

**SOCIAL AND ENVIRONMENTAL DETERMINANTS
OF CHANGING DISTRIBUTION AND INCIDENCE
OF TICK-BORNE ENCEPHALITIS IN WESTERN
EUROPE**

THESIS SUBMITTED FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY AT THE UNIVERSITY OF OXFORD

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Michaelmas Term 2012

Social and Environmental Determinants of Changing Distribution and Incidence of Tick-Borne Encephalitis in Western Europe

Thesis Submitted for the Degree of Doctor of Philosophy

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ABSTRACT

In Western Europe the incidence of tick-borne encephalitis (TBE) has increased over the last 30 years, coupled with changes in distribution. Modifications in the TBE enzootic cycle, through a combination of changes in temperature, vertebrate abundance and habitat suitability may have increased the risk of TBE in recent years. In Switzerland, analysis using satellite-derived climate data demonstrated that the environment of areas with TBE since the 1980s and areas that recently became endemic for TBE have become more similar between 2001 and 2009. This was coupled with an increase in April, May and June temperature, which could have affected the tick population and/or human exposure to ticks. Deer and boar abundance also changed in some cantons. In Germany, spatio-temporal modelling demonstrated the importance of temperature, vertebrate abundance and unemployment in the incidence and distribution of TBE between 2001 and 2009. Changes in TBE reporting, April, May and June temperature, vertebrate abundance and pesticide use may have contributed to increases in TBE in 1992 and 2001.

Human exposure patterns, however, appear to be as important as the enzootic cycle in shaping the incidence of TBE, not only in determining the overall trend but also in interacting with the weekly, seasonal and yearly patterns of tick hazard to give the observed incidence. In Switzerland, in weeks with warm, sunny weather, human exposure to ticks is promoted and short-term increases in tick bites are seen. Human outdoor activity also shifts the seasonal pattern of tick bites, when compared with tick questing. There was no apparent increase in time spent in outdoor activities between the 1990s and

2000s in Italy, Germany and Austria, but survey data demonstrated that walking and hiking were already popular activities across Europe by the 1990s. The popularity of mushroom and berry foraging as a source of income in Latvia, Lithuania and Poland, coupled with the expense of vaccination, provide an inverse link between economic wellbeing and TBE risk. Correspondingly, in 2009, the economic recession was associated with an increase with TBE in these three countries.

ACKNOWLEDGEMENTS

First, I would like to thank my supervisors Professor Sarah Randolph and Professor David Rogers for the opportunity to undertake my doctorate, and the continuing support, advice and assistance they have provided me with over the last three years.

I would also like to thank the other members of the Oxford Tick Research Group, Jenny Taylor and Andy Dobson, for useful discussions. Thanks are extended to the members of the Spatial Ecology and Epidemiology Group, including Dr. Luigi Sedda, Dr. David Morley, Nick Golding and David Benz for their friendship, support and advice over many tea breaks.

I would like to thank Ekkehardt Altpeter, at the Swiss Federal Office of Public Health for providing me with the tick bite data collected in Switzerland, HansPeter Zimmerman, at the Swiss Federal Office of Public Health, for access to the Swiss postcoded tick-borne encephalitis case dataset and Norbert Neuwirth, from the Austrian Institute for Family Studies, for the Austrian 2009 time-use survey data. I would also like to thank Kimberly Fisher of the Centre for Time Use Research at the University of Oxford, for access to the Multinational Time Use Survey data.

I would like to express my thanks to my family for their continued support and encouragement, specifically to Mum, Dad, Bernie, Kate, Ben and Louise. Thanks go also to my close friends, including Maggie Frost, Matt Nicholls and Holly Marsh. Specific thanks go to Pete Buckley, who has been an incredible source of support, time and patience; I genuinely couldn't have finished this without him.

Lastly, I would like to thank the UK Natural Environment Research Council for the funding to undertake this research.

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CHAPTER 1. INTRODUCTION

1.1. The importance of tick-borne encephalitis

Tick-borne encephalitis (TBE) is one of the most significant vector-borne diseases of humans in Europe. TBE is endemic in two large regions of Europe: (1) North-Eastern Europe including Latvia, Lithuania, Estonia, North East Poland and Russia; and (2) Central Europe including the Czech Republic, Southern Germany, Northern Switzerland, Austria, Slovenia and Western Hungary, Slovakia and parts of the Balkans and France. The number of cases has risen sharply in the last twenty years, with an average 1,450 cases from 1976-1989, rising to around 3,000 cases every year between 1990 and 2007 in mainland Europe (Suss, 2008). The rate of increase has been variable between countries; for instance, in Central and Eastern European countries the number of cases increased between two and thirty fold between 1992 and 1993, whereas in Germany, Switzerland and Italy the increase has been more gradual, and in Sweden and Finland two step increases occurred in 1984 and 2000 (Sumilo et al., 2008b), followed by on-going annual increases.

Investigations into TBE can shed light on increases in a number of other tick-borne diseases including Lyme borrelioses, ehrlichioses and babesioses (Randolph, 2004a). The study of TBE benefits from high quality data because it is a notifiable disease in 16 countries across Europe (Mantke et al., 2008) and has been reported for 30 years in many countries. However, this, as with all data, should be treated with caution as the case definition and diagnostic tests utilised show some variation across Europe (Mantke et al., 2008). Even so, temporal trends within any one country, but not relative incidence between countries, are indicated by the index of reported cases.

1.2. Tick-borne encephalitis

TBE was first recognised as a disease by Schneider in 1931 and the causative agent, tick-borne encephalitis virus (TBEV), identified soon after by Zilber working in Irkutsk,

Siberia in 1937 (Charrel et al., 2004). TBEV is a member of the family *Flaviviridae* and genus *Flavivirus* (Dumpis et al., 1999). Other members of the *Flaviviridae* include Omsk hemorrhagic fever, Langat virus, Alkhurma hemorrhagic fever virus, Kyasanur Forest disease virus, Powassan virus and Louping ill virus (Mansfield et al., 2009).

TBE can be contracted either: (1) via a bite from an infected tick; or (2) through consuming raw milk products from infected livestock, usually goats (Dumpis et al., 1999). Once infected, between 70% and 98% of people are thought to show no symptoms (Dumpis et al., 1999). In symptomatic patients, flu-like symptoms including fever, headache, joint and back pain, nausea and vomiting develop (Gunther et al., 1997; Kaiser, 1999) 7-14 days after the initial bite, and last 2-7 days (Dumpis et al., 1999). One third of patients with first stage symptoms then progress to the second stage of disease (Dumpis et al. 1999). Of these, around 75% of cases experience an asymptomatic period lasting c. 8 days before the onset of the second stage (Haglund and Gunther, 2003). The main syndromes of the second stage are febrile headache, meningoencephalitis, meningomyeloencephalitis and most commonly, aseptic meningitis (Dumpis et al., 1999). The fatality rate from TBE in Europe is around 1% (Charrel et al., 2004).

Following infection, a significant proportion of those infected suffer post-encephalitic syndrome, which is characterised by the development of a variety of chronic symptoms including headache, reduced stress tolerance, impaired ability to memorize, disorders of balance and coordination, hearing loss, tremor and chronic fatigue (Dumpis et al., 1999). TBE post-encephalitic syndrome was detectable in 80% of patients at 6 weeks and in 40% of patients at 1 year (Gunther et al., 1997). Using the same methods, 46% of patients were observed to have post-encephalitic symptoms at 1 year in Lithuania (Mickiene et al., 2002). In Germany, only 27% of patients retained symptoms at 3 months (Kaiser, 1999), but Haglund and Gunther (2003) suggest that the definitions used underestimate cognitive dysfunction and overestimate paretic symptoms.

Treatment of TBE is supportive only and involves the usage of aspirin, paracetamol and other non-steroidal anti-inflammatory drugs, and in serious cases, corticosteroids (Dumpis et al., 1999). Vaccination against TBE is available and there are two currently produced: (1) FSME-IMMUN (Baxter Vaccine AG, Vienna, Austria); and (2) Encepur, (Novartis, Marburg, Germany) (Dumpis et al., 1999). The vaccination protocol consists of two doses given a month apart followed by a further dose one year later. Booster vaccinations should be taken every 3-5 years (Kunz, 2003). The rate of protection following vaccination is 96-98%, and possibly as high as 99% (Kunz, 2003; Heinz et al., 2007).

In 1981 a mass vaccination programme was initiated in Austria, which has subsequently led to significant decreases in TBE case numbers, with between 294 and 677 cases per annum during 1975-81, dropping to 89-300 cases p.a. during 1985-91, and 41-178 cases p.a. since then. Vaccination coverage in 2001 was 86% across the country and as high as 90% in high-risk areas (Kunz, 2003). In 2006, vaccination was at 88% in Austria (Kunze, 2007). It is notable that the incidence of Lyme borreliosis in Austria is the highest in Europe, suggesting that without this level of TBE vaccination the number of cases could be significantly higher (World Health Organisation, 2004). Vaccination programmes are also active in Germany, Switzerland, Hungary, Slovenia, Russia, Latvia and Finland (Mantke et al., 2008); however, vaccination levels rarely exceed around 15% (Kunze, 2007). Exceptions to this are Latvia, where vaccination rates were 38% in 2006 (Kunze, 2007), probably due to a concerted campaign targeted initially at children in 1998, and in some areas of Southern Germany, e.g. Dingolfing and Passau in Bavaria, where vaccination coverage is 70% (Suss, 2009).

1.3. Ticks as vectors for TBE

There are three sub-types of TBEV: Western, Siberian and Far-Eastern TBEV (Ecker et al., 1999; Hayasaka et al., 2001). Western TBEV is carried and transmitted by the tick

Ixodes ricinus, whilst Siberian and Far-Eastern TBEV are carried by *Ixodes persulcatus* ticks (Charrel et al., 2004). The vector species for each subtype is crucial in determining the distribution of the disease; *I. persulcatus* is distributed in Eastern Europe, Russia and Asia whereas *I. ricinus* is distributed in Europe and European Russia (Lindquist and Vapalahti, 2008). The two tick species overlap in distribution in Estonia, Latvia, and Finland, and the three sub-types of TBEV are found to co-circulate there (Lundkvist et al., 2001; Golovljova et al., 2004; Jaaskelainen et al., 2006). This work will concentrate on the distribution and incidence of TBE in Europe, and so focuses predominantly on Western TBEV and *I. ricinus*.

Ixodid ticks, along with Argasid and soft ticks, are members of the Arachnida, subclass Acari. Ixodid ticks (hereafter, 'ticks') pass through three life stages; progression is from larvae to nymph to adult before mating and laying eggs (Fig. 1.1). Ticks are haematophagous and a single blood meal is needed for progression from one stage to the next and for the production of eggs in adult females. Ticks usually feed once a year and the average lifespan is therefore three years but can range from two to six (Randolph, 2004b).

Abiotic factors are important to the *I. ricinus* population size and the pattern of tick questing. For instance, the rate of development of ticks depends on temperature and the rate of mortality on the saturation deficit, which is a measure of the drying capability of the environment (Randolph, 2004b). Threshold temperatures are needed for tick questing, which are thought to be a weekly mean daily maximum temperature of c.7°C for nymphs and adults and c.10°C for larvae (Perret et al., 2000; Randolph, 2004b). As a result, tick questing activity is seasonal in European temperate climates with peak questing months in May to September (Lindquist and Vapalahti, 2008). Another key determinant of tick questing is humidity. Younger life stages suffer from moisture stress more so than older stages, due to a higher surface area to volume ratio, higher weight-specific metabolic rate

and limited energy reserves (Randolph and Storey, 1999). Moisture stress is thought to be the reason that ticks of different life stages ascend to quest for hosts at different heights. Juvenile ticks quest nearer to the ground and can attach and feed on hosts of all sizes, from small rodents to red deer. Nymphs and adults ascend to successively higher levels to quest and so usually attach to larger host species; adults rarely attach to hosts smaller than hares and roe deer (Gigon, 1985; Mejlun and Jaenson, 1997). Moisture stress, however, can drive larvae and nymphs to quest lower, thereby increasing their probability of attachment to smaller rodents (Randolph and Storey, 1999).

1.4. Transmission of TBEV between ticks

TBEV can be transmitted between an adult *I. ricinus* and its offspring transovarially (Fig. 1.1). The low probability of this route, however, makes it insufficient to support persistent cycles (Randolph, 2004b). The main transmission route requires a tick to feed on an infected competent host animal, retain the infection during development and moulting, and pass the infection back to a susceptible host during feeding by the next stage. Not all tick hosts are competent to support this route of TBEV transmission. Furthermore, the development of viraemia of a certain ‘threshold’ level is not necessary for transmission; instead TBEV may be transmitted from an infected tick to an uninfected one in the absence of a systemic infection, so-called non-viraemic transmission. The most important natural transmission hosts are rodents of the genus *Apodemus* and *Myodes*, of which *Apodemus* mice appear to be the most efficient (Labuda et al., 1993b; Labuda et al., 1997).

A wide range of other hosts, for example deer and other large mammals, are not competent for disease transmission but are the main source of food for adult female ticks, and can thus boost the overall tick population. An abundance of hosts may, however, act to reduce the number of ticks actively questing as they provide an easily accessible food source. For instance, if the abundance of deer is decreased, the number of questing ticks

may initially increase as questing ticks are not removed quickly from the vegetation, before the tick population declines (Rand et al., 2004).

TBEV incompetent hosts, such as deer, may also act to dilute TBEV prevalence by providing alternative food sources than competent hosts (Cagnacci et al., 2012), although the ability of such hosts to boost the tick population probably outweighs this in many situations (Randolph and Dobson, 2012). The role of vertebrate hosts in influencing the number of ticks and the prevalence of TBEV is therefore a complex one.

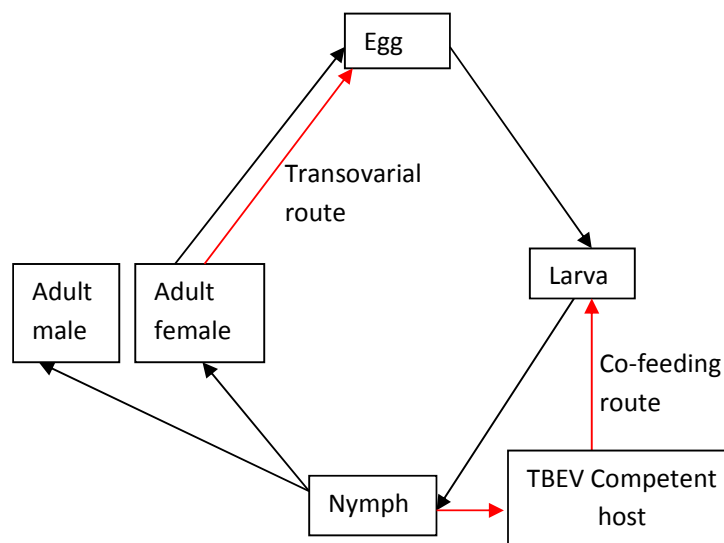


Figure 1.1. The lifecycle of *I. ricinus* ticks and TBEV transmission routes. Black arrows indicate development between tick life stages and red arrows indicate TBEV transmission routes.

Persistent transmission relies on feeding by ticks of different life stages on the same hosts, so called co-feeding, which is facilitated by aggregated tick distributions in time and space. Systemic viraemia lasts for only about 2-3 days in hosts (Kozuch et al., 1981), therefore for transmission via either the systemic or non-systemic viraemic route, feeding of uninfected ticks must occur within a few days of infected ticks. Feeding of ticks on the same host can transmit TBEV without systemic infection of the host, if ticks feed on the same area of the host (Labuda et al., 1993a; Randolph et al., 1996). In the rodent, TBEV enters the Langerhans cells at the site of an infected bite (Labuda et al., 1996). The

Langerhans cells then migrate to the lymph nodes where virus replication takes part and importantly, they are attracted to the sites of uninfected co-feeding ticks (Labuda and Randolph, 1999).

It is co-feeding between nymphs and larvae that is thought to be key for the amplification of TBEV in ticks as the relatively few infected nymphs transmit to the much more abundant larvae (Randolph, 2004b). Nymphs and larvae require different spring temperatures for questing, with nymphs requiring c.7°C to quest whereas larvae require c.10°C (Perret et al., 2000; Randolph, 2004b). Co-feeding is therefore promoted when there is least delay between spring temperatures reaching 7°C and 10°C (i.e. a rapid rate of spring warming) and questing by both stages is most synchronous. It is only in certain regions of Europe that this temperature profile is seen and this appears to account for the focal distribution of TBE within the range of *I. ricinus* (Randolph et al., 2000).

1.5. TBE as a zoonosis

TBE, like all zoonotic diseases, can be analysed by comparing it to an iceberg; the majority of transmission is within the enzootic cycle and the disease in humans is only the tip we are aware of (Randolph and Sumilo, 2007). The size of the enzootic cycle (the bulk of the iceberg) is a result of factors that affect the infected tick population. The size of the more easily visible tip above the water is controlled by the contact between humans and ticks; increased contact allows more transmission of TBEV from ticks to humans. Factors that influence TBE epidemiology can broadly be split into those that affect the size of the enzootic cycle and those that affect the amount of contact between ticks and humans.

1.6. Factors that influence the density of infected ticks

Within a TBE focus, it is the number of ticks rather than variation in the prevalence of infection in ticks that is thought to be the main driver of infected tick numbers (Ostfeld et al., 2006). The recorded prevalence of TBEV is relatively low in ticks: for instance in

Germany it is 0.38% in nymphs and 1.17% in adults (Suss et al., 2004); in Italy it is 0% in nymphs and 1.2% in adults (Carpi et al., 2009); and in the Czech Republic 0.4% in nymphs and 2.6% in adult females (Danielova et al., 2002). This may be an underestimate, however, because the prevalence is higher in ticks tested after a blood meal than unfed ticks (Suss et al., 2006), perhaps as a result of virus replication in feeding ticks (Belova et al., 2012). Factors that could influence the number of infected ticks include the number of vertebrate hosts, habitat availability and suitability e.g. land cover and pesticide use, the climate and weather.

Vertebrate hosts are important in providing a food source for ticks. Increasing numbers of ticks were associated with high densities of roe deer in both time and space in Denmark (Jensen and Frandsen, 2000; Jensen et al., 2000). Similarly, in Italy, TBE emergence was associated with abundance of roe deer, as well as forest favouring small rodent hosts of ticks (although rodents are less limited by habitat than deer) (Rizzoli et al., 2009). This also highlights the importance of land cover in the incidence of TBE, via its effect on the number of vertebrate hosts, as well as providing a favourable microclimate for ticks. Elements of land cover, such as the percentage of land that is forest, were important in predicting TBE in Latvia, as was land access, such as the percentage of forest owned by the State, which affects human outdoor activities (Vanwambeke et al., 2010). Habitat must be both available and suitable for tick proliferation and the use of products such as pesticides may make the environment unsuitable for ticks. Pesticide usage declined in Central and Eastern Europe from the mid-1980s to 2000, coincident with increases in TBE in these countries (Sumilo et al., 2008b).

Climate change has been suggested as a potential factor in the increase in TBE cases as climate can affect the tick, the host, the virus and the human. Northerly shifts in the limits of *I. ricinus* in Sweden (Lindgren et al., 2000) and increases in the altitudinal extent of *I. ricinus* in the Czech Republic (Materna et al., 2005) have been attributed to a warmer

climate. The altitude of TBE cases has increased in Slovakia, the Czech Republic and Austria (Zeman and Benes, 2004; Holzmann et al., 2009; Lukan et al., 2010). Statistical modelling of TBE in Europe using climate predictions until 2050 predicts there will be a shift to higher altitude and latitude but also a possible contraction from many European countries (Randolph and Rogers, 2000).

If changes in TBE incidence are purely a result of climate, concomitant changes in TBE and climate in time and space should be observed. In the Baltic States the heterogeneous trends in TBE incidence in different counties were not matched by similar trends in climate, and as such could not have been caused by changing climate alone (Sumilo et al., 2007). Similarly, in the Czech Republic, fluctuations in TBE case numbers observed on a fine scale are incompatible with temperature changes (Zeman et al., 2010).

1.7. The role of human behaviour

In 2006, TBE case numbers surpassed the average levels for the past decade by 79-183% in Switzerland, Germany, Slovenia and Czech Republic (Randolph et al., 2008). In Poland, Lithuania, Slovakia, Italy and France TBE numbers were also high, but did not exceed that seen in some previous years. Cold weather was seen across Europe in early 2006, followed by hot weather from the summer of 2006 into early 2007 (Randolph et al., 2008). Tick abundance data from several sites in each of those countries showed no consistent increase in the tick population in response to the unusual weather. Qualitative data instead highlighted the role of human response to unusual weather in causing the spike in TBE. In Switzerland, Germany, Slovenia and Czech Republic hot weather is thought to have promoted recreation and therefore contact with ticks. Smaller increases in Poland and Lithuania may have been a result of weather favourable for mushroom growth and collection, which provides an important source of income.

Any increase in human population or in human mobility for recreational, cultural or socioeconomic purposes may be relevant to the emergence of disease (Vorou et al., 2007).

For instance, economic vulnerability, indicated by the percentage of household expenditure spent on food, shows a strong correlation to the degree of the upsurge in TBE levels in the early 1990s following the break-up of the Soviet Union (Sumilo et al., 2008b).

The impact of humans in the TBE system is multifactorial; humans can influence many of the determinant factors in the enzootic cycle such as climate change, land use change and the number of vertebrates, as well as influencing the contact rate between humans and the enzootic cycle through changes in behaviour.

1.8. A framework of factors and applying this to Europe

Dana Sumilo increased the understanding of the factors that influence TBE in the Baltic States following the fall of the Soviet Union in the early 1990s (Sumilo et al., 2007; Sumilo et al., 2008b; Sumilo et al., 2009). This work suggests that no single factor can explain the dramatic increases in TBE experienced, and instead a ‘nexus of synergistic effects’ is invoked. Reform moved agriculture from large-scale public farms to smaller scale private farming. Reduced agriculture and industry caused large-scale unemployment, leading to an increasingly subsistence way of life for many. Abandonment of large swaths of agricultural land allowed the natural vegetation to grow which is an important habitat for ticks and their rodent hosts (Pupila and Bergmanis, 2006). Pesticide use and pollution decreased significantly. Forest produce, such as wood, mushrooms and berries provided food and income but in turn increased the likelihood of contact with ticks. A combination of all these changes, and more, in the early 1990s acted synergistically to cause the drastic increases in TBE cases observed.

While the increases in TBE incidence in the Baltic States and Poland following the fall of the Soviet Union were highly unusual, they allowed us insight into the various factors that contribute to change in TBE. The aim of this work is to extend this framework to apply not only to the Central and Eastern Europe, but also to the Western European TBE endemic area.

1.9. Thesis structure

The starting point of the thesis will be to examine the epidemiological situation in Switzerland and Germany (Chapter 2 and 3). In Switzerland climate change will be examined as a potential contributing factor to changes in incidence and distribution of TBE since 1984. A combined spatial and temporal analysis will be utilised, with satellite data giving climate information in high spatial resolution and meteorological stations providing long-term climate information. Changes in vertebrate population will also be assessed. In Germany, spatio-temporal analyses will be used to identify the factors important in predicting TBE cases in space and time. These factors will be subjected to temporal analysis to measure the extent to which they could have contributed to changes in case numbers between 1975 and 2010.

The remaining elements of the thesis predominantly examine the role of human behaviour in shaping TBE incidence and distribution. The balance between human behaviour and tick activity in shaping the seasonal pattern of human exposure to ticks will be examined using reports of tick bites from across Switzerland between 2008 and 2010 (Chapter 4). Variation in weekly tick bites will be modelled as a result of the weather conditions, which will indicate whether human or tick activity is most important in the weeks of unusually high tick bites.

The economic recession provided an unfortunate natural experiment that allows an examination of the potential impact of human socioeconomic factors on TBE incidence (Chapter 5). An ecological analysis across the countries of Europe will be used to test the hypothesis that changes in economic wellbeing can cause shifts in the number of TBE cases. A change in outdoor activity patterns, due to reduced economic wellbeing, is one factor highlighted in Chapter 5 as linking the recession and TBE incidence. The role of human behaviour in the increasing incidence of TBE across Western Europe will be examined using time-use data from Austria, Germany and Italy (Chapter 6). Outdoor

behaviour patterns between c.1990 and c.2000 will be examined for potential trends.

Differences in outdoor recreational patterns across demographic and socioeconomic groups will be assessed to understand the risk factors for TBE. More broadly, the first quantitative and qualitative review of outdoor activity patterns across Europe will be presented (Chapter 7), along with the legislation and social tradition that shapes these patterns. The importance of external factors such as weather and socioeconomic factors in outdoor activity will be examined.

Finally, Chapter 8 presents my conclusions about the causes of changes in TBE distribution and incidence in Western Europe.

CHAPTER 2. HAVE CHANGES IN THE ENVIRONMENT IN SWITZERLAND CAUSED THE EXPANSION IN THE SPATIAL DISTRIBUTION OF TBE CASES?

2.1. Introduction

Temperature and humidity are important factors in the survival and questing of *Ixodes ricinus* ticks (Randolph, 2004b; Dobson et al., 2011a). While climate change is therefore an attractive and convenient explanation of increases in TBE incidence, it could actually have a negative or positive effect on TBE incidence (Randolph, 2004a). Changes in ticks and tick-borne diseases since the 1990s at the altitudinal and latitudinal extremes of the distribution in Europe have been attributed to changes in climate. A northward expansion of ticks in Sweden was associated with milder winters (Lindgren et al., 2000). In Slovakia and the Czech Republic, an increase in the maximum altitude of TBE was associated with a trend for increasing temperature (Zeman and Benes, 2004; Lukan et al., 2010). However, climate is not the only potential limiting factor to the distribution of TBE. Density of deer were correlated with the emergence of TBE in districts of north Italy (Rizzoli et al., 2009), and in Denmark the spatial distribution of ticks was influenced by the abundance of roe deer (Jensen et al., 2000). Other large mammals, such as boar, are potential hosts to ticks and their abundance has increased in Sweden concurrent with changes in TBE incidence (Jaenson et al., 2012b).

The number of TBE cases has increased in Switzerland since the early 1990s (Randolph, 2001). Additionally, new areas associated with a risk of TBE infection have been identified in the western part of the country (Suss, 2008). This chapter will use satellite-derived variables to examine whether climate change is a causal factor in changes in the distribution and incidence of TBE in Switzerland. The variables important to the distribution of TBE in Switzerland will be assessed using satellite-derived climate data. A

change detection method will be used to identify if there has been a significant change between 2001 and 2009 in these environmental variables in areas newly endemic to TBE. Change detection methods use multi-temporal datasets to quantify the change in a phenomenon through time (Lu et al., 2004) and temporal trajectory analysis, such as that used here, have been used to detect changes in vegetation through time (Myneni et al., 1997; Kawabata et al., 2001). The environmental distance between newly endemic TBE districts and districts that have had reported cases of TBE since the 1980s will be measured and tracked between 2001 and 2009. This will show whether the environments of these two groups have become more similar.

These methods will be supplemented with temporal analysis of meteorological station data to examine changes in weather over the longer 1984 to 2009 period. Temporal analysis will also be used to identify changes in the abundance of red and roe deer and boar coincident with changes in TBE incidence through time. The temporal method uses six cantons of Switzerland which summarise the Swiss TBE situation.

2.2. Materials and Methods

2.2.1. TBE data

Over the period from 1984 to 2006, 1,784 cases of TBE were reported to the Swiss Federal Office of Public Health, of which 835 cases had their postcode of residence recorded (Table 2.1). The coverage of these data varied by canton and year (Table 2.2). The highest percentage of annual TBE cases for which a postcode was recorded was achieved in 1984 (87%). While this percentage has since decreased, since 1988 it has remained between 30 and 55 per cent. Cantons with high TBE case numbers tended to have a large proportion of them recorded to postcodes. For example over 40% of cases were recorded to postcodes in Aargau, Bern, Schaffhausen, St.Gallen, Thurgau and Zurich, each of which has a large number of TBE cases, but zero per cent were recorded to

postcodes in Basel-Stadt, which has only 12 TBE cases in total.

2.2.2. Distribution modelling of TBE in Switzerland

Satellite images taken by the Moderate Resolution Imaging Spectroradiometer (MODIS) satellite were used to predict the distribution of TBE across Switzerland. MODIS imagery has a resolution of 1/120th of a degree, which is about 1km² at the equator, giving a high spatial resolution for analyses. Similar to a photograph, the resolution dictates that images are provided as a surface of pixels, with each one giving the measurement for an area that is 1/120th of a degree long and wide. MODIS images are available for the daytime Land Surface Temperature (dLST), night-time Land Surface Temperature (nLST), Normalized Difference Vegetation Index (NDVI), Middle Infrared (MIR) and Enhanced Vegetation Index (EVI). MODIS data are available from 2001 to 2010 but to coincide with the TBE postcode data a series from 2001 to 2006 was used.

Table 2.1. Details of data used for analysis, including the years covered, spatial resolution and source.

Dataset	Years	Resolution	Source	Website
TBE	1984-2009	Canton	HansPeter Zimmerman, Swiss Federal Office of Public Health	
Boar & Deer	1984-2009	Canton	Swiss Federal Office for the Environment	http://www.wild.uzh.ch/jagdzt/index.php
Ground-based weather	1984-2009	1 site per canton	Idaweb system from Meteoswiss	http://www.meteoswiss.admin.ch/
TBE	1984-2006	Postcode	HansPeter Zimmerman, Swiss Federal Office of Public Health	
MODIS	2001-2006	1/120th of a degree	NASA	http://modis.gsfc.nasa.gov/index.php
GRUMP	2000	1/120th of a degree	Center for International Earth Science Information Network et al., (2005)	http://sedac.ciesin.columbia.edu/gpw/

Table 2.2. Proportion of cases in each a) canton and b) year which have a recorded postcode of residence.

a)	Canton	%Postcoded (1984-2006)	Number of cases	b)	Year	% Postcoded (All cantons)	Number of cases
	Aargau	56.06	198		1984	86.96	23
	Appenzell I.Rh.	0.00	1		1985	80	10
	Appenzell A.Rh.	0.00	3		1986	56	25
	Baselland	20.00	15		1987	70.83	24
	Basel-Stadt	0.00	12		1988	56.25	32
	Bern	62.99	154		1989	53.85	39
	Fribourg	60.00	30		1990	41.67	24
	Geneva	0.00	2		1991	39.39	33
	Glarus	50.00	2		1992	44.62	65
	Graubünden	59.26	27		1993	50	42
	Jura	0.00	3		1994	41.49	94
	Lucerne	63.22	87		1995	38.33	60
	Neuchâtel	50.00	2		1996	32.79	61
	Nidwalden	64.29	14		1997	45.38	119
	Obwalden	125.00	4		1998	27.27	66
	Schaffhausen	95.12	41		1999	56.03	116
	Schwyz	14.29	7		2000	40.45	89
	Solothurn	32.14	28		2001	46	100
	St.Gallen	56.00	75		2002	37.74	53
	Thurgau	45.50	211		2003	42.98	114
	Ticino	0.00	1		2004	48.89	135
	Uri	83.33	6		2005	50	206
	Valais	0.00	3		2006	51.02	245
	Vaud	62.50	24				
	Zug	54.55	11				
	Zürich	61.57	497				

As images are taken every eight days, MODIS images suffer from serial correlation, therefore data are decomposed into a series of uncorrelated sine curves through temporal Fourier analysis (TFA) (Rogers et al., 1996; Scharlemann et al., 2008). Summary aspects of the sine curves are used for further analysis and include the mean, maximum, minimum, variance, and the phases and amplitudes of the annual, biannual and triannual cycles of variation (Fig. 2.1). A combination of these cycles reconstructs the original data series.

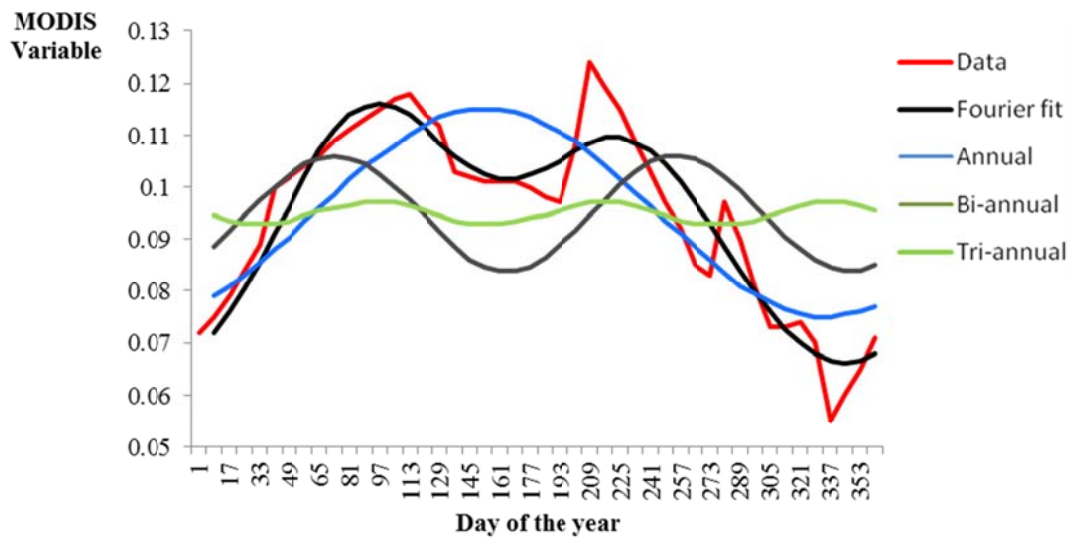


Figure 2.1. Demonstration of how the annual, biannual and triannual cycles combine to produce a Fourier fit for MODIS data.

Non-linear discriminant analysis (NLDA) was used to identify significant MODIS variables in predicting TBE distribution (Rogers, 2006). NLDA was performed using the eRiskMapper program (Morley et al., in prep). Presence of TBE (2001-2006) was used as the dependent variable and temporal Fourier analysed MODIS data, a model of digital elevation (DEM) and human population density known as GRUMP (Center for International Earth Science Information Network et al., 2005) were the independent variables. The NLDA algorithm examines the explanatory variables to identify those that maximise the discrimination between pixels where the disease is present or absent. Discrimination is based upon the Mahalanobis Distance, a co-variance adjusted measure of environmental distance.

As data were provided in a polygon form, presence pixels were selected using a clustering and filtering algorithm using the mean, minimum, maximum, variance and amplitudes of the cycles for MIR, dLST, NDVI and DEM data (McPherson et al., 2006). This algorithm first clusters all pixels from the presence polygons into a large number of groups. Those clusters that contain pixels from a large number of presence polygons are more likely to represent areas of TBE presence and are retained for the next round of

clustering, while small clusters (more likely to represent TBE absence) are discarded. Clustering and filtering continues for a number of rounds, the aim being to reduce as much as possible the total number of pixels, while retaining as many polygons as possible (since the disease occurred in all of them). Initially the number of pixels in all of the polygons totalled 5,197. 150 clusters were created and four rounds of clustering were undertaken, removing 3 per cent of pixels at each round. After clustering, 2,771 pixels were still classed as positive, but only 11 polygons from the initial total of 284 had been lost.

Places of absence of TBE are not specifically recorded in Switzerland, so pseudo-absence points were created that were sufficiently dissimilar to the presence points, providing an environmental comparison for future modelling. Pseudo-absences were selected on the basis of two different measures of ‘distance’: one physical (the Euclidean distance) and one environmental (the Mahalanobis Distance). A minimum distance is set to ensure that pseudo-absence points are not too close to presence points (and hence might have similar environmental conditions) and a maximum distance is set to ensure that such points are also not so different as to provide very little information to the discriminating algorithm (for example, arctic conditions cannot really help to define the distribution limits of a tropical species). Euclidean distances for pseudo-absence points were set to be between 0.01 and 0.30 degrees of latitude/longitude. eRiskMapper calculated the Mahalanobis Distances of all presence points from their local centroid (i.e. the multi-variate mean) and examining these distances suggested that a threshold of ten units should be chosen for the TBE data; thus pseudo-absence points were selected that were at least this distance away from the nearest presence centroid. This combination of both Euclidean and Mahalanobis distances was therefore used to select more than 7,000 pseudo-absence points for the analyses.

The first step of the analysis was to cluster the point data in the training set into three presence and two absence clusters. This ensures that the condition of multi-variate

normality, which is essential for NLDA, is met by the data. Point data were clustered using the mean, minimum, maximum, variance and amplitudes of the cycles for MIR, dLST, NDVI and DEM.

Modelling was carried out using multiple independent subsets ('bootstraps') of the total training set data. Each bootstrap sample consisted of 200 presence and 200 absence points selected at random, with replacement, from the 2,743 presence and 7,140 pseudo-absence points for which full environmental data could be extracted. 100 bootstrap samples were selected and each was used to generate one risk map prediction. Predictor variables were selected by step-wise inclusion, beginning with the variable that maximised the Mahalanobis Distance function, and continuing until a maximum total of ten variables had been selected. The discriminant analytical model arising from the selected variables was applied to the raster imagery of Switzerland to generate a risk map of the posterior probability of TBE presence. The 100 resulting risk maps were averaged to produce a single prediction of TBE risk in Switzerland. Across the 100 bootstraps, the ranks of the selected variables in each case were averaged to give a list of ten variables that had the highest average ranking for predicting TBE.

A map of current endemic areas for TBE in 2010 was available from the Federal Office of Public Health. Output for the predicted TBE risk map (based on the TBE data from 2001 to 2006) was compared with this 2010 map to examine whether any of the areas predicted to be suitable for TBE by the distribution model (but negative for TBE cases from 1984 to 2006) had indeed become TBE-positive between 2006 and 2010.

2.2.3. Change analysis 2001-2009

The appearance of TBE in new areas of Switzerland may have been precipitated by an environmental change causing such areas to be more suitable for TBE enzootic transmission. Those variables found to be significant in predicting TBE from the NLDA were submitted to change analysis which detected if there had been a significant change in

each variable through time. MODIS satellite images for dLST, nLST, NDVI, EVI and MIR were Fourier transformed as pairs of overlapping years from 2001 to 2010 (i.e. 2001/2, 2002/3 etc.). Each MODIS pixel in the Switzerland area was investigated for a change separately. A linear regression was applied for each temporal Fourier variable value against time in years. Significance was established using the appropriate level of Pearson's correlation coefficient corrected for serial correlation effects (i.e. greater than 0.667 (Chatfield, 2003)). A correlation map of Switzerland was created for each variable, in which each pixel had either a value of zero (no significant trend in environmental conditions) or a value of the calculated correlation coefficient (when the trend was significant). The series of correlation maps were overlaid with maps of the postcode locations of new TBE cases (2001-2006) to find if there was a spatial coincidence between significant changes in a particular variable or variables and the emergence of TBE.

2.2.4. Testing for increasing similarity in the environment between newly endemic TBE areas and the 'ancestral' TBE areas, 2001-2009

Postcodes that reported cases of TBE between 1984 and 1990 and predicted to be suitable for TBE by NLDA were classed as 'ancestral' sites (Table 2.3). These sites are still considered to be endemic by the Swiss Federal Office of Public Health. Postcodes with a first recorded case of TBE between 2004 and 2006 were used to create two groups of pixels; newly endemic pixels and out-group pixels for analysis, as follows. Only some pixels in each polygon would be suitable for TBE, as demonstrated when over half were removed by clustering analysis for the NLDA. Those pixels predicted to have TBE by the NLDA were included in the newly endemic class. The remaining pixels, which are thought to be unsuitable for TBE, were considered as the out-group. The newly endemic and out-group pixels should be considered as indicator sites to examine changes in the wider context of Switzerland.

Table 2.3. Three groups of pixels used for environmental similarity analysis

Name	Time when postcode had first reported case of TBE	How pixels were selected
Ancestral	1984-1990	Pixels from postcodes endemic from the 1980s and predicted to be suitable for TBE by NLDA
Newly Endemic	2004-2006	Predicted suitable for TBE by NLDA
Out-group	2004-2006	Not suitable for TBE by NLDA

The average for the MODIS variables selected from the NLDA was calculated for the ancestral pixels, using all nine years' data (hereafter the 'ancestral centroid'). The ancestral centroid is a fixed point in environmental space from which to measure trajectories of change in the environment. The Mahalanobis Distance (hereafter, 'MD') of each ancestral, newly endemic and out-group pixel for each year 2001-2009 to this ancestral centroid was then calculated. The MDs had a non-normal distribution so the logarithmic transformation was applied for analyses (hereafter, 'log(MD)').

The working hypothesis was that the environment in the newly endemic pixels and the ancestral pixels had become more similar. The out-group would be expected to remain too different from ancestral pixels to support TBE.

A general linear model ('GLM'), using R statistical software (R Development Core Team, 2012), was fitted to identify if there had been a statistically significant change in log(MD) in ancestral, newly endemic and out-group pixels between 2001 and 2009. An interaction between the year and TBE status of the pixel was included in the model and would be significant if there had been a different change between the groups. As the value of each pixel in a given year was likely to be correlated with the value in the following year, a model with an autocorrelated variance structure was fitted, using the function 'gls' from the package 'nlme' (Pinheiro et al., 2012). This model was compared with a model with no autocorrelation in the variance structure using an ANOVA.

To give a measure of the similarity of newly endemic or out-group pixels to the ancestral pixels the annual average log(MD) for the ancestral pixels was subtracted from

the log(MD) of each pixel by year, leaving annual anomalies in the log(MD).

2.2.5. Longer term temporal trends

Longer term temporal data were available for weather and vertebrates on a cantonal basis. 83 per cent of the TBE cases in Switzerland are restricted to only six cantons. These cantons are (in order of decreasing numbers of cases, 1984-2009): Zurich, Thurgau, Aargau, Bern, Lucerne and St.Gallen. Weather data were extracted for one site in each of these six cantons: Aadorf for Thurgau, Zurich Fluntern for Zurich, St.Gallen for St.Gallen, Wynau for Bern, Lucerne for Lucerne and Buchs for Aargau. These sites were chosen as they provided the most complete dataset for the relevant years, but are often in urban areas.

The rate of spring warming was calculated by fitting a linear regression to the daily maximum temperature data between February and April, and extracting the coefficient. The average monthly maximum temperature, number of sunny days (with greater than 50 per cent relative sunshine duration, June - September) and the number of rainy days (with precipitation >0.0mm May – September) were also calculated. The number of frosty days (minimum temperature less than 0°C) and total snowfall (measured at 5.40am daily) from October in the previous year to February completed the weather dataset.

Estimates of the combined number of red and roe deer were collected for each canton by the Swiss Federal Office for the Environment and are available from <http://www.wild.uzh.ch/jagdst/index.php>. The standing stock figures were estimated on the basis of expert opinion. Hunting bags for boar, the number of boar killed through other methods (e.g. roadkills) and number of reports of damage to land caused by boar, were also collected from the same website. TBE incidence, weather and vertebrate abundance were regressed against time to detect if there had been a significant trend in these variables between 1984 and 2009.

2.3. Results

2.3.1. The expanding distribution of TBE

The annual number of TBE cases in Switzerland has shown increases since the mid-1980s (Fig. 2.2a, R^2 for the linear trend = 0.64). The highest numbers of cases from 1984 to 2009 were in 2004, 2005 and 2006. The patterns of increase were variable from canton to canton (Fig. 2.2b). In Zurich, which is the canton with the highest number of cases, case numbers rose steadily from 12 in 1984 to 49 in 1994, before plateauing at this level, with a mean from then to 2009 of 37.7 cases ($\pm$ stdev 15.8 cases). Until 1993, the national total number of TBE cases strongly reflects the patterns in Zurich. After 1993 the other cantons' contribution to the number of TBE cases across Switzerland increases. For instance, the number of TBE cases in Aargau, Thurgau and Lucerne increased since the early 1990s and in Bern and St.Gallen began to rise in the latter half of the 1990s.

As well as the increase in the absolute number of cases of TBE in Switzerland, the distribution of TBE has changed throughout this period (Fig. 2.3). Between 1984 and 1991, cases were localised to the central northern region, including Zurich and Schaffhausen (Fig. 2.3a). Cases in Thurgau, Aargau, Lucerne, Bern and St.Gallen were patchy. Between 1992 and 1999, the distribution of TBE expanded within the same cantons, with more cases in Zurich, Thurgau, Aargau, Lucerne and Bern (Fig. 2.3b). This expansion can be considered as 'filling in the gaps' of the distribution, with new cases arising in areas surrounding those where previous TBE cases had been reported. From 2000 the distribution changed again, with cases occurring further west and in the south. There were first reported cases in the cantons Uri, Glarus and Obwalden, which fall further south than the previous distribution of TBE.

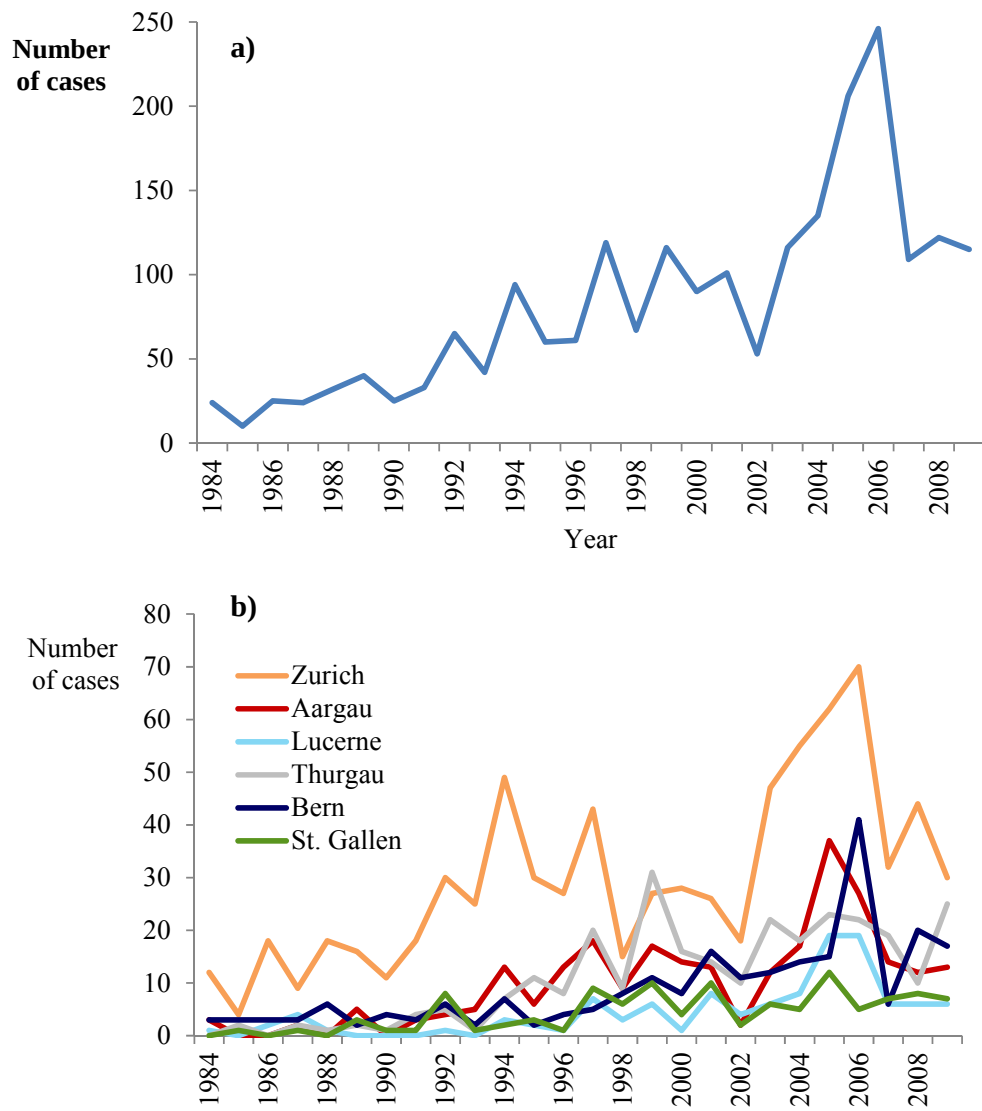


Figure 2.2. Number of TBE cases in a) Switzerland, and b) in 6 of the cantons between 1984 and 2009.

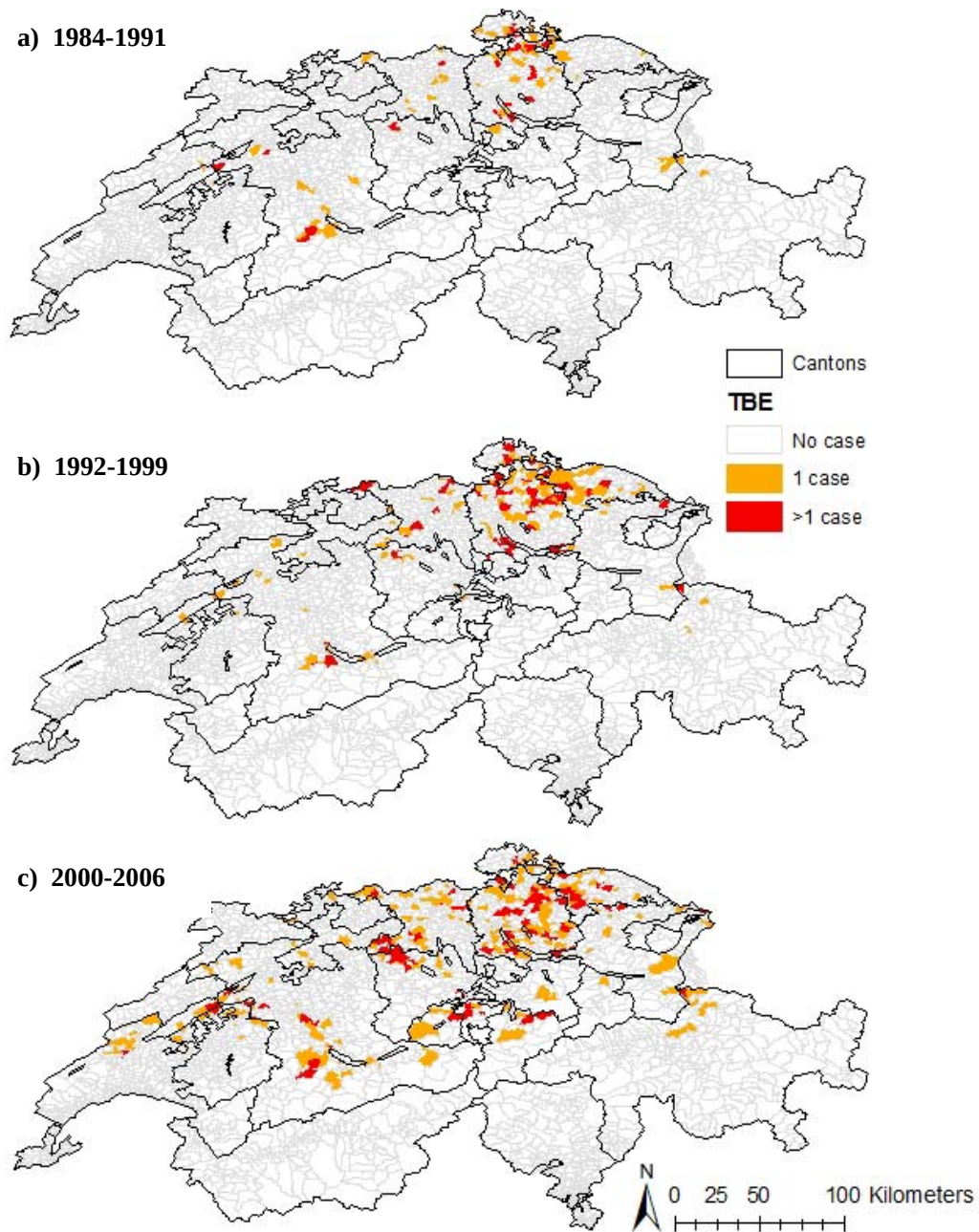


Figure 2.3. The changing distribution of TBE in Switzerland between 1984 and 2006. Postcodes in white reported no cases, those in yellow reported 1 case and those in red reported 2 or more cases (see legend). a) Cases of TBE in Switzerland between 1984 and 1991. b) Cases between 1992 and 1999. c) Cases between 2000 and 2006.

