

ORIGINAL ARTICLE

Coupling spatial statistics with social network analysis to estimate distinct risk areas of disease circulation to improve risk-based surveillance

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Abstract

Most animal disease surveillance systems concentrate efforts in blocking transmission pathways and tracing back infected contacts while not considering the risk of transporting animals into areas with elevated disease risk. Here, we use a suite of spatial statistics and social network analysis to characterize animal movement among areas with an estimated distinct risk of disease circulation to ultimately enhance surveillance activities. Our model utilized equine infectious anemia virus (EIAV) outbreaks, between-farm horse movements, and spatial landscape data from 2015 through 2017. We related EIAV occurrence and the movement of horses between farms with climate variables that foster conditions for local disease propagation. We then constructed a spatially explicit model that allows the effect of the climate variables on EIAV occurrence to vary through space (i.e., non-stationary). Our results identified important areas in which in-going movements were more likely to result in EIAV infections and disease propagation. Municipalities were then classified as having high 56 (11.3%), medium 48 (9.66%), and low 393 (79.1%) spatial risk. The majority of the movements were between low-risk areas, altogether representing 68.68% of all animal movements. Meanwhile, 9.48% were within high-risk areas, and 6.20% were within medium-risk areas. Only 5.37% of the animals entering low-risk areas came from high-risk areas. On the other hand, 4.91% of the animals in the high-risk areas came from low- and medium-risk areas. Our results demonstrate that animal movements and spatial risk mapping could be used to make informed decisions before issuing animal movement permits, thus potentially reducing the chances of reintroducing infection into areas of low risk.

KEYWORDS

disease spread, movement flows, non-stationary Gaussian models, risk areas mapping, social network analysis

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1 | INTRODUCTION

Equine infectious anemia virus (EIAV) is a widespread disease of equids caused by a lentivirus member of the *Retroviridae* family, subfamily Orthoretrovirinae (Leroux et al., 2004). EIAV affects members of the *Equus* genus worldwide, with horses presenting the highest infection rate in warm and wet regions (Issel & Foil, 1984; Oliveira et al., 2017; Tigre et al., 2017). EIAV transmission is often related to direct contact with infected blood, milk, and other fluids; however, biting flies such as the horse fly, stable fly, and deer flies are known to be EIAV vectors (Issel & Foil, 2015). Therefore, regions where environmental conditions favor high vector densities make vector or iatrogenic transmission more likely and consequently increase the risk for disease of spatial local transmission (Barros & Foil, 2007; Machado et al., 2021).

Between-farm movements of infected, untested, or false-negative animals have been associated with short- and long-distance disease spread events (Büttner & Krieter, 2021; Cárdenas et al., 2019; Prem et al., 2019; Spence et al., 2017, 2018, 2019). Thus, understanding how farms are connected through between-farm animal movements is critical to, for example, (i) identify high-risk movements, (ii) uncover disease spread routes, and (iii) design improved surveillance and control strategies (Cardenas, VanderWaal, et al., 2021; Guinat et al., 2016; Machado et al., 2020). For the most part, disease control and surveillance programs in Brazil have clear definitions for permitting animals to move from farm to farm. Often, a negative diagnostic test result is required before movement permits are granted to individuals or groups of animals. If an animal is classified as positive, it is mandatory to be removed from the herd and euthanized. This process is different from other countries, such as the United States, where euthanasia or slaughter is not mandatory but is the option generally selected (Cardenas, Pozo, et al., 2021; Machado et al., 2021; Napp et al., 2019; Schiller et al., 2011; Zhang et al., 2018). However, movement permitting does not consider the spatial risks associated with infection-related risks at the farm of origin or the destination farm, unless the disease in question is a foreign animal disease in which case, movements are much more restricted (Shamoun-Baranes et al., 2014). Nevertheless, in Brazil, for most endemic and even reportable diseases, such as EIAV, animals are allowed to be transported among areas regardless of known or unknown disease occurrence and anticipated risk of disease dissemination (Barzoni et al., 2018; Fèvre et al., 2006). Therefore, the use of animal movements alone (e.g., ranking farms based on the number of animals transported to and into farms (Ezanno et al., 2020; Firestone et al., 2012)) to identify farms at greater risk of becoming infected or infecting others does not account for the risk of reintroducing infection in areas with greater potential of local transmission risk (Bjørnham et al., 2020; Cárdenas et al., 2019; Tao et al., 2021).

The approach proposed here is especially useful where monitoring of disease spread is carried out through passive surveillance systems (Jones et al., 2019; Machado et al., 2019) in which animal movement data are recorded on a regular basis (Duncan et al., 2022; Lentz et al., 2016; Notsu et al., 2020; Pozo et al., 2019). We integrate social

network analysis with geostatistical analysis to map the distribution of EIAV, delineate risk areas, and quantify animal movements between diverse risk areas (e.g., movements from low-risk to high-risk areas) to assess the potential role of movement in spreading EIAV throughout the study region.

