High habitat richness reduces the risk of tick-borne encephalitis in Europe: A multi-scale study

Title: **High habitat richness reduces the risk of tick-borne encephalitis in Europe: a multi-scale study.**

Author names and affiliations: Francesca Dagostin[a], Valentina Tagliapietra[a,b], Giovanni Marini[a], Giulia Ferrari[a,b], Marco Cervellini[c,d], William Wint[e], Neil S. Alexander[e], Maria Grazia Zuccali[f], Silvia Molinaro[f], Nahuel Fiorito[g], Timothée Dub[h], Duccio Rocchini[c,i], Annapaola Rizzoli[a,b]

[a] Research and Innovation Centre, Fondazione Edmund Mach, San Michele all'Adige (TN), Italy

[b] NBFC, National Biodiversity Future Center, Palermo, Italy

[c] BIOME Lab, Department of Biological, Geological and Environmental Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy

[d] School of Biosciences and Veterinary Medicine, Plant Diversity and Ecosystems Management Unit, University of Camerino, Italy

[e] Environmental Research Group Oxford Ltd, c/o Dept Biology, Oxford, United Kingdom

[f] Azienda Provinciale Servizi Sanitari, Trento, Italy

[g] Unità Locale Socio Sanitaria Dolomiti, Belluno, Italy

[h] Department of Health Security, Finnish Institute for Health and Welfare, Helsinki, Finland

[i] Department of Spatial Sciences, Faculty of Environmental Sciences, Czech University of Life , Czech Republic

Corresponding author: Francesca Dagostin (francesca.dagostin@fmach.it), +393396716703, Via E. Mach 1, 38010 San Michele all'Adige (TN), Italy)

[1]HRI: Habitat Richness Index

Abstract

Background: The natural transmission cycle of tick-borne encephalitis (TBE) virus is enhanced by complex interactions between ticks and key hosts strongly connected to habitat characteristics. The diversity of wildlife host species and their relative abundance is known to affect transmission of tick-borne diseases. Therefore, in the current context of global biodiversity loss, we explored the relationship between habitat richness and the pattern of human TBE cases in Europe to assess biodiversity's role in disease risk mitigation.

Methods: We assessed human TBE case distribution across 879 European regions using official epidemiological data reported to The European Surveillance System (TESSy) between 2017 and 2021 from 15 countries. We explored the relationship between TBE presence and the habitat richness index (HRI[1]) by means of binomial regression. We validated our findings at local scale using data collected between 2017 and 2021 in 227 municipalities located in Trento and Belluno provinces, two known TBE foci in northern Italy.

Findings: Our results showed a significant parabolic effect of HRI on the probability of presence of human TBE cases in the European regions included in our dataset, and a significant, negative effect of HRI on the local presence of TBE in northern Italy. At both spatial scales, TBE risk decreases in areas with higher values of HRI.

Interpretation: To our knowledge, no efforts have yet been made to explore the relationship between biodiversity and TBE risk, probably due to the scarcity of high-resolution, large-scale data about the abundance or density of critical host species. Hence, in this study we considered habitat richness as proxy for vertebrate host diversity. The results suggest that in highly diverse habitats TBE risk decreases. Hence, biodiversity loss could enhance TBE risk for both humans and wildlife. This association is relevant to

support the hypothesis that the maintenance of highly diverse ecosystems mitigates disease risk.

Keywords: Biodiversity, Europe, Habitat Richness, One Health, Vector-borne disease, Tick-borne encephalitis

Funding: This work was supported by EU grant 874850 MOOD and is catalogued as MOOD 080. The contents of this publication are the sole responsibility of the authors and do not necessarily reflect the views of the European Commission.

Introduction

Tick-borne encephalitis (TBE) is one of the most severe tick-transmitted diseases in Eurasia, with more than 3000 confirmed cases reported annually in Europe [1]. During the last decade, European incidence of TBE human cases increased significantly from 2412 confirmed cases in 2012 to 3604 confirmed cases in 2020, concomitantly with a north-westerly spread [2] and the appearance of new foci of infection in previously non-endemic countries [3], making TBE a growing Public Health challenge in Europe.

TBE virus (TBEV) is a flavivirus that affects the central nervous system. It is transmitted mainly through the bite of ticks belonging to the *Ixodes ricinus* complex, such as *I, ricinus* and *I. persulcatus* [4], but can also be acquired through consumption of infected unpasteurized milk and dairy products [5].

The active circulation of TBEV among vectors and reservoir hosts occurs in specific hotspots and strongly depends on the co-occurrence of multiple ecological factors, such as abiotic conditions - which, in turn, determine vectors' activity and habitat suitability [6,7] - along with a subset of key vertebrate host species [8–10]. Tick larvae mainly feed on small mammals, nymphs feed on small- and medium-sized mammals, birds, and reptiles, and adults feed on large animals such as ungulates [11]. Ticks are both vectors and main viral reservoirs, remaining infected throughout their life cycle due to transstadial and transovarial transmission. Uninfected ticks can also acquire the infection via systemic transmission, while feeding on a viremic competent host, or via non-systemic transmission, while co-feeding with infected ticks [12,13].

Various animal species can act as dead-end hosts or maintain and amplify the virus (reservoir hosts), with or without evident symptoms of the disease. Rodents and

insectivores are considered the main reservoir hosts for TBEV maintenance and circulation. Once infected with TBEV, they may develop a chronic infection, although the duration of viraemia, and thus their infectivity to ticks, is commonly considered short (two to nine days) [14]. Symptoms and viremia have been rarely detected in wild ungulates [15], which are not competent for viral transmission, although they are important hosts for the amplification of tick populations [16,17].

The diversity of wildlife host species and their relative abundance is known to affect transmission of tick-borne diseases such as Lyme disease [18–20]. This relationship, denoted as *diversity-disease relationship*, might also apply to the TBEV transmission system, as the main TBEV vector, *I. ricinus,* parasitizes several different host species [21] and its infection prevalence is likely to be affected by host diversity and competence among hosts. Rodent species such as *Apodemus flavicollis* and *Clethrionomys glareolus* are considered the main reservoir hosts for TBEV circulation [22,23] as they simultaneously harbour multiple developmental stages of ticks [9,12]. Nonetheless, Apodemus spp. support higher tick burdens (Kiffner et al. 2011), higher tick- feeding success, and a more efficient TBEV transmission via co-feeding compared to C. glareolus [12].

Little is known about the effects of habitat and vertebrate host diversity on the emergence of tick-borne diseases in Europe, given the complexity of their transmission dynamics. Moreover, the lack of high-resolution, large-scale data on the abundance or density of key vertebrate host species, such as rodents and ungulates, is one of the main reasons why no attempt has been made to investigate the relationship between biodiversity and TBE risk in both local and large-scale geographical contexts. So far, few studies explored the interactions between ticks, vertebrate hosts, habitat and tick-borne pathogens in Europe [24–26]. To our knowledge, no studies have investigated the relationship between TBE and biodiversity in Europe.

