

# Descriptive spatiotemporal analysis of rabies in domestic carnivores and wildlife in Ukraine in 2012-2018\*

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### Summary

Ukraine leads Europe in the number of rabies cases reported in both wild and domestic animals. Endemic rabies in Ukraine poses a threat of rabies spreading into non-endemic neighbouring countries, including Poland, Slovak Republic, Hungary and Romania. This study is the first to collate and analyze rabies cases at the national level in Ukraine. Spatial and temporal analysis was performed to identify space-time clusters of rabies cases using nationally collated rabies surveillance data from 2012-2018. In the study period, 10,717 rabies cases were confirmed, with the majority in domestic carnivores (49.5%; cats: 28.5%; dogs: 21.1%) and the other primarily in foxes (34.0%). Rabies epidemic curves identified peak rabies incidence from October to December for foxes and from October to March for domestic carnivores. The kernel density of rabies for all species indicates a permanently high density in southwest Ukraine (Zakarpattia and Vinnytsia oblasts) and lower in northeast Ukraine (Poltava oblast). The highest density of rabies cases in foxes occurred in oblasts bordering European countries, while rabid domestic carnivores were concentrated near the border with the Russian Federation. The analysis identified 10 statistically significant clusters in foxes and 3 in domestic carnivores, mostly in the same high kernel density locations. Early clusters of foxes were recorded on January 3, 2012 in western Ukraine (ratio, 2.21), and early clusters of domestic carnivores on January 30, 2012 in western Ukraine as well (ratio, 6.39). These findings provide insight into the temporal patterns and distribution of rabies case clusters in wildlife and domestic carnivores in Ukraine. Our study provides policymakers with the first statistically valuable data on the hotspot regions and timing of rabies outbreaks. The analysis may contribute to improved rabies prevention and surveillance strategies by identifying regions for targeted prevention measures so that national programmes for the prevention, surveillance and control of rabies in Ukraine are executed more effectively.

**Keywords:** rabies cases, Ukraine, domestic carnivores, wildlife carnivores, foxes, temporal patterns, space-time clusters

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Globally, rabies is responsible for 59,000 human deaths a year, particularly in developing countries (9, 35, 37). Historically, *Carnivora* and *Chiroptera* species are the primary hosts of the rabies virus (RABV), but rabies affects both domestic and wild animals (3, 11, 13, 17). The World Health Organization's Rabies Information System reports that Ukraine, the Russian Federation, and the Republic of Belarus account for the highest number of rabies cases in Europe (available online at <https://www.who-rabies-bulletin.org/%20Queries/Surveillance.aspx>, accessed April 21, 2021).

Although rabies cases are subject to mandatory reporting in all European countries, including Ukraine, rabies control and surveillance efforts vary significantly among EU and non-EU European countries (4, 7, 39). Over the last century, a positive trend in control measures and active implementation of oral rabies vaccination (ORV) programmes for sylvatic rabies in European countries have facilitated the elimination of fox-mediated rabies (6, 15, 29).

In Ukraine, the first ORV programme for wild carnivores was introduced in the early 2000s, but, due to limited funding, this programme was targeted at areas with the highest rabies incidence (23, 34). ORV campaigns were usually carried out 1-2 times per year only across those targeted areas. For instance, ORV was carried out in 4 to 9 oblasts (out of 24) in springs and autumns of 2012-2014. In 2015-2017, it was performed only once per year in 3 to 6 oblasts, and in 2018 ORV was deployed across the whole territory of Ukraine, but again, only once (in autumn). As pointed out by Freuling et al. (16), in order to eliminate rabies in wild animals, ORV campaigns should be carried out twice a year. Parenteral vaccination campaigns for domestic carnivores in Ukraine were launched in 1954 and continue, but are not regarded as very effective (2). Despite ORV and parenteral vaccination campaigns, Ukraine remains endemic for rabies (12, 28, 34).

Unlike other countries in Eastern and Central Europe, Ukraine has a high circulation of rabies in domestic carnivores (including stray dogs and cats) with as many cases of rabies in wild carnivores (12, 34). As noted by Cliquet et al. (8), the proportion of rabid domestic animals (3,088 cases) in Europe in 2012 was almost analogous to that reported in wildlife, whereas domestic cases dominated in Ukraine (1,161 cases) and in the Russian Federation (893 cases), which suggests that rabies monitoring should focus on domestic species.

According to Kornienko et al. (20), between 1998 and 2018 in Ukraine, there were 33,079 cases of rabies among animals: 19,687 (59.5%) cases in domestic animals (10 species) and 13,392 (40.5%) cases in wild animals (18 species). Domestic cats (25.3%), dogs (19.3%), foxes (36.7%) and cattle (13%) accounted for 94.5% of all animal rabies cases. Among wild animals, the highest number of cases was recorded in foxes

(12,136; 90.6%) and a significantly lower number in other wild species. Among domestic animals, cats accounted for the highest proportion of cases (8,384 cases; 42.6%), with dogs (6,375 cases; 32.4%), cattle (4,311 cases; 21.9%), and sheep and goats (419 cases, 2.1%) accounting for the remaining cases (25).

The aim of this study was to investigate the spatial and temporal dynamics of rabies in animal populations (primarily, fox and domestic carnivore populations) at the national level in Ukraine between 2012 and 2018. To date, no previous studies have explored spatial and temporal dynamics of rabies at the national level, probably because of the lack of a centralized national database of rabies cases that contains GIS data. Initial attempts at consolidating rabies case data for GIS analysis were made in 2016, but that study was limited to 4 of the 24 oblasts of Ukraine (34). Since then, our research group has made significant efforts to compile a national-level database of rabies cases, with support and approval from Ukrainian authorities. This database contains data on rabies cases across Ukraine, starting from 2012. The present study is the first spatial and temporal analysis of rabies incidence at the national level in Ukraine. The results of this work are particularly relevant to planning effective rabies control measures and implementing more targeted awareness campaigns in both veterinary and public health sectors.

## Material and methods

**Study location.** Ukraine, with an area 603,628 km<sup>2</sup>, is located in Eastern Europe. The total length of Ukraine's land borders is 5,684 km, including 2,590 km of the borders with Central and Western Europe: Poland, Slovakia, Hungary, Romania, Moldova and Belarus. In the east and northeast, Ukraine borders the Russian Federation; in the south, Ukraine's maritime borders are in the Black Sea and the Sea of Azov.

Most of Ukraine's land borders do not have natural boundaries that would hinder animal migration. Within the country itself, such a boundary is the Dnieper River, which divides the country from north to south into 2 parts: the left-bank Ukraine and the right-bank Ukraine. Along the river, there are 6 water reservoirs with a maximum width of 7 km to 28 km (10). The country is administratively divided into 24 oblasts (Fig. 1), and each oblast is subdivided into administrative districts called rayons. The estimated human population is about 41.4 million (excluding Crimea and Sevastopol), and the population density amounts to 73.8 persons per km<sup>2</sup> (available online at <https://en.wikipedia.org/wiki/Ukrainehttps://cran.r-project.org/web/packages/epitools/index.html>, accessed May 24, 2021).

With regard to animal population, there are 116 species of mammal fauna across Ukraine. The most abundant predatory species relevant to this study include foxes, wolves, badgers, raccoon dogs, raccoons, martens and jackals. They numbered about 468 thousand in 2018, including about 50 thousand foxes, 11 thousand raccoon dogs, 2 thousand

wolves, the rest consisted of small wild animals according to the State Statistics Service of Ukraine (available online at <http://www.ukrstat.gov.ua>, accessed January 12, 2021).

**Disease data.** Ukraine conducted passive surveillance of the whole country. It was based on the testing of indicator animals each year. Indicator animals are generally animals that show clinical signs (or abnormal behaviour suggestive of rabies), animals found dead, road kills and animals which have potentially exposed humans to rabies. Active monitoring is used to determine the effectiveness of oral vaccination campaigns in wild animals and animals submitted by hunters. This active monitoring occurs one month after vaccination when foxes are shot at the rate of 2-4 foxes per 100 km<sup>2</sup> of vaccinated area, and the carcasses (heads) are sent to the laboratory and tested.

The State Regional Laboratories of Veterinary Medicine (SRLVM) received samples from animals as part of passive surveillance. In general, fresh carcasses of small animals, or heads and brains of large animals, are delivered by oblast (rayon) veterinary specialists to the SRLVM along with documentation specifying the animal species, name and address of the sender, animal owner or person who was in contact with the animal, vaccination status of the animal if known, anamnesis, as well as clinical and epidemiological information if available. Rabies was diagnosed from each sample using a fluorescent antibody test or a bioassay test in white mice; samples with positive results in either test was considered positive. In the case of the testing of vaccine intake by foxes, the lower jaw and serum samples from foxes are delivered by messenger to the State Scientific Research Institute of Laboratory Diagnostics and Veterinary and Sanitary Expertise (SRILDVSE) along with an appropriate document indicating the species of the animal, location where the shooting took place, date of vaccination, date of blood sampling, as well as name and series of the

vaccine used for immunization (available online at <https://zakon.rada.gov.ua/laws/show/z0054-94#Text>, accessed May 24, 2021).

Rabies surveillance data for the study period (2012-2018) were collected from the official annual reports of the SRLVM of the State Service of Ukraine for Food Safety and Consumer Protection and from the SRILDVSE. Data regarding positive samples included the serial number of the case, animal species (fox, dog, cat, raccoon dog, badger, cattle, etc.), location (oblast, district, settlement) and the date of rabies diagnosis confirmation. The geocoordinates of each case were found additionally by our research group. Data concerning negative samples were collected by laboratories only as a general number per oblast annually, without location or date, so we could not find geocoordinates or conduct deeper spatial and temporal analyses.

Although every effort was made to integrate data into the dataset accurately, there are limitations to data collection stemming from the lack of division according to the surveillance method (e.g., active and passive surveillance). The analysis was limited by the fact that the data sets were mixed. To address some of these limitations, the analysis was performed and presented separately for different species.

**Descriptive statistical analyses.** Rabies data were classified into four groups: foxes, domestic carnivores (including stray cats and dogs), other wild animals (e.g., raccoon dogs, martens, wolves, ferrets, rats, bats) and other domestic animals (e.g., cows, horses, goats and pigs) (Tab. 1). Foxes were allocated into a separate group because of their main role as a rabies reservoir. Dogs and cats (both domestic and stray) were combined into one group as they are a major source of human rabies infection in Ukraine (19, 25). The percentage of positive samples with an exact binomial confidence interval in each group was calculated

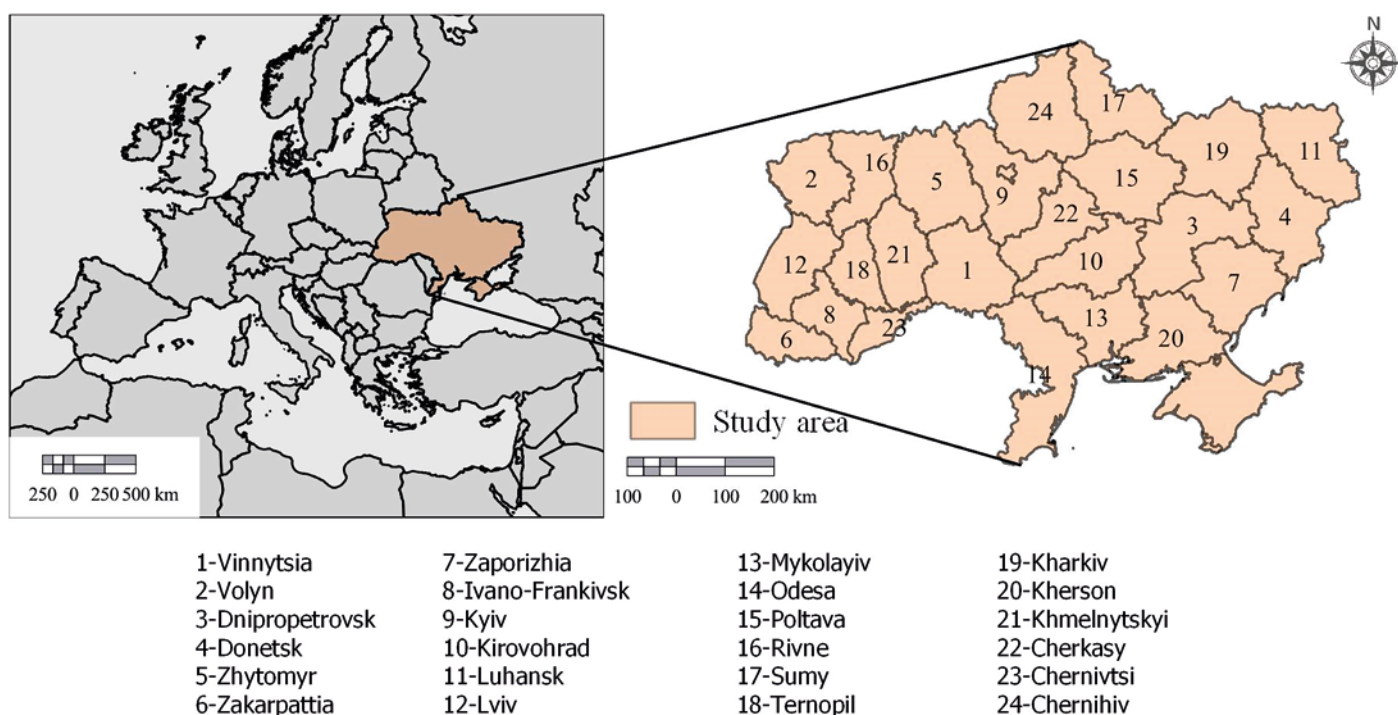


Fig. 1. Map of the study area with the boundaries and names of the oblasts of Ukraine