2 | MATERIAL AND METHODS

2.1 | Study population and data sources

In Brazil, the movement of food animal species is regulated by the animal health office at the state level. In the case of horses, movement permits are issued upon presentation of a negative EIAV test. We obtained records of all EIAV tests ($n = 45,857$) performed between 2015 and 2017 in the state of Rio Grande do Sul; each individual test has an expiration date of 6 months, which means that movement issues are valid for the same number of months. National regulations (MAPA, 2020) for equine movements mandate that all weaned animals older than 6 months be accompanied by official negative test results for EIAV; thus, the test results used in this study are official diagnoses all related to pre-movement permits (SEAPA, 2016). The total equine population reported for this area in 2017 was 347,220 (MAPA, 2017). In addition, we obtained records of all between-farm horse movements from 2015 to 2017 with a total of 1,235,383 records in which 1,877,215 horses were moved, which consisted of geolocations of farms of origin and destination, movement types (e.g., reproduction, veterinary care), and the number of transported animals. Between-farm movement data were curated before further analysis. An in-depth data quality analysis was conducted on between-farm movement data to determine the volume of missing information regarding the date of movement, number of transported animals, and geolocation. EIAV test results and between-farm movement data were obtained from the official veterinary service SEAPDR-RS under a data use agreement (SEAPI, 2017).

2.2 | Mapping the spatial distribution of equine infectious anemia virus

The Brazilian legislation accepts enzyme-linked immunoassay and commercial agar gel immunodiffusion (IDGA) as diagnostic test. However, the IDGA is the confirmatory test with a sensitivity of 98.8% and specificity of 100% (Coggins et al., 1972). A positive EIAV was defined as a horse farm with at least one positive test for EIAV between 2015 and 2017. In total, we identified 158 newly reported cases, and the control group was sampled from the list of farms that had issued at least one movement and in which all EIAV tests between 2015 and 2017 were negative. The movements of animals that have tested positive are banned; therefore, there are no records of the entry or exit of positive animals between Brazilian states. The case-control ratio was 1:5, with control farm samples from the same municipality of the pair(s) cases.

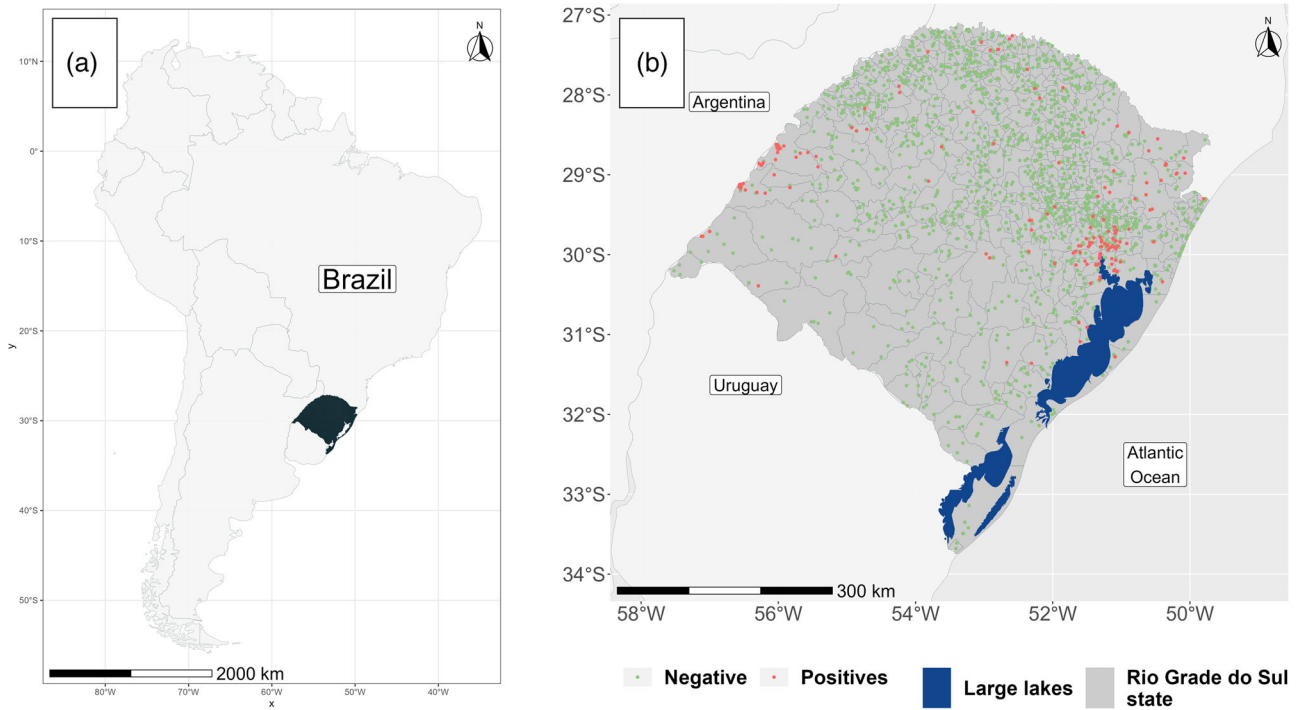


FIGURE 1 a) Map with South America showing the location of the study area (the Rio Grande do Sul) in the black fill shape. (b) Spatial distribution of 158 equine infectious anemia virus (EIAV)-positive farms in red and 2202 negative sites in green; major lakes are represented in blue.

In the case of municipalities where no cases were detected, five farms were sampled following the same criteria described above. In total, 2202 controls were sampled from 497 municipalities (Figure 1).