Postcodes were grouped according to the year of the first recorded TBE case in that area (Fig. 2.4). Over time, peaks in TBE cases arose when new areas became TBE-positive rather than when old areas produced more TBE cases. The group of postcodes with a first recorded case between 1984 and 1991 shows no trend in case numbers over the 1984 to 2009 period. Those postcodes with a first recorded case between 1992 and 1999 were largely responsible for peaks in the overall number of TBE cases during this period, but following 1999 they had fewer than 20 cases a year. The group of postcodes with a first recorded case between 2000 and 2006 were responsible for the peaks in cases in 2005 and 2006.

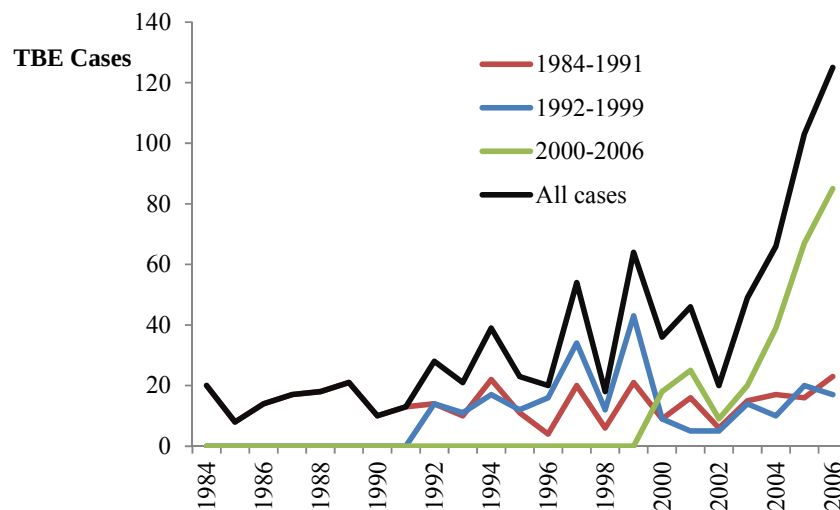


Figure 2.4. Annual TBE cases grouped by the year of the first recorded case in each postcode. The black line is total annual cases in all postcodes, the red line is annual cases in postcodes with a first recorded case between 1984 and 1991, the blue line is annual cases in postcodes with a first recorded case between 1992 and 1999 and the green line is annual cases in postcodes with a first recorded case between 2000 and 2006.

2.3.2. Results of distribution modelling

The distribution of TBE between 2001 and 2006 was predicted using NLDA with MODIS, GRUMP, and DEM as possible predictor variables. The distribution model with three presence and two absence clusters had a kappa value of 0.810 ± 0.035 , a sensitivity of 0.959 ± 0.013 and a specificity of 0.898 ± 0.022 . Amongst the top ten variables selected as

described above from the 100 bootstraps, the predictor with the highest average rank (i.e. the one that came consistently nearest to the top) is the minimum of dLST with an average rank of 4.16 (Table 2.4). Of the top ten variables, seven are aspects of daytime or nighttime LST. Additionally, five of the variables are from the biannual or triannual cycles, demonstrating the importance of the subtleties of the seasonal profile.

Average values for the top ten variables for each presence and absence cluster were calculated (Table 2.4). These give an insight into the environmental conditions that are suitable for TBE. For instance, suitability for TBE is associated with an nLST triannual phase of 2.41 or higher (i.e. the first peak of the triannual cycle occurs in month 2.41, which is mid March, or later) and an nLST annual phase of 6.68 or lower (i.e. peak in month 6.68, which is mid July, or sooner). Unsurprisingly in Switzerland, altitude is important, with the second absence group, for example, having an average altitude (given by DEM) of 1973m a.s.l., which would clearly be unsuitable for ticks.

Much of the area north of the Alps in Switzerland is predicted to be suitable for TBE by the NLDA model using 2001 to 2006 postcode data (Fig. 2.5). TBE cases between 1984 and 2006 broadly fit with the prediction, despite this being modelled with data from only 2001 to 2006 (Fig. 2.6). The effective prediction of the distribution of earlier cases of TBE suggests that the selected environmental variables are important in predicting the distribution of TBE since the 1980s. A number of cases occurred at the southern edge of the area predicted to support TBE. Efforts were made to improve the prediction to cover these areas more fully through more presence clusters in the model, but to no avail.

Table 2.4. Top ten variables selected in NLDA, with average values for the presence and absence groups. Variables highlighted in grey are those with clear thresholds between presence and absence pixels.

Average Rank	Variable	All Presence	Presence 1	Presence 2	Presence 3	All Absence	Absence 1	Absence 2
4.16	Daytime LST minimum	271.53	272.40	272.44	269.46	266.76	271.11	263.60
6.07	Night-time LST triannual phase	2.5124	2.4066	2.5676	2.5061	2.0998	2.1873	2.0364
6.66	Night-time LST triannual amplitude	0.6927	0.8121	0.6391	0.6863	0.7935	0.9535	0.6777
6.97	Daytime LST biannual amplitude	1.4676	1.1895	1.4123	1.7643	1.5251	1.6225	1.4546
8.02	Night-time LST annual phase	6.6484	6.6817	6.6140	6.6770	6.8379	6.7377	6.9106
8.36	Night-time LST minimum	265.47	265.73	266.15	264.20	261.32	264.67	258.90
9.00	DEM	613.87	546.26	472.34	886.48	1453.57	735.92	1973.30
9.09	NDVI biannual amplitude	0.0704	0.0571	0.0556	0.1038	0.0781	0.0948	0.0661
9.25	Middle infra-red triannual amplitude	0.0051	0.0043	0.0060	0.0043	0.0055	0.0055	0.0056
9.39	Night-time LST annual amplitude	10.443	10.015	10.518	10.651	10.527	9.892	10.988

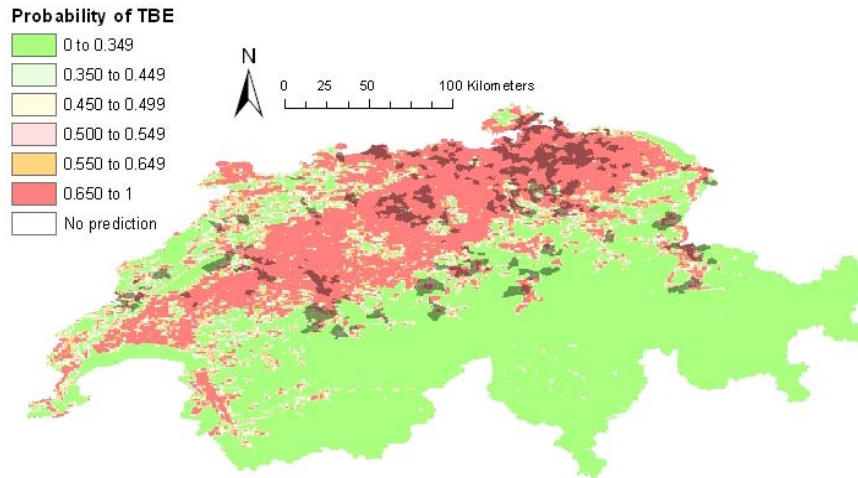


Figure 2.5. The probability of TBE occurrence across Switzerland during the period 2001-2006, as predicted by NLDA. The areas in pink through to red have a probability of TBE of 50% or greater (see legend), but green to yellow have less than a 50% chance of TBE. The postcodes with TBE cases 2001 to 2006 are shown in grey over the distribution map for comparison, and fall largely in the predicted areas.

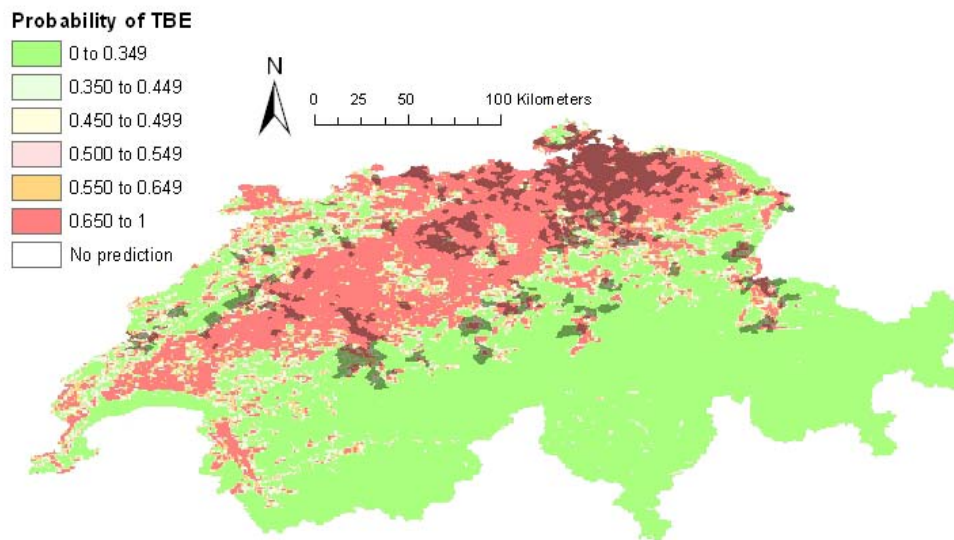


Figure 2.6. Postcodes with TBE cases from 1984 to 2006 (grey) shown over the area predicted to be suitable for TBE by NLDA produced using a training set of cases from 2001 to 2006. Areas coloured pink through to red are predicted to be suitable for TBE (see legend).

The NLDA model predicts that there are areas of Switzerland suitable for TBE transmission but have no recorded cases as of 2006. When the distribution of TBE in 2010 is compared with the prediction based on cases from 2001 to 2006, it is noticeable that a number of new cases have emerged in predicted areas (Fig. 2.7). For instance, the Rhône River valley was predicted to be suitable for TBE by the model, and in 2010 there were cases reported from this area. This is despite the training dataset of cases from 2001 to 2006 containing no cases in this region.

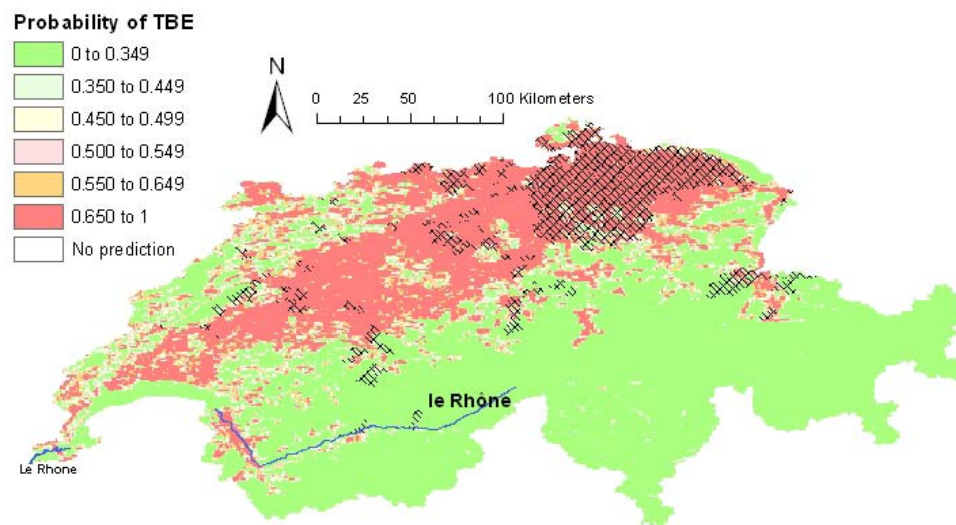


Figure 2.7. The predicted probability of TBE modelled with NLDA. The postcodes considered to be endemic by the Swiss Federal Office of Public Health 2010 are hatched. TBE is predicted to occur in areas of the Rhône valley (river shown in blue) where cases were first seen in 2010.

A clear discrepancy between the extent of the area predicted to be suitable for TBE, and areas where cases have actually been observed still remains, however. This is entirely expected for a number of reasons. First, places with over 50 per cent probability are considered suitable for TBE, but there is considerable variation in the level of suitability above this threshold and some areas have a probability approaching one (Fig. 2.8). Secondly, this distribution model does not account for other environmental factors such as the availability of vertebrate hosts (although some variables do reflect the forest type).

Thirdly, human factors can influence the predicted and observed distribution of TBE. For instance, cases may have been under-reported. TBE is notifiable in Switzerland, but the residence postcode was not recorded for all cases. The areas with the lowest percentage of cases recorded with a postcode were the cantons with low numbers of TBE cases, so new areas are likely to be underreported in this dataset. There may also be differences in the accessibility of different areas which are suitable for TBE (i.e. cases occur in those areas where TBE is predicted and where humans visit).

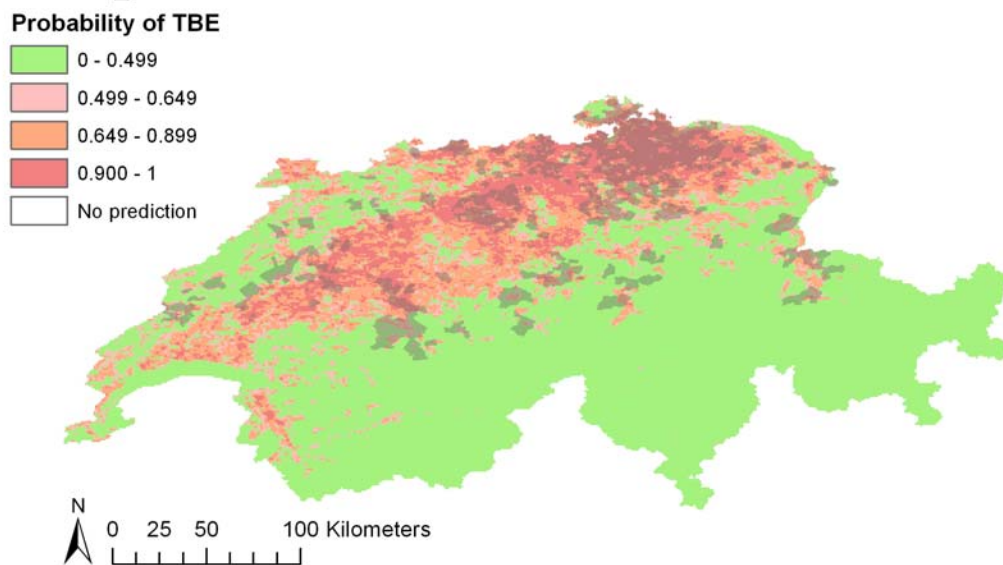


Figure. 2.8. The probability of TBE modelled with NLDA. The classification of probability is different to that seen in Fig. 2.5-2.7 to demonstrate the considerable variability in suitability in the areas predicted to be suitable to be TBE (i.e. with probability greater than 0.5). Postcodes of TBE cases (2001-2006) are shaded grey.

2.3.3. Change analysis of MODIS variables 2001-2009

NLDA identified the top ten variables for predicting TBE, which included seven variables that are aspects of daytime or night-time LST. Change analysis was applied to detect significant changes in the MODIS variables selected by NLDA (but not DEM, which is static). Change analysis applies a linear regression (using 2001 to 2009 data) to each pixel of Switzerland for each of the nine variables and significant trends were mapped. If changes in the climate had been the cause of changes in the TBE distribution

across Switzerland then the MODIS variables in the new TBE districts would be expected to have changed significantly. Given the standard threshold of significance ($p = 0.05$) in these regression analyses, five per cent of pixels would be expected to have a significant trend at random, so the maps will be visually examined for clusters of points. For the two most highly ranked MODIS variables, significantly changing pixels show very little spatial coincidence with those postcodes that had first cases of TBE between 2001 and 2006 (Fig. 2.9).

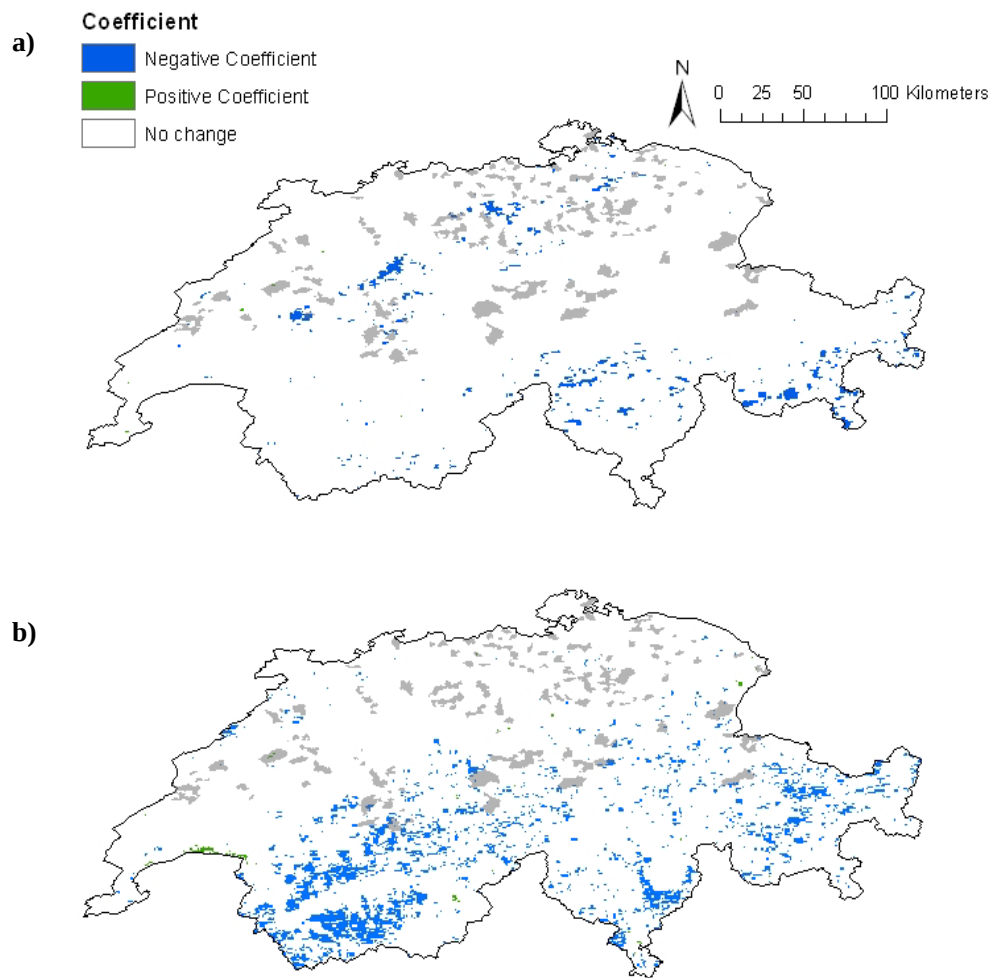


Figure 2.9. Maps of Switzerland showing pixels that experienced significant increases (in green) or decreases (in blue) in a) dLST minimum and b) nLST triannual phase over the period 2001-2009. Also shown in grey are postcodes where TBE was first recorded between 2001 and 2006.

The next two MODIS variables important to a prediction of the distribution of TBE

are nLST triannual amplitude and dLST biannual amplitude. Pixels which have undergone significant changes in these variables during the 2001-2009 period coincide with new TBE postcodes between 2001 and 2006 (Fig. 2.10).

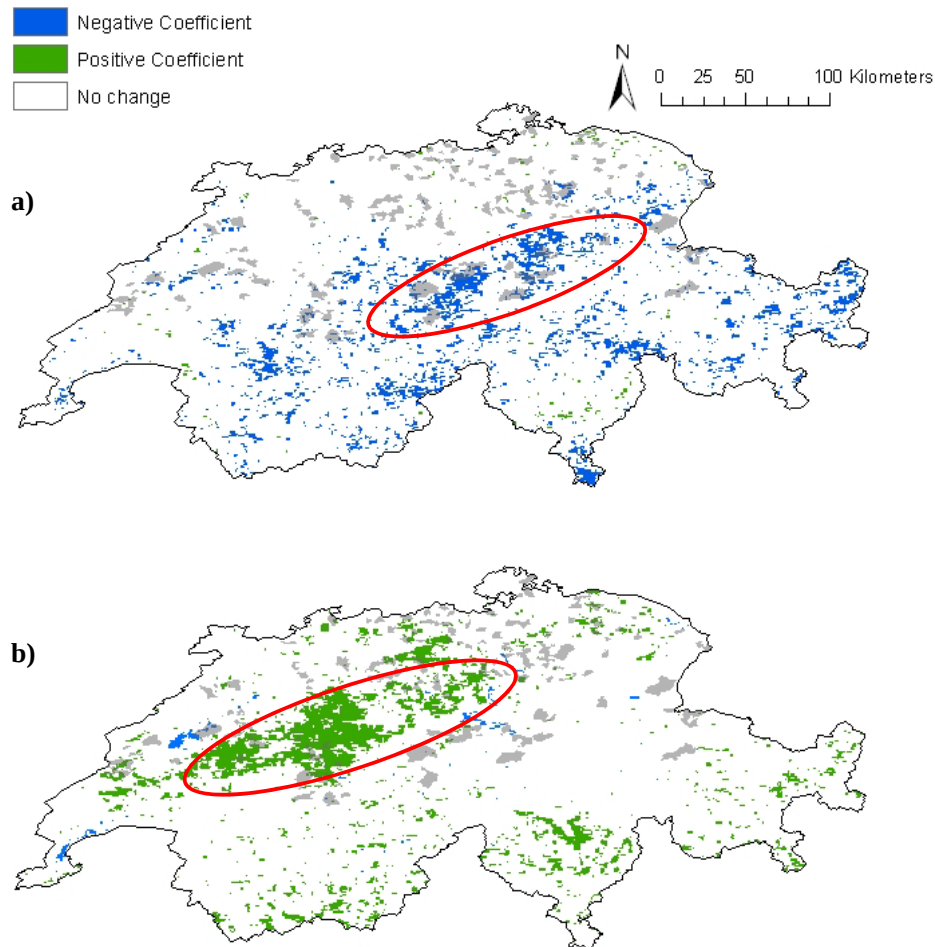


Figure 2.10. Maps of Switzerland showing pixels that experienced significant increases (in green) or decreases (in blue) in a) nLST triannual amplitude and b) dLST biannual amplitude over the period 2001-2009. Also shown in grey are postcode areas where TBE was first recorded between 2001 and 2006. Areas of particular interest, because they fall at the edge of the TBE distribution are shown in a red ellipse.

The remaining five MODIS variables appear to show no consistent patterns of change across Switzerland (Fig. 2.11). nLST annual phase and nLST minimum show no significant changes over the period of interest. Pixels with significant change in the MIR triannual amplitude are patchy across the country and not clustered in the TBE areas. NDVI biannual amplitude shows changes across the Alps, but not in the TBE areas.

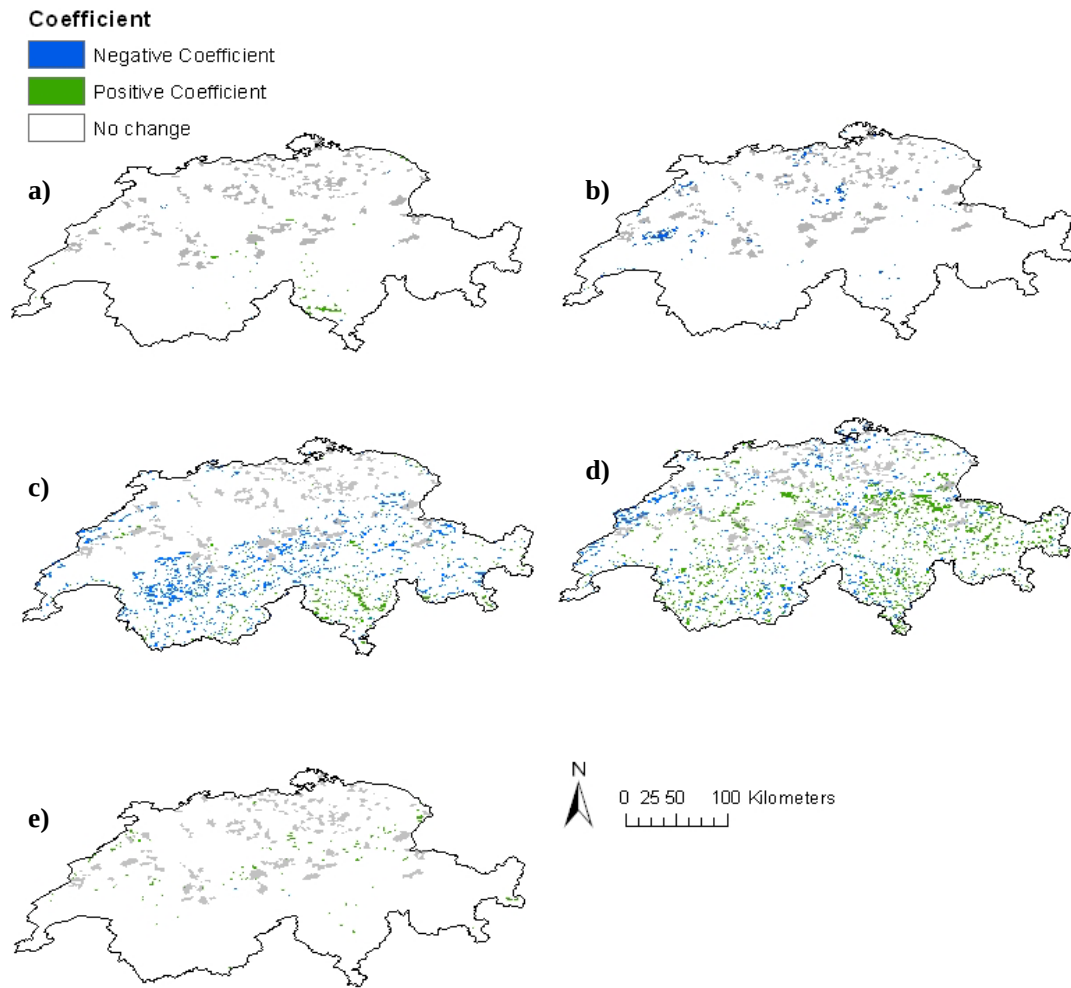


Figure 2.11. Maps of Switzerland showing pixels that experienced significant increases (in green) or decreases (in blue) in a) nLST annual phase, b) nLST minimum, c) NDVI biannual amplitude, d) MIR triannual amplitude and e) nLST annual amplitude over the period 2001-2009. Also shown in grey are postcode areas where TBE was first recorded between 2001 and 2006.

In Fourier analysis the biannual and triannual cycles of variables are important in modulating the shape of the annual cycle to fit the actual seasonal pattern (see Fig. 2.1). To investigate the effect of changes in the nLST triannual and dLST biannual amplitude, the full time series were reconstructed for a sample of pixels (Fig. 2.12). For each of the nLST triannual and dLST biannual amplitude, 50 pixels with significant changes and coincident with TBE postcodes newly endemic to TBE (between 2001 and 2006) were selected, known as test pixels. 50 control pixels 5-10 kilometres from test pixels, with no significant change in the relevant MODIS variable, were selected for comparison.

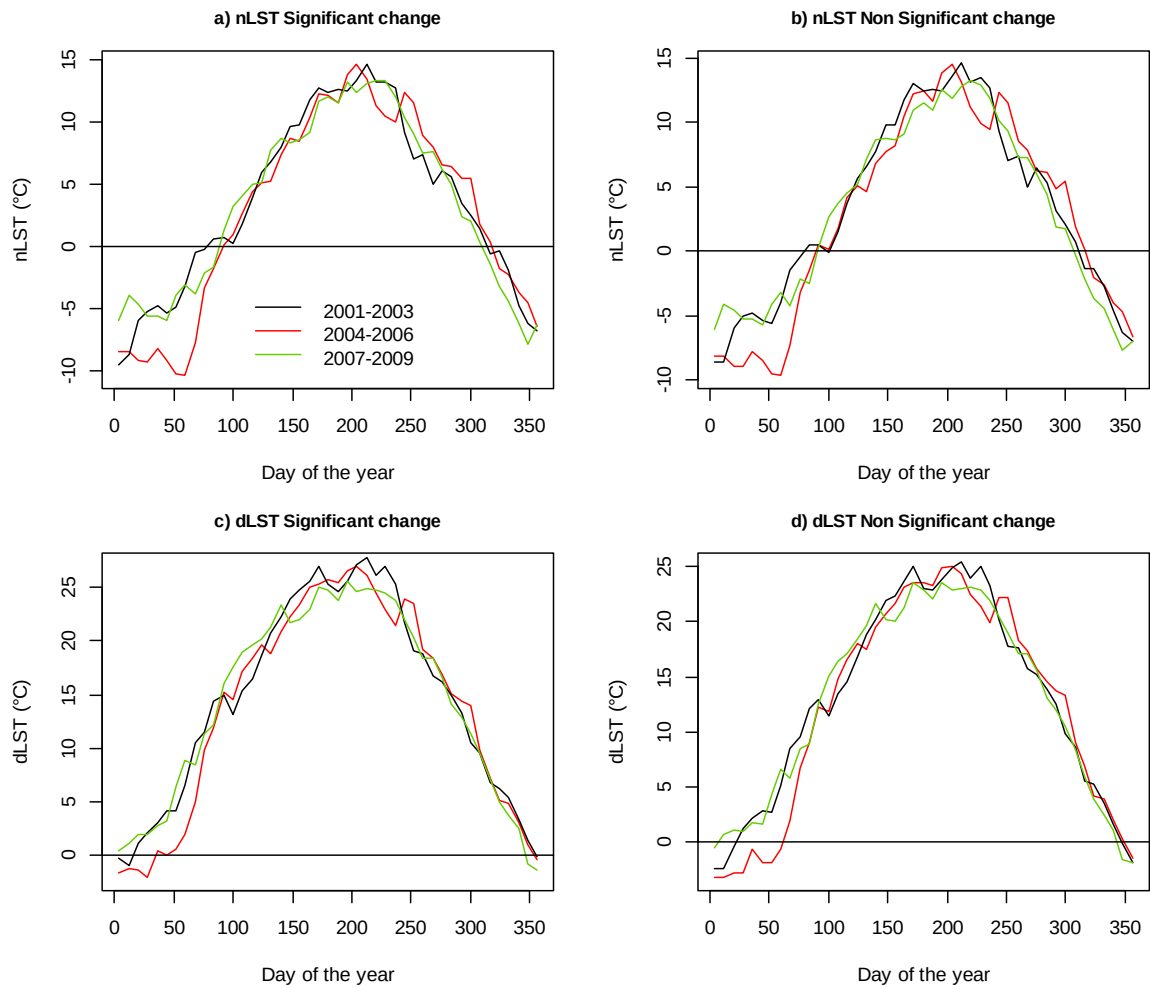


Figure 2.12. Time series of MODIS data for a) fifty test pixels with significant change in nLST triannual amplitude, b) fifty pixels with non-significant change 5-10km from test pixels, c) fifty test pixels with significant changes in dLST biannual amplitude and d) fifty pixels with non-significant change and 5-10km from test pixels. Horizontal lines are plotted at zero for comparison.

It is difficult to identify visually where the significant change has occurred in the reconstructed profile of nLST and dLST variables (Fig. 2.12). Potential differences between the changing and unchanging time series include at the peak in nLST and in the spring rise in temperature in dLST. An increase in the rate of spring warming in dLST could favour TBE endemism, so the 50 pixels with significant changes in the dLST biannual amplitude were tested for changes in spring warming. A linear regression was fitted between February and April and the coefficient taken as the rate of spring warming (Fig. 2.13). 2001 and 2002 were characterised by low rates of spring warming, and 2003

to 2009 appear to have higher rates of spring warming but not in any sequential order, suggesting that the rate of spring rate might have increased but not systematically. However, when the two unusual (lowest) years fall at the start of such a short time series, it is impossible to judge how representative they are of the preceding period, so an examination of change in a longer time series is needed. MODIS data has excellent spatial resolution but only has records between 2001 and 2009. For longer time series, ground based meteorological station data were used.

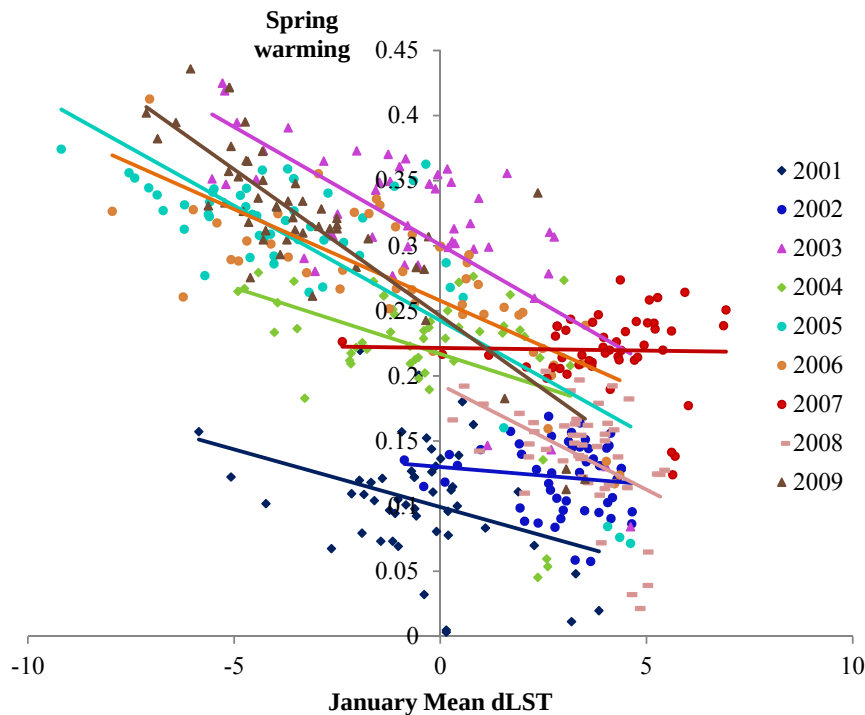


Figure 2.13 Rate of spring warming (fitted using a linear regression February to April) in 50 pixels with a significant change in dLST biannual amplitude, against the mean dLST in January, across different years.

The rate of spring warming in maximum temperature was measured for six Swiss cantons between 1984 and 2009. During this period TBE incidence increased in all six cantons. There appears to have been no increase in the rate of spring warming between 1984 and 2009 in Switzerland (Fig. 2.14). Considering only the 2000 to 2009 data in Figure 2.14 (coloured in blue and labelled) it is clear that the 2001 and 2002 years have the lowest rate of spring warming during this period, which is in agreement with the satellite-

derived data. The 2001-2009 points, however, have similar rates of spring warming to the points from before 2001, suggesting there has been no trend for increased spring warming. Zurich, Lucerne and Aargau have similar average January mean temperature, but on average Zurich has considerably higher rates of spring warming (mean =0.188 compared with 0.145 and 0.151 for Lucerne and Aargau respectively). St. Gallen has the lowest rate of spring warming.

If there is no significant trend in spring warming, are there other changes in the temperature throughout the year that could explain the significant changes observed in the MODIS variables? Applying a linear regression to average monthly temperature for each canton demonstrated a significant increase in temperature in April, May and June (Table 2.5, Fig. 2.15). April is the last month used in calculating the spring warming, but the positive trend in temperature for that month evidently has no influence on spring warming.

Table 2.5. Regression coefficients for TBE incidence, weather or vertebrate numbers against the year (1984-2009)

	Aargau	Bern	Lucerne	St. Gallen	Thurgau	Zurich
January	0.083	0.064	0.061	0.048	0.056	0.059
February	0.101	0.174	0.180	0.155	0.177	0.166
March	0.058	0.071	0.081	0.064	0.063	0.073
April	0.146 *	0.131 *	0.129 *	0.131 **	0.127 *	0.132 *
May	0.107 *	0.100	0.115 *	0.117 *	0.106 *	0.114 *
June	0.164 **	0.170 **	0.150 **	0.153 **	0.153 **	0.155 **
July	0.017	0.013	0.021	0.036	0.015	0.019
August	-0.013	-0.016	-0.001	0.004	-0.007	0.001
September	-0.006	-0.009	0.001	-0.010	-0.007	0.003
October	-1.729	-1.852	-1.304	-1.863	-1.654	-1.945
November	-0.361	-0.440	-0.457	-0.394	-0.382	-0.507
December	-0.875	-0.881	-1.326	-1.145	-1.076	-1.348

* denotes p-value<0.05, ** for p-value<0.01 and *** for p-value<0.001

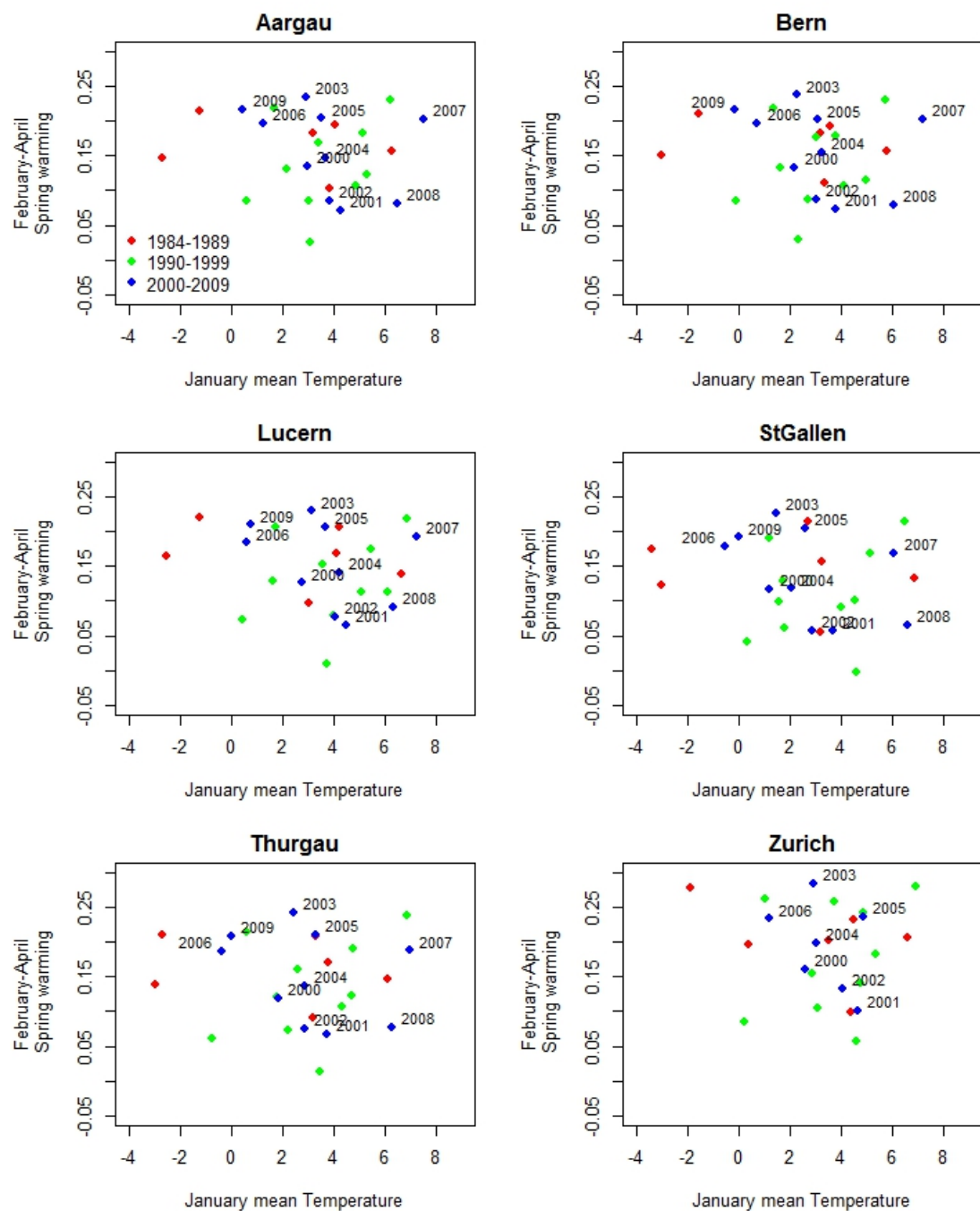


Figure 2.14. The rate of spring warming (February-April) in maximum temperature as a function of January average maximum temperature, calculated from meteorological station data 1984-2009. Points are coloured according to the year – red for 1984-1989 data, green for 1990-1999 and blue for 2000 to 2009 data. Data points for 2000 to 2009 data are labelled.

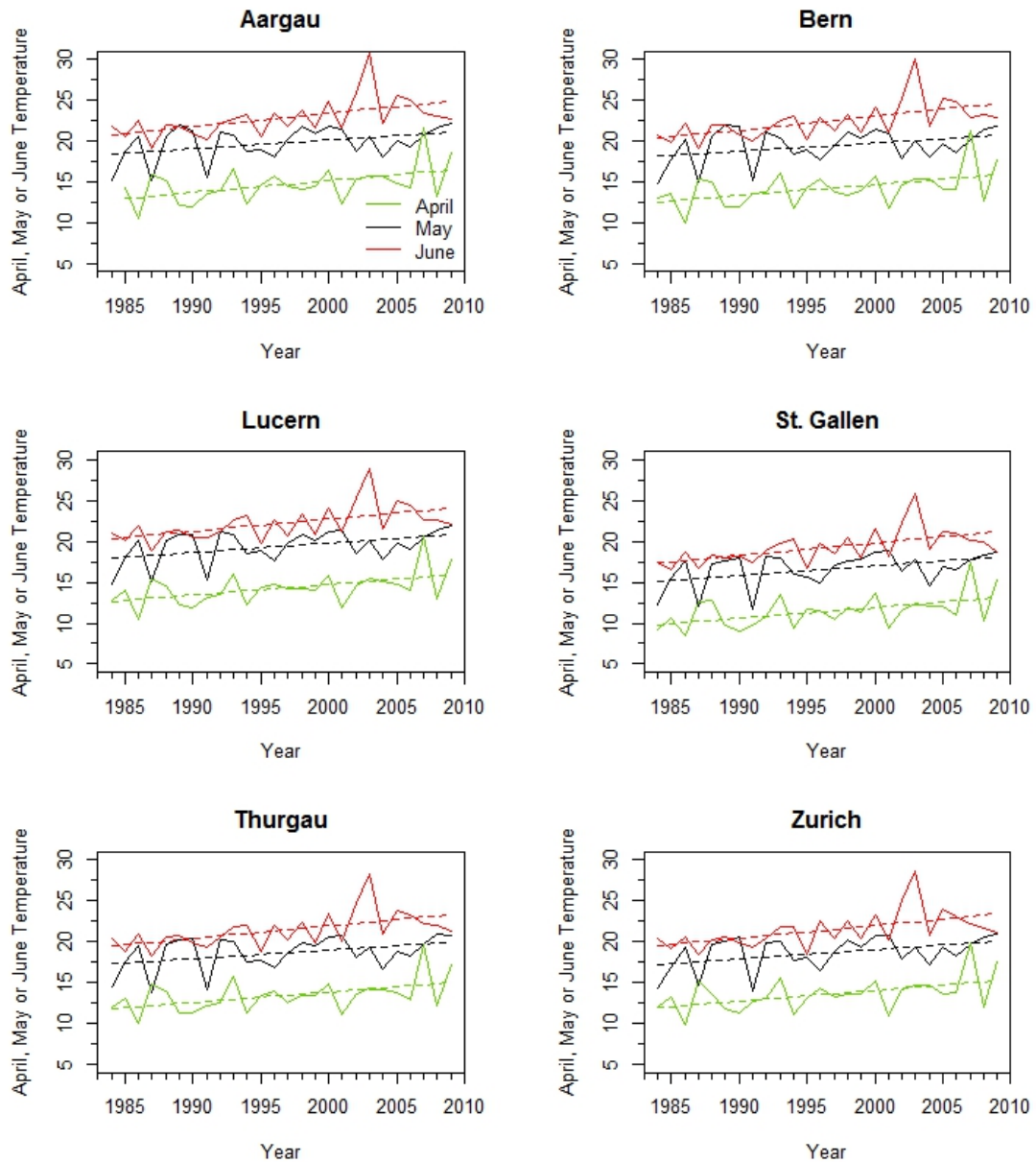


Figure 2.15. April (green line), May (black line) and June (red line) average maximum daily temperature 1984-2009 with linear model fits (shown with dashed line in green for April, black for May and red for June).

2.3.4. Environmental similarity between newly endemic and ancestral TBE areas

A statistical analysis using the MD was carried out to establish if areas with TBE since the 1980s and sites newly endemic for TBE in 2004-2006 have become more similar between 2001 and 2009. If so, this would support the hypothesis that environmental

change has precipitated distributional change in TBE. The MD to the ancestral centroid was calculated for each ancestral, newly endemic and out-group pixel and log transformed to normalise the values (known as 'log(MD)'). Across all years, 2001 and 2006 have the lowest log(MD) values, and 2004 and 2009 have the highest, but no year is considered unusual (Fig. 2.16a,c,e).

A GLM was fitted to the ancestral, newly endemic and out-group pixels with the response variable as the log(MD). The year, TBE status (ancestral vs. newly endemic vs. out-group), and an interaction between the two were included as explanatory variables. A significant ANOVA demonstrated a GLM fitted with generalised least squares, with an AR1 autocorrelation structure, was significantly better fit than that without (likelihood ratio 24,975.46, $p < 0.001$), but the results of both models show agreement (Table 2.6). The ancestral and newly endemic pixels show an increase in log(MD) between 2001 and 2009 (Table 2.6). Given that the ancestral centroid is a fixed point in environmental space, this demonstrates that the environments of ancestral and newly endemic pixels are changing through time.

When the annual average log(MD) of the ancestral pixels is subtracted from the log(MD) of each of the ancestral, newly endemic or out-group pixels, the result is the anomaly, a measure of the difference between the ancestral and other pixels. By definition, the anomaly for the ancestral pixels is zero between 2001 and 2009 (Fig. 2.16b). In newly endemic pixels, a reduction in this anomaly is observed between 2001 and 2009 (Fig. 2.16d), demonstrating that the newly endemic and ancestral pixels became more similar. The GLM results agree, as the ancestral pixels have a greater increase in the log(MD) between 2001 and 2009 than the newly endemic pixels, meaning they are converging (Table 2.6). The log(MD) of out-group pixels shows no great change between 2001 and 2009 (Fig. 2.16e), and the pixels remain significantly different from ancestral pixels (Fig. 2.16f).

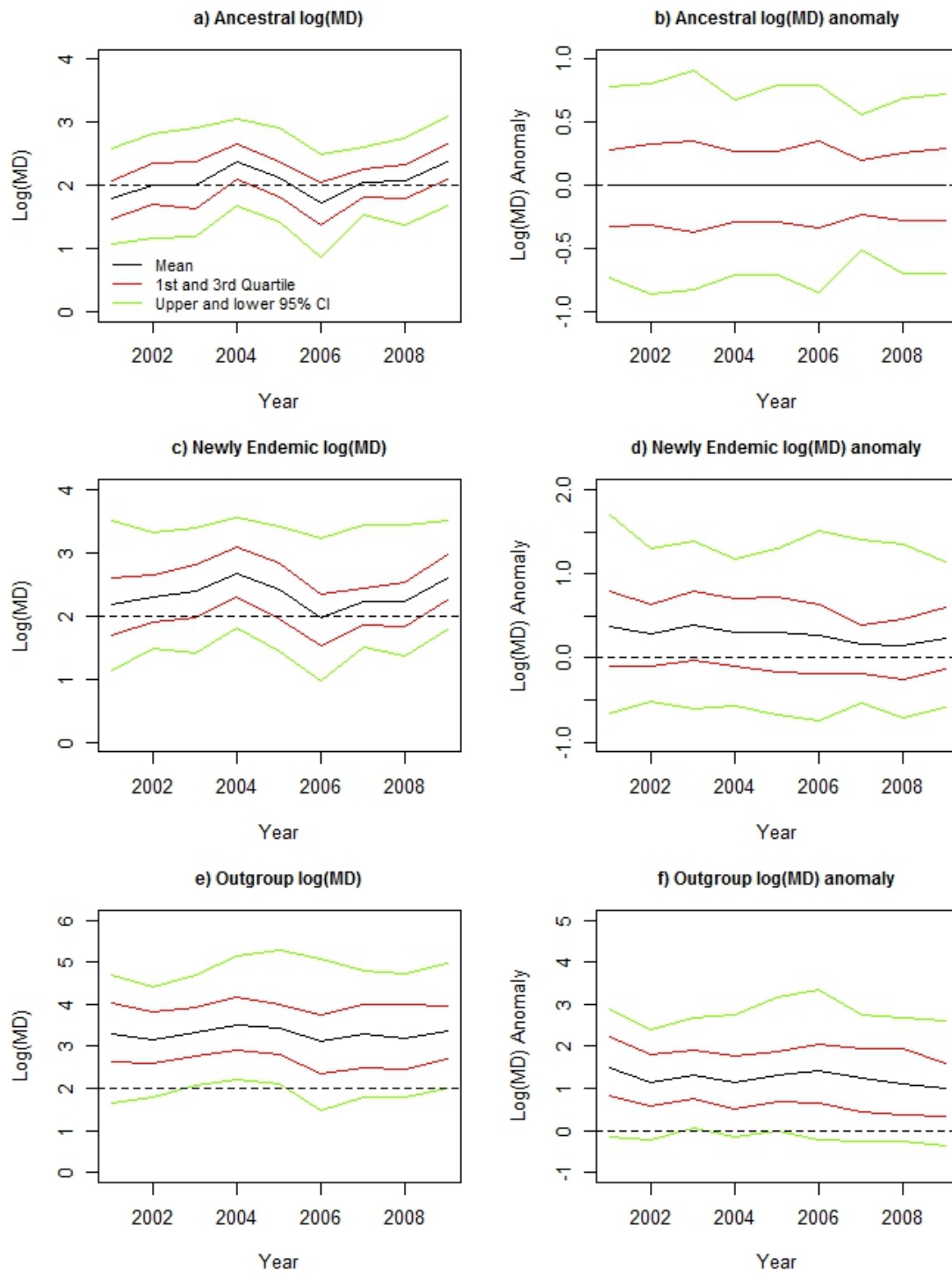


Figure 2.16. The log(MD) to the ancestral centroid in the a) ancestral, c) newly endemic and the e) out-group pixels and the anomaly in log(MD) from the annual average ancestral log(MD) in that year in b) ancestral, d) newly endemic and f) out-group pixels between 2001 and 2009.

Table 2.6. Results from GLM for the log(MD), with and without AR1 correlation structure per site.

	Not autocorrelated model			Autocorrelated model		
	Coefficient	t-value		Coefficient	t-value	
Intercept	1.904	104.503	***†	1.761	65.186	***
Ancestral	ref.			ref.		
Newly Endemic	0.392	16.754	***	0.381	10.979	***
Out-group	1.413	62.101	***	1.529	45.350	***
Year	0.031	9.488	***	0.061	14.675	***
Year*Newly Endemic	-0.024	-5.678	***	-0.019	-3.535	***
Year*Out-group	-0.034	-8.291	***	-0.056	-10.786	***

†*** denotes p-value<0.001

2.3.5. Longer term trends

To complement the spatial analysis of environmental change, a longer-term analysis of other potential factors was undertaken with climate variables other than temperature and vertebrate abundance. There was a significant quasi-linear increase in TBE incidence from 1984 to 2009 in the six cantons examined (Fig. 2.17, Table 2.7). Of the weather and vertebrate data, the abundance of deer showed significant trends through time in all cantons. In five cantons the abundance of boar also showed significant trends through time.