In this study we relied on the habitat richness index (HRI), a novel indicator that accounts for the diversity of European ecosystem types (sensu “Habitat Directive” - Council Directive 92/43/EEC). Habitat diversity, measured as the number of different habitats in a given area, has proven to be a prominent driver for species diversity of a variety of taxa at the landscape scale [27]. Indeed, the use of habitat amount in an equal-sized sample sites as biodiversity proxy is contextualized by the habitat amount hypothesis [28] and habitat richness or heterogeneity can be used as an explanatory variable for biodiversity modeling [29–31]. Furthermore, Habitat Directive types monitoring is the standardized and legally established tool for monitoring ecosystems in Europe (Council Directive 92/43/EEC).

Considering the need for a broad and scale-dependent understanding of the diversity-disease relationship [32] we applied HRI for the first time to evaluate its relationship with the occurrence of human TBE cases in Europe and in a local setting located in the northern-Italian provinces of Trento and Belluno, which are well known endemic areas for TBE [33].

Methods

Study areas

We carried out the statistical analysis at two different spatial scales, using regional-level data about TBE distribution and HRI across 15 European countries, i.e., “analysis at European scale”, and municipal-level TBE and HRI data in two northern Italian provinces, Trento and Belluno, i.e., “analysis at local scale”.

Epidemiological data

For the analysis at European scale, data for laboratory-confirmed human TBE cases were provided by the European Surveillance System (TESSy) and released by ECDC. They included, when available, the probable place of infection at NUTS-3 (Nomenclature of

territorial units for statistics, small regions for specific diagnosis) or NUTS-2 level (Nomenclature of territorial units for statistics, basic regions for the application of regional policies). In our study, we used cases reported to TESSy between 2017 and 2021, since the place of infection was unknown or not recorded in most countries prior to 2017. Patients infected abroad or whose location of exposure was unknown or not provided at high spatial resolution, were excluded. Only countries that reported the place of infection at the NUTS-3 or NUTS-2 level for at least 75% of the cases notified over the selected period were included. The 13 countries selected according to these criteria were: Austria, Czech Republic, Denmark, Germany, Finland, France, Hungary, Italy, Lithuania, Poland, Romania, Slovakia, and Sweden. To take into consideration areas with no recorded TBE presence, we included two countries with no autochthonous cases reported during the study period, namely Spain and Ireland.

Additionally, to perform the analysis at local scale, we used municipal-level human TBE cases recorded in the Trento and Belluno Provinces (Italy) from 2017 to 2021. These data were provided by local Public Health Agencies, Azienda Provinciale per i Servizi Sanitari Provincia Autonoma di Trento (APSS) and Unità Locale Socio Sanitaria Dolomiti (ULSS1).

Based on these data sources, we compiled two different dichotomous datasets ,depicting the presence and absence of human TBE cases, at European (Figure 1a) and at local scale (Figure 3a).

Ecological variables

The habitat richness index (HRI) was derived from the habitat distribution maps of 222 terrestrial habitats of community interest, obtained from the European Environment Agency [34] and based on the standard grid provided by EEA for habitat monitoring with a spatial resolution of 10 km (for more details on the computation of this index see [27]). HRI can be considered a proxy for biodiversity, as it is positively correlated with the richness of

the species listed in the Annex species of the Birds and Habitats Directives [27]. For our analysis, we used the normalized index (*i.e.*, habitat richness corrected for actual cell area), which values ranged from 0 to 1·5. To exclude potential extreme values, we computed the 95-th percentile value of HRI as a measure of the levels of biodiversity that characterize each spatial unit, in accordance with the spatial resolution of the available official epidemiological data provided by ECDC and local Public Health Agencies.

To assess the distribution of key vertebrate species across the European NUTS-2 and NUTS-3 regions included in our study, we used 1-km data about the probability of presence of critical TBEV reservoir and tick-amplification hosts (*i.e.,* rodents, *Apodemus flavicollis* and *Clethrionomys glareolus,* and cervids, *Dama dama*, *Capreolus capreolus* and *Cervus elaphus*) that were previously derived using long established ensembled Random Forest and Boosted Regression Trees based spatial modeling techniques, as described in [35].

Statistical analysis

We used binomial regression to describe the association between the occurrence of human TBE cases and HRI, at the two different spatial scales. For each epidemiological dataset, we considered models with both linear and quadratic covariate of the form:

$$\log(p/(1-p)) = a_0 + a_1 HRI + a_2 HRI^2 + \varepsilon$$

where p represents the probability of presence of at least one human TBE case, a_0, a_1 and a_2 are the model coefficients, ε is the random error component, and *HRI* indicates the 95-th percentile value of habitat richness (Table 1).

We tested both linear and quadratic models and ranked their performances based on the Akaike's Information Criterion (AIC) score [36]. Spatial autocorrelation was detected through Moran's I statistic and visual inspection of Moran's scatterplot [37] and was filtered out by including an autocovariate term that represents spatial dependence in the model

residuals [38]. In residuals autocovariate (RAC) models, spatial autocorrelation is accounted for by estimating the strength of the relationship between the model residuals and the values of those residuals at neighboring locations. This procedure leads to an autocovariate that captures only the variance unexplained by explanatory variables and therefore the RAC model better captures the true influence of these covariates, resulting in strong inferential performance [38]. Moreover, models with autocovariates typically provide unbiased estimates of fixed effects [39].

The strength of the correlation between HRI and the probability of presence of rodents and cervids across Europe was assessed using Pearson's correlation coefficient.

All analyses were performed using the statistical software R ver. 4.1.2 [40] and packages spdep [41], raster [42], and sf [43].

Results

Analysis at European scale

Based on the data released by ECDC, the current geographical distribution of human TBE cases in Europe extends to the west as far as the French region of Alsace, to the south as far as northern Italy and to the east as far as the Balkan countries and northward to Norway and Finland. During the period 2017-2021, 13 European countries (Austria, Czech Republic, Denmark, Germany, Finland, France, Hungary, Italy, Lithuania, Poland, Romania, Slovakia, and Sweden) reported at least one locally acquired human TBE case with known place of infection at NUTS-3 or NUTS-2 level, for a total of 381 different regions and 12,296 cases. The same countries reported no TBE cases from the remaining 442 regions, to which we added 56 regions from Ireland and Spain, for a total of 498 regions with no autochthonous cases reported (Figure 1a). The corresponding 95-th percentile values of HRI showed large variations across the continent (Figure 1b). Lower values were found in the agricultural plains of western France, and in the lowland plains of

Poland and Romania. Conversely, high levels of habitat richness were found in the major European mountain ranges, such as the Alps, the Pyrenees, the Scandinavian mountains, the Apennines, the Central Massif in south-eastern France and the Bohemian Forest highlands along the German-Czech-Austrian border, together with regions located along the coastlines of countries facing the Baltic Sea, featured high levels of habitat richness.