2.3 | Network analysis

From the movement data, we reconstructed yearly networks for 2015, 2016, and 2017, as well as the multiyear network that included the entire study period. Briefly, we utilized the unique identification of each municipality and the movements of animals to form the edges of the network. Thus, we considered the network as a graph $g = (V, E)$, where V represents the nodes (municipalities) of the network, and E represents the unique contact between two nodes or edges of the network. Network terminology is described in Table S1. Here, the graph was represented by an adjacency matrix A with $(A)_{ij} = 1$, if there was a connection between the source nodes i and destination nodes j , and $(A)_{ij} = 0$ otherwise. Directed contact networks were $(A)_{ij} \neq (A)_{ji}$ due to contacts having a particular origin (node i) and destination (node j) with a specific direction (Jackson, 2008). Movements with the same origin and destination were removed from this analysis since no edges were formed. To characterize the static network, the parameters derived from the social network analysis metrics in-degree, out-degree, PageRank (Brin and Page, 1998), clustering coefficient, closeness centrality, and betweenness (Freeman, 1978; Wasserman and Faust, 1994; Watts and Strogatz, 1998) were calculated by year,

and for the entire study period, all metrics used are described in Table S1. A more detailed network analysis of horse movements in this same study area was already described by Cárdenas et al. (2019); therefore, we only included a brief description of the network.

2.4 | Mapping covariates and data preparation

We identified four environmental covariates potentially affecting EIAV distribution by modifying vector populations, including two land cover covariates and two climate covariates. The geolocations of cases and control farms were then used to extract the following variables: land surface temperature represented by the annual average temperature (Krcmar, 2005), annual average precipitation (Mullens, 2019) in millimeters provided by WorldClim (worldclim, 2021), soil moisture (Blahó et al., 2013), and normalized difference vegetation index (NDVI) (Baylis et al., 1998), both obtained from the Copernicus Global Land Service (JRC, 2021). All covariate values were summarized by calculating the mean for the full study period. All variables listed above were at ~ 5 min of spatial resolution from the equator. Similarly, we used the between-municipality movement networks to calculate the following metrics: in-degree and out-degree, PageRank, cluster coefficient, closeness centrality, betweenness, in-degree, and out-degree centralization, which were later extracted for each farm based on their geolocation. These parameters are described in detail in Figure S2 and Table S3.

2.5 | Bayesian hierarchical spatial models framework

We implemented a spatial hierarchical model to account for the environmental and network metrics covariates, considering spatial stationarity and non-stationarity models. The specific farm locations i of cases and controls were defined as Y_i . Each farm location i ($i = 1, \dots, n$, $n = 2624$) is given as Y_i , where $Y_i = 1$ if EIAV was present and $Y_i = 0$ otherwise. The hierarchical generalized base spatial model for the first level is modelled as a logit model, Y_i via binomial distribution,

$$Y_i = \text{Logit}(\mu_i). \quad (1)$$

We constructed the following linear predictor:

$$\text{Logit}(\mu_i) = \alpha + \beta_j \cdot X_i + v(s_i) + \omega(s_i) \quad (2)$$

where μ is the probability of EIAV occurrence, α is the model intercept, $\beta_j \cdot X_i$ describes a matrix of all environmental and network metrics covariates, $v(s_i)$ is an independent and identically distributed (iid) random effect to account for variation between individual farms, and $\omega(s_i)$ provides a spatial random field (Gaussian field) to account for spatial errors. Since large lakes are present in the state of Rio Grande do Sul, the spatial processes were not assumed to be uniform (non-stationarity field) following the approach proposed by (Bakka et al., 2019; Elias T. et al., 2019).

Briefly, we used a stochastic partial differential equation (SPDE) approach to analyze the spatial point data and to calculate the marginal posteriors using the integrated nested Laplace approximations (INLA) approach implemented with the R-INLA framework in the R language environment (Bakka et al., 2018; Elias T. et al., 2019; van Niekerk et al., 2021), which first requires the creation of a mesh of Delaunay triangulation (Figure 2), including the specification of a maximum triangle edge length, a model domain boundary, and the location of barriers within the domain (Bakka et al., 2019). The maximum triangle edge length was specified as 10 km within the inner domain and 20 km in the outer domain; the boundary of the domain was constructed as a polygon of the state of Rio Grande do Sul, and the barriers were specified as the location of major lakes within the state. The resulting mesh created using R-INLA is presented in Figure 2 and consists of 2,766 triangle vertices. In addition, we specified a barrier model to prevent the estimated spatial error from terrestrial sampling sites from being extrapolated into open water areas as suggested elsewhere (Martínez-Minaya et al., 2018).

The default and recommended settings for priors were adopted; thus, we used penalized complexity priors (Fuglstad et al., 2019; Simpson et al., 2017) for the spatial random fields where the spatial range and standard deviation quantile and probability tailored to be higher than 1 is 0.01. (Rue et al., 2009; Sultaire et al., 2022). We explored the sensitivity to priors to the posterior random field values by comparing the Watanabe–Akaike information criterion (WAIC) and the random posterior mean distribution values (Table S3).

