Trends in the spatial spread of nephropathia epidemica and Lyme borreliosis incidence in Belgium

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Summary: Lyme borreliosis (LB) and nephropathia epidemica(NE) are zoonotic diseases caused by the bacterium *Borrelia burgdorferi* and the *Puumala* hantavirus, respectively. The reported number of cases has recently increased in Belgium and other European countries for both diseases. This study analyzed the spatial pattern of a risk estimator for NE/LB in the period 1996-2010 in Belgium. The results revealed the increase in risk of NE/LB in known infection foci and a noticeable expansion of infection risk. Vegetation seems to be a driver in disease spread. Yet, the spread and expansion of NE and LB is not always spatially correlated.

KEYWORDS: Lyme borreliosis, nephropathia epidemica, hantavirus, disease mapping, spatial epidemiology

1. Introduction

Interest in Lyme borreliosis (LB) and nephropathia epidemica (NE) has risen as consequence of recently reported increases in the number of reported cases and higher frequency of outbreaks (Clement et al.,2009, 2010; Ducoffre, 2010; Mailles et al., 2005). LB and NE are zoonoses caused by the bacterium *Borrelia burgdorferi* and *Puumala* virus (PUUV), respectively. The specific vector of PUUV in Western Europe is the bank vole (*Myodes glareolus*) and *B. burgdorferi* is transmitted to humans by means of bites of *Ixodes* ticks. Besides its prominent role in the transmission of PUUV, the bank vole is an important reservoir in the transmission chain of *B. burgdorferi*.

The analysis of the disease spread in space and time is the departure point for developing hypotheses on the mechanisms ruling spatial distribution, timing of outbreaks and expansion routes of these diseases. It may also allow the incorporation of spatial and/or temporal data sources such as satellite imagery and spatial databanks in epidemiology analysis.

In this paper we analyzed 15 years (1996-2010) of count data on NE and LB cases in Belgium at municipal level in order to *(i.)* assess changes in the spatial spread of both diseases, *(ii.)* determine whether the common aspects of their transmission mechanisms have led to similar spatial patterns of risk.

2. Background

Belgium has temperate climate, warm summer and no dry season (Peel et al., 2007). The country is divided in provinces that belong to either Flanders or Wallonia (Figure 1A). Official demographic data (Belgian Federal Government, 2010) indicate that the country's population density approximates

350 inhabitants/km^2. Local figures can differ significantly from this average. The maps in Figure 1 show that Flanders is a densely populated zone with prominence of artificial surfaces and fragmented vegetation patches. This situation is opposite in the south where the population density is much lower, the forested areas are larger and less fragmented and the artificial surfaces are not the dominant landscape feature.
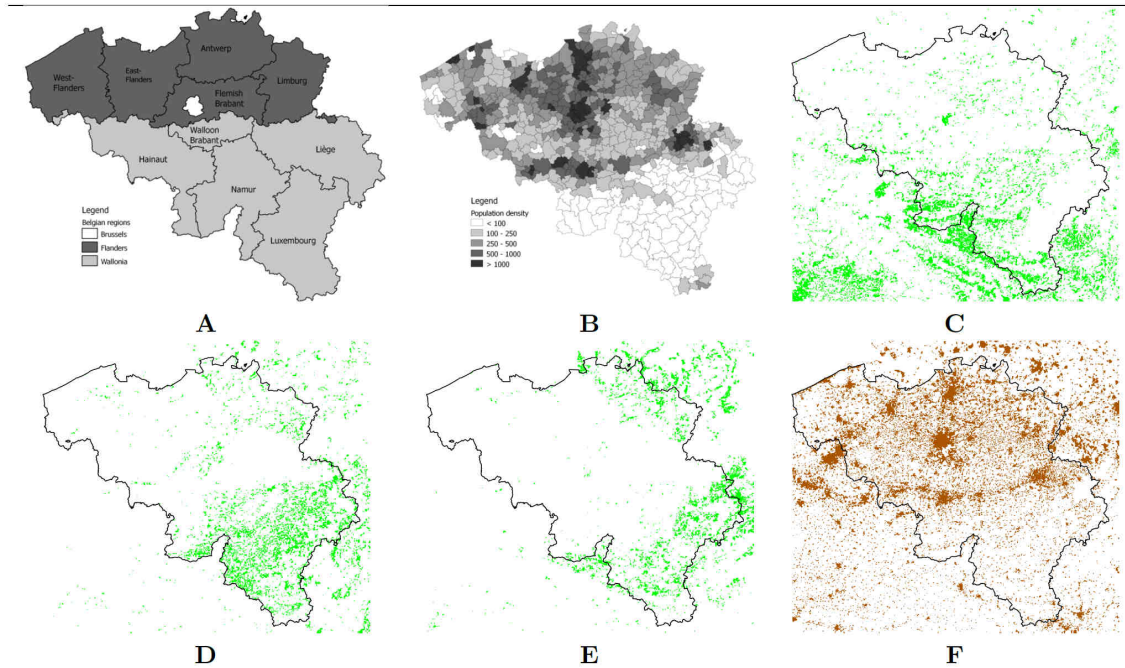