In Aargau, Bern and Lucerne the linear model suggested an increase in deer abundance between 1984 and 2009, but in St. Gallen, Thurgau and Zurich the abundance of deer decreased (Fig. 2.18). These inconsistencies are at odds with the increase in incidence of TBE in all six cantons. Additionally, although linear trends were fitted in all instances, there was considerable variation in the shape of the increase or decrease. For instance, changes in the abundance of deer in Aargau are not linear and show no resemblance to change in TBE incidence during the same period.

The boar hunting bag has increased in all cantons except Lucerne, where fewer than ten boars were hunted in the canton in any one year (Fig. 2.18). In Aargau, Bern, St. Gallen, Thurgau and Zurich virtually no boar were hunted in 1984. The hunting bag in

2009 is variable across the cantons, with around 1,000 animals in Aargau, but only around 25 in St. Gallen. Reported levels of damage caused by boar and boar killed of causes other than hunting demonstrate no trend in boar abundance in Bern and St. Gallen between 1992 and 2009 (Fig. 2.19). In Aargau and Zurich there was no increase after 2000. A linear positive trend is only seen during the entire period in Thurgau.

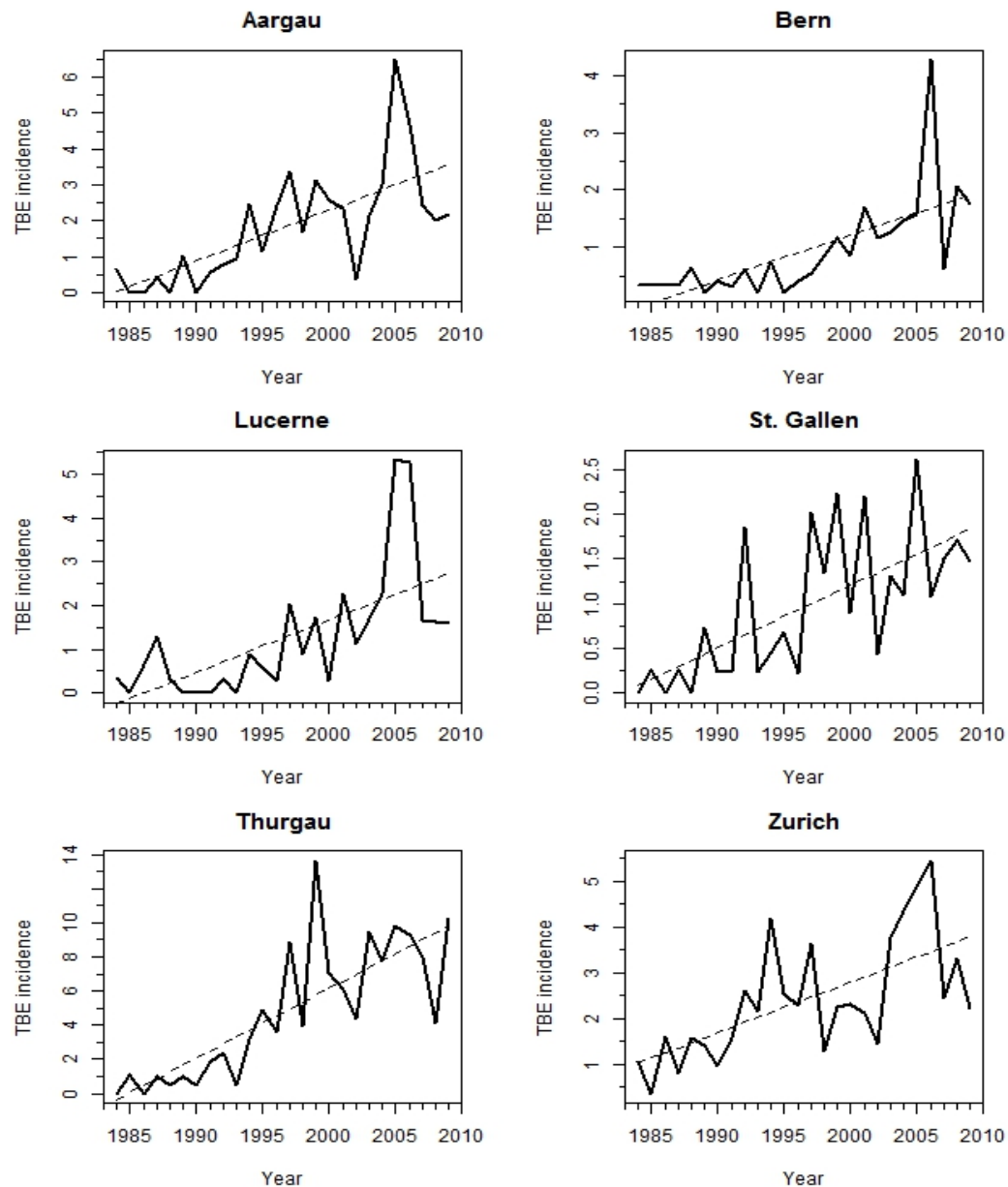


Figure 2.17. The incidence of TBE in six cantons of Switzerland 1984-2009, with a fitted linear model (dashed line).

Table 2.7. Regression coefficients of TBE incidence, weather or vertebrate numbers against the year (1984-2009).

	Aargau		Bern		Lucerne		St. Gallen		Thurgau		Zurich	
Incidence	0.141	***†	0.079	***	0.118	***	0.070	***	0.407	***	0.111	***
Sunny Days	0.162		0.363		0.019		0.210		0.196		0.086	
Frosty Days	0.148		-0.030		0.021		-0.175		-0.122		-0.017	
Rainy Days	0.190		0.167		0.019		0.099		-0.068		0.160	
Rainfall	-0.001		0.016		0.021		-0.009		0.017		0.007	
Snowfall	-0.072	*	-0.040		-0.074		-0.017		-0.020		-0.039	
Boar	48.00	***	7.22	***	-0.01		1.23	***	18.78	***	29.65	***
Deer	23.13	*	563.19	***	63.69	**	-136.05	***	-22.00	***	-27.63	*

† * denotes p-value<0.05, ** for p-value<0.01 and *** for p-value<0.001

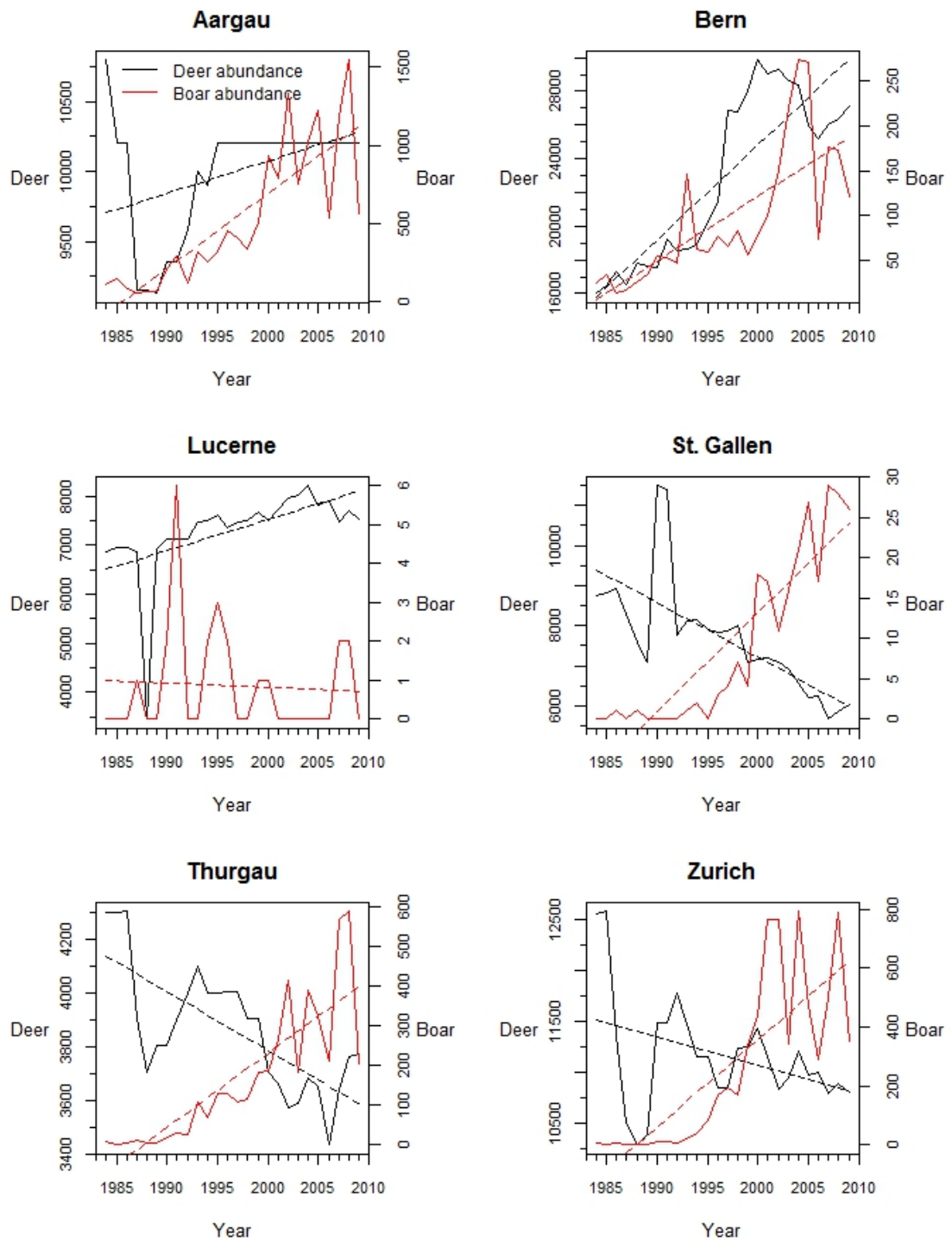


Figure 2.18. The abundance of deer (in black, left hand axis) and the hunting bag of boar (in red, right hand axis) in six cantons of Switzerland (1984-2009) with fitted values from a linear model against the year (shown in dashed red for boar and dashed black for deer).

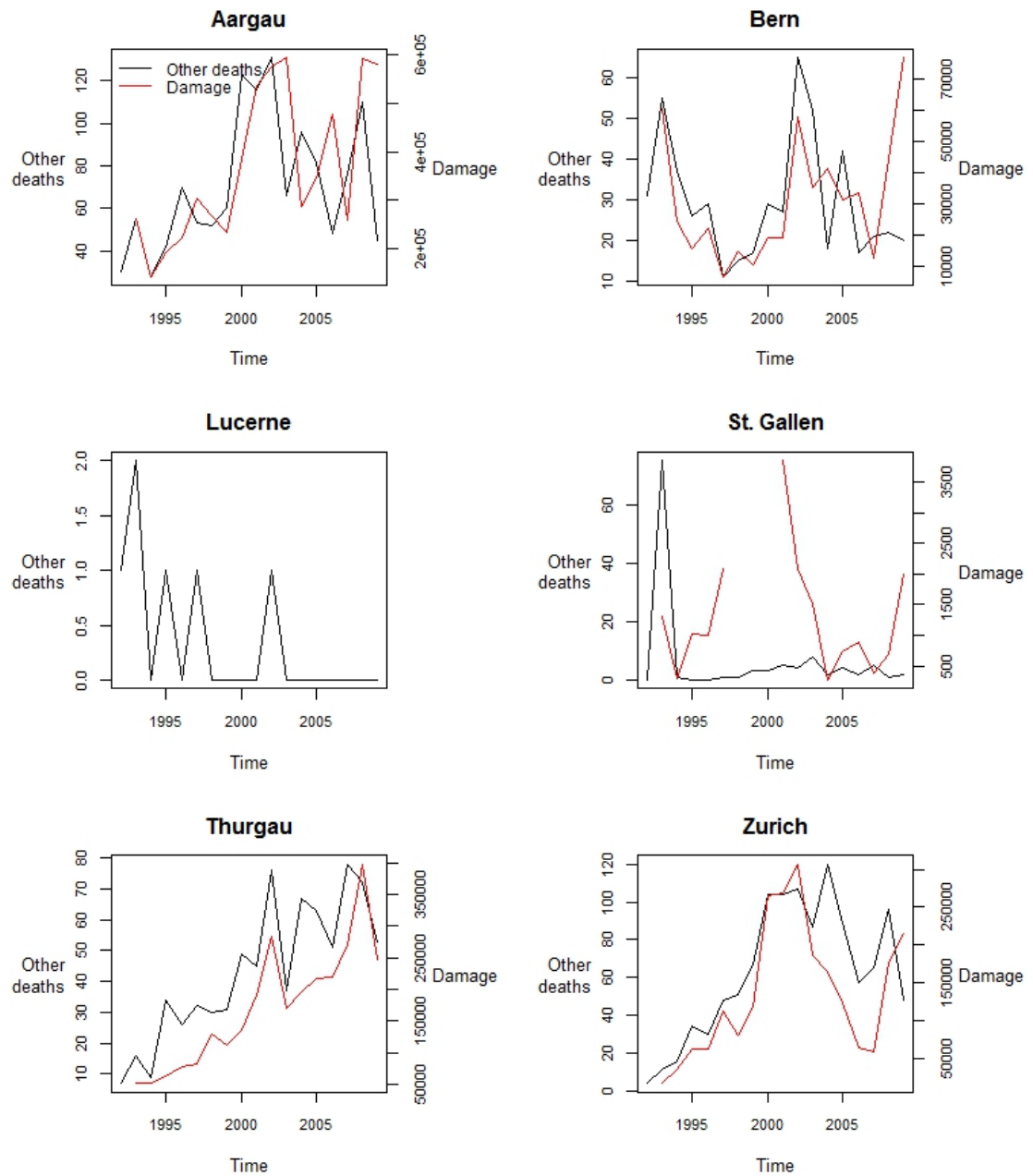


Figure 2.19. Number of reports of damage caused by boar and number of deaths of boar not as a result of hunting in six cantons of Switzerland (1992-2009). Deaths not as a result of hunting is shown in black (left hand axis) and records of damage caused by boar are shown in red (right hand axis). No damage was recorded in any year in Lucerne.

2.4. Discussion

2.4.1. The changing incidence and distribution of TBE in Switzerland 1984-2009

In Switzerland, between 1984 and 2009 the distribution of TBE expanded and the number of recorded cases increased. On average, there were 27 cases of TBE annually in Switzerland between 1984 and 1991, 78 cases annually between 1992 and 2000 and 129 cases annually between 2001 and 2009. Between 1984 and 1999, TBE occurred predominantly in the central northern cantons of Zurich, Schaffhausen, Thurgau, Aargau, Lucerne, Bern and St.Gallen. After 2000, the distribution of TBE expanded further west and south, with first cases of TBE being reported in the cantons of Uri, Glarus and Obwalden.

TBE cases in Switzerland with a recorded postcode of residence were grouped according to when the postcode had a first recorded case of TBE. Examination of these grouped cases demonstrated that increases in incidence came from areas recently endemic for TBE. Postcodes with a first reported case before 1990 show no trend in case numbers between 1984 and 2006, and the increase in TBE cases since 2000 was associated with areas with their first reported case during the same period. This situation seems extreme; changes in TBE incidence would be expected to originate from changes in the core and edge of the distribution.

In 2006, there was a spike in TBE case numbers in many European countries, including Switzerland (Randolph et al., 2008). It was argued that unusual weather patterns in 2006 promoted activities that exposed humans to ticks. This weather did not consistently increase tick abundance across the sites sampled, although it should be noted that higher numbers of ticks were counted in Switzerland in 2006 than 2007. Results presented here suggest the excess cases came from newly endemic sites, predominantly in

Zurich and Bern. No coincident increase in the rate of spring warming was seen in satellite-derived or meteorological station data. Changes in human behaviour, precipitated by the unusual weather situation, could have exposed people to areas previously not known to be endemic for TBE.

2.4.2. Environmental factors in the distribution of TBE

Using the postcode data, the area predicted to be suitable for TBE in Switzerland was modelled using satellite-derived variables and NLDA. The resulting predictive map suggests that much of the area north of the Alps is suitable for TBE. Based on the postcoded cases, TBE is thought to be restricted within this area, but this includes only around half of the actual TBE cases in Switzerland between 1984 and 2006. Cantons with comparatively low numbers of TBE cases have a lower percentage of cases recorded to the postcode of residence, so the breadth of the true TBE distribution may be underestimated. Other factors could also contribute to the discrepancy between the predicted and observed distribution of TBE. For example, human factors such as vaccination and activity patterns can affect the distribution of human TBE cases. Additionally, despite a large area being predicted to be suitable for disease, there is considerable variation in the level of predicted suitability across the region; areas with high numbers of cases are associated with a higher probability of endemicity in distribution models.

Distribution models have previously been produced for TBE for Europe with 8x8km resolution (Randolph, 2000). Despite the methodological differences with the model of TBE in Switzerland presented herein, the results are concordant. In the continental model, a combination of land surface temperature, normalised difference vegetation index and middle-infrared variables were selected as predictive for TBE.

Ixodes ricinus ticks are present throughout Switzerland (except above an altitude of around 1,000m (Krech, 2002)), but the predicted distribution of TBE is restricted within this area. This is common in TBE, which shows a focal distribution across Europe,

associated with synchrony in the questing of nymphs and larvae, allowing co-feeding on rodents and transmission of non-systemic viral infection (Randolph et al., 1999; Randolph et al., 2000). In Switzerland, an area without circulating TBE virus in sampled ticks was associated with a lower proportion of co-feeding ticks than three sites with TBE virus (Burri et al., 2011).

Synchrony in seasonal activity by nymphs and larvae, essential for co-feeding, is favoured by rapid spring warming; TBE foci typically have a high rate of temperature increase between February and April, when adjusted for January temperature (Randolph and Sumilo, 2007). It was found by NLDA that three of the ten variables associated with the distribution of TBE in Switzerland are biannual and triannual elements of daytime and night-time LST. These variables determine the seasonal temperature profile and therefore could be associated with the rate of spring warming.

2.4.3. Climate as a potential causal factor in changing incidence and distribution of TBE in Switzerland

An analysis using the MD to measure environmental similarity detected that the environment in areas with TBE since the 1980s (ancestral) and since 2004-6 (newly endemic) has become more similar between 2001 and 2009. These changes in environmental suitability could have contributed to the observed changes in TBE distribution, but more evidence is needed to identify exactly what changes occurred to make the environments more similar.

Using change analysis, changes in two temperature variables (dLST biannual amplitude and nLST triannual amplitude), that had been shown by NLDA to be important predictors of TBE, were observed in some, but not all, areas newly endemic for TBE. Significant changes in these variables could be associated with an increased rate of spring warming. Satellite data showed that 2001 and 2002 had a lower rate of spring warming than 2003-2009, but meteorological station data showed that the rates of spring warming in

2003-2009 were not different to rates in years previous to 2001. This suggests that the increased similarity in ancestral and newly endemic pixels is not because of changes in the rate of spring warming.

An increase in the April, May and June temperatures was observed between 1984 and 2009 in six key TBE cantons of Switzerland. The increased similarity between newly endemic and ancestral TBE areas may result from these changes in temperature, but the effect of this change in temperature on the TBE system is unknown; it could affect the abundance and/or questing activity of ticks and/or the behaviour of humans. The temperatures in April, May and June are already above that required for ticks to quest actively, which are thought to be around 7°C for nymphs and 10°C for larvae (Perret et al., 2000; Randolph, 2004b), therefore these temperature changes are not advancing the commencement of tick questing.

Fieldwork would be needed to measure whether temperature increases in April, May or June could boost the actively questing tick population and thus the mass of the TBE enzootic cycle. Population modelling for *I. ricinus* in the UK has suggested that increases in the average annual temperature can lead to increases in the nymphal tick abundance, due to more rapid development of ticks from one life stage to the next (Dobson and Randolph, 2011). This effect would, however, be more marginal in mainland Europe where the climate is warmer than the UK. Additionally, any increase in temperature would also increase the saturation deficit, which could adversely affect tick survival.

2.4.4. Vertebrate abundance and the changing incidence of TBE in Switzerland

Factors other than climate that could potentially affect the incidence of TBE in Switzerland were also considered, namely vertebrate abundance. Temporal analysis cannot rule out an additional possible effect of changes in vertebrate populations on TBE in Switzerland. Information on the estimated abundance of deer is available, but boar

abundance is estimated from three types of information: (1) the number of animals hunted; (2) the number killed through other means (e.g. roadkill); and (3) the number of reports of damage caused by boar. There were significant trends in boar and deer populations across many of the cantons observed, but the trends were not consistent. In Aargau and Zurich, the average deer abundance was fairly stationary over the 1984 to 2009 period, in St. Gallen and Lucerne substantial reductions in the deer abundance were observed and in Bern and Thurgau substantial increases were observed. Several hundred boar are now hunted annually in Bern, Aargau, Thurgau and Zurich, from almost zero in 1984 in all areas. Data on the number of boar killed by means other than hunting and damage caused by boar suggest growth in the abundance of boar in Thurgau, Aargau and Zurich, as it has in many European countries (Saez-Royuela and Telleria, 1986). Boar are not distributed throughout Switzerland, with almost no reported hunting, other kills or damage in Lucerne. It therefore seems unlikely that vertebrate populations are responsible for all the increase in TBE cases across Switzerland, but it could have contributed to changes in some cantons.

2.4.5. Conclusion

The seasonal profile of temperature is important in predicting the area suitable for TBE in Switzerland. Using MD and the satellite variables found to be important in predicting TBE in Switzerland, newly endemic areas of Switzerland and ancestral TBE areas were found to have become more similar between 2001 and 2009. MODIS variables significantly changed between 2001 and 2009 in some, but not all, places coincident with new TBE endemic areas. Longer term temporal data from meteorological stations showed no trend for an increased rate of spring warming between 1984 and 2009. Temporal data did, however, identify an increase in temperature in April, May and June between 1984 and 2009, but the effect of this change is unknown and could affect the tick and/or the human. Temporal analyses demonstrate that there have been significant changes in deer and boar abundance, but the trends are variable across the cantons considered. This variability

suggests that change in vertebrate populations could have contributed to changes in incidence in only some areas.

CHAPTER 3. SPATIAL AND TEMPORAL CHANGES IN TBE IN GERMANY 1975-2010

3.1. Introduction

The incidence of TBE in Germany, as in many European countries, is thought to have increased since the early 1990s (Randolph, 2001). The majority of TBE cases take place in the south German states of Baden-Württemberg and Bavaria with 85-100% of all the annual cases of TBE in Germany between 1991 and 2002 (Suss et al., 2004). Whereas it is thought to have been stable at a high level in Baden-Württemberg and Bavaria since around 2000 (Suss, 2008), incidence has increased in other low-risk states, such as Hessen, Thuringia and Rhineland-Palatinate (Suss et al., 2004). In 1998 there were 63 districts classed as risk areas which increased to 86 in 2002, suggesting a concomitant change in distribution with incidence (Suss et al., 2004).

In this chapter, a spatio-temporal framework model will be used to model the effects of environmental and socioeconomic covariates and spatio-temporal autocorrelation in shaping TBE in Germany between 2001 and 2009. Similar methods have been used to assess the role of weather conditions in malaria in Zimbabwe (Mabaso et al., 2006) and Kenya (Amek et al., 2012). The factors established to be important to TBE in Germany in space will then be examined for changes through time which are coincident with the observed change in TBE incidence. This combined spatial and temporal approach was previously used to examine TBE in the Baltic States (Sumilo et al. 2006).

Vertebrate abundance has previously been implicated in the distribution of TBE, and will therefore be included in the spatio-temporal framework model. In Southern Germany, human TBE risk was positively correlated with roe deer abundance and negatively correlated with red deer (Kiffner et al., 2010). Other ungulates, such as wild boar, have been hypothesised as a potential diluting host for tick-borne diseases, such as *Anaplasma*,

but no supporting evidence for this idea was found in Italy (Estrada-Pena et al., 2008). However, the role of boar in the broad scale epidemiology of TBE has not yet been examined.

Maximum daily temperatures of 7°C and 10°C are thought to be important thresholds for nymphal and larval activity, respectively (Perret et al., 2000; Randolph, 2004b). The focal nature of TBE is apparently related to the rate of spring warming, which allows *Ixodes ricinus* larvae and nymphs to feed at the same time and therefore potentially on the same TBEV competent hosts (Randolph & Sumilo 2007). Therefore, the seasonal temperature profile would be expected to be important to the distribution of TBE in Germany. Additional effects of temperature on tick questing (following the commencement of activity) may include limitation of activity due to desiccation in peak summer temperatures (Perret et al., 2000; Perret et al., 2004; Burri et al., 2007), so temperature variables from throughout the year will be included in the spatio-temporal model.

Both habitat availability and visits to this habitat by humans are important to TBE in spatial analyses. In Latvia, both land cover and land use variables were significant in predicting the distribution of TBE in space (Vanwambeke et al., 2010). Parishes with high levels of wild food gatherers (i.e. people who were unemployed or on low income and looking for alternative sources of food or income) had higher incidence of TBE (Vanwambeke et al., 2010). Variables associated with 'hikers' were not correlated with TBE incidence. Despite this, and other, (e.g. Randolph et al., 2008), evidence of the importance of human variables in TBE, a recent model of TBE in Germany only included abiotic and biotic factors, with no consideration of human variables, and failed to explain annual variation in incidence (Kiffner et al., 2010).

TBE incidence has been increasing in many European countries, but the nature of the change is variable. In almost all ex-communist Central and Eastern European countries

TBE incidence increased around 1993, but to different extents (Sumilo et al., 2008b). In Western Europe the increase in incidence has been gradual. For instance in Switzerland and Finland the increase was slow and steady (Randolph, 2001). Exceptions to these patterns include Hungary, where there was no increase and then a sudden decrease (Randolph, 2001) and Sweden, where a 3-fold increase was seen between 1983 and 1986, 2-fold increase in 2000 and exponential increase since then (Randolph, 2004a).

The timing of the change in a system is important for detecting the potential causal factors. Changes in the abiotic and biotic conditions and human behaviour, precipitated by agriculture and industrial changes following independence from Soviet rule contributed to upsurges in TBE in 1993 in Central and Eastern European countries (Sumilo et al., 2008b). An increase in TBE in Sweden in 1984 was linked to climate change (Lindgren and Gustafson, 2001), but the increase in temperature (1989) actually occurred after the change in TBE so could not have been responsible for it (Randolph, 2004a).

Temporal correlations between changes in TBE and potential explanatory variables (vertebrate abundance, land use and cover, temperature, pesticide use) will be examined with a breakpoint analysis. Breakpoint analysis is capable of detecting significant changes in the coefficient of a regression model (Zeileis, 2006), for instance a change in the constant, which would indicate a step change in the variable of interest (Zeileis et al., 2010). For a causal relationship, changes in the explanatory variables must precede or be concurrent with, but not post-date, changes in TBE.

One factor that cannot be examined spatially, but will be included in temporal analysis regardless, is pesticide use. It has already been mentioned that agricultural and industrial policies were implicated in the increase in TBE in Central and Eastern Europe in the early 1990s (Sumilo et al., 2008b).

This chapter will first present a spatio-temporal model which assesses the influence of vertebrate abundance, land use, climate and human socioeconomic variables on the

incidence and distribution of TBE. The variables found to be significant will be examined for changes through time that may coincide with changes in TBE case numbers between 1975 and 2010.

3.2. Materials and methods

3.2.1. Modelling of the distribution and number of cases of TBE by district 2001-2009

The number of TBE cases per district was extracted for each year between 2001 and 2009 (accessed on the 29 February 2012 from the Robert Koch Institute via the SurvStat website, <http://www3.rki.de/SurvStat>). The data for the districts of Berlin were combined to give comparability with the explanatory variables. Explanatory variables for the distribution and number of cases of TBE included satellite-derived environmental variables, socioeconomic variables, land use and vertebrate numbers.

The population size, Gross Domestic Product (GDP), percentage of the working population who are unemployed and number of cars in each district were available from the German Statistical Office. Land use data were only available from the German Statistical Office for 2000, 2004 and 2008 so linear interpolation was used to fill the intervening years. Woodland was expressed as the percentage of the area of each district.

To produce an estimate of the numbers of boar, roe deer and red deer, estimated population data were accessed from the German hunting association, Deutscher Jagdschutz Verband (www.jagd-online.de, accessed January 2010). These data were only available on a state level. The numbers of vertebrates per district were calculated by multiplying the density of animals per hectare of woodland over the state, by the woodland area in hectares for each district.

Altitude at the centroid of each district was extracted from a digital elevation model using ArcMap 10 (ESRI, 2011). Moderate Resolution Imaging Spectroradiometer

(MODIS) satellite images with a resolution of $1/120^{\text{th}}$ of a degree, which is about 1km at the equator, were used. The MODIS images used were daytime and night-time land surface temperature (dLST and nLST respectively), Middle Infrared Red (MIR) and the Normalized Difference Vegetation Index (NDVI). MODIS data were extracted for each month from 2001 to 2009. To create an estimate of each variable appropriate to each district, MODIS variables were extracted not only for the centroid, but also for four additional surrounding points. The placement of these points was dependent on the size of the district; the points were in a square around the centroid with each side as the square root of the area of the district (Fig. 3.1). This is based on the assumption that each district is roughly square and the result is that the conditions in the whole district are accounted for. The average size of a district in Germany was 865km^2 , so the average side length of the square was 29km. After the MODIS variables were extracted for these five points per district, they were averaged. Three-monthly moving averages of MODIS variables were created, i.e. for January, February, March, then for February, March, April, and so on until the December, January, February average. The three-monthly averages from September, October, November onwards were associated with TBE of the following year.

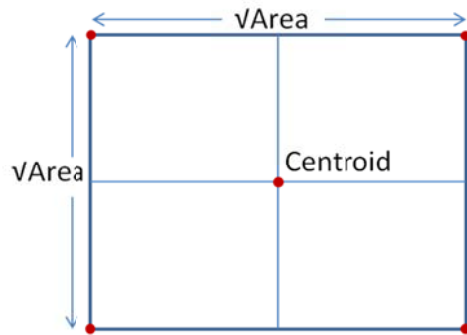


Figure 3.1. For each district, the MODIS variables were measured at five points. One point was the centroid. The remaining four points were selected as a square around the centroid, with the side length of the square as the square root of the district size. The average of each MODIS variable at these five points was used in spatio-temporal modelling.

Moran's I was used to measure the spatial autocorrelation of TBE across the districts of Germany (2001-2009) and was calculated in ArcMap 10 using the Moran's I based on

polygon contiguity (ESRI, 2011). As only contiguous polygons are used, the district of Landkreis Rügen was excluded as it shares no borders with other districts.

Using the yearly TBE data for each district and the explanatory variables already outlined, a model was created that accounted for covariates and spatio-temporal autocorrelation in the data. This model was created using a framework approach, which means that the effect of the covariates is modelled and then the spatio-temporal autocorrelation is estimated; this process is then iterated. The covariates and spatio-temporal autocorrelation shared a common posterior distribution.

First the significant covariates were selected. This was undertaken with an algorithm written in R (R Development Core Team, 2012) which searches the available variables for the best model, using Akaike's Information Criterion ('AIC') as the best fit criterion. This method, known as the headlong search strategy, is a stepwise variable selection method with two stages (Raftery and Dean, 2006). In the first stage, a variable is proposed for addition to the set of selected variables. To be selected a given variable should reduce the AIC of the model; if not, the proposed variable goes to the end of the list of potential explanatory variables, and another variable is considered. In the second stage of the algorithm, each of the variables currently in the model are tested using AIC to discover if they should be removed. The addition and removal of variables is iterated until no further variables are added or removed. The programme used a general linear model with a Poisson family because the yearly TBE data are 'counts'. To avoid local minima, an increase in AIC, i.e. a worse model, was tolerated at the beginning of the process of the algorithm.

The variables selected were included as covariates in a Bayesian spatio-temporal general linear model ('BSTGLM') of TBE in Germany (2001-2009). The model combines pre-built routines from the "ramps" package (Smith et al., 2008) in R (R Development Core Team, 2012), with additional elements written specifically for this task. The basis of

the model was a generalised linear model with covariates. The form of this model is given by the following function (Lindstrom and Bates, 1990; Pinheiro and Bates, 2000):

$$gi_{s,t} = \mathbf{X}\beta' + e_{s,t} \quad (\text{Equation 3.1})$$

where $gi_{s,t}$ is the number of TBE cases at a given time, t , and point in space, s ; β' is a vector of fixed-effects parameters of length p (where p is the number of covariates); $\mathbf{X}$ is the $(s \times t) \times p$ fixed-effect matrix of the covariates; and e is a normally distributed noise term. A spatio-temporal autocorrelation component, $\mathbf{Z}$, is included in this model:

$$gi_{s,t} = \mathbf{X}\beta' + \mathbf{Z} + e_{s,t} \quad (\text{Equation 3.2})$$

$\mathbf{Z}$ is a one column matrix, of length $s \times t$, which gives the spatio-temporal autocorrelation values of each point. The covariance matrix of $\mathbf{Z}$ is given by the product of the spatio-temporal variance and the variogram, a measure of the spatio-temporal relationship of TBE at one point with surrounding points in space and time (Oliver and Webster, 1991). $\mathbf{Z}$ is multivariate normally distributed, with mean zero. The variogram, γ , used here is a space-time non-separable exponential function (Cressie and Huang, 1999):

$$\gamma = \exp\left(-\frac{d}{\pi_d} - \frac{t}{\pi_t} - \lambda\left(\frac{d}{\pi_d}\right)\left(\frac{t}{\pi_t}\right)\right) \quad (\text{Equation 3.3})$$

where d is the Euclidean distance in space; π_d the spatial range; t the difference in time; π_t the temporal range; λ is a constant to rescale the space-time interaction.

The variances can be divided into those for the fixed effects, the spatial effects and the measurement error (Smith et al., 2008), allowing a better approximation of the likelihood. The measurement error can be split for each district according to the weights, which in this case are the area of the district (Cowles et al., 2009).

The Bayesian elements of the model are:

- a) the spatio-temporal covariance matrix estimated using the shrinkage method (Daniels, 1999);

- b) the coefficients for fixed effects are random variables;
- c) posterior inference achieved through applying an Monte Carlo Markov Chain (MCMC) method (Tierney, 1994).

Six variables were estimated as random variables through the MCMC method, with the following prior distributions:

$$\beta' \sim \text{flat distribution with infinite range} \quad (\text{Equation 3.4})$$

$$\sigma_e^2 \sim IG(\text{shape} = 3, \text{scale} = 0.1) \quad (\text{Equation 3.5})$$

$$\sigma_s^2 \sim IG(\text{shape} = 3, \text{scale} = 0.1) \quad (\text{Equation 3.6})$$

$$\pi_d \sim U(\text{min} = 25000, \text{max} = 75000) \quad (\text{Equation 3.7})$$

$$\pi_t \sim U(\text{min} = 6, \text{max} = 9) \quad (\text{Equation 3.8})$$

$$\lambda \sim U(\text{min} = 0.25, \text{max} = 0.75) \quad (\text{Equation 3.9})$$

where σ_e^2 and σ_s^2 are the residual error and spatial variances respectively. *IG* stands for Inverse Gamma distribution, a form chosen for two reasons: (i) computation; the *IG* is the conjugate prior for the variance of a Gaussian distribution; (ii) sampling exploration; the higher the value of the shape parameter, the less the information given by (i.e. required from) the prior, thus the result is more data-driven. The coefficients for the fixed covariates, β' are provided with an infinite prior allowing a full and un-biased exploration of the coefficients. The prior distributions for π_d , π_t and λ were uniform (*U*).

3.2.2. Long term data

TBE data prior to 2001 were collected from the International Scientific Working Group on TBE (ISWTBE). Since 2001 TBE data have been available from the Robert Koch Institute website (<http://www3.rki.de/survstat>, accessed December 2011). TBE data were collected for the country and the individual states when available.

Based on the above spatio-temporal model, changes in temperature, land use,

vertebrate numbers and pesticide usage were considered as factors that could have influenced TBE incidence (Table 3.1). Numbers of roe and red deer, and the wild boar hunting bag were available from the German hunting association, Deutscher Jagdschutz Verband. Pesticide and insecticide usage (tonnes of active ingredient) information for Germany was available from Eurostat. Data on the area of land used as woodland and for agriculture were available from Eurostat, and were supplemented with additional comparable data from the German statistical office, Destatis.

Temperature data were available from the German Meteorological Service, Deutscher Wetterdienst. Data were extracted for Baden-Württemberg (BW) and Bavaria (BV), which are the two most southern states in Germany. Six meteorological stations were selected for BW and seven for BV (Table 3.2). Stations were selected if they had temperature data from 1975 to 2010 to coincide with the TBE data. Monthly averages of the maximum temperature were calculated using data from the selected sites within each state. Ten-day (dekadal) averages were also calculated for the maximum temperature in April, May and June.

3.2.3. Temporal data analysis (1975 -2010)

Temporal analysis was undertaken in the R statistical package (R Development Core Team, 2012), using the package *strucchange* (Zeileis et al., 2002). *Strucchange* fits a regression model, but can detect if there are significant changes in the slope or constant term (Zeileis et al., 2003). Models for TBE in all Germany, and BW and BV separately, were fitted with a constant, i.e. $TBE \sim 1$, and then significant changes in this constant over the period of interest were sought (Zeileis et al., 2010). The Bayesian Information Criterion (BIC) was used to select the best number of breakpoints in the model. BIC is less sensitive to changes in the variable of interest than AIC because adjustment for the number of parameters is $\log(n)$, not n . BIC is the recommended criterion by which to select the number of breakpoints when modelling structural changes in a regression (Bai and Perron,

2003). Breakpoints are given as the last datapoint before the change. Monthly and dekadal temperature series, land use, vertebrate numbers and pesticide use were analysed in the same way. If one of these explanatory variables had contributed to changes in TBE, the two series (cause and effect) should show similar transitions, either at the same point or with the causal series slightly earlier in time. Although concurrent changes cannot prove causality, discordance can rule out factors and highlight potential routes for further investigation.

Table 3.1. Details of data used as potential explanatory variables in temporal breakpoint analysis, including the source and spatial resolution.

Data	Source	Website	Resolution	Dates Available	Accessed
Temperature	Deutscher Wetterdienst	www.dwd.de	State	1975-2010	June 2012
Roe & red deer, wild boar	Deutscher Jagdschutz Verband	www.jagd-online.de	State	1983-2010	January 2010
Pesticides and Insecticides	Eurostat	http://epp.eurostat.ec.europa.eu	Germany	1980-2008	June 2012
Woodland part 1	Eurostat	http://epp.eurostat.ec.europa.eu	State	1977-2006	June 2012
Woodland part 2	Destatis	https://www.destatis.de	State	1992-2010	June 2012
Utilised Agricultural Area	Eurostat	http://epp.eurostat.ec.europa.eu	State	1975-2010	June 2012

Table 3.2. Sites of meteorological stations used for temporal analysis.

State	Meteorological stations
Baden-Württemberg	Mannheim, Öhringen, Stötten, Freudenstadt, Stuttgart, Konstanz
Bavaria	Hohenpeißenberg, Oberstdorf, Hof, Weiden, Würzburg, Kempten, Nürnberg

3.3. Results

3.3.1. Changes in the distribution of TBE 1997 - 2010

The extent to which the distribution of TBE is expanding in Germany was assessed using TBE risk maps produced by the Robert Koch Institute (RKI) between 1998 and 2011. Before 2006 a risk area was classed as a district with at least five cases during a five-year period in the previous twenty years (Robert Koch Institute, 2007). Following 2006, a risk area was classed as a district or district region (where district region includes the adjacent districts) with an incidence of TBE significantly higher than 1 case per 100,000 people.

Only districts in the south of the country are considered by the RKI as risk areas, despite cases being seen in more northerly areas (Fig. 3.2). New TBE risk areas were seen between 1998 and 2005 in BW, BV (labelled Bayern, the German name), Thuringen, Hessen and Rheinland-Pfalz (shown in orange in Fig. 3.2). Of these, the greatest changes in the TBE distribution were in BV; in 2001 seven of the eight new risk areas were in BV. New risk areas can be split into two groups: those areas that are surrounded by earlier risk areas, and those areas that are further north of the previous 1997 distribution.

In 2006 a number of town districts that are entirely surrounded by high incidence counties, as well as a number of other districts close to risky districts, were newly classed as risky (shown in sky blue). Unfortunately, it is difficult to tell to what extent this is a genuine effect as the definition of a risk area changed in this year. The raw case data from 2001 to 2005 show that some of these new areas had TBE cases previous to 2006 (Fig. 3.3), suggesting a potential artefact in this year.

TBE Risk areas in Germany

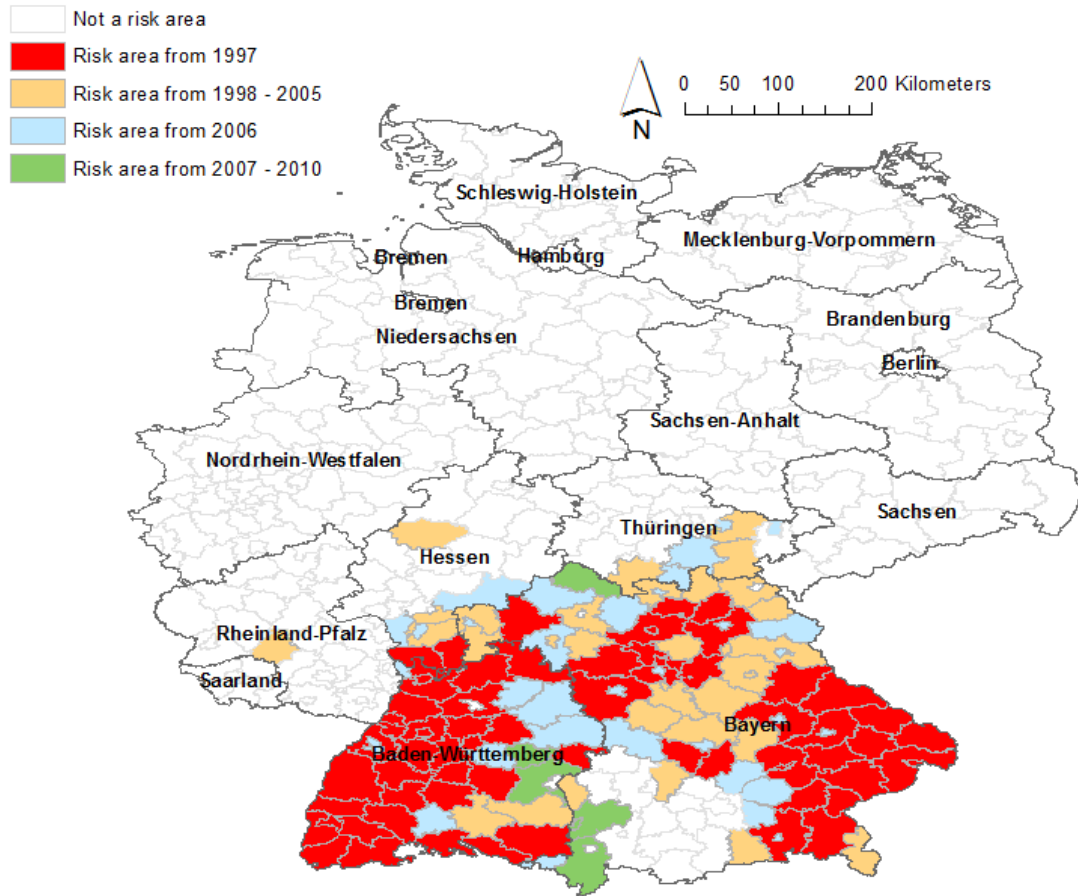


Figure 3.2. Risk areas for TBE in Germany based on maps issued by the Robert Koch Institute. Areas shaded in red have been considered risk areas since 1997. Orange shaded areas were first considered ‘risky’ between 1998 and 2005. Sky blue areas were first considered a risk area in 2006, when the definition of a risk area changed. Five districts were first considered risk areas between 2007 and 2010 (shown in green).

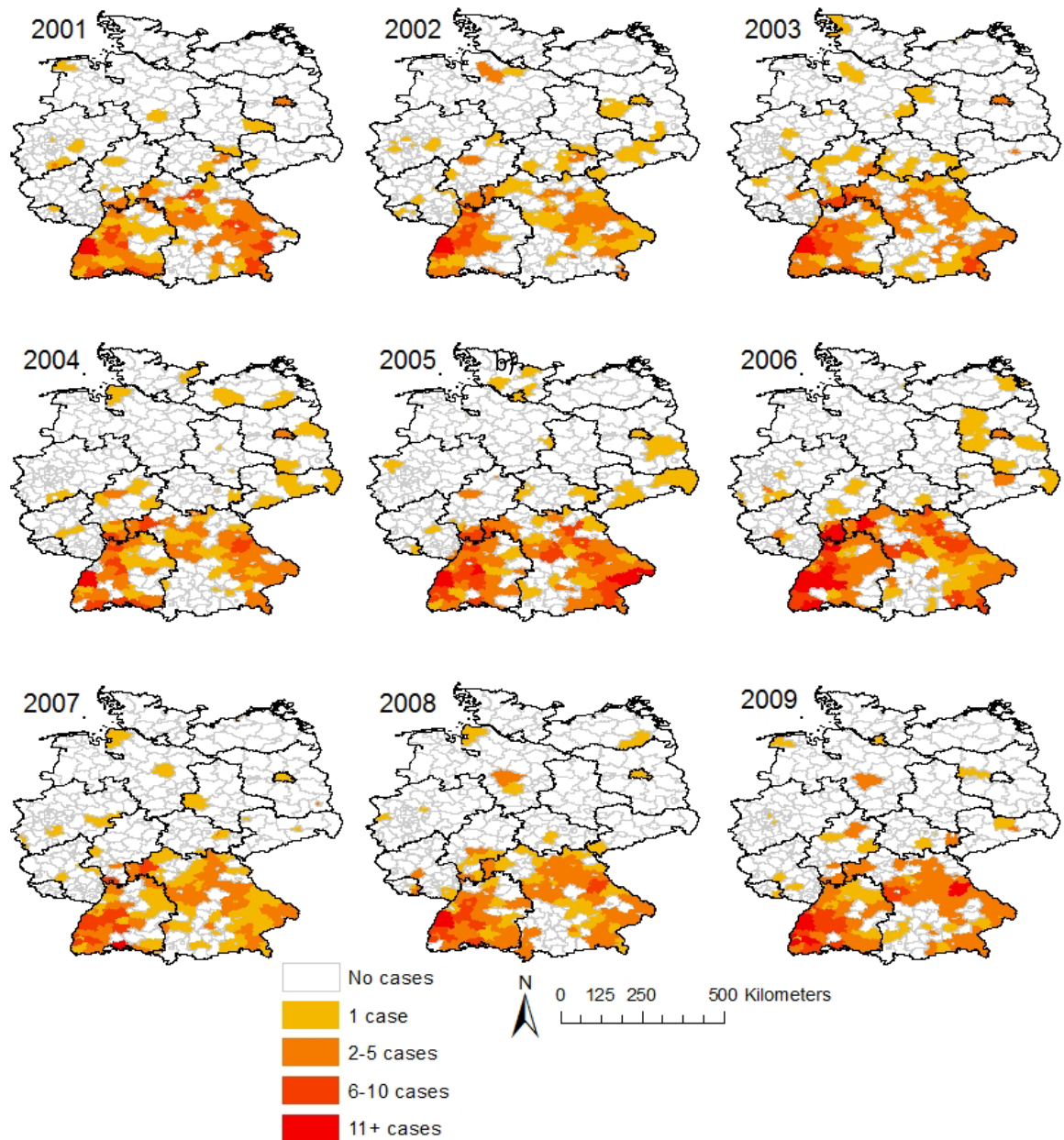


Figure 3.3. Maps detailing the annual distribution of TBE cases in Germany between 2001 (top left map) and 2009 (bottom right map).

From 2001 to 2009, 64-74% of cases were recorded in districts considered risky from before 1997, 12-17% in districts first considered risky between 1998 and 2005 and 3-8% from districts first considered risky in or after 2006. In 2006 there were 546 cases of TBE; this represents around 210 excess cases compared with the mean of 2005 and 2007. The peak in cases of TBE in 2006 was a result of extra cases in all districts, irrespective of when they were first designated a risk area (Fig. 3.4). The areas first considered a risk in

2006 were associated with only 12 of the ‘excess’ cases when compared with the 2005 and 2007 mean. Between 2001 and 2009 changes in incidence occurred in all areas regardless of when they were first considered risky, presumably through such effects as new micro-foci of disease, changes in tick biology or human behaviour.

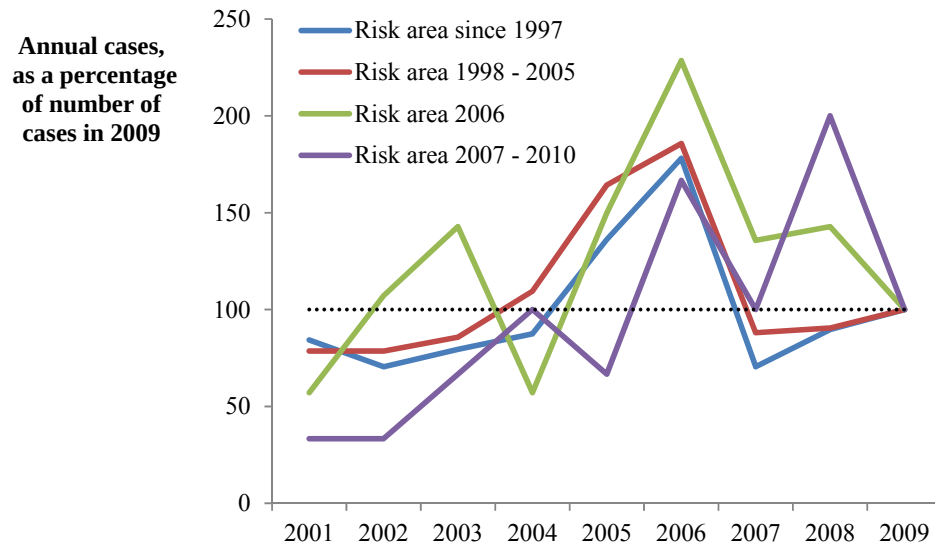


Figure 3.4. Annual TBE cases, as a percentage of the case numbers in 2009, in districts of Germany grouped according to the year the district was first considered ‘risky’.

3.3.2. The role of human and environmental factors in the distribution of TBE between 2001 and 2009

Covariates for a spatio-temporal model of TBE in Germany 2001 to 2009 were selected using the headlong search strategy, which selects the variables most capable of fitting the data, with AIC as the discriminating criterion. Models were fitted with a GLM with between three and seven variables, from a possible 61 (Fig. 3.5). The model with five variables was chosen because it showed a significant improvement on the four-variable model (a decrease in AIC of 550) but the difference between the five and six variable model was much lower (a decrease in AIC of 330). The first variable selected in all models (with between three and seven variables) was unemployment. After this, a combination of abiotic and biotic factors was included in the GLM (Table 3.3).

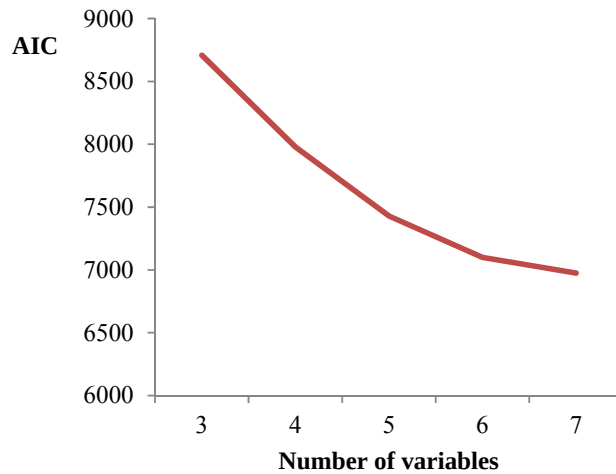


Figure 3.5. AIC for GLM models with between three and seven explanatory variables.