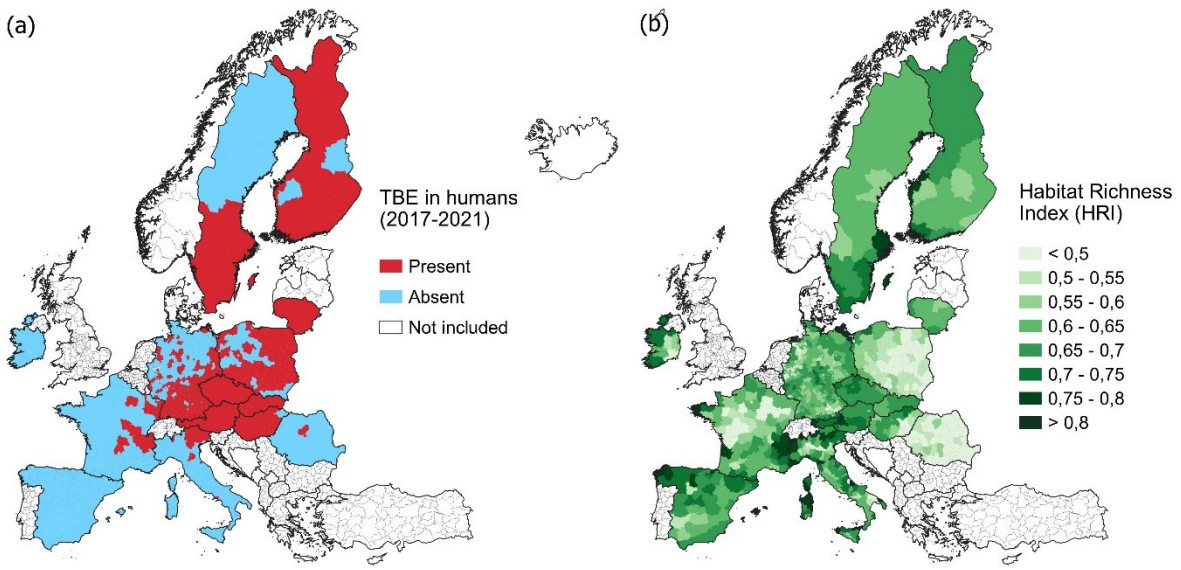

Figure 1 - Presence of human TBE cases and values of habitat richness index (HRI) in Europe. Panel (a): presence in red (n=381) and absence in light blue (n=498) of human TBE cases (2017-2021). Panel (b): 95-th percentile value of HRI at regional level.

Our analysis evidenced a significant, parabolic effect of HRI on the presence of human TBE cases in the European regions included in our dataset, as the binomial model with quadratic covariate (AIC = 1010·96) (Table 1) outperformed the linear one (AIC = 1026·3) (Supplementary Table S1).

Table 1 - Results of quadratic binomial regression. The habitat richness index (HRI) and autocovariate (ac) were used as predictors, for which the estimated regression

coefficients, standard errors SE, z-values, and p-values are given. Observations = 872. AIC = 1010·96.

Predictor	Coefficient	SE	z-value	p-value
Intercept	-8·14	2·22	-3·66	<0·001
HRI	25·06	7·28	3·44	<0·001
HRI^2	-19·69	5·93	-3·32	<0·001
ac	6·22	0·63	9·84	<0·001

Hence, the estimated probability of presence of human TBE cases in Europe showed a humped-shape curve, peaking in regions with intermediate values and then rapidly decreasing and zeroing at lower and higher values of HRI (Figure 2).

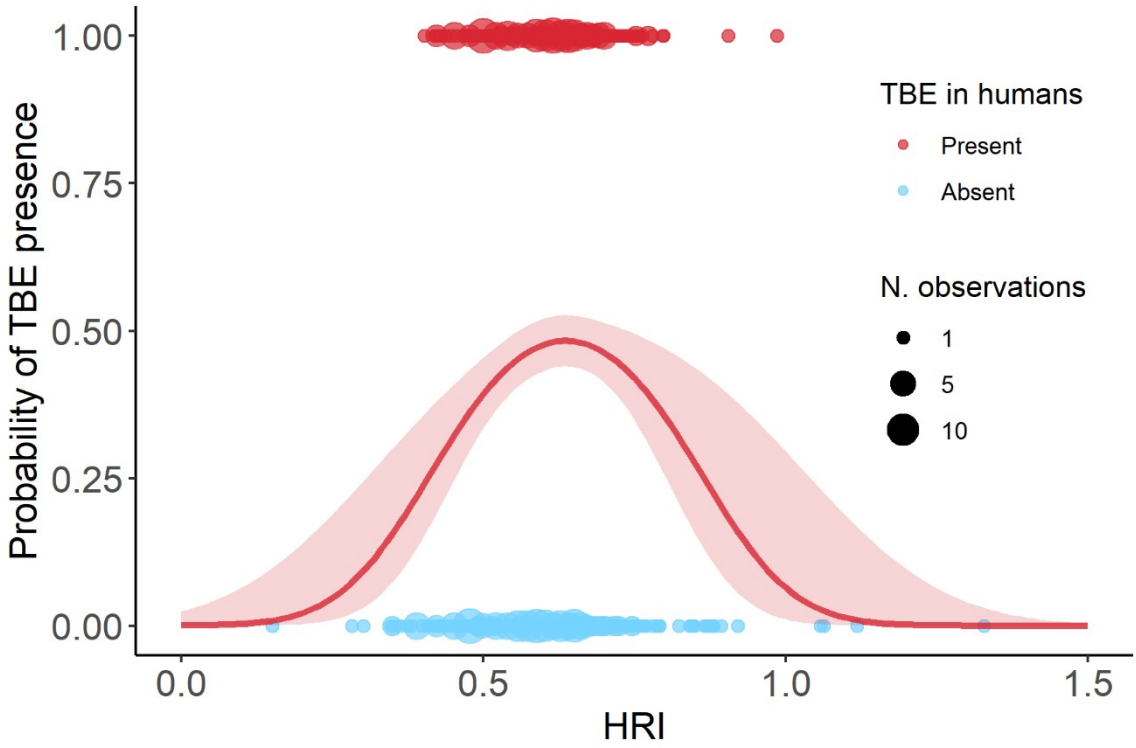

Figure 2) Estimated probability of TBE presence in Europe based on habitat richness index (HRI). Dots: Observed TBE presence (red) and absence (blue). Line: model prediction. Shaded bands: 95% confidence intervals.

In an analysis of the association between HRI and the probability of presence of key vertebrate hosts, we found a significant negative correlation with the presence of yellow-necked mouse, *A. flavicollis* (r = -0·16, p = 0·006), and a negative, although not significant, correlation with the presence of bank vole, *C. glareolus* (r = -0·06, p = 0·09), roe deer, *C. capreolus* (r = -0·04, p = 0·20) red deer, *C. elaphus* (r = -0·04, p = 0·43), and fallow deer, *D. dama* (r = -0·03, p = 0·44).

