Application of modern spatio-temporal analysis technologies to identify and visualize patterns of rabies emergence among different animal species in Kazakhstan

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Abstract

During the period 2013-2023, 917 cases of rabies among animals were registered in the Republic of Kazakhstan. Out of these, the number of cases in farm animals amounted to 515, in wild animals to 50 and in pets to 352. Data on rabies cases were obtained from the Committee for Veterinary Control and Supervision of Kazakhstan, as well as during expeditionary trips. This research was carried out to demonstrate the use of modern information and communication technologies, geospatial analysis technologies in particular, to identify and visualize spatio-temporal patterns of rabies emergence among different animal species in Kazakhstan. We also aimed to predict an expected number of cases next year based on time series analysis. Applying the 'space-time cube' technique to a time series representingcases from the three categories of animals at the district-level demonstrated a decreasing trend of incidence in most of the country over the study period. We estimated the expected number of rabies cases for 2024 using a random forest model based on the space-time cube in Arc-GIS. This type of model imposes only a few assumptions on the data and is useful when dealing with time series including complicated trends. The forecast showed that in most districts of Kazakhstan, a total of no more than one case of rabies should beexpected, with the exception of certain areas in the North and the East of the country, where the number of cases could reach three. The results of this research may be useful to the veterinary service in mapping the current epidemiological situation and in planning targeted vaccination campaigns among different categories of animals.

Introduction

Rabies is one of the deadliest of all infectious diseases and is estimated to have caused an average of 59 000 deaths worldwide each year (Hampson *et al.*, 2015). Dog bites are responsible for approximately 99% of human deaths from rabies, which mainly occurred in Africa and Asia (WHO, 2023). Dog rabies has been successfully eliminated in many countries in the western hemisphere, while the Pan American Health Organization (PAHO) and Latin American governments have achieved a sharp decrease in the prevalence of rabies in recent years through the implementation of large-scale and sustainable dog vaccination programmes (Cleaveland *et al.*, 2018). If adequate coverage to stop the enzootic transmission of rabies can be provided, dog vaccination is considered the single most effective strategy to reduce the burden of rabies disease (Monroe *et al.*, 2021).

A global program for the eradication of rabies under the concept of "One Health", adopted in 2018, provides excellent opportunities for many countries to defeat rabies once and for all (Tidman *et al.*, 2022; Shafaati *et al*., 2023). At the same time, the creation of a comprehensive strategy ensuring reliable control and prevention requires the use of modern technologies and computer tools. This is not only needed for analysis and forecasting, but also to further accelerate the decision-making process and organize timely and effective control measures. An important aspect in the application of these technologies directly is the obtaining of reliable information that will serve as the key to valid research and forecasting.

To date, the successful experience of rabies control in many countries is based precisely on the use of information and communication technologies, for example, the RabIDprogram (Blanton *et al.*, 2006) is an innovative example of the effectiveness of geographical surveillance of infectious diseases available via the Internet. This surveillance system was developed based on existing technology and is easily adaptable to other infectious diseases and can be especially useful in relation to zoonoses. In their research, scientists from China used a Bayesian hierarchical spatio-temporal model to determine the impact of environmental, economic, and demographic factors and describe trends in morbidity over the period 2004-2019 (Li *et al.*, 2023). Thanks to this approach, priority areas (provinces) where it is necessary to strengthen animal vaccination were identified as high-risk areas for rabies.

A successful approach to rabies epidemiology should include early detection and immediate response to new outbreaks and surveillance programs. Timely information on the spread of cases in space and time can facilitate the actions of veterinarians and/or public health officials. Several techniques are currently available for space-time analysis and visualization in medical epidemiology (Robertson & Nelson, 2010; Lan & Delmelle, 2023) as well as in veterinary medicine (Perez *et al.*, 2002; Moore *et al.*, 2005; Kabzhanova *et al.*, 2023).

Application of some of these techniques were successfully carried out in our previous rabies studies. We refer here to spatial-temporal analysis using SatScan software in the period from 2013 to 2022, which made it possible to make a significant contribution to improving the effectiveness of preventive measures against rabies. This study identified species-specific clusters for some regions of the country, upon which a vaccination proposal prepared (Kabzhanova *et al*., 2023). Another GIS-based technique, namely the 'space-time cube', was applied for analysis of anthrax burden in Kazakhstan over a long historical period by Abdrakhmanov *et al.* (2017), who was able to demonstrate specific trends. The latter approach, being an effective tool for spatiotemporal analysis and visualization and receiving extensive development in recent years, is still underrepresented in veterinary epidemiology (Bergquist, 2017).

