Title: **Modeling the spatio-temporal annual changes in human tick-borne encephalitis (TBE) risk in Europe**

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Introduction
Caused by the tick-borne encephalitis virus (TBEV), tick-borne encephalitis (TBE) is a zoonotic disease that can cause severe neurological symptoms. Despite the availability of a vaccine, it remains a public health concern in Europe, with an increasing number of reported human cases and new hotspots of virus circulation, also in previously non-endemic areas. To geolocate and predict new areas at risk of human TBE infections, we developed a spatio-temporal predictive model to infer the year-to-year probability of human TBE occurrence across Europe at the regional and municipal administrative levels.

Methods
We derived the distribution of human TBE cases at the regional (NUTS-3) level during the period 2017-2022 using data provided by the European surveillance system (TESSy, ECDC), while the distribution of human TBE cases at the municipal level during the same years was obtained using data from five European countries (Austria, Finland, Italy, Lithuania, and Slovakia). We modelled the probability of TBE occurrence at regional and municipal levels for the period 2017-2024 using a boosted regression trees approach, including both hazard and exposure variables affecting TBE

risk: climate, land cover, presence of tick hosts to account for the natural hazard of virus circulation, forest road density and human population density as proxies for the probability of human exposure to tick bites.

Results

Our modelling framework provides a multi-scale approach to predict yearly variations in the risk of occurrence of human TBE cases in Europe. Our results highlight a significant rising trend in the probability of human infection with TBE not only in north-western, but also in south-western European countries and show that areas at high risk of TBE are characterized by the presence of key tick host species, intense human recreational activity in forests, steep drops in late summer temperatures and high annual precipitation.

Discussion

Our study provides a modelling framework for the early annual assessment and identification of European regions and municipalities at risk of human TBE infection, based on covariates reflecting both the hazard and exposure dimensions. Being based on lagged covariates, our approach can also be used to predict risk areas one year in advance, thus supporting surveillance, prevention, and control of human TBE infections by public health authorities.

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Main text

Introduction

Tick-borne encephalitis (TBE) is a severe viral infection of the central nervous system caused by the tick-borne encephalitis virus (TBEV), a member of the Flaviviridae family [1,2]. Patients may experience flu-like symptoms in mild cases, while more severe cases can lead to inflammation of the brain or the membranes surrounding the brain and spinal cord, resulting in potentially life-threatening complications. Long-term neurological deficits may be experienced by survivors of severe TBE [1,2]. The most widespread TBEV subtype circulating in the EU/EEA is the European subtype (TBEV-Eu), while the Siberian subtype (TBEV-Sib) occurs in some northeastern European countries [3]. In TBEV-Eu infections, 80% generally remain asymptomatic. The remainder usually present with biphasic disease, of which 10% show symptoms with severe neurological sequelae and a mortality rate of 1% to 2%. [1].

TBEV is transmitted to humans primarily through the bite of infected ticks belonging to the *Ixodidae* family. However, transmission can also occur through non-vectorial routes of infection, such as the consumption of unpasteurised milk and dairy products from infected cattle [4], which stand for 1% of all TBE cases reported annually in the EU/EEA. In 2012, the European Commission included TBE in the list of notifiable diseases in the EU/ EEA. TBE reporting in the EU/EEA is compulsory in nineteen countries, voluntary in four (Belgium, France, Luxembourg, and the Netherlands) and 'not specified' in one country (Croatia). During the last decade, European incidence of TBE human cases increased from 2412 confirmed cases in 2012 to 3514 confirmed cases in 2022, with the appearance of new foci of infection in previously non-endemic countries [5,6]. The geographical occurrence of human TBE infections shows an irregular distribution with a patchy occurrence in restricted foci of limited size where it circulates among vertebrate hosts and ticks. Such hotspots are difficult to identify and often vary in space and time [7]. An explanation could be found in the complex interplay of the biotic and abiotic factors that characterise the transmission chain of the TBE virus, including climate, vegetation, and the presence of vertebrate hosts that act as either virus reservoirs (e.g. rodents) or amplifiers of the tick population (e.g., ungulates) [8,9]. These factors affect the distribution and abundance of tick vectors and the prevalence of TBEV within tick populations. Additionally, human behaviour and land use patterns can also significantly contribute to shaping the TBE risk, as humans can increase their likelihood of exposure to infected ticks during outdoor activities [10].

