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Short Communications

SPACE-TIME PERMUTATION MODEL APPLIED TO THE PAST OUTBREAK DATA OF LUMPY SKIN DISEASE IN THE BALKAN PENINSULA FROM AUGUST 2015 TO JULY 2017

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Abstract

Introduction: In August 2015, lumpy skin disease (LSD) was notified for the first time in mainland European Union when it was observed in cattle in Greece. From August 2015 to July 2017, 1,757 outbreaks were reported in cattle in Greece, Bulgaria, Macedonia, Albania, Serbia, and Montenegro.

Materials and Methods: The Kulldorff space-time permutation scan statistic contained in the software package SaTScan v 9.4.4 was used to analyse the epizootic past outbreak data and describe the spread of the disease in the 24 months after the first notification.

Results and Conclusions:: Seventy-six space-time disease clusters (62 significant and 14 non-significant) were identified. In 2015, 10 clusters with a monthly peak in October (n=5, 50%) were identified, in 2016, the most (n=57) clusters were detected with monthly peak in July (n=15, 26.3%), and up to July 2017, nine clusters with a monthly peak in May (n=3, 3.3%) were determined. Possible high-risk areas were identified using the presented methodology, and so this technique could guide national veterinary authorities to formulate strategies for mitigating the spread of LSD, allocating resources and for formulating epidemiological preparedness plans in neighbouring, LSD-negative, countries.

Key Words: Lumpy skin disease, space-time scan statistic, cluster, Balkan Peninsula, epizooty

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INTRODUCTION

Lumpy skin disease (LSD) is a viral disease affecting cattle, caused by one serotype of lumpy skin disease virus (LSDV) which belongs to the family *Poxviridae*, genus *Capripoxvirus*, characterized by nodules on the skin and other parts of the body. Transmission is primarily by biting insects (vector) and to a lesser extent through direct contact between animals (Animal Disease Information Summaries, not dated).

LSD is endemic in African countries, but unusually, from 2012, the disease reached the Middle East. In 2013, the disease spread in Turkey, and by May 2015, the disease reached the East Thrace area (European Food Safety Authority (EFSA), 2017). In August 2015, for the first time, LSD reached Greece near the border area with Turkey. In the following year, this disease spread into Bulgaria, Macedonia, Albania, Serbia and Montenegro (Animal Disease Information Summaries, not dated).

The goal of the study was to identified space-time disease clusters in the Balkan Peninsula by applying a permutation model of the space-time scan statistic on the past outbreak data from the first notification for the following 24 months.

MATERIALS AND METHODS

Study area and period

All countries from the Balkan Peninsula which reported LSD outbreaks were included i.e. Greece, Bulgaria, Macedonia, Albania, Serbia and Montenegro from August 2015 to July 2017.

Data sources

Freely downloaded data from the Global Animal Disease Information System (EMPRES-i) of the Food and Agriculture Organization (FAO) (EMPRES-i - Global Animal Disease Information System, not dated) were used for the purpose of space-time disease cluster analysis. Scanning for clusters was done with SaTScan v 9.4.4 free software (SaTScan - Software for the spatial, temporal, and space-time scan statistics, not dated) using the Space-Time Permutation model which requires only case data with information about the spatial location and time for each case, but does not need information about controls or risk factors for the background population (Kulldorff, 2006). Visualisation of the disease clusters and municipalities was made in an open source geographic information system-Quantum GIS (Welcome to the QGIS project!, not dated). Country-level data were used from freely downloaded spatial data DIVA-GIS (DIVA-GIS | free, simple & effective, not dated).

For space-time cluster analysis, several parameters were set: Maximum temporal cluster size was set at up to 50 % of the study period (Kulldorff, 2006); maximum size of the spatial window for a cluster was set at up to a 20 km radius which is the maximum distance according to the assumption that most LSD occurs over a relatively small distance**,** in agreement with the vector-borne pattern of LSDV (EFSA, 2017); significance of the clusters was evaluated with Monte Carlo simulation which was set as the default in section inference with a maximum number of 999 replications, under the null hypothesis of random distribution; the time aggregation period was set at up to a **7-**day block.

A space-time scan statistic is defined by a cylindrical window with a circular (or elliptic) geographic base and with a height corresponding to time (Kulldorff, 2006).