Tab. 1. Number of rabies cases in Ukraine in 2012-2018

| Species                       | Year               |                    |                    |                    |                    |                    |                    | Total               |
|-------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|---------------------|
|                               | 2012               | 2013               | 2014               | 2015               | 2016               | 2017               | 2018               |                     |
| <b>Domestic carnivores</b>    | <b>905 (45.7%)</b> | <b>693 (45.6%)</b> | <b>489 (45.7%)</b> | <b>723 (49.9%)</b> | <b>747 (56.1%)</b> | <b>845 (50.7%)</b> | <b>907 (53.2%)</b> | <b>5309 (49.5%)</b> |
| • Cat                         | 548                | 393                | 274                | 415                | 437                | 504                | 480                | 3051                |
| • Dog                         | 357                | 300                | 215                | 308                | 310                | 341                | 427                | 2258                |
| <b>Fox</b>                    | <b>739 (37.3%)</b> | <b>564 (37.1%)</b> | <b>414 (38.7%)</b> | <b>450 (31.1%)</b> | <b>415 (31.2%)</b> | <b>521 (31.3%)</b> | <b>548 (32.2%)</b> | <b>3651 (34.1%)</b> |
| <b>Other domestic animals</b> | <b>237 (12.0%)</b> | <b>174 (11.5%)</b> | <b>116 (10.9%)</b> | <b>186 (12.8%)</b> | <b>117 (8.8%)</b>  | <b>215 (12.9%)</b> | <b>167 (9.8%)</b>  | <b>1214 (11.3%)</b> |
| • Cow                         | 204                | 153                | 106                | 155                | 99                 | 185                | 136                | 1038                |
| • Goat                        | 25                 | 13                 | 10                 | 26                 | 16                 | 24                 | 28                 | 142                 |
| • Horse                       | 7                  | 7                  | 0                  | 1                  | 2                  | 3                  | 2                  | 22                  |
| • Pig                         | 1                  | 1                  | 0                  | 4                  | 0                  | 3                  | 0                  | 9                   |
| <b>Other wild animals</b>     | <b>98 (4.9%)</b>   | <b>88 (5.8%)</b>   | <b>51 (4.6%)</b>   | <b>89 (6.1%)</b>   | <b>53 (4.0%)</b>   | <b>84 (5.0%)</b>   | <b>83 (4.8%)</b>   | <b>545 (5.1%)</b>   |
| • Badger                      | 6                  | 11                 | 6                  | 7                  | 4                  | 4                  | 7                  | 45                  |
| • Bat                         |                    | 3                  | 1                  |                    | 3                  | 1                  | 1                  | 9                   |
| • Beaver                      | 3                  | 1                  | 1                  |                    | 1                  | 3                  | 2                  | 11                  |
| • Elk                         |                    |                    | 1                  | 2                  |                    | 1                  |                    | 4                   |
| • Ferret                      | 2                  | 5                  | 2                  | 3                  | 1                  | 1                  | 1                  | 15                  |
| • Hamster                     | 7                  | 2                  |                    | 3                  | 1                  | 3                  |                    | 16                  |
| • Jackal                      |                    |                    |                    | 3                  | 2                  | 1                  | 3                  | 9                   |
| • Lynx                        |                    |                    |                    |                    | 1                  | 1                  |                    | 2                   |
| • Marten                      | 31                 | 30                 | 12                 | 14                 | 6                  | 9                  | 14                 | 116                 |
| • Domestic cavy               |                    |                    | 1                  | 1                  |                    |                    |                    | 2                   |
| • Muskrat                     | 1                  |                    | 1                  | 2                  |                    | 1                  | 1                  | 6                   |
| • Otter                       |                    |                    |                    | 1                  |                    | 1                  | 1                  | 3                   |
| • Raccoon                     | 3                  | 2                  | 1                  | 2                  | 4                  | 5                  | 5                  | 20                  |
| • Raccoon dog                 | 27                 | 27                 | 15                 | 36                 | 25                 | 35                 | 33                 | 198                 |
| • Rat                         | 4                  | 3                  | 1                  | 3                  | 2                  | 6                  | 3                  | 22                  |
| • Roe deer                    | 1                  |                    | 1                  | 1                  | 1                  | 2                  | 2                  | 8                   |
| • Saiga antelope              |                    |                    | 3                  |                    |                    |                    |                    | 3                   |
| • Squirrel                    |                    |                    |                    |                    |                    |                    | 2                  | 2                   |
| • Weasel                      | 1                  |                    | 1                  | 1                  |                    |                    | 1                  | 4                   |
| • Wild boar                   | 1                  | 1                  |                    | 1                  |                    |                    |                    | 3                   |
| • Wolf                        | 11                 | 3                  | 3                  | 9                  | 2                  | 8                  | 7                  | 43                  |
| <b>Total</b>                  | <b>1979</b>        | <b>1519</b>        | <b>1070</b>        | <b>1448</b>        | <b>1332</b>        | <b>1665</b>        | <b>1704</b>        | <b>10 717</b>       |

using an epitools package in R and is shown in Table 2, Supplemental Table 1 and Supplemental Table 2. To assess the difference in the percentage of positives in each group across the years, we used Pearson's Chi-squared test in R (available online at <https://cran.r-project.org/web/packages/epitools/index.html>, accessed June 14, 2021). The results were considered statistically significant at  $p < 0.05$ . Epidemic curves of rabies cases among wildlife and domestic animals were created on a monthly basis for all oblasts (Fig. 4).

**Spatial and temporal analysis.** The spatial and temporal analysis was conducted for all species of animals and separately for foxes and domestic carnivores. The kernel density of cases (QGIS 3.4.6, Heatmap) was estimated to describe spatial heterogeneity in rabies distribution on an annual basis as described previously (18). The optimal

search radius responsible for smoothing power was calculated according to Fotheringham et al. (14).

Spatial-temporal clusters of rabies cases were identified using the SaTScan software 9.6. (available online at <https://www.satscan.org>, accessed January 12, 2021). Dataset limitations (lack of location and geocoordinates for all negative samples, absent GIS information on fox and domestic carnivore populations) restricted the selection of tools for analysis to the space-time permutation model (21). This model is capable of analysing cases without controls (negative samples), which made it possible to analyze data despite the dataset limitations. The maximum spatial cluster size and the maximum temporal cluster size were set to 50% of the population at risk and 50% of the study period, respectively. The time aggregation parameter was defined as up to 14 days.



The numbers of all samples from animals per oblast were mapped as an indicator of monitoring efforts (active and passive) and shown as choropleth maps (Fig. 2, 3) separately for foxes and domestic carnivores. In order to increase the comparability of surveillance efforts between regions of Ukraine, an index of surveillance efforts was also calculated as the number of animals tested in each oblast over the human population (i.e. a unit of 100,000 inhabitants) (38). Human population data were obtained from the State Statistics Service of Ukraine (available online at <http://www.ukrstat.gov.ua>, accessed January 12, 2021).

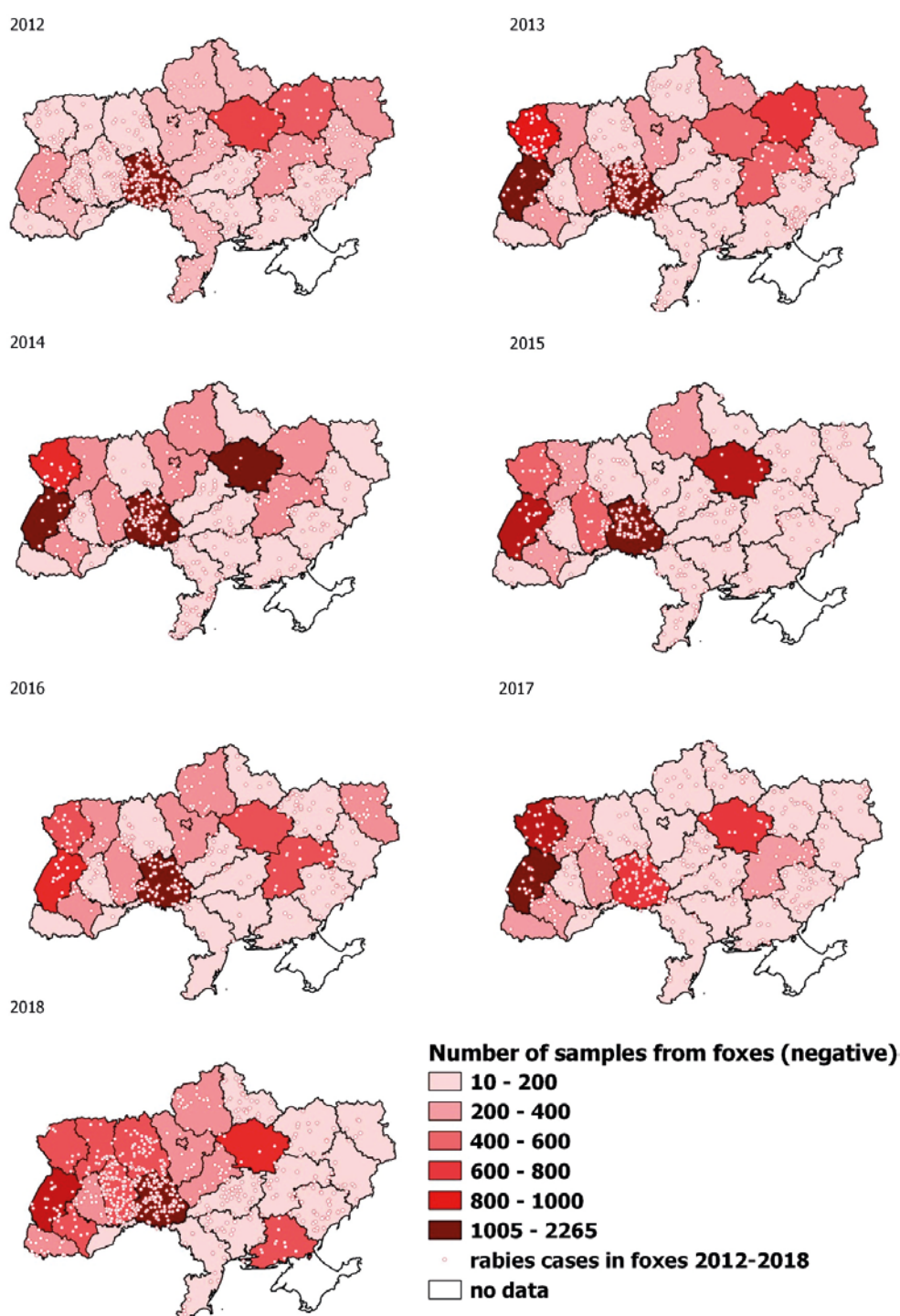
All maps and shapefiles were generated in QGIS 3.4.6. using projection CRS: EPSG:102013 – Europe\_Albers\_Equal\_Area\_Conic. Vector layers of Ukrainian borders were obtained using GADM (<http://gadm.org/>).

