such as sharing water sources (FAO, 1999; Fournié et al., 2018). PPRV natural and experimental infection studies have indicated possible source of PPRV infection from a range of atypical domestic livestock hosts such as pigs, cattle, camels and dogs, which therefore, need to be included in surveillance plans either as sources of infection or at least as surveillance indicators of PPR transmission (Gortázar et al., 2021; Rahman et al., 2020). Livestock species such as pigs have been experimentally proved to be sources and amplifiers of PPRV (Schulz et al., 2018). A significant number of wild artiodactyls have also been previously reported as susceptible although with low levels of infection believed insufficient for sustained transmission among wild ruminants (Jones et al., 2021).

The available PPR control measures include vaccination, animal movement restrictions (quarantine), good biosecurity measures such as proper carcass disposal, and proper management practices that restrict chances of direct contact between flocks, among others. To be able to achieve the 2030 PPR GCES, PPR endemic regions (or eco-zones) and individual countries first need to fully understand PPR eco-epidemiology (OIE-FAO, 2015). However, most disease endemic countries including Uganda have not documented the full eco-epidemiology of PPR. Isolated studies in Uganda indicate that PPR has been endemic in northeastern Uganda (Karamoja region) for the past decade. PPR recently extended to isolated districts in central and southwestern Uganda (Fernandez Aguilar et al., 2020; Lernfelt, 2013; Luka et al., 2012; Mulindwa et al., 2011; Ruhweza et al., 2010). Grey literature, namely PPR passive reports, from the Ugandan Ministry of Agriculture Animal Industry and Fisheries (MAAIF) further indicates that PPRV is rapidly spreading to previously non-endemic districts in Uganda.

Although spatiotemporal and broader epidemiological studies are necessary primers for designing and implementing PPR surveillance and risk-targeted control programs, for example vaccination (A. K. M. A. Rahman et al., 2021; Abdrakhmanov et al., 2022; M. H. Rahman et al., 2021; Ma et al., 2019; Ruget et al., 2019), such studies have not been undertaken for Uganda. As such, there is a dearth of information about PPR hotspot patterns, and epidemiological drivers of PPR transmission. Consequently, PPR has not been prevented from spreading from its initial northeastern Uganda (Karamoja) focus to other regions, even though effective attenuated PPRV vaccines are commercially available. This has put the population of 16 million small ruminants in Uganda at risk of PPRV infection. To bridge this information gap, we used spatiotemporal cluster analysis and statistical regression approaches to fit a purely spatial model to identify the high-level spatial conditions associated with places in which PPR tends to be present and characterize those places in which the disease is frequent using epidemiological factors, such as past laboratory-confirmed outbreak reports (2007–2020), animal movements and environmental data sets. This information will support the design and implementation of PPR GCES for Uganda.

2 | MATERIALS AND METHODS

2.1 | Study area

The study included all districts of Uganda that reported at least one PPR confirmed outbreak during the study period (2007–2020). Uganda is a landlocked country located in East Africa. It borders South Sudan to the north, Kenya to the east, Democratic republic of Congo to the west, Tanzania to the south and Rwanda to the southwest (Figure 1). Uganda is divided into nine subregions (Karamoja, Acholi, Lango, Western, South Western, Central, East Central, West Nile, Elgon and Teso) and five administrative divisions (districts, counties/municipalities, sub-counties/town councils, parishes/wards and villages).

In 2019, Uganda had 135 districts. Disease reporting is usually aggregated at district level where there is a functional veterinary services department. Due to the temperate climate in all but the northeastern parts of the country, the major economic activity in Uganda is agriculture, with crop growing and livestock keeping as the backbone of the economy. As such, Ugandans keep about 16 million small ruminants (12,344,407 goats and 3,410,371 sheep), 11,434,795 cattle, 3,184,297 pigs, 37,443,881 chickens, 1,458,253 ducks and 348,314 turkeys (MAAIF & UBOS, 2008).

2.2 | Data source and curation of dependent variables

We obtained PPR outbreak reports (passive and active surveillance) data from 2007 to 2020 from MAAIF. Reports with accompanying laboratory reports in which at least one of the samples tested positive by either OIE recommended polymerase chain reaction (PCR) or Enzyme-linked immunosorbent assay (ELISA) PPR protocols, were considered as confirmed PPR outbreaks. All reports with no corresponding laboratory report were excluded from the analysis. Two potential response variables, (i) discrete total number of confirmed outbreak reports per district and (ii) binary report data (whether 'yes' or 'no'; a district reported at least one confirmed outbreak), during the study period were generated. This was done in Microsoft Excel (Microsoft Office suite 365, version 2106, Build 14131.20320).

2.3 | Preparation of potential explanatory variables

Different sets of variables hypothesized to directly or indirectly facilitate/support the PPR mode of transmission were considered in this study as supported by recent scholarly literature and specific epidemiological aspects of PPR virus transmission. PPR transmission and spread is usually facilitated by human socioeconomic activities, bioclimatic conditions, topographic and environmental factors that tend to favour suitability of PPR disease occurrence (Gao et al., 2019). These factors, acting singly or in combination may contribute significantly to the transmission and spread of the PPR virus resulting into re-introduction or introduction of such infectious diseases into new areas. It is therefore paramount to evaluate the interplay between anthropogenic and bioclimatic factors for better control of infectious diseases (Niu et al., 2021). We obtained human population data from the Uganda Bureau of Statistics (UBOS) (UBOS, 2009). Livestock density data sets (goat, sheep, cattle, pig, horse and small ruminant) were obtained from the Gridded Livestock of the World v2.0 high resolution raster files at cell size 30s < https://livestock.geo-wiki.org/home-2 / > (Robinson et al., 2014). Environmental variables such as landcover type, soil water index and digital elevation were obtained from Copernicus global website < https://land.copernicus.eu/global / > (Buchhorn et al., 2020). Topographic slope was calculated from the elevation data using the geodesic method with GIS extension 'Slope' (Ligas & Banasik, 2012) in ArcMap v.10.7 (Esri, Redlands, CA, USA). We also obtained variables for wildlife protected areas, distance from major towns (as defined by the Uganda Bureau of statistics according to population size and infrastructure) as proxies for wildlife population density and livestock