Surveillance efforts for TBE aim to track the incidence and distribution of TBE infections in the human population, identify high-risk areas, and assess temporal trends in disease prevalence. Within this context, mapping the spatial risk of TBEV transmission at the finest spatial resolution, ideally at the municipal level, is essential for targeted public health interventions, including awareness and vaccination campaigns. Machine learning techniques have been increasingly used for predicting the potential distribution of vectors and infectious diseases as part of risk assessments, as they are flexible, can account for nonlinearity and interactions and can handle different types of predictor variables [11]. Such techniques have been successfully used to model the distribution of pathogens and disease cases (e.g., Dengue [12], Chikungunya [13], West Nile Fever [14,15]). Concerning tick-borne diseases, several studies conducted in Europe have used species distribution modelling techniques combined with environmental and climatic predictors to model the present and future distribution of tick vectors [16,17] and the natural hazard of TBEV

circulation in ticks and vertebrate hosts [18,19]. In the case of risk models for human TBE cases, recent publications focus only on limited areas or specific countries, such as Finland [20], Germany [21], or Sweden [22]. At the continental scale, maps depicting human TBE notification rates are available but usually have a rather coarse spatial resolution [23]. Hence, estimating the probability of human TBE infections at the finest administrative scale within a single modelling framework that uses easily accessible data on environmental, animal, climatic and anthropogenic factors, represents a step forward for TBE risk estimation and mitigation in Europe.

Here, we developed a modelling framework that integrates our understanding of the biological premises underlying TBEV circulation, with machine learning modelling in support of the evaluation and prediction of the short-term spatio-temporal TBE risk. Specifically, we aim to (i) predict in advance the annual risk of human TBE infections in European regions and municipalities before the start of tick questing activity, (ii) produce risk maps based on model predictions, and (iii) assess the spatio-temporal trend in the risk of human TBE infections.

Methods

Collection of epidemiological data

The observations of reported human cases of TBE were obtained from The European Surveillance System (TESSy), a database for the collection, validation, cleaning, analysis, and dissemination of data for public health activities hosted by the European Centre for Disease Prevention and Control (ECDC). Epidemiological data included, where available, the most likely place of infection at "nomenclature of territorial units for statistics" (NUTS) level 3 (which correspond to small regions for specific diagnosis, according to the NUTS classification system [24]). In our study, we used the human TBE confirmed and probable cases reported to TESSy between 2017 and 2022. Patients who acquired the infection abroad or whose place of exposure was unknown or not reported at the NUTS-3 administrative level were excluded. Specifically, we only included reporting countries that provided the location of infection at the NUTS-3 level for at least 75% of cases notified during the selected period. The 13 countries selected according to these criteria were: Czechia, Denmark, Germany, Greece, Finland, France, Hungary, Italy, Lithuania, Poland, Romania, Slovakia, and Sweden. To complement this dataset, we received data from Austria (Austrian Agency for Health and Food Safety, AGES) and Slovenia (University of Ljubljana). We also included Ireland and Spain, two countries in which, despite compulsory notification, no autochthonous cases were reported during the study period, to account for areas with no recorded presence of TBE.

We also received, upon formal request, data reported at a higher administrative level, namely the distribution of human TBE cases in Austrian districts between 2017 and 2022, provided by the Austrian Agency for Health and Food Safety (AGES), and data collected between 2017 and 2022 in the municipalities of Finland (provided by the Finnish Institute of Health and Welfare, THL), Slovakia (provided by the Public Health Authority of the Slovak Republic), Lithuania (provided by the National Public Health Centre under the Ministry of Health) and northern Italy (provided by the local public health agencies, Azienda Provinciale per i Servizi Sanitari Provincia Autonoma di Trento and Unità Locale Socio Sanitaria Dolomiti Belluno). Based on these sources, we compiled two different dichotomous datasets representing the presence and absence of human TBE cases between 2017 and 2022, at the regional (NUTS-3) and municipal levels. Presence locations were

defined by the administrative units that reported at least one confirmed human TBE case per year, while absence locations were defined as the remaining units with zero confirmed cases.