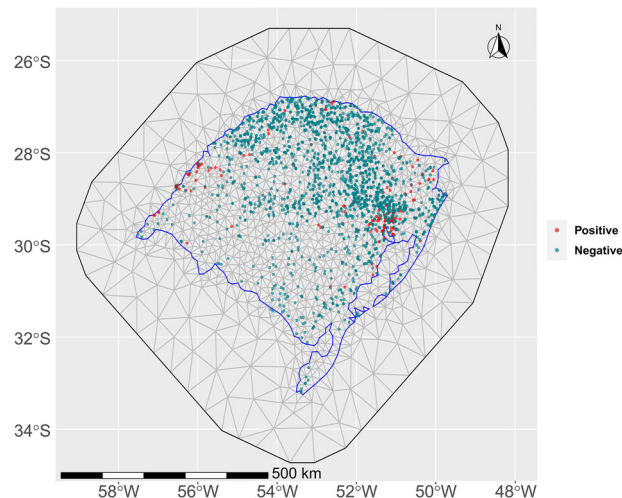


FIGURE 2 Equine infectious anemia virus (EIAV) data are plotted in red cases and in green controls. Grey triangles show the spatial mesh of Delaunay triangulations created using R-integrated nested Laplace approximations (INLA); the blue line represents the border for the state considering physical barriers (large lakes)

TABLE 1 Model nomenclature and selection

Model	Model formula	WAIC
Intercept model	$\text{Logit}(\mu_i) = \alpha + \beta_j \cdot X_i$	8,778.03
Spatial model	$\text{Logit}(\mu_i) = \alpha + \beta_j \cdot X_i + v(s_i)$	1,331.74
Barrier model	$\text{Logit}(\mu_i) = \alpha + \beta_j \cdot X_i + v(s_i) + \omega(s_i)$	1,267.89

Abbreviation: WAIC, Watanabe–Akaike information criterion.

2.6 | Model fitting and comparison

For model fitting and selection, we compared three candidate model structures (Table 1). The first model was constructed with an intercept only used to benchmark models with spatial terms. The second model considers the spatial-effect term (stationary GRF) without barriers, and the third model considers the presence of a physical barrier term (non-stationary GRF). The best model, without any covariates, was selected based on the WAIC.

We evaluated a number of candidate covariate models while following our conceptual framework (Figure 3), which rests on the following assumptions: temperature, along with precipitation, promotes the formation and maintenance of soil moisture that might contribute to the growth of vegetation, thus increasing EIAV vector densities and the stability of the virus in the environment (Barros & Foil, 2007). On the other hand, municipalities with the greatest movement of horses, thus highly connected via animal transportation contact networks, are more prone to receiving infected animals, thus increasing the chances of EIAV dissemination (Cárdenas et al., 2019). For covariate selection, we used the best model, which was the one with the non-stationary barrier term (Table 1). We first analyzed the candidate variable via univariable analysis (Table 4). Significant variables were selected for the multivariable backward elimination analysis, where all variables with 95% credible

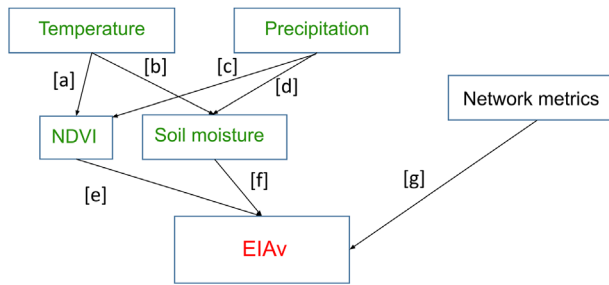


FIGURE 3 Conceptual model: The conceptual model describes the association between environmental characteristics and network metrics as a function of Equine infectious anemia virus (EIAV) cases

intervals (95% confidence interval [CI]) in which zero was not included were considered.

2.7 | Risk flow between risk areas

We used the final covariate barrier model to estimate the posterior mean probabilities of EIAV occurrence, which were then used to categorize each municipality into three EIAV risk areas by using Jenks's natural breaks of the aggregated posterior mean probability values. Thus, municipalities at high risk were between $\mu = 0.38$ and 2.45, municipalities at medium risk were between $\mu = 0$ and 0.38, and municipalities at low risk were between $\mu < 0$. Finally, we utilized the between municipalities' horse movements to identify and count the number of in-going and out-going movements among the three risk areas. We have also measured the distances (km) between the origin and the destination of each movement. Briefly, the Euclidean distance between the municipalities of origin and destination was calculated and further examined by plotting the empirical cumulative distribution and the distance in km for movements within the same risk areas (e.g., from high-risk to high-risk areas) and between different risk areas (from low-risk to high-risk areas) (Figure S7).

All the analysis and data visualization presented in this work were conducted in R software (Core Team, 2021) using the packages tidyverse (Wickham et al., 2019), INLA (Bakka et al., 2018), sf (Pebesma, 2018), ggspatial (Dunington, 2021, p. 2), brazilmaps (Prado Siqueira, 2021), INLAutils (W Redding et al., 2017), INLAoutputs (Santos Baquero, 2018), inlabru (E. Bachl et al., 2019), rgeos (Bivand & Rundel, 2021), circlize (Gu et al., 2014), and raster (J. Hijmans, 2021).