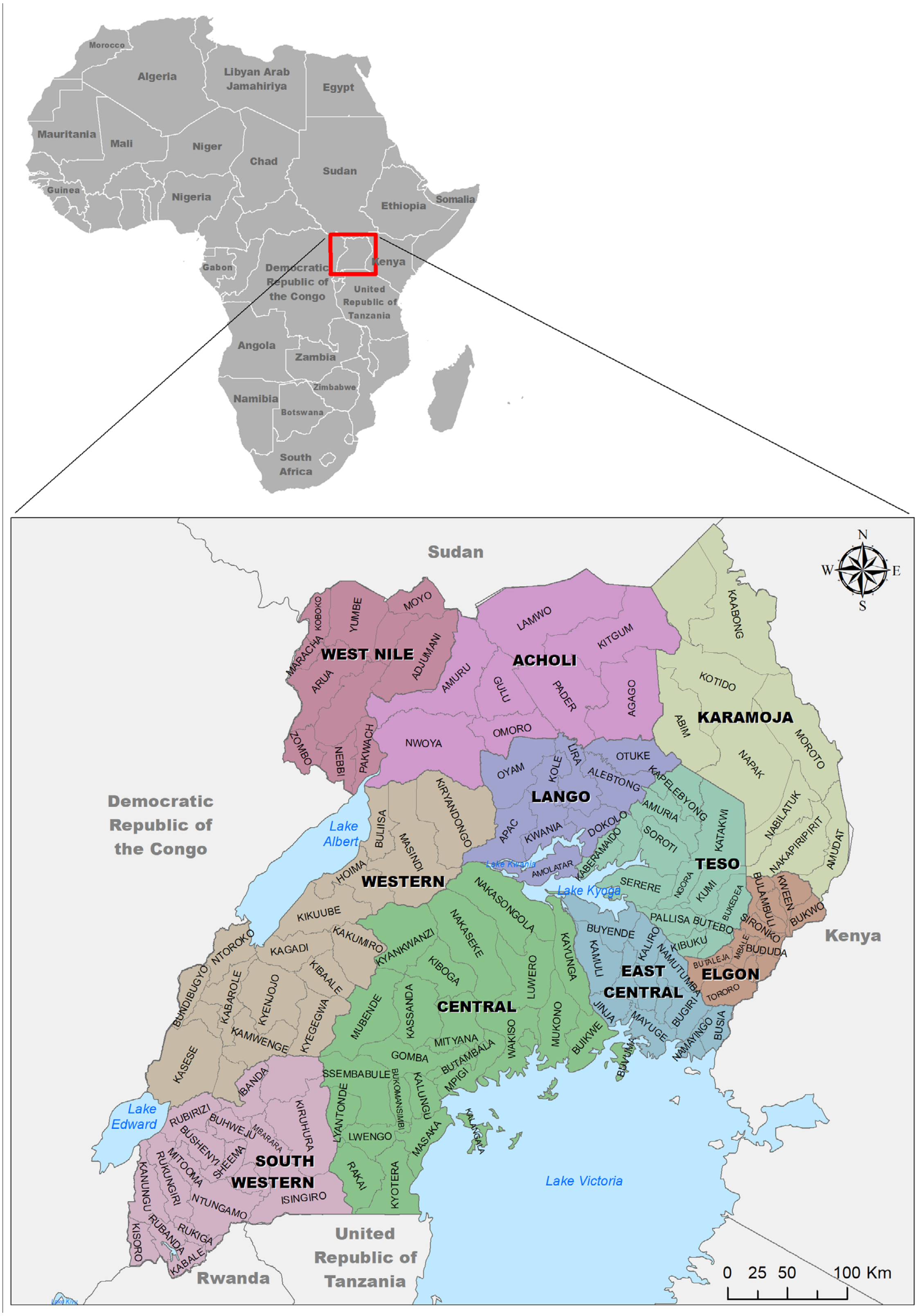

FIGURE 1 Uganda's location in Africa (in set) and national administrative sub-region boundaries

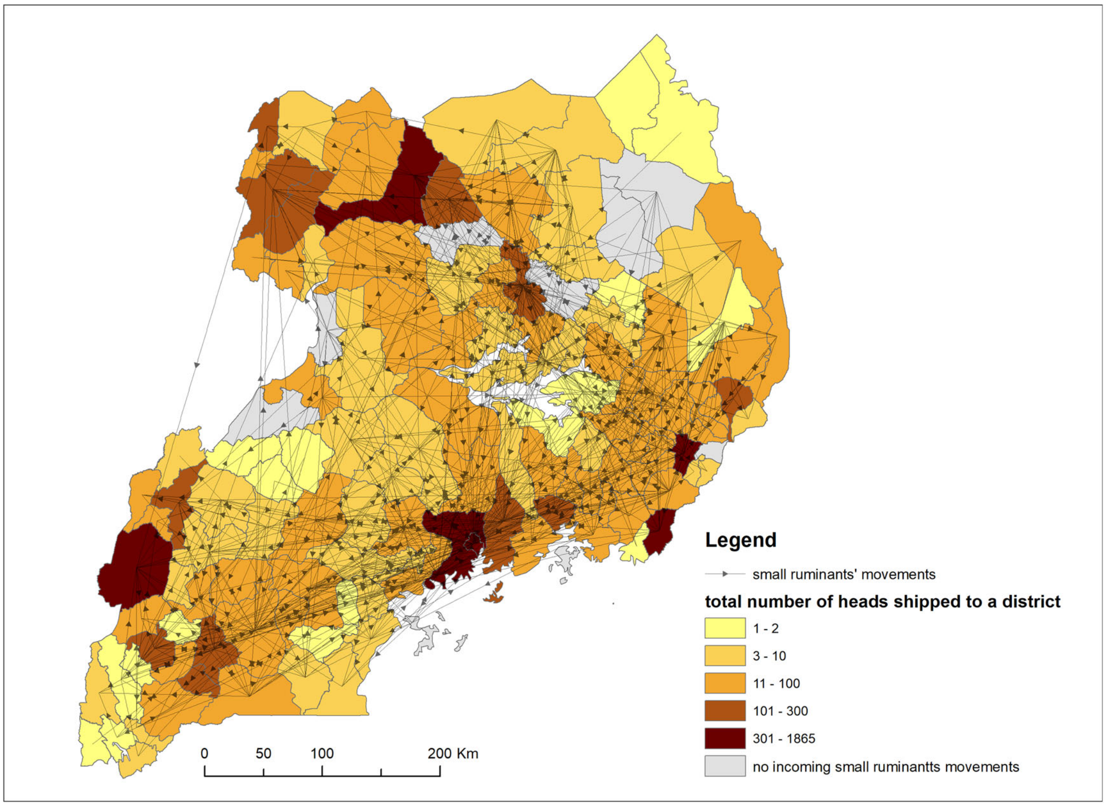

FIGURE 2 Animal movement transactions across Uganda districts (2010–2019). Each transaction line contains details pertaining to small ruminant origin, means of movement and purpose of movement as summarised using the SQL queries in ArcMap 10.7 software

markets/slaughterhouses respectively. The 19 bioclimatic variables along with solar radiation, wind speed, water vapour pressure were obtained from < https://www.worldclim.org/data/worldclim21.html > (Fick & Hijmans, 2017). Solar radiation has previously been reported to rapidly inactivate PPR virus within a couple minutes in an in vitro experiment (Latif et al., 2016), thus including such a variable might be useful in characterizing areas with likely high or low PPR transmission rates. The variables on road density and road length were computed from the roads dataset obtained from the Uganda Road network < https://geonode.wfp.org/layers/geonode:uga_trs_roads_osm > . A series of different variables were created from livestock movement data which was obtained from animal movement permits issued by officials at MAAIF (2013-2019). Movement permits were digitized in Microsoft Excel to generate a table containing all the attributes of the animal movement permit (animal species, mode of transportation, purpose of movement, number of heads moved, origin and destination among others). To this table, centroid GPS coordinates for animal origin and destination were calculated and added (since the movement permits did not include actual GPS coordinates) to create an animal movements geo-database. The frequency and the total number of heads of individual (and /combined) livestock species (goats, sheep, pigs and cattle) translocated to each destination district were computed from the created geo database (Figure 2).

All predictor variables, except for animal movement variables, were extracted from high resolution raster files available in open-source repositories. They were summarized by district followed by calculating the median values per district. Spatial Analyst, an ArcMap Desktop 10.7 extension (https://www.esri.com/en-us/arcgis/products/arcgis-desktop/resources), was used to perform raster calculations. The entire geo-database containing all 44 variables was then exported in a comma-separated (csv) file for further analysis (Supplementary Table S1).