Hazard and exposure covariates

We included in our study a comprehensive set of covariates that reflect both hazard and exposure dimensions, as risk assessment relies on the interaction between these two components (Figure 1). Specifically, hazard refers to any potential source of harm, while risk is the probability of harm occurring based on physical exposure to the hazard. Concerning tick-borne diseases, hazard can be defined as the presence of infected vectors in the environment, which depends on the interplay of complex ecological and environmental conditions that allow TBEV circulation among ticks and competent hosts [25]. Exposure, on the other hand, relates to human interactions with the environment that increase the likelihood of encountering infected ticks and depends on factors such as human outdoor activities and socio-economic variables [22].

We selected key hazard factors as identified by Dagostin *et al*. [26]. These predictors included: (i) the percentage of forested areas in each area, (ii) the total precipitation of the driest quarter one year prior, (iii) the autumnal cooling rate one year prior, (iv) the weighted probability of presence of selected critical host species originally produced using Random Forest and Boosted Regression Trees based spatial modelling techniques [27] (see Supplementary Material for a detailed description of covariates and data sources). The assumption of a constant distribution (presence or absence of key hosts) during the study period was made due to the lack of standardised, high-resolution data on annual and interannual variations in host abundance and density at the continental scale.

To account for human exposure to tick bites, assuming that roads increase access and that forests with roads are more likely to be entered by visitors, we computed the density of forest roads contained by OpenStreetMap as a proxy of accessibility to forested areas [22]. Human population density in each area, derived from the WorldPop dataset [28], was also included. Time-dependent predictors, the autumnal cooling rate and the precipitation of the driest quarter, were computed for each year of analysis with a 1-year lag (2016-2023). All explanatory variables were computed by averaging them for each administrative area included in the dataset, at the regional and municipal administrative levels (see Supplementary Material, Figure S1-S6, for the mapped values of predictors).

Boosted regression trees modelling framework

We modelled the probability of the presence of human TBE cases using a boosted regression tree (BRT), a machine learning technique based on regression trees and gradient boosting. BRT offer several advantages over other modelling techniques, including the capacity to handle diverse types of predictor variables, to fit complex nonlinear relationships, and to accommodate missing data [11]. We implemented the BRT algorithm using the "gbm" R package [29] using a spatial cross-validation to limit model overfitting. Specifically, we applied a leave-location-out (LLO) resampling method within the 'mlr3' R framework [30] in which a test set is selected and all observations that correspond to the same location across multiple time points are omitted from the training sample. To consider spatial autocorrelation, spatial folds selection was defined based on the block generation method described by Valavi and colleagues and implemented in the R package "blockCV" [31]. As BRT builds the trees on random subsamples, we ran 10 independent

model replicates and averaged the results. We trained the BRT model on TBE presence-absence data reported between 2017 and 2021 at the NUTS-3 spatial level, and assessed the model predictive performance by estimating the area under the receiver operating characteristic curve (AUC), the sensitivity and specificity, and the prevalence-pseudoabsence-calibrated Sørensen's index (SI_{ppc}) [32,33], as the use of the AUC metric alone has been repeatedly criticised in previous works because of its dependence on prevalence [34]. As the computation of this index needs binary presence-absence data, whereas our model instead returns predicted probability values, we performed an optimisation procedure by applying a threshold to the model's predictions to transform them into a presence-absence dataset. The threshold values were varied in the range [0, 1] with a 0.01 step increment, and the threshold that maximised the SI_{ppc} was eventually selected to compute the index (see [35] for the application of a similar approach). Performance metrics were calculated across the ten replicates. In addition, official TBE records from 2022, reported at the NUTS-3 level, were left out from model training and later used to externally assess the predictive power of the model. We trained the model at the regional administrative level and then applied it to predictors averaged at the municipal administrative level to obtain a higher resolution output [36], due to the lack of sufficient municipal-level data to develop a model based solely on them. The accuracy of of municipal risk maps was externally assessed based on the presence/absence dataset compiled at the municipal level for the period 2017-2022 (see Supplementary Material, Figure S7, for the presence/absence dataset of TBE at the municipal level). The model enables the prediction of TBE risk on an annual basis, using temporal covariates recorded one year prior. For example, the prediction for 2025 could be made in January 2025, based on the covariates recorded in 2024. A schematic representation of the modelling framework is shown in Figure 1.

Figure 1 - Schematic representation of the modelling framework.