Figure 1. Belgian maps of Regions and provinces (A), population density (B), broad-leaved forest (C), mixed forest (D), coniferous forest (E) and artificial surfaces (F) (source C, D, E, F: CORINE land cover map)

Likewise, reported NE and LB cases in north and south are contrasting. Figure 2 illustrates the official numbers of cases (Ducoffre, 2010). While the incidence of NE is larger in southern Belgium, the number of LB cases is much larger in the north. The graphs show also that the NE and LB records differ greatly across time.
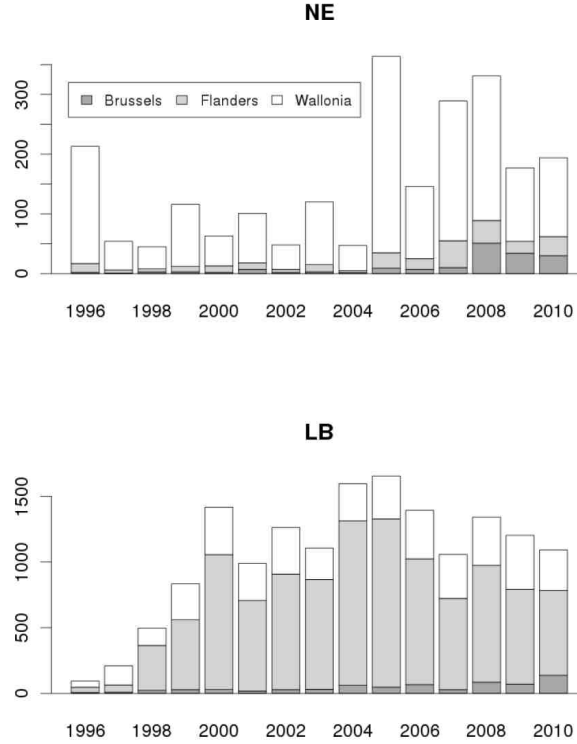
Figure 2. NE and LB reported cases in Belgium for the period 1996-2010

3. Methods

3.1 Risk Estimator

Various disease risk estimators exist, several of them being based on Bayesian statistics. By following a Bayesian approach for local risk assessment, data of geographical entities are weighted such that only neighbouring entities are used in the estimation. We followed the method proposed by Marshall (1991) for the computation of a local Empirical Bayesian Estimator of risk (EBE). Marshall's method shrinks the estimated value towards a local mean by considering only adjacent entities in its computation. The use of a local estimator was motivated by the spatial nature of disease determinants; i.e. vector habitat, landscape configuration, forest characteristics, etc. Adjacency among municipalities was defined by a first order Queen contiguity criterion, i.e. two municipalities were considered neighbours when their borders shared at least one point. Marshall's algorithm is represented by the following expression (Marshall, 1991):

$$\hat{\theta}_i = \hat{m}_i + \left(\theta_i - \hat{m}_i\right)\frac{\hat{a}_i}{\hat{a}_i + \dfrac{\hat{m}_i}{n_i}} \tag{1}$$

where, θ_i is the EBE for municipality i, $\hat{\theta}_i$ is the number of cases to person-years at risk (n) ratio in municipality i. $\hat{m}_i$ and $\hat{a}_i$ are the prior mean and variance of relative risk, respectively, calculated over municipalities adjacent to i.