## Results and discussion

**Descriptive statistical analysis.** Between 2012 and 2018, 81,314 samples from 28 different species were tested for rabies in oblast laboratories, and 10,717 of those samples tested positive. Table 1 details rabies cases across the four species groups in the study period. The most numerous were cases in domestic carnivores: 5,309 cases (49.5%), with 3,051 cases (28.5%) reported in cats and 2,258 cases (21.1%) in dogs. In other domestic animals, 1,214 rabies cases (11.3%) were confirmed, most of which occurred in cattle (1,038 cases, 9.7%). Among all wild animals, the vast majority, i.e., 3,653 cases (34.0%), were reported in foxes, whereas 541 cases (5.1%) were confirmed in other wild animals (Tab. 1).

The number of samples collected from foxes (Fig. 2) and domestic carnivores (Fig. 3) reflects the monitoring efforts in Ukraine. With regard to foxes, most oblasts provided a moderate to high number of samples. Only in few oblasts was monitoring more intensive (~1000-2000 samples per oblast per year) (Fig. 2).

Samples collected from domestic carnivores were much fewer than those collected from foxes across



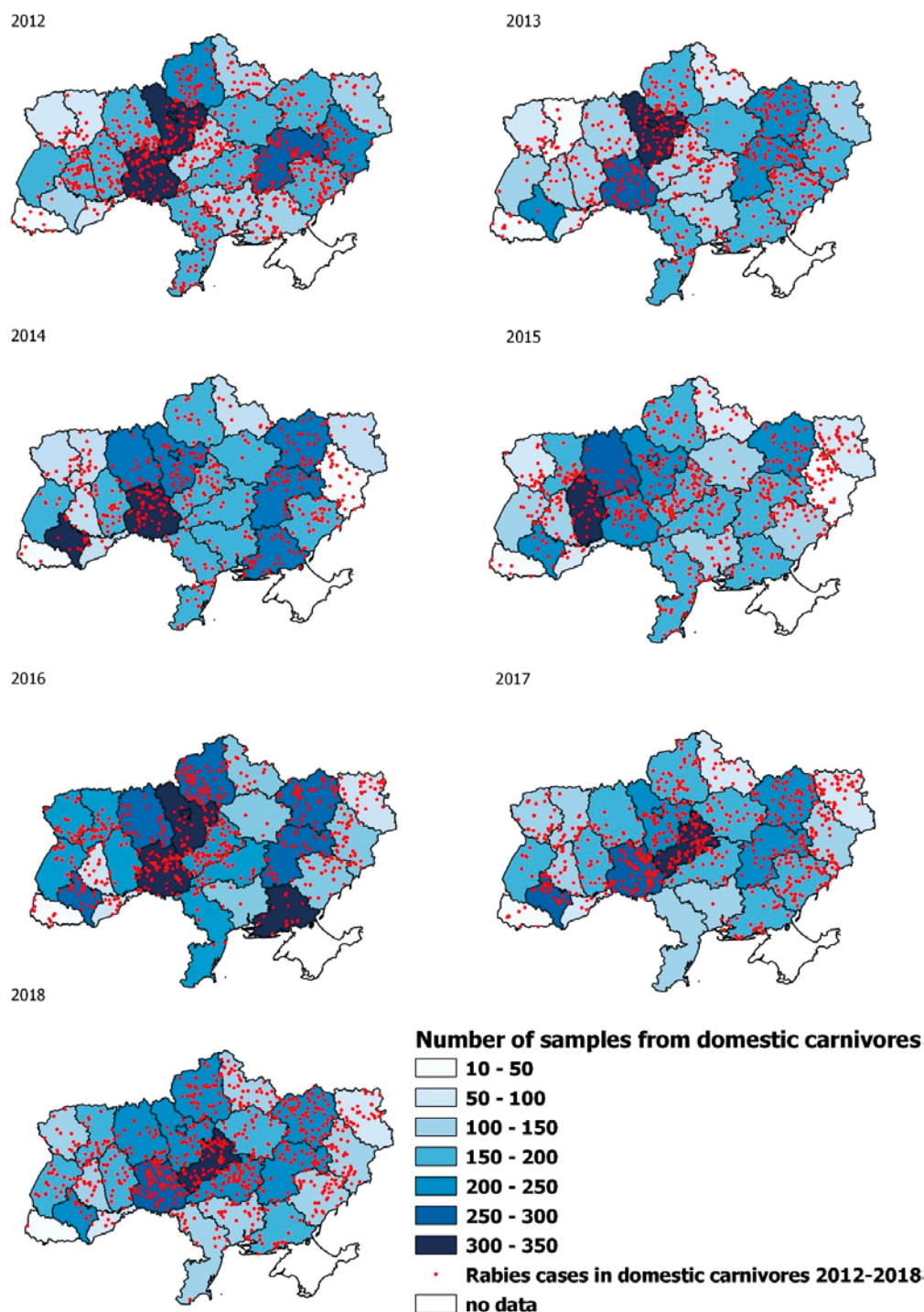
**Fig. 2. Collection of fox samples by oblast in 2012-2018**

Explanations: oblasts with a high level of collection of all samples are highlighted in a more intense red color, and oblasts with a low level of collection of all samples are less intense red

all Ukraine, with only central (Kyiv, Kirovograd) and western (Vinnytsia) Ukraine collecting moderate numbers of samples (~300-350 samples per oblast) (Fig. 3).

Figure 4 shows epidemic curves for all species identified in sample metadata. With regard to monthly variation, the last months of autumn and the first months of winter showed the highest number of reported cases for all species of animals, and spring and summer months had the fewest reported cases each year.

The highest number of rabies cases in foxes (among all species) were observed from 2012 to 2014 and in



**Fig. 3. Collection of domestic carnivore samples by oblast in 2012-2018**

Explanations: oblasts with a high level of collection of all samples are highlighted in a more intense blue color, and oblasts with a low level of collection of all samples are less intense blue

2018. In general, the epidemic curve for foxes shows a consistent increase in rabies incidence from October to December for each year of the study period.

The epidemic curve for domestic carnivores shows a consistent increase in incidence from October to March for each year with the highest annual picks (among all species) from 2015 to 2017. The full list of rabies prevalence in foxes, domestic carnivores, and other domestic and wild animals with a 95% exact binomial confidence interval over the years of the study is presented in Table 2.

As shown in Table 2, the percentage of positive cases in foxes was not consistent across all years of observation ( $\chi^2 = 74.291$ ,  $df = 6$ ,  $p\text{-value} = 5.371e^{-14}$ ). From 2012 to 2013, a decrease in the percentage of cases was observed (2012 – 7.58%, 2013 – 6.13%), followed by an increase in the following 2 years (2014 – 9.03%, 2015 – 9.96%), a decrease in 2016 (6.76%) and an increase in the last 2 years of the study (2017 – 7.29%, 2018 – 8.39%).

The percentage of positive cases in domestic carnivores was also inconsistent across the years of observation ( $\chi^2 = 192.7$ ,  $df = 6$ ,  $p\text{-value} < 2.2e^{-16}$ ). The lowest percentage of positive rabies cases was observed in 2013, and the highest in 2015. From 2012 to 2014, a decrease in the percentage of rabies cases in domestic carnivores was observed (2012 – 21.02%, 2013 – 17.55%), followed by an increase in the following 2 years (2014 – 24.15%, 2015 – 29.50%), a decrease in 2016 (18.26%) and an increase in the last 2 years of the study (2017 – 21.02%, 2018 – 21.25%) (Tab. 2).

**Spatial and temporal analysis.** In general, the density of rabies cases among all animal species in 2012-2018 was highest in southwestern Ukraine (primarily Vinnytsia oblast), close to the border with Moldova (Fig. 5). A high density of rabies cases was observed in central Ukraine

(in the eastern part of the Cherkasy oblast) and in eastern Ukraine (Zaporizhzhia, Donetsk, Lugansk, Dnipropetrovsk, and Kharkiv oblasts), near the border with the Russian Federation.

Interestingly, two southern oblasts (Odesa and Kherson) showed a decreasing rabies case density among all species in the study period, while several other areas in eastern and western Ukraine showed an increasing density of cases during the study period (Luhansk, Sumy, Kharkiv, Kirovograd, Khmelnytskyi and Lviv oblasts). Across Ukraine, only two locations,



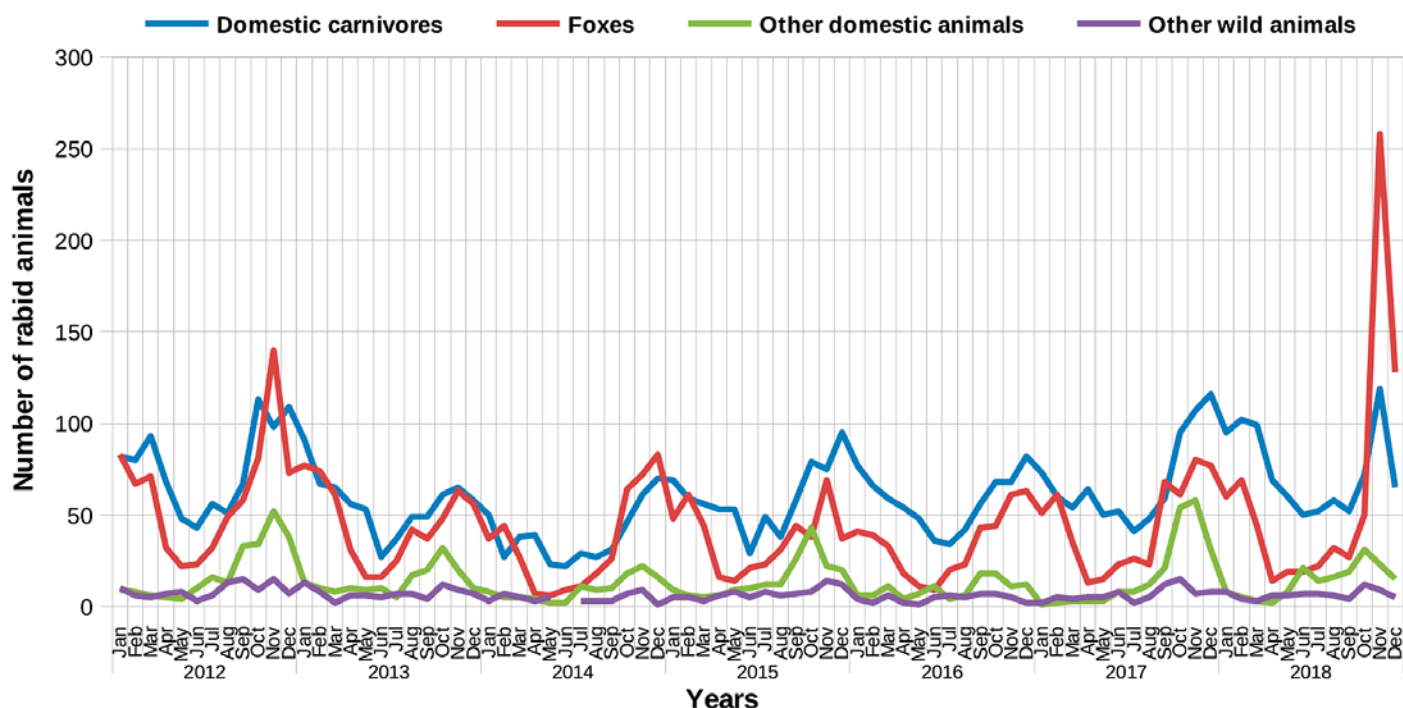


Fig. 4. Epidemic curves of rabies cases among wildlife and domestic animals in Ukraine, by month, 2012-2018