Finally, linear regressions were performed to identify areas with either an increasing or decreasing trend in the probability of human TBE cases over the specified years and across the two administrative scales. For this analysis, we fitted generalised linear models (GLMs) to the predicted risk probability, with the year as the predictor variable (formula: prediction ~ year). All analyses were performed using R Statistical Software v.4.1.2 [37].

Results

The current observed spatial distribution of human TBE cases across Europe extends westward to the Ain department of France, southward to northern Italy, eastward to the Balkan countries, and northward to Norway and Finland. Over the period spanning 2017 to 2022, 15 European countries reported at least one confirmed, autochthonous human case with a known place of infection at the regional level. Overall, this dataset comprised a total of 1,658 "presences" in NUTS-3 regions over the period of analysis, spanning 15 European countries (Austria, Czech Republic, Denmark, Germany, Greece, Finland, France, Hungary, Italy, Lithuania, Poland, Romania, Slovakia, Slovenia, and Sweden). The number of NUTS-3 positive regions (*i.e.*, that notified at least one human TBE case), increased from 255 regions in 2017 to 279 regions in 2022. Within the same timeframe, no human TBE cases were reported from 4,096 other regions within the 15 countries mentioned above, plus Spain and Ireland (Figure 2).

Figure 2 – Presence (in red) and absence (in blue) of human TBE cases at the NUTS-3 (regional) administrative level (2017-2022). Areas where TBE distribution is unknown at the NUTS-3 level are masked in grey.

TBE risk maps at the regional and municipal level

The predicted probability of occurrence of TBE human cases at the regional level is shown in Figure 3. Figure 4 provides more detailed risk maps, displaying the same probability at the municipal level. Both results are consistent with the observed spatial distribution of human TBE cases, but also suggest emerging risk areas in countries where TBE is not considered endemic, and a few autochthonous cases have recently been reported (e.g. Belgium and the United Kingdom). The mean AUC was 0.85 (standard deviation (SD) = 0.02) for the regional model, derived from internal cross-validation, and 0.82 (SD = 0.03) for the model at the municipal scale, derived from external validation. The predictive performance at the regional scale showed good sensitivity (0.82) and specificity (0.80), while specificity decreased when downscaling the results at the municipal scale (0.69). Similarly, the Sorensen's Index showed a variation from 0.71 (regional model) to 0.56 (municipal model). We also performed external validation on official TBE cases reported during 2022 at the regional level, which were not included in the training dataset. The external validation of regional risk maps yielded good results, with an AUC of 0.87, sensitivity of 0.81, specificity of 0.78, and SI_{ppc} of 0.73 (see Supplementary Material, Table S3, for detailed performance metrics).

Figure 3 - The predicted probability of the occurrence of human TBE cases at the regional (NUTS-3) level, 2017-2024. Interactive maps can be explored in detail at *https://mood-platform.avia-gis.com/core?tab=diseases*.

Figure 4 - The predicted probability of the occurrence of TBE human cases at the municipal level, 2017-2024. Interactive maps can be explored in detail at *https://mood-platform.avia-gis.com/core?tab=diseases* .

Fitted functions and relative importance of variables

BRT results comprise two main elements: fitted functions and the relative importance of variables. Fitted functions can be visualised using partial dependence plots. They show the effect of a predictor on the response after accounting for the average effects of all other variables and were interpreted here as the relative probability of reporting at least one human TBE case at various levels of the predictor variable. The contribution of each environmental factor is given by its relative influence (RI) in the BRT model and is computed as the number of times the variable is selected for splitting a tree, weighted by the squared improvement to the model resulting from each split averaged over all trees [11]. Variables which showed a positive trend are the probability of vertebrate hosts' presence (RI = 39.44); the density of roads and pathways in forested areas (RI = 21.39); the total precipitation of the driest quarter (RI = 20.19); the proportion of forested areas (RI = 14.85); and population density (RI = 2.37). The autumn cooling rate (RI = 1.77), which is negative by definition and measures the rate of decrease in late summer temperatures, showed a negative trend, meaning that the risk of TBE is higher when such temperature decrease is steeper (see Supplementary Material, Figure S8, for partial dependence plots).