Table 3.3. Coefficients for the covariates in a Poisson GLM for all Germany, a Poisson GLM including only BW and BV, and the full Bayesian spatio-temporal linear mixed model (BSTGLM).

Variable	GLM		GLM for Baden-Württemberg & Bavaria		BSTGLM (95% CI)	
Intercept	-81.70	***	-78.71	***	16.103	(11.950, 0.451)
Unemployment (%)	-0.1526	***	0.0151		0.0115	(0.00332, 0.0322)
dLST Dec, Jan, Feb	-0.1911	***	-0.0467	***	-0.107	(-0.13439, -0.0723)
nLST July, Aug, Sept	0.4701	***	0.3187	***	0.0459	(0.0266, 0.0579)
Red deer abundance	-0.0047	***	-0.0031	***	-0.00442	(-0.00445, -0.00414)
Roe deer abundance	0.0003	***	0.0003	***	0.00046	(0.00044, 0.00047)
Spatial range (metres)					25073	(25048, 25074)
Temporal range (years)					6.0305	(6.0301, 6.0309)
Spatio-temporal interaction					0.25032	(0.25031, 0.25036)

There is significant spatial autocorrelation in TBE in Germany between 2001 and 2009 (Moran's $I = 0.529$, score=18.9, p-value<0.0001), so a simple GLM is inappropriate, and a Bayesian spatio-temporal General Linear Model (BSTGLM) was fitted with the five selected covariates. The model converged on the coefficients after 2000 iterations, during which the loglikelihood of the model improved by 15.13%. The final Deviance Information Criterion was 8421. Cross-validation, where a single point is removed from the dataset and the model is refitted, was repeated 100 times to test the model fit. Ideally the mean error should be around 0 and the squared deviation ratio would be 1 when using

this method (Webster and Oliver, 2007). Validation gave a mean error of 0.11445 and a squared deviation ratio of 1.20551. The error distribution shows no spatial trend (Fig. 3.6d) but the response variable is over predicted in the north (Fig. 3.6b).

The spatio-temporal elements of the fitted BSTGLM show that the range of spatial autocorrelation is approximately 25,000m and the temporal autocorrelation is a little over 6 years (Table 3.3). The TBE status of districts within 25km of any given district therefore have an influence on its TBE status. Considering that the average district size in Germany is 865km², which given the model considers the district area as a circle would give an average radius of the district as 16.6km, this means that districts are only correlated with the closest two districts. TBE status in a district also influences the status of that district for the following 6 years. There is also an interaction between the spatial and temporal autocorrelation, so the status of surrounding districts in year one would have an influence on the status of a given district in year two. However, the coefficient for the spatio-temporal interaction is only 0.25, suggesting the separate spatial and temporal are more important in shaping TBE than the combined spatio-temporal effect.

The coefficients of all the covariates are significantly different from zero, indicated by the 95% confidence intervals which do not include zero (Table 3.3). The variables are therefore important in predicting the number and distribution of cases of TBE in Germany, even when spatio-temporal autocorrelation is accounted for. Some of the coefficients in the BSTGLM are considerably smaller than in the normal GLM, including that for unemployment and mean night-time LST for July, August and September (nLST JAS), because some of the variation in the data is explained by the spatio-temporal autocorrelation.

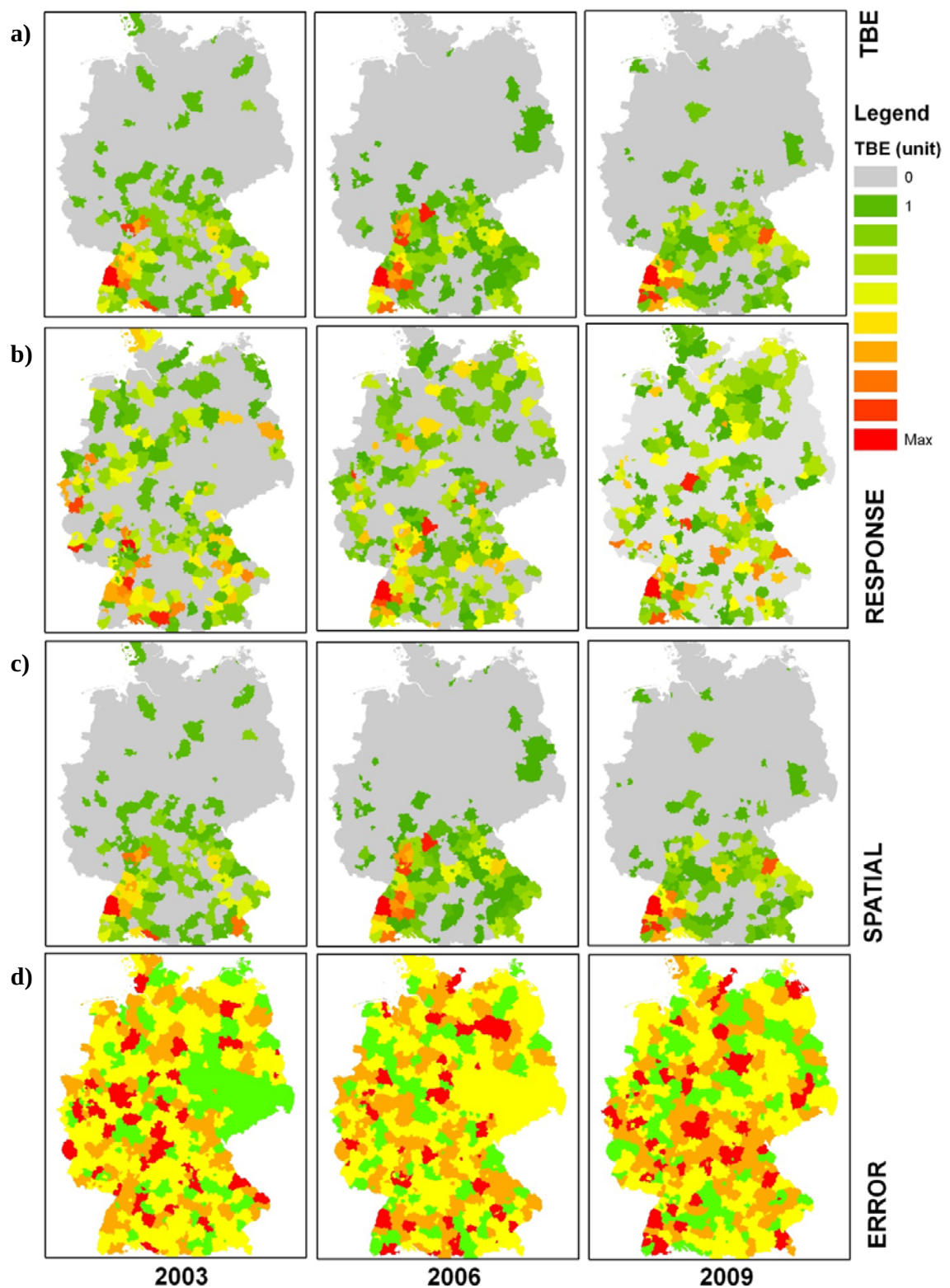


Figure 3.6 Maps for the distribution of a) the original TBE data, b) the fitted response, c) the spatial correlation and d) the error in the fitted model in 2003 (left-hand column), 2006 (middle column) and 2009 (right-hand column). In the error maps, red indicates an error of one standard deviation.

The two temperature variables included in the final BSTGLM are mean daytime LST for December, January and February and mean night-time LST for July, August and September. When the average daytime temperature in December, January and February in 2009 is mapped, it can be seen that it varies from warm in the north-west to cool in the south-east (Fig. 3.7b); this correlates with the clear latitudinal differences in TBE (Fig. 3.3). There is no latitudinal trend for night-time LST in July, August and September, but the warmest summer area is in north Baden-Württemberg (Fig 3.7a), where TBE is highest. Yearly variation in these temperature variables shows a particularly warm winter in 2007 and 2008 and warm summer in 2007 (Fig. 3.8c,d), but other years show similar temperature patterns.

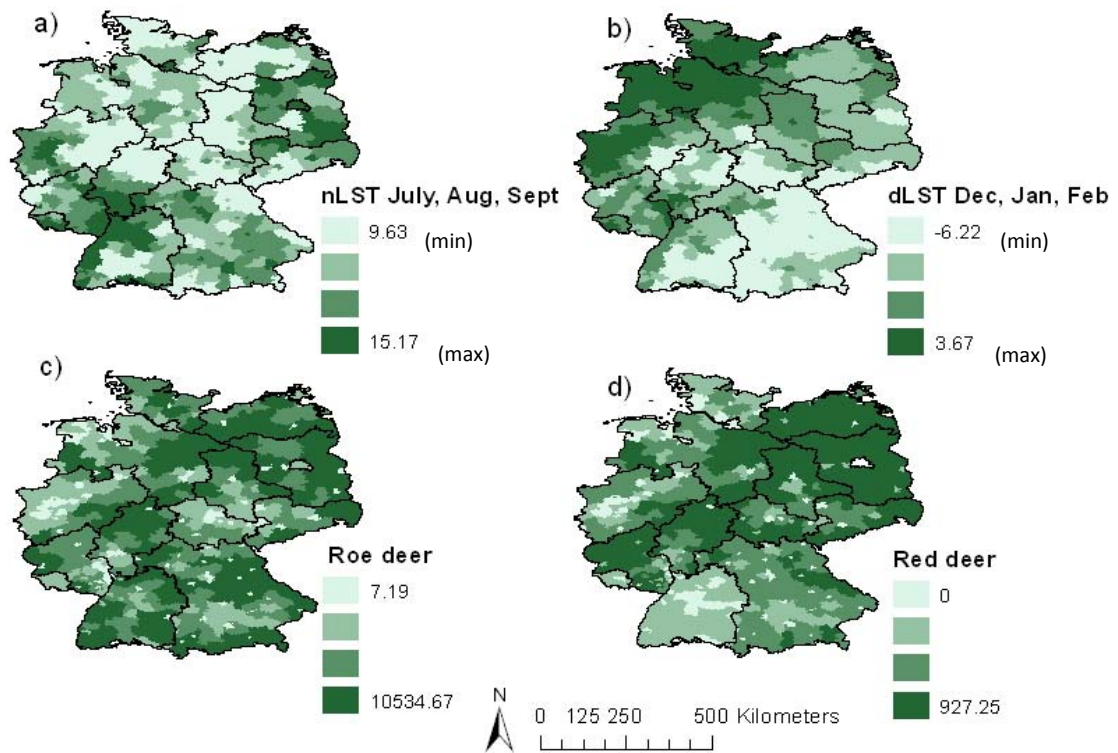


Figure 3.7. Distribution of (a) average nLST in July, August and September, (b) mean dLST in December, January and February, (c) roe deer abundance and (d) red deer abundance across Germany in 2009. The distribution is given in quartiles (i.e. <25%, 25-50%, 50-75% and >75% of the frequency distribution) with the minimum and maximum value for each variable given in the legend.

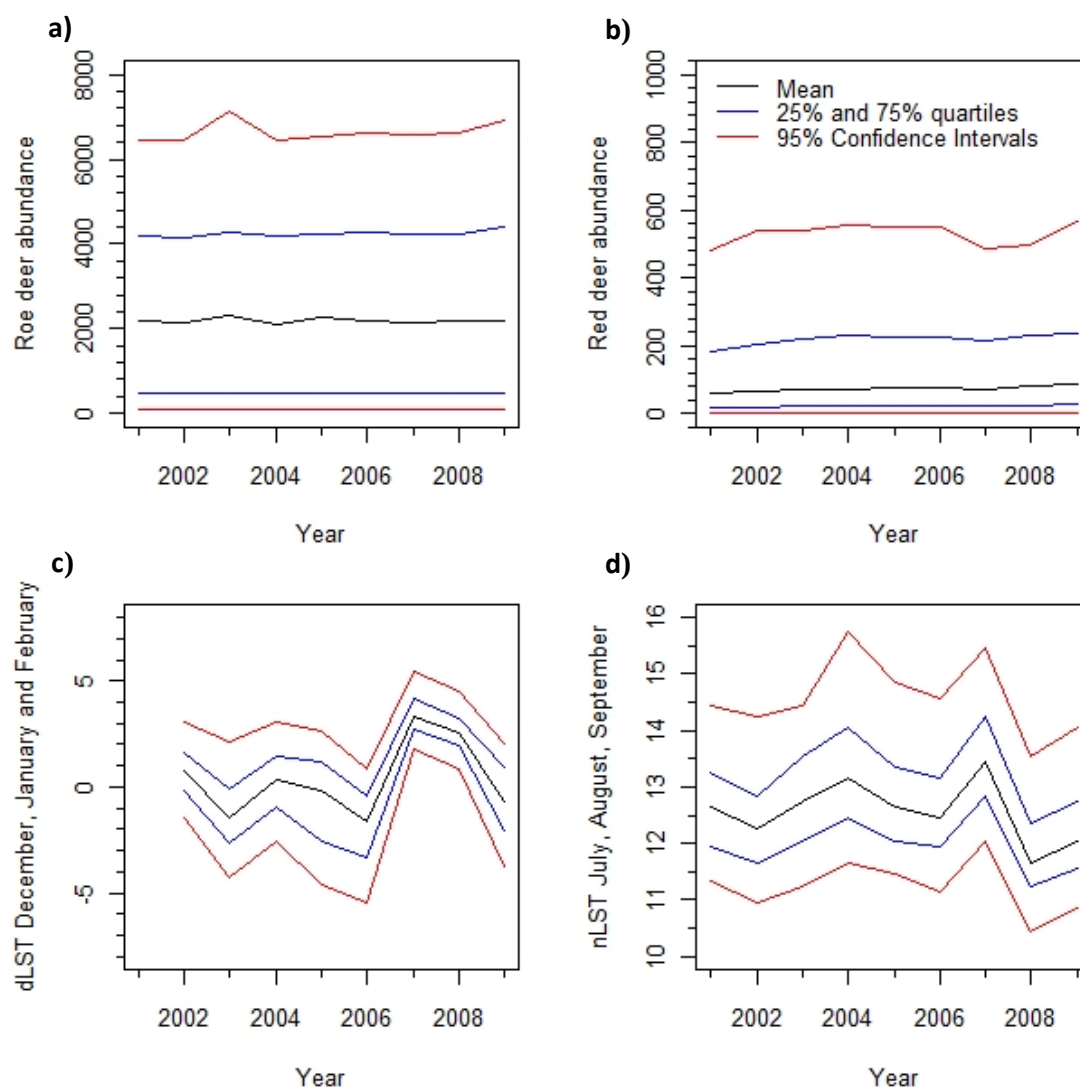


Figure 3.8. Yearly variation in a) roe deer abundance, b) red deer abundance, c) the average dLST in December, January and February and d) the average nLST in July, August and September (2001-2009). The annual average value for all districts is shown with a black line, the 25% and 75% quartiles with blue lines and the 95% confidence intervals (for the mean) in red.

The abundance of red and roe deer per district, calculated on the basis of the amount of woodland in each district and the state estimates of vertebrate abundance, were selected as significant predictors in the model. Red deer abundance is higher in the north-east of Germany, giving the negative correlation with TBE (Fig. 3.7d). Roe deer are distributed fairly evenly across the country and the differences in roe deer abundance within a state are related to the area of woodland per district. This suggests both roe deer abundance per state and the distribution of woodland between districts are important in predicting TBE.

Red and roe deer abundance are stable throughout the 2001 to 2009 period (Fig. 3.8a,b).

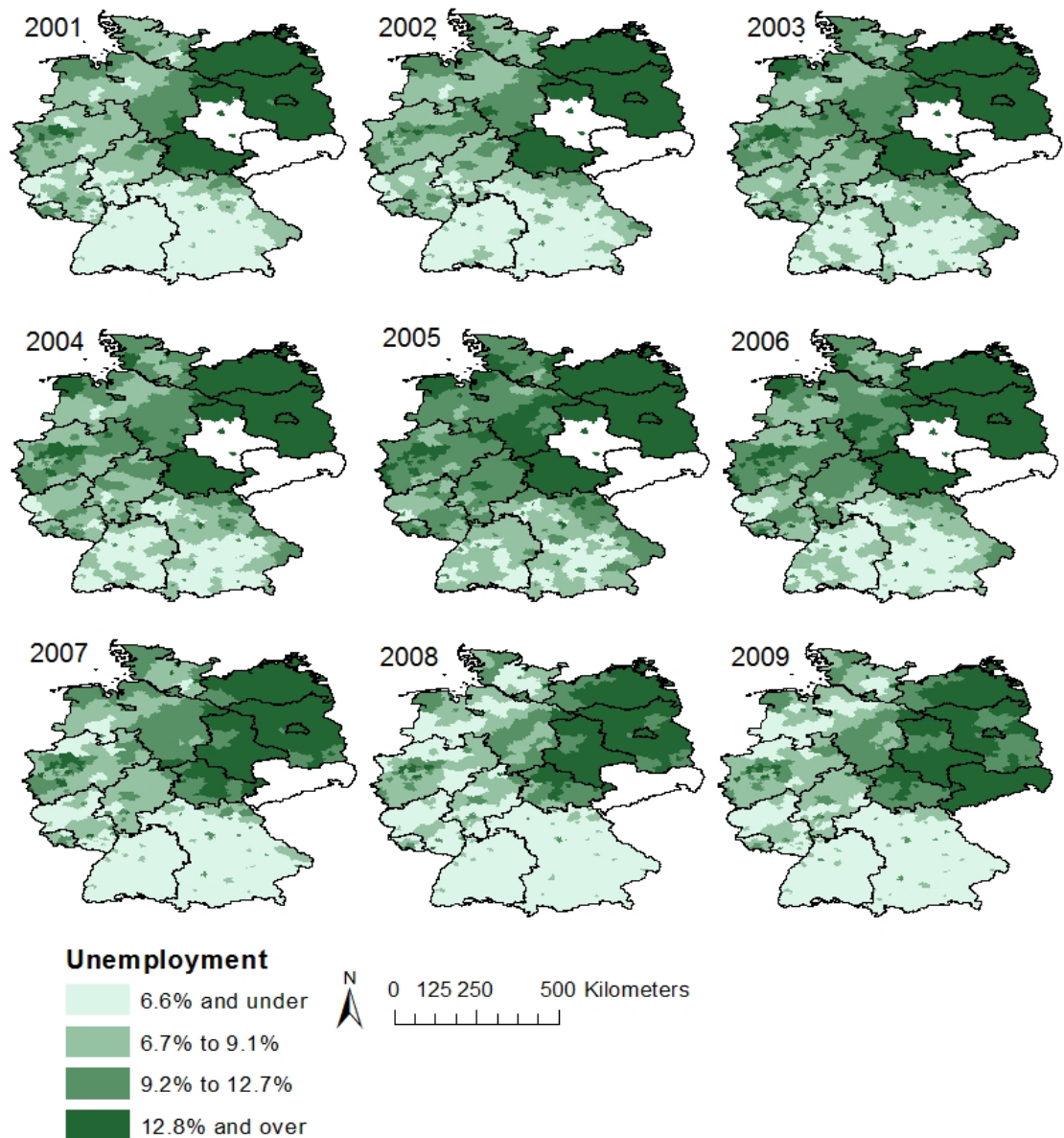


Figure 3.9 The proportion of the working age population who are unemployed across Germany (2001-2009). The darker colours indicate higher unemployment.

Unemployment has a negative coefficient in the GLM, but once spatio-temporal autocorrelation is accounted for in the BSTGLM, the coefficient is positive.

Unemployment is highest in the north-east of Germany (Fig. 3.9), which is why it was negatively correlated with TBE in the GLM. The gross latitudinal trend in unemployment obscures the finer detail of the relationship, and once this trend is accounted for with the

spatio-temporal autocorrelation in the BSTGLM, a positive relationship is revealed. To further demonstrate this, a GLM fitted with only data for BW and BV shows unemployment has a non-significant positive coefficient (Table 3.3).

3.3.3. TBE incidence 1975 - 2010

Having established that temperature and deer abundance per district (which is a function of the amount of woodland per district and abundance of deer across the state) are important to the distribution of TBE, these factors can be examined through time to see if any changes are coincident with changes in TBE incidence. Boar abundance and pesticide use through time were also examined.

TBE incidence in Germany showed two step increases between 1975 and 2010 (Fig 3.10). This is mirrored by increases in BW and BV. There are three clear phases in the pattern during the period; up to 1991, between 1992 and 2000 and from 2001 to 2010. Each of these three phases had a peak year of cases, which were 1982, 1994 and 2006 respectively. There was a five-fold increase in the average number of cases between the first and second phase and a two-fold increase between the second and third phase (Table 3.4).

Up to 1991, the annual pattern in the total number of TBE cases in Germany is due equally to the patterns in BV and BW, with slightly more cases recorded in BV than in BW. The step increase in TBE in Germany in 1992 is mostly a result of excess cases in BW, so in the second phase the total number of cases in Germany predominantly reflects cases in BW (Table 3.4). The average number of cases in BV in the first and second phase is relatively stable. This situation is reversed between the second and third phase, as cases in BW increased by an average of only around 30 cases a year (around 26%), but cases in BV increased 3-fold. This increase in BV, coupled with new cases in other areas of Germany, was the principal cause of the increase in national case numbers following 2000.

There is no significant trend during any of the three phases of TBE in Germany

(linear regression for trend, $p > 0.05$). Similarly, there is no significant trend before or since 1992 in BW. In BV, there is a weakly positive trend before 2001 (coefficient=1.113, $t=2.165$, $p=0.04$), but no trend since 2001.

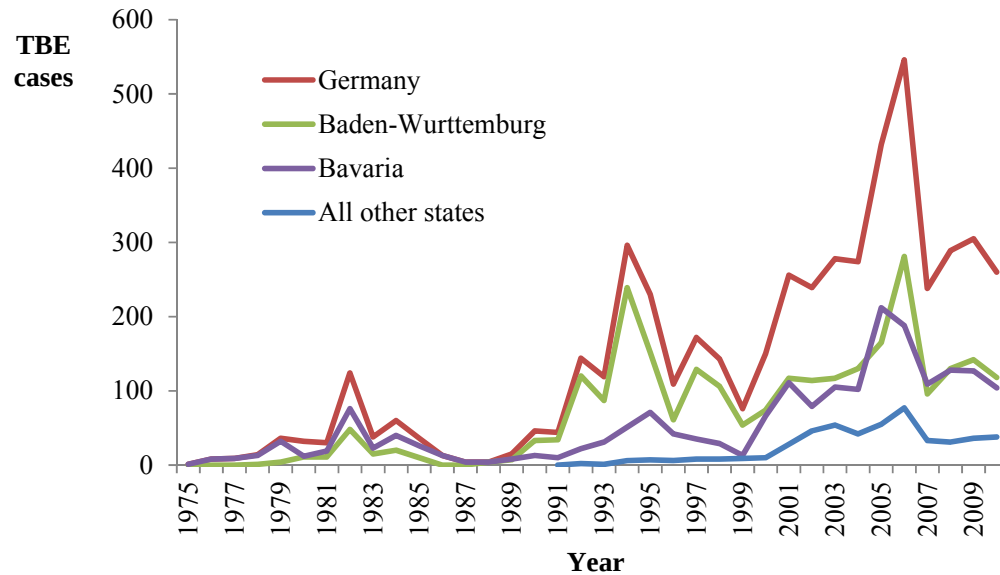


Figure 3.10. Cases of TBE in the whole of Germany, and in the states of Baden-Württemberg, Bavaria and all other areas of Germany between 1975 and 2010.

Table 3.4. Annual average TBE case numbers $\pm$ standard deviation, in Germany, BW and BV in three time periods between 1975 and 2010.

Area	1975 – 1991	1992 – 2000	2001 - 2010
Germany	30.24 $\pm$ 29.81	159.89 $\pm$ 66.64	311.70 $\pm$ 99.43
BW	11.65 $\pm$ 14.34	113.56 $\pm$ 57.15	141.00 $\pm$ 52.55
BV	18.29 $\pm$ 18.15	40.00 $\pm$ 19.50	126.50 $\pm$ 41.45

To test these observations more formally, linear models with only a constant (no trend through time) were fitted, but with breakpoints allowed in the constant, reflecting the step changes. BIC was used to measure the goodness of fit of models with differing numbers of breakpoints; the model with the lowest BIC is best. As suspected, total TBE cases for Germany demonstrate two breakpoints in 1991 and 2000 (Table 3.5, Fig. 3.11). The breakpoints method returns the breakpoint as the last year before the change, so the increases actually occurred in 1992 and 2001. These steps are associated with an increase in TBE in BW after 1991 and in BV after 2000 (Table 3.5, Fig. 3.12). This difference in

timing in the two southern states is highly valuable in assessing the potential causal factors.

Table 3.5. Breakpoint analysis results for the total number of cases in Germany, and in the states of BW and BV.

	BIC for Breakpoints†				Breakpoint 1 (95% CI)	Breakpoint 2 (95% CI)
	Zero	One	Two	Three		
TBE, all Germany	461.72	433.12	420.90	426.28	1991 (1988-1992)	2000 (1998-2004)
TBE, BW	415.81	382.25	385.09	389.92	1991 (1988-1992)	
TBE, BV	394.71	354.22	352.60‡	355.96	2000 (1998-2001)	

†Bold indicates best model

‡Although this BIC is lower than the model with 1 breakpoint, the confidence intervals of the breakpoints overlapped, so a model with one breakpoint was selected. The model with two breakpoints had breakpoints in 1999 and 2004.

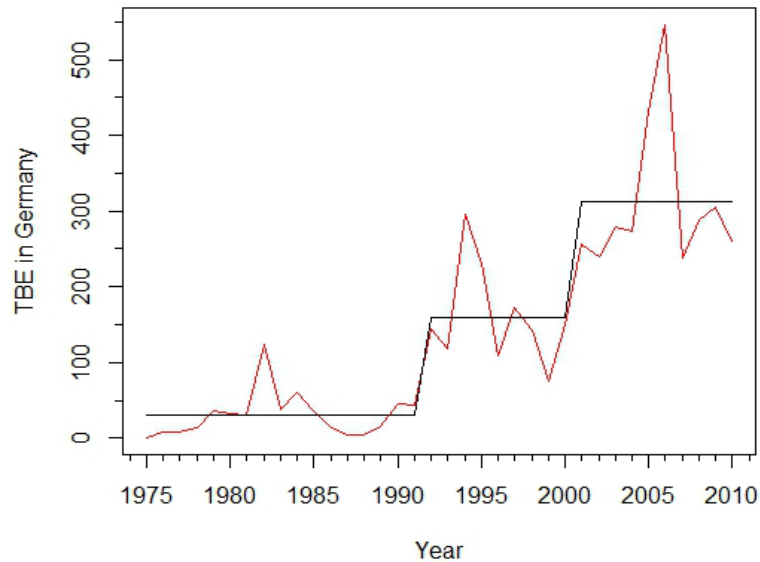


Figure 3.11. Number of cases of TBE in Germany (shown in red, between 1975 and 2010) with the model fitted with breakpoint analysis (shown in black). Three phases of TBE in Germany can be observed, with breakpoints in 1991 and 2000.

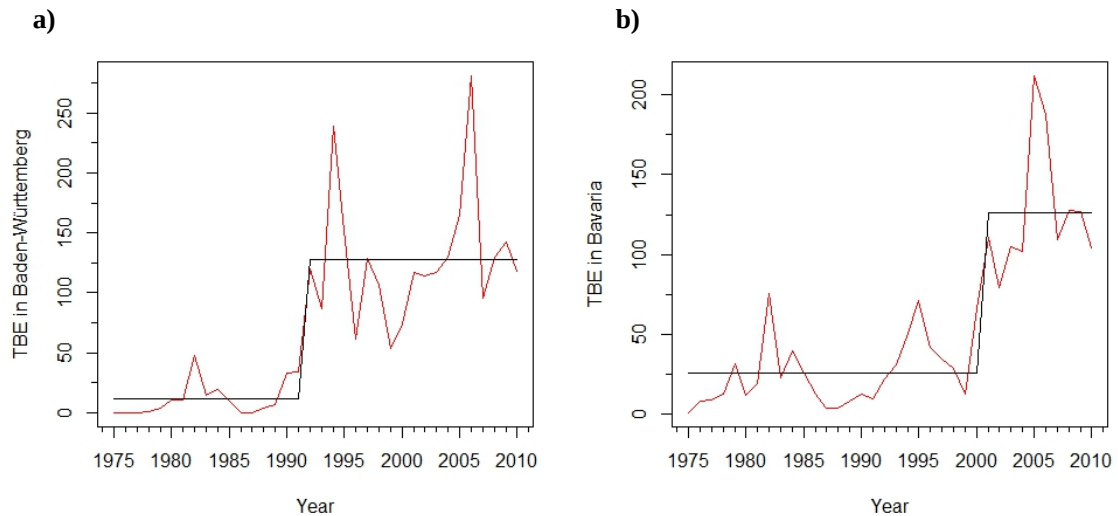


Figure 3.12. TBE cases in a) BW and b) BV (1975-2010, shown in red). Models with a single breakpoint were fitted to each dataset (fitted values shown in black)

3.3.4. Changes in the measurement of TBE

The possibility that changes in TBE case numbers are an artefact of changes in the way TBE is diagnosed and reported should first be examined. For the first step change in 1991, opinion is mixed as to whether the change is ‘real’ or an artefact. On one hand, increases in case numbers during the 1980s and 1990s were thought to be due to increased intensity of questioning of doctors, mostly in BW (Fiedler et al., 1999). The absence of increase in BV was attributed to an increase in vaccination levels in this state, especially in highly endemic Passau (Roggendorf, 1996). These statements are qualitative, however, with no quantitative evidence. Others suggest the changes in TBE are ‘real’, i.e. not an artefact. For instance, the peak in cases in 1994 was thought to be associated with warm winter and summer (Kaiser, 1995). Further, in 1997 and 1998 an extensive survey of doctors was undertaken (Fiedler et al., 1999), but the case numbers reported were in line with previous years, suggesting that at least by this point reporting was thorough enough.

In 2001 the Infection Protection Act made TBE a notifiable disease in Germany. In 2001, 106 cases were recorded in BV under the new surveillance system, compared with 54 which would have been recorded under the previous system (Suss, 2003). In BW 117

TBE cases were recorded under the new system compared with 95 cases under the previous system. Perhaps this more modest increase in BW, in comparison to BV, is because TBE was better known in BW so the majority of cases were already recorded under the previous system. Consistent with this idea is the fact that proportionally, the biggest increases after 2001 were seen in ‘the other states’, i.e. those outside BW and BV, where TBE was scarce in the past.

As well as the effect of changes in the recording system, changes in the method of diagnosis could have had an impact on the reported case numbers. In BW, between 1994 and 2000 TBE was diagnosed by identifying specific IgM and IgG activity in the serum with routine serological tests (Kaiser, 2002), and detection of specific IgM and IgG remains the main diagnostic method (Mantke et al., 2008). A positive Polymerase Chain Reaction (‘PCR’) using a blood or CSF sample is now also recognised (Mantke et al., 2008). PCR is, however, only useful for diagnosis during the first stage of disease (Saksida et al., 2005) and people do not usually present at hospital until the second stage, when TBE is diagnosed with traditional serology methods.

There is no doubt that TBE reporting in Germany has changed since 1975, but changes in the reporting system could have contributed to, or resulted from, increases in TBE cases. Unfortunately the majority of the statements relating to the effect of reporting are qualitative. The evidence for the changes in TBE being artefacts is insufficient to preclude other potential ‘real’ changes in the TBE system, which are also examined.

3.3.5. Land use, vertebrate abundance and pesticide use

Land cover, specifically woodland, and land use, for agriculture, were examined for potential step changes between 1975 and 2010. Visual examination shows that the area of woodland has increased in both BW and BV, but by relatively small amounts (Fig. 3.13). For instance, in BW between 1986 and 1992 there is approximately a 3% increase in woodland coincident with changes in TBE in this state. In BV, there was a 5% increase in

woodland between 1978 and 1989. The patterns of change are not identical in the two states, with an abrupt increase earlier in BV (1979) than in BW (1989), but then followed by more steady increases in both states.

Declines in the Utilized Agricultural Area were seen in BW and BV, with a step reduction in 1978, then a steady decline. Although it is expected that a reduction in agricultural area would favour increases in TBE, steady changes in land use, if they did have an effect on TBE, would be unlikely to cause a step change in case numbers. It is therefore considered more likely that land use changes set a scene permissive for abrupt TBE increases induced by other factors.

Both increases and decreases in the deer population could theoretically affect TBE through boosts to the tick population and the dilution effect. Roe deer populations varied sporadically between 1983 and 2010 in BW, including an increase in roe deer in 1987 (Fig. 3.14). Similarly in BV there was a small increase in roe deer numbers in 1997, which precedes the change in TBE in 2000. However, if increases in roe deer population were solely responsible for increases in TBE in BW in 1991 and in BV in 2000, it is unknown why TBE has not changed in response to the changes in deer population since this e.g. the apparent decrease in BW after 1994.

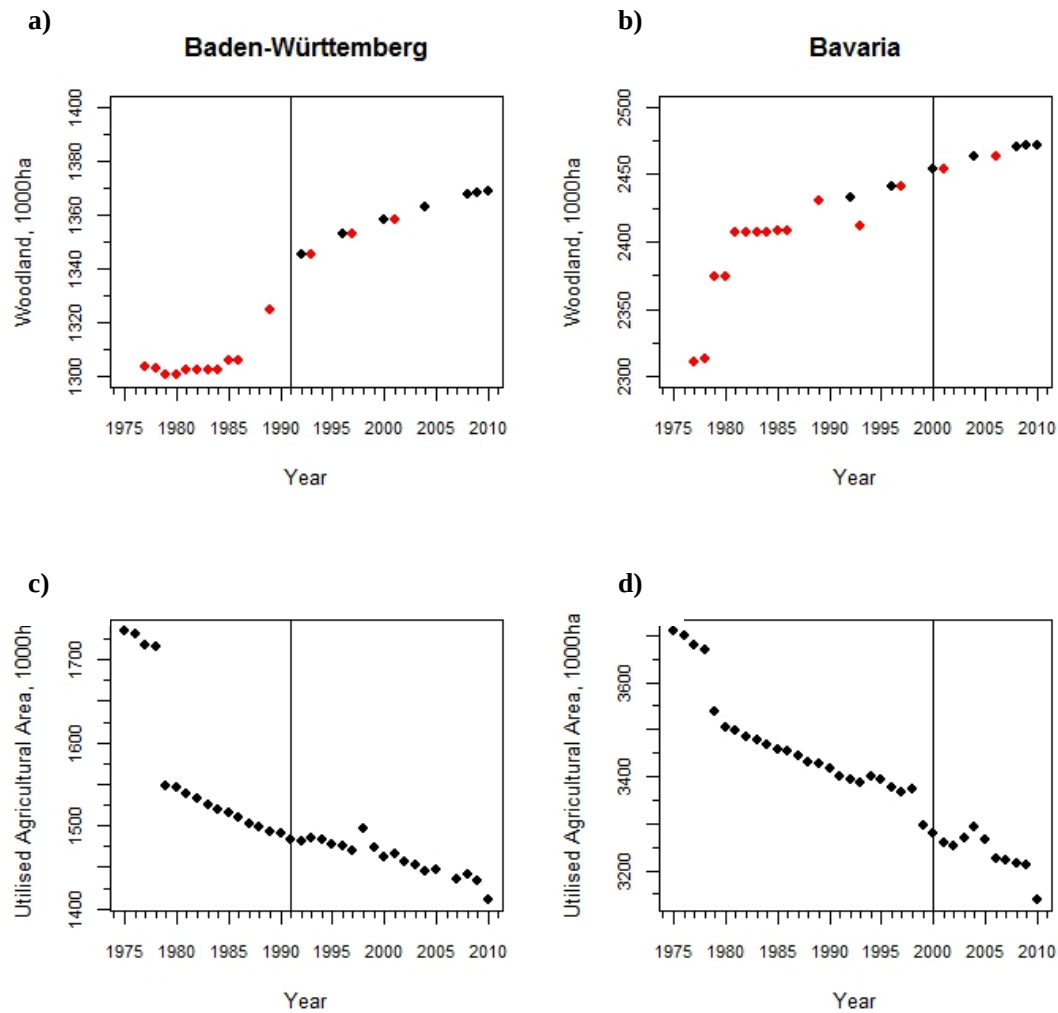


Figure 3.13. The area of woodland in a) Baden-Württemberg and b) Bavaria and the Utilised Agricultural Area in c) Baden Württemberg and d) Bavaria between 1975 and 2010. Red points for the area of woodland use data from Destatis and black use data from Eurostat. Vertical lines at 1991 in BW and 2000 in BV demonstrate the timing of the change in TBE incidence in each state.

Declines in the population of red deer were seen in both states into the 1990s (Fig. 3.14). Immediately before the increase in TBE (shown as the vertical line) red deer populations were declining in BW. In BV, red deer declined between 1983 and 1997, with a comparatively small increase between 1998 and 2000. There are, however, considerable differences in the total population of red deer, and in the size of the population decline previous to changes in TBE across the two states. As with roe deer, it is unclear why other changes e.g. decline in red deer abundance in 1991-2000 in BW, did not also result in

changes in TBE if they are the simple causal factor behind changes in TBE incidence.

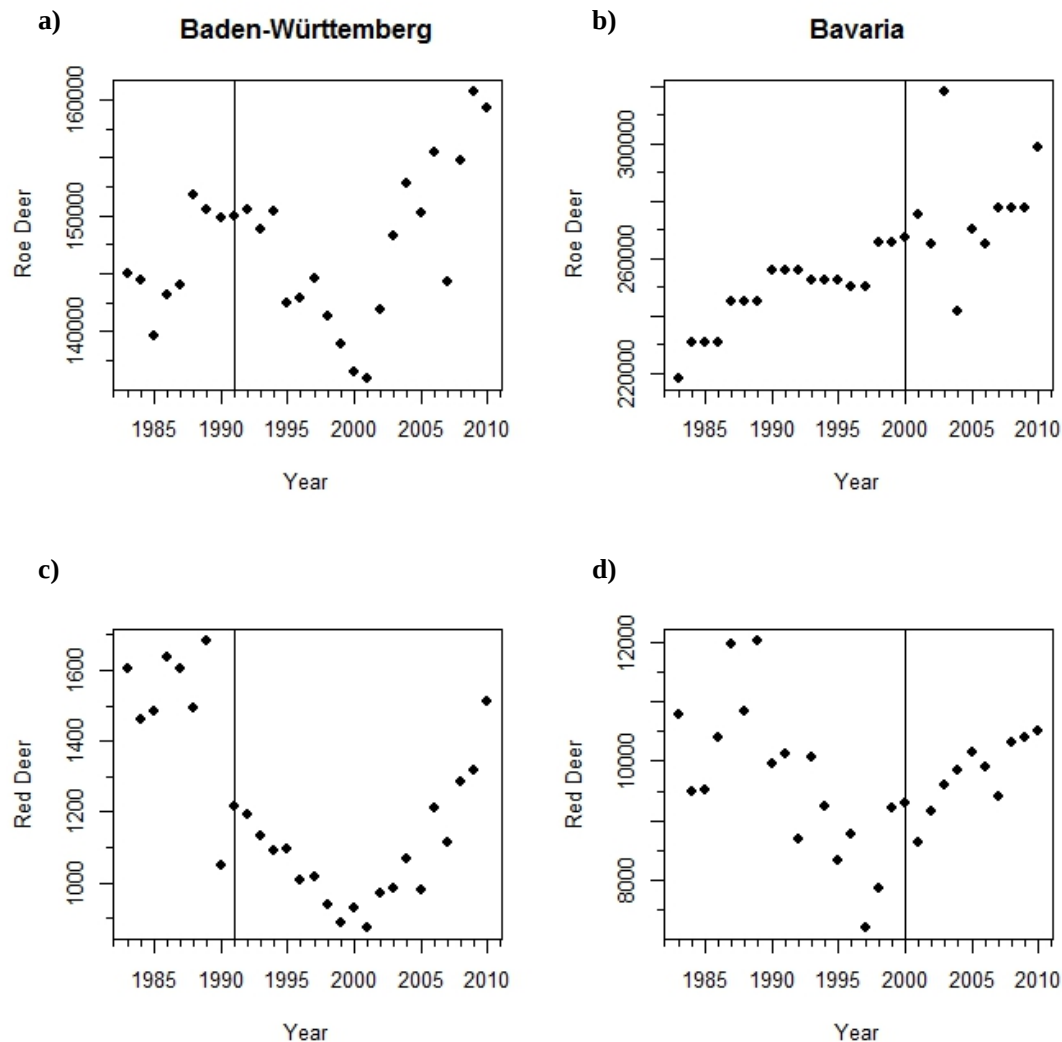


Figure 3.14. Abundance of roe deer in a) Baden-Württemberg and b) Bavaria, and abundance of red deer in c) Baden-Württemberg and d) Bavaria. Vertical lines at 1991 in BW and 2000 in BV demonstrate the timing of the change in TBE incidence in each state.

Although estimated boar population numbers are unavailable, the annual hunting bag suggests there have been substantial increases in boar abundance between 1983 and 2010 (Fig. 3.15). In BW the hunting bag increased from 2,936 to 32,969, with a peak of 51,086 boar in 2009. In BV, the hunting bag increased from 3,291 to 42,545, with a peak of 62,195 in 2009. Breakpoint analysis fits a breakpoint in boar hunting bag in 1990 in both BW and BV (so the first year with increased bag size is 1991), which coincides with the change in TBE in BW. A second breakpoint is fitted in 2001 in BV, therefore the boar

hunting bag increases in 2002, which is after the second step change in TBE (Table 3.6).

Although Figure 3.15 has been fitted with breakpoint analysis, there is in fact a linear trend for increase during the period, rather than step changes.

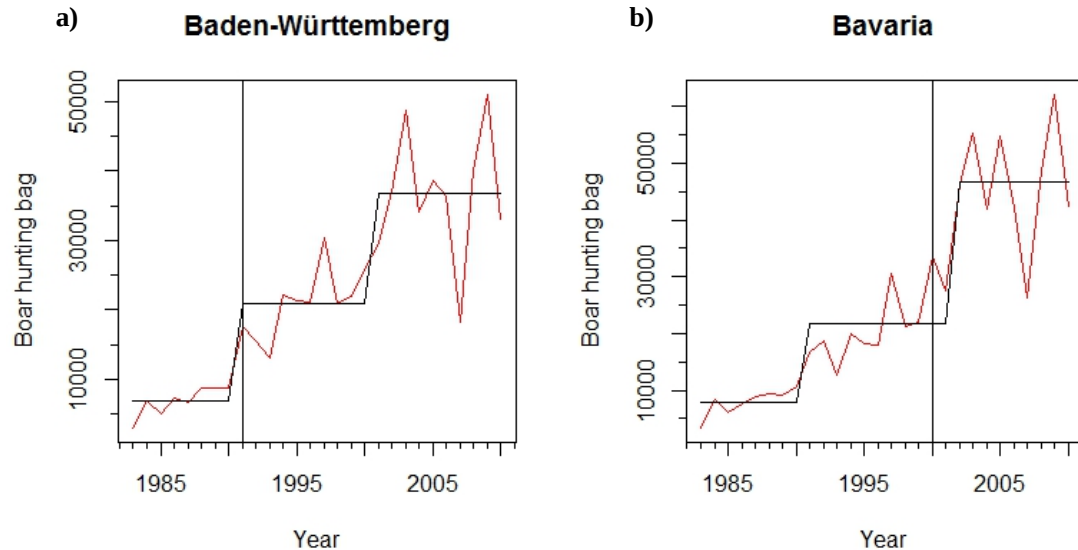


Figure 3.15. Boar hunting bag in a) Baden-Württemberg and b) Bavaria are shown in red, with the fitted model from breakpoint analysis shown in black. The vertical lines indicate the timing of breakpoints for TBE in each state.

Pesticide usage across Germany was stationary from 1980 to 1986, increased in 1987, but then declined again after 1991 (Fig. 3.16, Table 3.6). The decline in pesticide usage in 1992, from 1444 to 900 tonnes of active ingredient per year, coincides with increases in TBE in BW. Similarly, insecticides show a decline after 1984 and 1991. However, declines in pesticide usage in 1986 and insecticide usage in 1984 were accompanied by no coincident increases in TBE. The discrepancy could result from how the pesticide is used across Germany, information on which is unavailable. For instance, if the decline in pesticide use in 1986 occurred in northern Germany, its decline would have been of no consequence to the TBE system in BW and BV.

Table 3.6. Breakpoint analysis results for the boar hunting bag, pesticides and insecticides.

	BIC for Breakpoints†						Coefficient (i.e. average value)				
	Zero	One	Two	Three			Breakpoint 1 (95% CI)	Breakpoint 2 (95% CI)	Before Breakpoints	Between Breakpoints	After Breakpoints
BW Boar	618.21	595.93	587.08	589.90	1990	(1988-1991)	2000	(1996-2000)	6886.25	20987.60	36695.60
BV Boar	631.12	600.75	593.74	594.36	1990	(1987-1991)	2001	(1999-2002)	7915.75	21734.82	46639.11
Pesticides	544.19	542.87	539.99	540.14	1986	(1984-1987)	1991	(1988-1992)	31312.57	35044.20	30308.06
Insecticides	451.00	417.80	383.00	387.19	1984	(1983-1985)	1991	(1990-1992)	2234.20	1444.43	900.47

†Bold indicates the best model

For pesticides to have influenced TBE in the same year, tick populations would have had to respond immediately to changes. This is possible only if tick mortality in that year were the principal determinant of tick populations, because effects of pesticides on tick productivity would take longer to appear. A further recovery in tick populations following the initial step change might also be expected as tick productivity is also affected, which could have contributed to the peak of TBE cases in 1994.

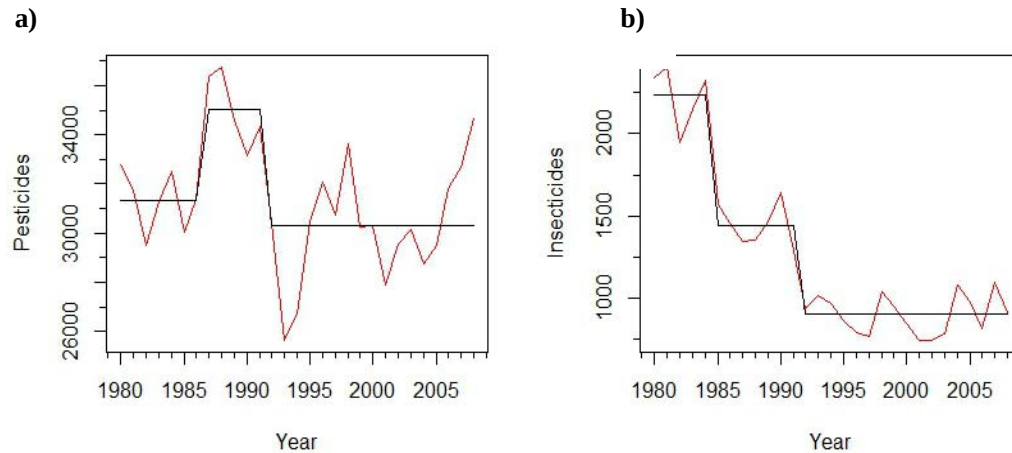


Figure 3.16. a) Pesticide and b) insecticide usage in Germany between 1980 and 2008 (tonnes of active ingredient, red line). The model fitted using breakpoint analysis is shown in black.

3.3.6. Temperature

Changes in temperature could precipitate a change in TBE, most likely through changes in the tick population (Randolph, 2004b; Dobson et al., 2011a) and/or their questing activities (Perret et al., 2000). Endemicity of TBE is associated with rapid spring warming, allowing co-feeding between TBE-infected nymphs and naïve larvae (Randolph and Sumilo, 2007). Although spring temperatures were not selected in the spatio-temporal model other aspects of temperature were, so the monthly mean of the maximum daily temperature throughout the year was examined for significant changes coincident with the changes in TBE. It should be noted that gradual changes in temperature could precipitate step changes in TBE, for instance through temperature thresholds for tick activity. Breakpoint analysis should also be able to detect a significant linear trend (as it did for the

boar hunting bag), which would be associated with significant breakpoints, giving a step effect across the underlying straight line. Visual examination of all data with significant breakpoints was used to assess the ability of breakpoints to summarise changes in temperature.

There are significant breakpoints in August mean daily maximum temperature in 1989 and 2004 in BW and BV (Table 3.7). The coefficients from the model show that the first step change was an increase in August temperature (from 22.12°C to 24.53°C) and the second was a decrease (to 21.04°C). If August temperature is important to the incidence of TBE, it is unclear why the system would only be responsive to the increase, and not to the decrease in temperature.

There was an increase in temperature in BW in May after 1987, preceding the first breakpoint in TBE in 1991. A significant breakpoint in June temperature is seen in 2001 in both states, which is after the 2000 breakpoint in TBE in BV. Significant breakpoints are seen in April in 1992 in BW and 2002 in BV. This is later than the change in TBE, but along with May and June temperatures were examined in further detail using dekads (ten-day periods). Dekads are more relevant than months for the biology of TBE virus transmission (Sumilo et al., 2007) and were subjected to the same breakpoint analysis.

Table 3.7. Months with at least one significant breakpoint in temperature in BW and BV.

	BIC for Breakpoints†				Breakpoint 1 (95% CI)		Breakpoint 2 (95% CI)	
	Zero	One	Two	Three				
BW								
April	161.46	156.87	158.57	163.78	1992	(1981-1997)		
May	160.24	156.95	163.09	169.35	1987	(1978-1994)		
June	156.64	149.07	153.50	157.67	2001	(1995-2004)		
August	166.22	167.55	162.13	167.61	1989	(1982-1991)	2004	(1997-2007)
BV								
April	161.82	157.57	157.27‡	162.95	2002	(1993-2006)		
June	152.19	147.43	152.38	155.48	2001	(1993-2006)		
August	161.86	163.09	158.98	164.36	1989	(1982-1991)	2004	(1996-2007)

†Bold indicates best model. ‡ This model has a marginally lower BIC than the one breakpoint model, but the difference was insufficient to justify an additional parameter in the model.

While no significant breakpoints were detected for the first dekad of April and the breakpoint in the second dekad (in 2002) was after changes in TBE occurred, a significant step increase was seen for the third dekad in 1991 in both states (Table 3.8, Fig. 3.17). The changing temperature is coincident with increases in TBE in 1991 in BW, but the temperature changes in both states. The dekadal mean of the daily maximum temperature rises to 17.73°C in BW and 16.95°C in BV, so the difference might be due to a threshold of activity between these two temperatures, but this is much higher than any previous estimate of temperature thresholds for tick activity.

In the first and third dekad of May increases in temperature occurred a few years before the increase of TBE in 1991 in BW. Of the temperature changes observed, the increase in temperature in May 1987 is considered to be the most likely to be related to an increase in TBE in 1991 because it only occurred in BW. During this time temperature increased from an average 17.55°C to 20.03°C.

Table 3.8. Results from breakpoint analysis of ten-day average daily maximum temperature in BW and BV.