RESULTS

From August 2015 to July 2017, six countries in the Balkans reported a total of 1,757 outbreaks and 3,139 cases. Albania reported the most (n=858, 48.8%) and Montenegro the fewest (n=63, 3.6%) outbreaks.

Overall, 76 disease clusters, among which 62 were significant ($p<0.05$) and 14 were non-significant (Figure 1, Table 1) were identified.

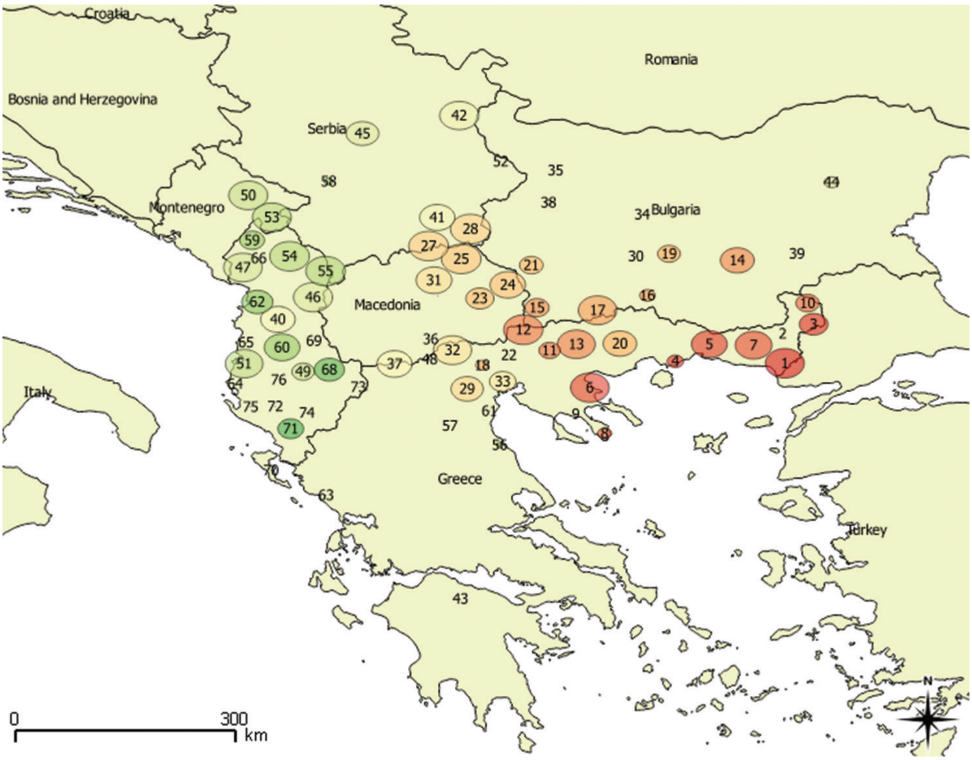

Figure 1. LSD clusters (circles) in the Balkans, detected from August 2015 to July 2017 by use of the permutation model of the time-space scan statistic. The numbers refer to the chronological designation of clusters. The first and earliest cluster is dark red colour towards the last one identified in dark green.

Table 1. Chronological order of LSD space-time disease clusters in Balkans epidemiology from August 2015 to July 2017.

Cluster	Radius (km)	Start date	End date	Duration of cluster (Days)	p-value	Number of outbreaks	Observed (O)	Expected (E)	O/E
1	19.94	2015/8/18	2015/10/5	48	<0.001	50	324	42.11	7.69
2	1<	2015/8/25	2015/8/31	6	<0.001	1	35	1.45	24.15
3	14.57	2015/9/8	2015/9/21	13	<0.001	3	23	0.78	29.34
4	8.39	2015/9/22	2015/11/2	41	<0.001	17	48	1.83	26.28
5	18.24	2015/9/22	2015/11/23	62	0.02	4	6	0.28	21.43
6	19.84	2015/10/6	2015/12/14	69	<0.001	7	42	1.71	24.56
7	18.76	2015/10/6	2015/12/14	69	<0.001	6	9	0.37	24.32
8	7.20	2015/10/13	2015/11/30	48	<0.001	10	15	0.43	34.88
9	1<	2015/10/20	2015/10/26	6	<0.001	1	8	0.05	160
10	11.81	2015/10/20	2015/10/26	6	0.11	2	3	0.03	100
11	10.93	2016/4/5	2016/4/18	13	<0.001	6	10	0.17	58.82
12	19.98	2016/4/12	2016/5/23	41	<0.001	23	92	9.68	9.50
13	19.28	2016/4/12	2016/5/16	34	<0.001	17	53	4.24	12.50
14	17.00	2016/4/12	2016/5/9	27	<0.001	12	21	1.39	15.11
15	12.26	2016/5/3	2016/5/23	20	<0.001	3	17	1.21	14.05
16	7.82	2016/5/10	2016/5/23	13	0.99	2	3	0.09	33.33
17	19.51	2016/5/10	2016/6/6	27	<0.001	24	59	7.43	7.94
18	6.54	2016/5/17	2016/5/23	6	<0.001	2	6	0.17	35.29
19	11.37	2016/5/24	2016/6/6	13	<0.001	3	39	2.63	14.83
20	17.07	2016/5/24	2016/6/6	13	<0.01	3	8	0.59	13.56
21	11.85	2016/5/24	2016/5/30	6	0.12	3	5	0.22	22.73