2.4 | Building the regression models

Variable testing and regression analysis were performed with R software, version 4.05 (R Core Team, 2021). We tested all the 44 variables for multicollinearity by calculating the Variance Inflation Factor (VIF) for each independent variable. Before computing VIF, the ‘alias’ function in R was used to check for and later remove any perfectly correlated independent variables. Using R software packages ‘car’ and ‘plyr’ (Fox & Weisberg, 2019; Wickham, 2011), we fitted a linear regression model to the data and set out to sequentially drop all predictor variables with VIF threshold greater than 2.5 (Table 1) (Robinson et al., 2014).

Using R software package MASS (Venables & Ripley, 2002), we used a Generalised Linear Negative Binomial Regression (GLMNB) method for the count data. This was the preferred method of choice because our dependent variable [discrete total number of outbreaks

TABLE 1 A list of potential explanatory variables that were deemed eligible for use in the regression models selected based on variance inflation factor (VIF) threshold of 2.5

Variable (unit of measure)	VIF	Range	Source	Reference
Annual Precipitation (mm)	1.74	721–1935	https://www.worldclim.org/data/worldclim21.html	(Fick & Hijmans, 2017)
Precipitation Seasonality (mm)	1.83	31–60		
Digital elevation (m)	1.53	646–2219		
Median annual wind speed (ms^{-1})	1.94	1.7–2.5		
Soil Water Index for June 2019	1.46	0–250	https://land.copernicus.eu/global/products/swi	(Yao et al., 2021)
Land cover type (km^2)	2.20	2–21		
Road density (length per km^2)	2.07	0.3–15	https://geonode.wfp.org/layers/geonode:uga_trs_roads_osm	(UBOS, 2009)
Road length (km)	1.77	0–458		
Cattle density (head per km^2)	1.85	0–336	https://livestock.geo-wiki.org/home-2/	(Robinson et al., 2014)
Pig density (head per km^2)	1.50	0–122		
Sheep density (head per km^2)	2.37	0–79		
Neighbouring country reporting PPR cases	1.61	0 or 1	MAAIF	This study
Number of cattle movement transactions	1.55	0–2233		
Number of shipped heads by hoof, 2016–2020	1.22	0–3773		
Distance to the nearest 'major' city (km)	1.28	1977–79048	https://geonode.wfp.org/layers/geonode:uga_trs_roads_osm	(UBOS, 2009)
Protected area within a district (km^2)	1.49	0–2302		
Percentage of wetland areas (km^2)	1.51	0–42		

per district for the entire study period (2007–2020)] was over dispersed (i.e. the ratio between the conditional variance to conditional mean was 3.2, three times greater than the recommended 1). The GLMNB was applied using the stepAIC function that uses the Akaike information criterion (AIC) to sequentially remove all variables that are not statistically significant ($p > .05$) and generate the best-fitting model with the lowest AIC. To further assess the accuracy of our findings, we also similarly attempted fitting a logistic regression model on the cases data (yes/no; for a district that had reported a confirmed outbreak for the entire study period).

2.5 | Testing whether animal movements could explain the observed outbreaks

We performed a logistic regression test to determine whether the animal movements by year for each district were associated with the presence of PPR outbreaks so as to justify applicability of either pure spatial or spatiotemporal models. Three movement types passed the multicollinearity test [with variance inflation factor (VIF) less than 2.5]: (i) movements of small ruminants, (ii) movements by hoof (trekking) and (iii) the total numbers of movement transactions to each district were considered in the analysis.

Using SQL queries on the animal movement data (Figure 2), corresponding movement types were segregated by year and by destination district. Logistic regression models for each of the three movement types were then fit to test whether each of the movement type was significantly associated with the presence of PPR outbreaks (Outbr_bin).

2.6 | Testing for spatial autocorrelation of the model and residuals

The final model residuals and fitted values were annexed to the attributes table containing all Ugandan districts in ArcGIS. Global Moran's I method was used to test the observed and fitted values for spatial autocorrelation (Mitchell, 2005) in order to detect potential clustering and to decide whether or not the obtained set of explanatory variables allows adjusting for spatial autocorrelation. Spatial autocorrelation was tested using the Row standardization of features' spatial weights that allows for mitigation of bias due to features having different number of neighbours. Results of the analysis include *Z*-scores and *p* values, which together indicate a statistical significance of the observed pattern (standard deviations and corresponding probabilities). Moran's I index represents a measure of statistically significant *Z* and *p* values. Positive values of I indicate a tendency towards clustering while negative values indicate a tendency towards dispersion.

2.7 | Space–time analysis and visualization

To analyse and visualize the change in PPR infection status at the district level throughout the study period (2007–2020), we applied a space–time analysis using the space–time cube data aggregation approach (Abdrakhmanov et al., 2017; Kraak & Koussoulakou, 2005). This technique generates space–time hotspots and their trends across the entire study area. The total number of confirmed PPR outbreaks was aggregated by Ugandan districts as space units, while 1 year was used as a time step for the analysis. The Getis-Ord Gi* statistics was used to generate hotspots in each location (Ord & Getis, 1995). An *Emerging Hot Spot* analysis was applied to identify trends in the clustering of outbreaks in neighbouring space–time cells. This was followed by the Mann–Kendall statistics approach that detects trends in hotspot emergence (Hamed, 2009). Depending on the trend category revealed, this analysis assigns each district a particular pattern of a hotspot emergence through time (new, consecutive, oscillating, diminishing etc.), thus allowing conclusion making about the tendency of outbreaks to emerge or to fade within each district over the considered period (2007–2020 in our case).

3 | RESULTS

3.1 | Descriptive statistics

During the study period (2007–2020), a total of 221 PPR passive surveillance reports were recorded at the National Animal Disease Diagnostics and Epidemiology Centre (NADDEC) of MAAIF. Of these, 172 reports were confirmed as PPR outbreaks based on ELISA and/or PCR test results and covered about 40% (55/134) of districts in Uganda. Confirmed outbreaks per district in the entire 14-year period ranged between 0 and 12. The average number of confirmed PPR outbreaks per year and per district were 13 and 2, respectively (Figure 3). The spatial distribution of each of the 17 potential explanatory variables in Uganda was also generated (Figures S1–S3)

3.2 | Logistic regression model analysis of the animal movement variables

All the three logistic regression models revealed that animal movements were not significantly associated with the likelihood of outbreaks in any district (Outbr_bin). In our case therefore, animal movements were not significant predictors of the observed outbreaks ($p > .1$ and Null deviance nearly equals Residual deviance) (Table 2).

These results demonstrate that animal movement does not contribute to the explanation of the observed outbreaks, so the final regression models did not lose their goodness of fit with the exclusion of this variable. This further validates the fact that this set of variables was not statistically significant and was thus eliminated during the stepwise best model selection based on AIC criteria.

3.3 | Negative binomial regression (NBR) analysis

A total of 17 independent variables were fit into the negative binomial regression (NBR) model. The final model contained a set of seven variables with six of them being significantly associated with number of outbreaks in each district ($p < .05$). Increase in the road length, cattle density and soil water index were significantly associated with increase in PPR outbreaks. The model further revealed that as road density, annual precipitation and wildlife protected areas decrease in a district, the number of outbreaks tends to significantly increase (Table 3). The goodness-of-fit chi-squared test was not statistically significant ($p = .2875$); AIC: 384.48; thus, this model fits our data reasonably well.