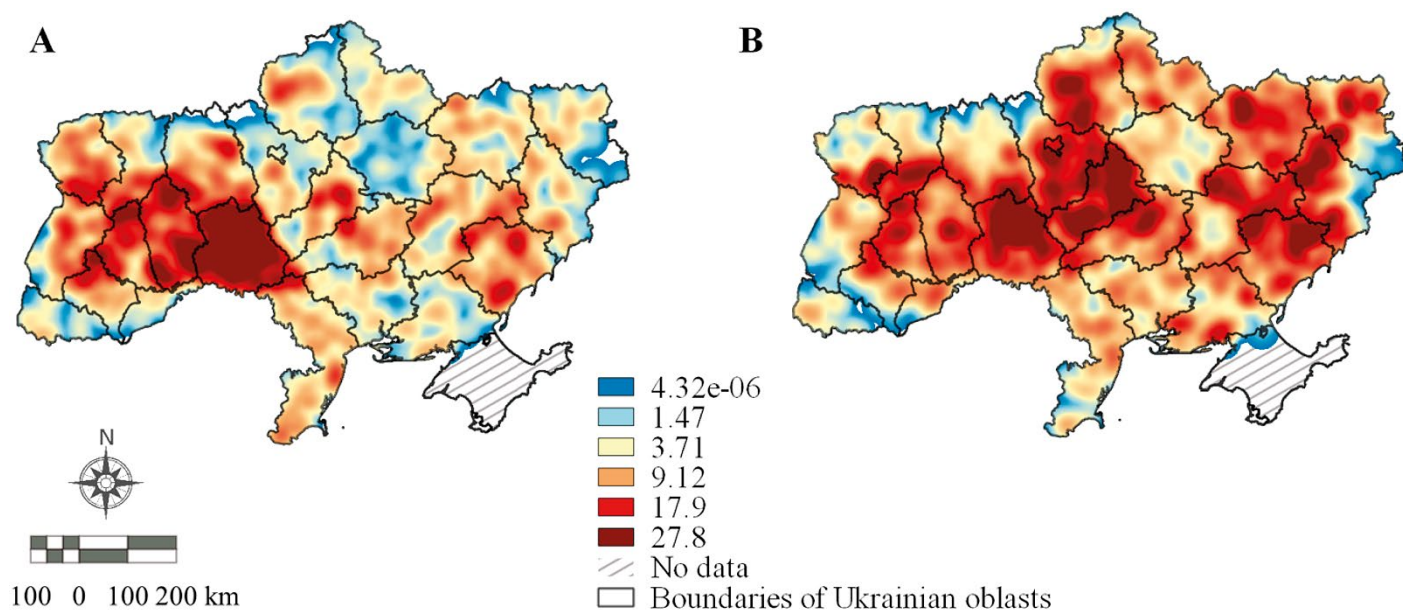


Fig. 5. Kernel density estimation of rabies cases in foxes (A) and in domestic carnivores (B) for 2012-2018. Explanations: areas with the highest density of rabies cases are highlighted in red, and the areas with the lowest density are blue across all years

northeast Ukraine (Poltava oblast) and southwest Ukraine (Zakarpattia oblast), showed a consistently low rabies case density year-over-year for the study period.

A spatio-temporal analysis performed separately for foxes and domestic carnivores data revealed that the density of rabies cases in foxes (Fig. 5A) was highest in three areas: southwestern Ukraine (especially in the Vinnytsia oblast, near the border with Moldova), western Ukraine (Khmelnyskyi, Ternopil and Ivano-Frankivsk oblasts), and close to the border with Poland (Lviv and Volyn oblasts). A lower density of rabies cases among foxes was observed in central

Ukraine (Zhytomyr, Chernihiv, Cherkasy, Kirovograd, Dnipropetrovsk, and Zaporizhzhia oblasts).

Areas with a high density of rabies cases in domestic carnivores (Fig. 5B) were more uniformly distributed across Ukraine than those for foxes. Rabies cases peaked in central (Kirovograd, Kyiv oblasts), western (northern section of the Vinnytsia oblast) and eastern Ukraine (Zaporizhzhia, Donetsk, Luhansk, Kharkiv oblasts) along the border with the Russian Federation and near the border with the Republic of Belarus (Chernihiv oblast). The year-over-year density of rabies cases was also analyzed separately for foxes and domestic carnivores during the whole study period

Tab. 2. Rabies prevalence by year (2012-2018) with an 95% exact binomial confidence interval (BCI)

| Species                   | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence<br>(%) | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|---------------------------|------|---------------|--------------|------------------------|---------------------|---------------------|
| Foxes                     | 2012 | 739           | 8988         | 8,22                   | 7,66                | 8,81                |
|                           | 2013 | 564           | 9150         | 6,16                   | 5,68                | 6,68                |
|                           | 2014 | 414           | 7545         | 5,49                   | 4,98                | 6,02                |
|                           | 2015 | 450           | 7146         | 6,30                   | 5,74                | 6,89                |
|                           | 2016 | 415           | 6194         | 6,70                   | 6,09                | 7,35                |
|                           | 2017 | 521           | 7133         | 7,30                   | 6,71                | 7,93                |
|                           | 2018 | 548           | 8347         | 6,57                   | 6,04                | 7,12                |
| Domestic<br>carnivores    | 2012 | 905           | 4100         | 22,07                  | 20,81               | 23,37               |
|                           | 2013 | 693           | 3926         | 17,65                  | 16,47               | 18,88               |
|                           | 2014 | 489           | 3035         | 16,11                  | 14,82               | 17,47               |
|                           | 2015 | 723           | 3627         | 19,93                  | 18,64               | 21,27               |
|                           | 2016 | 747           | 4090         | 18,26                  | 17,09               | 19,48               |
|                           | 2017 | 845           | 4049         | 20,87                  | 19,63               | 22,15               |
|                           | 2018 | 907           | 4174         | 21,73                  | 20,49               | 23,01               |
| Other domestic<br>animals | 2012 | 237           | 378          | 62,70                  | 57,61               | 67,59               |
|                           | 2013 | 174           | 316          | 55,06                  | 49,39               | 60,64               |
|                           | 2014 | 116           | 226          | 51,33                  | 44,61               | 58,01               |
|                           | 2015 | 186           | 304          | 61,18                  | 55,45               | 66,69               |
|                           | 2016 | 117           | 181          | 64,64                  | 57,20               | 71,59               |
|                           | 2017 | 215           | 295          | 72,88                  | 67,43               | 77,87               |
|                           | 2018 | 167           | 245          | 68,16                  | 61,93               | 73,95               |
| Other wild<br>animals     | 2012 | 98            | 600          | 16,33                  | 13,46               | 19,54               |
|                           | 2013 | 88            | 687          | 12,81                  | 10,40               | 15,54               |
|                           | 2014 | 51            | 319          | 15,99                  | 12,14               | 20,48               |
|                           | 2015 | 89            | 418          | 21,29                  | 17,46               | 25,53               |
|                           | 2016 | 53            | 477          | 11,11                  | 8,43                | 14,28               |
|                           | 2017 | 84            | 475          | 17,68                  | 14,36               | 21,42               |
|                           | 2018 | 83            | 439          | 18,91                  | 15,35               | 22,89               |

(2012-2018), which confirmed the permanence of rabies among foxes in the west of Ukraine and among pets mostly in the central part.

Tab. 3. Space-time clusters of fox rabies cases in Ukraine from 2012 to 2018

| Cluster<br>No. | Start date        | End date          | Observed/expected<br>= ratio | Radius,<br>km | p-value      |
|----------------|-------------------|-------------------|------------------------------|---------------|--------------|
| One*           | January 3, 2012   | April 8, 2012     | 43/19.44 = 2.21              | 69.81         | p = 0.019    |
| Two            | August 27, 2012   | November 4, 2012  | 37/15.14 = 2.45              | 168.54        | p = 0.011    |
| Three*         | November 5, 2012  | December 30, 2012 | 92/52.70 = 1.75              | 134.35        | p = 0.020    |
| Four           | December 3, 2015  | December 16, 2015 | 6/0.28 = 21.14               | 40.02         | p = 0.00050  |
| Five*          | November 5, 2016  | November 18, 2016 | 6/0.43 = 13.89               | 54.48         | p = 0.012    |
| Six            | November 19, 2016 | December 30, 2016 | 36/12.81 = 2.81              | 150.27        | p = 0.000049 |
| Seven*         | November 19, 2016 | December 16, 2016 | 14/2.77 = 5.05               | 75.53         | p = 0.0024   |
| Eight*         | January 30, 2017  | February 26, 2017 | 36/14.42 = 2.50              | 174.43        | p = 0.0026   |
| Nine*          | February 11, 2018 | June 30, 2018     | 37/14.42 = 2.57              | 176.70        | p = 0.0031   |
| Ten*           | November 4, 2018  | December 15, 2018 | 204/105.79 = 1.93            | 111.42        | p = 1e-17    |

Explanation: \* – indicates clusters that overlap with higher density from the kernels

**Space-time cluster analysis.** Fig. 6 shows the spatial-temporal clusters using the permutation space-time model. Ten statistically significant clusters were detected in foxes (Tab. 3), with the earliest cluster identified on January 3, 2012, in western Ukraine (Ternopil oblast). In domestic carnivores, we detected three likely clusters (Tab. 4), The earliest of them, found on January 30, 2012, in western Ukraine, intersected in space and time with the cluster in foxes.

Most of the clusters in foxes (7 out of 10) and one cluster in domestic carnivores (1 out of 3) coincide with high kernel density locations. These overlapping areas are indicated in Table 3 and 4.

The level of surveillance of animal rabies in foxes and domestic carnivores in Ukraine for the entire study period (number of samples per 100,000 people) is described in Table 5. For foxes, the index of surveillance efforts varied from 1.86 to 79.59 samples. It was highest in the west and centre of the country (Vinnytsia, Volyn and Poltava oblasts), and lowest in the east and south of Ukraine (Donetsk, Odesa and Zaporizhia oblasts). The level of sampling from domestic carnivores was low in all oblasts, and the index ranged from 2.06 to 17.30, with the lowest rates observed in the east (Donetsk, Luhansk) and in one oblast in the west (Zakarpattia).

This study describes, for the first time, the temporal and spatial dynamics of rabies epidemic in domestic and wild carnivore populations across all Ukraine. Our study used the newly developed national dataset for rabies, which incorporates data obtained between 2012 and 2018 from multiple sources. The dataset contains a remarkable amount of data. Between 2012 and 2018, more than 81,000 samples were analyzed, and more than 10,000 cases in different species were confirmed.

The analysis performed in this study shows that, in addition to foxes, about 50.0% of rabies cases (5,309 cases) were observed in domestic carnivores, a pattern which is different from other regions of Europe, where rabies occurs primarily in wild carnivores (12, 39). Our results show that, among domestic carnivores,

cats (28.5%) are affected more than dogs (21.1%). This result is explained mostly by the high population density of domestic carnivores, especially cats, and the absence of mandatory full vaccination of cats against rabies at the national level, as pointed out by Kornienko et al. (20). According to the current official regulation "About measures to combat animal rabies" (available online at <https://zakon.rada.gov.ua/laws/show/z0054-94#Text>, accessed May 24, 2021), cats ought to be vaccinated in the area of



**Tab. 4. Space-time clusters of rabies cases among domestic carnivores in Ukraine from 2012 to 2018**

| Cluster No. | Start date        | End date          | Observed/expected = ratio | Radius, km | p-value     |
|-------------|-------------------|-------------------|---------------------------|------------|-------------|
| One *       | January 30, 2012  | February 12, 2012 | 14/2.19 = 6.39            | 73.11      | p = 0.00061 |
| Two         | August 14, 2013   | August 27, 2013   | 9/1.22 = 7.37             | 131.05     | p = 0.028   |
| Three       | November 18, 2018 | December 15, 2018 | 17/3.49 = 4.87            | 78.60      | p = 0.0014  |

Explanation: as in Tab. 3

outbreaks, which are only limited to quarantine zones. Rabies (or suspected rabies) cases in domestic carnivores are often identified because most pets in Ukraine are under some veterinary supervision. Interestingly,