cont. Table 1.

Cluster	Radius (km)	Start date	End date	Duration of cluster (Days)	p-value	Number of outbreaks	Observed (O)	Expected (E)	O/E
22	1<	2016/5/24	2016/5/30	6	0.32	1	4	0.12	33.33
23	14.18	2016/5/31	2016/6/13	13	<0.001	20	50	3.87	12.92
24	17.89	2016/5/31	2016/6/6	6	<0.001	14	17	0.83	20.48
25	19.89	2016/6/7	2016/6/27	21	<0.001	62	110	16.67	6.60
26	1<	2016/6/7	2016/6/13	6	<0.001	1	20	0.76	26.32
27	19.89	2016/6/7	2016/7/25	48	0.88	13	17	5.12	3.32
28	19.97	2016/6/14	2016/7/25	41	<0.001	78	111	29.55	3.76
29	16.57	2016/6/14	2016/6/20	6	<0.001	8	9	0.57	15.79
30	1<	2016/6/14	2016/6/20	6	0.07	1	5	0.19	26.32
31	18.00	2016/6/14	2016/6/27	13	0.86	6	6	0.58	10.34
32	19.46	2016/6/21	2016/7/4	13	<0.001	13	52	6.69	7.77
33	13.56	2016/6/21	2016/6/27	6	<0.001	8	27	1.97	13.71
34	1<	2016/6/21	2016/6/27	6	<0.001	1	12	0.70	17.14
35	1<	2016/6/21	2016/6/27	6	<0.001	1	10	0.58	17.24
36	1<	2016/6/28	2016/7/4	6	<0.001	1	9	0.42	21.43
37	17.96	2016/6/28	2016/7/4	6	0.06	4	6	0.33	18.18
38	3.17	2016/6/28	2016/7/4	6	0.45	2	5	0.28	17.86
39	1<	2016/7/5	2016/7/11	6	<0.001	1	22	0.79	27.85
40	17.52	2016/7/5	2016/9/12	69	<0.001	20	88	31.19	2.82
41	17.54	2016/7/5	2016/7/11	6	<0.001	15	11	0.76	14.47
42	19.10	2016/7/5	2016/7/18	13	<0.01	6	9	0.69	13.04

cont. Table 1.

Cluster	Radius (km)	Start date	End date	Duration of cluster (Days)	p-value	Number of outbreaks	Observed (O)	Expected (E)	O/E
43	1<	2016/7/12	2016/7/18	6	<0.001	1	30	0.99	30.3
44	7.26	2016/7/12	2016/7/25	13	<0.001	3	17	1.15	14.78
45	16.01	2016/7/12	2016/7/18	6	0.41	3	4	0.13	30.77
46	19.71	2016/7/19	2016/12/19	153	<0.001	54	244	84.13	2.90
47	19.33	2016/7/19	2016/12/19	153	<0.001	12	55	19.59	2.81
48	1<	2016/7/19	2016/7/25	6	<0.01	1	6	0.21	28.57
49	11.49	2016/7/19	2016/7/25	6	0.22	4	5	0.24	20.83
50	19.34	2016/7/26	2016/8/1	6	<0.001	22	52	3.89	13.37
51	19.19	2016/7/26	2016/11/21	117	<0.001	13	39	11.21	3.48
52	1<	2016/7/26	2016/8/1	6	<0.001	1	10	0.66	15.15
53	19.37	2016/7/26	2016/8/1	6	<0.001	7	10	0.79	12.66
54	19.91	2016/8/2	2016/11/28	118	<0.001	31	92	22.94	4.01
55	19.85	2016/8/9	2016/12/19	135	<0.001	24	35	9.14	3.83
56	3.72	2016/8/23	2016/8/29	6	<0.001	2	10	0.20	50
57	1<	2016/8/23	2016/8/29	6	<0.01	1	5	0.10	50
58	4.22	2016/8/30	2016/10/3	35	<0.001	6	14	0.64	21.88
59	12.41	2016/8/30	2016/9/26	27	0.54	2	4	0.14	28.57
60	18.15	2016/9/13	2017/2/13	153	<0.001	12	49	6.86	7.14
61	1<	2016/9/27	2016/10/3	6	0.04	1	3	0.02	150
62	15.73	2016/11/1	2017/1/2	62	<0.001	5	9	0.61	14.75
63	1<	2016/11/22	2016/11/28	6	<0.001	1	5	0.05	100