Short-term variability of TBE risk in Europe

To examine potential upward or downward trends in the spatio-temporal variation of TBE risk from 2017 to 2024, we conducted GLM analyses for each administrative unit, considering the BRT prediction as the response variable and the year as the predictor variable, and mapped statistically

significant coefficients both at the NUTS-3 (Figure 5a) and municipal (Figure 5b) administrative levels. The results suggest an increase in TBE probability of presence across central-western European countries (e.g. Switzerland and Germany), with the emergence of new risk areas extending in a north-westerly and potentially south-westerly direction (e.g. Belgium, France, and the United Kingdom). Areas with larger significant increases in human TBE infection risk can be identified at both regional (Figure 5a) and municipal (Figure 5b) levels and are concentrated in western Germany, southern Belgium, eastern France, and Switzerland (dark red areas), suggesting a non-negligible short-term increase in TBE risk in recent years, and so possibly in the coming years.

Figure 5. Significant coefficients (p < 0.05) of linear regression models applied to each area over 2017-2024 with year as predictor, at the NUTS-3 (a) and municipal (b) administrative levels.

Discussion

The observed spread and emergence of new TBE hotspots across Europe highlights the need to provide public health authorities with high-resolution risk models as a tool to improve surveillance and preventive measures aimed at reducing the burden of TBE among European citizens. Here, we present a machine learning modelling framework that improves our current understanding of the spatial and temporal distribution of TBE risk in Europe while enabling the assessment of the probability of changes in TBE risk one year in advance. The model outputs, which can be visualised and interpreted as risk maps highlighting areas where new TBE outbreaks are likely to occur, will be regularly updated and could become a complementary tool for disease surveillance and control, allowing prevention and response efforts to be focused on high-risk areas. Overall, the spatio-temporal risk maps suggest a shift of TBE suitability towards northern, western, but possibly also southwestern countries, with a significant positive trend in areas where TBEV is recognised as endemic, such as Germany and Switzerland, and countries where so far only a few

autochthonous cases have been reported, such as Belgium [38], France [39], and the UK [40]. These results are consistent with the recent longitudinal and latitudinal shifts, which imply retraction from some areas as well as expansion into others, that was observed in cases reported to ECDC [6,23] but also suggest a possible new pathway of TBE emergence towards southwestern areas, which we assume could be driven by changes in climatic and ecological factors, such as the spatio-temporal expansion of ticks and their range of activity, coupled with host movements, changes in land use patterns and rise in exposure driven by changes in human behaviour and increase use of green areas also in relation to a warmer climate [41].

In our modelling framework, we provide a more comprehensive understanding of the human TBE risk pattern and its drivers as model predictions are determined by both hazard factors, such as climate, vegetation, and presence of vertebrate hosts, which influence tick abundance and TBEV prevalence in ticks, and exposure drivers, which include human behaviour. Abiotic factors directly affect the off-host stages of ticks, particularly temperature and humidity, which influence tick body hydration [42]. Our results suggest that areas with higher cumulative rainfall lead to higher TBE risk, as rainfall has an indirect positive effect on relative humidity (and therefore on saturation deficit) that enhances tick survival and favours questing also during the driest months of the year [17]. Moreover, a high rate of autumnal cooling (i.e. a rapid drop in late summer temperatures) affect the critical seasonal point of diapause induction in ticks by favouring a behavioural diapause in larvae and nymphs that are ready for synchronised questing the following spring. This scenario enhances TBEV transmission from infected nymphs to co-feeding uninfected ticks on rodents, supporting TBEV circulation [43–45].

Concerning environmental variables, forests, especially well-connected coniferous, deciduous, and mixed forests, provide suitable habitats and resources for tick hosts, facilitating their encounter and resulting in higher TBE suitability [8,46]. Human activity and behaviour can act in synergy with these ecological factors by increasing the likelihood of encountering infected ticks, as people who engage in recreational or occupational outdoor activities in green areas are at increased risk of tick bites [22,47]. Therefore, forest road density and population density, included in the model as proxies for forest accessibility and human exposure to infected ticks, are both associated with higher TBE risk. Our results also highlight the relevance of including information on the occurrence of competent and tick-feeding hosts when modelling TBE risk. In small-scale studies, this is usually achieved by relying on locally recorded game population densities [8,48,49]. However, high-resolution data on host abundance or density are not available at the continental scale, which is why this information is generally not considered in European-wide studies. For this reason, we included in our modelling framework a variable describing the habitat suitability of critical host species, which was originally obtained using random forest and boosted regression trees-based spatial modelling techniques [27] and has already been shown to be a good predictor of TBE incidence across Europe [26]. Rodents are known TBEV reservoir hosts, supporting both virus circulation and tick feeding, while ungulates are capable of greatly increasing tick abundance while diverting tick bites from competent hosts [50–53]. Hares and red foxes may also play a similar role, as high host species diversity and population numbers weaken the incidence of TBE-infected ticks on a given host [54,55]. A limitation of this study is that the variable used as a proxy for TBE host distribution does not consider the actual annual and interannual variations in host population density and is constant throughout the study period. However, it was found to significantly