Analysis at local scale (Italy)

During the period 2017-2021, 104 and 56 human TBE cases were reported in the Trento and Belluno provinces, respectively. Overall, 73 different municipalities were indicated by patients as the place where they likely acquired the infection during this period (Figure 3a). The entire area is characterized by medium to high values of habitat richness, which peaks in correspondence of natural parks and reserves (Figure 3b).

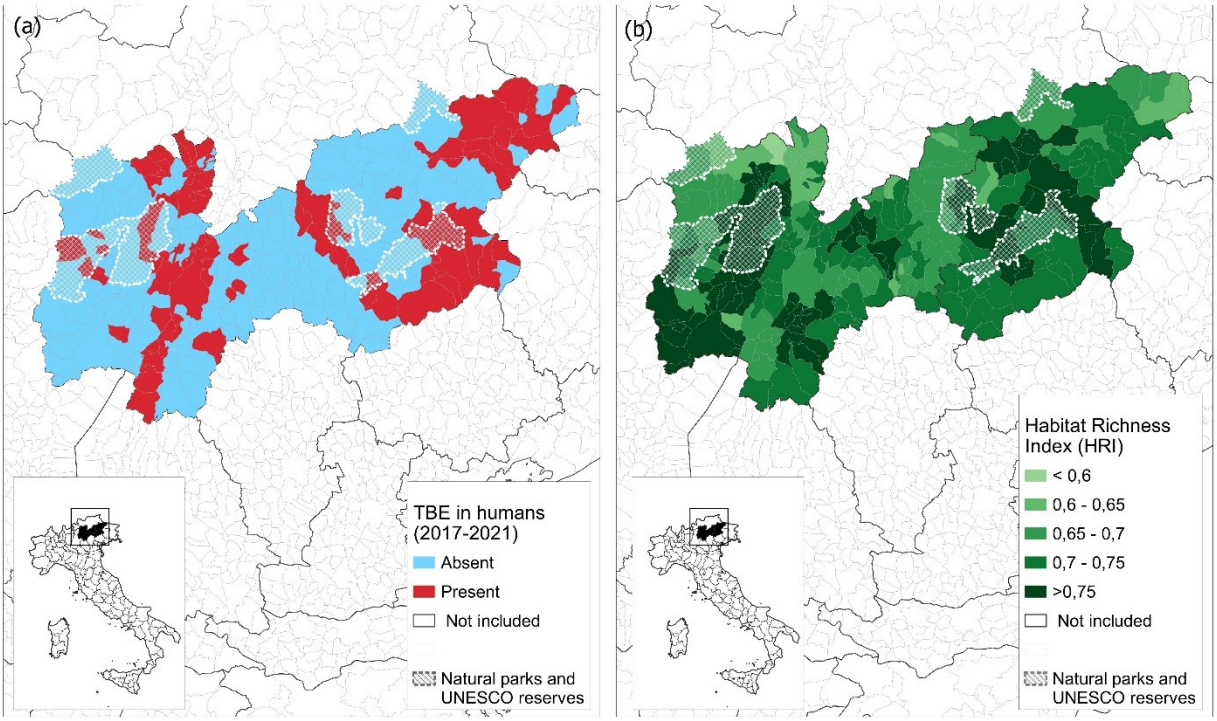

Figure 3 - Presence of human TBE cases and values of habitat richness index (HRI) in Trento and Belluno provinces (Italy). Panel (a): presence in red (n=73) and absence in light blue (n=164) of human TBE (2017-2021). Panel (b): 95-th percentile value of HRI at municipal level.

We found a significant negative association between the levels of HRI in each municipality, and the corresponding presence of human TBE cases (Table 3).

Table 3 – Results of linear binomial regression. The habitat richness index (HRI) and *autocovariate (ac) were used as predictors, for which the estimated regression coefficients, standard errors SE, z-values, and p-values are given. Observations =237. AIC =270·7.*

Predictor	Coefficient	SE	z-value	p-value
Intercept	6·34	2·03	3·13	<0·001
HRI	-9·93	2·84	-3·49	<0·001
ac	0·88	0·24	3·68	<0·001

In this case, the probability of presence of human TBE cases is higher in those regions with low to medium values of HRI, and then dramatically decreases as HRI becomes higher (Figure 4).

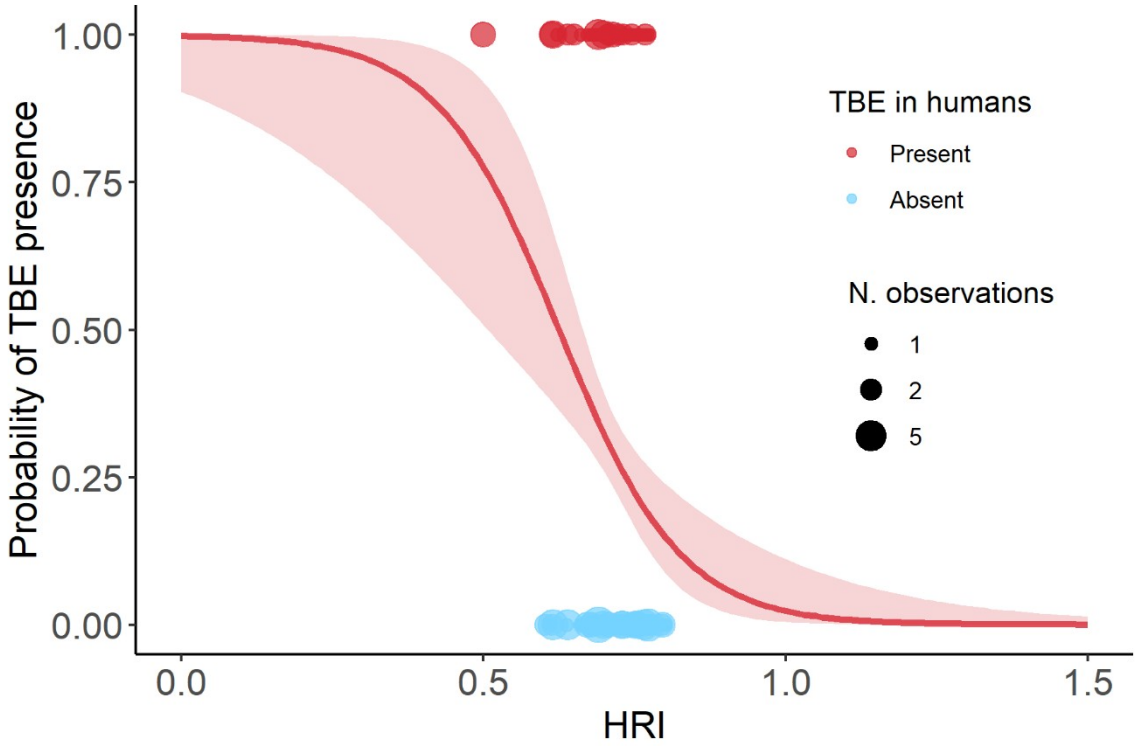

Figure 4) Estimated probability of TBE presence in the Trento and Belluno provinces (Italy) based on HRI. Dots: Observed TBE presence (red) and absence (blue). Line: model prediction. Shaded bands: 95% confidence interval.