cont. Table 1.

Cluster	Radius (km)	Start date	End date	Duration of cluster (Days)	p-value	Number of outbreaks	Observed (O)	Expected (E)	O/E
64	1<	2016/11/29	2016/12/5	6	<0.01	1	4	0.03	133.33
65	1<	2016/12/27	2017/1/9	13	<0.001	1	25	0.61	40.98
66	1<	2016/12/27	2017/1/30	34	<0.001	1	23	0.81	28.40
67	1<	2016/12/27	2017/1/16	20	<0.001	1	15	0.46	32.61
68	15.43	2017/1/3	2017/2/6	34	<0.001	8	14	0.69	20.29
69	1<	2017/2/7	2017/2/13	6	0.09	1	2	0.0025	800
70	1<	2017/2/21	2017/2/27	6	<0.001	1	12	0.05	240
71	13.33	2017/4/18	2017/6/5	48	<0.001	3	56	2.01	27.86
72	1<	2017/5/2	2017/6/19	48	<0.001	1	45	2.14	21.03
73	1<	2017/5/23	2017/6/5	13	<0.001	1	8	0.15	53.33
74	1<	2017/5/23	2017/6/19	27	<0.01	1	6	0.20	30
75	1<	2017/6/6	2017/6/19	13	<0.001	1	24	0.37	64.86
76	1<	2017/6/6	2017/6/12	6	0.97	1	2	0.01	200
Sum	/	/	/	/	/	703	2360	35.74	3319.49
Range	1< - 19.98			6-153		1-78	2-324	0-84.13	2.81-800
Median	11.83			13		3	14	0.66	21.23
Mean	10.05			28.89		9.25	31.05	4.62	43.68
Mode	<1			6		1	6	0.05	21.43
SD	± 8.26			±37.13		± 14.36	± 49.51	± 12.02	± 98.07

The first cluster was identified in Alexandroupoli, Greece, in August 2015, with a radius of 19.9 km and the last one in June 2017, in the region of Velabisht, Albania, with a radius of less than 1 km (Figure 1, Table 1).

Correlations, using Pearson's coefficient of correlation, between the radius of the spatial window and the number of outbreaks or observed cases were 0.57 ($p<0.001$) and 0.40 ($p<0.001$), respectively. Correlations using Pearson's coefficient of correlation, between duration of the outbreak (in days), the number of outbreaks or observed cases, and the radius of the spatial window were 0.41 ($p<0.001$), 0.46 ($p<0.001$) and 0.48 ($p<0.001$), respectively.

Distribution of the clusters per month showed that in 2015, 10 clusters with a monthly peak in October (n=5, 50%) were identified, 57 clusters occurred in 2016 with a monthly peak in July (n=15, 26.3%), and 9 clusters were determined in 2017 (up to July) with a peak in May (n=3, 3.3%) (Figures 1, 2).