3.4 | Predicted number of outbreaks by NBR model results

The negative binomial regression model predicted a range of 5–11 outbreaks in the Karamoja subregion and about 1–2 in the Lake Victoria crescent area (east central region). The model also predicted between 2 and 3 outbreaks to occur in the central and southwestern regions of Uganda except for Rakai and Isingiro districts with a similar range of predicted outbreaks like the Karamoja region (Figure 4a). The model residuals exhibited a nearly random pattern (Figure 4b), indicating a fairly good fit.

3.5 | Logistic regression model analysis of the likelihood of occurrence of confirmed outbreaks

A total of 17 independent variables were fit into the logistic regression model. The final model revealed a combination of five variables, with four of them being significantly associated ($p < .05$) with the likelihood of occurrence of confirmed PPR outbreaks. All the variables in this model were similar to those predicted by the NBR model except for the median annual windspeed that was negatively associated with PPR outbreak in a district (Table 4). The goodness-of-fit chi-squared test was not statistically significant ($p = .072$); AUC = 0.811, AIC = 165.22; thus this model fits our data reasonably well.

3.6 | Predicted probability of outbreaks by logistic regression model results

The logistic regression model predicted that the Ugandan districts that lie at international borders have the highest probability of having PPR outbreaks. Just like in the negative binomial regression model, it is similarly observed that the highest probability of having PPR

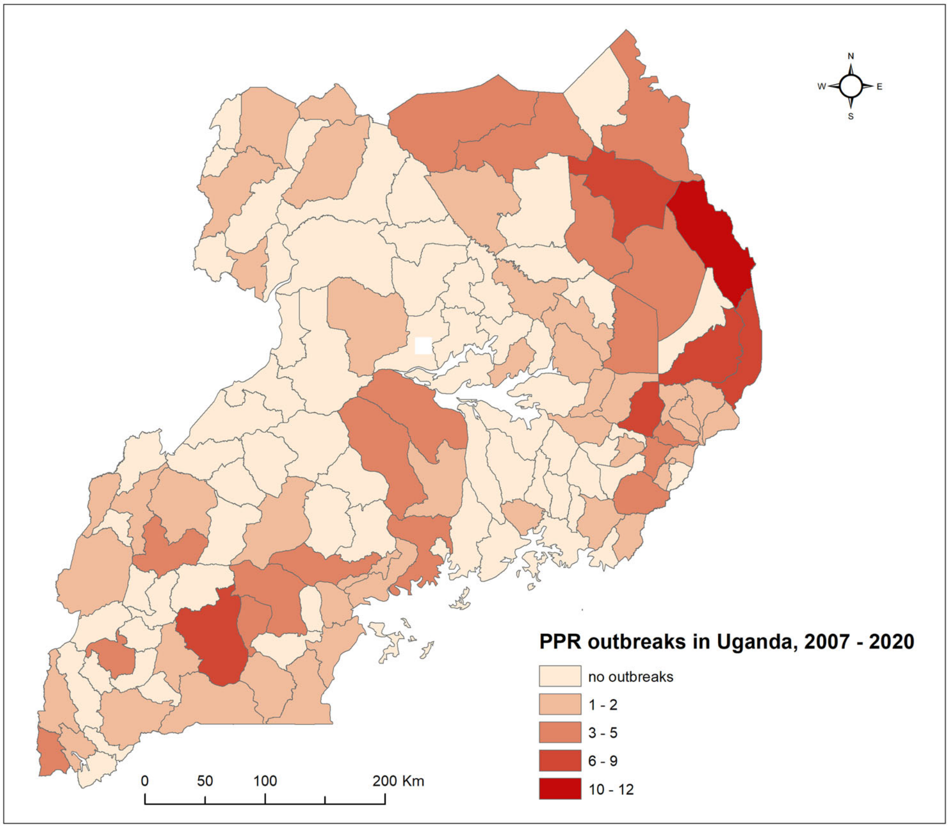

FIGURE 3 Spatial distribution of confirmed Peste des Petits Ruminants (PPR) outbreaks (2007–2020) in Uganda

TABLE 2 Logistic regression modelling of animal movement parameters as predictors of PPR outbreaks in Uganda; 2007–2020

Model	Variable *p* value	Null deviance	Residual deviance	Pseudo R^2
Outbr_bin ~ Total movements	.159	636.58	634.96	0.002
Outbr_bin ~ Livestock movement by all methods	.170	636.58	635.05	0.002
Outbr_bin ~ Livestock trekking	.122	636.58	624.24	0.019

TABLE 3 Negative binomial regression (NBR) predictors of PPR outbreaks in Uganda; 2007–2020

PPR outbreak predictor	Coefficient	Standardized coefficient	Standard error	z Value	Pr(>|z|)
(Intercept)	0.572		1.135	0.504	0.61431
Annual precipitation	−0.003	−0.283	0.001	−4.469	7.85e-06***
Digital elevation	0.001	0.106	0.000	1.899	0.05755
Road density	−8.321	−0.238	2.542	−3.274	0.00106**
Road length	0.005	0.200	0.001	3.048	0.00230**
Cattle density	0.005	0.107	0.002	2.134	0.03286*
Soil Water Index, June 2019	0.013	0.279	0.003	4.087	4.37e-05***
Protected area within a district	−0.001	−0.148	0.000	−2.189	0.02859*

Significance levels: ***$p < .001$, **$p < .01$ and *$p < .05$.

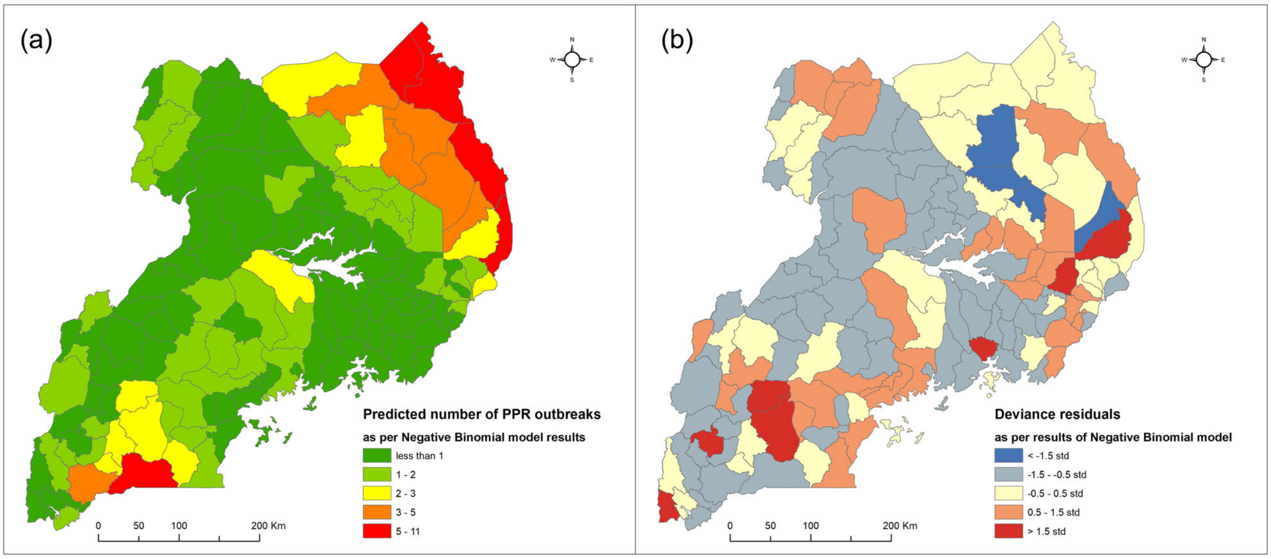

FIGURE 4 The predicted number of PPR outbreaks in Uganda as estimated by the negative binomial regression model and the distribution of the associated model residuals as visualised in ArcMap 10.7 software