3 | RESULTS

3.1 | Animal movement description and data quality analysis

A total of 1,877,215 horses were transported between 2015 and 2017, which amounted to 1,235,383 movements among 497 municipalities. A moderate increase in EIAV cases was seen for the period from 2015 to 2016 (Table 2). A total of 1,170,471 (94.74%) between-farm

TABLE 2 Yearly horse movement frequency, total animals moved, and the number of equine infectious anemia virus (EIAV) cases in the state of Rio Grande do Sul, Brazil

Year	Number of movements	Total number of transported animals	Number of EIAV cases
2015	266,334	428,665	47
2016	497,566	740,349	66
2017	471,483	708,201	45

movements had at least one data-related issue (e.g., missing geolocation), which limited our ability to reconstruct farm-to-farm contact networks. The main issue with the movement data was related to origin and destination farms having the same farm identification in the origin and destination present in 1,148,789 (92.98%) of between-farm movements. Missing geolocation was the second most prevalent issue, with 452,616 (36.63%) movements; however, 100% of the movements, 1,235,383, had accurately identified municipalities of origin and destination, date, and the number of moving animals, which allowed for the reconstruction of the contact network among municipalities.

3.2 | Between-municipality movement networks

Our results did not show a significant variation in the number of horses transported between municipalities over the course of the 3 years. The majority of the municipalities (441, 88.73%) received or sent at least one animal throughout the study period. Over time, the number of edges and the total number of horses increased from 2015 to 2016; consequently, it is reflected in the increasing values in graph density (Table 3). Last, the average in-degree and out-degree also increased from 33.50 to 43.32 from 2015 to 2017 (Table 3).

3.3 | Model formulation and selected covariate variables

Of the three spatiotemporal models (Table 4), the model with the barrier effect had the most suitable fit and was used in the covariate selection procedure. Univariate analysis showed that precipitation, in-degree, and out-degree were significantly associated with EIAV (Table 4). Because in-degree and out-degree were correlated and in-degree was a better fit than out-degree, we eliminated out-degree from the final model. Additionally, variables that included number one within the quantile 0.25–0.75 in the distribution of the fixed effect were not considered significant and were removed from the final barrier model (Table 4). Thus, the selected final model considered precipitation and the number of movements into municipalities (in-degree).

Higher risk values were observed closer to the border with Argentina, Porto Alegre metropolitan area, and near large lakes in the Southwest (Figure 5a). We identified 56 (11.3%) municipalities at high risk for EIAV, while 48 (9.66%) were estimated to have medium spatial

TABLE 3 Between-municipality networks metrics for 3 years of between-municipalities movements. Overall and yearly graph density, number of edges, nodes, the total number of horses transported between municipalities, and in-degree and out-degree averages with their 95% confidence interval (CI 95%)

Year	Graph density	Nodes	Edges	Mean of in-degree (CI 95%)	Mean of out-degree (CI 95%)
All years	0.12	497	31,726	63.83 (68.02, 71.78)	63.83 (59.51, 68.15)
2015	0.06	487	16,317	33.50 (30.76, 36.24)	33.50 (30.72, 36.28)
2016	0.08	493	21,157	42.91 (39.86, 45.96)	42.91 (39.81, 46.01)
2017	0.08	496	21,489	43.32 (40.35, 46.29)	43.32 (40.28, 46.36)

TABLE 4 Summary statistics of the fixed effects of the barrier model

Covariate	Univariate				Multivariate			
	Mean	Quantile 0.025	Quantile 0.975	WAIC	Mean	Quantile 0.025	Quantile 0.975	WAIC
In-degree	1.006	1.003	1.009	1,261.19	1.006	1.003	1.009	1256.16
Out-degree	1.006	1.003	1.009	1,262.19	-	-	-	-
PageRank	7.10	-5.72	9.64	1264.91	-	-	-	-
Clustering coefficient	0.002	-2.662	0.002	1259.69	-	-	-	-
Closeness centrality	1.95	4.89e-26	3.01	1267.62	-	-	-	-
Betweenness	1	0.99	1	1268.95	-	-	-	-
Precipitation	1.019	1.003	1.037	1261.95	1.016	1.002	1.033	-
Soil moisture	1.011	0.989	1.037	1267.77	-	-	-	-
Temperature	0.998	6.99e-01	1.377	1268.85	-	-	-	-
NDVI	1	1	1	1270.50	-	-	-	-

Abbreviation: NDVI, normalized difference vegetation index; WAIC, Watanabe–Akaike information criterion.

risk and 393 (79.1%) were considered low risk (Figure 4b). Finally, high standard deviation values were observed in the south of Rio Grande do Sul (Figure S6); therefore, risk estimates for this area should be interpreted with caution. Our sensitivity analysis did not reveal significant differences between the priors tested (Table S4 and Figure S5).

3.4 | The movement of horses between risk areas

We used the spatial posterior mean at the municipality level of the final barrier model (Figure 4b) and the animal movements between municipalities to identify key areas in which in-going and out-going movements were more prone to facilitate disease dissemination. The spatial distribution of the risk areas and the movement flows among them are shown in Figure 5a. The majority of the movements were between low-risk areas, representing 848,433 (68.68%) of all animal movements. The remainder of the movements were 117,060 (9.48%) and 76,640 (6.2%) for high- and medium-risk areas, respectively. Only 5.37% of the animals transported into low-risk areas came from high-risk areas. On the other hand, 92,148 (4.91%) of the animals in high-risk areas came from low- and medium-risk areas (Figure 5b and Table S7). Finally, we recovered the distribution of EIAV cases within each risk

zone. We observed a total of 29 cases in low-risk areas, 17 in medium-risk areas, and 112 in high-risk areas. The number of cases was divided by the total number of municipalities for each risk-zone area, which amounted to 3.28% cases per municipality in low-risk areas and 14.9% and 81.8% for medium-risk and high-risk areas, respectively.