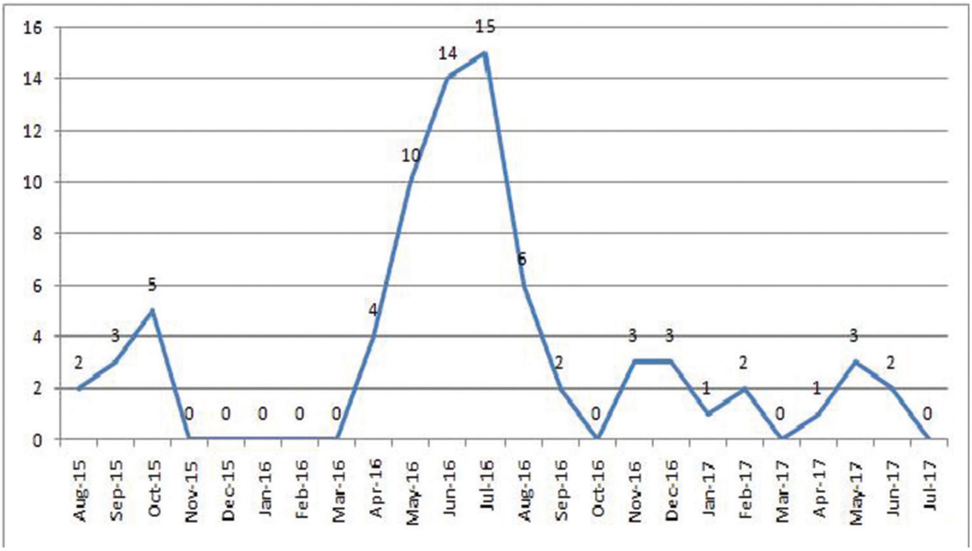

Figure 2. Monthly distribution of detected LSD clusters in the Balkans from August 2015 to July 2017

From autumn 2016 to the middle of summer 2017, no clear seasonal clustering pattern was observed, with skewed clusters detected in almost all months and a moderate peak in May 2017 (Figure 2).

Disease clusters which comprised the highest number of outbreaks were identified near border areas: Serbia-Bulgaria-Macedonia (cluster number 28), Macedonia-Serbia-Bulgaria (cluster number 25), Albania-Macedonia (cluster number 46), Greece-Turkey (cluster number 1) (Figure 1, Table 1). Cluster numbers 68 to 76 in the period from January to July 2017 were located in Albania and one cluster, number 70, occurred on the island of Corfu (Figure 1, Table 1).

A visual analysis in QGIS of 76 disease clusters according to the administrative region where the label of the centre of the spatial window was located produced the following results (Figure 1):

Greece: Alexandroupoli, Sintiki, Topeiros, Aristotelis, Serres, Soufli, Kalouryta, Almpoia, Didymoteicho, Corfu, Delta, Sithonia, Polygyros, Irakleia, Agia, Maroneia-Sapes, Parga, Veria.

Bulgaria: Hadzidimovo, Maritsa, Tundzha, Dimitrovgrad, Varbitsa, Strumyani, Karlovo, Montana, Pazardzhik, Kocherinovo, Kostinbrod, Smolyan.

Macedonia: Rankovce, Radovish, Lozovo, Delchevo, Prilep, Sveti Nikole.

Albania: Gjrokastër, Qendër i Tomin, Fshat Memaliaj, Kotr, Luz i Vogël, Fieaz, Postribë, Papër, Komsi, Zall Bastar, Dardhas, Hogisht, Gradishtë, Rrethinat, Shishtevac, Lar, Novoselë, Qendër i Piskovë, Hotolisht, Kodoujat/Skendribegas, Shrel,Velabisht.

Serbia: Bosilegrad, Novi Pazar, Vranje, Pirot, Zajechar, Trstenik, Preshevo.

Montenegro: Mojkovac, Plav.

DISCUSSION

This study focused on applying a space-time permutation model to past outbreak LSD data in the Balkan Peninsula in the 24 months after these data were first notified. Space-time cluster analysis is a valuable method to examine how spatial patterns change over time (Banu et al., 2012). Most of the identified clusters were observed in Greece and Albania, and therefore, both countries could be regarded as higher risk areas for LSD (Figure 1).

The results in the current study regarding the location of clusters, with highest numbers of outbreaks being near border areas, are similar to another study in the Balkans (Mercier et al., 2017). In that study, LSD transmission hot spots were mainly located in the border areas and the observation was in line with assumptions about the influence of vaccination campaigns on the spread of the disease (Mercier et al., 2017).

Moderate positive correlations were observed between the radius of spatial windows and numbers of both outbreaks and observed cases, indicating that increasing the geographical area captured more outbreaks as well as observed cases. Because of possible under-reporting, both the radius of spatial windows and the location of clusters are probably unstable.