The estimation of person-years at risk n_i in equation (1) was based on demographic data per municipality from official data sources (Belgian Federal Government, 2010; European Commission - Eurostat, 2011) that were adjusted according to the breakdown of officially reported cases per age and

sex class (Ducoffre, 2010). In order to visualize the temporal variations of risk $\hat{\theta}_i$ values were calculated at a time step of 2 years.

3.2. Spatial correlation

Assessing the spatial correlation between LB and NE EBE is a first step in exploring connections in the infection mechanisms of both diseases. It is particularly interesting to assess whether high/low EBE values for one disease in a certain area correspond to high/low EBE values of the other disease. In this respect a bivariate Moran scatterplot, as proposed by Anselin et al. (2002), can provide valuable insight. The scatterplot was built by plotting the standardized EBE values of one disease against the standardized spatially lagged EBE values of the second disease.

4. Results

The calculation of EBE values at a biannual time step allowed the visualization of changes in magnitude of infection risk and trends in spatial expansion of changing risk conditions. Figure 3 presents a sequence of maps that show that spatial expansion is a common aspect for both diseases. The expansion of high NE EBE values seems to depart from the southwest where the infection risk remained high throughout the period.

As for LB, the maps in Figure 3 show a continuous expansion of the area in risk in the north-east. The increase in EBE in the municipalities at the east side of Brussels region is remarkable too. Also for southern Belgium, a spatial expansion of LB risk has been observed where EBE values have gradually increased towards the border with the Luxembourg. The Franco-Belgian border, the area with the highest NE risk of the country, has also exhibited high LB EBE values throughout the period.