Strengthening rabies surveillance is of particular importance and Information and Communication Technologies (ICT) are vital for lasting success. With the development of ICTs, various processes are being improved and optimized so that reliable information can be obtained for decision-making. The objective of the current study was to employ new techniques to reveal and visualize trends of animal rabies emergence through 2013-2023, and to predict an expected number of cases by district that could indicate the primary areas subject to enhanced surveillance.

Materials and Methods

Study area

The Republic of Kazakhstan is a landlocked state in central Asia, occupying the 9th place in the world in terms of area. The country measures 2,900 km west to east, and 1,600 km from north to south. Seventy percent of the territory is suitable for animal husbandry including transhumance, *i.e.* the practice of moving livestock from one grazing ground to another in seasonal cycles. The average population density is 7.3 people/km^2. Administratively, the country is divided into 17 regions (oblasts) and three cities of significance (administrative division of the first level). In turn, the regions are subdivided into 178 second–level administrative districts. In our research, districts constituted the minimum unit of analysis to which the analyzed attributes were linked (Figure 1).

Rabies data

Data on rabies cases among various animal species were obtained from the Committee for Veterinary Control and Supervision of the Ministry of Agriculture of the Republic of Kazakhstan (https://www.gov.kz/memleket/entities/vetcontrol?lang=en) as well as collected from local veterinary authorities during expeditionary trips of the research team duringthe period 2013-2023. In this study, the case refers to the geographically localized (*i.e.* defined by geographical coordinates) detection of one or more animals infected with the rabies virus. The diagnosis of animal rabies is laboratory-confirmed by the regional branches of the Republican Veterinary Laboratory using a direct fluorescent antibody test and alsoby the RSE "National Reference Center for Veterinary Medicine" using a reverse transcription polymerase chain reaction (RT-PCR) test. For modelling purposes, all infected animals were divided into three categories: livestock (cows, small ruminants, horses, camels, donkeys); wild animals (wolfs, foxes, jackals) and pets (cats and dogs). Due to the confidentiality of the data, individual cases could not be mapped in this study. Instead, a yearly number of cases was calculated for each district.

Spatiotemporal trend analysis and visualization

To assess the temporal trends of animal rabies emergence in districts of Kazakhstan through the study period, a 'space-time cube' Geospatial Information Systems (GIS) technique was applied (Kraak, 2003). This technique, developed for commercial purpose by ESRI (https://pro.arcgis.com/en/pro-app/latest/tool-reference/space-time-pattern-mining/learnmorecreatecube.htm) allows aggregating spatio-temporal count data by space-time cells creating time series of data for each location. A range of analysis methods may then be applied to the time series in order to reveal spatial and temporal patterns. In our case, the spatial basis of the cells was the districts of the Republic of Kazakhstan, and the time step, represented by the vertical axis, was one year. Emerging Hotspot (EHS) analysis by Ord and Getis, 1995 was first applied to detect clusters of districts demonstrating higher than expected concentration of rabies cases both in space and time (with a null hypothesis of their random distribution). Further, trend analysis using Mann-Kendall statistics (Hamed, 2009) was applied i) to reveal hotspots and coldspots: and ii) to prepare an individual, district-based time series. For each district, the following characteristics were reported: i) its attribution to a hotspot or a coldspot; ii) the temporal trend of emergence of these spots; and iii) the temporal trend of the number of cases per district. Each of these characteristics was supported by a confidence level, where $p<0.1$ was considered statistically significant.

Hotspots and coldspots here were defined as places (districts) demonstrating a statistically significant excess/scarcity of the number of rabies cases over the number expected under the null hypothesis of their random distribution. Depending on the specific pattern formed by these areas over time revealed categories that could be described as 'New', 'Sporadic', 'Oscillating', 'Decreasing', etc. (https://pro.arcgis.com/en/pro-app/3.2/tool-reference/space-time-pattern-mining/learnmoreemerging.htm).