improve model performance compared to the same model built excluding this predictor (see Supplementary Material, Table S4, for the predictive performance of the BRT model without this variable). Hence, our results highlight the need for a standardised and systematic collection of high-resolution data on animal host density and accurate population estimates which will be crucial to improve the accuracy of future modelling studies, as host density is known to be a key determinant also for tick-borne disease transmission dynamics [49,52,56]. Layers representing the distribution of the vectors, *Ixodes ricinus* and *Ixodes persulcatus* were initially considered as predictors but had no significant impact on the model's performance and were therefore excluded from further analyses. This can be explained by the fact that the mere presence of the vector, which is widely distributed, is not sufficient for the circulation of the virus. Instead, specific ecological and environmental conditions are necessary, given the focal distribution of TBEV.

To implement actual one-health surveillance, it will also be essential to incorporate data on food-borne TBE infections, which were not included in this study due to the unavailability of information on the specific mode of TBEV transmission (either tick bites or infected food sources, such as unpasteurised milk and derived products), and data on the occurrence of cattle, sheep and goats, which act as sentinel and source of TBEV. Consequently, at this stage, our approach does not differentiate between tick-borne and food-borne human TBE infections and the model indicates potential risk areas for disease transmission regardless of the infection mode. In the future, vaccination rates should also be considered to model changes in the true incidence of TBE in the human population, which we could not assess in this study due to lack of available vaccination data coverage in all countries considered in this study.

We downscaled our results to the municipal administrative level to explore local TBE risk patterns, as TBEV circulates in restricted hotspots depending on local climatic and ecological conditions. These higher-resolution risk maps provide a more detailed picture of the pattern of TBE risk areas across Europe and could allow more effective and targeted surveillance efforts. The enhanced resolution of the municipal risk maps shown in Figure 4 highlights the geographical heterogeneity of TBE risk areas over the years studied, which is consistent with the known patchy distribution of TBE infections across Europe. However, we were only able to validate these results using a limited dataset of recorded human TBE cases provided by five European countries upon special agreement. To facilitate future efforts to model TBE risk at high spatial resolution, it would be beneficial to collect epidemiological data in an integrated and standardised manner across Europe, not only at the regional level but also at the municipality level. Overall, our model has shown good predictive performances, although with a slight tendency to overestimate positive areas, especially when results are downscaled to the local level, implying that the higher resolution maps are more likely to contain a high number of false positives and may incorrectly predict high risk in areas where TBE is not present. This is not necessarily a drawback, as the primary purpose of the maps is to define risk areas where surveillance could be strengthened, and local authorities should use their specific knowledge of the area to put the predicted risk level in context.

Overall, estimating and predicting the risk of transmission of TBEV under a global change scenario is essential for planning public health interventions, including awareness campaigns, vaccination programmes, and complementary risk assessments are fundamental to inform and educate local populations in endemic regions, but also travellers, to take appropriate prophylactic measures to

avoid tick bites and tick-borne infections. In this study, we provide a solid framework for early TBE risk assessment one year in advance, based on standardised and biologically consistent covariates that are easily accessible to public health practitioners, and we establish its validity as a tool to support public health surveillance.

A further strength of our approach lies in the interpretability of the results and the sustainability of the modelling framework since the easy access to covariates selected for this study will allow a continuous updating of the spatio-temporal risk predictions on an annual basis. Outputs are obtained by integrating data on tick habitat suitability, wildlife tick hosts and TBEV reservoirs, environmental and climatic variables, and proxies for human behaviour, and our results indicate non-negligible short-term changes in the epidemiology of TBE over the years considered, especially in western countries. Ultimately, the risk maps developed in this study will be regularly updated and used to predict one year in advance the expected changes in TBE risk across Europe, as a useful tool to strengthen and inform disease surveillance, control and prevention strategies aimed at mitigating the public health impact of TBE.

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