	BIC for Breakpoints†				Breakpoint (95% CI)	Coefficient (i.e. average value)	
	Zero	One	Two	Three		Before	After
						Breakpoint	Breakpoint
BW							
April 2	189.22	186.59	190.63	197.31	2002 (1993-2008)	11.73	15.29
April 3	201.97	191.22	195.44	201.45	1991 (1993-2008)	13.19	17.73
May 1	192.02	190.39	196.34	201.24	1986 (1993-2008)	14.46	17.65
May 3	179.15	178.09	181.29	187.24	1987 (1993-2008)	17.55	20.03
June 2	186.03	182.96	189.55	195.09	1999 (1986-2004)	19.86	23.00
June 3	194.27	193.24	198.58	203.24	2000 (1977-1998)	21.29	24.57
BV							
April 2	190.52	187.22	190.95	197.16	2002 (1994-2007)	10.67	14.40
April 3	203.61	193.14	196.85	201.98	1991 (1987-1997)	12.33	16.95
May 1	189.50	188.74	194.87	198.20	1986 (1975-1993)	14.13	17.07
May 3	178.69	180.75	185.31	191.18			
June 2	183.37	180.88	186.90	191.59	1999 (1984-2003)	19.12	22.06
June 3	191.61	192.35	197.96	202.32			

†Bold indicates best model

There are two step changes in temperature which on first inspection could be relevant to the increase in TBE in 2001 in BV: the second dekad of April and the second dekad of June. However, temperature in the second dekad of April rose in 2003 (indicated by a breakpoint in 2002), too late to have caused the increase in TBE in 2001. The temperature increased in the second dekad of June in 2000, but in both states, which is not consistent with increases in TBE only in BV.

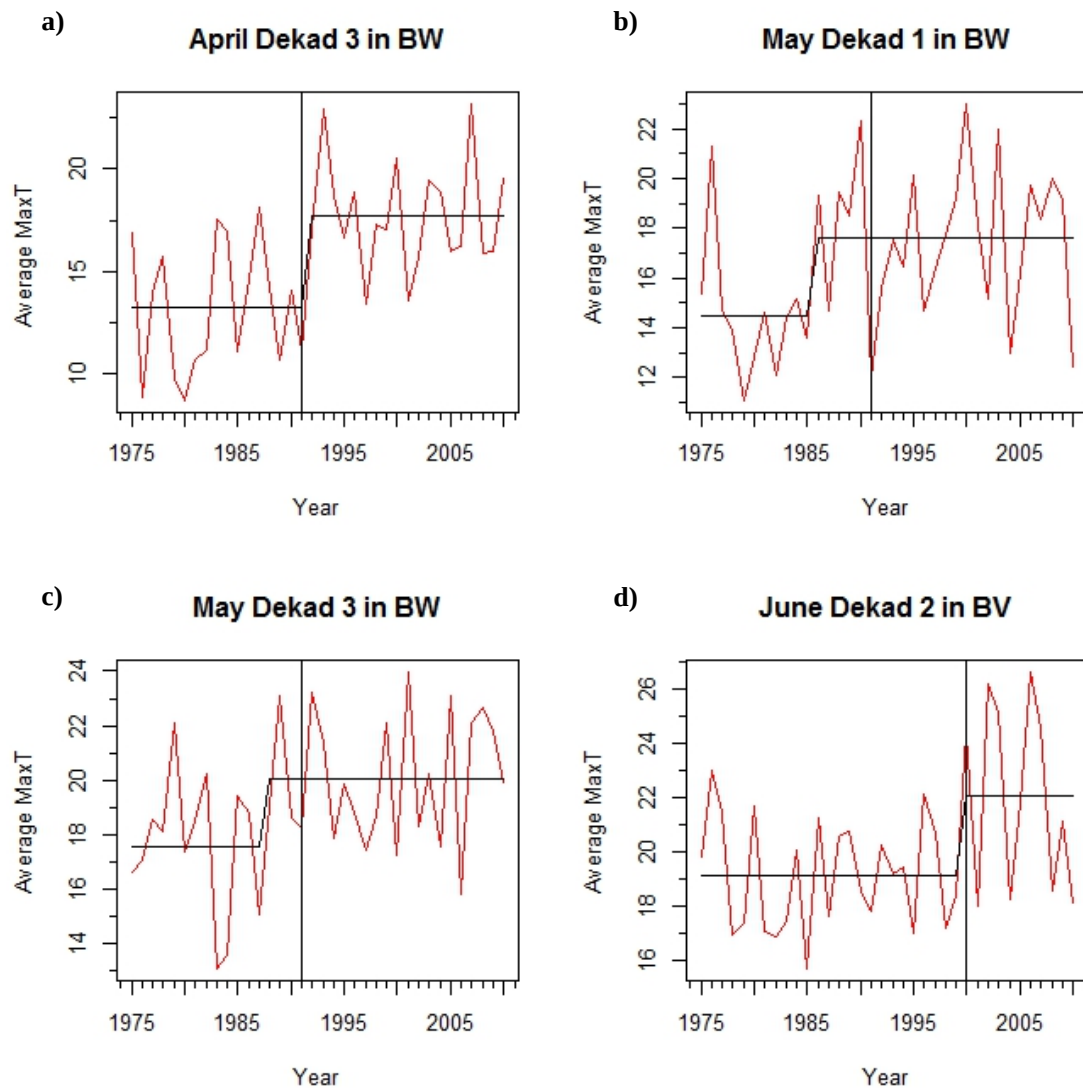


Figure 3.17. The ten-day average daily maximum temperature (in °C) in a) April dekad 3 in BW, b) May dekad 1 in BW, c) May dekad 3 in BW and d) June dekad 2 in BV between 1975 and 2010, shown in red. Fitted breakpoint models are shown in black, with a vertical line denoting the breakpoint in TBE in each state.

3.4. Discussion

TBE incidence in Germany since 1975 shows 3 distinct phases: before 1992, between 1992 and 2000, and after 2000. These changes are associated with an increase in TBE in Baden-Württemberg in 1992, followed by an increase in 2001 in Bavaria accompanied by more cases in a wider range of states. Changes in recording might have contributed to increases in TBE in the 1980s and 1990s (Fiedler et al., 1999), with enhanced vaccination possibly accounting for the absence of TBE increases in BV at that time (Roggendorf, 1996). These are, however, only qualitative statements and no quantitative evidence is given. The increase after 2000 could have resulted, at least partially, from the Infection Protection Act, which was introduced in 2001. It remains to be seen why a greater increase in recorded cases was observed in BV than BW. TBE has been diagnosed with serology for many years (Kaiser, 2002). The addition of PCR tests may help with diagnosing cases of TBE during the first stage, but is little use during the second stage of disease (Saksida et al., 2005). Changes in the recording system and diagnostics, while important, do not preclude other effects acting on 'real' incidence concurrently.

TBE is endemic throughout Bavaria and Baden-Württemberg, but also in Thuringen, Hessen, Sachsen, Rhineland-Pfalz and Saarland. Sporadic cases are seen in the states further north. Between 1997 and 2010 the distribution of TBE has changed. Based on the areas considered to be 'risky' by the Robert Koch Institute, the new risk areas identified from 1998 to 2005 were mostly around previously risky areas. Additionally, new risk areas occurred north of the previous distribution, further into Hessen and for the first time in Thuringen and Rhineland-Pfalz. In 2006 the definition of a risk area changed, which might have precipitated new risk areas which 'fill in the gaps' as risk, under the new definition, was based on the surrounding districts as well. There was a spike of cases in 2006 in Germany (and other countries (Randolph et al., 2008)), which could also have contributed to changes in the distribution. This spike was associated with additional cases in TBE risk

areas, irrespective of when they first became endemic for TBE (Fig. 3.4). Only 12 of the additional 210 cases (relative to the mean for 2005 and 2007) came from areas first classed as risk areas in 2006. Long- and short-term changes in incidence were therefore a result of changing dynamics at both the edge and core of the distribution in Germany.

3.4.1. Human socioeconomic factors in TBE

The spatio-temporal model of TBE in Germany demonstrated the need to include human socioeconomic factors, such as unemployment, in spatial models of TBE. A negative relationship between unemployment and TBE was identified using a GLM, due to the north-east to south trend in unemployment. When spatial autocorrelation was accounted for in the BSTGLM, a positive relationship between unemployment and TBE was revealed. Further, when the GLM was run with only BW and BV (which represent the majority of cases) there was a non-significant positive relationship with unemployment, suggesting the country-wide trend is not seen in local circumstances.

In a similar spatial model, TBE in Latvia was positively associated with parishes with high proportions of the population with low education and receiving a pension, and negatively associated with the proportion with higher education and an economic activity (Vanwambeke et al., 2010). The proportion with low educational status and receiving a pension were used to characterise a group of people, called ‘pickers’, who were thought more likely to utilise the forest for alternative sources of income or food. Although this is unlikely to be the case in Germany (see chapter 7), unemployment may be associated with increased time available to spend outdoors (see chapter 6) and reduced likelihood of vaccination, as seen in Latvia (Sumilo et al., 2008a), although vaccination is available on German health insurance in risk areas (Mantke et al., 2008).

3.4.2. Vertebrate abundance and land use

The positive correlation between roe deer abundance and TBE in the spatio-temporal model is a function of both the distribution of roe deer and the proportion of each district utilised as woodland; both of these would have contributed to a permissive environment for ticks.

In BW, between 1989 and 1991 the amount of land used as woodland increased from around 1,300,000 to 1,340,000 ha, representing a 3% increase, and in 1988 roe deer abundance increased from 145,000 to 150,000, concurrent with the step-change in TBE in 1992. However, changes in roe deer abundance of a much greater magnitude occurred after 2000. Additionally, a 4% increase in woodland in 1978 was also seen in BV independent of any change in TBE. Each individual change in roe deer abundance and woodland availability is therefore not unique. Perhaps instead it is the combination of these changes, potentially with other changes in the environment, which precipitated an increase in TBE in BW in 1992. In BV both the step increase in woodland observed in 1978 and the increase in roe deer abundance between 1983 and 1990 are considerably earlier than the 2001 rise in TBE, suggesting these changes were of little influence.

A negative correlation is observed between red deer abundance, which shows a strong latitudinal trend, and TBE case numbers in the spatio-temporal model of TBE. This correlation was also observed in a spatio-temporal study of TBE in just Bavaria and Baden-Württemberg (Kiffner et al., 2010). This is not surprising given the similarity of the data used, but reassuring that it is not an artefact of the gross latitudinal trend in red deer abundance across Germany. Red deer prefer open habitats including open deciduous woodland, upland moors, open mountainous areas, natural grasslands, pastures and meadows (Lovari et al., 2008). As such, the negative relationship between TBE incidence and red deer in space may actually represent a negative relationship between TBE incidence and the red deer's open habitat, which is less likely to provide a microclimate

suitable for ticks. For instance, in Slovenia, ticks were found in open areas only in early spring, and virtually no ticks were found in such habitats in the summer (Knap et al., 2009). If there is a negative correlation between red deer and TBE in space, there may also be one through time. For instance, if red deer abundance has reduced because the habitat has become less open through time more ticks may be able to survive, and TBE may consequently increase.

Red deer abundance decreased from around 1600 to 1200 animals in 1989, as part of a greater decline between 1984 and 2000 in BW. This was mirrored by a steady decline until 2000 followed by recovery in red deer abundance in BV. The declines are therefore concomitant with the change in TBE, but there is no indication of why similar changes at other points would not have similar effects.

No correlation was found between boar abundance and TBE in a spatio-temporal model of TBE Germany. However, the changes in abundance of this mammal are so great that they are still worth consideration. In BV the boar hunting bag increased steadily from around 8,000 animals before 1990 to 45,000 since 2002. In BW the hunting bag was around 7000 animals previous to 1990, rising to 37,000 since 2001. Two breakpoints were fitted to the BW and BV boar hunting bag data, although a linear trend seems more appropriate in both cases. Although this pattern might be an effect of changes in hunting procedure, it is thought that changes in the hunting bag are largely a reflection of the underlying population size. In Thurgau, Switzerland, the boar hunting bag was correlated with the number of boar killed on the roads and the amount of damage caused to agricultural land by boar (Geisser and Reyer, 2005). The increases are thought to be driven at least partially by increased food supplies from agriculture, specifically maize cultivation (Neet, 1995; Geisser and Reyer, 2005). The acreage for maize increased in Germany between 1950 and 1985, and is prominent in BW and BV with 15% and 18% of agricultural devoted to this purpose, respectively (Finke et al., 1999).

Hunting is also an activity that is likely to expose people to ticks, so a correlation between the boar hunting bag and TBE incidence may be the result of a double effect; the increased abundance of boar boosts the TBE enzootic cycle and the hunting boosts the human exposure to ticks.

Changes in land cover and red deer, roe deer and boar abundance are therefore concurrent with the step change in TBE incidence in BW in 1992. Changes in only red deer and boar abundance were seen immediately prior to the change in TBE incidence in BV in 2001. However, similar changes in these factors at other time points appear to have had no impact on the TBE system. It is conceivable, but untested, that it is the interactions between changes in the environment in 1992, and perhaps also in 2001, that caused a step change in TBE. This step change could result from combined changes in the enzootic cycle (through increased vertebrate abundance and habitat suitability) and human exposure (through increased hunting).

3.4.3. Pesticide use

While pesticide use in Germany increased in 1986 and then declined in 1991, insecticide use declined first in 1984 and then again in 1991. Reductions in pesticide and insecticide usage in the mid 1980s and subsequently, result from a changing attitude to farming across Europe. In 1985 EU policy was reformed for the first time to include measures which ensured environmental protection and provided national aid in environmentally sensitive areas (Kleijn and Sutherland, 2003). Specifically, in 1986 the Plant Protection Act was amended in Germany, to control the application of pesticides and the use of active ingredients (Wossink and Feitshans, 2000). The biotic elements of the TBE virus transmission system were inadvertently part of the newly protected environment. Only the second of the reductions, in 1991, in insecticide use was directly concomitant with changes in TBE, and this may relate to the spatial application of insecticides, but without further information about insecticide application, this remains

untested.

3.4.4. Changes in the climate

Two temperature variables were selected in spatio-temporal modelling of TBE in Germany suggesting warm summers and cold winters combine to shape TBE in space and time. The temperature profile across Germany demonstrates particular warmth in BW in summer and cold winters in the south, which explains the correlations seen in the model.

Other aspects of the seasonal temperature profile have been identified elsewhere as important to the epidemiology of TBE. Ticks are highly sensitive to the temperature at the beginning of the questing season and 7°C and 10°C are important thresholds for nymphal and larval activity, respectively (Perret et al., 2000; Randolph, 2004b). Rapid attainment of these temperature thresholds promotes co-feeding of nymphs and larvae and therefore the transmission of TBEV between different tick life stages (Sumilo et al., 2007). Climate changes leading to rapid spring warming may therefore lead to an increase in TBE incidence.

Between 1975 and 2010 increases in temperature concomitant with an increase in TBE incidence were identified at four points in the year: April dekad 3 in BW in 1991; May dekad 1 in BW in 1986; May dekad 3 in BW in 1987; and June dekad 3 in BV in 1999. Of these, only the increase in temperature in May dekad 3 occurred only in the state where TBE increased. The step changes in temperature, however, occurred well above the 7 and 10°C thresholds for tick activity. The earliest (and therefore coolest) temperature change was that of dekad 3 of April when daily maximum temperature rose from 13.19°C on average to 17.73°C. These higher temperatures will increase the period of each day that is suitable for tick questing activity and the rates of development of engorged ticks but higher temperatures are also associated with increased mortality from moisture stress (Dobson and Randolph, 2011), so the actual effect of these temperature changes on the enzootic cycle remains to be seen.

Higher temperatures later in the summer can inhibit tick questing activity (Perret et al., 2000; Perret et al., 2004; Burri et al., 2007) and so reduce contact with humans. Two step changes in temperature were observed in August in 1989 and 2004 in both BW and BV (Table 3.7). The first step change was an increase in August temperature and the second was a decrease. The timing and direction of changes does not match the change in TBE.

Although temperature changes were concomitant with the increases in TBE incidence in 1992 and 2001, the majority of changes (the exception being May 3) are seen in both BW and BV. Temperature change is therefore unable to explain the heterogeneity of changes in TBE in Germany. This is in agreement with findings from Latvia (Sumilo et al., 2007) and the Czech Republic (Zeman et al., 2010). It is concluded that there is insufficient evidence that temperature is the sole cause of the change in TBE, especially because the effect of changes in temperature in April, May and June on the TBE system is yet to be elucidated.

3.4.5. A nexus of factors?

In conclusion, there were two step increases in TBE cases in Germany in 1992 and 2001. A variety of abiotic and biotic factors underwent changes concurrently with the first increase in 1992 in Baden-Württemberg. Increases in temperature, in the land covered with woodland, in roe deer and boar abundance and declines in red deer populations and pesticide use all occurred in the same year, or previous to, the change in 1992. Many of these changes were not unusual or unique. For instance, the changes in roe and red deer were of the same magnitude as other changes at other points. Perhaps then, it is the sum and the interaction between these factors that warrants further examination as the cause of the increase in TBE.

The 2001 step increase in TBE in Germany, associated with an increase predominantly in Bavaria, but also in states where TBE is less common, might have been

the result of the introduction of the Infection Protection Act in 2001, but it is not clear why this did not apply equally to Baden-Württemberg. The evidence for a shift in TBE risk is less compelling than previous to the increase in 1992. Roe deer numbers were stable between 1990 and 2000, red deer numbers declined steadily between 1985 and 2000 and boar increased throughout. Temperature also increased in June but no concurrent changes are seen in pesticide or insecticide use, or woodland at this point.

CHAPTER 4. WHAT IS THE DIFFERENTIAL CONTRIBUTION OF QUESTING TICK ABUNDANCE AND HUMAN EXPOSURE IN DETERMINING THE WEEKLY NUMBER OF TICK BITES IN SWITZERLAND?

4.1. Introduction

Human tick-borne diseases (TBDs), such as TBE and Lyme Borreliosis (LB), are contracted in Europe through a bite from an infected tick of the species *Ixodes ricinus*. Questing ticks must coincide with humans in time and space for a tick bite to occur. The number of tick bites will depend on the limiting factor in the system at that point, whether that is the abundance of questing ticks or human exposure. Interventions targeted on the limiting factor may be more effective; for instance, there is little point reducing the questing tick population if ticks are always abundant and it is the patterns of human behaviour that shape tick bites. This applies in both space and time, but this analysis will consider temporal patterns. Climate change, which may have an impact on the abundance of infected ticks, has been suggested as a factor in increased TBD incidence (for example Lindgren, 1998, Danielova et al., 2008 and Gray et al., 2009). However, in the debate on the effect of climate change on TBDs, the question of how tick questing patterns translate into tick bites in humans has so far been ignored.

The supposition that climate change may have an impact on the questing tick population comes from established relationships between the weather and the questing tick population. Once ticks are recruited to the questing population and environmental conditions become consistently suitable for questing, the number of ticks actively questing is a function of daily saturation deficit ('SD'), a measure of moisture stress (Perret et al., 2004). Ticks respond to moisture stress by descending the vegetation and no longer questing for hosts. In the laboratory, *I. ricinus* demonstrated positive geotropism at

SD >4.4 mmHg (MacLeod, 1935), while in the field, reductions in numbers of questing ticks were seen when maximum (i.e. near midday) SD exceeded 4.4 mmHg (Perret et al., 2000).

Following engorgement, the daily developmental rate of the tick to the next life stage is higher in warmer temperatures. Therefore, at higher temperatures, ticks complete their inter-stadial development period more rapidly (if there is no diapause to consider (see below)) and suffer lower total mortality. However, higher mortality of ticks is also associated with high SD (Mount et al., 1997).

Shortening day length triggers ticks that engorge during late summer to enter developmental diapause, which delays the onset of development to the next life stage until temperatures rise after the winter. Unfed ticks may enter behavioural diapause, whereby they have the potential to quest but do not do so over the winter period, although the triggers for this are less well understood (Dobson et al., 2011a). In spring, the combination of lengthening day length and rising temperature creates a permissive environment for unfed ticks to break their diapause and begin questing. A weekly mean daily maximum temperature of around 7°C is required for nymphal ticks to quest (MacLeod, 1935; Perret et al., 2000).

This chapter will examine the extent to which these relationships between the weather and questing ticks translate into the number of tick bites. A unique dataset of weekly tick bites reported to doctors in Switzerland between 2008 and 2010 will be used. Both tick questing and human outdoor activities have a seasonal pattern, and both can limit the number of tick bites humans incur. The human exposure and tick questing season will be compared with the tick bite season to identify any periods when ticks are questing but not biting humans, or humans are active outdoors but not being bitten. The tick questing season is described using empirical data collected in east Switzerland and the seasonal human exposure pattern will be assessed through leisure activity data.

Weekly variations in numbers of tick bites are due to short-term fluctuations in tick questing or human exposure. Weather is an important external factor in determining both tick questing and human behaviour, and therefore weather will be used as a proxy for short-term tick and human activity patterns. Sunny, warm days without rainfall promote exposure of humans to ticks through outdoor recreational activities (see chapter 7). If tick-relevant weather (i.e. low SD, which is a function of temperature and humidity) is predictive of weekly variation in bites, it is the tick questing that is causing short-term fluctuations in tick bites and *vice versa* with human-relevant weather. To measure the short-term fluctuations in tick bites, the seasonal pattern will be accounted for using a series of sine and cosine curves to reconstruct and account for the seasonality, leaving only the weekly variation in bites to compare with the weather. This method has previously been used to examine cholera epidemics in response to rainfall (Hashizume et al., 2008; Luque Fernandez et al., 2009).

4.2. Methods and materials

4.2.1. Tick bite data

Ekkehardt Altpeter at the Swiss Federal Office of Public Health provided data on the number of tick bites reported by a network of general practitioners (GPs) in the Sentinella reporting system. Data were available from 2008 until 2010. In 2008, 179 GPs took part in the Sentinella system, in 2009, 132 GPs and in 2010, 173 GPs took part. Weekly data collected from Saturday until Friday included the number of confirmed LB, the number of tick bites and the total number of doctors' consultations. When a bite was recorded by the doctor, the patient was asked if he/she received the bite during leisure time, during work, or during leisure or work (i.e. unknown which). The information was provided in six regions of Switzerland (Fig. 4.1) as the resolution of the Sentinella system is inadequate for information at a cantonal level.

TBE data were registered through the mandatory surveillance system and diagnosis requires evidence of seroconversion, a positive IgM and at least a four-fold increase in IgG. The diagnostic criteria for LB in Switzerland depend on the form of the illness. For instance, diagnosis of erythema migrans requires a tick bite with local redness or livid discolouration and expansion in the middle without marked elevation of the skin surface. In contrast, diagnosis of Lyme arthritis requires repeated brief attacks of swelling of one or a few large joints and laboratory confirmation by detection of IgG in the blood or by cultural and molecular biological detection of infection in synovial fluid or biopsy. Definitions for these and other presentations, including lymphocytoma, early neuroborreliosis, Lyme carditis, acrodermatitis chronica atrophicans and chronic neuroborreliosis, are based on the definitions developed by the European Concerted Action on Lyme Borreliosis (EUCALB) and are available from the Swiss Federal Office for Public Health (www.bag.admin.ch).



Figure 4.1. Map of Switzerland, with cantons coloured according to the Sentinella region in which they fall. Region 1 (orange) includes the cantons of Geneva, Neuchâtel, Valais and Vaud. Region 2 (yellow) includes Bern, Jura and Freiburg. Region 3 (blue) includes Basel-Stadt, Basel-Landschaft, Aargau and Solothurn. Region 4 (purple) includes Luzern, Obwalden, Nidwalden, Uri, Schwyz, Zug and Glarus. Region 5 (green) includes Schaffhausen, Zürich, Thurgau, Appenzell Innerrhoden, Appenzell Ausserrhoden and St. Gallen. Region 6 (turquoise) includes Ticino and Graubünden.

4.2.2. Questing tick data

Peer-reviewed articles written by members of the University of Neuchâtel with data pertaining to the season of tick questing in Switzerland were sourced from the Web of Knowledge. Data referring to the seasonality of tick questing since 1995 were collated (Table 4.1). To allow comparison of data from different sites and years, questing ticks per month were calculated as a proportion of the annual total. Data for questing tick abundance in four sites across Bern in 2006 to 2009 were available as part of the EU FP6 Emerging Diseases in a Changing Environment (EDEN) project.

Table 4.1. Sources of data on the tick questing season.

Reference	Site(s) of study dataset	Year(s) of study dataset
Perret et al., 2000	Periurban forest in Neuchatel	1996, 1997, 1998
Jouda et al., 2004	Chaumont mountain at 900m, 740m and 620m, Neuchatel	1999, 2000, 2001
Moran Cadenas et al., 2007	North & South side of Chaumont mountain, Neuchatel	2003, 2004, 2005
Burri et al., 2011/ EDEN project	Thun, Belp, Kiesen & Trimstein in Bern	2006, 2007, 2008, 2009

4.2.3. Human leisure data

To provide a measure of human leisure activities that may result in exposure of humans to TBDs, tourism data from the Swiss Tourism Association (<http://www.swisstourfed.ch/>) and the Swiss Statistical Offices (<http://www.bfs.admin.ch/bfs/portal/de/index/themen/10/22/lexi.html>) were collated. Data were available for the monthly occupancy of hotels, campsites and youth hostels. School holiday information was collated, where available, from <http://www.feiertagskalender.ch>.

4.2.4. Weather data

Weather data were provided by MeteoSwiss, the Swiss Federal Office of Meteorology and Climatology. Data were extracted from IDAweb, a data portal provided

for research (http://www.meteoswiss.admin.ch/web/en/services/data_portal/idaweb.html).

Sites were selected from a network of ground-based weather monitoring stations across Switzerland (Table 4.2). The ‘detailed Swiss network’ of stations suggested by MeteoSwiss was modified to remove those weather stations at high altitudes (>1100m above sea level) where ticks are unlikely to be actively questing, and to add some additional sites in cantons which were unrepresented.

Table 4.2. MeteoSwiss ground-based meteorological stations included in weather data for each region

Region	MeteoSwiss sites included
1	Geneva, Chaux-de-Fonds, Neuchatel, Pully, Sion
2	Bern, Interlaken, Plaffeien
3	Basel, Buchs, Grenchen
4	Altdorf, Einsiedeln, Glarus, Luzern, Engelberg
5	Schaffhausen, St. Gallen, Zurich
6	Chur, Locarno, Lugano

Rainfall (mm) and the duration of sunshine (minutes) each day were taken from IDAweb. The daily maximum temperature and daily average humidity were also extracted. Average humidity and maximum temperature measurements were also taken each hour, and these were used to calculate the SD (Equation 4.1) (Randolph and Storey, 1999). Maximum SD is a measure of how challenging the environment is to the tick, as high SDs cause the tick to lose moisture rapidly and limit the time spent questing for a host. The SD was calculated for each hour and the maximum SD for each day collated.

$$SD = \left(1 - \frac{Humidity}{100}\right) \times 4.9463 \times e^{0.0621Temperature} \quad (\text{Equation 4.1})$$

Weekly summaries of the mean daily maximum temperature, mean daily maximum SD, mean daily maximum humidity, mean hours of sunshine and the number of days which were rainy were calculated. Multiple sites were available for each region, although not every weather variable was available at each site. The data at each site were examined to look for comparability across the region. Region six, which includes the cantons of

Graubünden and Ticino, was geographically highly variable and the weather variables were heterogeneous across the sites. Therefore, only regions one to five were included in those parts of the study that consider the relationship between the weather and tick bites. When weekly data for each site were correlated with all other sites within the region, there were strong correlations between sites (0.98 for maximum temperature, 0.93 for maximum SD, 0.88 for sunshine duration, 0.66 for humidity and 0.60 for the number of rainy days per week). The mean across the sites in each region for each weather variable were used in the analysis.

4.2.5. Analysis

Data were analysed in Microsoft Excel, the R statistical package (R Development Core Team, 2012) and Stata v12 (StataCorp, 2011). Regression models were used to investigate the link between LB or TBE case numbers and the number of tick bites. Initially, a general linear model (GLM) was fitted between the cases of disease and tick bites. The number of cases of LB or TBE followed a Poisson distribution and an offset was included to account for the number of doctor consultations or the population respectively. This offset inserts a term into the regression model but constrains the coefficient to one, with the effect of a denominator for the dependent term. The partial autocorrelation of residuals was plotted for each region to identify significant autocorrelation (using the `pacf` function in R). The presence of significant autocorrelation necessitated the use of general estimating equations (GEE) to estimate a GLM accounting for an autoregressive correlation structure (Liang and Zeger, 1986). Residuals showed second order autocorrelation in LB and fourth order autocorrelation in TBE. GEE models were implemented in Stata and compared using the quasi-likelihood under the independence model criterion (QIC) implemented in the `qic` command in Stata (Cui, 2007). Lags were included to assess whether there was a temporal lag between the reporting of tick bites and the cases of disease, consistent with a disease incubation period. In Slovenia,

mean time to development of erythema migrans was 20 days in 892 patients in 1993 (Strle et al., 1996a) and 24 days in 231 patients in 1994 (Strle et al., 1996b). A lag of about three weeks is therefore expected between the tick bite and diagnosis of LB. The incubation period for TBE is 7-14 days, but the first stage of disease is flu-like symptoms, which are often undiagnosed as TBE (Dumpis et al., 1999). After a non-symptomatic period of two to 10 days, patients may develop a more serious second phase of disease. As such, cases of TBE may be diagnosed between one and five weeks after a bite, with an average of around four weeks. Based on the LB and TBE literature, lag periods of up to five weeks were included between the tick bite and disease case.

Modelling was used to examine the relationship between tick bites and the weekly weather. To remove potential collinearity between temperature, sunshine, rain and humidity, principal components analysis was used to produce axes of variation in the weather data. PCA was undertaken in Stata and all axes were retained. Six sine and cosine terms were fitted to the weather PCA axes using a GLM to account for the seasonality in weather. The weather PCA residuals from this model can be considered as the deviance of weather from its usual seasonal pattern.

Seasonality in the tick bite data was removed using a GEEGLM model with a Poisson response for the bite 'counts', an offset variable for the number of doctor consultations and a fourth order autocorrelation structure (fitted after visual assessment with the `pacf` function in R). An explanatory variable for the region was added as a factor to account for the underlying regional differences in the number of tick bites. Six sine and cosine variables were included to account for the seasonal pattern. Residuals from this model were considered the weekly variation in case numbers and were regressed against the residuals of the PCA axes with up to five weeks lag. The residuals for the tick bites were normally distributed, so a GEE with a Gaussian response and a third order autoregressive correlation structure (fitted after visual assessment with the `pacf` function in

R) was used. The model with the lowest QIC was selected, before testing for additional significant terms.

4.3. Results

4.3.1. Tick bites and disease

4.3.1.1. Relationship between tick bites and LB or TBE cases

A lag between a tick bite and TBD case is expected and will be equal to the incubation period for disease development in the Sentinella system if the bite was reported to doctors immediately after it occurs. Before analysis of the Sentinella dataset, the duration of this lag must be verified to ascertain if tick bites were reported immediately after they occurred.

The reports of tick bites to doctors are considerably higher than the numbers of confirmed cases of LB or TBE. In the six regions over three years, 1,141 tick bites, 583 cases of LB and 223 cases of TBE were recorded. There is a clear linear relationship between the weekly number of bites and the number of cases of disease (Fig. 4.2).

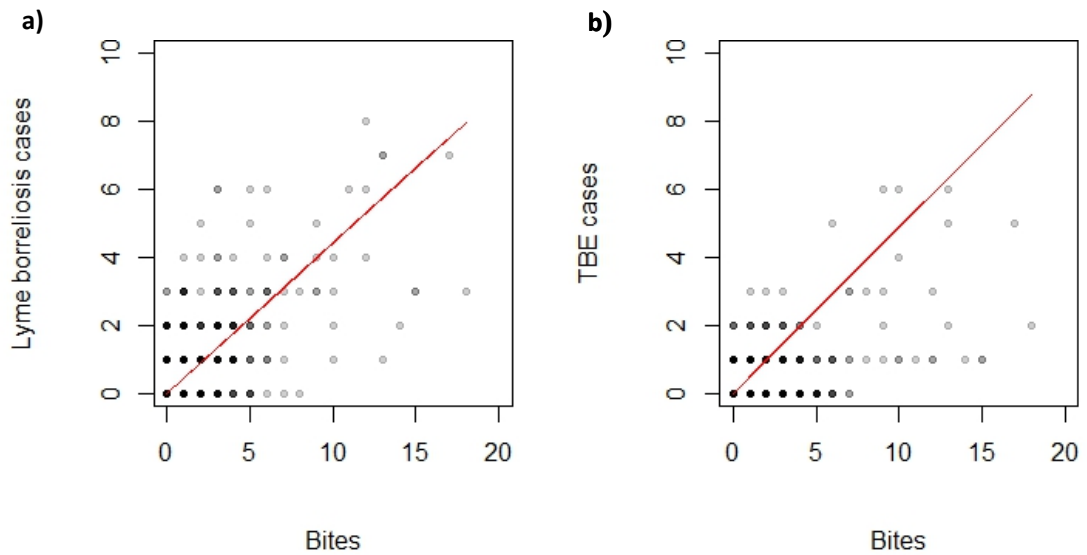


Figure 4.2. a) LB and b) TBE cases against the number of tick bites reported each week. Data points are opaque, so that if four points are overlaid it appears black in colour. The red line is fitted with the coefficient from the GEE models (Table 4.3). The correlation between LB cases and tick bites is 0.638 ($t=25.381$, $df=940$, $p<0.001$) and between TBE and tick bites is 0.557 ($t=20.568$, $df=940$, $p<0.001$).

The GEE models fitted with no lag between the bites and cases of TBE or LB were found to be best using the QIC measure of goodness of fit (Table 4.3). This, coupled with the high rate of bites that are accompanied by disease, suggests that the majority of bites were reported at the same time as the cases of disease, i.e. some weeks after they actually occurred. If this is the case, and bites were reported when disease was suspected, then the bite would have had to occur sometime earlier. This finding must be accounted for in later models that consider the relationship between weather and tick bites.

Table 4.3. Results of GEE regression models between cases of LB or TBE and the number of tick bites reported to doctors.

	Lyme borreliosis						Tick-borne encephalitis					
	Coeff	p-value	P*	Trace**	QIC	QIC (u)	Coeff	p-value	P*	Trace**	QIC	QIC (u)
Bites	0.4426	<0.001	2	3.748	499.897	496.401	0.4871	<0.001	2	2.539	330.432	329.353
Bites Lag1	0.2124	<0.001	2	3.747	571.818	568.325	0.3619	0.001	2	5.565	351.619	344.490
Bites Lag2	0.1904	0.003	2	5.023	575.051	569.004	0.4359	<0.001	2	3.417	333.799	330.964
Bites Lag 3	0.2721	<0.001	2	0.853	530.362	532.656	0.4237	<0.001	2	1.896	331.018	331.227
Bites Lag 4	0.2091	<0.001	2	2.154	557.125	556.817	0.3111	<0.001	2	1.223	345.748	347.303
Bites Lag 5	0.2405	<0.001	2	2.768	546.469	544.932	0.1339	0.02	2	1.387	371.954	373.181

* P is the number of explanatory variables in the model, in this case two for the number of bites and the region.

**If the trace is similar to P, then the QIC (u) can be used, which is an estimation of the QIC. The results of QIC and QIC (u) are in agreement over the best model.

4.3.2. Tick bite season

4.3.2.1. The tick questing season

Empirical data demonstrate that tick questing in Switzerland has a strong seasonal pattern (Fig. 4.3). The data were presented as proportions to demonstrate the seasonality of tick questing, but the absolute number of ticks represented by these figures is variable across the studies. Tick questing typically starts around March, peaks in May and then declines from this peak. There is variation in the timing of the peaks in 2004 and 2005 across the data series, which may result from the differences in aspect as three sites are south facing and four are north facing. In 2004 tick questing peaks slightly later than other years, with five of seven series peaking in June. Following this, in 2005 only one series, which is north facing at the highest altitude, peaks in June, so no trend in delayed peaks is apparent. The additional autumn peak in questing varies in strength, but is almost always apparent. This autumn questing peak is most marked in 2000 and 2005.

Questing ticks in four locations across Bern (2006-2009) show the same seasonal pattern (Fig. 4.4). Questing by nymphs begins in February, March or April and ends in around November. Altitudinal differences in the sites are reflected in the shape of the seasonal pattern, with lower sites showing a very spiky distribution and higher sites a flatter distribution. The flatter distribution in Belp means the annual peak in tick questing is only marginally above the surrounding months and can be as early as May and as late as August in 2008. Additionally, the lowest altitude site, Kiesen, peaks first in 2007 and 2008. Altitude is therefore important in shaping the tick questing season, but there are similarities across all sites.

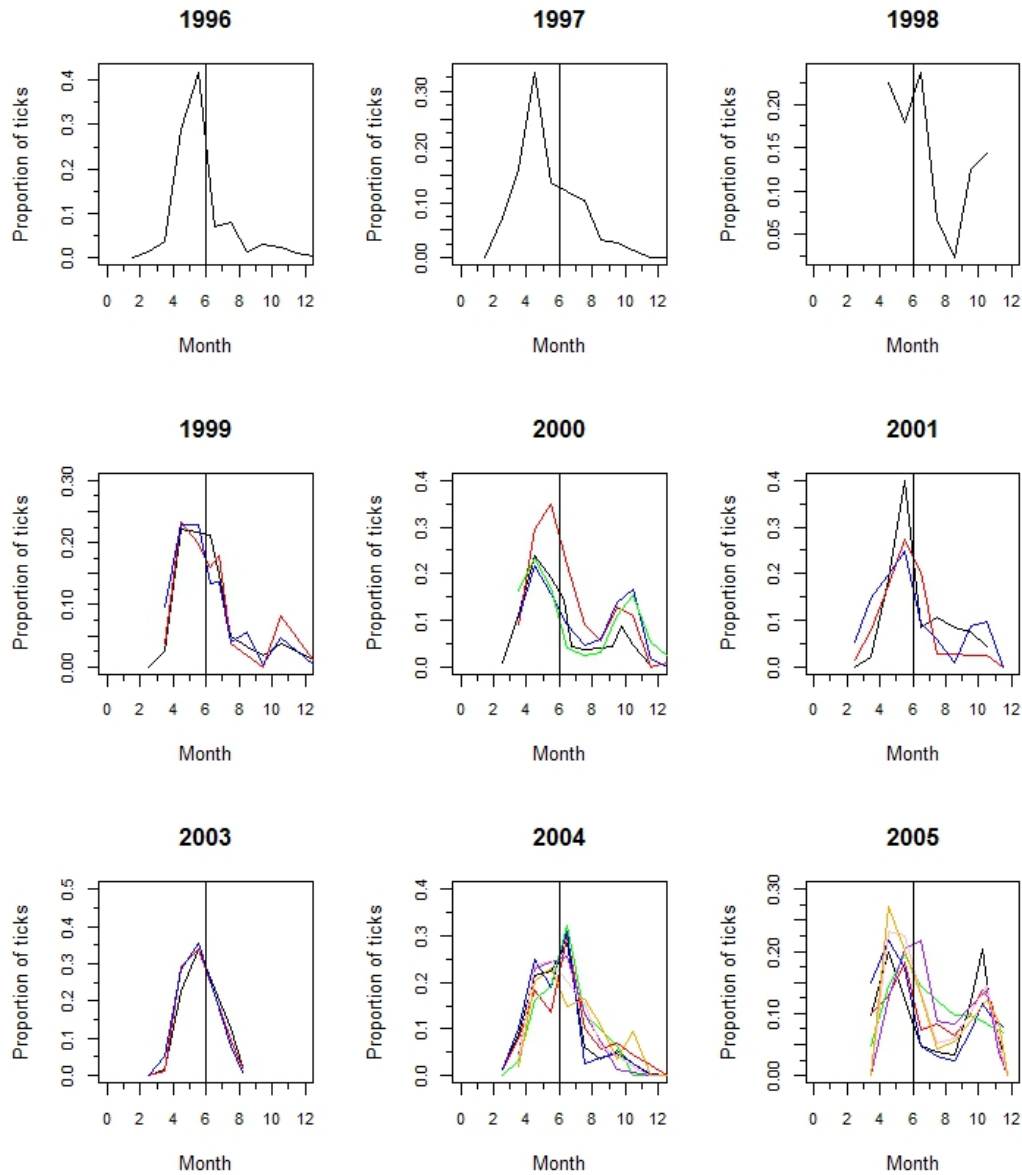


Figure 4.3. Seasonal distribution of questing nymphal ticks in Switzerland from 1996 (top left) until 2005 (bottom right). Each colour within a plot represents a different tick sampling site. 1996 – 1998 data are from Perret et al., 2000, 1999 – 2001 from Jouda et al., 2004, 2000 from Perret et al., 2004, 2003 - 2005 from Moran Cadenas et al., 2007.

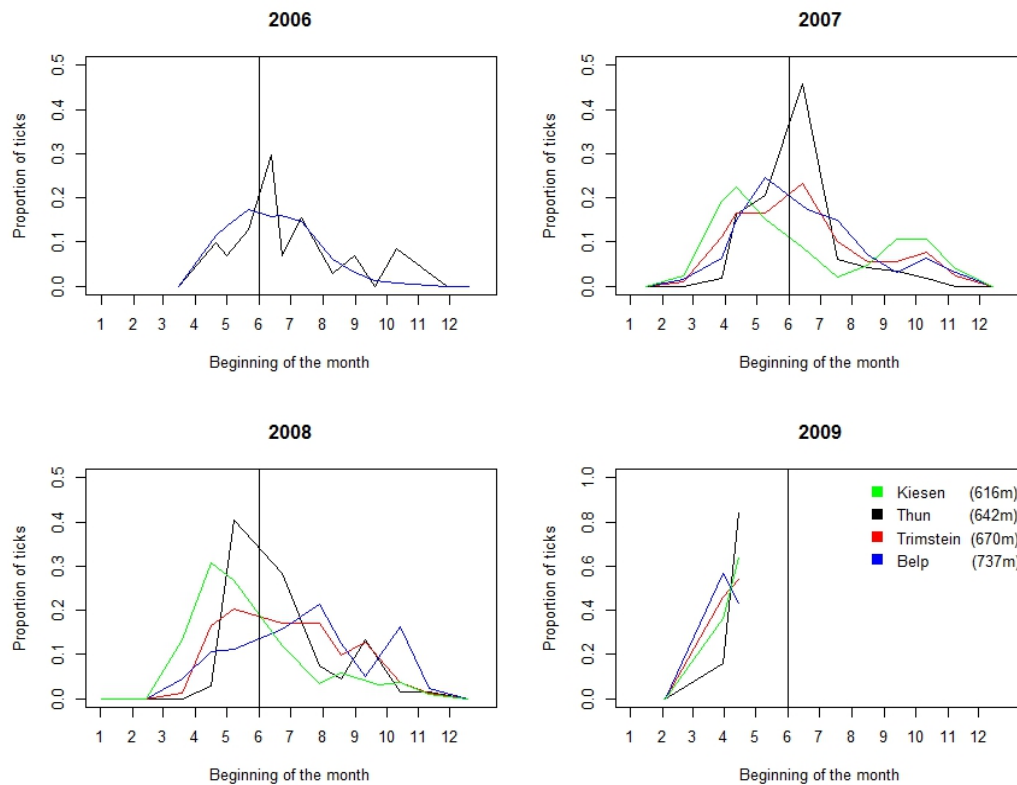


Figure 4.4. Tick seasonality at four sites across the canton of Bern from 2006 to early 2009 collected during the EDEN project, and available in Burri et al., 2011 . Data were collected until April in 2009, so only a small section of the pattern is available for that year. As would be expected, the proportion of ticks in any month is therefore higher in 2009 than in other years.

The seasonal distribution of questing ticks is shaped by the underlying population processes (as depicted in Fig. 4.5). At the beginning of the season, recruitment adds to the pool of questing ticks at a greater rate than host attachment and death removes ticks. After the peak in the questing tick population, recruitment is adding to the pool of questing ticks at a lower rate than the combined effects of death and host attachment are removing ticks. Recruitment ceases, and the questing tick population is increasingly exhausted as ticks find a host or die and the remaining ticks have low energy reserves (Randolph et al., 2002; Perret et al., 2004). In the autumn, a new cohort of each tick life stage emerges following development, leading to the autumn rise in questing ticks.

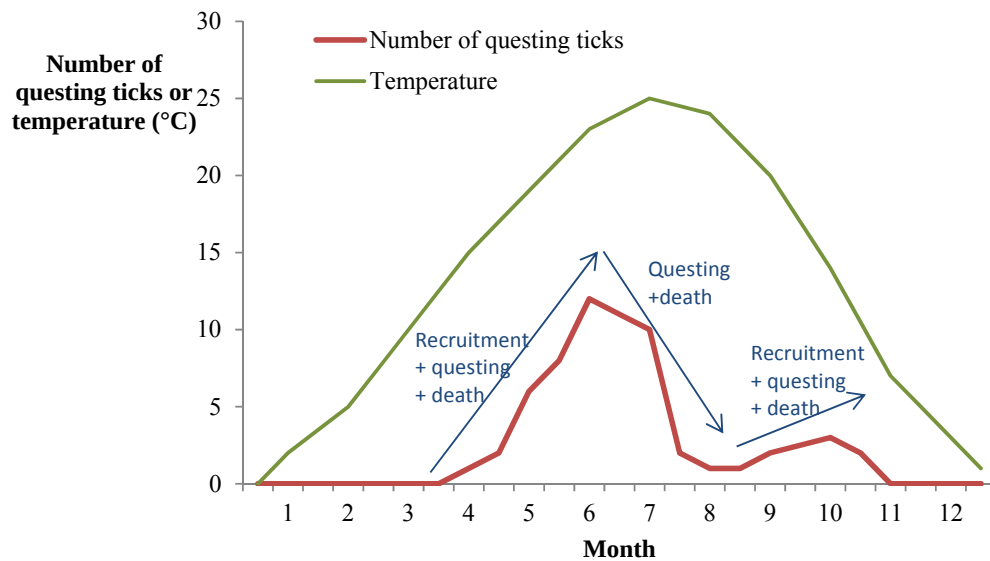


Figure 4.5. Model for the population processes that shape the questing tick population. Blue arrows and labels describe the population processes shaping the questing tick population (shown in red) and how this relates to temperature (green line).

4.3.2.2. The tick bite season

The seasonal pattern of tick bites is much the same across all regions, but variable in the absolute number of bites (Fig. 4.6). The highest incidence of bites per week throughout the period is seen in Region 6 with almost six bites in every 1,000 doctor consultations. Across the six regions there are no consistent patterns of years with higher or lower numbers of bites. The very few tick bites recorded between week 50 and week 10 is consistent with the weather being unsuitable for tick questing during the winter period. The first bites occur in April and May, and the peak in bites often occurs close to the mid-year point (depicted by the vertical line at week 27 in Fig. 4.6). Following the peak, bites continue to occur often into October and November, frequently with an autumn peak in bites, similar to the autumn peak in tick questing (Fig. 4.3 & 4.4).

Tick bite seasonality shows similarity to the shape of the tick questing season, but with differences in the timing of the start of the season and of the peak. Given the data on tick questing patterns for 2008 from the EDEN project, the relationship between tick questing and reported tick bites can be examined further. The start of the season of tick

bites is delayed by around 10 weeks compared with tick questing in Kiesen and around three weeks compared with tick questing in Thun (Fig. 4.7a). When tick bites first occur in week 16, 13% of the questing tick population is already active (Fig 4.7b). In week 20, 33% of questing ticks have been collected, but only 7% of tick bites have occurred. Towards the end of the season, at around 33 weeks, the cumulative distribution of questing ticks and tick bites are re-aligned. Given that bites are reported at the time of suspected disease, a delay of about three weeks would be expected between tick questing and the reporting of a tick bite. However, the delay at the beginning of the season is greater than this and variable throughout the season, suggesting it is not caused simply by the disease incubation period. Re-alignment later in the season would suggest that the number of actively questing ticks then becomes the limiting factor determining the number of bites. In confirmation of the earlier modelling (see Table 4.3), the seasonal pattern of tick bites closely resembles that of LB and TBE cases (Fig. 4.7b).

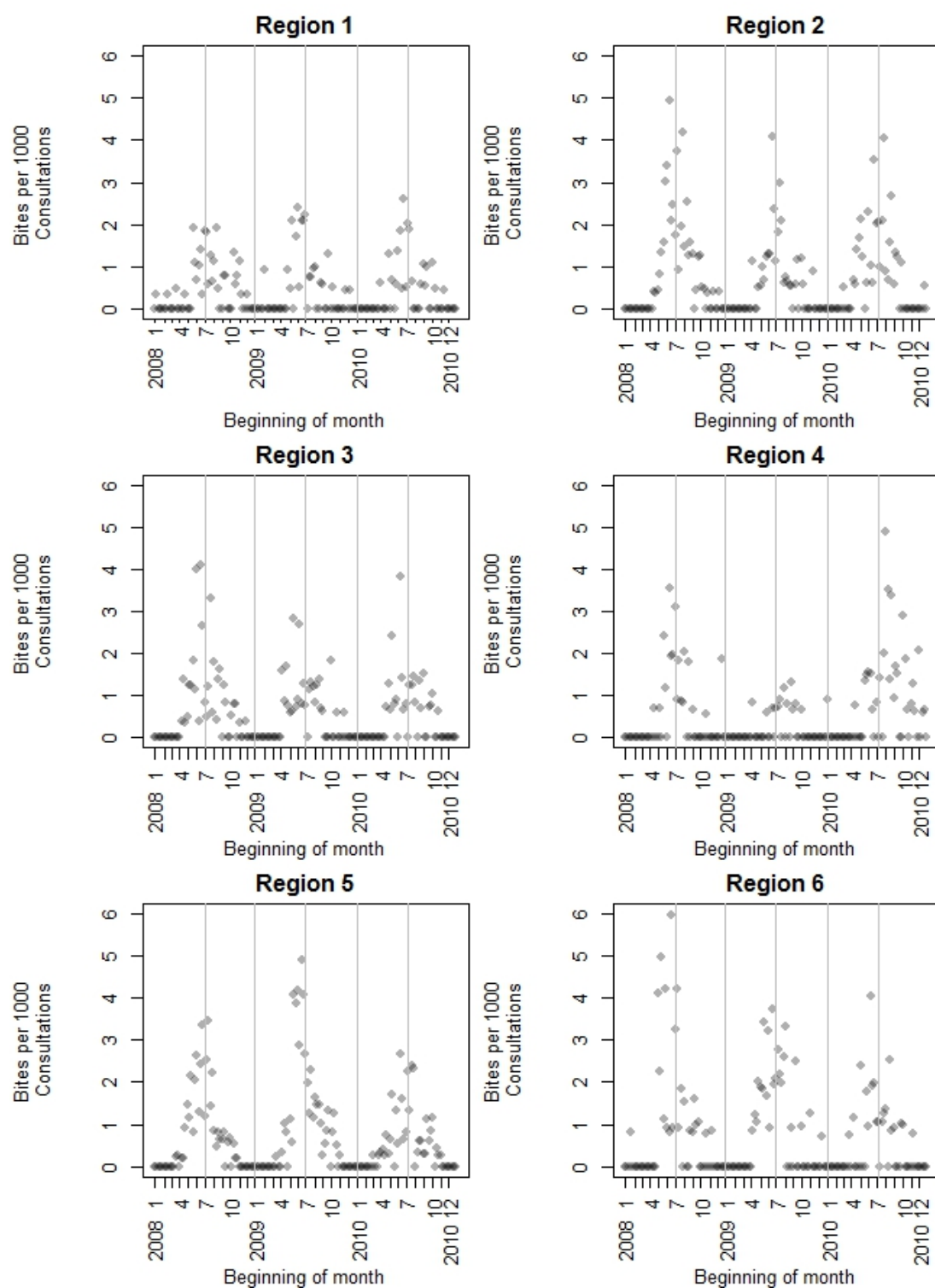


Figure 4.6. The weekly number of tick bites per 1,000 doctor consultations between 2008 and 2010 in the six regions. Lines mark the first week of the new year and week 27 for reference.