Forecasting the number of rabies cases

To estimate the expected total number of cases of rabies in each district of the Republic of Kazakhstan in 2024, we applied the method of forecasting time series using the forest-based technique (Breiman *et al.*, 2017; Goehry *et al.*, 2021). For each time series, revealed at the previous step within a space-time cube, a regression model was fitted based on the random forest approach, where the dependent variable was the number of cases of rabies and the explanatory variable the time step. This forest was then used to predict the next time step. Including this predicted value, the fore-

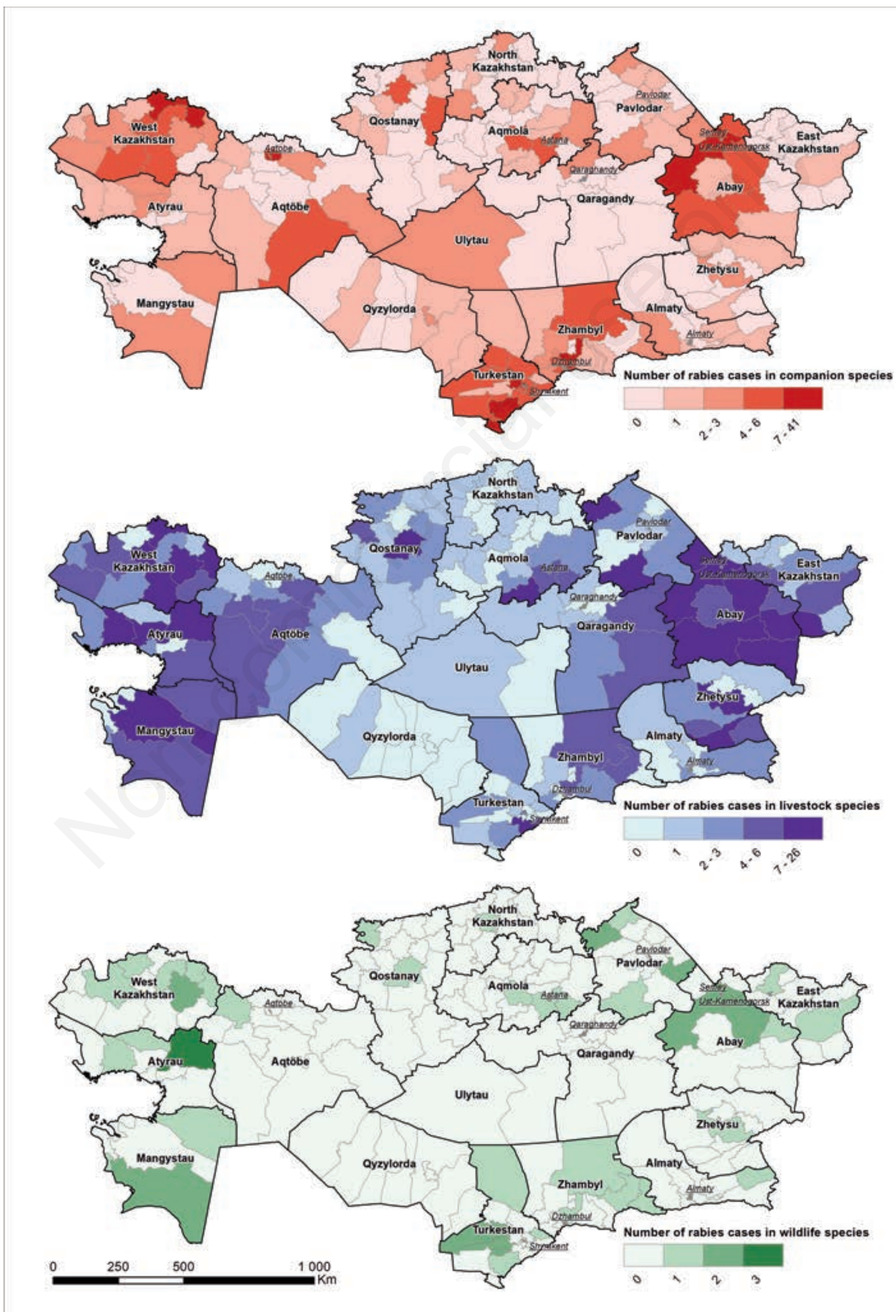

Figure 1. The administrative division of the Republic of Kazakhstan and number of rabies cases among various categories of animals in 2013-2023.

cast of the next time step occurs, thus generating a recursive process that continues through all subsequent time steps. The match for each time series was measured using the Root Mean Square Error (RMSE) that shows the average difference between a statistical model's predicted values and the actual values. The spatial distribution of RMSE was then tested for spatial autocorrelation using Moran's I (Mitchell, 2005), where index values close to zero with a high p-value (>0.05) suggests absence of autocorrelation and thus indicates spatial randomness of the error distribution. To test the accuracy of the prediction, validation was applied during forest-based regression modelling. The validation was performed by withholding a number of time steps at the end of time series (two-time steps in our case) forecasting values for these steps using the model trained by the previous steps and comparing the forecasting performance with the actual values using the RMSE error calculation.