Discussion

Tick-borne encephalitis (TBE) has become a growing public health concern in Europe, with an increasing number of reported human cases, despite the availability of a safe vaccine, and new natural foci of viral circulation appearing in previously non endemic areas.

The study of the relationship between biodiversity and disease risk in Europe is challenging due to the lack of quantitative data on abundance and density of wildlife species. We overcame this limit by using a newly developed indicator, the habitat richness index (HRI), to predict the probability of occurrence of human TBE cases at different spatial resolutions. Our results suggested that, at European scale, intermediate HRI maximizes TBE risk, which decreases at extreme (low and high) HRI values. This can be explained by the fact that European NUTS-2 and NUTS-3 regions included in the European-scale analysis are characterized by a great variety of habitat types, including habitats that are unsuitable for vector and host occurrence (compare Figure 1b and Figure 3b).

These findings were validated also at local scale, despite the narrower HRI range, where high TBE risk corresponds to areas with intermediate HRI. At the local scale, we found high TBE risk also at low HRI values. This result likely depends on the areas included at local-scale analysis, which feature habitat types that are generally suitable for ticks and host presence, as opposed to those corresponding to low TBE levels at European scale.

To fully understand the ecological implications of our findings, they need to be discussed in the context of the complex ecological mechanisms that underpin the viral circulation in the environment. TBEV circulation in the enzootic cycle is restricted to suburban and natural settings, as the establishment of a TBEV hotspot depends on environmental and behavioral factors associated with the presence of vectors and key animal hosts [8,9,44,45]. In this study, we found a negative, although non-significant, correlation between HRI and the presence of three species of cervids. This result is not surprising as

spatial behavior of deer species is conditioned not only by habitat and environmental features, but also by other factors such as, for example, human hunting pressure.

A. flavicollis and *C. glareolus* are widespread common forest species at European level although they differ in habitat selection and food diet composition. Our results confirmed the tight connection between the probability of presence of these species, *A. flavicollis* and *C. glareolus* (which are indeed the main reservoirs for TBEV), habitat richness, and, in turn, the occurrence of human TBE cases. Specifically, the significant negative correlation between HRI and *A. flavicollis* presence, found at the European scale, suggests a higher chance to find *A. flavicollis* in medium to low-diversity habitats, given its tendency to occupy mainly mature forested areas with little or no shrub vegetation diversity [46,47]. Its low presence in highly diversified habitats may decrease TBE risk thereafter. The same negative relationship with HRI has been found for *C. glareolus*, although not significant. This is probably due to its widespread occurrence in European forestry habitats with different levels of vegetation diversity [48]. Overall, our results suggest a lower probability of occurrence of TBEV reservoirs and tick-amplification hosts (i.e., rodents and deer), and therefore a lower probability of TBEV circulation, in regions with higher habitat richness.

As high habitat richness is also related to high species richness [27] we speculate that richer host communities with higher relative abundance of non-competent species could affect the role of *A. flavicollis* and other competent rodent species on tick infection prevalence by diverging blood meals of infected vectors away from competent hosts, and consequently reducing the natural hazard of TBEV circulation, in accordance with the dilution effect hypothesis [20,32]. Moreover, habitat destruction and the fragmentation of landscapes into small, isolated units are known to cause reduction or elimination of some vertebrate species and therefore diversity [49,50]. Often, species that occupy high trophic levels (i.e. predators) are the most sensitive to such habitat destruction. Loss of these species, although generally non competent reservoirs for vector-borne zoonoses, may

increase disease risk (i) via reduction of diverted blood meals from these incompetent hosts and (ii) via the loss of a regulatory ‘predator’ effect on typically more reservoir-competent hosts (Ostfeld et al., 2004; Levi et al., 2012). In fact, mesocarnivore predators (such as, for example, red foxes and mustelids) or birds of prey are known to regulate the density of small mammals [18,51,52].

So far, we have taken into consideration the ecological aspects that play a fundamental role in the natural hazard of TBE viral circulation and discussed how they might be affected by habitat and species richness. However, habitat richness might also have an impact on human exposure to infected ticks. Indeed, *I. ricinus*, the principal vector of TBEV in Europe, is mainly found in pastures, deciduous and mixed forests with abundant undergrowth [53] but can also be found in public greenspaces within peri-urban environments. Hence, human exposure to tick bites is enhanced when tourism or occupational activities take place not only in the proximity of forests and easily accessible areas with low vegetation, but also in urban or peri-urban recreational areas that feature low to moderate habitat diversity [54,55].

CONCLUSIONS

To our knowledge, this is the first attempt at understanding the relationship between TBE occurrence and habitat richness in Europe. Our findings suggest a broad, dampening effect of habitat richness on potential disease burden. As a result, the ongoing human driven reduction in biodiversity, coupled with climate change, could lead to more widespread disease [56,57]. However, such a conclusion is not definite, and we are aware of the limitations of this study. In fact, many crucial aspects of this interaction remain to be explored, such as the role of low-quality hosts, the characteristics of host competence or the vector preference. To have a thorough understanding of the TBE-diversity paradigm, these aspects should be carefully investigated in *ad hoc* empirical analysis aimed at

assessing how species diversity and host community composition influences local TBEV circulation.

In this study, we aimed to provide new evidence on the conditions (including direct or indirect roles of biodiversity, wildlife and land use) that promote the emergence and spread of TBE. Disentangling the relationship between habitat richness and TBE risk on an EU-wide basis is important to consistently inform public health authorities and support their prevention and control activities in areas where TBE viral circulation is more likely to occur. Furthermore, this study could support community efforts, such as the recently approved EU Nature Restoration Law, that are aimed at the conservation and protection of species and ecosystems in the European Union.

Statements

Contributors: Francesca Dagostin: Conceptualization, Methodology, Data Curation, Formal analysis, Writing - Original Draft. Valentina Tagliapietra: Conceptualization, Methodology, Writing - Review & Editing. Giovanni Marini: Conceptualization, Methodology, Writing - Review & Editing. Giulia Ferrari: Writing - Review & Editing. Marco Cervellini: Resources, Writing - Review & Editing. William Wint: Resources, Writing - Review & Editing. Neil S. Alexander: Resources, Writing - Review & Editing. Maria Grazia Zuccali: Resources, Writing - Review & Editing. Silvia Molinaro: Resources, Writing - Review & Editing. Nahuel Fiorito: Resources, Writing - Review & Editing. Timothée Dub: Writing - Review & Editing. Duccio Rocchini: Resources, Writing - Review & Editing. Annapaola Rizzoli: Conceptualization, Methodology, Supervision, Writing - Review & Editing.

