Modeling the Epidemiological Processes of Economically Significant Infections of Animals

Sarsenbay Abdrakhmanov[1], Ersyn Mukhanbetkalyev[1], Altay Ussenbayev[1], Dina Satybaldina[2(✉)], Ablaikhan Kadyrov[2], and Nurlan Tashatov[2]

[1] S. Seifullin Kazakh Agrotechnical University, 010011 Nur-Sultan, Kazakhstan
[2] L.N. Gumilyov Eurasian National University, 010008 Nur-Sultan, Kazakhstan
satybaldina_dzh@enu.kz

Abstract. Analysis of the retrospective and current states of the epidemiological situation on economically significant zoonoses (rabies, anthrax, and animal foot and mouth disease) in Kazakhstan over the past eight decades is considered. A reliable factual data for computer simulations and modern quantitative epidemiology methods were provided by the state veterinary and public health services. Historical and modern trends of the spatial and geographical distribution, the presence of cluster foci and the potential occurrence of infections outbreaks by country regions were assessed by mapping the incidence of diseases among animals and humans and using an environmental niche modeling, a space-time cube technology, as well as a negative binomial nesting density model, a linear regression and a generalized linear models. As a research result the statistically reliable visualization of the cluster zoning of Kazakhstan territory by risk emergent outbreaks categories of animals' and humans' infectious diseases was obtained. It allows predicting the likelihood of zoonoses outbreaks in the country regions.

Keywords: Computer modeling · Epidemiology · Geographical information systems

1 Introduction

In connection with the entry of Kazakhstan into the World Trade Organization, the need for socio-economic stability, including animal epidemics that can spread to humans, is becoming increasingly important for each administrative unit of the country [1–3].

The list of the most economically significant diseases of the World Organization for Animal Health (OIE) includes animal infections such as rabies, anthrax and foot and mouth disease (FMD), and global control of their outbreaks is a new challenge for modern human and animal medicine because of rabies and anthrax are dangerous zoonoses and can cause human deaths. FMD has an economic perspective because of a decrease in productivity in food-producing animals, trade restrictions imposed on the countries in which the disease is present [1–4].

© Springer Nature Switzerland AG 2019
S. Misra et al. (Eds.): ICCSA 2019, LNCS 11621, pp. 551–560, 2019.
https://doi.org/10.1007/978-3-030-24302-9_39

A retrospective spatiotemporal analysis of outbreaks of foot and mouth disease among livestock in Kazakhstan from 1955 to 2013 showed that during this period several strategies for foot and mouth disease controlling were implemented in the country, which led to the recognition of Kazakhstan by the OIE as a foot and mouth disease-free country with partial vaccination (2015) [4].

As in many endemic countries, animal rabies is recorded annually in Kazakhstan. There is also a vaccination program for domestic dogs, cats, farm animals and a limited fox vaccination program by distributing vaccines-soaked baits. However, a decrease in the incidence in animals was not observed [1, 2].

The first reliable information about anthrax in Kazakhstan was provided at the end of the 19th century, while anthrax foci began to be officially registered since the early 1930s. Stationary foci of natural infection were formed and maintained their activity over a long period of time in a significant part of the territory of Kazakhstan [3].

Currently, the prevention strategy for the above diseases is provided by their constant monitoring in all territorial units of the country. In today's world, the decision to control of these diseases is only possible by analyzing the epidemiological behavior of these dangerous zoonoses using computer technologies to simulate the spatial distribution and population dynamics of infectious agents among animals and humans.

The goal of this article is to review our latest research results on analysis the epidemiological situation for economically significant zoonoses - rabies, anthrax, and FMD - in the RK performed by computer simulation using modern quantitative epidemiology methods.

2 Materials and Methods

2.1 Studies Area

The epidemics of infections in the territory of Kazakhstan covering 2,724,900 km^2 were analyzed, including 14 oblasts (oblasts) and 179 districts; average population density here is 6.58 individuals/km^2.

2.2 Data

To analyze the epidemic situation of infections in Kazakhstan, we used the data of registered anthrax outbreaks in the period 1933–2014, outbreaks of foot and mouth disease from 1955 to 2013, and outbreaks of rabies in 2010–2013 in animals and people. The database was provided by official veterinary statistics and public health statistics of the country and the OIE, as well as data from veterinary research institutions and laboratories, supplemented by their own data collected during the expedition visits to assess preserved infection foci throughout the country. Recorded for each outbreak information included geographical coordinates, the date of confirmation of the disease, the name and administrative affiliation of the settlement, infected species, the number of infected and susceptible animals in infected herds.