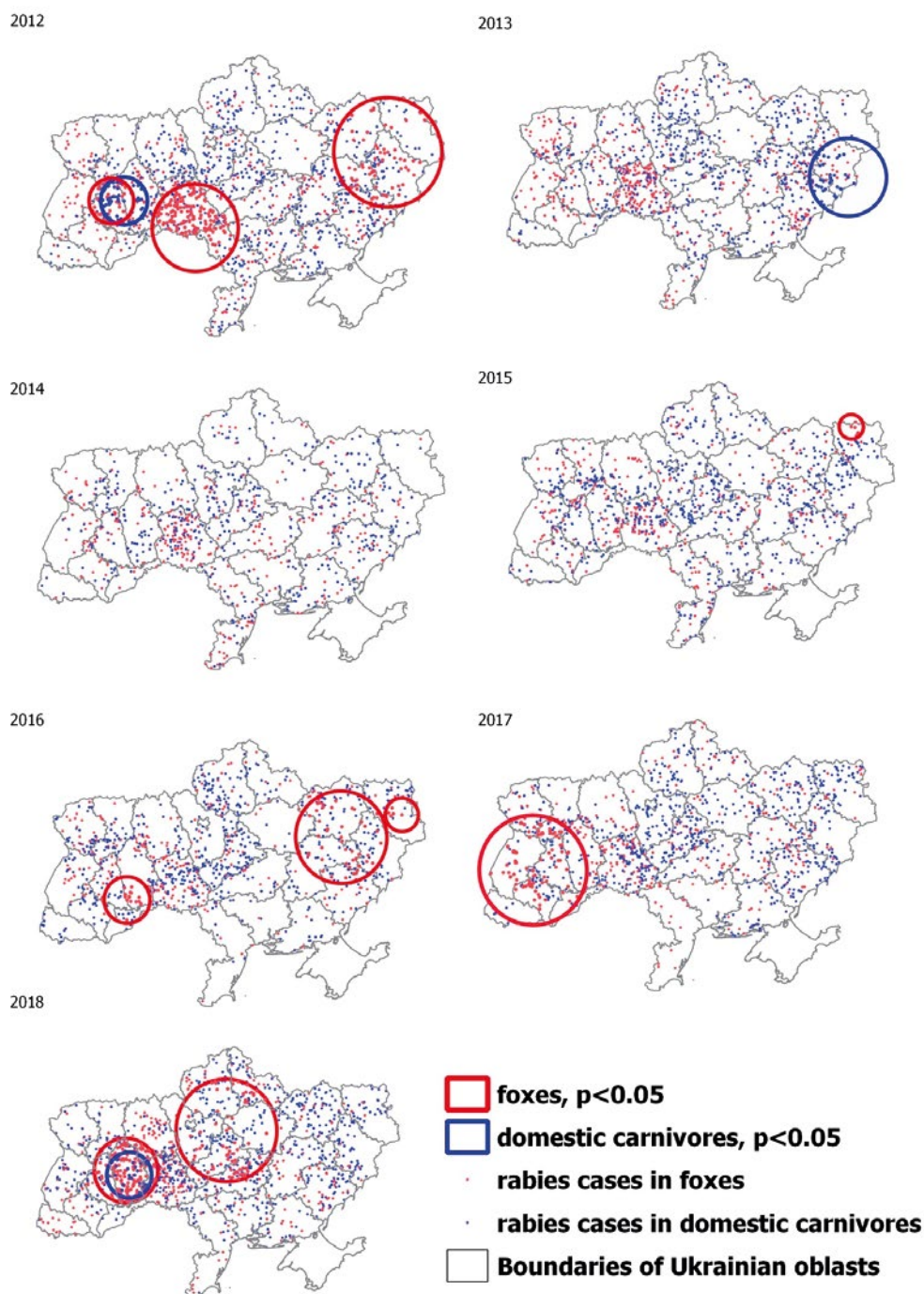
due to the greater responsibility of the owners and the fewer stray domestic carnivores in Poland.

During the study period, the highest number of rabies cases was reported in 2012 (1,979 cases), and the

lowest number of cases (1,070) in 2014. The decrease in 2014 may have been due to the occupation of eastern Ukraine, particularly the Luhansk and Donetsk oblasts, and the annexation of the Autonomic Republic of Crimea by the Russian Federation. These developments affected rabies surveillance strategies in those areas, reducing the number of samples and data collected across Ukraine, as well as decreasing the reliability of reports from those three regions.

This opposite situation may be

The epidemic curves for foxes and domestic carnivores are remarkably similar (Fig. 4). The peaks of rabies epidemic in fox populations in autumn and winter (from October to February) are driven mainly by fox ecology, with peak numbers of cases coinciding with fox resettlement due to breeding, habitat expansion and aggressive behaviour which facilitates fighting over territory (28, 31). Fluctuations in fox numbers also depend on the availability of food and the number of infected individuals in the population (5). In addition to ecological factors, the disease dynamic in foxes may be partially influenced by hunting and culling practices in Ukraine. These are concentrated in autumn, which results in an increased number of samples (and positive cases). Although culling occurs throughout Ukraine, each oblast regulates the cull



**Fig. 6. Spatiotemporal clustering of rabies cases in foxes (red circles) and domestic carnivores (blue circles) from 2012 to 2018 was detected using a space-time permutation model in SaTScan**

Tab. 5. Level of surveillance in Ukraine from 2012 to 2018 (e.g. number of animals tested/100.000 humans)

| No | Oblasts         | Average size of the human population during 7 years | Average number of samples from domestic carnivores and foxes | Average number of samples (negative) from domestic carnivores and foxes per 100,000 humans | Average number of samples (negative) from foxes | Average number samples from foxes per 100,000 humans | Average number of samples from domestic carnivores | Average number samples from domestic carnivores per 100,000 humans |
|----|-----------------|---|--|--|---|--|--|--|
| 1  | Vinnytsia       | 1,595,985.00  | 1545.29  | 96.82  | 1270.29   | 79.59  | 275.00   | 17.23  |
| 2  | Volyn           | 1,037,732.14  | 725.86   | 69.95  | 612.57  | 59.03  | 113.29   | 10.92  |
| 3  | Dnipropetrovsk  | 3,261,931.57  | 544.43   | 16.69  | 330.71  | 10.14  | 213.71   | 6.55   |
| 4  | Donetsk         | 4,274,368.71  | 196.14   | 4.59   | 79.57   | 1.86   | 116.57   | 2.73   |
| 5  | Zhytomyr        | 1,251,246.86  | 332.14   | 26.54  | 137.00  | 10.95  | 195.14   | 15.60  |
| 6  | Zakarpattia     | 1,254,407.29  | 218.29   | 17.40  | 192.43  | 15.34  | 25.86  | 2.06   |
| 7  | Zaporizhia      | 1,755,218.71  | 316.29   | 18.02  | 153.43  | 8.74   | 162.86   | 9.28   |
| 8  | Ivano-Frankivsk | 1,377,686.71  | 573.57   | 41.63  | 357.14  | 25.92  | 216.43   | 15.71  |
| 9  | Kyiv            | 1,728,721.43  | 457.71   | 26.48  | 206.29  | 11.93  | 251.43   | 14.54  |
| 10 | Kirovohrad      | 969,650.00  | 289.00   | 29.80  | 121.29  | 12.51  | 167.71   | 17.30  |
| 11 | Luhansk         | 2,209,247.29  | 287.43   | 13.01  | 201.14  | 9.10   | 86.29  | 3.91   |
| 12 | Lviv            | 2,516,805.29  | 1156.14  | 45.94  | 1001.00   | 39.77  | 155.14   | 6.16   |
| 13 | Mykolaiv        | 1,157,929.43  | 230.00   | 19.86  | 109.00  | 9.41   | 121.00   | 10.45  |
| 14 | Odesa           | 2,379,265.29  | 299.14   | 12.57  | 147.14  | 6.18   | 152.00   | 6.39   |
| 15 | Poltava         | 1,434,079.71  | 959.14   | 66.88  | 810.43  | 56.51  | 148.71   | 10.37  |
| 16 | Rivne           | 1,158,635.71  | 443.43   | 38.27  | 317.00  | 27.36  | 126.43   | 10.91  |
| 17 | Sumy            | 1,116,179.43  | 251.14   | 22.50  | 150.43  | 13.48  | 100.71   | 9.02   |
| 18 | Ternopil        | 1,062,600.14  | 282.71   | 26.61  | 157.86  | 14.86  | 124.86   | 11.75  |
| 19 | Kharkiv         | 2,703,744.71  | 547.29   | 20.24  | 334.71  | 12.38  | 212.57   | 7.86   |
| 20 | Kherson         | 1,062,019.86  | 365.57   | 34.42  | 188.86  | 17.78  | 176.71   | 16.64  |
| 21 | Khmelnytskyi    | 1,292,369.29  | 521.00   | 40.31  | 338.86  | 26.22  | 182.14   | 14.09  |
| 22 | Cherkasy        | 1,241,660.00  | 402.57   | 32.42  | 202.14  | 16.28  | 200.43   | 16.14  |
| 23 | Chernivtsi      | 904,816.57  | 177.43   | 19.61  | 99.43   | 10.99  | 78.00  | 8.62   |
| 24 | Chernihiv       | 1,040,871.57  | 409.71   | 39.36  | 233.00  | 22.39  | 176.71   | 16.98  |

differently, and hence large regional variation in fox population density across Ukraine. Although veterinary and sanitary requirements aim at a fox population density of 0.5-1 head per 1000 ha at the end of culling, fox population density in most oblasts (in the western and central parts of Ukraine) exceeds that rate up to 3-3.5 head per 1000 ha (31). The culling foxes for evaluation of the effectiveness of ORV, which was conducted by hunters mainly in autumn in different numbers, also influencing the reporting efforts depending on each oblast. In domestic carnivores, our data reveal a seasonal distribution in the epidemic curve of rabies incidence, with a higher incidence in the period between October and March every year, similar to that identified in the fox data. The cause of this temporal pattern in domestic carnivores is not completely clear and deserves further attention. One possibility is the synantropization of foxes (proximity of foxes to human habitats), a well-known phenomenon in Ukraine (21, 24). As reported by the Ministry of Health of Ukraine, 500-600 people per year report to medical facilities as a result of fox attacks (1, 27). This statistic suggests that foxes may attack domestic animals, as well

as humans, which could lead to an increase in rabies incidence in domestic carnivores. A similar correlation between rabies in domestic carnivores and foxes was observed between 1995 and 2005 in Germany, where a decrease in rabies cases in domestic carnivores correlated with a decrease in rabies cases in foxes (16, 30). The high incidence of stray domestic carnivores provides an environment conducive to the spillover of rabies between foxes and domestic carnivores (36, 40). It is, therefore, plausible that interaction between foxes and domestic carnivores (both domestic and stray) in rural and suburban areas may influence to some extent the seasonal patterns described above. However, an additional ecological study on contact patterns and a genetic analysis of animal populations are necessary to further investigate this hypothesis.

Prevalence data varied between species, with fox and domestic carnivores presenting narrower intervals (min-max) across the years (6.1-8.4% for foxes and 17.5-29.5% for carnivores) compared to other species. It is also clear that rabies prevalence differed between oblasts and across the years in each oblast (see Tab. 1, 2 in the supplementary documentation). Factors influ-

**Supplemental Tab. 1. Rabies prevalence by year (2012-2018) in foxes with a 95% exact binomial confidence interval. The table presents the percentage of positive samples from foxes from each oblast by year (2012-2018)**