The maps in Figure 3 show that southern and northeastern Belgium were the most dynamic areas in terms of increase and expansion of infection risk. This dynamism is not always geographically coincident for both diseases. Figure 4 shows bivariate Moran scatterplots that relate standardized NE and spatially lagged LB EBE values in the north-east and south. These plots show that NE and LB correlate negatively in a great part of northeastern Belgium whereas the opposite occurs in southern Belgium. This suggests the existence of elements in the landscape configuration in southern Belgium that are common favourable factors for the spread of both NE and LB. The negative spatial correlation in northern Belgium points at the presence of determinants for LB spread that do not translate into significant NE occurrence.
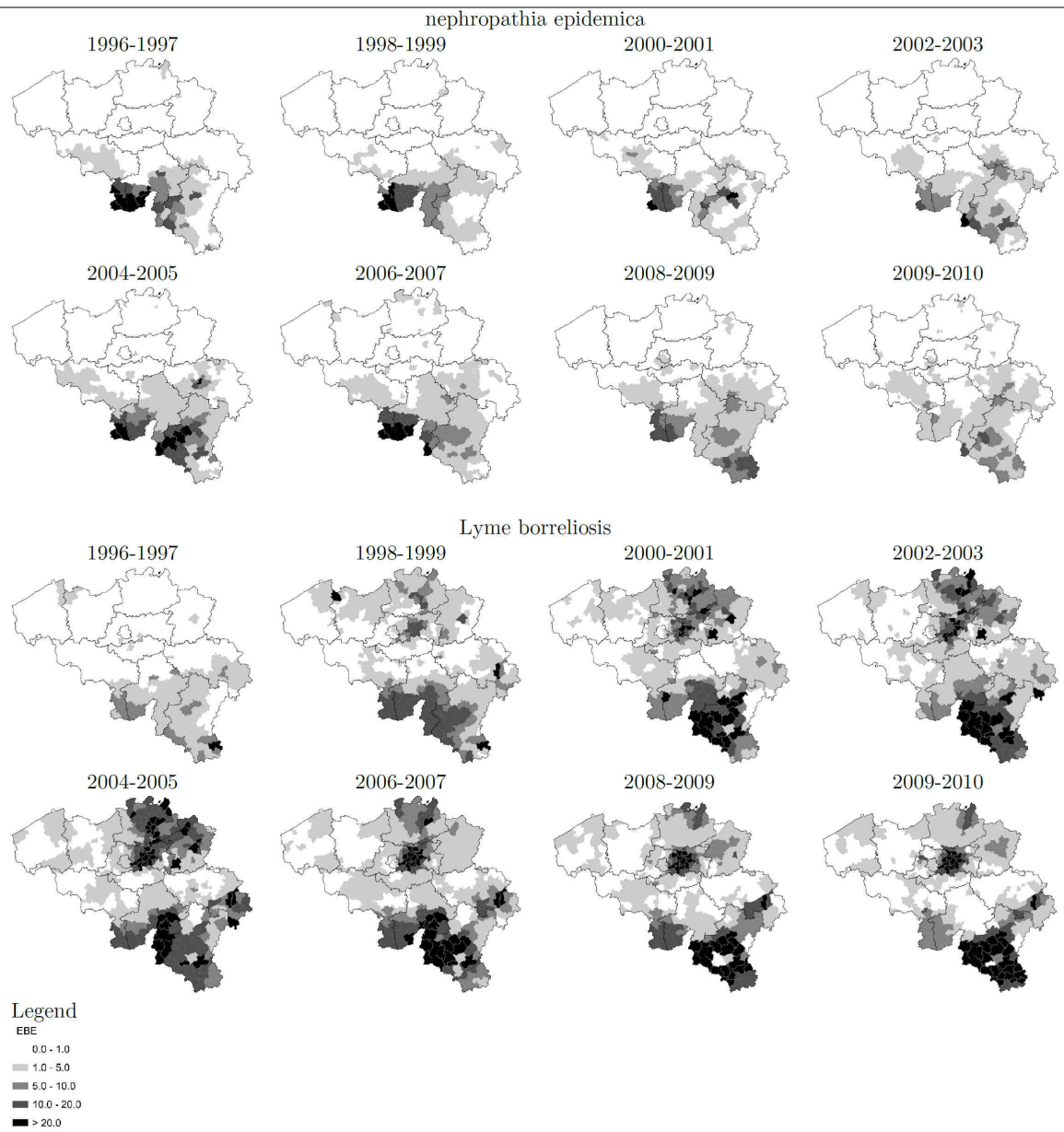
nephropathia epidemica

1996-1997	1998-1999	2000-2001	2002-2003

2004-2005	2006-2007	2008-2009	2009-2010

Lyme borreliosis

1996-1997	1998-1999	2000-2001	2002-2003

2004-2005	2006-2007	2008-2009	2009-2010

Legend

EBE
- 0.0 - 1.0
- 1.0 - 5.0
- 5.0 - 10.0
- 10.0 - 20.0
- > 20.0

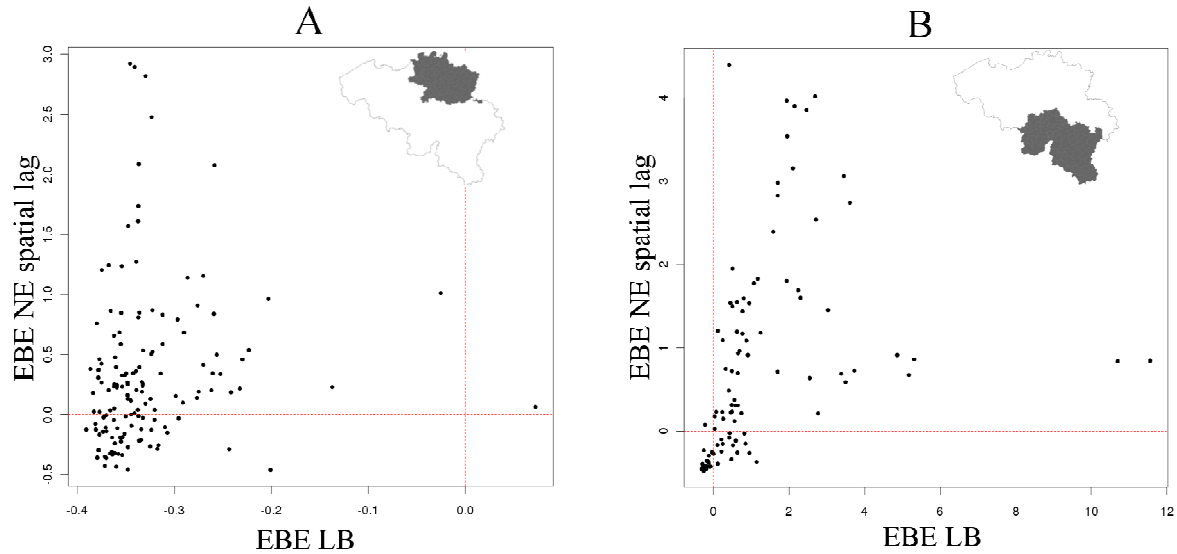**Figure 3.** EBE values with a bi-annual time step for NE and LB in Belgium for the period 1996-2010

