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ORIGINAL ARTICLE

Spatiotemporal distribution of classical swine fever in Cuba, 2007 - 2013

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ABSTRACT: Classical swine fever (CSF) is an endemic disease in Cuba with significant economic impact on the swine industry, not only for the animal losses, but also for the operating expenses of the national coverage control program (technical staff, surveillance, diagnosis, vaccines, disinfectants, etc.). For implementing more effective control and eradication measures, the epidemiological analysis is necessary for a better understanding of the disease spatial and temporal distribution. With this aim, it was used the information about municipalities with CSF outbreaks during a seven-year period (2007-2013) registered by the Epizootiological Surveillance System. The spatiotemporal scan statistics analysis was performed; a Bernoulli probabilistic model was used to detect clusters of outbreak occurrence. Also, a temporal analysis was made through logistic regression. Three significant clusters (p<0.05) of high rates were detected, two of them from 2007 to 2009 with relative risks (RR) of 1.99 and 1.8, respectively. The third cluster had a RR=2.46 in 2008. Also two low rates clusters were observed, the first with a RR= 0.08 from 2009 to 2011, and the second with a RR= 0.43 from 2011to 2012. Furthermore, a tendency to a decreasing percentage of affected municipalities was observed in the studied period; a low risk of the municipalities to be affected were observed in 2011 (OR: 0.518, 0.332-0.809, I.C. 95%, p=0.004) and 2012 (OR: 0.577, 0.371-0.897, I.C 95%, p=0.015). Finally, to investigate the factors associated with the clusters of disease outbreak occurrence is the next step to progress in the CSF control and eradication campaign in the country.

Key words: Classical swine fever, Cuba, spatiotemporal distribution, clusters, tendency.

Distribución espaciotemporal de la peste porcina clásica en Cuba, 2007 - 2013

RESUMEN: La peste porcina clásica (PPC) es endémica en Cuba, con un impacto económico significativo en la industria porcina, no solo debido a la mortalidad, sino también a gastos operacionales (personal, vigilancia, diagnóstico, vacunas, desinfectantes, etc.). Para implementar medidas de control y erradicación más efectivas es necesario realizar análisis epidemiológicos para comprender mejor la distribución espacial y temporal de la enfermedad. Con este propósito, se utilizó la información registrada por el Sistema de Vigilancia Epizootiológica sobre los municipios con brotes de PPC durante un periodo de siete años (2007-2013). Se realizó un análisis espaciotemporal mediante *scan statistics* con el empleo del modelo probabilístico de Bernoulli para detectar conglomerados de ocurrencia de brotes. También, se realizó un análisis temporal a través de regresión logística. Se detectaron varios conglomerados significativos (p<0.05); dos de ellos, de altas tasas, desde el 2007-2009 con riesgo relativo (RR) de 1,99 y 1,8, respectivamente. El tercer clúster mostró un RR= 2,46 y ocurrió en 2008. Asimismo, se observaron dos conglomerados de bajas tasas: el primero con RR= 0,08, desde 2009-2011, y el segundo con RR= 0.43, desde 2011-2012. Además, en el periodo estudiado se observó una tendencia decreciente en el porcentaje de municipios afectados; y los años 2011 (OR: 0,518; 0,332-0,809; I.C. 95%; p=0,004) y 2012 (OR: 0,577; 0,371-0,897; I.C 95%; p=0,015) mostraron un riesgo bajo de afectación en los municipios. Finalmente, investigar los factores asociados con los conglomerados de ocurrencia de brotes es el primer paso para progresar en la campaña de control y erradicación de la enfermedad.

Palabras clave: Peste porcina clásica, Cuba, distribución espaciotemporal, conglomerados, tendencia.

INTRODUCTION

Classical swine fever (CSF) is considered one of the most important and economically damaging pig diseases worldwide(1). It is caused by CSF virus, a *Pestivirus* belonging to the *Flaviviridae* family (2). The disease remains endemic in many countries of South and Central America, Africa, and Southeast Asia, and sporadic outbreaks have been affecting the European countries (3).