Declaration of interest: We declare no competing interests.

Data sharing: The data that support the findings of this study are available from ECDC, Azienda Provinciale per i Servizi Sanitari Provincia Autonoma di Trento (APSS) and Unità Locale Socio Sanitaria Dolomiti (ULSS N.1 Dolomiti). Restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Code sources are available from the corresponding author upon reasonable request.

Disclaimer: The views and opinions of the authors expressed herein do not necessarily state or reflect those of ECDC. The accuracy of the authors' statistical analysis and the findings they report are not the responsibility of ECDC. ECDC is not responsible for conclusions or opinions drawn from the data provided. ECDC is not responsible for the correctness of the data and for data management, data merging and data collation after provision of the data. ECDC shall not be held liable for improper or incorrect use of the data.

Acknowledgments: GF, VT and AR acknowledges the support of NBFC to Fondazione Edmund Mach, funded by the Italian Ministry of University and Research, PNRR, Missione 4 Componente 2, "Dalla ricerca all'impresa", Investimento 1.4, Project CN00000033.

Bibliography

[1] European Centre for Disease Prevention and Control, Tick-borne encephalitis. In: ECDC. Annual epidemiological report for 2020. Stockholm: ECDC., 2022.
[2] J. Van Heuverswyn, L.K. Hallmaier-Wacker, J. Beauté, J. Gomes Dias, J.M. Haussig, K. Busch, J. Kerlik, M. Markowicz, H. Mäkelä, T.M. Nygren, H. Orlíková, M. Socan, J. Zbrzeźniak, M. Žygutiene, C.M. Gossner, Spatiotemporal spread of tick-borne encephalitis in the EU/EEA, 2012 to 2020, Eurosurveillance. 28 (2023). https://doi.org/10.2807/1560-7917.ES.2023.28.11.2200543.
[3] A. Stoefs, L. Heyndrickx, J. De Winter, E. Coeckelbergh, B. Willekens, A. Alonso-Jiménez, A.-M. Tuttino, Y. Geerts, K.K. Ariën, M. Van Esbroeck, Autochthonous Cases of Tick-Borne Encephalitis, Belgium, 2020, Emerg. Infect. Dis. 27 (2021) 2179–2182. https://doi.org/10.3201/eid2708.211175.
[4] T.S. Gritsun, V.A. Lashkevich, E.A. Gould, Tick-borne encephalitis, Antiviral Res. 57 (2003) 129–146. https://doi.org/10.1016/s0166-3542(02)00206-1.

[5] E. Martello, E.L. Gillingham, R. Phalkey, C. Vardavas, K. Nikitara, T. Bakonyi, C.M. Gossner, J. Leonardi-Bee, Systematic review on the non-vectorial transmission of Tick-borne encephalitis virus (TBEv), Ticks Tick-Borne Dis. 13 (2022) 102028. https://doi.org/10.1016/j.ttbdis.2022.102028.
[6] J.P. Borde, K. Kaier, P. Hehn, A. Matzarakis, S. Frey, M. Bestehorn, G. Dobler, L. Chitimia-Dobler, The complex interplay of climate, TBEV vector dynamics and TBEV infection rates in ticks—Monitoring a natural TBEV focus in Germany, 2009–2018, PLOS ONE. 16 (2021) e0244668. https://doi.org/10.1371/journal.pone.0244668.
[7] S.E. Randolph, D.J. Rogers, Fragile transmission cycles of tick-borne encephalitis virus may be disrupted by predicted climate change, Proc. R. Soc. Lond. B Biol. Sci. 267 (2000) 1741–1744. https://doi.org/10.1098/rspb.2000.1204.
[8] A. Rizzoli, H.C. Hauffe, V. Tagliapietra, M. Neteler, R. Rosà, Forest Structure and Roe Deer Abundance Predict Tick-Borne Encephalitis Risk in Italy, PLoS ONE. 4 (2009) e4336. https://doi.org/10.1371/journal.pone.0004336.
[9] R. Rosà, V. Tagliapietra, M. Manica, D. Arnoldi, H.C. Hauffe, C. Rossi, F. Rosso, H. Henttonen, A. Rizzoli, Changes in host densities and co-feeding pattern efficiently predict tick-borne encephalitis hazard in an endemic focus in northern Italy, Int. J. Parasitol. 49 (2019) 779–787. https://doi.org/10.1016/j.ijpara.2019.05.006.
[10] E. Tkadlec, T. Václavík, P. Široký, Rodent Host Abundance and Climate Variability as Predictors of Tickborne Disease Risk 1 Year in Advance, Emerg. Infect. Dis. 25 (2019) 1738–1741. https://doi.org/10.3201/eid2509.190684.
[11] A.I. Krawczyk, G.L.A. van Duijvendijk, A. Swart, D. Heylen, R.I. Jaarsma, F.H.H. Jacobs, M. Fonville, H. Sprong, W. Takken, Effect of rodent density on tick and tick-borne pathogen populations: consequences for infectious disease risk, Parasit. Vectors. 13 (2020) 34. https://doi.org/10.1186/s13071-020-3902-0.
[12] M. Labuda, O. Kozuch, E. Zuffová, E. Elecková, R.S. Hails, P.A. Nuttall, Tick-Borne Encephalitis Virus Transmission between Ticks Cofeeding on Specific Immune Natural Rodent Hosts, Virology. 235 (1997) 138–143. https://doi.org/10.1006/viro.1997.8622.
[13] S.E. Randolph, D. Miklisová, J. Lysy, D.J. Rogers, M. Labuda, Incidence from coincidence: patterns of tick infestations on rodents facilitate transmission of tick-borne encephalitis virus, Parasitology. 118 (1999) 177–186. https://doi.org/10.1017/S0031182098003643.
[14] A. Michelitsch, B.A. Tews, C. Klaus, M. Bestehorn-Willmann, G. Dobler, M. Beer, K. Wernike, In Vivo Characterization of Tick-Borne Encephalitis Virus in Bank Voles (Myodes glareolus), Viruses. 11 (2019) 1069. https://doi.org/10.3390/v11111069.
[15] G. Da Rold, F. Obber, I. Monne, A. Milani, S. Ravagnan, F. Toniolo, S. Sgubin, G. Zamperin, G. Foiani, M. Vascellari, P. Drzewniokova, M. Castellan, P. De Benedictis, C.V. Citterio, Clinical Tick-Borne Encephalitis in a Roe Deer (Capreolus capreolus L.), Viruses. 14 (2022) 300. https://doi.org/10.3390/v14020300.
[16] L. Bolzoni, R. Rosà, F. Cagnacci, A. Rizzoli, Effect of deer density on tick infestation of rodents and the hazard of tick-borne encephalitis. II: Population and infection models, Int. J. Parasitol. 42 (2012) 373–381. https://doi.org/10.1016/j.ijpara.2012.02.006.