Figure 4. Bivariate Moran scatterplots for NE and spatially lagged LB risk estimator (1996-2010) at municipal scale in northeastern (A) and southern (B) Belgium

4. Discussion

Interesting parallels can be highlighted regarding the temporal and spatial behaviour of NE and LB risk estimator. Firstly, the infection risk for both diseases has expanded in a relatively short period. This denotes a boosting in the infection mechanisms and is coincident in time for both diseases. Although an increase in risk could be noticed for both diseases, interannual variations and differences in spatial spread pattern are the effect of the disease specific factors governing risk. On one hand NE incidence depends on bank voles population which is greatly influenced by cyclic masting of beech (*Fagus sylvatica*) and oak (*Quercus sp.*) trees (Clement et al., 2009). On the other hand, since the set of organisms enabled to host *B.burgdorferi* is not restricted to rodents, infected ticks spread via other organisms as well (Lindgren and Jaenson, 2006) and the vegetation-related conditions affecting LB incidence is larger and more complex. Recent literature ascribes the rise in NE cases to climate-induced changes in vegetation. Specifically, related to increase in mast production in broad-leaved trees (Clement et al., 2010, 2009) and phenological changes that alters the conditions for rodents to breed (Barrios et al., 2010). The latter aspect, and particularly the length of vegetation growing season, is known to increase the period of tick activity and to enlarge the proportion of the tick population that hibernates in an advanced developmental stage (Lindgren and Jaenson, 2006). Besides the effect of vegetation dynamics on vectors populations and on pathogens prevalence, changes in vegetation and climatic conditions alter human behaviour and thus, exposure to infection (Barrios et al.,2010; Lindgren and Jaenson, 2006).

The visual examination of the forest maps in Figure 1 suggests correspondence between landscape configuration and spatial distribution of risk. These maps show, for instance, that a prominent landscape attribute in the south is the presence of broad-leaved and/or mixed forests. The forests in the north-east are scarce and fragmented and the existence of an important LB risk zone here is an indicator of the wider spectrum of habitat conditions that favour ticks as compared to bank voles. This preliminary evidence as well as previous studies referring to the connections between landscape and NE/LB spread (Lambin et al., 2010; Brownstein et al., 2005) motivated on-going research aiming at exploring numerical relationships between landscape attributes and NE/LB infection risk.

5. Conclusions

This study revealed that the increase in NE and LB cases in Belgium ocurred in the form of both, *(i.)* more cases in known infection foci (the Franco-Belgian border); and, *(ii.)* the geographical expansion of infection risk.

The spatial expansion of NE appeared to follow a west-east direction in the south in line with the distribution of broad-leaved forest. The risk values seemed to diminish as the mixed forest becomes the dominant forest type. Southern Belgium experienced also a remarkable increase in LB infection risk. The expansion was generalized in the south, with remarkable high EBE values in the vicinity of the Franco-Belgian border. A significant rise of infection risk was coincident in this area for both diseases. Northeastern Belgium was another important expansion zone for LB.

6. References

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8. Biography

J. M. Barrios does research at the Katholieke Universiteit Leuven on remote sensing and spatial analysis applications for epidemiology. He has a particular interest for open source tools for addressing spatial analysis problems.