Economic losses in the event of an outbreak are often very extensive, due to both direct and indirect impacts. They can be experienced due to pig deaths, reduced reproductive and growth performance, as well as implemented control strategies where compulsory slaughter and movement restriction further increase costs (4).

In Cuba, after a long period without CSF cases, the disease has become endemic since 1993 with several outbreaks each year despite the implemented control program (5, 6). Difficulties in vaccine production and conservation (cold chain) and the increase of backyard producers with the well-known breaches on biosecurity have been factors with a decisive influence on case occurrences. In 1996, it became necessary to declare a national emergency and to activate the Civil Defense System and its respective provincial offices(7). Until now, several human and financial resources have been used without the expected success in the control of the disease (8).

Pork meat is one of the most important protein sources of animal origin for the Cuban population. Every year, CSF outbreaks cause enormous losses to commercial farms, but also to the economy of a great number of backyard pig producers for their own consumption or sale of live animals or their products. Therefore, as CSF affects food security, its control as soon as possible is considered a priority in Cuba.

The Cuban Official Veterinary Service, along with pig producers and other organizations have developed a CSF eradication strategy. This strategy proposes to start the campaign by two provinces, Pinar del Río, the most western province, and Guantánamo, the most eastern province. The goal is to eradicate the disease in Cuba before 2020.

One of the first steps for developing a control and eradication campaign is to analyze the spatial and temporal distribution of the disease in the country to detect its geographical patterns (e.g., clusters). Disease clusters can help in identifying common environmental factors or sources of exposure (9). Scan statistics is an effective and accurate method for analyzing spatial, temporal and space-time data (10).

The aim of this study was to identify the spatial and temporal distribution of CSF outbreaks in Cuba, detect high and low-risk areas, and support the control strategy for the disease eradication.

MATERIALS AND METHODS

- Study area

The study area was the entire country. Cuba is located in the entrance of the Gulf of Mexico, in the western part of the Caribbean Sea, from 19º49´ - 23º16´ north latitude and 74º08´ - 84º57´west longitude, and has a total surface of 109 884.1 km2. Cuba is divided into 15 provinces and one special municipality (Isla de la Juventud). Each province is also divided into municipalities (168 in the whole country). Furthermore, Cuba is geographically divided into three regions (Figure 1), the Western region with five provinces (Pinar del Río, Artemisa, Mayabeque, La Habana, and Matanzas), Central region with five provinces (Cienfuegos, Villa Clara, Sancti Spiritus, Ciego de Ávila, and Camagüey), and the Eastern region with five provinces (Las Tunas, Granma, Holguín, Santiago de Cuba, and Guantánamo).

- Data sources and case definition

We used data of CSF outbreaks compiled by the National Surveillance Epizootiological System (Sistema de Vigilancia Epizootiológica, SIVE) during a seven-year period (2007 - 2013). The cases considered were those municipalities where at least one CSF outbreak occurred during each year, whereas those with no outbreaks during each corresponding year were the controls.

- Spatiotemporal analysis

Isla de la Juventud was excluded of the study because of the effect due to absence of geographical continuity. We assume the centroid of municipalities as a location of cases and controls. A retrospective spatiotemporal analysis for clustering detection was made using the Bernoulli probabilistic model in SaTScan, Scan Statistics Software, v 9.3 (10).The models assumed that the affected municipalities were randomly distributed in space and time under the null hypothesis. The maximum cluster size was set at 25% of the population at risk. The statistical significance of clusters was evaluated through Monte Carlo simulation using 99999 repetitions. The scan was made for detecting areas with high and low rates of outbreak occurrences with no geographical overlap. The output was geographically represented through ArcGIS 10.2 (ESRI).