The forest model was chosen for forecasting in our case, when the number of rabies cases within the time series demonstrated a high variationsince it, unlike more traditional regression models, does not impose significant restrictions on the input data.

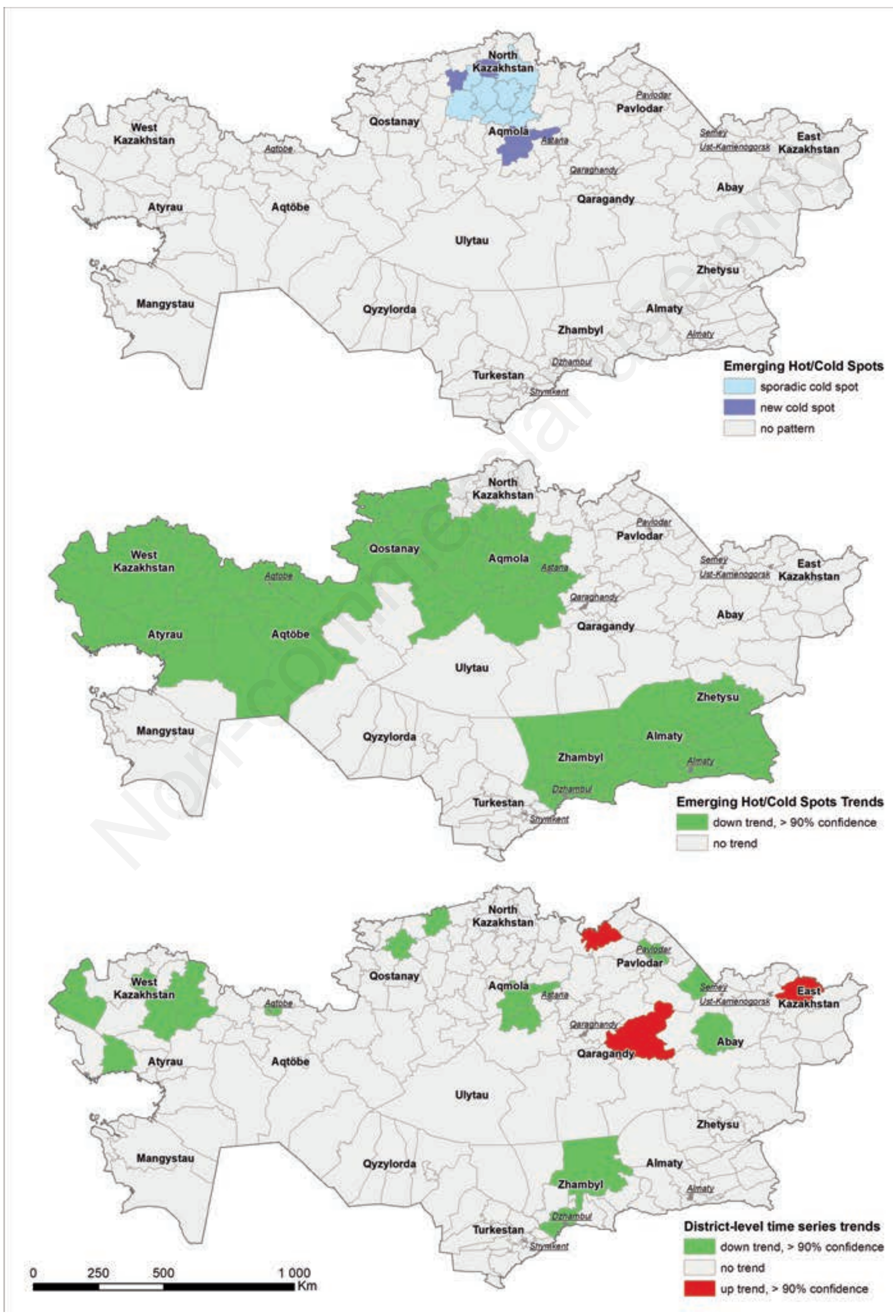

Figure 2. Results of space-time cube based emerging hot spot analysis and trend visualization of rabies cases among various categories of animals in the Republic of Kazakhstan, 2013-2023.