2.3 Methods

Rabies. Spatio-temporal clusters of rabies outbreaks were identified using Kuldorf scan statistics. Preliminary data analysis using the Multi-distance Spatial Cluster Analysis software tool (Ripley K-function) was performed to determine the maximum distance of spatial outbreak clustering. The curves were plotted for the selected clusters based on the available data on the dynamics of cases of rabies in the second stage analysis. The time step of the epidemic curve implies a period equal to the average incubation period of rabies for the respective animal category, the duration of the infectious periods were modelled using the Pert distribution. In order to simulate the possible number of new outbreaks of rabies in the event of an epidemic in a new territory, a technique based on the concept of basic reproductive ratio was used [1]. The geographical distribution of rabies cases was also analyzed by mapping the cases of the disease in animals according to the corresponding coordinates. The distribution and density of common rabies cases were analyzed using the kernel density function smooth Scatter. Economic losses and disease burden were estimated using Monte Carlo simulations. They were summed up for Disability Adjusted Life Years (DALY) or for cost estimation and repeated 10,000 times. The total number of cases in farm animals and people by regions was also analyzed in a generalized linear model (GLM) with the number of confirmed cases in foxes and dogs as independent variables. The negative binomial regression model was used as a statistical model [2].

Anthrax. For assessment the risk of anthrax in each area, the maximum entropy technique (Maxent) was used. Using this approach, the values of the assumed risk factors represented by geospatial variables are determined at the locations of the recorded outbreaks. A regression equation was compiled for each location based on the Gibbs distribution. It was described the likelihood of observing a disease outbreak in each location. The values of the constants were selected using several iterations applying the Monte-Carlo method, which ensured the maximum probability distribution corresponding to the observed distribution of the disease outbreaks.

Then there was developed a risk map based on the distribution of infection obtained throughout the study area. The following factors were chosen as the proposed explanatory variables: a set of 19 climate variables included in BIOCLIM (the altitude above sea level in m; the maximum green vegetation fraction, reflecting the presence and intensity of vegetation cover; the land cover type, reflecting the category of land use; the soil type) (FAO 2016).

All geospatial variables were obtained in raster format, cropped along the border of Kazakhstan, processed with a resolution of 1×1 km^2, and converted to ASCII format, according to the requirements of Maxent software. The output of the Maxent model was a solid surface, which was the most appropriate distribution of areal suitability for the appearance of anthrax.

After developing a continuous risk surface, which is characterized by the distribution of suitability to anthrax outbreaks throughout the study area, a generalization was applied to compare risk categories in accordance with administrative divisions of

the second level (districts). The results of this rating were presented in the form of a risk map, which was the main result of research.

Foot and Mouth Disease. There was used Kuldorf space-time scan statistics to detect the statistically significant groups of foot and mouth disease outbreaks, called a space-time clusters, for each of the three lines. A group of infected farms located close to each other was interpreted as the cluster, it was suggested that the farms were epidemiologically linked either to local transmission processes or to common risk factors. The resulting p-values of the scan statistic, adjusted for multiple hypotheses testing, denote the probability that the observed space–time cluster resulted from a random spatiotemporal distribution of outbreaks. The space–time density of outbreaks (STDO) was used to define the speed of the outbreak's spread within space–time clusters. At last, values of the STDO were compared using ANOVA to know whether STDOs were influenced by serotype.

2.4 Software

Geospatial analysis, processing the raster and vector data, converting the data into different formats and visualizing the results were carried out using the ArcGIS 10.4 and 10.5 geographical information system (ESRI, Redlands, CA, USA), Global Position System receivers (eTrex Legend, Global Sat GH-801 and Shturman SVG-40). Identification of space-time clusters was performed by means of SatScan 9.1 software package.

The distribution and density of rabies cases was analyzed in R using the function smooth Scatter; calculations of economic losses and disease burden from rabies were undertaken with glm.nb function from the MASS package. Statistical analysis was performed by Monte Carlo simulation method with @Risk 6.2 software (http://www.palisade.com/risk/) based on a standard Microsoft Excel package (Microsoft, USA).

Modelling by maximum entropy method was performed with the Maxent software [1–4].