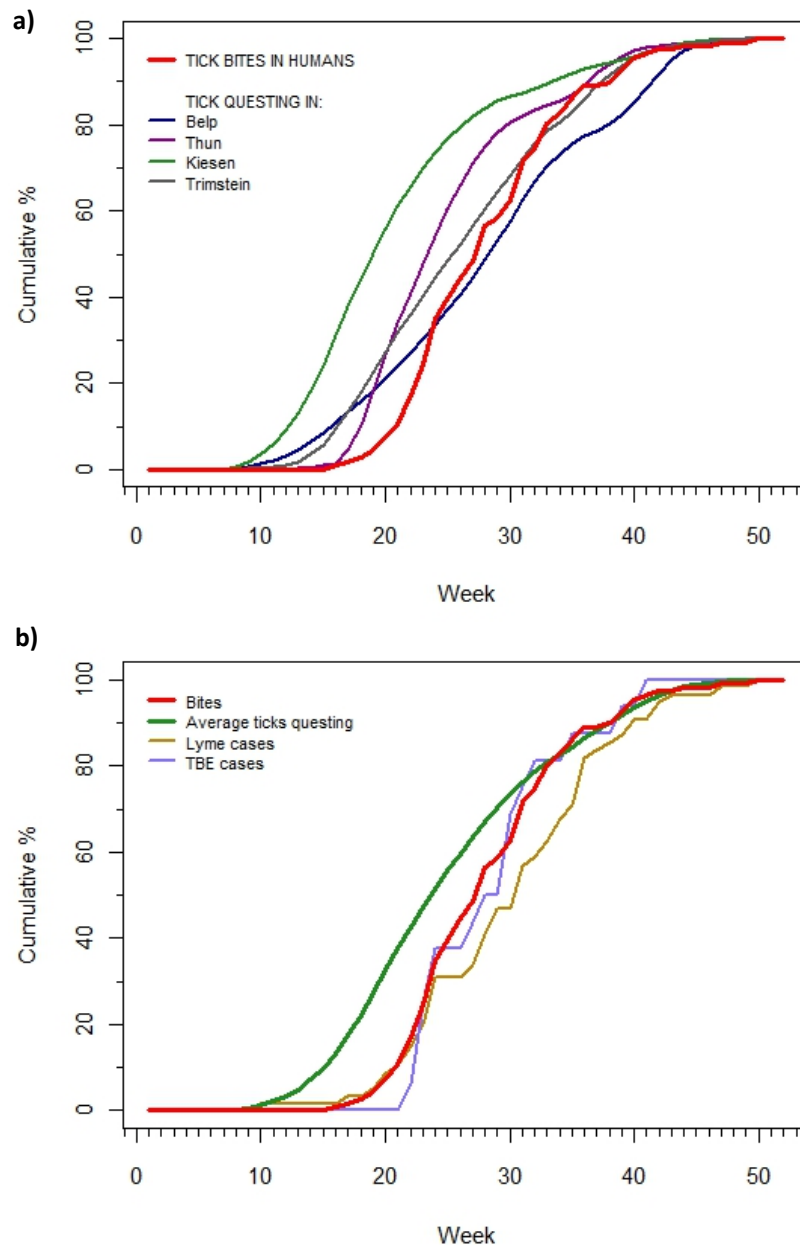


Figure 4.7. Cumulative percentage distribution of questing tick abundance, tick bites, LB and TBE cases in 2008. a) The cumulative distributions of tick bites (shown in bold red) and questing ticks in four locations in Bern. b) The cumulative distribution of tick bites, average questing ticks, LB and TBE.

4.3.2.3. Temperature, SD and tick bites

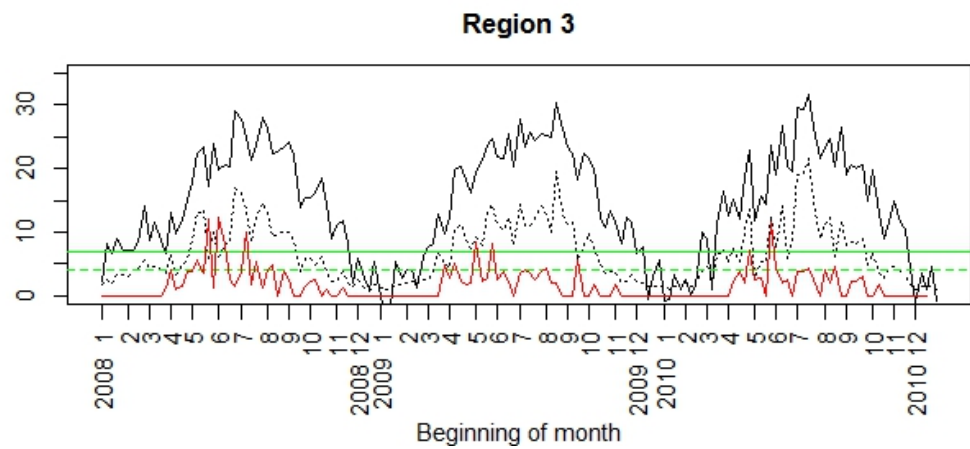
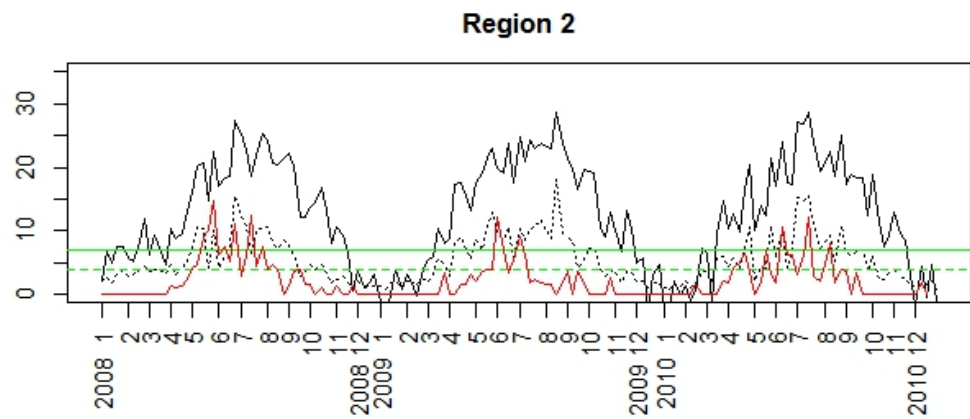
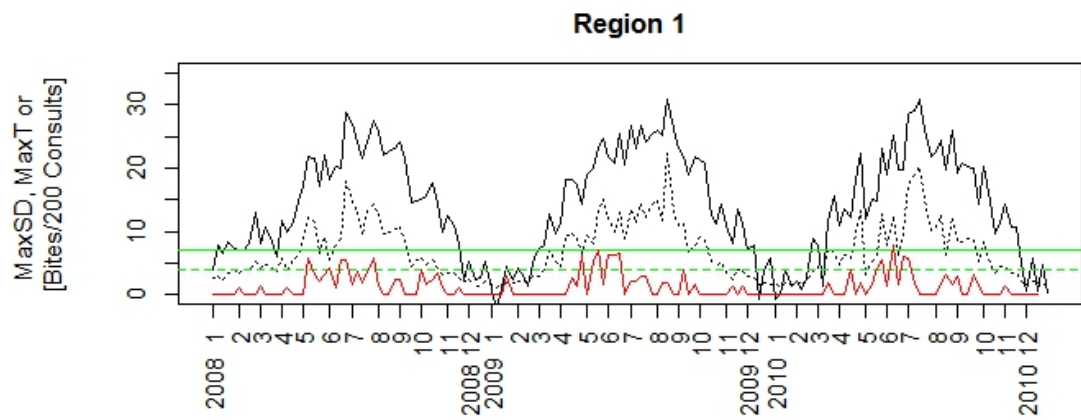
There are clear relationships between the tick questing season and weather.

Temperature has a crucial role, as weekly mean daily maximum temperatures greater than about 7°C are thought to be required for nymphal ticks to become active. SD, as a measure of the drying power of the environment, is negatively correlated with tick questing; when

the SD exceeds c.4mmHg, ticks escape desiccation by descending the vegetation to the moist litter layer and so do not quest actively.

The role of these variables in affecting the probability of tick bites on humans is less well known, because that depends on both tick and human activity. The three-year record of tick bites was compared with the SD and temperature for each of the five regions (Fig. 4.8). The data are justified by two weeks so that weather in week one is compared with the number of bites in week three, which is consistent with the idea that people report bites when disease is suspected. Across the five regions there are consistent seasonal patterns for SD and temperature.

Tick bites seem to occur at a considerable interval after daily maximum temperature exceeds 7°C, (Fig. 4.8) consistent with the delay seen between questing ticks and tick bites (Fig. 4.7). The 4mmHg SD threshold for tick questing seems largely unimportant in influencing tick bites on a seasonal scale. This may be because weather data were collected from meteorological stations, which might not reflect the microclimate in the tick environment. For instance, in the UK, tick habitat rarely meets this threshold in forest and undergrowth, so it may be of no practical importance in these environments (Dobson et al., 2011b).



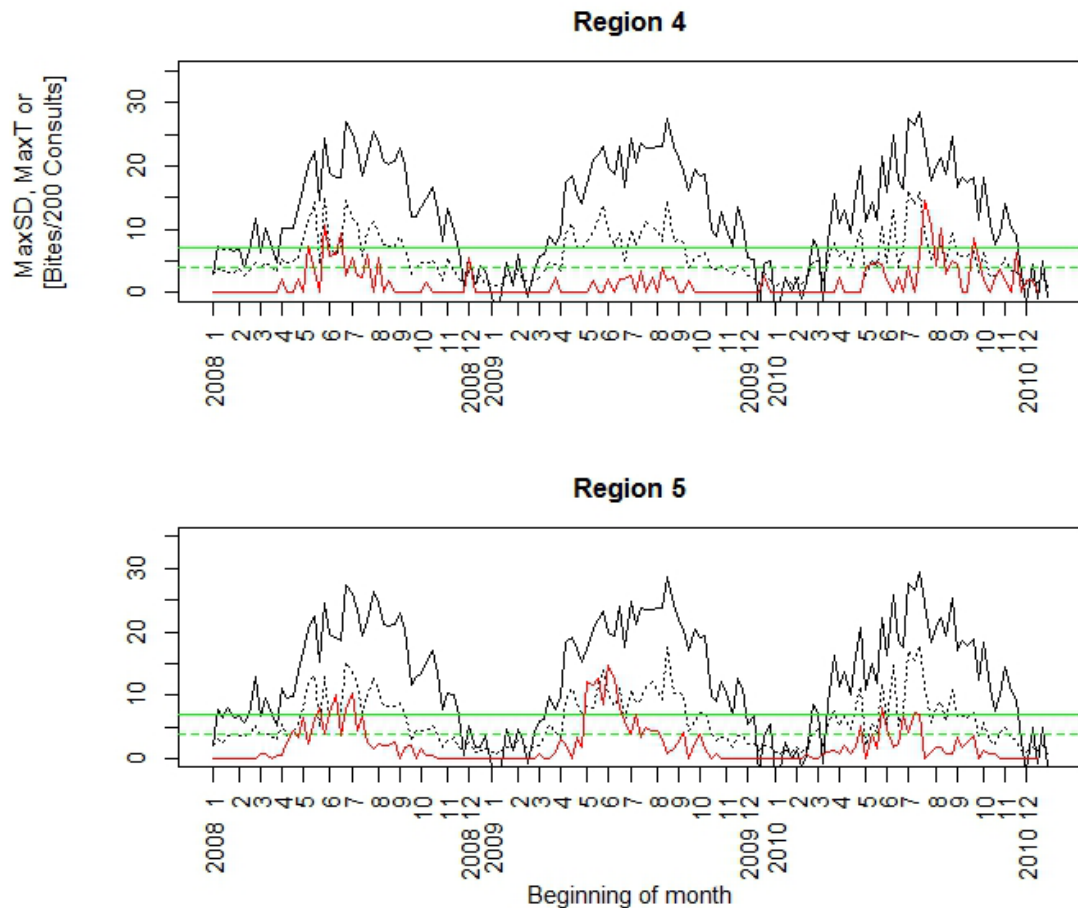


Figure 4.8. Weekly average maximum temperature ($^{\circ}\text{C}$, solid black line), maximum SD (mmHg, dashed black line) and tick bites per 200 doctors consultations (solid red line) for years 2008-2010 in five Sentinella regions of Switzerland (region labelled above each individual plot). Thresholds are depicted by the green lines, at 7°C for temperature (solid line) and at 4mmHg for maximum SD (dashed line).

Given the predictable influence of environmental determinants on tick activity (see Fig. 4.5), we can predict that tick bites will increase in line with increasing temperature in spring but after the peak in bites, no correlation will be seen (as questing ticks are removed through host attachment or death more rapidly than they are recruited). To test this hypothesis, for each year and region the correlation between the temperature and tick bites per 1,000 doctor consultations before and after the peak in the tick bite season was measured (using data from weeks nine to 39, Table 4.4). Before the peak in 12 of 15 series, the incidence of tick bites is significantly correlated with the temperature, whereas

only one shows a correlation following the peak. This is consistent with the idea that temperature in the spring provides an increasingly permissive environment for questing, but is less influential after this (see Fig. 4.5 for model for tick questing). Increasing temperatures in spring may also promote human exposure through recreation, but after a period of warming, temperature is no longer a limiting factor to human exposure as it is consistently warm enough.

Table 4.4. Correlation coefficients between tick bites and temperature before and after the peak in tick bites.

Year	Region	Peak week	Before peak		After peak
2008	1	21	0.178		0.046
2008	2	24	0.687	**	0.337
2008	3	25	0.540	*	0.143
2008	4	24	0.352		0.328
2008	5	29	0.806	***	0.347
2009	1	23	0.571	*	-0.051
2009	2	25	0.688	**	0.013
2009	3	21	0.795	**	0.144
2009	4	35	0.476	**	0.811
2009	5	25	0.758	***	-0.010
2010	1	25	0.622	*	0.339
2010	2	30	0.455	*	0.279
2010	3	23	0.615	*	0.116
2010	4	31	0.304		0.710 *
2010	5	23	0.688	**	0.356

* denotes p-value<0.05, ** denotes p-value<0.01, *** denotes p-value<0.001

The indirect measure of weather thought to be permissive and optimal for tick questing for 2008-2010 (Fig. 4.8) demonstrates that the seasonal pattern of recorded weekly tick bites is influenced somewhat by the availability of questing ticks, i.e. the environmental hazard. The spring rise in tick bites is likely to relate to the progressive recruitment of ticks to the questing population. The decoupling of tick bites and temperature after the peak is likely because of exhaustion of the questing tick population. However, tick bites do not correspond to weather in exactly the same way as tick questing: for example, tick bites occur with considerable delay after the temperature threshold for

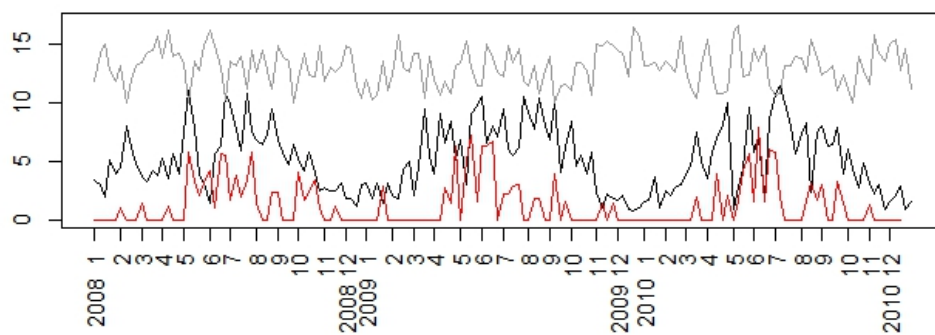
nymphal activity (7°C) is crossed, and high SD, thought to limit tick activity, does not appear to prevent tick bites from occurring.

4.3.2.4. *Rainfall, sunshine and tick bites*

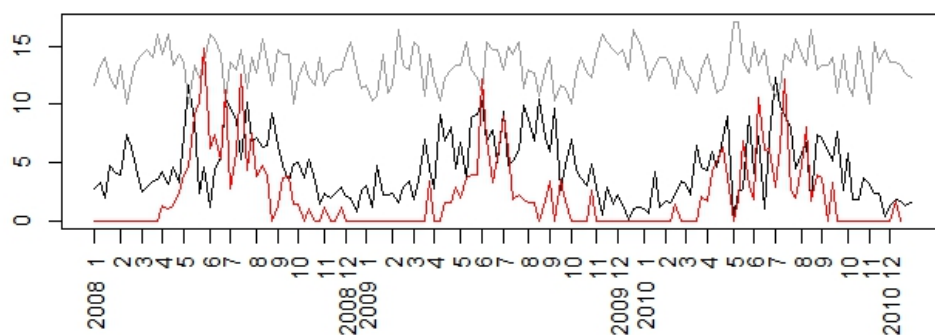
Tick bites are a function of not only the abundance of questing ticks, but also human exposure behaviour. For instance, the rate of the spring rise in tick bites may be a result of a combination of tick recruitment and increasing human exposure in spring as the temperature becomes more favourable for outdoor activities. Human outdoor behaviour is linked to temperature, but also a lack of rain and high levels of sunshine. No additional insight into the tick bite season (e.g. the causes of the early season delay in bites), is given by rain or sunshine variables (Fig. 4.9). Sunshine has a seasonal profile similar to temperature, so it is difficult to separate the two effects, and rainfall shows little seasonality. Instead, factors other than weather e.g. social factors, might be shaping human exposure, and therefore the observed season of tick bites.

(Rainy days+10), Sunshine Hours or
[Bites/200 Consults]

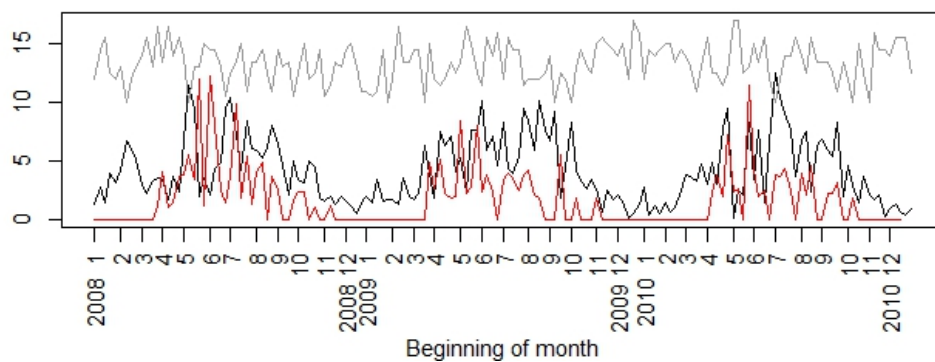
Region 1



Region 2



Region 3



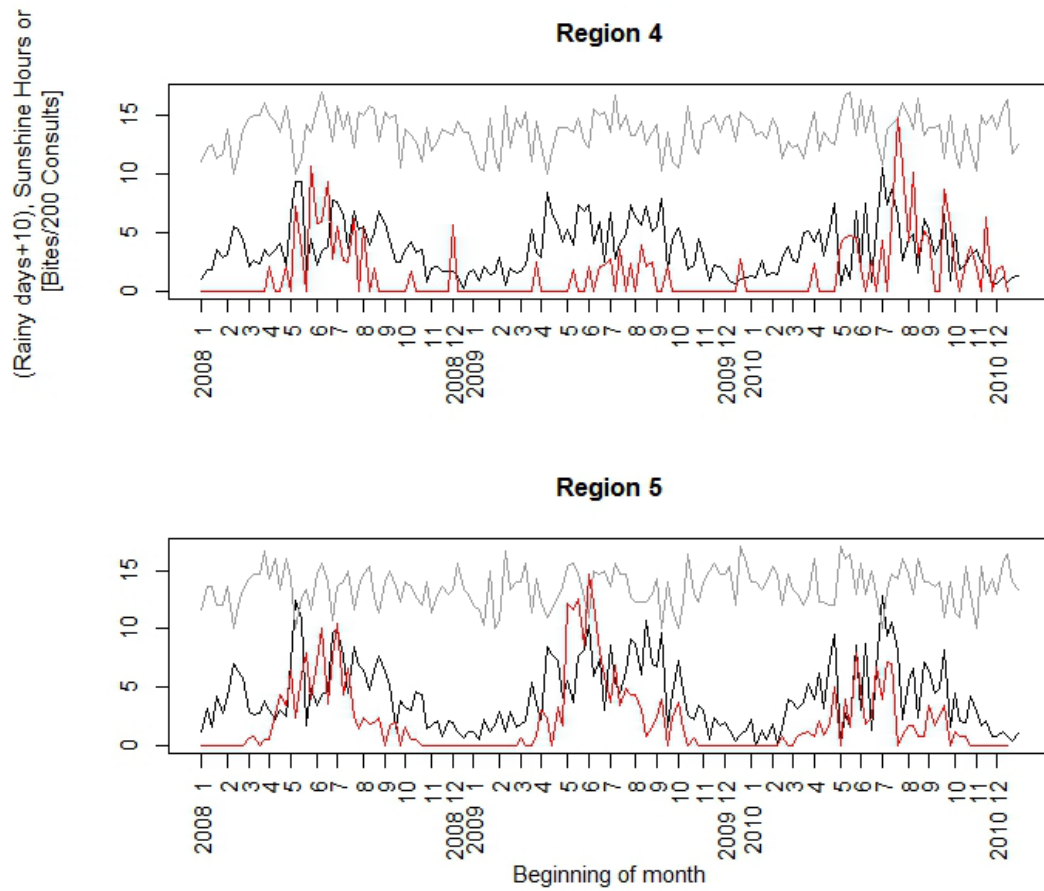


Figure 4.9. Weekly tick bites per 200 doctors consultations (red line), average daily hours of sunshine (solid black line) and the number of rainy days (solid grey line, plus ten for clarity) for years 2008-2010 in Sentinella regions 1-5 of Switzerland (region labelled above each plot).

4.3.2.5. Human behaviour and tick bites

Human exposure is not simply a function of weather, but of other social factors such as school holidays. Tourism data can be used to assess the seasonal pattern of human exposure on tick bites. A strong bimodal seasonal pattern is seen in the number of Swiss hotel and health establishment arrivals across Switzerland (Fig. 4.10a). The peak month for tourism arrivals and overnight stays is seen in August in 2008 and July in 2009 and 2010, but with additional peaks in the late winter (which can be considered irrelevant as ticks are not actively questing until around March). The place of residence of these Swiss tourists within Switzerland is unknown, but the most popular tourism cantons are Graubünden, and Bern (Fig. 4.10b). Graubünden, a canton with many skiing facilities,

demonstrates a very seasonal pattern of tourism. with large summer and winter peaks. In contrast, Ticino, which is south of the Alps and has little skiing trade, sees no winter peak in tourism. In Zürich, a major Swiss city, all year round visitation would be expected *a priori* and indeed there is very little seasonal variation in tourism.

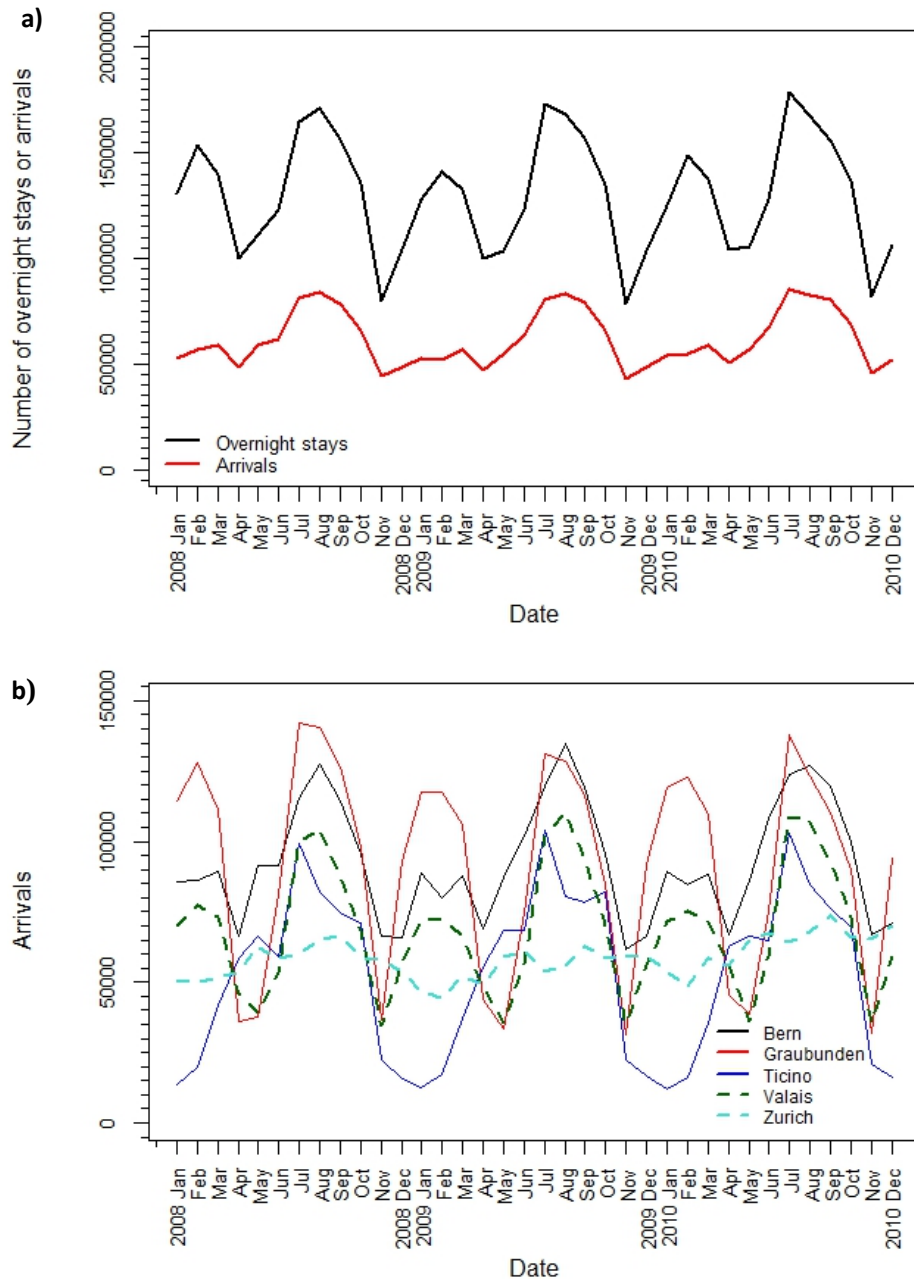


Figure 4.10. The number of Swiss tourists staying at a hotel or health establishment by month from 2008 to 2010. a) The number of arrivals (solid red line) and total overnight stays (solid black line) in Switzerland. b) The number of tourist arrivals in the top five most visited cantons.

Along with the bimodal seasonal pattern in hotel tourism, there is a strong seasonal

element to camping trips in Switzerland (Fig. 4.11). Peak campsite occupancy is seen in July in 2008, 2009 and 2010, but unlike hotel visits, there are no overnight stays between November and March. In 2009, there were around 35 million overnight stays in hotels and health establishments and 3.6 million visits to campsites in Switzerland.

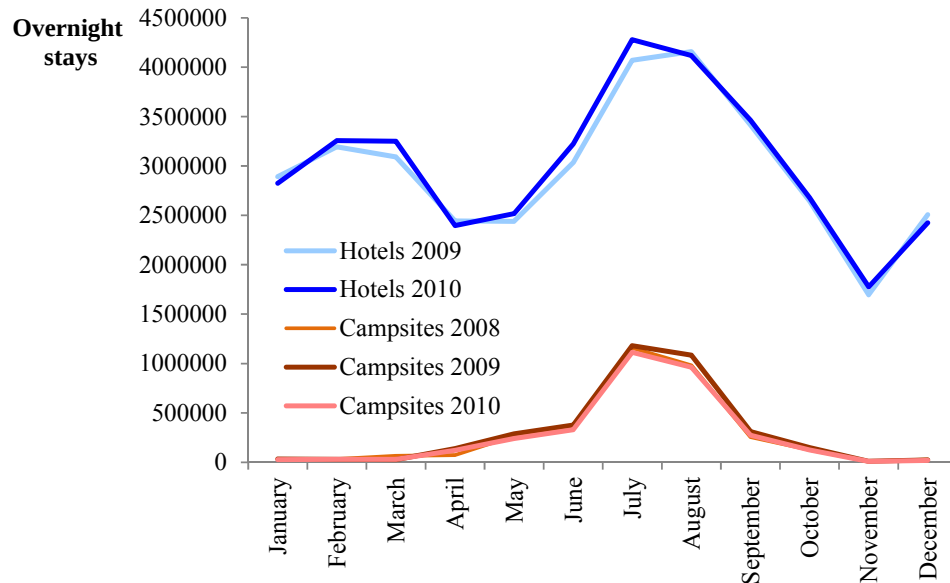


Figure 4.11. The number of overnight stays per month in hotels or health establishments and in campsites in Switzerland between 2008 and 2010.

The majority of cantons in Switzerland have a similar system of school holidays (Fig. 4.12). In Figure 4.12 each of the five plots is a different Sentinella region and within each region each canton is represented by a colour, which is slightly transparent. If cantons in the same region have holidays at the same time, the overlaid blocks show a colour made up of the underlying cantons. For instance, in August of 2009 in Region 1, a brown colour is shown because three cantons have school holidays and the green for Geneva, red for Vaud and blue for Neuchâtel are overlaid. Data were only available for three cantons of Switzerland in 2008: Geneva in Region 1 and Aargau and Basel County in Region 3. All cantons have school holidays for Easter and Christmas, and during much of July and August. Schools often have an additional holiday in February and October, but the exact dates are variable. There is only a weak relationship between the holidays and

tick bites, suggesting direct causality is unlikely, but tick bites do commonly occur during school holiday time. Bites may even peak during the summer holiday, for example in 2010 in Regions 2 and 4. This is despite the peak in tick questing occurring in June at the latest.

The peak month for holidays in hotels or campsites in Switzerland is July or August and the peak in questing ticks is in April or May but the tick bites peak in June. It is hypothesised that the peak in tick bites seen in June is because this is the time of maximum coincidence between the questing tick and human exposure seasons. This was verified by combining the seasonal curves of questing ticks and human holiday arrivals and overlaying this with the tick bite season (Fig. 4.13). The holiday data had been adjusted by removing the arrivals in the lowest tourism month (November) so as to give only the seasonal element of travel, which is thought to be most indicative of human exposure to ticks. As previously discussed, travel to cities such as Zürich shows no seasonal patterns, but in rural areas, such as Graubünden or Bern, there is a considerable seasonal pattern. By simply multiplying the questing tick activity and human exposure behaviour curves, a seasonal profile is created which is very similar to the actual seasonal pattern of tick bites. Specifically, the delay at the beginning of the tick bite season (when compared with the questing tick season) is predicted and the peak month of this new curve is July, which is a month with a high number of bites. This easily demonstrates how both tick and human behaviour are important in dictating the seasonal pattern of tick bites in Switzerland.

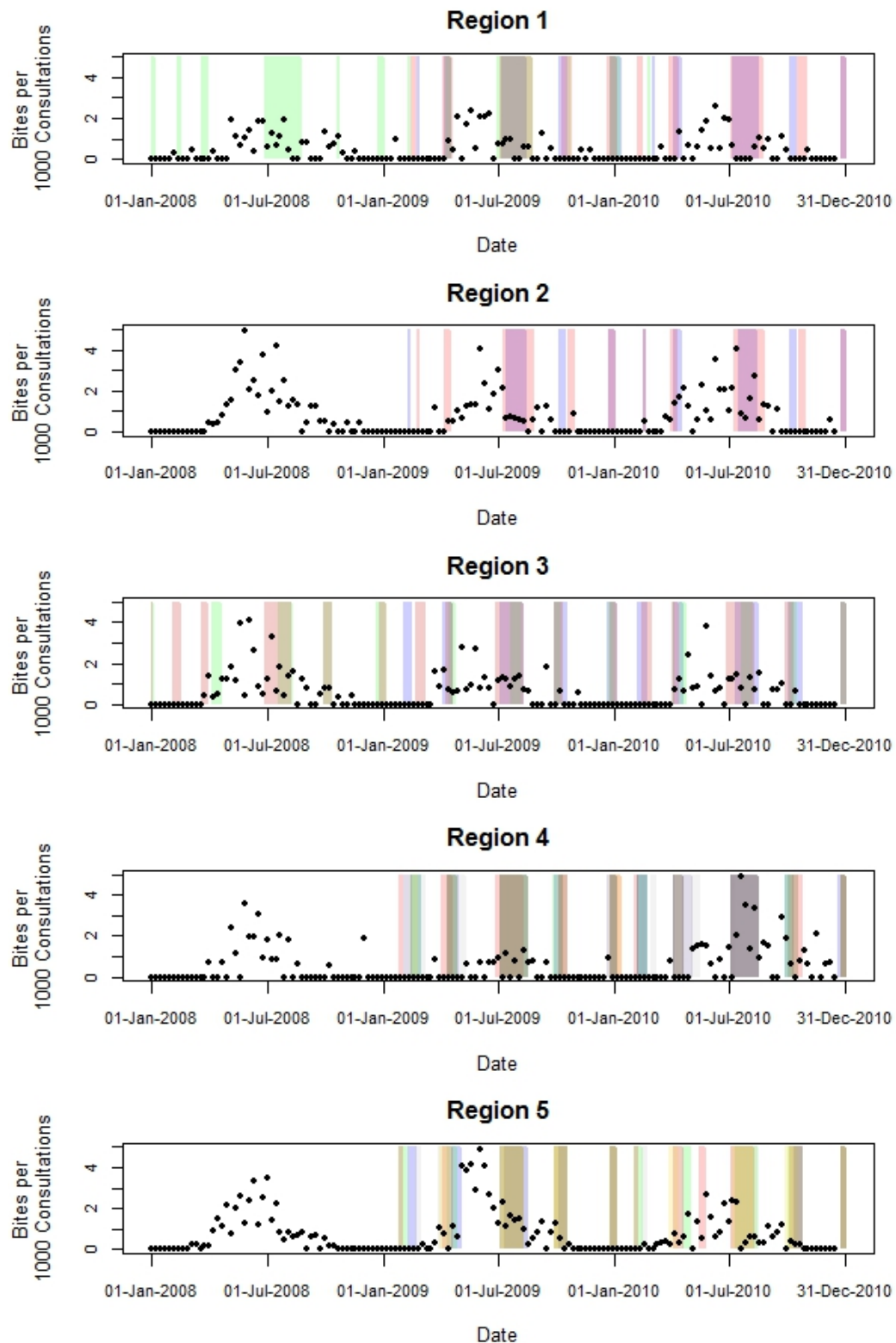


Figure 4.12. Weekly tick bites per 1000 doctor consultations between 2008 and 2010 (shown as black dots). The coloured blocks in the figure represent school holidays. In each region (labelled above the plot), a canton is represented by a different colour, which is semi-transparent. When the blocks are overlaid, the periods where most of the cantons are on holiday are seen in brown.

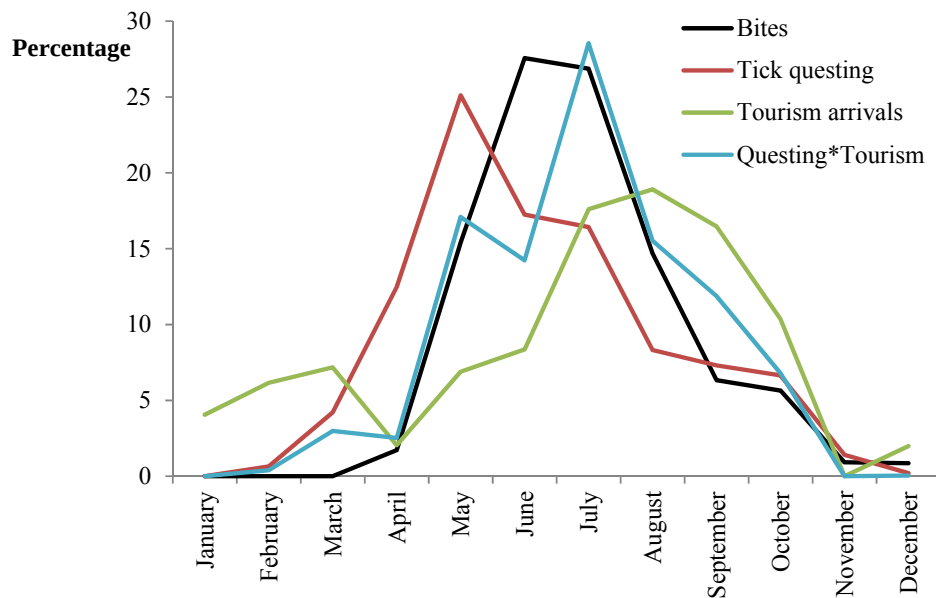


Figure 4.13. The annual seasonal pattern of tick questing in Bern, tourism in Switzerland, tick bites in Sentinella Region 2, and tourism multiplied by questing tick population (Questing*Tourism), presented as monthly percentages of the yearly total, in 2008. The ‘Tourism arrivals’ were adjusted by subtracting the number of arrivals in the lowest tourism month (November).

4.3.2.6. Occupation and leisure tick bites

It is hypothesised that the differences between the tick questing and tick bite season due to human exposure behaviour will be larger for bites gained during leisure time than those gained during work hours. Of the 1,023 bites recorded from 2008 to 2010 in this study, 89.7% were incurred during leisure time. Only 7.5% of bites recorded occurred during work time (however, it seems likely that those often exposed may be less inclined to report the bite). This has made it difficult to draw conclusions regarding differences in the tick bite season due to work or leisure exposure because the seasonal distributions showed no significant differences (Fig. 4.14).

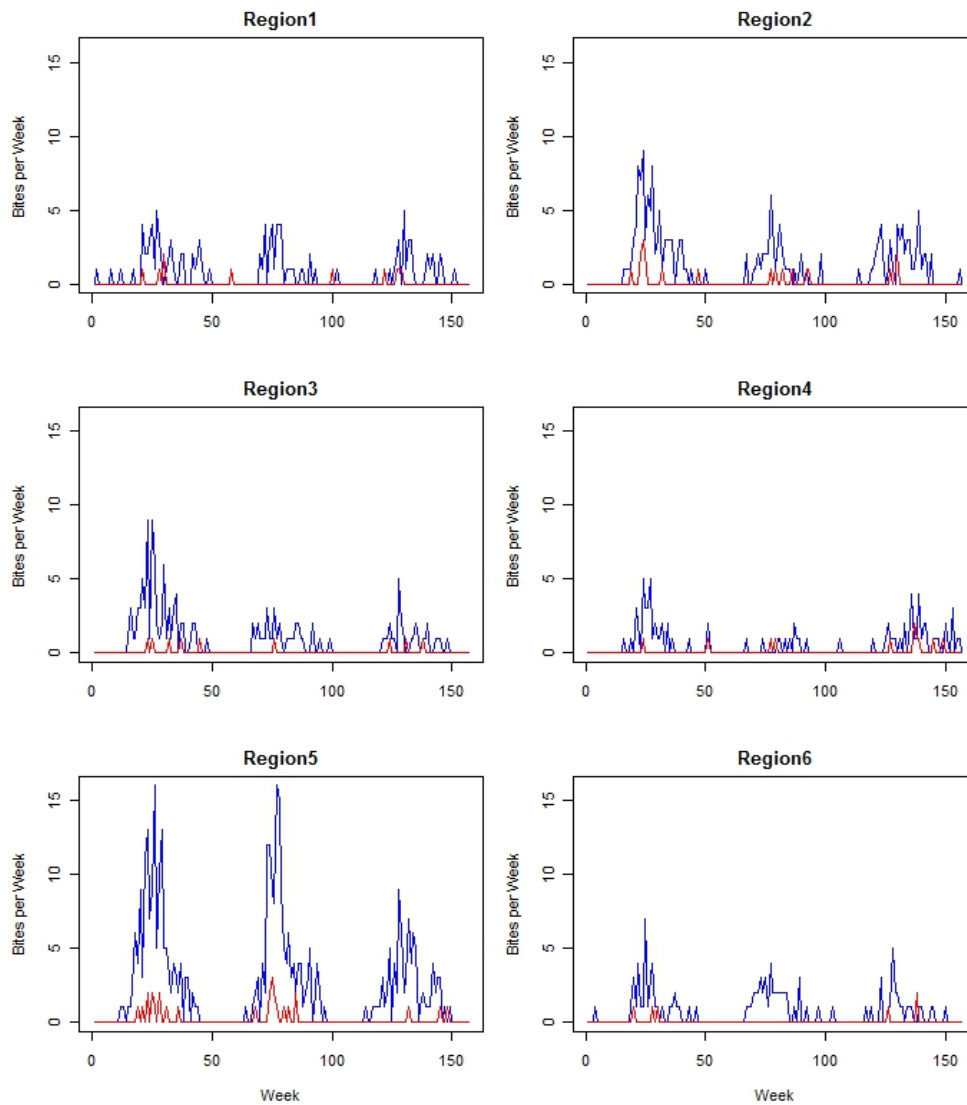


Figure 4.14. The seasonal distribution of bites incurred during leisure (blue) and work (red) time in 2008-2010 across the six regions of the Sentinella system (region labelled above each plot).

4.3.3. Weekly variation in tick bites

The influence of the weather in shaping the seasonal pattern of tick bites has been examined. The weekly variation in tick bites, aside from the seasonal pattern, could also relate to the weather, which might influence either the short-term questing activity of ticks or outdoor exposure of humans. The hypothesis tested here is that particularly sunny weeks or weeks with little rain would promote human outdoor behaviour resulting in short-term increases in tick bite numbers. The alternative hypothesis is that spikes in tick bites

relate to high numbers of questing ticks due to suitable weather.

Principal components analysis was applied to account for collinearity between the temperature, humidity, rainy days and sunshine, and four axes of variation for the weather data were extracted (Table 4.5). The first axis accounted for more than 60% of the variation in the weather data and was positively correlated with temperature and sunshine and negatively correlated with humidity and rainy days. It seems likely therefore that the weather described by axis one would promote human outdoor activity as it describes warm, sunny days, with low rainfall and humidity. Axes two, three and four account for 24%, 10% and 3% of the remaining variation in the data, respectively, and therefore have considerably less explanatory power. Axis two is strongly related to rainfall, axis three to high humidity and temperature, and axis four relates to cold but sunny days. Of these, any positive correlation between tick bites and axis three, with warm temperatures and high humidity, is likely to be mediated through changes in tick questing activity.

Table 4.5. Principal components analysis axes loadings for the four weather variables

	PCA1	PCA2	PCA3	PCA4
Maximum temperature	0.5305	0.3861	0.532	-0.5353
Rainy days	-0.2705	0.9144	-0.1126	0.2795
Humidity	-0.5316	-0.1175	0.815	0.1984
Sunshine	0.6024	-0.0331	0.2001	0.772
% variation explained	62.18	23.99	10.49	3.34

Seasonality in the weather PCA axes and tick bites were accounted for by fitting models with six sine and cosine terms, leaving residuals which were the weekly variation in weather and tick bites, respectively. Weekly residuals for the tick bites were regressed against the weekly residuals for the weather PCA axes. A null model for tick bite residuals, which included a constant term but no weather variables, had a QIC of 1,454. The best model fitted included the first PCA axis with a two-week lag and had a QIC of 1,443. The first PCA axis had a positive coefficient of 0.144 in the model which demonstrates that

warm, sunny weather with low humidity and rainfall promotes short-term increases in tick bites.

A model including the third PCA axis, with a two-week lag, had a QIC of 1,452. The third PCA axis was associated with a negative regression coefficient of -0.1386, which would suggest bites are associated with low humidity and temperature. Extra variables, included in addition to the first PCA axis, had p-values greater than 0.05, so were not included.

Although an increase in temperature could favour both tick questing and human outdoor activity, the influence of humidity and sunshine allow the causal factors in short-term fluctuations in tick bites to be more thoroughly elucidated. There is a positive relationship between bites and the first weather PCA axis, which is strongly related to sunshine. Sunshine would have no impact on ticks, but would promote human outdoor activities, suggesting it is human behaviour which shapes the weekly fluctuations in tick bites. In the model with the third weather PCA axis, a negative correlation is observed between humidity and tick bites. A positive correlation between humidity and tick bites would probably be expected given that high saturation deficit limits the tick's ability to actively quest for hosts. No correlation between humidity and tick bites might also be expected if meteorological station data did not accurately reflect conditions in the tick microclimate. However, a significant negative relationship suggests that short-term changes in the number of tick bites are not associated with changes in the questing tick abundance.

4.4. Discussion

4.4.1. Questing tick, human behaviour and tick bite season

In Switzerland, numbers of questing ticks increase rapidly from March to a peak in May, before declining as the questing tick population becomes exhausted. Tick bite

frequency shows a similar general seasonal pattern, with an increase, a peak and then decline. Between 2003 and 2005, physicians collected ticks which had bitten humans in the Neuchâtel region (Huegli et al. 2009). Tick collection peaked in May in 2005 and in June in 2003 and 2004. Tick bites begin in April, and extend into October in all years, just as they do in the Sentinella dataset.

Correlation analysis for two parts of the year, before and after the peak in tick bites, shows that bites are significantly correlated with the temperature prior to the peak in tick bites, but not after. This supports the hypothesis that increasing temperature in the spring is permissive to the progressive activation of questing ticks and after the peak, tick bites are independent of temperature as tick populations are exhausted. Rising spring temperature will likely also promote an increase in human exposure.

A comparison of the distributions, however, shows a delay in the timing of the onset of the tick bite season and of the peak in tick bites relative to the seasonal distribution of questing ticks. Additionally, the threshold in temperature thought to permit nymphal tick questing (7°C), does not correspond to the start of the tick bite season. In 2007, this seasonal delay was also seen, as questing nymphs were observed earlier in the year in Bern, Switzerland, but the seasonal distribution of TBE showed no change (Randolph and EDEN-TBD Sub-Project Team, 2010). This situation was mirrored in Germany and Slovenia, suggesting this early season delay in tick bites does not only apply to Switzerland.

This delay would seem to be a result of human behaviour, which has a much later seasonal distribution than questing tick abundance. In Slovenia, 90% of park visits occurred between May and September (Randolph et al., 2008). The observed seasonal peak in tick bites in the middle of the summer corresponds to the period of maximum coincidence between human exposure (measured using tourism data) and the tick questing season.

When predicting the seasonality of tick bites, both the tick questing season and the patterns of human exposure should be considered. Additionally, factors that influence the commencement of tick questing in the spring may have little influence on tick bites, and consequently TBDs at this point, because of the absence of human exposure. Advances in the commencement of the tick questing season, for instance as a result of global warming, may therefore have relatively little impact on the tick bite season. Nevertheless, rising spring temperature may also promote an increase in human exposure early in the year, although this may be constrained to some extent by cultural and societal schedules (e.g. traditional vacation seasons).

Towards the end of the season, around mid-August, the patterns of questing ticks and tick bites are re-aligned, which suggests that the number of tick bites is limited by the abundance of questing ticks from this point onwards. Humans are expected to show their peak exposure due to holidays during this month, so it is not surprising that the availability of the rapidly diminishing questing ticks should become limiting to the number of tick bites later in the year.

4.4.2. Weekly variation in tick bites as a result of human exposure patterns

After accounting for the effect of seasonality, warm, sunny weather with low humidity and rainfall evidently enhances the probability of tick bite occurrence. This weather profile is most likely to be associated with human exposure patterns. Tick questing is particularly reliant on high humidity to avoid desiccation, but weeks with anomalously high tick bites are significantly associated with low humidity weather. In previous empirical studies, reductions in humidity were found to have precipitated declines in tick questing (Perret et al., 2004), and to have no significant relationship with tick questing at all (Perret et al., 2000). The negative correlation found between weekly tick bites and humidity in this study therefore underlines the importance of human behaviour, not variability in tick questing, in determining the weekly number of tick bites.

This interpretation is in accordance with the events in Switzerland in 2003: it was very warm and people visited the forest, leading to a high number of tick bites (Huegli et al., 2009), despite a decline in the free-living tick population density (Moran Cadenas et al., 2007).

Increased human outdoor activity, as a result of favourable weather associated with mushroom foraging, was also implicated in weeks with peak tick bites in Latvia (Sumilo et al., 2008a). The number of tick bites reported to the State Public Health Agency in Riga, Latvia between January 2002 and December 2003 showed no relationship to the number of ticks counted in a forest close to Riga, but instead to rain-free weekends with mean maximum air temperature above 15°C and heavy rainfall in the previous week (Sumilo et al., 2008a). This effect of increased tick contact in favourable weather was evidently taken to its extreme in 2006 when a spike in TBE was observed across Europe, due not to an increase in the questing tick population but to favourable weather conditions for recreation (Randolph et al., 2008).

Forcing of short-term disease dynamics by weather variables has previously been observed. For instance, significant relationships between rainfall and cholera in Zambia (Luque Fernandez et al., 2009) and Bangladesh (Hashizume et al., 2008) have previously been recorded. However, in the present case of TBDs the mechanism for the relationship between disease and weather is the change in human behaviour which increases exposure to the vector.

**CHAPTER 5. ECONOMIC DOWNTURN RESULTS IN TICK-
BORNE DISEASE UPSURGE**

RESEARCH

Open Access

Economic downturn results in tick-borne disease upsurge

Elinor R Godfrey, Sarah E Randolph*

Abstract

Background: The emergence of zoonoses is due both to changes in human activities and to changes in their natural wildlife cycles. One of the most significant vector-borne zoonoses in Europe, tick-borne encephalitis (TBE), doubled in incidence in 1993, largely as a consequence of the socio-economic transition from communism to capitalism and associated environmental changes.

Methods: To test the effect of the current economic recession, unemployment in 2009 and various socio-economic indices were compared to weather indices (derived from principal component analyses) as predictors for the change in TBE case numbers in 2009 relative to 2004-08, for 14 European countries.

Results: Greatest increases in TBE incidence occurred in Latvia, Lithuania and Poland (91, 79 and 45%, respectively). The weather was rejected as an explanatory variable. Indicators of high background levels of poverty, e.g. percent of household expenditure on food, were significant predictors. The increase in unemployment in 2009 relative to 2008 together with 'in-work risk of poverty' is the only case in which a multivariate model has a second significant term.

Conclusion: Background socio-economic conditions determine susceptibility to risk of TBE, while increased unemployment triggered a sudden increase in risk. Mechanisms behind this result may include reduced resistance to infection through stress; reduced uptake of costly vaccination; and more exposure of people to infected ticks in their forest habitat as they make greater use of wild forest foods, especially in those countries, Lithuania and Poland, with major marketing opportunities in such products. Recognition of these risk factors could allow more effective protection through education and a vaccination programme targeted at the economically most vulnerable.

Background

Zoonotic infections, that circulate amongst wildlife and only infect humans accidentally, are not usually thought of as one of the ill effects of economic recessions. Tick-borne encephalitis (TBE), however, appears to be so in some parts of Europe. It is quantitatively and medically the most severe European vector-borne disease, caused by a flavivirus transmitted by *Ixodes ricinus* ticks in most countries in western, central and eastern Europe, and characterized by extreme spatial and temporal variability in its incidence. Dramatic upsurges in the early 1990s in most central and eastern European (CEE) countries have been related to environmental and socio-economic changes associated with the end of communist rule [1,2].