Software

ArcGIS Desktop 10.8.1 and ArcGIS Pro 3.2 (ESRI, Redlands, CA, USA) were used to visualize the results and process spatiotemporal data.

Results

Descriptive analysis

During the period 2013-2023, 917 cases of rabies among animals were registered in the Republic of Kazakhstan, out of which 515 (56.2%) were cases among farm animals, 352 (38.4%) among pets and only 50 (5.4%) among wild animals (Figure 1). The results of the EHS analysis and the corresponding temporal trends are represented in Figure 2. Most parts of Kazakhstan do not show a significant tendency towards formation of hotspots or coldspots, except the large area of North Kazakhstan Oblast and part of Aqmola Oblast around the capital Astana. These regions were identified as 'sporadic' and 'new' coldspots. Indeed, a significantly lower number of cases in these areas was found within the study period, and for may during the last few years. With respect to hotspots, 94 of 176 districts (together 53%) demonstrated a statistically significant trend toward a decrease, suggesting an improve-

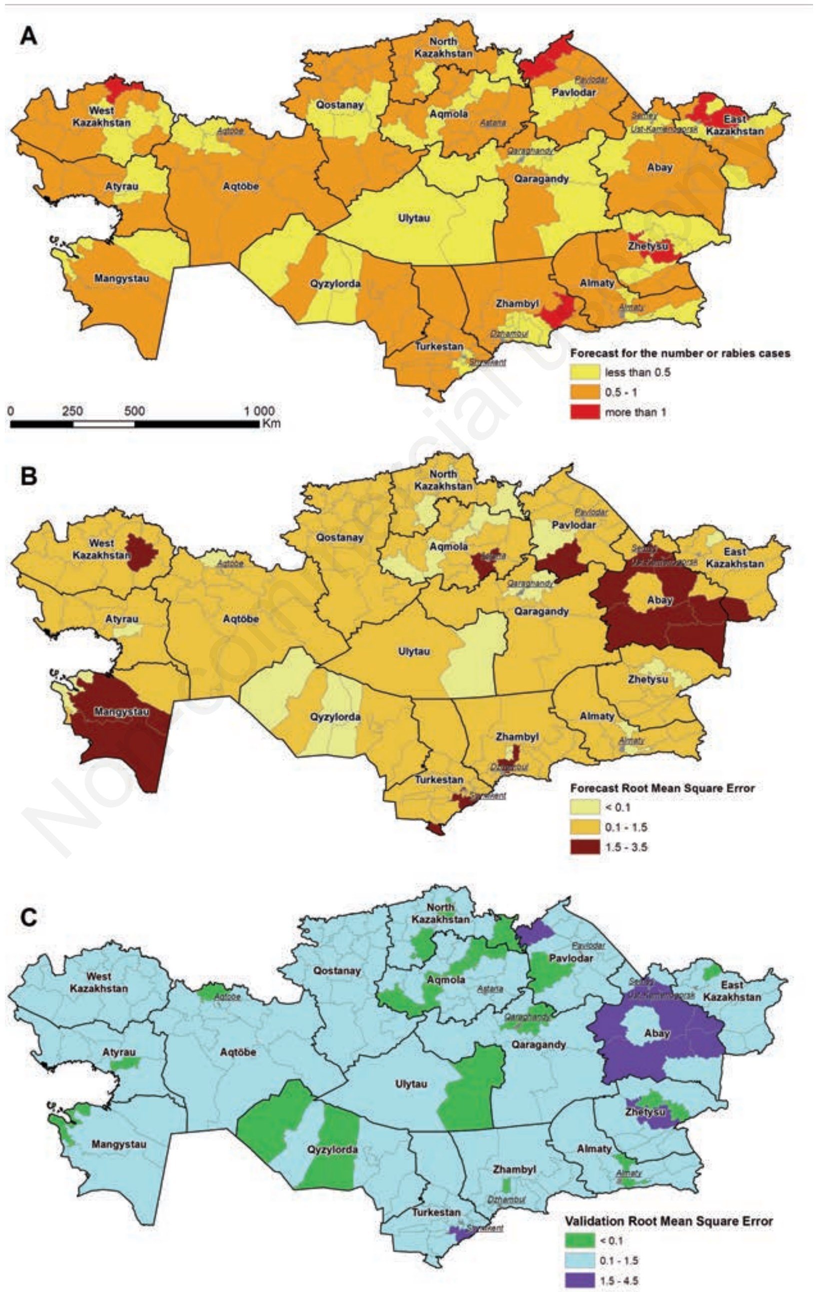

Figure 3. The predicted number of rabies cases among various animals in Kazakhstan in 2024. (**A**), Predicted number of rabies cases; (**B**), Root Mean Square Error of the forecast; (**C**), Root Mean Square Error of the validation