[17]F. Cagnacci, L. Bolzoni, R. Rosà, G. Carpi, H.C. Hauffe, M. Valent, V. Tagliapietra, M. Kazimirova, J. Koci, M. Stanko, M. Lukan, H. Henttonen, A. Rizzoli, Effects of deer density on tick infestation of rodents and the hazard of tick-borne encephalitis. I: Empirical assessment, Int. J. Parasitol. 42 (2012) 365–372. https://doi.org/10.1016/j.ijpara.2012.02.012.
[18]F. Keesing, L.K. Belden, P. Daszak, A. Dobson, C.D. Harvell, R.D. Holt, P. Hudson, A. Jolles, K.E. Jones, C.E. Mitchell, S.S. Myers, T. Bogich, R.S. Ostfeld, Impacts of biodiversity on the emergence and transmission of infectious diseases, Nature. 468 (2010) 647–652. https://doi.org/10.1038/nature09575.
[19]F. Keesing, R.S. Ostfeld, Dilution effects in disease ecology, Ecol. Lett. 24 (2021) 2490–2505. https://doi.org/10.1111/ele.13875.
[20]K.A. Schmidt, R.S. Ostfeld, BIODIVERSITY AND THE DILUTION EFFECT IN DISEASE ECOLOGY, Ecology. 82 (2001) 609–619. https://doi.org/10.1890/0012-9658(2001)082[0609:BATDEI]2.0.CO;2.
[21]J.F. Anderson, Epizootiology of Lyme borreliosis, Scand. J. Infect. Dis. Suppl. 77 (1991) 23–34.
[22]P.J. Brandenburg, A. Obiegala, H.M. Schmuck, G. Dobler, L. Chitimia-Dobler, M. Pfeffer, Seroprevalence of Tick-Borne Encephalitis (TBE) Virus Antibodies in Wild Rodents from Two Natural TBE Foci in Bavaria, Germany, Pathogens. 12 (2023) 185. https://doi.org/10.3390/pathogens12020185.
[23]A. Michelitsch, K. Wernike, C. Klaus, G. Dobler, M. Beer, Exploring the Reservoir Hosts of Tick-Borne Encephalitis Virus, Viruses. 11 (2019) 669. https://doi.org/10.3390/v11070669.
[24]S.C. Ruyts, D. Landuyt, E. Ampoorter, D. Heylen, S. Ehrmann, E.C. Coipan, E. Matthysen, H. Sprong, K. Verheyen, Low probability of a dilution effect for Lyme borreliosis in Belgian forests, Ticks Tick-Borne Dis. 9 (2018) 1143–1152. https://doi.org/10.1016/j.ttbdis.2018.04.016.
[25]K. Takumi, H. Sprong, T.R. Hofmeester, Impact of vertebrate communities on Ixodes ricinus-borne disease risk in forest areas, Parasit. Vectors. 12 (2019) 434. https://doi.org/10.1186/s13071-019-3700-8.
[26]T.R. Hofmeester, P.A. Jansen, H.J. Wijnen, E.C. Coipan, M. Fonville, H.H.T. Prins, H. Sprong, S.E. van Wieren, Cascading effects of predator activity on tick-borne disease risk, Proc. R. Soc. B Biol. Sci. 284 (2017) 20170453. https://doi.org/10.1098/rspb.2017.0453.
[27]M. Cervellini, M. Di Musciano, P. Zannini, S. Fattorini, B. Jiménez-Alfaro, E. Agrillo, F. Attorre, P. Angelini, C. Beierkuhnlein, L. Casella, R. Field, J. Fischer, P. Genovesi, S. Hoffmann, S.D.H. Irl, J. Nascimbene, D. Rocchini, M. Steinbauer, O.R. Vetaas, A. Chiarucci, Diversity of European habitat types is correlated with geography more than climate and human pressure, Ecol. Evol. 11 (2021) 18111–18124. https://doi.org/10.1002/ece3.8409.
[28]L. Fahrig, Rethinking patch size and isolation effects: the habitat amount hypothesis, J. Biogeogr. 40 (2013) 1649–1663. https://doi.org/10.1111/jbi.12130.
[29]L. Heidrich, S. Bae, S. Levick, S. Seibold, W. Weisser, P. Krzystek, P. Magdon, T. Nauss, P. Schall, A. Serebryanyk, S. Wöllauer, C. Ammer, C. Bässler, I. Doerfler, M. Fischer, M.M. Gossner, M. Heurich, T. Hothorn, K. Jung, H. Kreft, E.-D. Schulze, N. Simons, S. Thorn, J. Müller, Heterogeneity–diversity relationships differ between and within trophic levels in temperate forests, Nat. Ecol. Evol. 4 (2020) 1204–1212. https://doi.org/10.1038/s41559-020-1245-z.

[30] D. Leclère, M. Obersteiner, M. Barrett, S.H.M. Butchart, A. Chaudhary, A. De Palma, F.A.J. DeClerck, M. Di Marco, J.C. Doelman, M. Dürauer, R. Freeman, M. Harfoot, T. Hasegawa, S. Hellweg, J.P. Hilbers, S.L.L. Hill, F. Humpenöder, N. Jennings, T. Krisztin, G.M. Mace, H. Ohashi, A. Popp, A. Purvis, A.M. Schipper, A. Tabeau, H. Valin, H. van Meijl, W.-J. van Zeist, P. Visconti, R. Alkemade, R. Almond, G. Bunting, N.D. Burgess, S.E. Cornell, F. Di Fulvio, S. Ferrier, S. Fritz, S. Fujimori, M. Grooten, T. Harwood, P. Havlík, M. Herrero, A.J. Hoskins, M. Jung, T. Kram, H. Lotze-Campen, T. Matsui, C. Meyer, D. Nel, T. Newbold, G. Schmidt-Traub, E. Stehfest, B.B.N. Strassburg, D.P. van Vuuren, C. Ware, J.E.M. Watson, W. Wu, L. Young, Bending the curve of terrestrial biodiversity needs an integrated strategy, Nature. 585 (2020) 551–556. https://doi.org/10.1038/s41586-020-2705-y.

[31] M. Anderle, M. Brambilla, A. Hilpold, J.G. Matabishi, C. Paniccia, D. Rocchini, J. Rossin, E. Tasser, M. Torresani, U. Tappeiner, J. Seeber, Habitat heterogeneity promotes bird diversity in agricultural landscapes: Insights from remote sensing data, Basic Appl. Ecol. 70 (2023) 38–49. https://doi.org/10.1016/j.baae.2023.04.006.

[32] R.S. Ostfeld, F. Keesing, Biodiversity series: The function of biodiversity in the ecology of vector-borne zoonotic diseases, Can. J. Zool. 78 (2000) 2061–2078. https://doi.org/10.1139/z00-172.