| Oblast          | Year | Positive | Samples | Prevalence | Lower 95% BCI | Upper 95% BCI |
|-----------------|------|----------|---------|------------|---------------|---------------|
| Vinnytsia       | 2012 | 182      | 2265    | 8.04       | 6.95          | 9.23          |
|                 | 2013 | 175      | 1390    | 12.59      | 10.89         | 14.45         |
|                 | 2014 | 87       | 1143    | 7.61       | 6.14          | 9.30          |
|                 | 2015 | 75       | 1201    | 6.24       | 4.94          | 7.77          |
|                 | 2016 | 75       | 1073    | 6.99       | 5.54          | 8.68          |
|                 | 2017 | 90       | 706     | 12.75      | 10.38         | 15.44         |
|                 | 2018 | 145      | 1114    | 13.02      | 11.10         | 15.13         |
| Volyn           | 2012 | 20       | 127     | 15.75      | 9.89          | 23.27         |
|                 | 2013 | 40       | 892     | 4.48       | 3.22          | 6.06          |
|                 | 2014 | 21       | 671     | 3.13       | 1.95          | 4.74          |
|                 | 2015 | 23       | 444     | 5.18       | 3.31          | 7.67          |
|                 | 2016 | 25       | 465     | 5.38       | 3.51          | 7.83          |
|                 | 2017 | 25       | 1126    | 2.22       | 1.44          | 3.26          |
|                 | 2018 | 9        | 563     | 1.60       | 0.73          | 3.01          |
| Dnipropetrovsk  | 2012 | 47       | 428     | 10.98      | 8.18          | 14.33         |
|                 | 2013 | 30       | 520     | 5.77       | 3.93          | 8.13          |
|                 | 2014 | 27       | 386     | 6.99       | 4.66          | 10.01         |
|                 | 2015 | 20       | 142     | 14.08      | 8.82          | 20.91         |
|                 | 2016 | 14       | 430     | 3.26       | 1.79          | 5.40          |
|                 | 2017 | 32       | 213     | 15.02      | 10.51         | 20.54         |
|                 | 2018 | 26       | 196     | 13.27      | 8.85          | 18.83         |
| Donetsk         | 2012 | 36       | 254     | 14.17      | 10.13         | 19.08         |
|                 | 2013 | 24       | 156     | 15.38      | 10.11         | 22.02         |
|                 | 2014 | 4        | 26      | 15.38      | 4.36          | 34.87         |
|                 | 2015 | 3        | 9       | 33.33      | 7.49          | 70.07         |
|                 | 2016 | 11       | 35      | 31.43      | 16.85         | 49.29         |
|                 | 2017 | 12       | 21      | 57.14      | 34.02         | 78.18         |
|                 | 2018 | 9        | 56      | 16.07      | 7.62          | 28.33         |
| Zhytomyr        | 2012 | 24       | 86      | 27.91      | 18.77         | 38.62         |
|                 | 2013 | 27       | 107     | 25.23      | 17.33         | 34.55         |
|                 | 2014 | 11       | 85      | 12.94      | 6.64          | 21.98         |
|                 | 2015 | 22       | 92      | 23.91      | 15.63         | 33.94         |
|                 | 2016 | 31       | 91      | 34.07      | 24.45         | 44.75         |
|                 | 2017 | 24       | 88      | 27.27      | 18.32         | 37.81         |
|                 | 2018 | 71       | 410     | 17.32      | 13.78         | 21.33         |
| Zakarpattia     | 2012 | 4        | 61      | 6.56       | 1.82          | 15.95         |
|                 | 2013 | 2        | 175     | 1.14       | 0.14          | 4.07          |
|                 | 2014 | 1        | 98      | 1.02       | 0.03          | 5.55          |
|                 | 2015 | 3        | 172     | 1.74       | 0.36          | 5.01          |
|                 | 2016 | 0        | 112     | 0.00       | 0.00          | 3.24          |
|                 | 2017 | 1        | 339     | 0.29       | 0.01          | 1.63          |
|                 | 2018 | 19       | 390     | 4.87       | 2.96          | 7.50          |
| Zaporizhia      | 2012 | 46       | 197     | 23.35      | 17.63         | 29.89         |
|                 | 2013 | 49       | 176     | 27.84      | 21.36         | 35.08         |
|                 | 2014 | 24       | 156     | 15.38      | 10.11         | 22.02         |
|                 | 2015 | 25       | 137     | 18.25      | 12.17         | 25.75         |
|                 | 2016 | 27       | 136     | 19.85      | 13.51         | 27.55         |
|                 | 2017 | 33       | 129     | 25.58      | 18.31         | 34.01         |
|                 | 2018 | 35       | 143     | 24.48      | 17.68         | 32.36         |
| Ivano-Frankivsk | 2012 | 9        | 272     | 3.31       | 1.52          | 6.19          |
|                 | 2013 | 15       | 391     | 3.84       | 2.16          | 6.25          |
|                 | 2014 | 17       | 300     | 5.67       | 3.34          | 8.92          |
|                 | 2015 | 15       | 357     | 4.20       | 2.37          | 6.84          |
|                 | 2016 | 11       | 272     | 4.04       | 2.04          | 7.12          |
|                 | 2017 | 36       | 396     | 9.09       | 6.45          | 12.36         |
|                 | 2018 | 11       | 512     | 2.15       | 1.08          | 3.81          |
| Kyiv            | 2012 | 17       | 216     | 7.87       | 4.65          | 12.30         |
|                 | 2013 | 16       | 267     | 5.99       | 3.46          | 9.55          |
|                 | 2014 | 14       | 242     | 5.79       | 3.20          | 9.52          |
|                 | 2015 | 8        | 124     | 6.45       | 2.83          | 12.32         |
|                 | 2016 | 8        | 207     | 3.86       | 1.68          | 7.47          |
|                 | 2017 | 1        | 161     | 0.62       | 0.02          | 3.41          |
|                 | 2018 | 10       | 227     | 4.41       | 2.13          | 7.95          |
| Kirovohrad      | 2012 | 36       | 142     | 25.35      | 18.43         | 33.33         |
|                 | 2013 | 18       | 112     | 16.07      | 9.81          | 24.21         |
|                 | 2014 | 14       | 117     | 11.97      | 6.70          | 19.26         |
|                 | 2015 | 18       | 128     | 14.06      | 8.55          | 21.31         |
|                 | 2016 | 9        | 100     | 9.00       | 4.20          | 16.40         |
|                 | 2017 | 21       | 118     | 17.80      | 11.37         | 25.91         |
|                 | 2018 | 36       | 132     | 27.27      | 19.89         | 35.71         |
| Luhansk         | 2012 | 6        | 477     | 1.26       | 0.46          | 2.72          |
|                 | 2013 | 2        | 475     | 0.42       | 0.05          | 1.51          |
|                 | 2014 | 0        | 36      | 0.00       | 0.00          | 9.74          |
|                 | 2015 | 11       | 39      | 28.21      | 15.00         | 44.87         |
|                 | 2016 | 21       | 247     | 8.50       | 5.34          | 12.70         |
|                 | 2017 | 13       | 81      | 16.05      | 8.83          | 25.88         |
|                 | 2018 | 5        | 53      | 9.43       | 3.13          | 20.66         |
| Lviv            | 2012 | 27       | 558     | 4.84       | 3.21          | 6.96          |
|                 | 2013 | 18       | 1273    | 1.41       | 0.84          | 2.23          |
|                 | 2014 | 10       | 1167    | 0.86       | 0.41          | 1.57          |
|                 | 2015 | 17       | 1090    | 1.56       | 0.91          | 2.49          |
|                 | 2016 | 16       | 783     | 2.04       | 1.17          | 3.30          |
|                 | 2017 | 20       | 1258    | 1.59       | 0.97          | 2.44          |
|                 | 2018 | 16       | 878     | 1.82       | 1.05          | 2.94          |



| Oblast   | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|----------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Mykolaiv | 2012 | 16            | 117          | 13.68           | 8.02                | 21.26               |
|          | 2013 | 12            | 135          | 8.89            | 4.68                | 15.01               |
|          | 2014 | 11            | 104          | 10.58           | 5.40                | 18.14               |
|          | 2015 | 8             | 132          | 6.06            | 2.65                | 11.59               |
|          | 2016 | 1             | 62           | 1.61            | 0.04                | 8.66                |
|          | 2017 | 7             | 93           | 7.53            | 3.08                | 14.90               |
|          | 2018 | 19            | 124          | 15.32           | 9.48                | 22.89               |
| Odesa    | 2012 | 51            | 216          | 23.61           | 18.11               | 29.85               |
|          | 2013 | 25            | 178          | 14.04           | 9.30                | 20.03               |
|          | 2014 | 65            | 169          | 38.46           | 31.09               | 46.24               |
|          | 2015 | 43            | 154          | 27.92           | 21.00               | 35.71               |
|          | 2016 | 7             | 115          | 6.09            | 2.48                | 12.14               |
|          | 2017 | 17            | 96           | 17.71           | 10.67               | 26.83               |
|          | 2018 | 14            | 100          | 14.00           | 7.87                | 22.37               |
| Poltava  | 2012 | 6             | 1063         | 0.56            | 0.21                | 1.22                |
|          | 2013 | 2             | 582          | 0.34            | 0.04                | 1.24                |
|          | 2014 | 3             | 1018         | 0.29            | 0.06                | 0.86                |
|          | 2015 | 7             | 1091         | 0.64            | 0.26                | 1.32                |
|          | 2016 | 3             | 595          | 0.50            | 0.10                | 1.47                |
|          | 2017 | 14            | 617          | 2.27            | 1.25                | 3.78                |
|          | 2018 | 5             | 707          | 0.71            | 0.23                | 1.64                |
| Rivne    | 2012 | 8             | 192          | 4.17            | 1.82                | 8.04                |
|          | 2013 | 11            | 328          | 3.35            | 1.69                | 5.92                |
|          | 2014 | 6             | 240          | 2.50            | 0.92                | 5.36                |
|          | 2015 | 18            | 295          | 6.10            | 3.66                | 9.47                |
|          | 2016 | 13            | 236          | 5.51            | 2.97                | 9.24                |
|          | 2017 | 30            | 380          | 7.89            | 5.39                | 11.08               |
|          | 2018 | 20            | 547          | 3.66            | 2.25                | 5.59                |
| Sumy     | 2012 | 5             | 227          | 2.20            | 0.72                | 5.07                |
|          | 2013 | 6             | 201          | 2.99            | 1.10                | 6.38                |
|          | 2014 | 4             | 156          | 2.56            | 0.70                | 6.43                |
|          | 2015 | 4             | 178          | 2.25            | 0.62                | 5.65                |
|          | 2016 | 7             | 85           | 8.24            | 3.38                | 16.23               |
|          | 2017 | 18            | 69           | 26.09           | 16.25               | 38.06               |
|          | 2018 | 27            | 137          | 19.71           | 13.41               | 27.36               |
| Ternopil | 2012 | 60            | 174          | 34.48           | 27.45               | 42.05               |
|          | 2013 | 15            | 168          | 8.93            | 5.08                | 14.30               |
|          | 2014 | 15            | 168          | 8.93            | 5.08                | 14.30               |
|          | 2015 | 24            | 120          | 20.00           | 13.25               | 28.28               |
|          | 2016 | 21            | 119          | 17.65           | 11.27               | 25.70               |
|          | 2017 | 16            | 102          | 15.69           | 9.24                | 24.22               |
|          | 2018 | 27            | 283          | 9.54            | 6.38                | 13.58               |

| Oblast       | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|--------------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Kharkiv      | 2012 | 15            | 837          | 1.79            | 1.01                | 2.94                |
|              | 2013 | 8             | 782          | 1.02            | 0.44                | 2.01                |
|              | 2014 | 12            | 290          | 4.14            | 2.16                | 7.12                |
|              | 2015 | 19            | 110          | 17.27           | 10.73               | 25.65               |
|              | 2016 | 41            | 115          | 35.65           | 26.94               | 45.12               |
|              | 2017 | 24            | 113          | 21.24           | 14.11               | 29.93               |
|              | 2018 | 15            | 96           | 15.63           | 9.02                | 24.46               |
| Kherson      | 2012 | 19            | 192          | 9.90            | 6.06                | 15.02               |
|              | 2013 | 7             | 142          | 4.93            | 2.00                | 9.89                |
|              | 2014 | 13            | 168          | 7.74            | 4.18                | 12.87               |
|              | 2015 | 16            | 169          | 9.47            | 5.51                | 14.92               |
|              | 2016 | 10            | 49           | 20.41           | 10.24               | 34.34               |
|              | 2017 | 16            | 198          | 8.08            | 4.69                | 12.79               |
|              | 2018 | 11            | 404          | 2.72            | 1.37                | 4.82                |
| Khmelnytskyi | 2012 | 48            | 191          | 25.13           | 19.15               | 31.90               |
|              | 2013 | 28            | 238          | 11.76           | 7.96                | 16.55               |
|              | 2014 | 16            | 338          | 4.73            | 2.73                | 7.57                |
|              | 2015 | 39            | 423          | 9.22            | 6.64                | 12.39               |
|              | 2016 | 30            | 336          | 8.93            | 6.11                | 12.50               |
|              | 2017 | 28            | 332          | 8.43            | 5.68                | 11.96               |
|              | 2018 | 115           | 514          | 22.37           | 18.84               | 26.23               |
| Cherkasy     | 2012 | 24            | 249          | 9.64            | 6.27                | 14.00               |
|              | 2013 | 6             | 149          | 4.03            | 1.49                | 8.56                |
|              | 2014 | 14            | 186          | 7.53            | 4.18                | 12.31               |
|              | 2015 | 16            | 162          | 9.88            | 5.75                | 15.54               |
|              | 2016 | 14            | 168          | 8.33            | 4.63                | 13.59               |
|              | 2017 | 25            | 197          | 12.69           | 8.38                | 18.16               |
|              | 2018 | 31            | 304          | 10.20           | 7.03                | 14.16               |
| Chernivtsi   | 2012 | 5             | 71           | 7.04            | 2.33                | 15.67               |
|              | 2013 | 2             | 57           | 3.51            | 0.43                | 12.11               |
|              | 2014 | 5             | 110          | 4.55            | 1.49                | 10.29               |
|              | 2015 | 2             | 109          | 1.83            | 0.22                | 6.47                |
|              | 2016 | 1             | 109          | 0.92            | 0.02                | 5.01                |
|              | 2017 | 4             | 101          | 3.96            | 1.09                | 9.83                |
|              | 2018 | 0             | 139          | 0.00            | 0.00                | 2.62                |
| Chernihiv    | 2012 | 15            | 314          | 4.78            | 2.70                | 7.76                |
|              | 2013 | 15            | 85           | 17.65           | 10.23               | 27.43               |
|              | 2014 | 9             | 206          | 4.37            | 2.02                | 8.13                |
|              | 2015 | 15            | 264          | 5.68            | 3.21                | 9.20                |
|              | 2016 | 23            | 248          | 9.27            | 5.97                | 13.59               |
|              | 2017 | 12            | 198          | 6.06            | 3.17                | 10.35               |
|              | 2018 | 22            | 316          | 6.96            | 4.41                | 10.35               |