The former favoured increased abundance of infected ticks, while the latter promoted contact between those ticks and humans as they utilized tick-infested forests for either recreation or food harvest, depending on their economic status [3]. In western Europe, increases in incidence have been more gradual [4,5]; in Italy, for example, emergence has occurred in areas where forest types favour roe deer (*Capreolus capreolus*), the principal host for ticks [6,7]. Against this background, spikes in annual incidence occur sporadically in some countries for reasons that are not always apparent (e.g. in 2003 in the Baltic States - Estonia, Latvia and Lithuania - and Poland), but exceptional ones in 2006 in Switzerland, Germany, Slovenia, and the Czech Republic have been related to the unusual weather conditions during the second half of that year, apparently favouring both mushroom growth and outdoor recreation [8,9]. The response

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to such weather again varied with the national cultural and socio-economic contexts.

Low economic status has been identified as a significant risk factor for TBE infection in some parts of Europe. For eight CEE countries, the differential degree of TBE upsurge in the early 1990s was significantly positively correlated with contemporary poverty indicators, including the percentage of total household expenditure spent on food [1]. In Latvia, low income is linked to a greater probability of frequent visits to forests (tick habitat) for the purpose of collecting mushrooms or berries and a lower probability of being protected against TBE by vaccination [3]; furthermore, rural parishes with a low proportion of people with an economic activity have a higher probability of TBE cases [10]. Likewise, in Poland, replies to a questionnaire amongst 442 families involved in the harvest of non-wood forest products (NWFP) (principally mushrooms and fruit, but also fuel, decorative items and herbs) testify to the importance of income from the sale of these products for the economically disadvantaged [11]. The emergent prediction, tested here, is that the current economic recession might precipitate an upsurge in TBE incidence in certain countries where the response to poverty is more likely to include, amongst other things, activities leading to greater contact with tick-infested habitats and reduced protection through costly vaccination. Variations in both temperature and rainfall during the tick activity season have been shown to determine the weekly number of reported tick bites [3] and the monthly incidence of TBE [8], more through their impacts on human behaviour than on ticks. Therefore, we first tested the alternative hypothesis that any change in TBE incidence in 2009 was caused by unusual weather; it is discarded. Although we used time series data to derive our relative indices for 2009, we are actually taking a static view to make comparisons across countries.

Methods and data

Data sources

Information on the annual case numbers of TBE in each of 14 countries (with >10 cases per year) was acquired directly or indirectly from national Public Health Agencies via their web sites or the International Scientific Working Group on Tick-borne encephalitis (ISW-TBE). In addition to data at the national level, regional data for 2009 were available for most countries. For Hungary and Slovenia, data from the national diagnostic laboratories were used in favour of case numbers reported by doctors to Public Health Institutes, because the latter habitually suffer from under-reporting. These data are available from 1970 for most countries, but only those for the past six years are relevant to this present analysis. For Lithuania only, data on TBE incidence within different

employment groups were also made available from the Lithuanian Public Health Agency. Figures for annual unemployment were extracted from Eurostat http://epp.eurostat.ec.europa.eu/cache/ITY_SDDS/EN/une_esms.htm; for Switzerland equivalent data were taken from the national statistics department <http://www.bfs.admin.ch>. These statistics were based on the International Labour Organisation's definition of unemployment: persons of a certain age who were not employed during the reference week, had actively sought work during the past four weeks and were ready to begin working immediately or within two weeks. They therefore represent responses to the immediate economic situation better than would figures for long-term unemployment. A variety of other socio-economic indicator variables for the period 2004-08 was extracted from Eurostat and the United Nations Development Program to explore any further socio-economic influences on TBE occurrence; these included GDP, expenditure on food (available for 2005), the Gini coefficient (a measure of inequality of income or wealth), poverty gap, at-risk of poverty, and in-work risk of poverty [12] (Table 1 for definitions). These socio-economic indices changed very little over this short period, so we used values for 2008 (apart from food expenditure) to indicate the most immediate background levels of poverty against which unemployment increased in 2009. Not all these additional data were available for Switzerland.

To derive summary indices of the relevant weather during the tick activity season (typically April-October, giving TBE cases typically reported during May-November - [8]) monthly mean daily maximum temperature and daily precipitation (mm) were calculated from daily records downloaded from the European Climate Assessment web site <http://eca.knmi.nl> [13] for a representative site for each

Table 1 Definitions of poverty indices

GDP - gross domestic product:
The market value of all final goods and services produced within a country in a given period of time.
Equivalised disposable income (used below):
Income adjusted for household size, achieved by assigning different members of a household the following weighting (taken from OECD): 1 for the first adult (>14 years), 0.5 for each subsequent adult and 0.3 for each person ≤14 years old.
At-risk of poverty:
The share of persons with an equivalised disposable income below the at-risk-of-poverty threshold, which is set at 60% of the national median equivalised disposable income.
Relative median at-risk-of-poverty gap (abbreviated to poverty gap):
The difference between the at-risk-of-poverty threshold and the median equivalised disposable income of persons below the at-risk-of-poverty threshold, expressed as a percentage of the at-risk-of-poverty threshold.
In-work risk of poverty:
The share of persons who are employed whose household equivalised disposable income is below 60% of national median equivalised income.

country over 1989-2009. Given the very similar weather patterns within any one country, and even between neighbouring countries, each site is taken as representative of the relative conditions in each year. For Hungary, it was necessary to use data from a meteorological station just across the national border in Croatia, but within the same TBE endemic region. To derive comparable measures of any unusual annual weather pattern, for each country the particular conditions for each month from April to October in each year were summarized as the deviations from the monthly means over the whole period (1989-2009), i.e. seven monthly anomalies per year per country.

Analyses

As the purpose of this study was to test for unusually high incidence of infection in 2009 compared with recent years, rather than to compare incidence between countries, raw case numbers were used without correcting for population sizes, which have changed very little over the period of interest. This avoids the unnecessary complication of the differential extent of TBE distribution within each country. As TBE incidence varies from year to year (see above and Table 2), case numbers in 2009 were compared with the mean level over the previous five years in each country (to give a '2009 TBE index'); this avoids any exaggeration in the measure of upsurge in 2009 due to randomly low numbers in 2008. This relatively short time series was chosen deliberately to maximize the uniformity of background forces operating across Europe, and specifically to avoid the long-lasting, slowly resolved effects of the major socio-economic transition that occurred in central and eastern Europe in the early 1990s [1], in order to test the specific hypothesis concerning the exceptional economic recession. Because of the

highly variable patterns of recent trends in unemployment in each country (Figure 1b), change in unemployment levels was calculated as the ratio of 2009 to 2008 percentages to test the immediate effect of increased unemployment irrespective of recent trends. In fact, the ratio of unemployment 2009/2008 is highly correlated with the ratio for 2009/2004-08: correlation coefficient = 0.926, df 12, $p < 0.001$. The results of the analyses (below) were virtually identical (apart from very slight differences in values) whichever ratio was used.

To remove any co-variation in the weather variables taken from consecutive months, a principal components analysis (PCA) was performed on the monthly anomalies in temperature and precipitation, using the 'prcomp' function in the R statistical package [14]. Four PCA axes, that captured 76% of the variance in temperature and 71% in precipitation, were used for further analysis. Summary indices of the variation in weather by year and country were calculated as the Euclidean distance to the PCA centroid. As the conditions of normality were not met in several years, non-parametric t-tests (Mann-Whitney U-test) were used to compare the mean index across countries for each year against the mean for all other years to identify any unusual annual weather pattern. A comparable PCA for socio-economic conditions was not possible because there were too few indicators (8) relative to the number of countries.

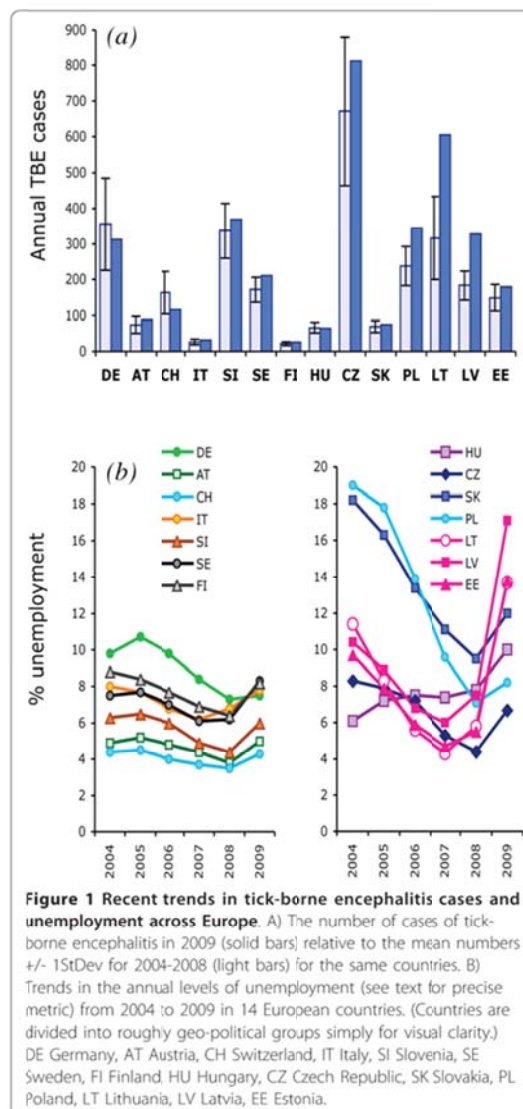
Instead, univariate and multivariate normal linear regression analyses with normally distributed errors for the 13 countries with full socio-economic data were undertaken in the R statistical package [14]. All factors used in univariate analyses were then included in the multivariate analyses. Forward stepwise selection was used, i.e. to each explanatory variable each other explanatory variable was added until no further improvement in the model was achieved. Model selection was based on the Akaike's Information Criterion corrected for small sample size (AICc). PCA Euclidean distances for temperature and precipitation in 2009 were also included in these analyses.

Results

In Latvia, Lithuania and Poland, TBE cases in 2009 exceeded the mean plus one standard deviation (StDev) for the years 2004-08 (Figure 1a) and were also 1.7-2.8 times higher than in 2008 (Table 2). Although the increase in these countries was not statistically significant (i.e. not more than 2 StDev greater than the mean), it was considerable compared with the long-term normal year-to-year variation, and was much greater than for any other country. In Estonia, there were twice as many cases in 2009 as in 2008 due to the unusually low numbers in 2008, but the number for 2009 fell within the ± 1 StDev range for 2004-08. Case numbers in

Table 2 Tick-borne encephalitis cases recorded from 2004 to 2009 in those countries in Europe in which there were more than 10 cases per year

	2004	2005	2006	2007	2008	2009
Germany	274	432	546	238	289	313
Austria	54	100	84	45	86	88
Switzerland	132	208	245	111	123	116
Italy	31	19	30	17	34	32
Slovenia	264	375	446	266	334	369
Sweden	160	130	163	182	224	211
Finland	31	17	18	20	23	26
Hungary	89	52	56	62	70	64
Czech Republic	507	643	1029	546	633	812
Slovakia	70	50	91	57	79	75
Poland	262	174	316	238	201	345
Lithuania	425	243	462	234	220	605
Latvia	251	142	170	171	184	328
Estonia	182	164	171	140	90	179



2009 in all other countries fell within the $\pm$ 1 StDev range for 2004-08, and differed from 2008 by no more than 13% (apart from the Czech Republic, 28% higher). In Sweden case numbers in 2009 just exceeded (by 5) the mean + 1 StDev for 2004-08, but did not exceed those in 2008, due to the on-going upward trend since 2000. The geographical pattern is shown in Figure 2.

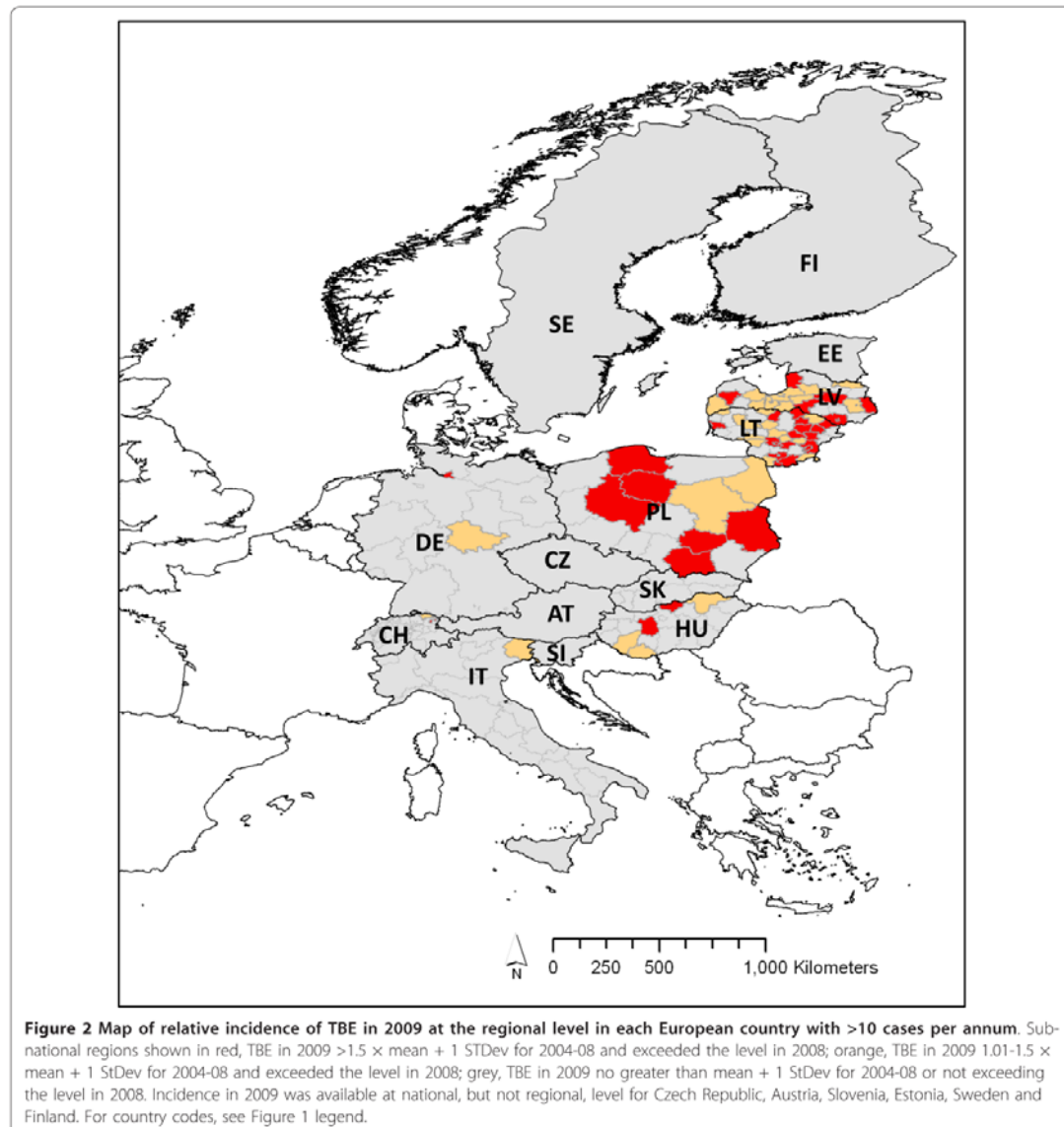
The weather in 2009 showed no statistically significant difference from the average conditions for 1989-2009 (Figure 3). Furthermore, the Euclidean distances from the PCA centroid for Latvia, Lithuania and Poland

(highlighted in Figure 3) were not consistently greater than for other countries. The weather in 2008, when the TBE virus-infected nymphal ticks that were active in 2009 would have been feeding as larvae and thus acquiring their infection, was even closer to the long-term average conditions. Only in 2006 were the patterns in both temperature and precipitation significantly different from the norm; for each specific country that suffered a spike in TBE incidence in 2006, the Euclidean distances in temperature were particularly large (>1 StDev above the overall mean for 1989-2009) (see discussion). In some other years, either temperature (1991, 2000, 2003) or precipitation (1994), but not both, showed significantly unusual patterns.

Unemployment increased in all countries in 2009, reversing the universal trend of steady decrease over the previous five years (except for Hungary, which showed an upward trend throughout this period) (Figure 1b). In all three Baltic countries, the increase had already started in 2008 (from the 3rd quartile) and exceeded two-fold from 2008 to 2009. Noteworthy is the sharp decline in unemployment in Poland and Slovakia from very high levels in 2004, followed by relatively modest increases in 2009 (15% and 25%, respectively). Amongst the CEE countries, Slovenia and the Czech Republic showed overall patterns most similar to those in 'western' Europe (in the political rather than geographical sense), although both showed higher rates of increase from 2008 to 2009 (36% and 55%, respectively) than seen in the 'west' (3-34%).

Univariate analyses showed that national '2009 TBE indices' were significantly correlated with seven of the nine tested socio-economic indices, but not with the weather indices (Table 3). In all cases, the greater the poverty, the greater the 2009 TBE index. Because the dominant relationship with 'percentage food expenditure for 2005' was non-linear (2nd order polynomial), the squared term of this variable was included in both univariate and multivariate analyses, and proved to be the most significant single correlate. This was not improved upon by adding any other variable to 'food expenditure'. The list of significant variables indicates that background socio-economic conditions are as important as the sudden increase in unemployment in triggering activities associated with the increased risk of TBE. The high degree of co-variation between these socio-economic indices is revealed by the fact that the selection of 'in-work risk of poverty' as a second significant variable with 'unemployment ratio 2008/09' is the only case in which a multivariate model has a second significant term.

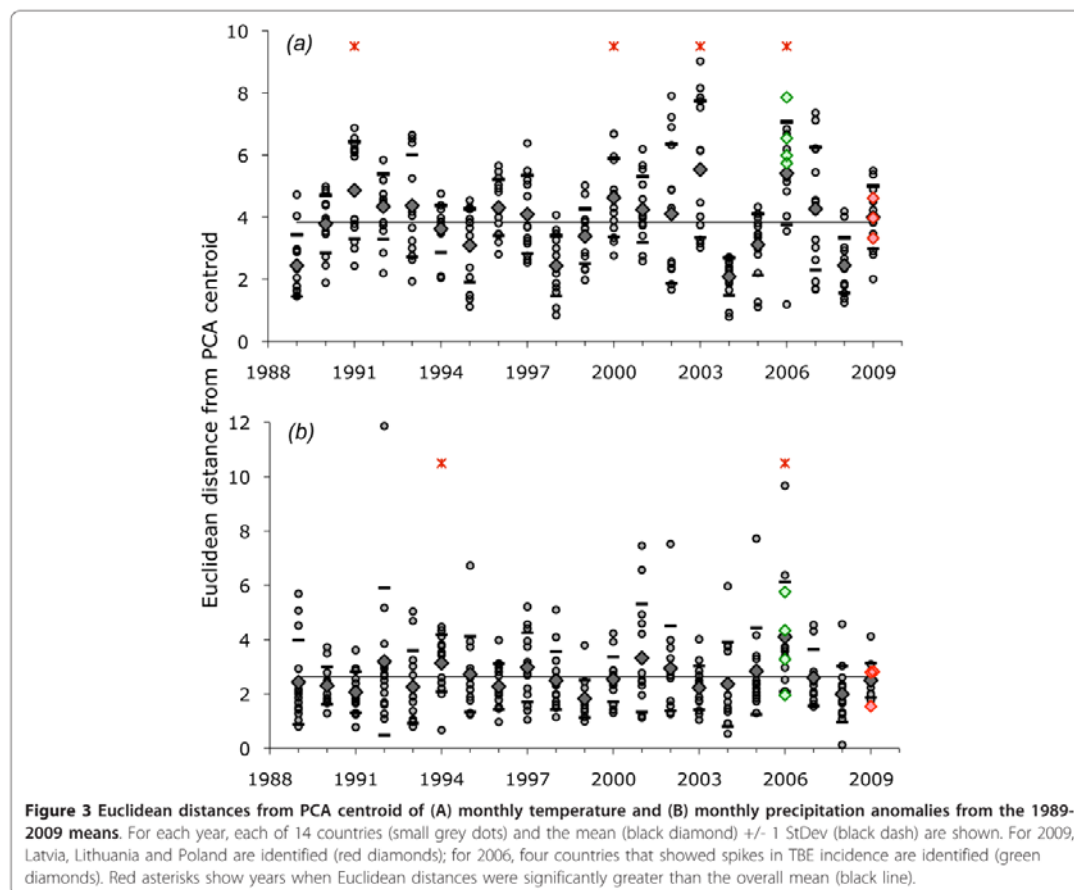
These conclusions are visually apparent from the univariate regressions (Figure 4) that highlight the outliers and exceptions to the overall effects of unemployment, most marked amongst CEE countries. In the three



countries with exceptional increases in unemployment in 2009, TBE cases did indeed almost double in Lithuania and Latvia, but increased by only 20% in Estonia (Figure 4a). Conversely, the very modest increase in unemployment in Poland was associated with a 45% increase in TBE. This seems to be largely explained by the in-work risk of poverty (Figure 4b), which is highest in Poland (12) and much lower in Estonia (7 relative to a range of 5-9 amongst western countries). Tellingly, in

Lithuania, the increase in TBE incidence was significantly greater amongst the unemployed (157%) than the employed (96%) ($\chi^2 = 4.57$, $p < 0.05$), or pensioners (47%) ($\chi^2 = 6.66$, $p < 0.01$).

With respect to socio-economics, as would be expected, 'western' European countries habitually fall in the lower left quartile of these plotted relationships and showed no significant effect of poorer socio-economic conditions on TBE incidence. Some CEE countries,



notably Slovenia, the Czech Republic, Slovakia and Hungary also consistently fall there. Clearly, people's responses to the recession differ between countries, and only in some are these responses associated with activities likely to raise the risk of TBE infection, discussed below.

Discussion

We report considerable increases in national mean TBE incidence in 2009 relative to average levels over the previous five years in three countries. Latvia, Lithuania and Poland, suffered 91, 79 and 45% increases in TBE case numbers, respectively, compared with <25% increase elsewhere and even 12-29% reduction in Germany and Switzerland. The propinquity of Latvia, Lithuania and Poland could suggest spatial autocorrelation that would undermine the statistical analyses, but this is highly unlikely in this case. Contiguity *per se* does not result in similar patterns of TBE incidence or change in incidence

[1-3,8]; TBE is not contaminative and the vector ticks do not fly. Estonia is also contiguous with and part of the same geographic and politico-historical group as Latvia and Lithuania, but shows neither the same current poverty levels nor TBE spike in 2009. TBE is largely absent in central Poland, and the TBE spike in NE Poland was no greater in the regions closest to Lithuania than in other parts of this large country (Figure 2). Plausible mechanisms for spatial autocorrelation in this disease system that could explain the sharp increase in incidence in 2009 (as distinct from simply the presence of TBE) are human habits and conditions associated with the geography of poverty due to history, or geographically coherent weather anomalies.

The hypothesis concerning the effect of the weather was tested and discarded. Across all 14 countries included in this analysis, neither temperature nor precipitation during the tick activity periods in 2009 or 2008 was unusual. Moreover, Latvia, Lithuania and Poland did not differ

Table 3 Significant socio-economic variables to predict the degree of change in tick-borne encephalitis cases in 2009 relative to the mean for 2004-08

Explanatory variables	factor 1 p-value	factor 2 p-value	AICc
Food expenditure 2005 ²	0.0013		0.078
Food expenditure 2005 ² + At-risk of poverty 2008	0.0194	0.1061	0.847
Food expenditure 2005 ² + Gini coefficient 2008	0.0322	0.1239	1.180
Food expenditure 2005 ² + In-work risk of poverty 2008	0.0131	0.1269	1.232
Food expenditure 2005 ² + Poverty gap 2008	0.0290	0.2465	2.577
Food expenditure 2005 ² + Ratio unemployment 2009/08	0.0317	0.3138	3.026
Food expenditure 2005 ² + Unemployment rate in 2009	0.0249	0.9508	4.407
Gini coefficient 2008	0.0051		3.102
At-risk of poverty 2008	0.0075		3.960
Poverty gap 2008	0.0107		4.743
Ratio unemployment 2009/08	0.0120		4.985
Ratio unemployment '09/08 + In-work risk of poverty '08	0.0142	0.0162	1.432
In-work risk of poverty 2008	0.0138		5.295
Unemployment rate in 2009	0.0295		6.931
GDP 2009	0.0898		9.222
Unemployment rate in 2008	0.8496		12.733
Temperature PCA Euclidean distance	0.8897		12.754
Precipitation PCA Euclidean distance	0.9471		12.773

Factor 1 and factor 2 refer to the predictor variables in the multi-variate analyses. Significant p-values are shown in bold.

Only some results of the multivariate analyses are presented to illustrate that second variables made significant contributions to the explanatory power of the models in only one case.

²For food expenditure, the squared term was used because a non-linear (2nd order polynomial) relationship with TBE increase is dominant.

In all cases, n = 13 (Switzerland omitted for lack of some data); df = 3 for uni-variate, 4 for bivariate models.

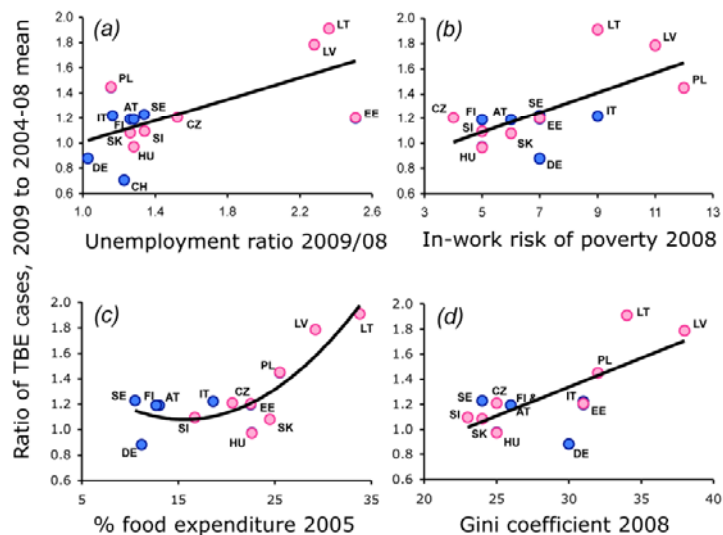


Figure 4 Relationships between relative changes in TBE case numbers in 2009, unemployment and various socio-economic indices. A) Increase in unemployment in 2009 relative to 2008, $R^2 = 0.437$, $p = 0.010$. **B)** In-work risk of poverty 2008, $R^2 = 0.437$, $p = 0.014$. **C)** Percentage expenditure on food, $R^2 = 0.745$, $p < 0.001$. **D)** Gini coefficient 2008, $R^2 = 0.524$, $p = 0.005$. Countries as listed in Figure 1 legend: 'western' European countries (blue dots), central and eastern European countries (pink dots).

from the other countries in this respect. This contrasts with 2006 when both temperature and precipitation were significantly different from average (warmer and drier), particularly in those countries (Switzerland, Germany, Czech Republic and Slovenia) that showed a spike in TBE incidence in that year (Ref 8 and this study), and in ways that encouraged outdoor activity and thus greater contact with ticks [8]. In 2003, however, weather conditions were very close to the 21-year norm in the Baltic countries and Poland where there were spikes in TBE whose cause has not yet been investigated. The conclusion is that marked variation in annual TBE incidence can be, but is not always, driven by changes in the weather; it was not in 2009.

Rather than with the weather, the increase in TBE in 2009 was correlated with differential socio-economic contexts within which increased unemployment was induced by the recent recession. This context, which changes rather slowly (relative food expenditure, for example, barely changed between 1999 and 2005, the most recent index available), determines susceptibility to risk, while increased unemployment triggered a sudden increase in risk. The greater increase in TBE amongst the unemployed in Lithuania is consistent with this. In other words, only specific pre-existing socio-economic conditions give rise to the potential for certain countries to be at risk of an abrupt increase in TBE incidence during a recession accompanied by unemployment. Under-pinning this statistical result are several plausible mechanisms whereby economically disadvantaged people may be less protected against infection and/or be brought into greater contact with infected ticks in their forest habitat.

Two anti-TBE vaccines ('FSME ImmunTM' produced by Baxter and 'EncepurTM' produced by Novartis) are effective, but their cost may be inhibitive for the poorest people. Vaccination coverage (at least one dose) has increased over recent years, reaching 39% in Latvia by 2008 due to a vigorous campaign started in 1998, but only 9% in Lithuania and 18% in Estonia (unrecorded in Poland), in line with the range in most other European countries. Lack of personal exposure, awareness, knowledge, convenience and money are the most common reasons for not getting vaccinated, and one in three do not complete the 3-dose course in Latvia and Lithuania (GfK Group survey, reported by Astrid Essl, 12th annual ISW-TBE meeting, Vienna, January 2010). Low economic status was also identified as a negative factor in TBE vaccination in Latvia in 2000 [3,15]. During 2008 and 2009, the cost of vaccination increased by 40% in Lithuania (followed by a decrease of 12% in 2010), which is likely to have had a negative effect on uptake across the whole population, especially in financially straitened times (Milda Zygiute, Centre for

Communicable Diseases and AIDS, Vilnius, Lithuania, and Aukse Mickiene, Kaunas University, Clinic of Infectious Diseases, Kaunas, Lithuania, personal communication). Concomitantly, sales of TBE vaccine decreased by 23% in 2009 and by a further 30% in 2010.

Another possible factor is an increase in the proportion of viral infections that progress to clinical disease (i.e. recorded TBE cases) as a result of poorer nutrition in impoverished households. This proportion is generally rather low [16], but symptoms are more severe, and therefore recorded incidence disproportionately high, in immunologically compromised patients, as illustrated by the elderly [17,18]. The same might apply to people under stress economically and, as a result, physiologically and/or emotionally.

Any activity that brings people into closer contact with the tick-infested forests for their earned or subsistence livelihood would increase the risk of TBE infection. This could include forestry or simply gathering wood from forests, but the most significant may be the harvest of forest foods that is associated with higher TBE risk to people in Latvia [3,15] and a higher incidence of TBE in the northeastern voivodeships of Poland [11]. This activity has always been associated more with eastern Europe (and Russia) than western Europe [19,20]. In Poland and Russia, the harvest of such foods for generating additional family earnings is associated with low income [11,21]. Increased harvesting and exposure to ticks is not confined exclusively to the unemployed or even the very poorest, but in Poland, 47% of survey respondents in 2004 gave worse financial status of the family as the main reason for increased harvest, while for better off families it represents recreation [11,21]. In Finland, in contrast, mushroom harvest is not a necessity related to the income of the picker, but rather a luxury for the more highly educated, and so less likely to increase in response to unemployment [22,23].

People living in economic uncertainty characterized by high levels of in-work poverty would be expected to react rapidly, probably changing their daily activities when faced with economic downturns. Capitalizing on pre-existing habits and market outlets for NWFP, whether for major exports as from Lithuania and Poland [24] or home markets in Latvia (SER personal observations), would be an obvious route, for which there is some evidence. For instance, in Lithuania, the official bulk purchase of fungi from forests increased from c.1300-2700 tonnes annually during 2004-08 to 5666 tonnes in 2009 <http://www.stat.gov.lt>. Furthermore, the Private Forest Centre of Estonia reports that 2009 was a good year for mushrooms, which has allowed the unemployed, possibly from the recession, to earn money mushroom picking (translated from Estonian) <http://www.eramets.ee/?op=body&id=25&>

art=498#art498. In contrast, in 'western' Europe, reactions to the relatively modest increases in unemployment are less likely to include more frequent visits to tick-infested forests.

Conclusion

This is the second of two natural experiments in recent years, both of which reveal the immediacy of the impact of disparate factors on TBE incidence acting through changes in human activities, rather than via the slower responses of the natural enzootic cycles of the virus between ticks and wildlife hosts. First, in 2006, differential responses to unusual weather conditions apparently encouraged outdoor activity for recreation and/or mushroom harvest [9], but left tick populations little changed [8]. Secondly, the current global economic crisis appears to include increased TBE incidence in some European countries as one of its less expected effects. This constitutes an unfortunate opportunity to test conclusions from previous descriptive and analytical studies that identified correlations in time and space between the equally sudden and widespread, but sustained, upsurge in TBE incidence in 1993 and human-induced environmental changes and socio-economic shifts, many arising as an unintended consequence of political independence after the fall of communist powers [1,2]. Food expenditure was identified as a significant correlate of that upsurge too. In one way or another, the multi-factorial drivers of these epidemiological changes affected the living conditions of all four partners, the virus, ticks, wildlife hosts and humans. They differed in force in time and space, however, thereby generating the observed heterogeneous patterns in TBE incidence. The point is not that the variability in TBE incidence is always due to economic forces, but that economic forces are one factor amongst several in causing variability, and in 2009 such factors appear to have been particularly powerful in some countries, specifically Latvia, Lithuania and Poland. Vector-borne diseases, and especially tick-borne diseases for which the risk of exposure to infectious agents depends so much on human behaviour [25,26], are prime examples of complex systems; the output of interest, the incidence of human infections, can vary abruptly due to changes in any one of a diverse range of factors, some of them unexpected.

Attempts to limit the risk of TBE infections will be most effective if targeted at high-risk groups, which, on the basis of these findings, appear to include economically disadvantaged people. Furthermore, if this greater risk arises from habitual activities determined by their economic status, such people are also least likely to be able to change their behaviour to control that risk. Effective practical steps for public health authorities include the promotion of awareness and protection

against tick bites, and making either of the two anti-TBE vaccines both accessible and affordable. Given the moderate to severe neurological sequelae that adversely affect the ability to work in c.30-50% of TBE patients [27], subsidization would surely outweigh the costs of such disablement.

Acknowledgements

We thank Emőke Ferenzi and Tatjana Avsic-Zupanc for supplying data from their national diagnostic laboratories on TBE incidence in Hungary and Slovenia, respectively; Milda Zygiute, Aukse Mickiene and Macej Kondrusik for information on vaccination and forest food harvest in Lithuania and Poland, respectively; and Luigi Sedda and David Rogers for advice on statistics. This study is funded by a graduate training grant for EG from the UK Natural Environment Research Council. SER was partially supported by the EU grant GOCE-2003-010284 EDEN; this paper is catalogued by the EDEN Steering Committee as EDEN0205 <http://www.eden-fp6project.net/>. The contents are the sole responsibility of the authors and do not necessarily reflect the views of the European Commission.

Authors' contributions

The study arose out of previous work by SER, who wrote the manuscript. ERG carried out the data analysis, and contributed significant ideas, interpretation and improvements to the final manuscript.

Competing interests

SER attends the annual meetings of the International Scientific Working Group on TBE, fully funded by Baxter.

Received: 19 January 2011 Accepted: 15 March 2011

Published: 15 March 2011

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doi:10.1186/1756-3305-4-35

Cite this article as: Godfrey and Randolph: Economic downturn results in tick-borne disease upsurge. *Parasites & Vectors* 2011 **4**:35.

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CHAPTER 6. HAVE CHANGES IN OUTDOOR ACTIVITIES CONTRIBUTED TO INCREASES IN TICK-BORNE DISEASES AND CHANGES IN THE DEMOGRAPHY OF PATIENTS?

6.1. Introduction

TBE and other tick-borne diseases (TBDs) have shown significant increases across Europe in the last twenty years. In Germany, for example, between 1991 and 1995 there were on average 166.6 cases of TBE per year ($\pm$ stdev 98.2), whereas between 2001 and 2005 there were 295.4 cases per year ($\pm$ stdev 77.8). There were only 3.2 cases of TBE per year ($\pm$ stdev 2.4) in Italy between 1991 and 1995 but this increased to 20.0 cases per year ($\pm$ stdev 5.7) between 2001 and 2005. Although less is known about the incidence of Lyme Borreliosis (LB), limited data suggests that there have also been increases across Europe. For example, in six eastern States of Germany incidence increased from 17.8 cases per 100,000 in 2002 to 37.3 cases per 100,000 in 2006 (Fülöp and Poggensee, 2008). This chapter will examine whether there have been changes in outdoor activity patterns that could have contributed to the increase in TBD incidence between the early 1990s and 2000s, through greater exposure of humans to ticks.

TBDs are thought to be associated with certain demographic and socioeconomic groups, including retirees, the unemployed and affluent. For instance, recent increases in TBE incidence have been associated with so-called ‘Golden Agers’ who are more active post-retirement (Kunze et al., 2005). At a conference of the International Scientific Working group on TBE (ISWTBE), most TBE patients in the Czech Republic were shown to be occupationally inactive (for example, young, retired or housewives) (Danielova and Benes, 1997). A case-control study of TBE in Poland revealed that unemployment increases the risk of TBE infection (Stefanoff et al., 2012). The changes in incidence have been attributed in part to increases in exposure activity amongst both the most affluent,

who have an increased appetite for the outdoor recreation, and the poor, who access wooded areas to increase income (Kunz, 1999; Kilpatrick and Randolph, In press).

The hypotheses to be tested are therefore fourfold:

1. TBD incidence varies with age and sex, and changes in TBD incidence have not occurred uniformly across these groups;
2. age, sex, unemployment, retirement and student status increase exposure to TBDs, leading to increased case numbers in these groups;
3. there has been an increase in outdoor activities that expose people to ticks; and
4. increases in TBD exposure have occurred most markedly amongst the most affluent and the poor.

Time-use data, which uses diaries to record the activity patterns of people, will be used to quantify the exposure to TBD through outdoor activities. A wealth of sociological information is available from time-use data including activity patterns by demographic group and by season. The statistical offices of many European countries now undertake national time-use surveys. These data can be used to quantify exposure to environmental diseases. For instance, Georgopoulos et al., (2008) used time-use data to model exposure to arsenic through ingestion of food and drink in the United States. Also, based on time-use diaries completed by 249 people in China, it was found that *Schistosoma japonicum* prevalence was significantly related to exposure to river water, and most importantly to fishing (Ross et al., 1998a; Ross et al., 1998b; Li et al., 2000). However, there has been no similar work on arthropod-borne diseases to date.

To create a measure of risk of recreational exposure to TBD using time-use data, the particular outdoor activities that are important in exposing people to TBD must be identified. There have been a small number of case-control studies for TBD in Europe.

A recent case-control study for TBE in Poland found that spending over ten hours per week in mixed forest did not significantly increase the risk of contracting TBE, but

combining this with foraging for forest foods was the most significant risk factor (Stefanoff et al., 2012). Spending time camping and swimming, however, had a protective effect, presumably because these latter activities do not take place within tick habitats.

In Germany, LB has been associated with spending time in gardens, especially if they are less than 200 metres from woodland (Fitzner et al., 2002). Cases in this study were more likely to have skin contact with garden and countryside bushes. Surprisingly, there was no significant influence of recreational activities in the countryside.

An additional rich resource for examining exposure to TBDs is the American LB literature. There is no systematic reason why these results should not broadly apply to TBD in Europe, but they should be considered carefully because the cultural context has an effect on exposure factors. LB cases in New Jersey were significantly related to rural residences, brush clearing and the presence of a bird feeder in the residence (Orloski et al., 1998). There was no effect of outdoor activities such as gardening, walking or jogging. This study included only 62 LB cases, however, so there may be insufficient power to detect relationships.

In California there was a significant relationship between LB and walking for more than five hours per week on wide maintained trails (Ley et al., 1995). Although non-significant, the authors noted that patients were more likely to have taken part in jogging and hiking. Once again, small sample size is identified as a possible cause for the lack of significant relationships.

In a larger study in Pennsylvania, with 294 cases and 449 controls, more significant relationships were detected, including a higher risk associated with gardening, yard work and visiting parks (Smith et al., 2001). In under 10- and over 50-year olds there was an increased risk associated with walking and jogging in the woods.

Gardening, foraging and walking (hereafter, the “Exposure Activities”) will be used as part of the analysis to measure differences in exposure to ticks by demographic and

socioeconomic group, before examining whether changes in exposure could have led to increases in TBD due to greater exposure to ticks.

6.2. Methods

6.2.1. Demography data

Data referring to the demography of TBE and LB were collected from a variety of sources. The primary resource for TBE data in Germany and TBE and LB data in Italy was the EU FP6 Emerging Diseases in a Changing Environment (EDEN) project. German TBE data between 2001 and 2009 were also available at www.rki.de/SurvStat/QueryForm.aspx. Additionally, the International Scientific Working group on TBE (ISWTBE) provided useful information on the demographics of disease in Austria. Older German TBE demography data were sourced from published, peer-reviewed literature and acted as a benchmark against which to measure trends (Kaiser, 1999). Non peer-reviewed reports which refer to the demography of LB in Germany were collected directly from the Robert Koch Institute (available at www.rki.de).

6.2.2. Time-use data

Time-use data, where people record their activities throughout a day in diaries, were used to investigate patterns of leisure activities that might expose people to TBD. This resource has been found to be a more reliable record of how time is spent than recall surveys (Bonke, 2005; Rossi and Scappini, 2011). Survey methodologies vary through time and space, and so the comparability of survey information must be considered. For instance, participants may be asked to record their activities in time slots of five to 15 minutes, or may be asked to describe the timing of all the activities they undertake without using an underlying time framework. The raw diary data are then classified into activities by the relevant statistical authority using a national codebook; this is found to be a more flexible method of diary collection than providing a codebook to the participant (Harvey,

1993). To ensure sufficiently high participation, surveys are restricted to one or a few days. As such, short-term diary data are used to infer longer-term patterns and trends in activities (Frazis and Stewart, 2010).

The Multinational Time-use Survey (MTUS) collate time-use surveys from a variety of countries and includes surveys from as early as the 1960s (Fisher et al., 2000). The MTUS re-format the surveys to their own harmonised codebook so that trends in activity patterns through time and space can be investigated. The MTUS have designed two universal code schemes: the AV and the Main/Sec. While Main/Sec has more codes, with 69 separate activities, a greater number of the available surveys are harmonised with the 41 AV codes.

For this analysis, data from Italy, Germany and Austria were used. These countries are endemic for TBDs including TBE and LB. Two surveys were available for each country, allowing the investigation of leisure trends through time. For Germany the surveys were undertaken in 1991 and 2001, for Italy in 1989 and 2002 and for Austria in 1992 and 2009 (Table 6.1). The Austria 2009 survey is not yet available in the MTUS dataset, but data referring to the activity codes of interest were made available by Norbert Neuwirth, an economist at the Austrian Institute for Family Studies.

Table 6.1. Details of the time-use surveys used.

Survey	Code	Survey period	Age range	Survey size	No. of diary days	% 'good' diaries	Original survey codes included in AV9 by MTUS	Original survey codes included in AV21 by MTUS
Austria 1992	Aus1992	Feb - Oct 1992	10-98	25233	1	98.2	351 Gardening	354 Walk the dog (up to one hour), 832 Walking 833 Hiking, climbing 838 Gathering mushrooms, berries
Austria 2009	Aus2009	March 2008 - March 2009	9-99	8234	1	98.0	tam159 Gardening tam161 Maintenance of flowers and plants	tam165 Walk the dog tam327 Taking a walk tam338 Forage (mushrooms, berries etc.) tam328 Hiking
Germany 1991/1992	Ger1991	Oct-Nov 1991, Jan, Feb, March, April, June, July 1992	12-75	25812	2	99.7	41 Care of ornamental and useful plants 42 Care of ornamental plants 43 Care of useful plants 49 Not exactly allocable activities of field 04	722 Taking a walk (incl. window shopping)
Germany 2001/2002	Ger2001	April 2001 - March 2002	10+	37724	3	92.2	zh340 Gardening and pet care, not specified zh341 Plant care, outside zh343 Other plant care zh349 Other gardening and pet care activities	zh346 Walking dog zh611 Walking zh612 Other walking zh613 Jogging zh642 Berries, mushrooms and herbs collect
Italy 1988/1989	Ita1988	June 1988 – May 1989	3+	38110	1	99.0	2321 Gardening 2322 Gardening of edible plants	5201 Going for a walk 5202 Walking without a specific goal

Survey	Code	Survey period	Age range	Survey size	No. of diary days	% 'good' diaries	Original codes included in Av9	Original codes included in Av21
Italy 2002/2003	Ita2002	April 2002 - March 2003	3+	55773	1	91.4	34 Gardening and animal care 341 Plants care 3411 Comestible plants care 3412 Non-comestible plants care 349 Other specified gardening and animal care activities	344 Walking dog 611 Walking, trekking 6111 Walking, trekking 622 Picking mushrooms, etc... 629 Other activities to collect products of the nature

As identified above, activities such as gardening, walking and foraging for foods were classed as Exposure Activities. In the AV codebook the two relevant codes for TBD exposure are therefore AV21 (walking, including hiking and foraging for wild foods) and AV9 (gardening). Other codes such as AV19 (active sport) may also include activities that expose people to ticks, but are more heterogeneous which might create a biased estimate of exposure. Comparable codes to the AV9 and AV21 codes were created using the raw activity data for the Austria 2009 survey (Table 6.1). The exposure measure was therefore a sum of the time spent by each individual in AV9 or AV21 activities. Data manipulation was undertaken in PASW Statistics 18 (SPSS Inc. an IBM company, 2009).

A number of factors (for instance, age, sex and employment status) are important in determining the time spent in leisure activities. Additionally, the season and day of the week can be important to the amount of time spent in outdoor activities. Time-use surveys require the quantitative contribution of each individual person to be adjusted so that the survey population is representative of the general population. This is achieved through the use of survey weights, which adjust for the underlying demography, seasonal variation in activities and weekend versus weekday differences in activities. The weighting variable inflates the importance of those surveys which are under-represented so that statistics such as average time spent in an activity represent that of the underlying population. The MTUS produces weights which are comparable across the dataset, allowing cross-country comparisons (Fisher et al., 2011). As the Austria 2009 survey is not yet included in the MTUS, comparable weights were created. The Austrian statistics agency had already carried out significant work to create weights which were representative of the demographic, seasonal and daily population. The resulting weights were not entirely balanced by day (as is the case for the other surveys in the MTUS), but given the complexity of the weights provided by the Austrian statistics agency, further adjustment was not undertaken. Some modifications were, however, made to the weights to align the

Austria 2009 survey with the MTUS as much as possible. Following the MTUS protocol, cases which were deemed to be bad quality were given a weight of zero so they were excluded from all analyses. The remaining case weights were inflated so that they had a mean of 1 and a sum of the number of diaries. The percentage of ‘good’ diaries from the original survey (which were used in this analysis) are detailed in Table 6.1.

Along with the weights, there is one other significant difference between the MTUS harmonised surveys and the Austria 2009 survey that should be identified. The MTUS methodology utilises the imputation of time based on the sequences of activities. For instance, if a diary has one hour of work, followed by an hour of unknown activity, followed by a second hour of work with no other intermittent activities or travel, the missing activity will be imputed as work. The Austria 2009 data were only provided for the total time spent in a small number of relevant activities, so the imputation of missing time using the sequence of activities was not possible. As such, not all time in the Austria 2009 diaries is accounted for. The imputation of time through the MTUS is, however, a very small percentage of time; otherwise the resource would not be reliable. Austria 2009 estimates may therefore contain a small underestimate of the true amount of time spent in the Exposure Activities.

6.2.3. Data analysis

Diaries from people aged under 16 or over 75 years were excluded to allow comparability across the surveys. Participation and time spent in the Exposure Activities were investigated for significant differences across demographic and socioeconomic groups. Differences were examined by age and sex, employment, unemployment, retirement and student status. Additionally, discrepancies were investigated across three levels of educational status: (1) less than secondary education; (2) secondary education; and (3) tertiary education. Family structure was considered as it was thought that time spent in Exposure Activities would depend on the presence or absence of children. For the

two German surveys, and the 1992 Austrian survey, income data were available and people could be split into three categories according to this information (lower 25%, middle 50% and upper 25%). Average time spent in the Exposure Activities was calculated using the weights previously described. T-tests and ANOVA were applied, as appropriate, to identify significant differences between demographic and socioeconomic groups. Basic analysis was undertaken in PASW Statistics 18 (SPSS Inc. an IBM company, 2009).

Changes in the average time spent by the population in the Exposure Activities through time may be a result of two things: (1) people spending more or less time in these activities; or (2) the demographic and socioeconomic make-up of the population has changed, thus creating the illusion of changes in the time spent in Exposure Activities. To control for demographic changes while assessing the time spent in Exposure Activities, multivariate regression models were created. These models include the survey as an independent variable, allowing the assessment of changes through time, but also include all the demographic and socioeconomic variables already discussed and therefore control for changes in the characteristics of the population.

Two models were created: a logistic model with participation or non-participation as the response variable and a Tobit model which models the time spent in Exposure Activities. Tobit models are often used in time-use studies (e.g. Gustafsson and Kjulin, 1994 , Bianchi and Robinson, 1997, Stalker 2011) as they allow the censorship of the response variable at zero, meaning negative values of time cannot be predicted (Tobin, 1958). Tobit model coefficients should be interpreted as the probability that time spent in the activity is above zero multiplied by the change in the response variable above zero (McDonald and Moffitt, 1980). As the level of participation increases, the coefficient estimates move towards the estimates of time spent in an activity created by ordinary linear regression. Models were also fitted with an ordinary linear model, with similar results. All models were undertaken in Stata version 12 (StataCorp, 2011).

In the German time-use surveys, multiple-day diaries were used, which cannot be considered as independent samples. One way to account for this would be to sample one diary day per person, but this significantly reduces the sample size. Instead, robust errors clustered according to the person were used in Stata (Williams, 2000).

6.3. Results

6.3.1. Demography of LB and TBE

6.3.1.1. Age distribution

First, the demography of TBD cases will be examined to provide a baseline with which to measure the validity of the time-use outdoor activity marker; if the marker can successfully predict age and gender distributions, it can be used further to examine temporal and socioeconomic trends in exposure to TBD.

TBE incidence shows clear differences between age groups (Fig. 6.1). Generally, there is a trend of increasing incidence with age up to middle-age, followed by a drop in the over 65s. In Italy the trend is less smooth than in Germany, probably because the incidence of TBE is much lower, so the lower incidence in the 35-44 age group may not be meaningful.

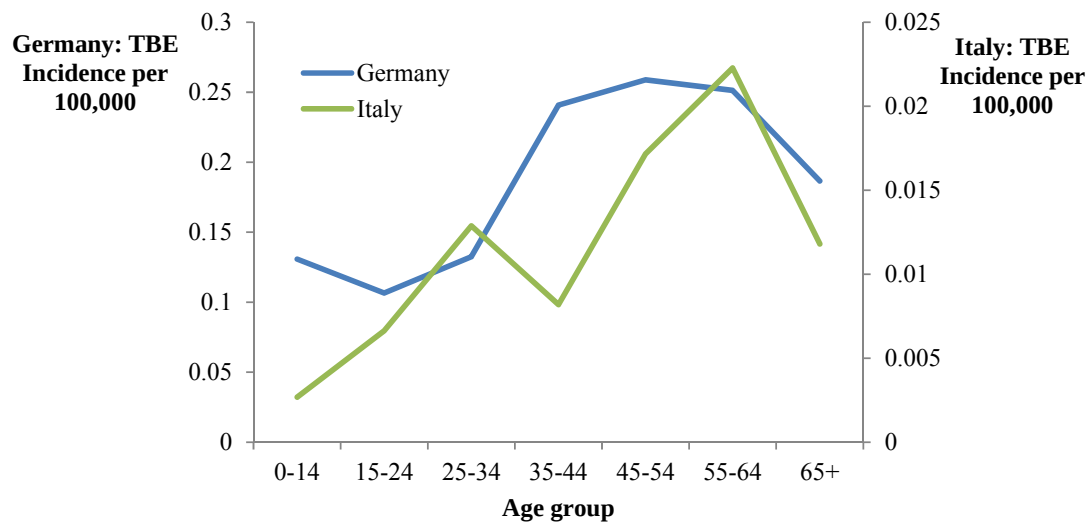


Figure 6.1. TBE incidence per 100,000 in Germany from 2001 to 2010 (shown in blue on the right hand axis) and in Italy between 1994 and 2004 (shown in green on the left hand axis).