3 Results

3.1 Rabies

Analysis of cases of rabies in 2010–2013 showed that clusters were mainly found among cattle in the category of farm animals, dogs – in domestic animals, and foxes – in wild animals. The initial segments of the epidemic curves were constructed for the three identified clusters, they included the fitted exponential curves.

The calculation of the main reproductive ratio confirms the hypothesis about the secondary nature of epidemics in domestic animals, since it appears that epidemics in these animal populations do not develop independently, but epidemics are supported by contact with wild world animals [1].

Mapping the official data of the public health and veterinary surveillance in 2003–2015 showed that rabies in farm animals have been occurred over most of Kazakhstan,

but in its distribution regional variations were revealed. There were two distinct districts (Zhambyl and Kostanay Oblasts) where large clustering of outbreaks was observed (Fig. 1).

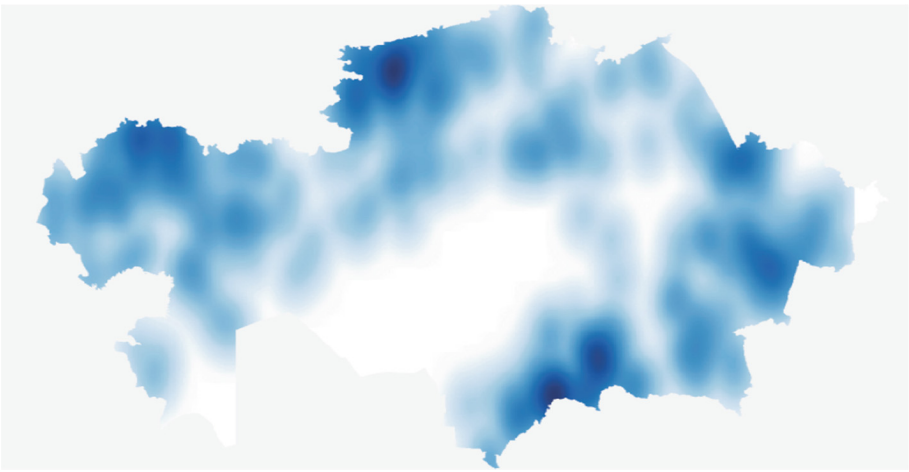


Fig. 1. Rabies in Kazakhstan (2003–2013): kernel density assessment in animals. A higher density of rabies cases is defined with darker shading. There are no outbreaks in white parts of the map [2].

There were treated an average 64,289 individuals with per annum underwent post exposure prophylaxis (PEP). Annually, it might result in 1140 DALYs. Every year PEP is protected 118 cases of human rabies or possibly 1184 at an estimated cost of $1193 or $119 averted respectively per DALY. It was estimated that in Kazakhstan an economic impact of rabies per annum is $20.9 million, with approximately half of it being attributed to the PEP and the income loss whilst persons were treated. There were annually assessed $5.4 million to be the life time income loss in lethal cases. An animal vaccination and control programs also particularly contributed to the economic losses [2].

3.2 Anthrax

A model was developed, the resulting predictive ability of which was rated as “good”. To anthrax outbreak distribution existing most significantly contributed such variables as the maximum green vegetation fraction, the precipitation level of the most humid month, the precipitation level of the most humid quarter and the soil type. Regarding moisture and vegetation, an increase in variables had led to a corresponding monotonic increase in fitness, what was illustrated by response curves.

The continuous surface, showing the distribution of suitability to the outbreak of anthrax and taking into account considered geospatial factors, was converted into a grid format and superimposed on the map of Kazakhstan.

Averaged over the districts values of the risk had constructed the last map of risk, what reflected the influence of districts of country on the appearance of anthrax and accompanied by the map demonstrated the 95th percentile of risk (Fig. 2).