TABLE 4 Logistic regression predictors of PPR outbreaks in Uganda; 2007–2020

Variable	Coefficient	Adjusted coefficient	Standard error	*z* Value	Pr (>|z|)
(Intercept)	6.408		2.514	2.549	0.01081*
Annual precipitation	−0.002	−0.852	0.001	−1.735	0.08269
Road length	0.007	1.231	0.003	2.591	0.00957**
Cattle density	0.012	1.057	0.006	2.043	0.04103*
Soil Water Index for June 2019	0.011	1.055	0.005	2.091	0.03653*
Median annual wind speed	−3.609	−1.385	1.175	−3.071	0.00213**

Significance levels: $^{**}p < .01$ and $^{*}p < .05$.

outbreaks was in the Karamoja region followed by the southwestern part of Uganda (Figure 5a). The model residuals were also randomly distributed (Figure 5b).

3.7 | Spatial autocorrelation analysis on various model inputs and outputs

The M values close to zero suggest randomness of the distribution (Figure 6). Spatial clustering of PPR outbreaks in Uganda was confirmed by testing distribution of the dependent variable (discrete total number of confirmed PPR outbreaks per district) for the NBR model that was found to be clustered with (M = 0.239, Z = 4.779 and p = .000002). Similarly, the distribution of the dependent variable (binary cases per district) for the logistic regression model was also clustered ($M = 0.143, Z = 2.805$ and $p = .005026$). The residuals of both models were close to random distribution with supported metrics: NBR model ($M = 0.049, Z = 1.058$ and $p = .289$) and logistic regression model ($M = 0.018, Z = 0.486, p = .627$).

3.8 | Space–time analysis and visualization

We identified two trend categories, 'Up Trend' and 'Down Trend' with varying degrees of confidence (90%, 95% and 99%) for the entire study period (2007–2020). The districts in the Karamoja subregion exhibited a general 'Down Trend' whereas districts around the Lake Victoria crescent (central Uganda) and southwestern Uganda exhibited a general 'Up Trend' in PPR outbreaks. There was generally no obvious pattern observed in the districts of the West Nile region and around the Lake Kyoga plains. The islands on Lake Victoria (Kalangala district) were also identified in 'Up Trend' category (Figure 7).

The 99%, 95% and 90% confidence 'Up Trend' categories consisted of 22, 19 and 10 districts respectively. The 99% 'Down Trend' category consisted of only Agago district, 12 districts in the 95% 'Down Trend' and only two districts in the 90% 'Down Trend' category (Table 5). The rest of the districts did not exhibit any significant trend.

Following the clustering pattern of PPR outbreaks through time (2007–2020), three hotspot trend categories (new, consecutive, and sporadic) were identified. Only 13 Uganda districts exhibited a

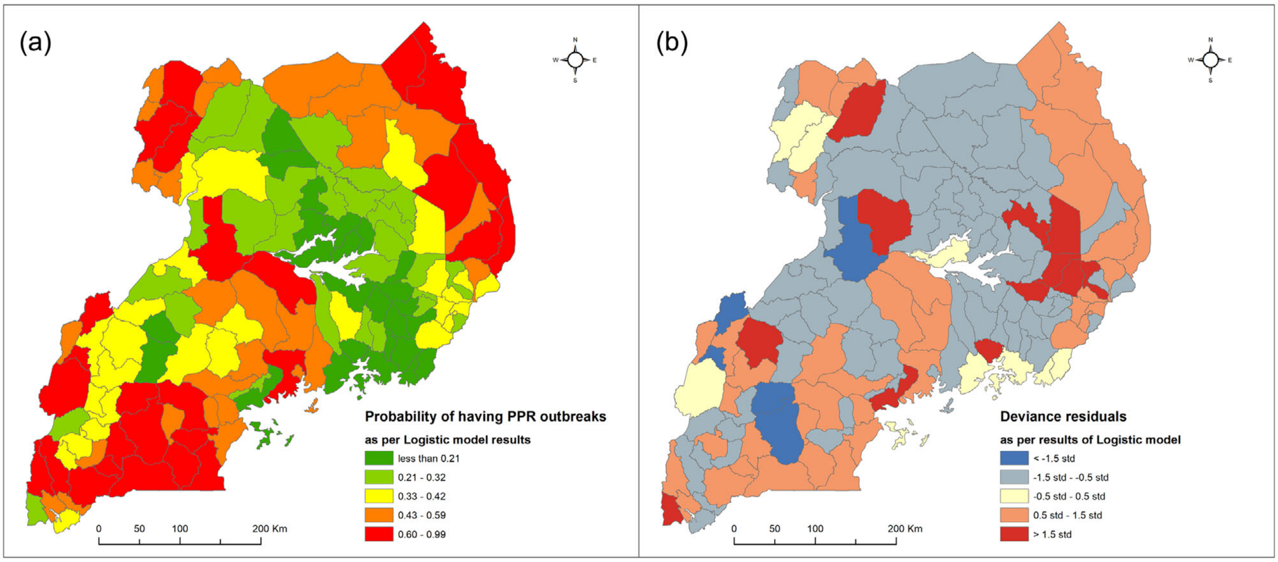

FIGURE 5 The predicted number of PPR outbreaks in Uganda as estimated by the logistic regression model and the distribution of the associated model residuals as visualised in ArcMap 10.7 software

TABLE 5 Uganda district clusters with significant (90–99%) PPR trend categories

PPR trend category (% confidence level)	Uganda district (2019)	Subregion (number of districts)
Down Trend (99)	Agago	Acholi (1)
Down Trend (95)	Kaabong, Karenga, Kotido, Abim, Napak, Kaberamaido, Kapelebyong, Lira, Kwania, Dokolo, Kitgum, Pader	Karamoja (5), Teso (2), Lango (3), Acholi (2)
Down Trend (90)	Amuria, Serere	Teso (2)
Up Trend (90)	Kabarole, Masindi, Bunyangabu, Kyenjojo, Kasese, Kamwenge, Ntoroko, Bundibugyo, Kiryandongo, Apac	Western (9), Lango (1)
Up Trend (95)	Kampala, Wakiso, Mukono, Masaka, Buikwe, Mubende, Nakasongola, Kyotera, Rukungiri, Kanungu, Ibanda, Rubirizi, Kisoro, Ntungamo, Mitooma, Buhweju, Kitagwenda, Kyegegwa, Kibaale,	Central (8), Southwestern (8), western (3)
Up Trend (99)	Kalangala, Luwero, Bukomansimbi, Mpigi, Lwengo, Lyantonde, Ssembabule, Butambala, Nakaseke, Kiboga, Gomba, Kasanda, Mityana, Kalungu, Rakai, Mbarara, Kiruhura, Sheema, Bushenyi, Isingiro, Rwampara, Kazo	Central (15), Southwestern (7)

significant trend and were categorised in at least one of the trend categories whereas the rest of the districts exhibited no significant pattern (Figure 8). Four districts of Masaka, Mubende, Gomba and Rwampara were identified as new emerging hotspots. Eight districts (Ibanda, Mbarara, Lwengo, Lyantonde, Ssembabule, Kiruhura, Isingiro and Kazo) were identified as consecutive PPR outbreak hotspots whereas only one district (Rakai) was identified as a sporadic hotspot.