4 | DISCUSSION

Our findings are the result of an integrated approach that coupled Bayesian hierarchical non-stationary spatial analysis (Battle et al., 2019; Emch et al., 2012; van Niekerk et al., 2021) with social networks analysis (Chen & Lanzas, 2016), which allowed us to demonstrate significant evidence of horse movements among areas of distinct risk for EIAV circulation. We estimated the probabilities of EIAV occurrence, which was used to classify municipalities into three risk areas, (1) high-risk, (2) medium-risk, and (3) low-risk, which were later used in conjunction with animal movement to calculate the number of movements among the distinct risk areas. Our results showed that the majority of movements (84.35%) were within areas of the same risk classification, while 15.65% of animal movements occurred between areas with different risk classifications (e.g., high risk to low risk). We

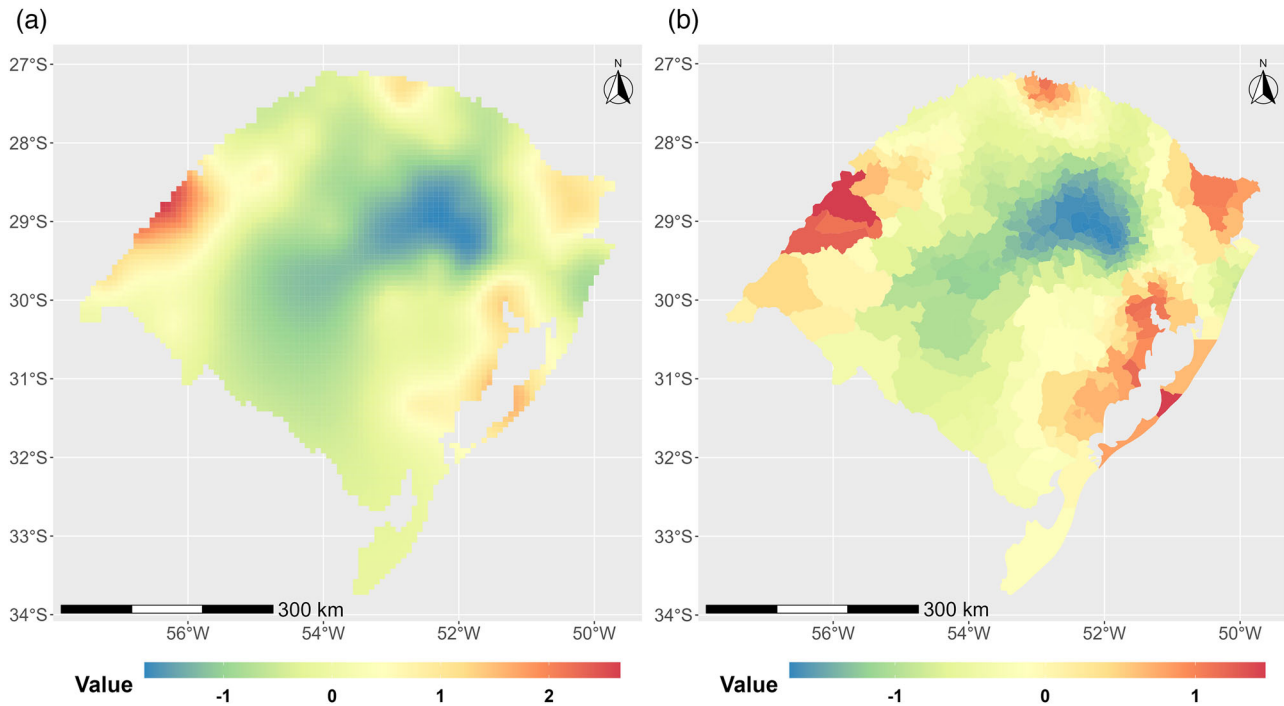


FIGURE 4 Spatial variation in posterior fitted values. (a) The posterior predictive mean values per pixel area of 56 km². (b) The aggregated posterior mean probabilities for each municipality in the state of Rio Grande do Sul, Brazil.