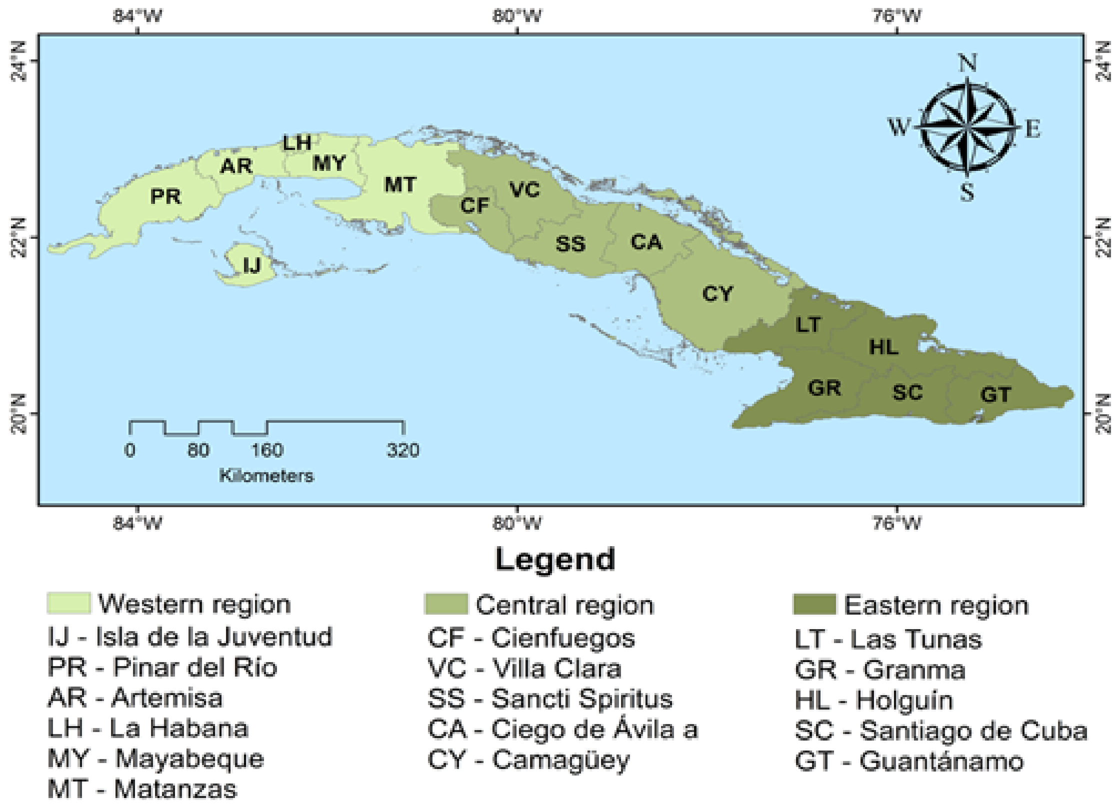

FIGURE 1. Cuban regions and provinces. / *Regiones y provincias de Cuba.*

- *Trend analysis*

A logistic regression was used to evaluate the temporal tendency of the proportion of affected municipalities by years through IBM SPSS Statistic software (Version 21.0.0.0). As dependent variable was used the presence (1) or absence (0) of outbreaks by year. Time (years) was considered as an independent variable. In the first analysis, the variable «Years» was included without categorization and in the second analysis was analyzed as a categorical variable.

RESULTS

- *Space-time scan statistics*

During the studied period, an average of 41.4% of the municipalities was affected by CSF each year. The highest percentage (53.9%) of the affected municipalities occurred in 2008, and the lowest percentage (31.7%) was observed in 2011.

Scan statistics identified three significant high rate spatiotemporal clusters, located each one in the three different regions: central, eastern and western regions, respectively (Figure2 and Table 1). Also, two low rate spatiotemporal clusters were detected in the western and eastern regions (Figure 3 and Table 1).

- *Temporal analysis*

A maximum number of affected municipalities was observed in 2008, and a minimum in 2011. A decreasing tendency (OR: 0.891, 0.84 - 0.945, I.C. 95%, p=0.000121) was also exhibited by the proportion of affected municipalities (Figure 4). The risk of a municipality to be affected was 10.9% less each year.

Using as a reference the first year (2007) of the studied period, the years 2011 (OR: 0.518, 0.332 - 0.809, I.C. 95%, p=0.004) and 2012 (OR: 0.577, 0.371 - 0.897, I.C 95%, p=0.015) had the significantly lowest risk of a municipality to be affected by CSF (Table 2).

Taking into account the tendency of the CSF affected municipalities, it can be seen that, if this tendency is maintained over time, approximately 18 % of the Cuban municipalities will be affected in 2020 (Figure 5).