4 | DISCUSSION

In this study, we present a holistic assessment of the PPR epidemiological situation in Uganda using retrospective confirmed outbreak reports, socioeconomic factors, and environmental variables. We further identified disease clusters (hotspots) and their predictors using advanced epidemiology and statistical modelling approaches.

We tested risk factors for transmission of PPRV reported in the literature against the outcomes of interest (total number of outbreaks per district or whether a district has reported an outbreak) (A. K. M. A. Rahman et al., 2021; Ruget et al., 2019). As previously reported (Ma et al., 2019), our regression models indicated a strong negative association between annual precipitation with the likelihood of PPR outbreaks implying that lower rainfall increases the chance of PPR outbreaks. During the dry season, the pastoral communities in Uganda tend to move animals over long distances within and sometimes outside the national borders in search for pastures and water for their livestock.

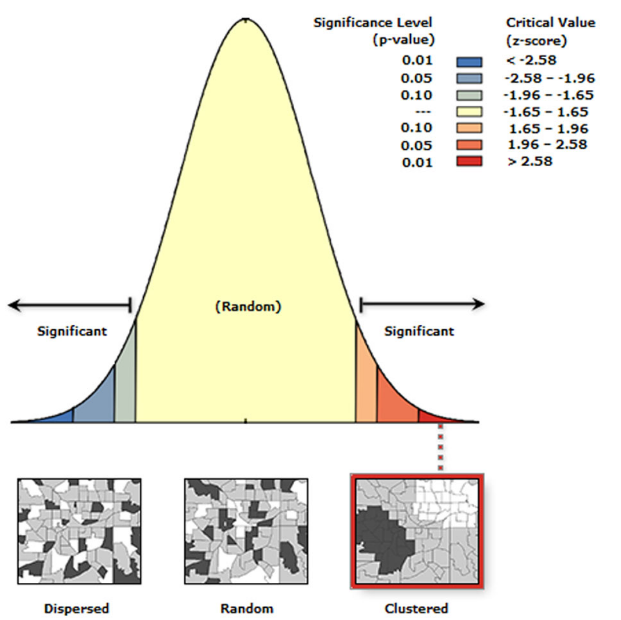

FIGURE 6 Graphical representation of acceptable regions for the measure of standard deviations and corresponding probabilities of Moran I's metrics of spatial autocorrelation

This husbandry practice increases chances of infected and naïve flocks interacting hence potentially facilitating PPRV transmission and increasing the number of outbreaks (Herzog et al., 2020). Additionally, the likelihood of animal nose-to-nose contact and therefore PPRV transmission especially at communal watering points increases during the dry season (VanderWaal et al., 2017). As well, dry seasons are associated with animal trekking for long distances in search of pastures and water which often increases stress for animals. Poor immunity compounded by inadequate/poor nutrition in the dry season will ultimately result into an increase in PPR outbreaks (Abubakar et al., 2009). It would be helpful to monitor precipitation levels and carry out vaccination exercises before onset of drought and/or at the end of the rains before susceptible animals gather at communal watering points.

Conversely, an increase in soil water index (SWI) was significantly associated with the likelihood of PRR outbreaks in Uganda. The Soil Water Index (SWI) provides an estimate of the level of moisture at different soil depths. The SWI varies significantly on small scales depending on the amounts of rainfall received, soil drainage and infiltration capacity of the soil in question (Yao *et al*., 2021). It is highly likely that as soil water index increases, the quality and volume of palatable forages increases, which in turn leads to congregation of small ruminants in such areas. Animal congregation, co-mingling and movement have previously been reported to be strongly associated with transmission of viral infectious pathogens (Kambarage & Kusiluka, 1996; VanderWaal

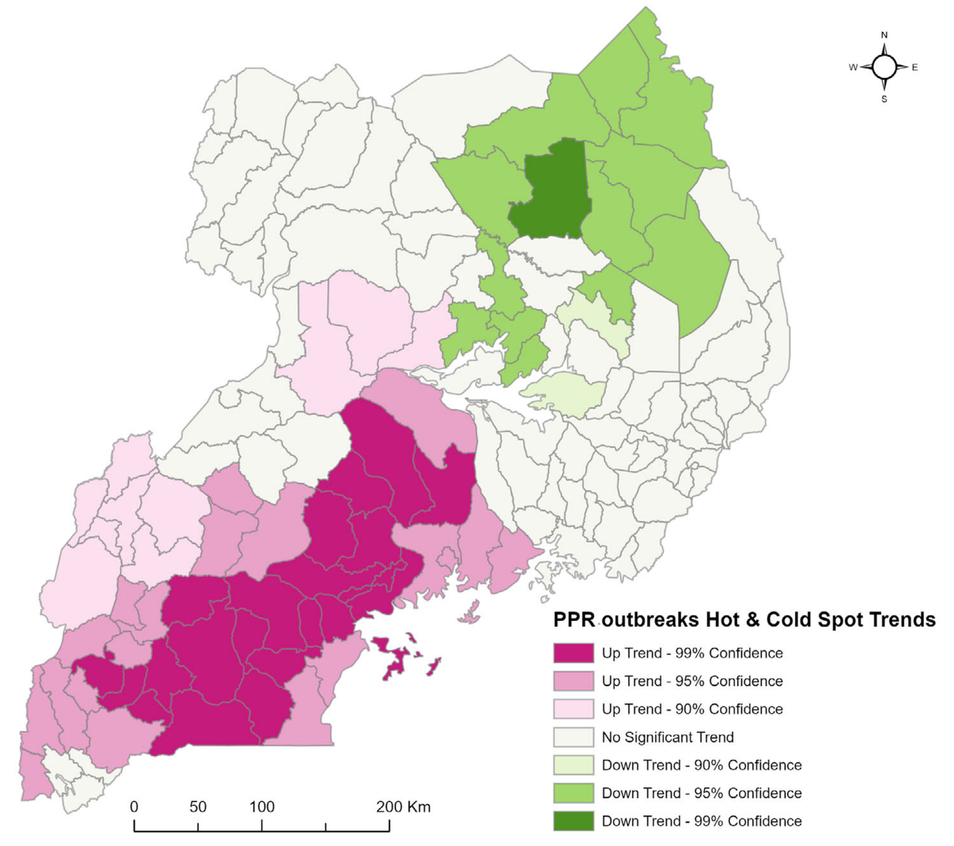

FIGURE 7 Space–time PPR hotspots and their trends across Uganda. A space–time cube data aggregation analysis, with the total number of confirmed PPR outbreaks reported per district and 1 year set as space units and time step, respectively