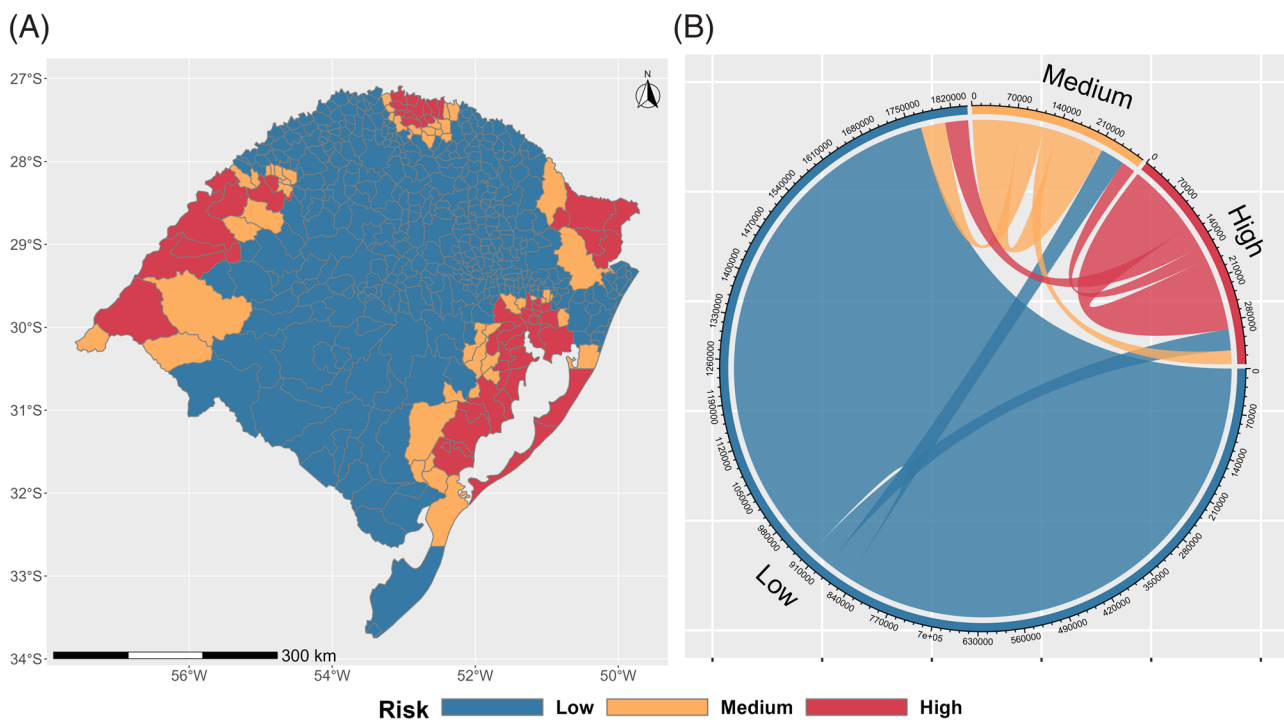


FIGURE 5 Spatial distribution of risk areas for each municipality and the number of movements between them. (a) The spatial patterns of the equine infectious anemia virus (EIAV) probability of occurrence in the state of Rio Grande do Sul, Brazil. (b) The circular plot shows the horse movement plot among the municipalities considering the three risk levels. The origins and destinations of movements are each assigned risk colors. The origin of the flow movements is encoded by the external ring area, and the bandwidth represents the total of in-going and out-going movements

remark that the described movement patterns restricted within high-risk areas could be driving the current endemic levels of EIAV, as indicated by the 129 (81.64% of the total cases) cases being in high- to medium-risk areas (Figure 5a), and only 29 (18.36%) cases were found in low-risk areas.

Comparing the non-stationary fields (barrier model) and stationary models, we found that including geographical barriers (large lakes in the southeast of Rio Grande do Sul) significantly improved the model fitting. A possible explanation could be associated with the vector-borne transmission of EIAV, which is the main mode EIAV is transmitted locally (short distances between farms). Biting flies such as horse flies, deer flies, and stable flies have been described as efficient vectors (Barzoni et al., 2018; Nogueira et al., 2017) that can only fly 4.9–6.8 km away from the initial marking station within 5 days. However, a significant percentage of tabanid flies were able to transmit EIAV to other horses within a range of 5–25 m, still limiting feasible transmission to short distances (Barros & Foil, 2007). Briefly, the barrier model disconnected the spatial process across the physical barriers (large lakes), blocking spurious dependence from EIAV traveling between two farms that were near each other in Euclidean distance but far away in geodesic distance in the spatial domain. Not only is the barrier model superior when compared with the spatial model (Table 1), but Figure S6 reveals that the standard deviation resulting from the barrier model appears to be substantially reduced by the addition of barrier term $\omega(s_j)$. Even with the development of the R-INLA, inlabru, and rSPDE packages (E. Bachl et al., 2019; Bolin & Kirchner, 2020; van Niekerk et al., 2021), more specifically the work done by Bakka et al. (2019) that implemented the option for a non-stationary barrier model directly via R-INLA, the vast majority of non-stationary models have been limited to ecology (Bell et al., 2021), fisheries (Monnahan et al., 2021), and theoretical studies (Lindgren et al., 2022; Sanz-Alonso & Yang, 2021). One reason for a lack of studies that include the explicit effect of barriers in animal disease epidemiology may be associated with the challenges of model implementation, which have been resolved by Bakka et al. (2019). The relevance of non-stationary field approaches in animal disease epidemiology is mainly targeted at diseases that disseminate locally, such as West Nile virus (Siqueira et al., 2022), Brazilian spotted fever (Moraes Filho et al., 2019), and piroplasmiasis (Minervino et al., 2020).

Our proposed model identified two covariates associated with the increased probability of EIAV occurrence: precipitation and in-degree. The association between increased precipitation and EIAV may be due to the formation and maintenance of water bodies and favourable conditions for vector breeding sites and enhanced environmental suitability (Hemming-Schroeder et al., 2018). This is especially true for regions where EIAV is endemic, and hot, humid rainforest environments support a very high density of horse and deer fly populations throughout the year (Resende et al., 2021). On the other hand, we also found that municipalities with high in-degree are more likely to have farms that tested positive for EIAV, as expected since the most relevant mode of between-farm transmission has been related to the transportation of infectious animals between farms (Firestone et al., 2011, 2012; Spence et al., 2017; Squarzoni-Diaw et al., 2021).