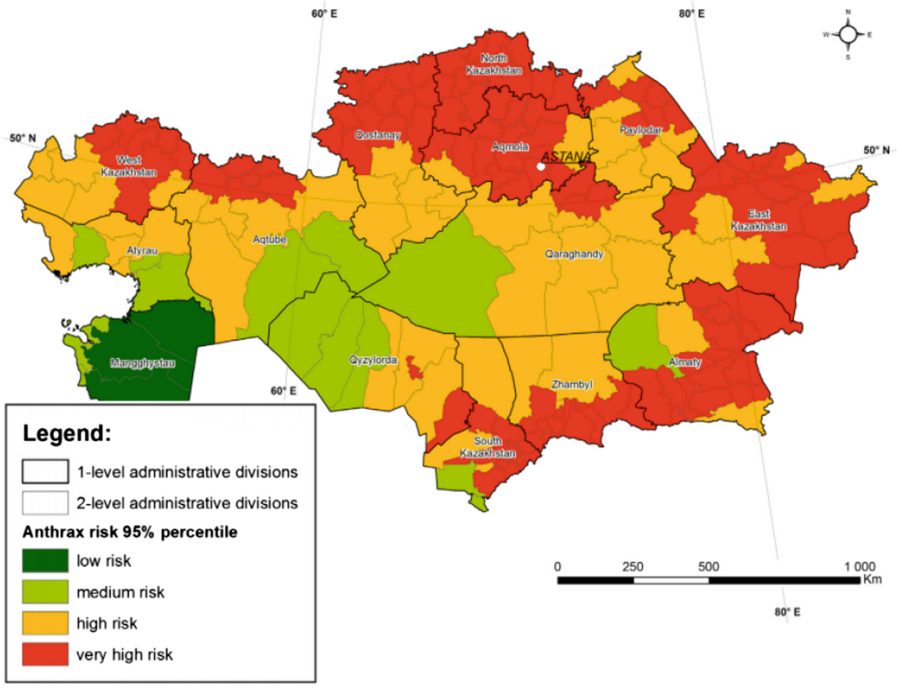


Fig. 2. Values of the 95th percentile in zoning of Kazakhstan by the risk of re-occurrence of anthrax (Maxent modelling) [3].

According to mapping the lowest risk of anthrax was indicated in western and central areas, and higher risk – in other geographical regions of the country [3].

3.3 Foot and Mouth Disease

In the study period there were revealed 35 statistically significant clusters for serotype A lineages, 41 clusters for serotype O and 13 clusters for lineage A22 by the spatiotemporal cluster analysis (Fig. 3).

In the late 1960s, there was a significant cessation of outbreaks of serotypes O and A clusters, which coincided with the onset of mass prophylactic livestock vaccination in 1970s.

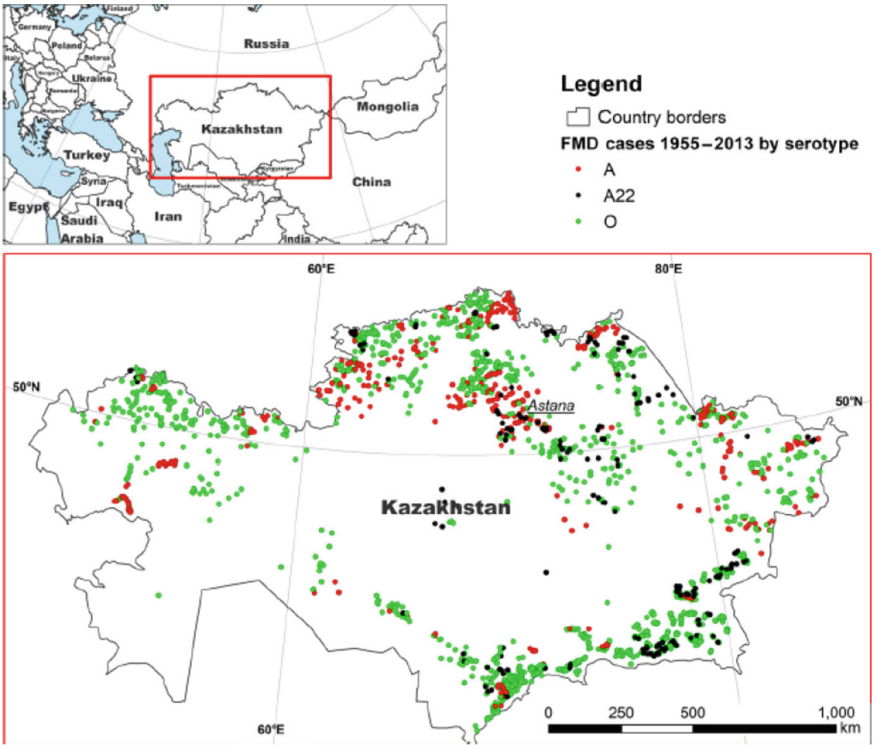


Fig. 3. Map of recorded foot and mouth disease outbreaks' location in 1950–2013 with serotypes [4].