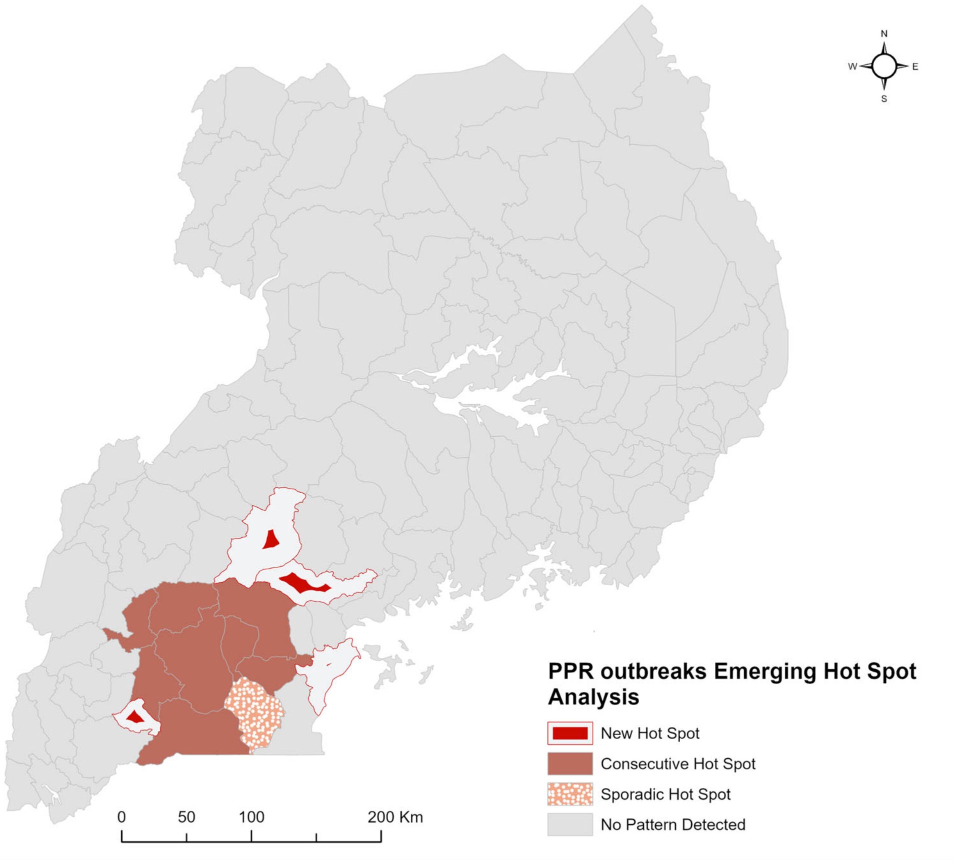

FIGURE 8 Clustering trends of PPR outbreaks in neighbouring space–time cells and hotspots. An *Emerging Hot Spot* analysis and Getis-Ord Gi* statistics analysis. Emerging hotspot trends through time; new, consecutive and sporadic PPR trends were identified following the Mann–Kendall statistics approach

et al., 2017). This could explain the significant association between the soil water index (SWI) and the likelihood of PRR outbreaks in Uganda given that PPR transmission is largely through direct contact as compared to environmental transmission (Mariner et al., 2016).

PPRV is quickly destroyed by ultraviolet light and high temperatures and thus does not survive long in the environment (Latif et al., 2016; Mariner et al., 2016). This attribute suitably explains our result of median wind speed being negatively correlated with PPR outbreaks. PPRV is majorly transmitted through direct contact between susceptible and PPRV infected animals. PPRV environmental transmission (aided by wind-propelled aerosolised virus particles) plays little or no role in PPR epidemiology as compared to increased small ruminant contact rates.

Cattle density was found to be positively correlated with PPR outbreaks. In Uganda, cattle density and small ruminant density are significantly positively correlated (r = 0.71, p = 2.2e-16, 95% CI: 0.61–0.78) (Figure S3F). Thus, the association between cattle density and PPR outbreaks could be explained by the mere fact that cattle keepers in Uganda often keep small ruminants as well. As cattle density (and indeed small ruminant density) increases in an area, the likelihood of animal congregation that improves chances of contact between flocks increases. This in turn may explain the increase in the outbreaks in such geographical areas. In addition, the production systems in which majority of Uganda's cattle populations are kept attach higher value to their livestock and are therefore more likely to report PPR outbreaks to the District Veterinary officers. Although cattle are always considered as dead-end hosts for PPR, their role in PPR epidemiology in Uganda has not been explored and should not be ignored. It is suggested by previous studies that cattle should be included as sentinels in PPR surveillance systems and also monitor their role in PPR transmission (Agga et al., 2019; Lembo et al., 2013).

The significantly positive correlation between road length and PPR outbreaks can be attributed to long distance translocation of small ruminants for sale for instance to livestock markets and for breeding purposes. The districts with longer roads are more likely to participate in long distance transportation of livestock within or outside the district boundaries which might increase the chances of importing (or exporting) a PPRV positive animal resulting into PPR outbreaks as observed in previous studies (A. K. M. A. Rahman et al., 2021). Road length signifies highways (longer road stretches) that are used for inter-district and across frontiers small ruminant movement hence fuelling PPR outbreaks as well as spread of PPR from its initial Karamoja focus to the central and southwestern Uganda foci (emerging PPR foci). Previously, highways were fewer in

Karamoja region explaining why the outbreaks took longer to expand to other districts. Road density, which signifies short distance livestock movement (Ruget et al., 2019), was negatively correlated with PPR outbreaks. Intra-district movements facilitated by dense feeder roads is important for intra-district transmission; hence playing a lesser role in inter-district PPR outbreaks that seems to describe the PPR trends in the analysed data sets.

The share of protected areas in a district was negatively associated with PPR outbreaks. Protected areas in Uganda include the land mass covered by wildlife and game reserves making up a total of approximately 4.6% of Uganda's total land mass (Munsey et al., 2019). Given that the government restricts livestock grazing in protected areas, it likely limits opportunities for contact between flocks resulting into a reduced chance of PPR outbreaks (Ruget et al., 2019). Having protected areas also minimizes contact with possible atypical wildlife hosts.

We identified diminishing PPR hotspots in the northeastern Uganda districts comprised largely the Karamoja region. This is most likely to be due to mass and ring PPRV vaccination efforts in response to outbreaks that have been undertaken in this region since 2007, leading to a herd-immunity level that affects transmission rates. At least 12 outbreaks have been confirmed in the Karamoja region resulting in an unknown percentage of small ruminant immunoprotection through natural disease challenge. There is no published literature on the actual PPR vaccine coverage in Uganda, however, with the current ring vaccination control approach following outbreaks over the past 14 years, a modest number of PPR vaccine doses has been applied in the Karamoja subregion by the Food and Agricultural Organization of the United Nation (FAO), the government of Uganda and other non-governmental organisations (Abebe, 2016). Interestingly, previous prevalence studies in this region indicate high levels (63%–85%) of seroconversion (Luka et al., 2011; Mulindwa et al., 2011) among small ruminants in Karamoja subregion. Much as there has been a significant vaccination effort in this region, it does not seem substantial enough to eliminate virus circulation, but may have been sufficient to slow down transmission. However, it may also have resulted into disease suppression and long term persistence as circulation/outbreaks would be difficult to recognise (Mariner et al., 2016), especially considering the inadequate animal disease surveillance system in Uganda.