**Supplemental Tab. 2. Rabies prevalence by year (2012-2018) in domestic carnivores with a 95% exact binomial confidence interval. The table presents the percentage of positive samples in domestic carnivores from each oblast by year (2012-2018)**

| Oblast         | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|----------------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Vinnytsia      | 2012 | 65            | 310          | 20.97           | 16.57               | 25.93               |
|                | 2013 | 51            | 251          | 20.32           | 15.52               | 25.83               |
|                | 2014 | 51            | 239          | 21.34           | 16.32               | 27.08               |
|                | 2015 | 58            | 247          | 23.48           | 18.34               | 29.27               |
|                | 2016 | 74            | 280          | 26.43           | 21.36               | 32.00               |
|                | 2017 | 93            | 299          | 31.10           | 25.90               | 36.69               |
|                | 2018 | 95            | 298          | 31.88           | 26.62               | 37.50               |
| Volyn          | 2012 | 10            | 88           | 11.36           | 5.59                | 19.91               |
|                | 2013 | 14            | 91           | 15.38           | 8.67                | 24.46               |
|                | 2014 | 11            | 66           | 16.67           | 8.62                | 27.87               |
|                | 2015 | 25            | 96           | 26.04           | 17.62               | 36.00               |
|                | 2016 | 38            | 183          | 20.77           | 15.13               | 27.37               |
|                | 2017 | 24            | 137          | 17.52           | 11.56               | 24.94               |
|                | 2018 | 14            | 132          | 10.61           | 5.92                | 17.15               |
| Dnipropetrovsk | 2012 | 74            | 271          | 27.31           | 22.09               | 33.02               |
|                | 2013 | 54            | 209          | 25.84           | 20.05               | 32.33               |
|                | 2014 | 31            | 166          | 18.67           | 13.06               | 25.45               |
|                | 2015 | 51            | 190          | 26.84           | 20.69               | 33.74               |
|                | 2016 | 30            | 227          | 13.22           | 9.10                | 18.33               |
|                | 2017 | 39            | 216          | 18.06           | 13.17               | 23.85               |
|                | 2018 | 43            | 218          | 19.72           | 14.66               | 25.63               |
| Donetsk        | 2012 | 57            | 219          | 26.03           | 20.35               | 32.37               |
|                | 2013 | 38            | 168          | 22.62           | 16.53               | 29.70               |
|                | 2014 | 7             | 39           | 17.95           | 7.54                | 33.53               |
|                | 2015 | 14            | 41           | 34.15           | 20.08               | 50.59               |
|                | 2016 | 46            | 123          | 37.40           | 28.84               | 46.58               |
|                | 2017 | 52            | 116          | 44.83           | 35.59               | 54.34               |
|                | 2018 | 41            | 110          | 37.27           | 28.24               | 47.01               |
| Zhytomyr       | 2012 | 52            | 163          | 31.90           | 24.83               | 39.65               |
|                | 2013 | 27            | 132          | 20.45           | 13.93               | 28.35               |
|                | 2014 | 18            | 154          | 11.69           | 7.08                | 17.84               |
|                | 2015 | 26            | 256          | 10.16           | 6.74                | 14.53               |
|                | 2016 | 28            | 242          | 11.57           | 7.83                | 16.29               |
|                | 2017 | 21            | 171          | 12.28           | 7.77                | 18.16               |
|                | 2018 | 22            | 248          | 8.87            | 5.64                | 13.12               |
| Zakarpattia    | 2012 | 10            | 28           | 35.71           | 18.64               | 55.93               |
|                | 2013 | 9             | 35           | 25.71           | 12.49               | 43.26               |
|                | 2014 | 2             | 16           | 12.50           | 1.55                | 38.35               |
|                | 2015 | 6             | 25           | 24.00           | 9.36                | 45.13               |
|                | 2016 | 9             | 22           | 40.91           | 20.71               | 63.65               |
|                | 2017 | 7             | 31           | 22.58           | 9.59                | 41.10               |
|                | 2018 | 2             | 24           | 8.33            | 1.03                | 27.00               |

| Oblast          | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|-----------------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Zaporizhia      | 2012 | 72            | 184          | 39.13           | 32.03               | 46.58               |
|                 | 2013 | 58            | 195          | 29.74           | 23.42               | 36.69               |
|                 | 2014 | 42            | 148          | 28.38           | 21.28               | 36.36               |
|                 | 2015 | 38            | 146          | 26.03           | 19.12               | 33.93               |
|                 | 2016 | 35            | 146          | 23.97           | 17.30               | 31.73               |
|                 | 2017 | 69            | 177          | 38.98           | 31.76               | 46.59               |
|                 | 2018 | 54            | 143          | 37.76           | 29.80               | 46.25               |
| Ivano-Frankivsk | 2012 | 2             | 125          | 1.60            | 0.19                | 5.66                |
|                 | 2013 | 1             | 220          | 0.45            | 0.01                | 2.51                |
|                 | 2014 | 13            | 227          | 5.73            | 3.08                | 9.59                |
|                 | 2015 | 10            | 218          | 4.59            | 2.22                | 8.27                |
|                 | 2016 | 24            | 235          | 10.21           | 6.65                | 14.81               |
|                 | 2017 | 31            | 251          | 12.35           | 8.55                | 17.07               |
|                 | 2018 | 10            | 239          | 4.18            | 2.02                | 7.56                |
| Kyiv            | 2012 | 57            | 326          | 17.48           | 13.52               | 22.05               |
|                 | 2013 | 67            | 343          | 19.53           | 15.47               | 24.13               |
|                 | 2014 | 42            | 185          | 22.70           | 16.88               | 29.42               |
|                 | 2015 | 38            | 195          | 19.49           | 14.17               | 25.75               |
|                 | 2016 | 31            | 251          | 12.35           | 8.55                | 17.07               |
|                 | 2017 | 53            | 243          | 21.81           | 16.79               | 27.54               |
|                 | 2018 | 38            | 217          | 17.51           | 12.70               | 23.23               |
| Kirovohrad      | 2012 | 44            | 163          | 26.99           | 20.35               | 34.50               |
|                 | 2013 | 35            | 132          | 26.52           | 19.21               | 34.90               |
|                 | 2014 | 12            | 144          | 8.33            | 4.38                | 14.10               |
|                 | 2015 | 31            | 173          | 17.92           | 12.51               | 24.46               |
|                 | 2016 | 22            | 155          | 14.19           | 9.11                | 20.70               |
|                 | 2017 | 34            | 166          | 20.48           | 14.62               | 27.43               |
|                 | 2018 | 86            | 241          | 35.68           | 29.64               | 42.09               |
| Luhansk         | 2012 | 15            | 137          | 10.95           | 6.26                | 17.42               |
|                 | 2013 | 7             | 132          | 5.30            | 2.16                | 10.62               |
|                 | 2014 | 3             | 52           | 5.77            | 1.21                | 15.95               |
|                 | 2015 | 33            | 56           | 58.93           | 44.98               | 71.90               |
|                 | 2016 | 35            | 58           | 60.34           | 46.64               | 72.95               |
|                 | 2017 | 59            | 93           | 63.44           | 52.81               | 73.19               |
|                 | 2018 | 44            | 76           | 57.89           | 46.02               | 69.14               |
| Lviv            | 2012 | 6             | 151          | 3.97            | 1.47                | 8.45                |
|                 | 2013 | 5             | 139          | 3.60            | 1.18                | 8.19                |
|                 | 2014 | 10            | 153          | 6.54            | 3.18                | 11.69               |
|                 | 2015 | 8             | 109          | 7.34            | 3.22                | 13.95               |
|                 | 2016 | 14            | 187          | 7.49            | 4.15                | 12.24               |
|                 | 2017 | 9             | 166          | 5.42            | 2.51                | 10.04               |
|                 | 2018 | 21            | 181          | 11.60           | 7.33                | 17.19               |

| Oblast   | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|----------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Mykolaiv | 2012 | 39            | 126          | 30.95           | 23.02               | 39.80               |
|          | 2013 | 15            | 123          | 12.20           | 6.99                | 19.32               |
|          | 2014 | 9             | 120          | 7.50            | 3.49                | 13.76               |
|          | 2015 | 19            | 116          | 16.38           | 10.16               | 24.39               |
|          | 2016 | 5             | 120          | 4.17            | 1.37                | 9.46                |
|          | 2017 | 4             | 109          | 3.67            | 1.01                | 9.13                |
|          | 2018 | 27            | 130          | 20.77           | 14.16               | 28.76               |
| Odesa    | 2012 | 51            | 194          | 26.29           | 20.24               | 33.07               |
|          | 2013 | 31            | 170          | 18.24           | 12.74               | 24.87               |
|          | 2014 | 31            | 146          | 21.23           | 14.91               | 28.76               |
|          | 2015 | 36            | 166          | 21.69           | 15.68               | 28.74               |
|          | 2016 | 10            | 160          | 6.25            | 3.04                | 11.19               |
|          | 2017 | 1             | 121          | 0.83            | 0.02                | 4.52                |
|          | 2018 | 20            | 102          | 19.61           | 12.41               | 28.65               |
| Poltava  | 2012 | 15            | 189          | 7.94            | 4.51                | 12.75               |
|          | 2013 | 12            | 168          | 7.14            | 3.75                | 12.14               |
|          | 2014 | 6             | 107          | 5.61            | 2.09                | 11.81               |
|          | 2015 | 7             | 103          | 6.80            | 2.78                | 13.50               |
|          | 2016 | 5             | 114          | 4.39            | 1.44                | 9.94                |
|          | 2017 | 31            | 178          | 17.42           | 12.15               | 23.80               |
|          | 2018 | 32            | 183          | 17.49           | 12.28               | 23.78               |
| Rivne    | 2012 | 14            | 93           | 15.05           | 8.48                | 23.97               |
|          | 2013 | 11            | 50           | 22.00           | 11.53               | 35.96               |
|          | 2014 | 18            | 89           | 20.22           | 12.45               | 30.07               |
|          | 2015 | 34            | 177          | 19.21           | 13.68               | 25.79               |
|          | 2016 | 29            | 193          | 15.03           | 10.30               | 20.86               |
|          | 2017 | 20            | 128          | 15.63           | 9.81                | 23.09               |
|          | 2018 | 26            | 154          | 16.88           | 11.33               | 23.75               |
| Sumy     | 2012 | 26            | 112          | 23.21           | 15.76               | 32.14               |
|          | 2013 | 17            | 91           | 18.68           | 11.28               | 28.22               |
|          | 2014 | 9             | 83           | 10.84           | 5.08                | 19.59               |
|          | 2015 | 22            | 96           | 22.92           | 14.95               | 32.61               |
|          | 2016 | 24            | 105          | 22.86           | 15.23               | 32.07               |
|          | 2017 | 19            | 95           | 20.00           | 12.49               | 29.46               |
|          | 2018 | 45            | 123          | 36.59           | 28.09               | 45.75               |
| Ternopil | 2012 | 54            | 187          | 28.88           | 22.50               | 35.94               |
|          | 2013 | 12            | 145          | 8.28            | 4.35                | 14.01               |
|          | 2014 | 9             | 88           | 10.23           | 4.78                | 18.53               |
|          | 2015 | 28            | 116          | 24.14           | 16.68               | 32.96               |
|          | 2016 | 19            | 99           | 19.19           | 11.97               | 28.34               |
|          | 2017 | 19            | 116          | 16.38           | 10.16               | 24.39               |
|          | 2018 | 22            | 121          | 18.18           | 11.76               | 26.22               |