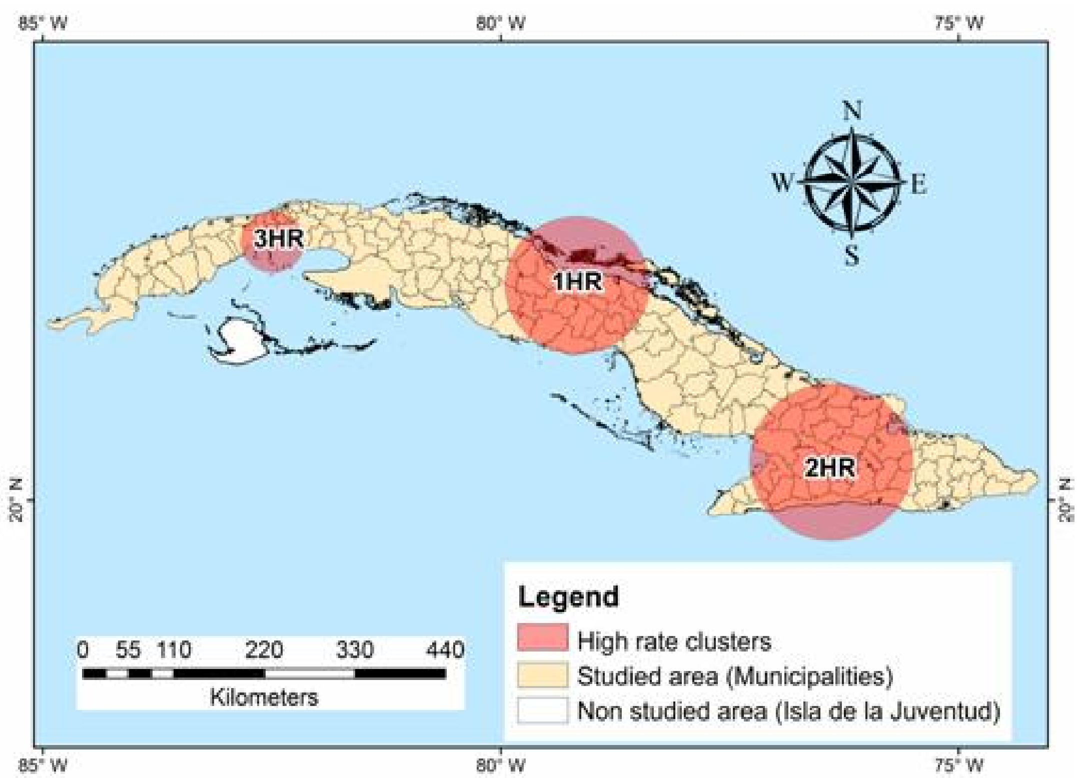

FIGURE 2. Representation of the high rate spatiotemporal clusters./ *Representación de los conglomerados espaciotemporales de altas tasas.*

TABLE 1. High and low rate spatiotemporal clusters./ *Conglomerados espaciotemporales de altas y bajas tasas*

CLUSTER	REGION	PROVINCES	INVOLVED MUNICIPALITIES/ TOTAL (%)	RADIUS (KM)	PERIOD	P-VALUE	RR*
1HR	Central	Villa Clara Sancti Spíritus Ciego de Ávila	6/13(46.2) 7/8(87.5) 7/10(70.0)	81.2	2007-2009	0.00007	1.99
2HR	Eastern	Las Tunas Holguín Granma Santiago de Cuba	4/8(50.0) 10/14(71.4) 9/13(69.2) 9/9(100)	92.8	2007-2009	0.00013	1.80
3HR	Western	Artemisa La Habana Mayabeque	7/11(63.6) 3/15(20.0) 4/11(36.4)	35.7	2008	0.01045	2.46
1LR	Western	La Habana	10/15(66.7)	10.2	2009-2011	0.0000001	0.08
2LR	Central & Eastern	Ciego de Ávila Camagüey Las Tunas Holguín Granma	1/15(6.67) 13/13(100) 8/8(100) 2/14(14.3) 13/13(100)	137.6	2011-2012	0.0011200	0.43