ment in the situation for animal rabies in those districts located in the North-west and South-east of the country. For 155 (88%) of the districts 176 no statistically significant trend was observed in the local time series, suggesting a rather uneven and heterogeneous distribution of rabies cases in those districts throughout the study period. Only three districts demonstrated a statistically significant upward trend, namely Zyryanovsky District in East Kazakhstan Oblast, Karkaralinsky District in Qaragandy Oblast and IrtyshskyDistrict in Pavlodar Oblast.

Forecasting

Forecasting the possible number of outbreaks for 2024 allowed us to obtain the expected spatial distribution of cases shown in Figure 3A. The largest number of outbreaks, up to three, is expected only in some particulardistricts of the country: Zhelezinka and Irtysh Districts in the region of Pavlodar, Zelenovsky District in West Kazakhstan, Glubokovsky District in East Kazakhstan and AksuDistrict of the region of Zhetysu. No more than one case of rabies was predicted in most other regions. The spatial distribution of RMSE demonstrated a random pattern (Figure 3B), suggesting absence of autocorrelation (Moran's I = 0.046; z-score=0.47 and p=0.64). For most of the study districts, the validation error did not exceed 1.5 and demonstrated no spatial autocorrelation (Moran's I = 0.05 z-score=0.53 and p-value=0.59) (Figure 3 C).

Discussion

The purpose of this research was to demonstrate the use of modern GIS analysis methods to identify the most common patterns of distribution of cases of rabies in animals in the Republic of Kazakhstan and to predict their expected number for the next year. In the previous work (Kabzhanova *et al.*, 2023), a multivariate cluster detection method was applied, which revealed clusters with a predominance of cases among one of the three categories of animals. An essential task on the national veterinary service, however, requires not only retrospective study, but strongly demand scientifically-based forecasts allowing targeted concentration of monitoring and vaccination efforts. Given the multiplicity of factors influencing the strength of the rabies epidemic situation in any particular region, we made an attempt to rely on a probabilistic approach dealing with a temporal sequence of data, deriving patterns and building prediction for future. We employed a popular GIS technique of data analysis that divides the entire study area into space-time cells (the spase-time cube) and performed an in-depth analysis of both spatial and temporal trends. Being a common tool in multiple disciplines based on geography (Bach *et al.*, 2014; Putrenko *et al.*, 2018), the space-time cube approach still lacks application in veterinary epidemiology (Abdrakhmanov *et al.*, 2017; Xu *et al.*, 2023).

The use of EHS analysis for visualization of epidemic situation trend has been demonstrated elsewhere (Abdrakhmanov *et al.*, 2017). The temporal trends revealed the emergence of hotspots suggesting a decrease in the intensity of the rabies epidemic situation in roughly half of the districts analyzed. The absence of any observed trend in the rest of the districts probably resulted from a relatively small number of cases and anuneven distribution over the study period.

Regarding the projected number of cases of rabies for 2024, it can be noted that the applied forecasting method only used the time series of cases for the period 2013-2023. The number of cases during this period is low and shows significant variation over the years, the final estimate has a fairly high RMSE error, but the spatial distribution suggests an absence of spatial autocorrelation, which supports the accuracy of the modelling. To improve the accuracy of the forecast, additional variables affecting the intensity of the epidemic rabies manifestation could be used – first of all, the size of susceptible populations and the vaccination coverage in different populations. A country-wise survey is now being conducted to build databases of livestock species distribution throughout the country, which should enable the application of more robust models to analyze disease spread patterns and reveal high-risk areas (Abdrakhmanov *et al.*, 2022).

The use of modern geoinformation methods is in line with the country's current course towards improving surveillance strategies and digitalizing national agriculture (Sultanov *et al.*, 2016) and our study results underline the importance of raising awareness of the Kazakhstani veterinary service and optimize planned vaccination campaigns.

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