ANOVA analysis of STDOs did not reveal significant differences between the lineages, and therefore, STDOs could be combined between lineages. The value could be used as an indicator of the possible development of the epidemic situation in the event of a new outbreak, especially in the absence of prophylactic vaccinations. Analysis of the seasonality showed that two seasonal peaks of the incidence were observed: in spring and autumn. There was no clear seasonality evident at the location of the clusters [4].

4 Discussion

Rabies is one of the dangerous lethal viral zoonotic diseases what transmitted to humans through bites of infected animals. Now the infection registered in more than 100 countries. The disease caused neurological clinics and had 100% fatality ratio if clinical signs present. Annually in the world 55,000 people and average a million animals die from this viral infection. Economical losses from rabies each year achieve more than EURO 4 billion [5].

According to the WHO the rabies problem must be researched by medical and veterinary professionals together. The epidemic curves developed in these studies were constructed for the three identified clusters, and the fitted exponential curves support the hypothesis about the secondary nature of the epidemics in domestic animals, since it is believed that these animals were infected by contact with wild animals. The found results agree well with the data of other authors [6, 7].

The reviewed research showed that 36% of animals should be vaccinated in the farm animals' category, while the figure increased to 41% for the wild animals' category. The obtaining vaccinations' ratio of the productive animals and wild carnivores corresponds to the current vaccination in Kazakhstan. It should be denoted the closeness of two clusters to the country's border, for it could be interpreted as a possible cross-border transfer of rabies in wildlife populations and the further spread in farm and pet animals' populations. Obtained data indicate that PEP was prophylactic for 713 rabies deaths in a 6 year period or an average of 119 annually deaths. The financial sums expended to control and destruction of stray and infected animals were $3.4 million annually. It was established that in spite of using the vaccination, the amount of areas with rabies cases in livestock or in the total numbers of cases was not reduced. The economic influence of rabies might be reduced by modifications of the vaccination program [1, 2].

It was known that for period 1961–2016 annual morbidity from anthrax in Kazakhstan decreased by more than 100 times [8]. But in the last decade there were described several endemic cases of disease among people [9]. In modern science environmental modelling is widely used for simulation the probability of a disease emergence with reference to certain territorially limited risk factors [10, 11].

In this research interpretive representation and statistical significant assessment of results was obtained with convenient maximum entropy method, applied in the anthrax research. The model's results approved the strong dependence of anthrax outbreaks locations from environmental conditions. Simulations showed a growth of local applicability to anthrax connected with an increase in the territorial ecological variables. Results were fitted to the foci in pastures and other places for animal feeding where anthrax was identified historically. Taking into account the range of relative pH values, it can be assumed to be associated with slightly acidic soils. The continuous probability surface was aggregated by averaging the values of risk by districts.

Research results produces more illustrative material in view of practical applicability and gives possibilities for official Kazakhstan veterinary service to make right decisions on planning of control measures against anthrax. So it gives an opportunity to identify districts where maximum plausible risk raises against a mean level, and decision-makers may refer to a continuous risk surface to reveal districts with significantly exposure to anthrax [3].

The present analysis has shown that the efficacy of the foot and mouth disease's outbreaks controlling strategy in Kazakhstan was clearly evidenced through the interruption of spatiotemporal clustering. There was suggested that immunity after vaccination developed decreasing the susceptibility of neighbour population and stopped the virus local spreading. After implementation the vaccination strategy clusters of A and O serotype strains of the foot and mouth disease no longer distributed in the country.

The space-time patterns of A22 lineage outbreaks allowed suggesting that trade relations of Kazakhstan with neighbour countries and transboundary movements of wild animals could be a cause of A22 lineage importation into Kazakhstan. Seasonality patterns described with peaks of infection prevalence in spring could be referable to productive animal farming practices in Kazakhstan where livestock is moved from winter location to pastures in the spring.

Applied in the research parameter STDO shows the amount of new outbreaks per unit area in a certain time interval. This parameter is very important for practical goals to compare the local epidemics intensity and to prognosis the expected number of outbreaks in bigger areas. It may be served to predict the expected amount of foot and mouth disease outbreaks within a particular area, and thus easily applicable to decision makers [4].

5 Conclusion

The reviewed studies give a detailed overview of the distribution and burden of infections as rabies, anthrax and foot and mouth disease in Kazakhstan. The results are largely based on detailed surveillance and budgetary data provided by the veterinary and public health services and demonstrate that in Kazakhstan there is a substantial economic cost and health impact of such diseases of animals and humans.