*RR= Relative Risk

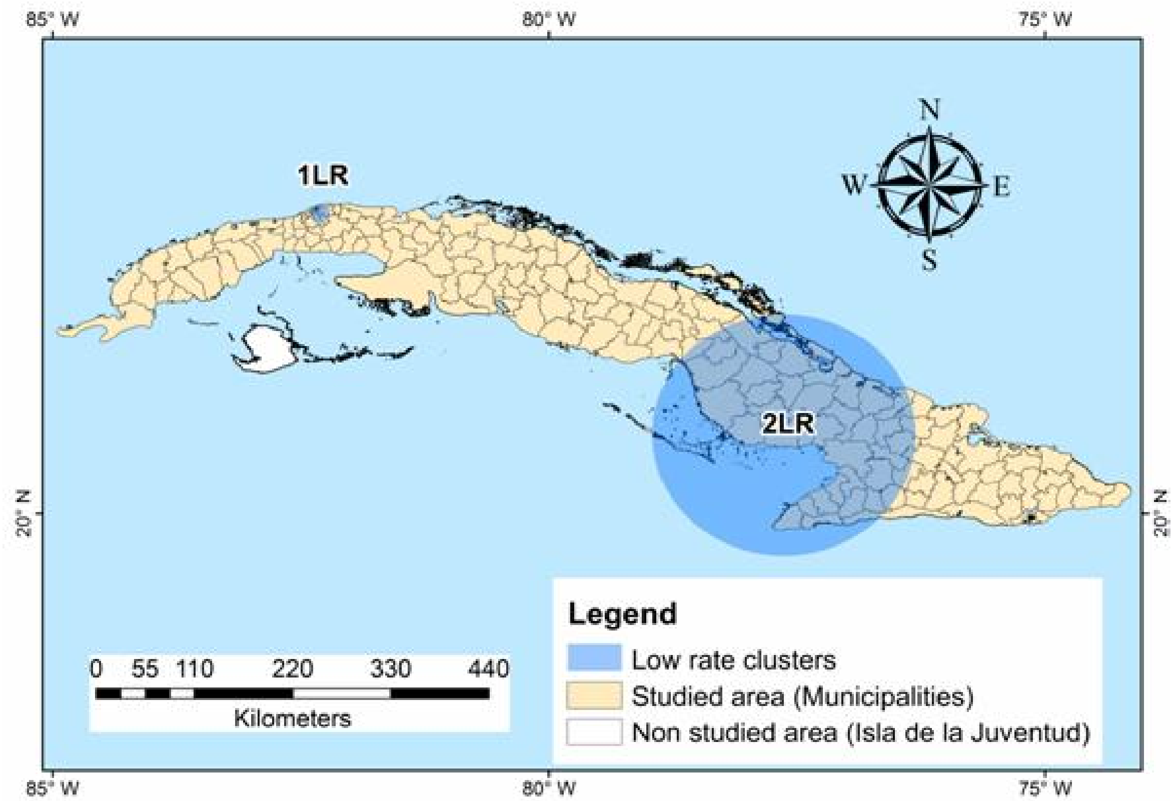

FIGURE 3. Representation of the low rate spatiotemporal clusters./ *Representación de los conglomerados espaciotemporales de bajas tasas.*

DISCUSSION

So far as we know, this is the first study describing the spatiotemporal distribution and clustering of CSF outbreaks in Cuba. The results of this study allowed the identification the geographical areas of high CSF occurrence making possible to target effors for the disease control with further eradication purposes. Spatial statistics in the analysis of disease spread or outbreak surveillance data are becoming standard practice in the study of infectious diseases. Scan statistics have been used with important results in many epidemiological investigations such as the detection of tuberculosis outbreaks (11), the spatial distribution of foot and mouth disease in Zambia (12), the identification and characterization of space and space-time clusters of seroreactivity to individual Leptospira serovars among dogs (13), the description of the spatial and temporal patterns of the high pathogenic avian influenza H5N1 outbreaks (14).