[33] G. Rezza, F. Farchi, P. Pezzotti, M. Ruscio, A. Lo Presti, M. Ciccozzi, V. Mondardini, C. Paternoster, M. Bassetti, M. Merelli, P.G. Scotton, R. Luzzati, J. Simeoni, P. Mian, R. Mel, V. Carraro, A. Zanin, R. Ferretto, E. Francavilla, TBE Virology Group, Tick-borne encephalitis in north-east Italy: a 14-year retrospective study, January 2000 to December 2013, Eurosurveillance. 20 (2015). https://doi.org/10.2807/1560-7917.ES.2015.20.40.30034.

[34] EEA, European Environment Agency (EEA). (2020). Article 17–2015 dataset – III report of Habitat distribution and of species occurrence data., (2020). https://www.eea.europa.eu/data-and-maps/data/article-17-database-habitats-directive-92-43-eec-2.

[35] W. Wint, D. Morley, Jolyon Medlock, N. Alexander, A first attempt at modelling red deer (Cervus elaphus) distributions over Europe, (2014). https://doi.org/10.6084/M9.FIGSHARE.1008334.V1.

[36] K.P. Burnham, D.R. Anderson, K.P. Burnham, Model selection and multimodel inference: a practical information-theoretic approach, 2nd ed, Springer, New York, 2002.

[37] L. Anselin, The Moran scatterplot as an ESDA tool to assess local instability in spatial association. Spatial analytical perspectives on GIS., in: Taylor Francis Lond., London, 1996.

[38] B. Crase, A.C. Liedloff, B.A. Wintle, A new method for dealing with residual spatial autocorrelation in species distribution models, Ecography. 35 (2012) 879–888. https://doi.org/10.1111/j.1600-0587.2011.07138.x.

[39] D.C. Bardos, G. Guillera-Arroita, B.A. Wintle, Valid auto-models for spatially autocorrelated occupancy and abundance data, Methods Ecol. Evol. 6 (2015) 1137–1149. https://doi.org/10.1111/2041-210X.12402.

[40] R Core Team, R: A language and environment for statistical computing. R Foundation for Statistical Computing., Vienna, Austria, 2022. https://www.R-project.org/.

[41] R.S. Bivand, D.W.S. Wong, Comparing implementations of global and local indicators of spatial association, TEST. 27 (2018) 716–748. https://doi.org/10.1007/s11749-018-0599-x.

[42]R.J. Hijmans, raster: Geographic Data Analysis and Modeling. R package version 3.5-15., 2022. https://CRAN.R-project.org/package=raster.
[43]E. Pebesma, Simple Features for R: Standardized Support for Spatial Vector Data, R J. 10 (2018) 439. https://doi.org/10.32614/RJ-2018-009.
[44]V. Tagliapietra, R. Rosà, D. Arnoldi, F. Cagnacci, G. Capelli, F. Montarsi, H.C. Hauffe, A. Rizzoli, Saturation deficit and deer density affect questing activity and local abundance of Ixodes ricinus (Acari, Ixodidae) in Italy, Vet. Parasitol. 183 (2011) 114–124. https://doi.org/10.1016/j.vetpar.2011.07.022.
[45]J.-F. Varlacher, S. Hägglund, M. Juremalm, G. Blomqvist, L. Renström, S. Zohari, M. Leijon, J. Chirico, Tick-borne encephalitis: -EN- -FR- Encéphalite transmise par les tiques -ES- Encefalitis transmitida por garrapatas, Rev. Sci. Tech. OIE. 34 (2015) 453–466. https://doi.org/10.20506/rst.34.2.2371.
[46]S.M. Hille, A. Mortelliti, Microhabitat partitioning of Apodemus flavicollis and Myodes glareolus in the sub-montane Alps: a preliminary assessment, Hystrix Ital. J. Mammal. 21 (2011). https://doi.org/10.4404/hystrix-21.2-4458.
[47]M. Mazurkiewicz, E. Rajska-Jurgiel, Spatial behaviour and population dynamics of woodland rodents, Acta Theriol. (Warsz.). 43 (1998) 137–161. https://doi.org/10.4098/AT.arch.98-11.
[48]F. Ecke, O. Löfgren, D. Sörlin, Population dynamics of small mammals in relation to forest age and structural habitat factors in northern Sweden, J. Appl. Ecol. 39 (2002) 781–792. https://doi.org/10.1046/j.1365-2664.2002.00759.x.
[49]B.F. Allan, F. Keesing, R.S. Ostfeld, Effect of Forest Fragmentation on Lyme Disease Risk, Conserv. Biol. 17 (2003) 267–272. https://doi.org/10.1046/j.1523-1739.2003.01260.x.
[50]D.A. Wilkinson, J.C. Marshall, N.P. French, D.T.S. Hayman, Habitat fragmentation, biodiversity loss and the risk of novel infectious disease emergence, J. R. Soc. Interface. 15 (2018) 20180403. https://doi.org/10.1098/rsif.2018.0403.
[51]H. Khalil, F. Ecke, M. Evander, M. Magnusson, B. Hörnfeldt, Declining ecosystem health and the dilution effect, Sci. Rep. 6 (2016) 31314. https://doi.org/10.1038/srep31314.
[52]R.S. Ostfeld, R.D. Holt, Are predators good for your health? Evaluating evidence for top-down regulation of zoonotic disease reservoirs, Front. Ecol. Environ. 2 (2004) 13–20. https://doi.org/10.1890/1540-9295(2004)002[0013:APGFYH]2.0.CO;2.
[53]A. Estrada-Peña, Distribution, Abundance, and Habitat Preferences of <I>Ixodes ricinus</I> (Acari: Ixodidae) in Northern Spain, J. Med. Entomol. 38 (2001) 361–370. https://doi.org/10.1603/0022-2585-38.3.361.
[54]P. Stefanoff, M. Rosinska, S. Samuels, D.J. White, D.L. Morse, S.E. Randolph, A National Case-Control Study Identifies Human Socio-Economic Status and Activities as Risk Factors for Tick-Borne Encephalitis in Poland, PLoS ONE. 7 (2012) e45511. https://doi.org/10.1371/journal.pone.0045511.
[55]M.C. VanAcker, E.A.H. Little, G. Molaei, W.I. Bajwa, M.A. Diuk-Wasser, Enhancement of Risk for Lyme Disease by Landscape Connectivity, New York, New York, USA, Emerg. Infect. Dis. 25 (2019) 1136–1143. https://doi.org/10.3201/eid2506.181741.

[56] G.M. Mace, R.S. Hails, P. Cryle, J. Harlow, S.J. Clarke, REVIEW: Towards a risk register for natural capital, J. Appl. Ecol. 52 (2015) 641–653. https://doi.org/10.1111/1365-2664.12431.
[57] D. Roe, Biodiversity loss—more than an environmental emergency, Lancet Planet. Health. 3 (2019) e287–e289. https://doi.org/10.1016/S2542-5196(19)30113-5.