The widespread use of post exposure prophylaxis (PEP) prevents annually at least 118 and up to 1184 fatalities of humans bitten by rabid animals. The annually economic costs of this disease are exceeding $20 million.

In studies employed a data-driven approach to quantify suitability of Kazakhstan districts to anthrax re-emergence with relation to environmental conditions. The research allowed illustrating the niche nature of anthrax and strong dependence of its historical outbreak locations in the country on a combination of environmental factors. There was creating a map of anthrax re-emergence risk categories that could be applied by the veterinary service to plan a vaccination and surveillance activity. The availability of this map also enables consideration of risks of preserved soil foci reactivation when developing projects of construction works that impact historically formed landscapes.

Using historical data on foot and mouse disease incidence in Kazakhstan, there was demonstrated that quantitative methods for analysis of spatiotemporal data can effectively evaluate the trends of local epidemic formation and illustrate the impact of different disease control strategies. In addition, estimated values of within-herd prevalence by species, size and duration of space–time clusters by serotype, and seasonal patterns of incidence contribute to our epidemiological understanding of foot and mouse disease distribution in endemic regions attempting eradication.

Acknowledgements. This work has been accomplished under the National Budgetary Program # 249 “Providing conditions for the development manufacturing, processing and sale of livestock production”.

References

1. Abdrakhmanov, S.K., Beisembayev, K.K., Korennoy, F.I., Yessembekova, G.N., Kushubaev, D.B., Kadyrov, A.S.: Revealing spatio-temporal patterns of rabies spread among various categories of animals in the Republic of Kazakhstan, 2010–2013. Geospat. Health **11** (455), 199–205 (2016)
2. Sultanov, A.A., Abdrakhmanov, S.K., Abdybekova, A.M., Karatayev, B.S., Torgerson, P.R.: Rabies in Kazakhstan. PLOS Negl. Trop. Dis. **10**(8), 1–15 (2016)
3. Abdrakhmanov, S.K., et al.: Maximum entropy modeling risk of anthrax in the Republic of Kazakhstan. Prev. Vet. Med. **144**, 149–157 (2017)
4. Abdrakhmanov, S.K., et al.: Spatiotemporal analysis of foot-and-mouth disease outbreaks in the Republic of Kazakhstan, 1955–2013. Transbound Emerg. Dis. **65**(5), 1235–1245 (2018)
5. Botvinkin, A.D., Otgonbaatar, D., Tsoodol, S., Kuzmin, I.V.: Rabies in the Mongolian steppes. Dev. Biol. **131**, 199–205 (2008)
6. Aikimbayev, A., Briggs, D., Coltan, G., et al.: Fighting rabies in Eastern Europe, the Middle East and Central Asia—experts call for a regional initiative for rabies elimination. Zoonoses Public Health **61**, 219–226 (2014). https://doi.org/10.1111/zph.12060. PMID: 23782901
7. Fooks, A.R., Banyard, A.C., Horton, D.L., Johnson, N., McElhinney, L.M., Jackson, A.C.: Current status of rabies and prospects for elimination. Lancet **384**, 1389–1399 (2014). https://doi.org/10.1016/S0140-6736(13)62707-5. PMID: 24828901
8. Lukhnova, L. Yu., Aikimbayev, A.M., Pazylov, E.K.: Epidemic process of anthrax in Kazakhstan. Bull. Agric. Sci. Kazakhstan 'Bastau' **7**, 44 (2004)
9. Abdrakhmanov, S.K., Mukhanbetkaliyev, Y.Y., Beysembayev, K.K., Kushubayev, D.B., Kadyrov, A.S.: Spatio-temporal analysis of the epidemiological situation on anthrax in Kazakhstan. In: Proceedings of 4th Conference of ISOCARD «Silk Road Camel: The Camelids, Main Stakes For Sustainable Development», 8–12 June, Almaty, Kazakhstan, pp. 222–224 (2015)
10. Stevens, K.B., Pfeiffer, D.U.: Spatial modelling of disease using data - and knowledge-driven approaches. Spat. Spatiotemporal Epidemiol. **2**, 125–133 (2011)
11. Korennoy, F.I., Gulenkin, V.M., Malone, J.B., Mores, C.N., Dudnikov, S.A., Stevenson, M.A.: Spatio-temporal modeling of the African swine fever epidemic in the Russian Federation, 2007–2012. Spat. Spatiotemporal Epidemiol. **11**, 135–141 (2014)