Moderate positive correlations were also found between duration (days) and numbers of outbreaks or observed cases, and radius of the spatial window, which could indicate that with increasing time, new outbreaks and cases occurred in the cluster zones.

The measure of association obtained using Pearson’s coefficient of linear correlation does not imply causation, nor point out the significance of clusters. Values of observed/expected higher than 1 indicate there were more outbreaks within a cluster than expected if the disease was evenly distributed in time and in space (Iglesias et al., 2010).

Monthly peaks were observed in October 2015, July 2016 and May 2017 (data were up to July), which implies that each year, peaks were probably earlier due to the control measures implemented by veterinary services. Vaccination campaigns, after introduction of the virus to a country, must have strongly influenced the spread of the virus, as such campaigns are the most effective option for controlling the spread of LSD (EFSA, 2016). A faster spread of LSDV in 2016 (Mercier et al., 2017), capturing Bulgaria, Macedonia, Albania, Serbia and Montenegro, was probably caused by dissemination of infection vectors by wind (Mercier et al., 2017). In addition, other control measures such as movement control inside the country, stamping out or modified stamping out, desinsection, zoning, surveillance (Animal Health - Regulatory Committee - presentations - Food Safety - European Commission, not dated), and re-vaccination campaigns in cattle in 2017 probably helped to avoid re-emergence and further spread of LSDV.

In the current analysis, the biggest peak of disease clustering was observed at the end of spring and summer 2016 in the months May, June and July, with a monthly peak in July. This was similar to other studies in the Nile Delta, Egypt, showing that outbreaks peaked in June, July and August 2015 (Abdelgawad, 2017) or in Turkey from July to November 2014 (Turan et al., 2017).

The centre of a spatial window which was located in a municipality or region does not imply that the entire territory was involved in the disease cluster, and larger clusters captured neighbouring areas as well. Rather, the techniques used were a methodology to locate administrative regions, because the most of the veterinary inspection services are organized according to municipality competence.

CONCLUSION

Our results emphasized two characteristics of LSD epidemiology in the Balkans: geographical regions where LSD had increased incidence and the times when this occurred.

Our findings do not oblige national authorities to follow these results but suggest areas which could be used by policymakers to formulate disease surveillance strategies as well as allocate resources and guide epidemiological emergency efforts and preparedness in neighbouring LSDV-free countries. Future research should focus on the investigation of climatic and ecological determinants of LSD in clustered areas.

Conflict of interest statement

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

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PERMUTACIONI MODEL PROSTOR-VREME PRIMENJEN NA PODATKE O BOLESTI KVRGAVE KOŽE (LSD) NA BALKANSKOM POLUOSTRVU OD AVGUSTA 2015 DO JULA 2017

STOJMANOVSKI Zharko

Kratak sadržaj

Uvod: Bolest kvrgave kože po prvi put je zabeležena na teritoriji Evropske Unije u avgustu 2015., kada je dijagnostikovana kod goveda u Grčkoj. U periodu avgust 2015. - juli 2017., od izbijanja bolesti prijavljeno je 1.757 žarišta u Grčkoj, Bugarskoj, Makedoniji, Albaniji Srbiji i Crnoj Gori.

Materijal i metode: Statističko skeniranje za permutaciju prostor-vreme po Kulldorff-u sadržano u softverskom paketu SaTScan v 9.4.4 korišćeno je da se analiziraju podaci o prethodnim izbijanjima ove bolesti kao i da se epizootija opiše 24 meseca posle prvog pojavljivanja.

Rezultati i zaključak: Identifikovano je sedamdeset šest klastera oboljenja (62 značajnih i 14 nesignifikantnih). U toku 2015. identifikovano je 10 klastera sa mesečnim maksimumom u oktobru (n=5, 50%), u toku 2016. detektovan je najveći broj od 57 klastera sa mesečnim maksimumom u julu (n=15, 26.3%), a do jula 2017. devet klastera sa mesečnim maksimumom u maju (n=3, 3.3%). Identifikovanje mogućih oblasti visokog rizika dobijeno je pomoću prezentovane metodologije i ono bi moglo da pomogne nacionalnim veterinarskim službama pri formulisanju strategija za ublažavanje širenja bolesti, alokaciju resursa kao i pravljenje planova za pripremu odgovarajućih mera u susednim zemljama.

Ključne reči: bolest kvrgave kože, statističko skeniranje prostor-vreme, klaster, Balkansko poluostrvo, epizootija