The best method is to analyze the data using the smallest area units for which data are available, e.g., farms (15), or alternatively aggregate data using a regular frame (16). The aggregation of cases to administrative divisions may negatively affect the accuracy of the analysis (17). In the present study, the lack of information in databases of many quadrants (around 50%) where outbreaks occurred made impossible to perform the cluster detection analysis at a quadrant level. The municipality was the smallest area unit for which the data were available.

Regardless of the CSF endemism in Cuba for a very long period and outbreak occurrences in the whole country(8), the results demonstrated the existence of high and low cluster rates of municipalities and the years when they occur, and rejection of the null hypothesis that the affected municipalities showed a random distribution in space and time.

Detected high rate clusters of affected municipalities in the three regions (western, central and eastern) showed that the situation of CSF occurrence was complicated from the epidemiological point of view. The presence of high-risk areas implies an important threat to surrounding territories because of the dissemination of the disease.

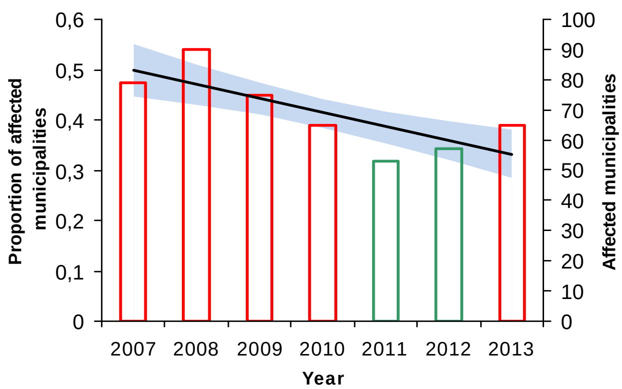

FIGURE 4. Affected municipalities by CSF from 2007 - 2013 (Green bars show the years of low-risk for municipalities being affected; the black line represents the probability of being affected and the blue area are the95% C.I. of a municipality being affected in each year)./ *Municipios afectados por PPC desde 2007 - 2013 (Las barras verdes muestran años con bajo riesgo de afectarse lo smunicipios, la línea blanca representa la probabilidad y el área azul muestra el I.C. 95%).*

The endemic condition of CSF in Cuba (6) could also have a certain influence on this result, with cases in all provinces. It is interesting to say that the provinces of the geographical extremes of the island, western (Pinar del Río) and eastern (Guantánamo) do not have any high rate cluster; it is important because the eradication campaign is thought to be started by these two extreme provinces. Then, it could facilitate the actions at the starting points for the absence of unfavorable epidemiological conditions in these provinces.

The first low rate cluster (LR1) was located in La Habana, and it occurred from 2009 to 2011. It could be due to the low activity in terms of pig production and the low pig population and number of farms because they are urban zones. The secondary low rate cluster (LR2) placed in the eastern region was the highest cluster detected and involved a great number of municipalities and it occurred during the period from 2011 to 2012. It can be observed that the results by scan statistics from the temporal point of view agreed with the results obtained by logistic regression, and they showed that the municipalities had significantly less risk of been affected during 2011 and 2012.

Moreover, all high rate clusters were before 2010. On the contrary, the low rate clusters were detected in the period from 2009 to 2012. Therefore, this observation and the decreasing tendency of municipalities to be affected demonstrated the reduction of cases in the period, which, in general, could indicate the positive effect of the control measures.

The results obtained in this work are interesting. However, factors like the sanitary measures or actions taken in general to make them possible are not enough well known, and they should be precisely analyzed to determine which factors influenced on this reduction of CSF cases so that this knowledge could be used to enhance management of the disease in the field. Factors such as inadequate vaccination or low vaccine quality, vaccination coverage, movement of pigs without veterinary control, low biosecurity in pig farms (18-20), among others, could have played an important role in the clusters formed. The difference of risks between the areas located inside and outside the clusters requires further investigation.