| Oblast      | Year | Posi-<br>tive | Sam-<br>ples | Preva-<br>lence | Lower<br>95%<br>BCI | Upper<br>95%<br>BCI |
|-------------|------|---------------|--------------|-----------------|---------------------|---------------------|
| Kharkiv     | 2012 | 34            | 198          | 17.17           | 12.19               | 23.16               |
|             | 2013 | 57            | 229          | 24.89           | 19.43               | 31.01               |
|             | 2014 | 31            | 181          | 17.13           | 11.94               | 23.42               |
|             | 2015 | 36            | 203          | 17.73           | 12.74               | 23.70               |
|             | 2016 | 68            | 213          | 31.92           | 25.72               | 38.64               |
|             | 2017 | 76            | 235          | 32.34           | 26.40               | 38.73               |
|             | 2018 | 78            | 229          | 34.06           | 27.95               | 40.59               |
| Kherson     | 2012 | 50            | 139          | 35.97           | 28.01               | 44.54               |
|             | 2013 | 25            | 161          | 15.53           | 10.31               | 22.06               |
|             | 2014 | 28            | 167          | 16.77           | 11.44               | 23.31               |
|             | 2015 | 23            | 163          | 14.11           | 9.16                | 20.42               |
|             | 2016 | 28            | 256          | 10.94           | 7.39                | 15.42               |
|             | 2017 | 33            | 177          | 18.64           | 13.19               | 25.17               |
|             | 2018 | 25            | 172          | 14.53           | 9.63                | 20.70               |
| Khmelnyskyi | 2012 | 42            | 160          | 26.25           | 19.62               | 33.78               |
|             | 2013 | 25            | 136          | 18.38           | 12.26               | 25.93               |
|             | 2014 | 28            | 145          | 19.31           | 13.23               | 26.69               |
|             | 2015 | 30            | 313          | 9.58            | 6.56                | 13.40               |
|             | 2016 | 12            | 161          | 7.45            | 3.91                | 12.66               |
|             | 2017 | 20            | 177          | 11.30           | 7.04                | 16.91               |
|             | 2018 | 13            | 183          | 7.10            | 3.84                | 11.84               |
| Cherkasy    | 2012 | 41            | 145          | 28.28           | 21.12               | 36.35               |
|             | 2013 | 48            | 149          | 32.21           | 24.80               | 40.35               |
|             | 2014 | 43            | 146          | 29.45           | 22.20               | 37.55               |
|             | 2015 | 77            | 164          | 46.95           | 39.13               | 54.89               |
|             | 2016 | 75            | 193          | 38.86           | 31.94               | 46.12               |
|             | 2017 | 83            | 306          | 27.12           | 22.22               | 32.48               |
|             | 2018 | 72            | 301          | 23.92           | 19.21               | 29.15               |
| Chernivtsi  | 2012 | 5             | 84           | 5.95            | 1.96                | 13.35               |
|             | 2013 | 7             | 61           | 11.48           | 4.74                | 22.22               |
|             | 2014 | 2             | 62           | 3.23            | 0.39                | 11.17               |
|             | 2015 | 6             | 78           | 7.69            | 2.88                | 15.99               |
|             | 2016 | 12            | 84           | 14.29           | 7.61                | 23.62               |
|             | 2017 | 5             | 95           | 5.26            | 1.73                | 11.86               |
|             | 2018 | 5             | 82           | 6.10            | 2.01                | 13.66               |
| Chernihiv   | 2012 | 52            | 215          | 24.19           | 18.62               | 30.48               |
|             | 2013 | 41            | 158          | 25.95           | 19.31               | 33.51               |
|             | 2014 | 13            | 112          | 11.61           | 6.33                | 19.03               |
|             | 2015 | 36            | 168          | 21.43           | 15.48               | 28.41               |
|             | 2016 | 73            | 216          | 33.80           | 27.52               | 40.53               |
|             | 2017 | 46            | 167          | 27.54           | 20.93               | 34.98               |
|             | 2018 | 47            | 201          | 23.38           | 17.72               | 29.85               |



encing these differences may be very different, and the results, as mentioned above, are influenced by the surveillance mechanisms in place.

Data for foxes were obtained primarily through active monitoring by hunters, and by official veterinarians in cases of reported bites of humans or animals by foxes. In addition, data from ORV monitoring are generated only in oblasts where vaccination campaigns have been implemented. Data for domestic carnivores were obtained primarily from cases of rabies suspected on the basis of clinical signs and when humans or animals had been bitten.

The choice of the permutation model for cluster detection was determined by the fact that some data on the population density of domestic and stray carnivores, as well as foxes, are missing. Similarly, the estimation of the kernel density of cases did not take into account the underlying population of domestic or wild animals. Extraction mapping is a valuable methodological option to address this limitation and should be considered in future studies of population data (32).

Although the dataset included data from all oblasts across Ukraine, variability in surveillance methods and reporting is inherent in these systems, which depends mainly on the frequency of ORV campaigns and the quality of control measures used to verify the effectiveness of vaccines. As a consequence, samples submitted from each oblast are inconsistent in terms of numbers (from 20 to 2,000 samples), and therefore reporting peaks are disconnected from the disease dynamic. As can be seen from Supplemental Table 1, laboratories in Vinnytsia, Volyn, Ivano-Frankivsk, Lviv and Poltava oblasts received more samples from foxes and therefore could identify the higher number of rabies cases in foxes. In other oblasts (Kyiv, Kirovograd, Odesa, Mykolaiv), where active monitoring of foxes was less intensive, fewer rabies cases were confirmed. These data are also influenced by the size of the territory and fox population and by the epizootic situation in each oblast. In some oblasts (Fig. 2, 3) with intensive monitoring efforts (1000-1500 samples), the rabies incidence was also higher (up to 500 cases). This, however, was not always the case, as in some oblasts (i.e., Poltava), despite intensive monitoring, the incidence of rabies was consistently low (up to 10 cases).

The estimates of the kernel density of rabies cases in foxes and domestic carnivores revealed a consistent presence of rabies across the years in most of the oblasts of Ukraine, but the densities were different. Density differences may be explained by ecological and environmental factors, the presence of natural barriers (for instance, the Dnieper River, which divides the territory of Ukraine into two parts, mountains in western Ukraine, etc.). On another side, the density of rabies cases depended from different results of the effectiveness and quantity of ORV campaigns and vaccination of domestic carnivores. In general, ORV campaigns should be carried out twice a year, but due

to the limited finance in most oblasts, the campaigns were implemented irregularly and only in autumn.

With regard to rabies in foxes, a higher density of cases was found in southwestern Ukraine (especially in the Vinnytsia oblast). It must be acknowledged that reporting efforts may have influenced this pattern, as the number of samples analyzed was larger in the west of Ukraine (supplemental Tab. 1) compared to other regions. The higher density of cases in Vinnytsia and other southwestern regions may be influenced by the larger fox population (24, 25, 31). The lower density of rabies cases in the western regions near the border with EU countries (especially the Zakarpattia oblast) may be partially explained by the mountainous environment, which can influence fox presence and density, and may limit the movement of wild animals, resulting in a slower progression of rabies. In addition, those oblasts (Lviv, Volyn, and Zakarpattia) benefited in recent years (2012-2016) from regular ORV campaigns with support from the EU (34).

In those eastern oblasts of Ukraine, where ORV campaigns were implemented regularly (especially in the Poltava oblast), we identified a lower circulation across the years. As noted by Kornienko et al. (20), spring and autumn oral vaccination campaigns in 2011-2014 were carried out on hunting grounds in Luhansk, Kharkiv, Donetsk, Sumy, Poltava and Dnipropetrovsk regions. The intensity of rabies in those areas decreased significantly between 2011 and 2014. In addition, the natural barriers in these areas (Dnieper River and Kremenchuk Water Reservoir) decreased the migration of infected animals from the endemic western regions and probably reduced the spread of rabies. According to Zecchin et al., the presence of natural or artificial barriers may affect the ecology of rabies reservoirs and thus the dynamic of infection (41). The above relationship was observed by Picard-Meyer et al. (33) during their study. Previously, Ivanov et al. (19) showed that the Dnieper River served as a natural barrier to the spread of the rabies virus, since rabies isolates circulating on either side of the Dnieper River belonged to two separate clusters, which suggests that similar environmental barriers may influence the dynamics of rabies spread.

Density plots of cases in domestic carnivores were also consistently high in most oblasts, but especially in the central and eastern regions and along the border with the Russian Federation. The highest density was observed in Khmelnytskyi, Vinnytsia, Cherkasy, Kirovograd, Zaporizhzhia, Donetsk, and Luhansk oblasts. These regions are highly industrialized, characterized by a larger human population density and large numbers of domestic carnivores in towns surrounded by vast suburban areas (Dnipro, Kharkiv, Zaporizhzhia). Due to the high density of domestic carnivores in these oblasts, vaccination coverage was imperfect. In general, approximately 2 million cats and 3.5 million dogs are immunized against rabies annually in Ukraine (25). But this coverage is insufficient,

because of the extremely high density of pets. Various sources estimate that up to approximately 6 million dogs and 7.5 million cats are kept in Ukraine (20). The low vaccination rate is attributed to multiple factors, including the owners' poor commitment, lenient laws on cat non-vaccination and the lack of penalties for non-vaccination of household pets (26). The density of rabies cases in domestic carnivores was lowest in Poltava, Odesa, Mykolaiv and Zakarpattia oblasts as a result of better coverage by campaigns of parenteral vaccination.

Categories were split to evaluate clusters within each and determine the presence of overlapping clusters. The analysis of space-time clusters identified a total of thirteen clusters in wild and domestic carnivores during 2012-2018. Most clusters in foxes and one cluster in domestic carnivores were located in high kernel density locations (Tab. 3 and 4). In western oblasts (Khmelnyskyi, Ternopil) in 2012 and, more clearly, in 2018 (Vinnitsia, Khmelnyskyi, Ternopil), clusters of rabies in domestic carnivores intersected with clusters in foxes during the same time period (partially in January-February 2012 and November-December 2018). These findings may indicate regions with a higher risk of rabies transmission between species. We acknowledge, however, that, although intriguing, this result may be due to differences in surveillance of the two species. Additional data from a consistent surveillance programme are needed for verification. Ideally, this hypothesis could be tested through molecular surveillance, including the typing of rabies virus isolates in the context of contact pattern studies.

The risk factor data in the dataset, including ecological factors (i.e. fox density, pattern of interaction with domestic populations), as well as environmental and human-related factors (i.e. human density, artificial barriers, vaccination of domestic populations) were not thoroughly and statistically analyzed in the current study, as the focus was on a description of the spatial and temporal dynamics of rabies. The intent of this project was to support the Ukrainian authorities in improving rabies control by identifying high-risk regions at the national level. This study also described some of the limitations of the current dataset and rabies surveillance measures.

This study analyzed national-level data, which revealed limitations of the current rabies control measures implemented in Ukraine. These analyses show that the current methods fail to reduce the numbers of rabies cases in wild and domestic animals. The current rabies control measures in Ukraine should be revised to use a data-driven strategy for monitoring and surveillance. The authors recommend increasing compliance with animal welfare requirements, enforcing pet vaccination, improving the monitoring of wild, domestic and stray animal population density, and improving the effectiveness of vaccination campaigns (including ORV twice a year) in wild animals. Additionally, we

recommend improving the current rabies surveillance and monitoring systems by integrating GIS technologies to improve the monitoring of the effectiveness of the programmes.

Taking into account the limitations of surveillance efforts across Ukraine, the results presented here support efforts by the Ukraine State Food and Consumer Service to develop a risk-based national control programme for rabies. Revised control programmes will improve surveillance strategies and prioritize regular ORV campaigns in regions with a higher number of rabies cases and a higher risk of rabies spread. Interaction between domestic carnivores and foxes could potentially influence the disease dynamics in some regions of Ukraine and should be further studied.

## References

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