Uptrend PPR hotspots were identified largely among districts along the cattle corridor in Western Uganda. This is a region where majority of the national livestock population are kept. In this cattle corridor, the majority of the famers communally graze their livestock, resulting into flock congregation which increases the likelihood of PPRV transmission. The observed PPR outbreak pattern is consistent with what has been reported in other East African countries with similar production systems (Mdetele et al., 2021). Over 50% and 17% of the national sheep and goat population respectively are kept in the 9 districts of Karamoja region (MAAIF & UBOS, 2009). With rampant uncontrolled inter-district animal movements supported by the recent extension of the motor way network system, it is not surprising that PPR is now spreading from northeastern Uganda (Karamoja) to southwestern and central region districts of Uganda. As a result, we identified emerging PPR hotspots in the southwestern part of Uganda categorised as new, consecutive and sporadic. The new PPR hotspot districts of Masaka, Mubende, Gomba and Rwampara have relatively high number of livestock including small ruminants per square kilometre. High density of livestock increases the likelihood of contact between infected and susceptible animals and therefore PPR transmission.

The consecutive and sporadic hotspot districts of Isingiro and Rakai respectively are characterised by communal pastoral livestock management and movement of animals across the international border, to and from the Republic of Tanzania. Transborder animal movements along this border point have previously been reported to contribute significantly to the spread and maintenance of contagious viral pathogens such as foot-and-mouth disease (Ayebazibwe et al., 2010; Di Nardo et al., 2011; Kerfua et al., 2018). This is likely the case with PPR transmission in the Rakai district sporadic hotspot and consecutive hotspot in Isingiro district. These factors increase the likelihood of contact between PPRV infected and susceptible animals. This partly explains why these districts are now consecutive and sporadic PPR hotspots. Unless targeted for control, these districts (new, consecutive and sporadic hotspots) will most likely become the new foci/epicentres for PPRV transmission.

4.1 | Study limitations

The outbreak data used in this study were based on clinical observations or outbreak reports (rather than seroprevalence data collected using robust epidemiological methods). The results and their interpretation that we report here are therefore determined using data based on the farmers' ability to primarily identify PPR outbreaks and report them to MAAIF technical personnel for confirmation. Such reports constitute just a fraction of the true PPR incidence over the study period. Additionally, there is limited capacity to accurately detect let alone investigate all the PPR outbreaks in all districts in Uganda due to majorly resource constraints. This is particularly true for Uganda where an efficient animal disease surveillance system is lacking and there are neither incentives nor penalties for livestock disease reporting or under and/no reporting respectively. The livestock disease surveillance system in Uganda suffers a number of setbacks which have affected the quality and volume of data transmitted from the lower level (livestock keeper) to the top level (disease control officers at MAAIF). These challenges include poor laboratory diagnostic services, budgetary constraints and inadequate data transmission systems precise enough to deliver data in a timely manner. Additionally, the system faces poor communication challenges among the stakeholders (Namayanja et al., 2019).

We were not able to find precise PPR vaccination data for all the districts in Uganda over time and thus we could not use vaccination data in the model. However, vaccines were applied in those places in which disease was prevalent, so, in a purely spatial model, that would come up as an association between vaccine and disease further complicating our objective of characterizing the setting. We therefore could only discuss vaccination coverage in general terms for the few regions that have somewhat vaccinated their flocks against PPR.

The key underlying assumption we employ in this study is that the parameters we used serve as a proxy for the true value of the variables, thus, allowing for spatial characterization of the settings. However, one limitation is that, because a time–space model could not be fit given limitations in the data, it is unclear whether those associations are influenced by other factors that were not measured here. Nonetheless, we believe that a purely spatial model will be helpful, novel and needed to support institution of interventions in the context of Uganda. The findings of this study provide useful information as a baseline for a more guided animal disease control interventions such as targeted vaccination and animal movement control.

4.2 | Conclusions and recommendations

The study identified three PPR disease hotspot trend categories with 90–99% confidence across different subregions in Uganda. Diminishing hotspots were identified in the Karamoja region whereas consistent, sporadic, new and emerging hotspots were identified majorly in central and southwestern districts of Uganda. The study further identified high small ruminant density, longer road length, reduced annual precipitation, high soil water index as the most important drivers of Peste des Petits Ruminants (PPR) transmission in Uganda. Findings of this study provide a basis for more robust timing and prioritization of control measures including vaccination to contribute to the global goal of control and eradication by 2030. For instance, these findings can be used to test a risk based PPR vaccination program by prioritising vaccination of small ruminants in PPR Up Trend districts. Prioritization of interventions in terms of both space and time and for example districts with uptrend, drought-prone and those with high density of small ruminants and the time of the year when the amount of rainfall is low.

ACKNOWLEDGEMENTS

This work was funded by the German Federal Ministry of Economic Cooperation and Development (BMZ) through the project Boosting Uganda's investment in livestock development (BUILD) (Grant number BMZ001). Additional support was received from the CGIAR Research Programs on Livestock and Agriculture for Nutrition and Health. We also acknowledge the CGIAR Fund Donors (https://www.cgiar.org/funders). Drs Peninah Nsamba and Dennis Muhanguzi were funded by the Research and innovations Fund (RIF) of Makerere University (grant number **MAK/DVCFA/481/19**)

We would like to thank Ms Esther Nambo, Ms Mary Nanfuka Lovincer and Mr Franklin Mayanja of the National Disease Diagnosis and Epidemiology Centre (NADDEC), Ministry of Agriculture, Animal Industries, and Fisheries (MAAIF) for their technical support during acquisition of the passive disease reports and laboratory reports.

We are sincerely grateful to the Dahlem Research School (DRS) and Univ.-Prof. Dr. Klaus Osterrieder for PhD supervision of Joseph Nkamwesiga.

Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. Administrative clearance to access and use disease outbreak reports and laboratory data was sought from the office of the Commissioner Animal Health, Ministry of Agriculture Animal industry and Fisheries. The work described under this study was approved by the Makerere University School of Veterinary Medicine and Animal Resources Institutional Animal care and Use committee (SVAR-IACUC) (Reference number: **SVAR_IACUC/58/2020**) and the Uganda national council of science and technology (reference number: **A103ES**). This work was also approved by the ILRI Institutional Animal Care & Use Committee (Reference number: **ILRI-IACUC2021-08**) and ILRI Institutional Research Ethics Committee (Reference number: **ILRI-IREC2021-07**).

AUTHOR CONTRIBUTIONS

JN: study conceptualization and design, data acquisition and analysis, writing and reviewing. FK: data analysis, visualization, writing and editing. PL, PN, FNM: writing and reviewing. KR: grant acquisition, writing and reviewing. HK and DM: study conceptualization, writing and reviewing. AP: data analysis, reviewing. BW: study conceptualization, design, writing and reviewing. All authors have read and approved this manuscript for publication.

DATA AVAILABILITY STATEMENT

The PPR outbreak reports data may be available on reasonable request from the corresponding author.

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How to cite this article: Nkamwesiga, J., Korennoy, F., Lumu, P., Nsamba, P., Mwiine, F. N., Roesel, K., Wieland, B., Perez, A., Kiara, H., & Muhanguzi, D. (2022). Spatio-temporal cluster analysis and transmission drivers for Peste des Petits Ruminants in Uganda. *Transboundary and Emerging Diseases*, *69*, e1642–e1658. https://doi.org/10.1111/tbed.14499