The number of EIAV cases at the border between Brazil, Argentina, and Uruguay have been high for the past several years. Of these, Uruguay is the only country where this disease is not endemic, while northeast Argentina and most Brazilian territories are in an endemic situation (Barzoni et al., 2018; Nogueira et al., 2017; Sandrigo et al., 2021). The recurrent spread has been associated with the illegal transport of untested horses across the borders. In the current study, we demonstrate that most transportation events were between municipalities in proximity to each other, with movements from and to high-risk areas being shorter than movements among municipalities of low risk (Figure S7). Therefore, our result suggests that EIAV dissemination may remain to be contained within high-risk municipalities, which for the most part may be explained by the structure of the between-farm contact networks with most movements within the same risk areas (Martínez-López et al., 2014; Sintayehu et al., 2017). In the same vein, a previous study described how glanders was disseminated among farms within the same study area, with most cases within one network step from infected farms (Cárdenas et al., 2019). Nevertheless, we cannot exclude the changes in EIAV dissemination into low-risk areas, since those areas have suitable environmental conditions and host a wide range of EIAV vector species (Hemming-Schroeder et al., 2018) while also receiving approximately 6.16% of horses from high-medium risk areas. Ultimately, our results suggest that the risk of further spatial propagation of EIAV seems to be limited. Restricting the movement within the same risk level to minimize long-distance transmission appears to be the next logical step in reducing EIAV infections. The highest number of horses is located in the southern region of the state, with some specific exceptions in the municipalities of 'Capão da Canoa' and 'Chuvisca', where the population was high in proportion with their area (Figure S8). Interestingly, the horse density was not correlated with the high-risk areas, suggesting that animal density is not related to the high-risk areas of EIAV at the municipality level.

5 | LIMITATIONS AND FURTHER REMARKS

This study had some limitations. First, the selection of control farms was sampled from sites that moved at least one animal between 2015 and 2017. However, we cannot exclude the possibility that there were other animals in the place of origin, which may be infected with EIAV (Machado et al., 2021). Additionally, the EIAV tests are valid for 6 months, which does not guarantee that negative animals will remain negative for the entire six months. On the other hand, due to the volume of horses that are tested from 495 municipalities, we are confident that the data used here were able to capture the spatial pattern of the disease. Even though the literature suggests the effect of seasons in the dissemination of EIAV, often driven by the increase in the population of EIAV competent vectors (e.g., horse flies) (Lucas et al., 2020), we remark on the challenges in explaining the role of iatrogenic transmission. Another limitation was the lack of accounting for illegal or unreported movements and their influence on the network. Legal movements can be detected and banned when cases are caught.

However, the unlawful movements could contribute to the EIAV spread. In addition, we may have missed infected movements coming from other states. Despite great efforts from the local government to improve the current movement data system, the quality of the data precluded the proper identification of the farm of origin and destination. For this reason, we work at the municipality level, which manages to capture the equine movement patterns at the state level quite well. Finally, combining Bayesian hierarchical non-stationary barrier mode and social network analysis warrants further research and would benefit from an in-depth evaluation compared to more traditional approaches (van Niekerk et al., 2022). In addition, we cannot inform the stability of these areas over large periods of time given variations due to climate change and animal movement patterns. Therefore, future work will be necessary to support or update these findings.

6 | CONCLUSION

Our proposed methodological approach that combines social network analysis and non-stationary spatial regression not only sheds light on where EIAV may persist but also demonstrates the risk of transporting animals between different risk areas. The current study demonstrated a methodological approach that combined social network analysis and non-stationary spatial regression to determine where EIAV may persist and determine the risk of transporting animals into specific areas. The majority of the movements were contained within municipalities of high-risk areas, which could explain the restricted number of EIAV in those areas ($n = 112$ cases). EIAV is hard to control, mainly because infected animals show little to no clinical signs; thus, infected individuals are detected via passive surveillance, serological testing, and testing necessary for movement permits. Such delay in detection reinforces the need for a better understanding of EIAV distribution, which may be achieved by estimating the spatial and spatiotemporal patterns of the disease. Animal health authorities may use this information to make decisions about animal movement permits by restricting or enhancing the monitoring of horses transported from high-risk municipalities into low-risk municipalities. The approach established here may be applied in the future at a larger scale in other Brazilian states, and the results may be integrated into movement permits of other food-animal systems.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Nicolas C. Cardenas and Gustavo Machado conceived the study. Nicolas C. Cardenas and Gustavo Machado participated in the design of the

study and model formulation. Francisco P. N. Lopes coordinated the movement data collection. Nicolas C. Cardenas conducted data processing and coding. Nicolas C. Cardenas, Felipe Sanchez, and Gustavo Machado wrote and edited the manuscript. Gustavo Machado secured the funding. All authors discussed the results and critically reviewed the manuscript.

DATA AVAILABILITY STATEMENT

The raw data that support the findings of this study are not publicly available and are protected by confidential agreements; therefore, the data are not available.

ETHICS STATEMENT

The authors confirm the ethical policies of the journal, as noted on the journal's author guidelines page. Since this work did not involve animal sampling or questionnaire data collection by the researchers, there was no need for ethics permits.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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