TABLE 2. Results of the logistic regression analyzing the probability of a municipality to be affected by year./ *Resultado de la regresión logística en el que se analiza la probabilidad de afectarse un municipio por año.*

Variable (Year)	B	Sig.	Odds Ratio	C.I. 95%	
				Lower	Upper
2007	Baseline				
2008	0.264	0.229	1.302	0.847	2.001
2009	-0.096	0.661	0.908	0.59	1.397
2010	-0.343	0.122	0.71	0.46	1.096
2011	-0.658	0.004*	0.518	0.332	0.809
2012	-0.55	0.015*	0.577	0.371	0.897
2013	-0.343	0.122	0.71	0.46	1.096
Constant	-0.108	0.486	0.898		

* Significant difference p<0.05

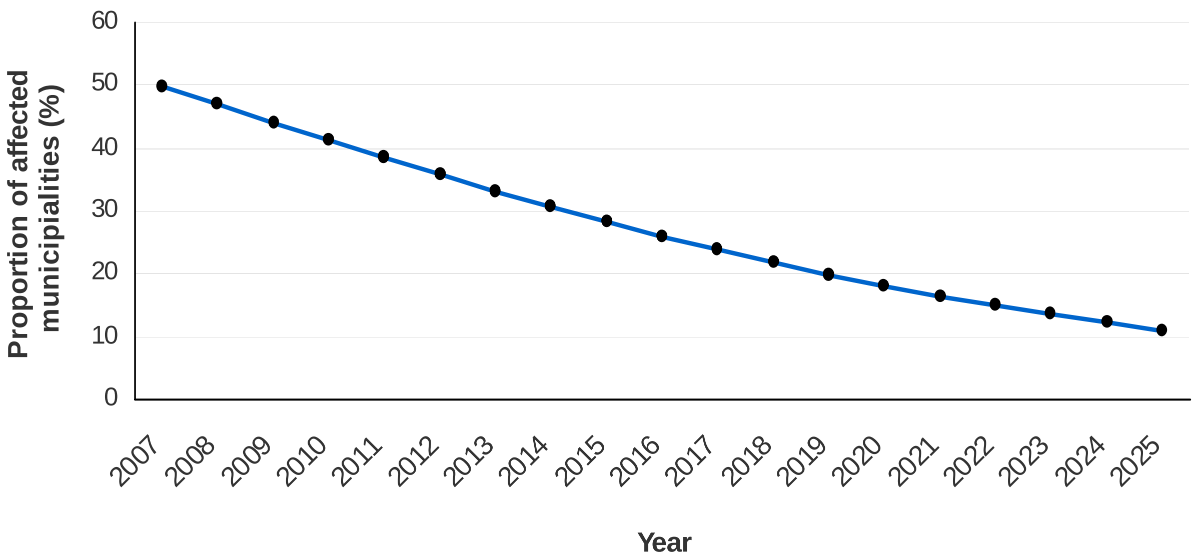

FIGURE 5. Predicted proportion of municipalities affected by CSF in Cuba over time./ *Pronóstico de la proporción de municipios afectados por CSF en Cuba a través del tiempo.*

A decreasing tendency of the proportion of municipalities affected with CSF was observed, but it was not considered enough because our goal is to make Cuba free of CSF by 2020 (21). Thus, the current strategy to control CSF must be profoundly analyzed to detect its inaccuracies and find methods that allow accelerating this process because the advances have been discrete.

In the high risk clusters, some measures should be enhanced, e.g., disease surveillance intensification, strengthening of biosecurity measures, etc. (22). On the other hand, the low risk clusters identified must be taken into account since they could be others starting points for the disease control and eradication campaign due to their better epidemiological conditions.

The safest way to prevent an infectious disease is by eradicating the pathogen. To achieve eradication of a disease, good surveillance systems and monitoring, reliable diagnostic techniques, and capability of identifying animals or infected farms are essential. In addition, a correct technical infrastructure and an appropriate management are indispensable to stop the infection spread and eliminate its source; re-introduction of the infection into zones where the disease has already been eradicated must also be prevented (22).

The identification of the spatiotemporal distribution of CSF in Cuba is an important step that could contribute to the decision-making process of our policy makers, in order to achieve more successful actions in a near future, which is demanded by the CSF eradication planned for 2020. An analysis to identify other risk factors is recommended to be made, especially in areas with high and low risks. It must include, among others, factors such as farm density, pig density, pig population, density of roads, human population, percentage of non-vaccinated pig population, proportion of farms with different technification levels (23, 24). This analysis will undoubtedly help to a better understanding of CSF patterns.

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