In Germany, there are considerable differences in the age distribution of TBE in 1994-1998 and 2001-2010 (Fig 6.2). While all groups have shown increases in incidence, changes are differential with age. At the earlier date, there is a steady trend for increasing incidence with age between the 11-20 and 61-70 age groups, but at the later date there has been a relatively much greater increase in incidence amongst the 30- and 40-year olds. Declines in incidence from the peak in the over 70s are seen in both datasets, but after 2000 the over 70-year olds show an incidence greater than the age groups under 30 years old, which is not the case in the 1990s. In Austria, there may also have been increases in TBE in older groups during the last decade; Walder et al., (2008) identified a significant increase in the proportion of TBE cases that were over 60 years old from 27% in 2000-4 to 56% in 2005-6.

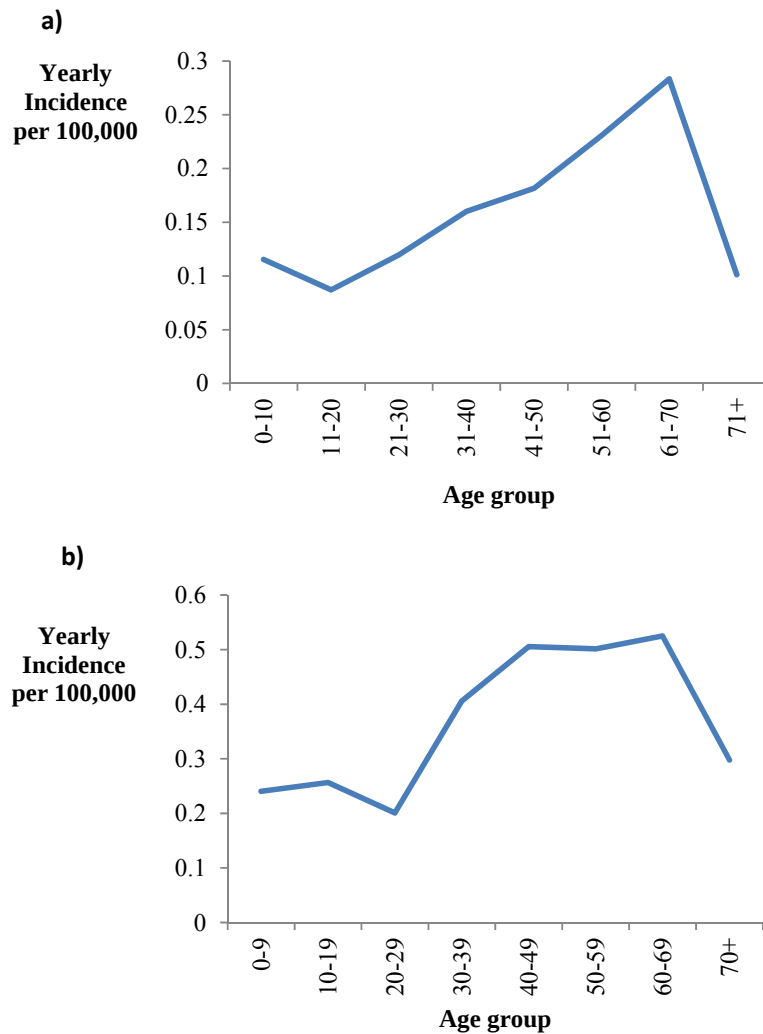


Figure 6.2. TBE by age in Germany in a) 1994-8 (data from Kaiser 1999) and b) in 2001-10.

LB is endemic in Italy, Germany and Austria, but incidence estimates are less reliable than for TBE. In Italy, LB shows a similar age distribution to TBE, with a lower incidence in the under 14s and 15-24s than the older age groups (Fig. 6.3). Once again, the 45-54 and 55-64 age groups have the highest incidence, with a decline in the over 65s.

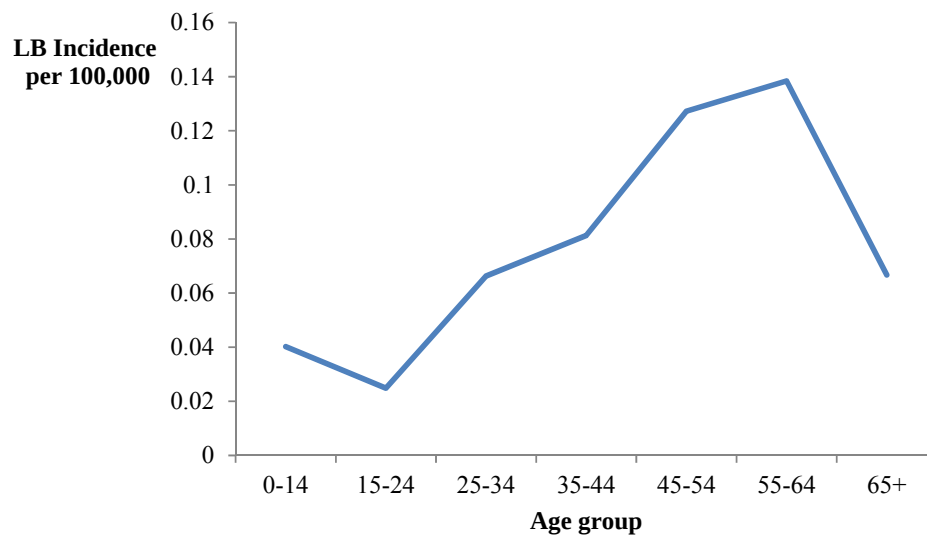


Figure 6.3. LB incidence in Italy by age groups for the period 1994-1998.

6.3.1.2. Sex distribution

Males have a higher incidence of TBE than females in both Italy and Germany (Fig. 6.4). In Italy, this skewed sex ratio seems to have become more pronounced since 2000. In Germany, between 2001 and 2010 64% of TBE cases were men (Fig. 6.4), while between 1994 and 1998 66% of cases were men, so there has been no change in the sex ratio of TBE cases in Germany in the last 20 years (Kaiser, 1999). The same skewed sex ratio in TBE is also seen in Austria, with 65% of cases in men from 2000 to 2006 (Lindquist, 2009).

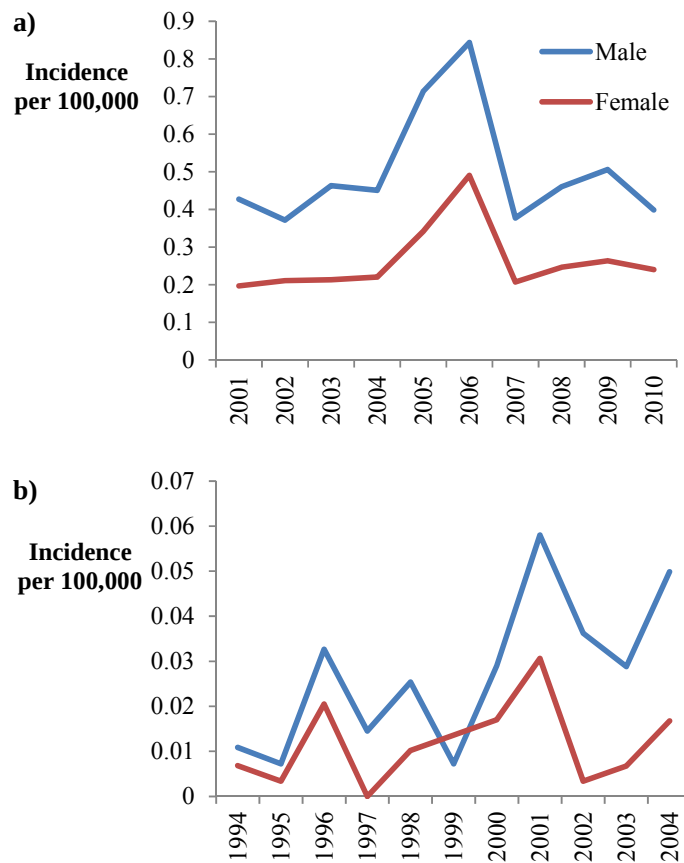


Figure 6.4. Incidence of TBE per 100,000 by sex in Germany (a) and Italy (b) shows higher disease in men than women.

For LB, there appears to be no skewed sex ratio in Italy; at least until 2002 when consistently higher incidences occurred in men for three years (Fig. 6.5). This different sex ratio for LB (when compared to TBE) was also seen in Germany. In 2002-2004 there was a higher incidence in women than men; respectively 20.9 and 18.0 cases per 100,000 in 2002, 25.3 and 21.6 per 100,000 in 2004 and 28.5 and 24.2 cases per 100,000 in 2004 (Robert Koch Institute, 2005). Between 2007 and 2009 over 55% of cases were women (Robert Koch Institute, 2010).

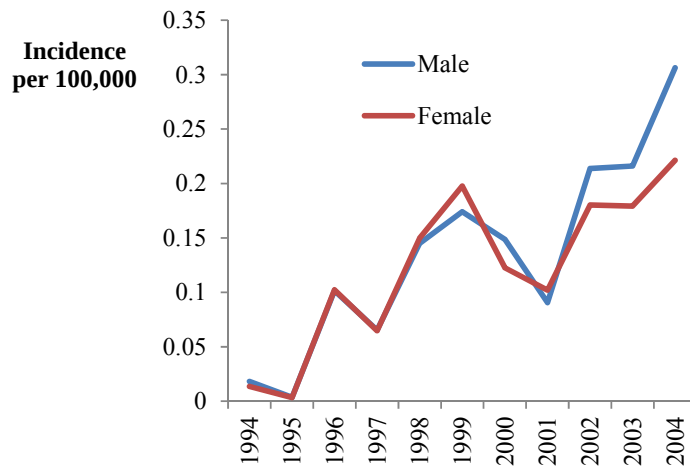


Figure 6.5. Incidence of LB in Italy is similar in males and females.

Based on TBD demography data it has been established that if the exposure marker created from time-use data is effective, it should identify increasing exposure levels with age, a peak exposure between around 55 and 69 years of age and then a decline in over 70s. The TBE and LB data show different case sex ratios. Time-use data and the measure for outdoor activity levels can be used to investigate whether the LB or TBE data give a true representation of exposure to ticks and thereby infection.

6.3.2. Description of time-use data

6.3.2.1. Time spent in exposure activities by age and sex

Most surveys indicate that people spend an increasing amount of time between late teens and 65 in activities that would expose them to TBDs (Fig. 6.6, ANOVA, p -values < 0.001). The only exception is in Italy 1989 where there was no such progressive trend and the 16-25 age group had almost as great an exposure time as the 56-65 year and 66-75 year olds. In the 2002 Italian survey, however, the difference between young and old was restored due largely to a decrease in the 16-25 age group from an average exposure time of 48.25 minutes per day in 1989 to 24.97 minutes per day in 2002. The trend in exposure with age is in line with that observed for TBD, where the 60-69 age groups have

the highest incidence. The 66-75 age group, however, spend more time in Exposure Activities than any other group, in contrast to the declines in incidence seen in the over 70s in TBE and LB.

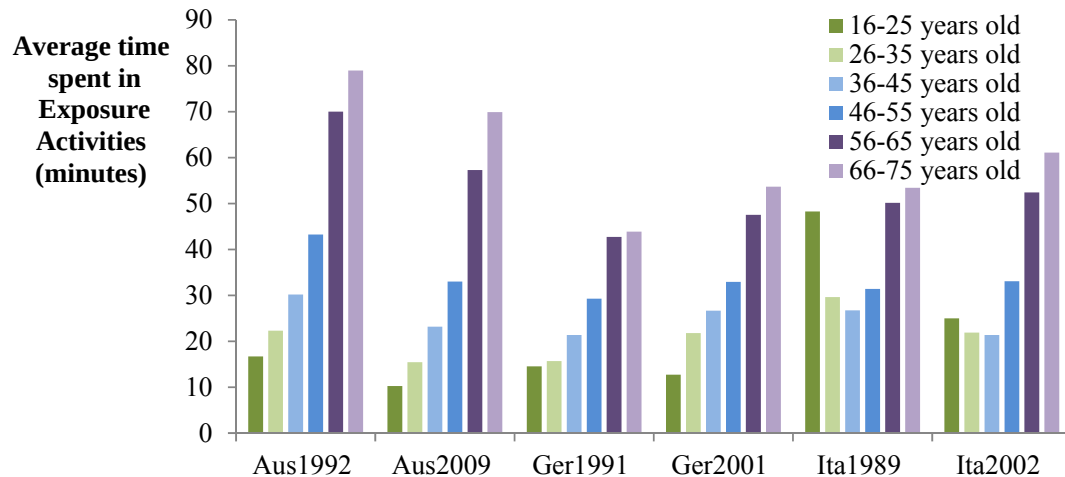


Figure 6.6. Average time spent in Exposure Activities (minutes) across the age groups.

Both Austrian surveys and the 1991 German survey show no significant difference in Exposure Activities by gender (Fig. 6.7). In the 2001 German survey men spend on average two more minutes exposed per day than women (t-test, $p < 0.05$). Both Italian surveys show that men spend a considerably longer time in Exposure Activities (t-tests, $p < 0.001$).

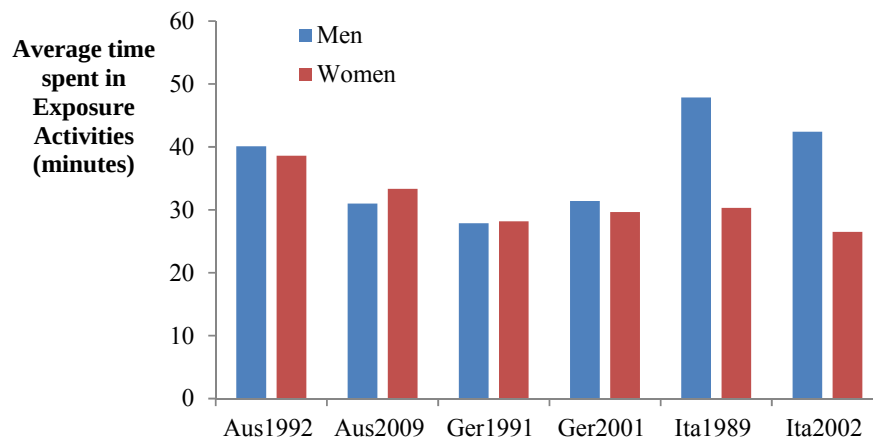


Figure 6.7. Average time spent in Exposure Activities by sex in Austria, Germany and Italy. The later German survey and the two Italian surveys show a significantly higher exposure in men ($p < 0.05$).

6.3.2.2. *Changes in time spent in exposure activities through time*

Across the whole population, the average time spent in Exposure Activities was found to have decreased in Austria from 39.30 minutes per day in 1992 to 32.21 minutes per day in 2009 (Table 6.2). Similarly, a decrease in exposure time was seen in Italy from 38.88 minutes per day in 1989 to 34.23 minutes per day in 2002. In Germany, however, the time spent exposed increased from 28.04 minutes per day in 1991 to 30.45 minutes per day in 2001. Changes in the average time spent in Exposure Activities could result from changes in the number of people who participate in the activity and/or changes in time spent by participants in the activity. In Austria, the decline in overall time spent in Exposure Activities is a result of declines in time spent per participant in the activity, as the percentage participation actually increases between 1992 and 2009 from 29.6% to 33.0%. In Italy, the decline in average time spent in Exposure Activities is a combination of a decline in the level of participation and the time spent by each participant. The increase in average time spent exposed in Germany is despite a decline in the proportion of the population who take part in this activity from 44.3% to 34.7%.

Table 6.2. Details of participation and time spent in Exposure Activities for the total population across six time-use surveys.

	Aus 1992	Aus 2009	Ger 1991	Ger 2001	Ita 1989	Ita 2002
Sample size	21772	7054	22121	29937	28915	40952
Mean time spent (mins)	39.30	32.21	28.04	30.45	38.88	34.23
Standard deviation	82.16	64.28	54.95	59.31	72.37	70.30
Range (mins)	0-870	0-840	0-550	0-630	0-705	0-720
Number of participants	6450	2324	9796	10374	9997	12981
Participation %	29.63	32.95	44.28	34.65	34.57	31.70
Mean of participants (mins)	132.66	97.77	71.32	87.88	112.45	107.99
Standard deviation of participants	102.00	78.30	67.78	71.43	82.93	87.32

6.3.2.3. Time spent in exposure activities by employment, education, income and family status

Apart from age and sex, it was hypothesised that socioeconomic factors would affect the time spent in exposure activities. Employed people spend less time in the Exposure Activities than people who are not currently employed (which include the unemployed, students, retirees, Table 6.3). There is a higher exposure in people who are retired when compared with those who are not retired. In Germany and Italy, the unemployed had significantly higher exposure than those not unemployed, but in both cases the difference has decreased between the first and second survey. In Austria, there are no significant differences between the unemployed and those not unemployed. In all surveys except Italy 1989, non-students spent a significantly greater time exposed than students. This survey in Italy in 1989 also showed that younger people spent more time in Exposure Activities, so this difference with students is unsurprising.

In MTUS surveys, education is harmonised to three international levels: (1) not achieved secondary level education; (2) secondary level education; and (3) tertiary level education. In both Austrian and Italian surveys and the 1991 German survey the highest exposure is seen in the lowest educational group and the lowest in the highest educational group.

Living with children in the household significantly decreased the time spent in Exposure Activities in all cases. Only the 1992 Austrian survey and the two German surveys provided data on the income of the diarist. In all instances the lowest income group had the highest exposure time, followed by the middle-income group. It would appear that in general, based on simple statistics, employment, a higher education, living with children and being a student all reduce time spent in Exposure Activities. In contrast, being retired or unemployed increases time spent in Exposure Activities.

Table 6.3. Mean time spent in exposure activities (with standard deviations) by socioeconomic variables and family status.

	Aus1992		Aus2009		Ger1991		Ger2001		Ita1989		Ita2002	
Income:												
Missing/NA	41.11 (83.12)				22.95 (48.16)		29.62 (59.79)					
Lowest 25%	46.96 (92.92)				34.46 (59.09)		34.71 (62.88)					
Middle 50%	35.94 (78.22)				29.49 (56.70)		30.55 (59.88)					
Upper 25%	25.55 (70.01)	***†			23.19 (50.66)	***	27.49 (53.95)	***				
Not employed	61.52 (97.13)		52.39 (79.27)		38.56 (63.50)		41.62 (68.88)		49.19 (47.24)		46.79 (82.32)	
Employed	24.89 (97.13)	***	20.83 (50.59)	***	20.45 (46.38)	***	25.40 (53.67)	***	28.55 (60.21)	***	22.60 (54.43)	***
Not unemployed	39.28 (82.12)		32.13 (64.24)		27.69 (54.40)		29.86 (58.57)		37.08 (70.17)		33.94 (70.16)	
Unemployed	40.43 (84.80)	NS	35.30 (65.60)	NS	52.87 (81.94)	***	43.52 (72.46)	***	66.43 (96.09)	***	39.99 (72.68)	***
Not retired	28.09 (70.18)		25.53 (56.99)		22.67 (49.27)		26.77 (55.32)		33.67 (66.00)		25.65 (58.01)	
Retired	79.35 (105.93)	***	68.14 (85.79)	***	46.26 (67.84)	***	54.29 (76.27)	***	66.77 (95.04)	***	71.92 (100.62)	***
Not a student	40.25 (82.69)		34.83 (66.16)		29.73 (56.28)		31.30 (59.89)		38.21 (72.03)		35.08 (71.36)	
Student	20.48 (68.28)	***	8.85 (36.52)	***	14.96 (41.07)	***	16.79 (46.82)	***	47.62 (76.17)	***	23.68 (54.39)	***
No children in house	47.92 (90.43)		38.46 (71.14)		34.49 (60.66)		35.82 (63.90)		40.14 (74.15)		39.66 (75.42)	
Children	27.22 (67.10)	***	21.97 (49.37)	***	19.69 (45.19)	***	24.93 (53.62)	***	36.01 (69.65)	***	23.02 (56.71)	***

Education:

Missing						17.54 (45.78)						
Not completed secondary	41.53 (83.63)		37.48 (66.32)		30.11 (56.40)		26.00 (55.55)		39.62 (74.12)		51.09 (88.27)	
Secondary	34.25 (79.12)		31.41 (64.95)		26.28 (55.94)		31.94 (60.07)		38.30 (69.21)		29.05 (63.20)	
Tertiary	30.70 (74.59)	***	28.03 (58.11)	***	24.47 (50.71)	***	31.75 (60.93)	***	30.11 (55.51)	***	28.58 (59.17)	***

†* denotes p-value<0.05, ** denotes p-value<0.01 and *** denotes p-value<0.001 in t-tests or ANOVAs that examine differences in the average time spent in Exposure Activities between socioeconomic and demographic groups within that survey. The lines denote the groups (to the left) compared in the test. For instance, no significant difference in time spent in exposure is seen between unemployed and not unemployed people in the Austria 1992 or Austria 2009 survey, but significant differences are seen between the income groups.

6.3.3. Multivariate modelling

Trends in participation and the average time spent in Exposure Activities could be due to a genuine change in activity levels, or could be a result of demographic and socioeconomic changes in the population, which cause a change in the estimates of means. Multivariate models, which control for changes in the demographic and socioeconomic make-up of the population of interest, allow us to identify if there have been real changes in the behaviour of the population. These changes in behaviour would be observed as a modification in the coefficient of an independent variable in the regression model with time. Interaction terms between the marker for the survey date and the variable of interest e.g. age, can identify these significant modifications in the regression coefficients. Model output from the logit and Tobit models show strong similarities (Table 6.4), with non-significant coefficients highlighted in red. Non-significant effects were retained if an interaction including them was significant.

6.3.3.1. Overall time spent in exposure activities

When adjusting for sex, age, employment variables, education and income (for Germany), a decline in exposure time across all countries is observed, indicated by a negative coefficient for the survey variable. The only significant decline in participation occurred in Italy. This suggests that the decline in exposure time in Austria and Germany was associated with reductions in the time spent by participating individuals.

6.3.3.2. Variables with consistent effects on time spent or participation in Exposure Activities

In multivariate models, some socioeconomic variables have consistent relationships to time spent or participation in Exposure Activities across the surveys. For instance, being a student or employed decreased exposure participation and time in all surveys. Unemployment and retirement increased exposure time and participation in Italy and

Germany but had no significant impact in Austria.

The effect of education in the multivariate model seems to contradict that seen in the earlier univariate analyses where increasing education had a negative impact on exposure time. In the multivariate analysis highly educated groups have increased participation in Italy and Germany.

6.3.3.3. Variables with inconsistent effects on time spent or participation in Exposure

Activities

In both the logit regression model for exposure participation and the Tobit model for time spent in Exposure Activities, age is included as a significant predictor variable across all countries. In Germany and Austria there is a simple trend for increased exposure with age. Italy is an exception to this rule. This is observed because there was an anomalously high activity level in the 16-25s in 1989. This caused the coefficients for age to become negative in both the logit and Tobit models as the 16-25 age group is the reference group in the regression models.

There is an inconsistent effect of gender on exposure participation and time. In Italy and Germany, being female has a significant impact on exposure participation and time, but with positive coefficients in Germany and negative in Italy when compared with males. In Austria, gender appears to have no significant impact on participation in 1992, but an interaction between survey date and sex indicates that this is not the case in 2009, where women have higher exposure than men. Women have a lower time of exposure in 1992, but a higher exposure in 2009.

6.3.3.4. Demonstration of changes through time using interaction terms

6.3.3.4.1. Exaggeration of effect in time

Significant interactions between the survey date and age group are seen in the Tobit model for Italy, Austria and Germany. The positive coefficient of the interactions indicates

that the later surveys have larger discrepancies between age groups in the time spent in Exposure Activities. There are no significant interactions for the logit model in Germany or Austria, indicating no change in participation. As discussed earlier, in Italy there are negative coefficients for the age groups, due to the high exposure of young adults in 1989. However, a significant interaction between the survey date and the age group coefficients in both the logit and Tobit models demonstrates that this is no longer the case in 2002.

6.3.3.4.2. Changes in the significance of factors through time

In Germany, higher income increases the likelihood of participation and time spent in Exposure Activities, but only in the 2001 survey. This is indicated by the non-significant coefficients in the income term of the model, but a significant interaction between the survey date and the highest income group.

Interactions between the survey date and sex further demonstrate there is no clear influence of gender on exposure. Significant interaction terms in Germany and Italy in both cases indicate a decline in the gender difference in exposure in the second surveys. In Austria, gender appears to have no significant impact on participation in 1992, but an interaction between survey date and sex indicates that in 2009 women have higher participation than men. With respect to the time in Exposure Activities in Austria, women have a shorter average time than men in 1992, but a longer time in 2009.

In the 1989 Italian survey, living with children is associated with increased participation and time in Exposure Activities but significant interactions reverse this relationship so that in 2002 children are associated with negative participation and time of exposure. In contrast, in the 1991 German survey, living with children is associated with lower participation and exposure time but significant interactions suggest that by 2001 this effect is almost non-existent. In Austria there is no significant impact of children in the earlier 1992 survey, but there is a significant increase in the time spent in exposure in 2009. So there appears to be no consensus on the effect of children on exposure to TBDs across

the three countries.

The effect of socioeconomic variables is much more consistent across surveys and time but there are still some significant interaction terms. An interaction term in the German model suggests the impact of unemployment on participation is removed by 2001. A negative interaction between the survey and student marker in Austria shows an increased impact of student status on participation in Exposure Activities in 2009. In Austria, there is a large negative interaction term for retirement in the Tobit model. Therefore, in the later survey the time spent by retired people in Exposure Activities is very similar to that in the non-retired population.

So, in summary, the effect of age is exaggerated between the first and second surveys in all countries considered and the effect of income only becomes significant in the second survey in Germany. With the markers for gender, living with children and socioeconomic variables the effect of interactions seems mixed across the countries so no general statement can be made about a trend through time.

Table 6.4. Coefficients from the multivariate logit and Tobit models. Coefficients in red are non-significant.

	Logit model for participation in Exposure Activities			Tobit model for time spent in Exposure Activities		
	Italy	Germany	Austria	Italy	Germany	Austria
SIGNIFICANT FACTORS						
Early survey	ref.	ref.	ref.	ref.	ref.	ref.
Later survey	-0.6243	-0.1186	0.0867	-50.4883	-21.0167	-37.9623
Male	ref.	ref.	ref.	ref.	ref.	ref.
Female	-0.4235	0.5226	-0.0118	-49.8326	12.0489	-8.9603
16-25 years old	ref.	ref.	ref.	ref.	ref.	ref.
26-35 years old	-0.2891	0.3973	0.4988	-33.6675	14.6093	36.9960
36-45 years old	-0.4152	0.6535	0.7276	-43.5286	37.6841	67.0069
46-55 years old	-0.3312	0.9426	1.0465	-36.2087	54.8594	95.7305
56-65 years old	-0.2175	1.1404	1.2252	-25.6733	67.3415	107.6628
66-75 years old	-0.2554	1.0225	1.2713	-35.6199	55.4666	107.8955
Not employed	ref.	ref.	ref.	ref.	ref.	ref.
Employed	-0.5245	-0.4101	-0.6481	-50.3315	-28.3440	-66.7486
Not unemployed	ref.	ref.	ref.	ref.	ref.	ref.
Unemployed	0.3039	0.3592		29.1526	13.3246	
Not a student	ref.	ref.	ref.	ref.	ref.	ref.
Student	-0.1623	-0.2893	-0.3895	-18.9939	-17.5229	-50.5344

	Logit model for participation in Exposure Activities			Tobit model for time spent in Exposure Activities		
	Italy	Germany	Austria	Italy	Germany	Austria
Not retired	ref.	ref.	ref.	ref.	ref.	ref.
Retired	0.4533	0.1434	0.2459	55.2414	10.2367	35.5610
Not completed secondary education	ref.	ref.		ref.		
Secondary education	0.0941	0.0731		11.8632		
Tertiary education	0.2649	0.1142		12.6949		
No children in household	ref.	ref.		ref.	ref.	ref.
Children in household	0.0777	-0.1596		8.4538	-10.0479	-6.7708
Income						
Lowest 25%		ref.			ref.	
Middle 50%		0.0353			2.3956	
Highest 25%		-0.0401			-4.8628	
INTERACTIONS						
Survey*Children	-0.3462	0.1506		-30.2683	10.4583	19.7869
Survey*Female	0.0983	-0.3695	0.2670	8.0081	-10.3103	25.0091
Survey*Income						
Lowest 25%		ref.			ref.	
Middle 50%		0.0724			4.2959	
Upper 25%		0.1740			13.6270	

	Logit model for participation in Exposure Activities			Tobit model for time spent in Exposure Activities		
	Italy	Germany	Austria	Italy	Germany	Austria
Survey*Agegroup						
16-25 years old	ref.			ref.	ref.	ref.
26-35 years old	0.3377			34.4711	23.5297	20.4786
36-45 years old	0.6224			56.3839	13.6066	10.7969
46-55 years old	0.7398			68.5997	15.1941	20.7734
56-65 years old	0.5587			54.0657	19.8676	49.1274
66-75 years old	0.5696			61.9174	30.8869	69.4865
Survey*Education						
Not completed secondary education				ref.		
Secondary education				-12.5040		
Tertiary education				-0.6432		
Survey*Retired	0.1639					-49.5161
Survey*Unemployment		-0.3669				
Survey*Student			-0.5288			

6.4. Discussion

6.4.1. The sex ratio of LB and TBE

LB and TBE both show a characteristic age pattern whereby incidence increases with age until a peak in middle age when it begins to decline. LB demonstrates a balanced sex ratio between men and women, whereas men predominate in TBE. It has been suggested that the skewed sex ratio in TBE results from differences in outdoor exposure across the sexes (Daniel et al., 2008). This seems unlikely, however, if LB does not show the same pattern as they are transmitted by the same tick vector, *Ixodes ricinus*. It would also seem unlikely that there is a difference in the preferences of the tick in biting humans when infected by different pathogens.

Alternative causes of this discrepancy could consider the capability of each parasite to cause infection by gender after it has been transmitted to the human through a tick bite. The testable hypothesis would therefore be that once bitten, males and females differ in their susceptibility to infection to LB and TBE. One possible mechanism for this difference in susceptibility is a difference in hormones affecting the adaptive immune system (Petri and Beran, 2009). This hormonal difference could be the higher level of testosterone in males. In bank voles, treatment with testosterone increases the peak parasitaemia and duration of infectivity with *Babesia microti*, a tick-borne infection (Hughes and Randolph, 2001). Testosterone has been shown to suppress the immune system of humans (Oertelt-Prigione, 2012) and immune responses tend to be more vigorous in females resulting in increased autoimmune diseases (Whitacre et al., 1999). Testosterone has also been positively associated with viraemia in Venezuelan Equine Encephalitis in macaques (Muehlenbein et al., 2006) and fecal intestinal parasite load in chimpanzees (Muehlenbein and Watts, 2010).

The question then becomes, if testosterone is increasing the susceptibility of males to

TBE, why does it not affect the sex ratio of LB? Only a very low proportion of those bitten by ticks infected by TBE virus become symptomatic (c.5%) so subtle differences in immune response may have a greater influence. Although the percentage of people who become infected with LB who demonstrate symptoms is unknown, it appears to be considerably higher, so small discrepancies in the quality of the immune response are less important. Therefore the equal sex ratio of LB can be considered an accurate reflection of the exposure to ticks, and the skewed sex ratio of TBE is not.

6.4.2. Outdoor exposure levels and TBD demography

The measure of Exposure Activities must be able to predict the age and sex distributions of TBD accurately if it is going to be considered as an adequate tool for looking at changes in exposure to ticks. TBD incidence increases with age to a peak incidence in the 45 to 64 year olds and then declines in the over 70s group. Exposure Activities, however, are highest in the 66-75 age group. The heterogeneous nature of the over 70 group for TBD incidence, which includes a high exposure group of 66-75 year olds but also the over 75s who are likely to experience declines in activity levels, could account for this discrepancy. The split between well and unwell seniors is thought to be around 73 years (Eagles, 2004).

The match between the equal sex ratio of LB and the exposure marker is not as clear cut. Sex is a significant predictor in the multivariate models in all three countries, but the coefficients do not show consistencies. Additionally, the interaction terms work to reduce the effect of sex in the later Italian and German surveys, but increase the effect in the later Austria survey. As such, there is no conclusive evidence that the measure of Exposure Activities is inconsistent with the balanced sex ratio of LB.

6.4.3. Outdoor exposure patterns in context.

Data from the broader recreational literature show strong similarities to that from the

time-use data. Age distributions of visits to parks and other outdoor recreational areas from a variety of European countries indicate highest visit levels in the 40-60 age group. In the Czech Republic, in National parks people 40-59 were the predominant age group of visitors (Cihar et al., 2002). Elsewhere in the Czech Republic it was found that 15-19 year olds spend the least time relaxing in forests (12%), compared with 32.6% of 50-59 year olds who spend most relaxation time in forests (Vítková, 2006). There is also a suggestion of decreased visits by people over 60 in Germany (Loesch, 1980 cited in Schmithusen and Wild-Eck, 2000). In a different study cited in the same review, Baillon (1975) states that people younger than 25 and older than 55 years of age visit less than those in between.

The literature suggests that there is no consistent evidence for a gender bias in visitation of forests, which agrees with the findings from the use of time-use diaries. In the Czech Republic, men are found to visit forests more than women; across four sites, the percentage of visitors that were male varied from 53 to 60% (Cihar et al., 2002). In Finland, however, there was no significant impact of gender on the number of visits to national parks (Pouta et al., 2004) and in Austria, while on-site interviews at the River Danube National Park show that males make up 62.1% of local residents only 46.3% of regional visitors are male (Arnberger and Brandenburg, 2007).

6.4.4. Socioeconomic variables and exposure to ticks

Employment and student status are negatively associated with time spent in Exposure Activities. Conversely, unemployment and retirement are positively associated with the time spent in Exposure Activities. This finding marries well with the recent direct link between unemployment and TBE in a case-control study in Poland (Stefanoff et al. 2012). Additionally, most TBE patients in the Czech Republic were shown to be occupationally inactive, e.g. young, retired or housewives (Danielova and Benes, 1997). The time-use data suggest that this relationship extends from Central and Eastern Europe to Western Europe. The retired or unemployed evidently use their greater available time to take part

in Exposure Activities, but this is not the case for students, who spend low amounts of time in Exposure Activities.

As well as unemployment, higher income may also be associated with greater exposure to TBDs (Kilpatrick and Randolph, In press). In Belgium, the spatial distribution of LB was positively associated with income (Linard et al., 2007) and in a case-control of TBE in Poland there was a dose-responsive, but non-significant, relationship with increasing income (Stefanoff et al., 2012). Income data were available for Germany to investigate if this relationship is mediated through higher exposure time amongst high-income people. There is no impact in the 1991 survey, but in 2001 the upper 25% of the population by income are associated with higher participation and time spent in Exposure Activities.

Perhaps the 2001 relationship is not as surprising as the lack of association in 1991 given that a positive association between recreational time and income has been identified since the 1980s. For instance, in 1980 decreased visits to German recreational areas was observed in people in low income groups (Loesch, 1980 cited by Schmithusen and Wild-Eck, 2000). Visits to recreational areas in Finland are higher amongst white-collar employees or entrepreneurs, who would tend have a relatively high income (Pouta et al., 2004). White-collar workers are also the most common occupational group seen amongst visitors to recreational areas in the Czech Republic (Cihar et al., 2002).

6.4.5. Human exposure and the changing incidence of TBE

Modelling, so far, has been successful at matching the demographic and socioeconomic patterns of TBD incidence, where available, to measures of outdoor exposure taken from the literature. The results of multivariate models are therefore considered accurate when they suggest that increases in TBD between around 1990 and 2000 are not a result of increases in behaviour associated with exposure to ticks. There was no change in participation in Austria and Germany, but a decline in the total time spent

in Exposure Activities. In Italy, there was a decline in both participation and the average time spent in Exposure Activities.

Interactions in the multivariate model demonstrate that a number of demographic and socioeconomic factors are becoming more important in predicting the participation and time spent in Exposure Activities. For instance, based on data from Germany, disparities in time spent in Exposure Activities across income groups are growing, as are differences between age groups. The effect of other socioeconomic factors, such as education and employment status, has been relatively stationary through time.

Social scientists have for some time been discussing significant changes in the levels of outdoor recreation. Repeated surveys in Sweden in 1977 and 1997 show there are no changes in visits to forests in the under 45 age group (Lindhagen and Hornsten, 2000). There was, however, a doubling in the group that visit more than three times a week, which was made up entirely of over 45-year olds. This increasing disparity is consistent with the trend of widening age differences seen in the time-use data.

A survey in Denmark repeated in 1976-8 and 1993-5 shows that the same percentage of the population visited the forest at least once a year (Jensen and Koch, 2004). This constant participation is consistent with the findings in Germany and Austria. The survey also finds an increase of around six hours a year spent in forest recreation (Jensen and Koch, 2004). This is inconsistent with the time use findings presented, but occurred somewhat earlier (1970s and 1990s) than the surveys considered by my time-use marker (1990s and 2000s).

Despite time-use data suggesting there has been relative stability in participation in outdoor activities between 1990 and 2000, there have been increases in park visit rates (Eagles, 2004). For instance, National Park visits in Finland have nearly doubled from 714,000 in 1996 to 1,410,000 in 2005, with year-on-year increases (Bell et al., 2007). In a more affluent society people have more money to spend on leisure, changing work patterns

and a desire for new experiences (Bell et al., 2007). These factors combine to result in people trying to get the most from their ‘outdoor time’ by visiting recognised national parks and sites of beauty.

Time use data have proved useful in monitoring trends in outdoor activity patterns and has demonstrated that in Western Europe, it seems unlikely that increases in tick-borne disease between 1990 and 2000 are a result of increases in exposure due to outdoor recreational behaviour during this period. It is, however, possible that changes in recreational patterns previous to 1990 played a role in the changing incidence of TBD. Similar studies in America found increases in outdoor activity between 1965 and 1990, but no change since then (Siikamäki, 2009). This putative earlier increase in time spent in outdoor activity remains to be tested in Europe, but surveys from Sweden and Denmark repeated in the 1970s and 1990s both show an increase in outdoor activity during this period (Lindhagen and Hornsten, 2000; Jensen and Koch, 2004). If it is the case, a growing enthusiasm for outdoor activities between 1970 and 1990 could have contributed to changes in incidence during this period. Following 1990, the continuing relatively high (compared to 1970) levels of outdoor activities could mean any changes in the enzootic cycle are more completely reflected in the incidence of TBD.

CHAPTER 7. THE FACTORS THAT INFLUENCE OUTDOOR ACTIVITY PATTERNS - A CROSS-COUNTRY PERSPECTIVE.

7.1. Introduction

Tick-borne encephalitis (TBE) is a significant vector-borne disease of humans in Europe, which is contracted through a tick bite. People who visit forests are four to five times more likely to be bitten by a tick than those who do not (Sumilo et al., 2008a) because forests provide the high humidity and sufficient vertebrate hosts needed by ticks to survive.

In Latvia, most people visit forests for recreation, but the primary reason for frequent visits to forests is to collect mushrooms and berries (Sumilo et al., 2008a). Furthermore, the activity of mushroom and berry (M&B) picking increases the risk of a tick bite when compared to walking (Sumilo et al., 2008a). There is evidence that patterns of M&B foraging can influence the incidence of TBE. In 2006, an unusually high number of TBE cases were seen in a number of European countries. In the Czech Republic this was attributed to an excellent mushroom picking season (Daniel et al., 2008). High TBE case numbers in Poland and Lithuania may also have been the result of weather that promoted collection of mushrooms (Randolph et al., 2008). Furthermore, the economic recession of 2009 was linked to increases in TBE cases in Poland, Latvia and Lithuania (Godfrey and Randolph, 2011). One of the mechanisms cited was an increased use of mushrooms and berries as a source of food and income, thus increasing the chance of TBE infection.

Other popular outdoor activities, such as hiking and walking, frequently take place in forests. In Latvia, after M&B picking, the next most likely reason for visiting forests is walking (Sumilo et al., 2008a). In the Czech Republic 55.8% of people visit forest for walks, either individually or with children or a dog, while 24.5% cited M&B foraging as the main reason for forest visits (Vítková, 2006). A high number of visitors (48%) to two

forests in Belgium visited for walking, alongside 29% for biking, 16% for jogging and 7% for horse riding (Roovers et al., 2002). In Switzerland, a national survey of 2,000 people showed that walking is the primary reason to visit forests (for 41% of the population), followed by recreation (19.1%) and hiking/sport/health (18.2%) (SAEFL, 2000). Similarly, in Germany, 86% of visitors came for walking or hiking, 11% for cycling and 3% for jogging or other activities (Elsasser 1996, cited in Schmithusen and Wild-Eck, 2000). In Sweden, in both 1976 and 1994, around two thirds of those visiting forests did so to go for a walk (Lindhagen and Hornsten, 2000).

A variety of outdoor activities, such as M&B foraging and walking/hiking, heighten the exposure of humans to ticks to forests. The aim of this chapter is to investigate the extent of national differences in outdoor activities and the reasons behind these patterns, before examining what external factors might influence daily and annual patterns of outdoor activities. Highlighting the influence of these factors will shed light on future drivers of TBE incidence, acting through human activity patterns. The following review is the first attempt to provide comparative information across Europe, both qualitatively and quantitatively, on the various outdoor activities considered to be relevant to risk of TBE infection.

7.2. Materials and methods

Information for this review was collated from published literature accessed from the Web of Knowledge and Google Scholar. Time-use data were available online from the Harmonised European Time-use Surveys (HETUS, <https://www.h2.scb.se/tus/tus/>).

HETUS are designed to create a comparable resource of surveys that measure how people from a variety of European countries spend their time (Eurostat, 2005). Harmonisation is a process of a common data collection method and survey coding (Eurostat, 2004).

Activities covered include employment, domestic work, personal care, and free time.

Within this there are codes for productive exercise and walking and hiking. Productive exercise includes hunting and fishing, picking berries, mushrooms and herbs, and other specified or unspecified productive exercise. Tables can be created online at <https://www.h2.scb.se/tus/tus/> which record the average time spent and percentage participation in these activities by country, age, sex, education, employment status and income. Access to the HETUS tool to create individual tables was granted by Mikael Molen of Statistics Sweden.

7.3. Results and discussion

7.3.1. Outdoor activities across Europe

Walking and hiking are popular activities in many European countries, with a daily percentage participation of between 12% in Hungary and 29% in Finland (Fig. 7.1).

Walking and hiking are most popular in the Scandinavian countries. However, the time spent walking and hiking gives a more accurate measure of tick-borne disease risk for the population and participants from the Scandinavian countries do not spend the longest time in these activities. It is Germans, Polish, Italians, Slovenians who spend the longest time walking or hiking, while the lowest time spent is seen in the Baltic States and Hungary.

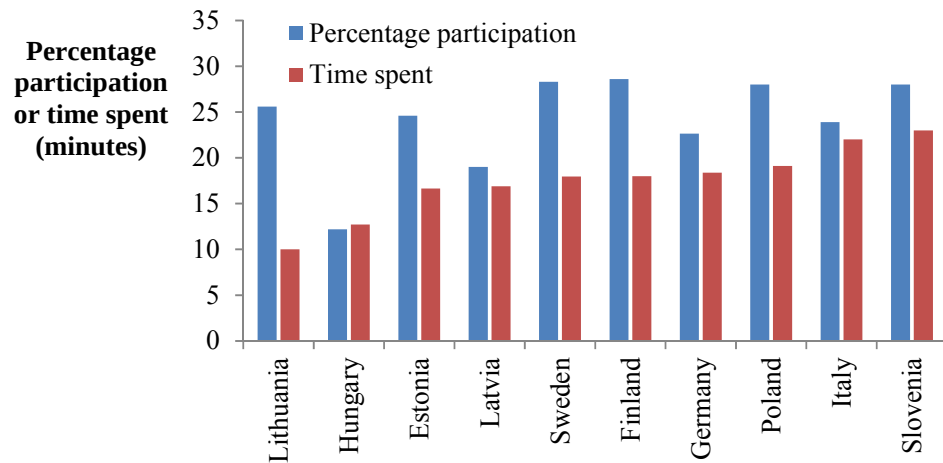


Figure 7.1. Time spent or participation in walking and hiking, with or without a dog (sorted by time spent) across 10 European countries.

A much smaller proportion of the population of each country takes part in productive exercise, with the peak participation in Lithuania of 6% (Fig. 7.2). The Baltic countries dominate in this activity in both participation and time spent. Participation and time spent in productive exercise activities is much lower in Italy, Germany and Hungary.

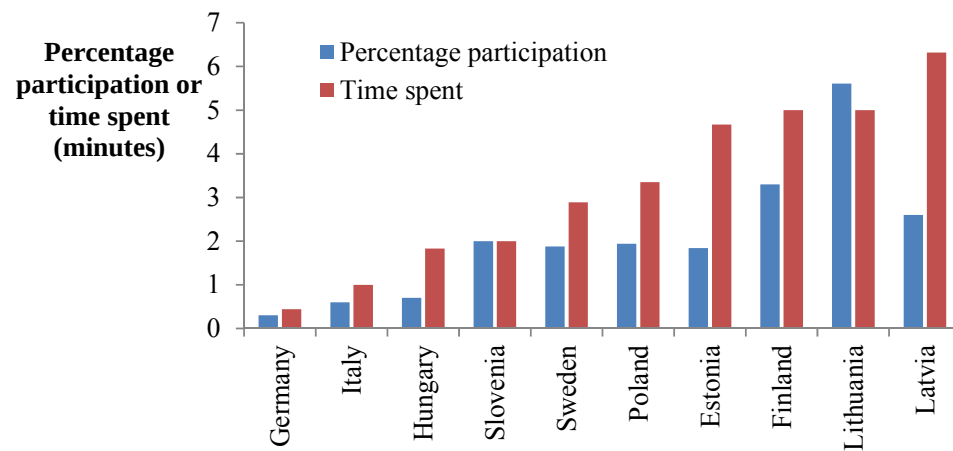


Figure 7.2. Time spent or participation in productive exercise activities (sorted by time spent) across 10 European countries.

Survey estimates of the yearly participation in M&B foraging are in line with the country-based differences in participation in productive exercise seen in HETUS (Table 7.1). For instance, Italy has the second lowest participation in the HETUS data and the survey data. Survey data reiterates that Estonia, Finland, Latvia and Poland have high

participation in foraging. One surprise from the HETUS data is that Sweden has participation levels similar to Poland and Estonia, even though survey data suggests low participation, which is also thought to be declining (Lindhagen and Hornsten, 2000).

The amount of M&B product collected in survey data can give an indication of the time spent in the activity, to match with the HETUS data. The highest collection amounts are seen in Poland and Finland, which is similar to the time-use data. Estonia and Sweden have considerably lower collection amounts, but these are per person, not per household. Additionally, there appears to be an impact of observation bias; surveys could not be found for Germany or Hungary, which have low participation levels in HETUS data.

Table 7.1. Percentage participation rates in mushroom and berry collection and amount of the product collected.

Country	% Participation in mushroom collection	% Participation in berry collection	Collection of mushrooms (kg/household)	Collection of berries (kg/household)	Reference
Czech Republic	72§	47*§	5.36	2 61*	(Šišák, 1997; Šišák, 2006)
Estonia		48†	2.36 ‡	1.85 ‡	(Paal and Saastamoinen, 1998; Vítková, 2006)
Finland	38	60		25.8	(Saastamoinen et al., 2000)
Italy	9.9	6.3			(Scrinzi et al., 1994)
Latvia		33†			(Sumilo et al., 2008a)
Poland		41†	79.5	126.4	(Barszcz, 2006)
Sweden		12, 4†		3litres*‡	(Lindhagen and Hornsten, 2000; Statistics Sweden, 2001; Kajala, 2006)
Switzerland		23, 9.8†			(SAEFL, 2000; Seeland et al., 2007)

§Household participation not individual,* Bilberries, † Participation rate for mushroom and berry collection, ‡ Per person, not per household.

7.3.2. What contributes to these country-based differences?

7.3.2.1. Walking and hiking

There appears to be fairly uniform enthusiasm for walking and hiking across Europe. This may be because most countries considered have a policy where the public have access to private forest land for recreational purposes (Table 7.2). That said, a small number of countries including Hungary and Poland allow private property rights to supersede public access (UN-ECE/FAO, 2000).

Recreational access policies have not changed over time in the majority of countries, suggesting it will not substantially impact patterns of walking and hiking in the future (UN-ECE/FAO, 2000). In some countries (e.g. Czech Republic), ownership distribution of land has changed but public access is guaranteed on public and private land so this has no impact. There are some trends though. In some of the former Eastern Bloc countries, restitution of forest has led to modifications in the land that can be used for recreational purposes. In Lithuania and Estonia there was increased access to private land. Decreasing private land access was reported in Hungary, Poland and Slovakia. In Hungary and Slovakia access to public land has also decreased, mostly due to restrictions based on nature protection initiatives.

7.3.2.2. Mushroom and berry foraging

Broadly speaking, European countries can be split into “nations with weak economies, usually with a significant local traditions of using wild edible fungi and some which also export” and “wealthier countries that import but may not have a strong tradition of collecting” (Boa, 2004). The former group includes Estonia, Finland, Hungary, Italy, Latvia, Lithuania, Poland, Slovakia, Slovenia and the Czech Republic according to the classification by Boa. In reality, not all these countries truly have a weak economy e.g. Finland, but are nonetheless the countries where we might expect mushrooms and berries

to be an important source of income. The latter group of countries includes Germany, Sweden and Switzerland, where collection is essentially for occasional individual use. Despite this, Statistics Sweden estimate that 30 million kilograms of berries and 10 million kilograms of mushrooms are produced by the Swedish Forest Ecosystem and sold each year with a value of €23m for berries and €7m for mushrooms, based on international trade price statistics (Statistics Sweden, 2001).

Although many European countries allow M&B collection for personal needs, the Baltic and Scandinavian countries are the only ones that widely allow collection for commercial purposes (Table 7.3). Commercial collection may be why the estimates of the time spent in productive exercise (from HETUS data) in these countries are higher than countries where commercial collection is not permitted. The causal relationships between the legislation and popularity of the activity are, however, hard to define and it seems more likely the tradition of commercial M&B picking in Baltic and Scandinavian countries leads to the legislation allowing commercial collection, rather than the other way around. Furthermore, if the tradition of commercial M&B collection is strong, legislation may be ignored. For instance in Poland, although collection for commercial purposes requires a contract, in practice this is largely ignored (Niskanen, 2006)

Utilisation of wild M&B products by one person limits utilisation by another, increasing the pressure on finite, if abundant, resources. Legislation can be imposed to limit conflict. For instance in Cansiglio, foraging for mushrooms was forbidden up until 1994 when a permit system was introduced (Mantau et al., 2001). In contrast, in the Baltic States and Scandinavian countries these products are open source and therefore cannot be excluded and private. This freedom to collect can sometimes lead to tension between local and immigrant collectors, as seen in the Scandinavian countries (Saastamoinen, 1999). However, in many cases the available quantities are considerably greater than the amount foraged. For instance, in Finland it is estimated that there is a yearly crop of about 500-

1,000 million kg of wild berries, of which 30% is collectable and only 5% is utilised, and in Lithuania, of the approximately 5,000 tonnes of exploitable berry harvest, no more than 2,000 tonnes were used (Olmos, 1999).

In summary, many European countries allow foraging for personal use. M&B are associated with significant monetary value, so sometimes foraging for commercial purposes can lead to conflicts. Differences between countries seem largely associated with tradition, which changes slowly, if at all.

7.3.2.3. *Hunting*

European hunting traditions have been classified by country based on the ratio of hunters to the total population size (Pinet, 1995). Scandinavian countries have many hunters with a ratio of around 1:25 hunters to population (Table 7.4). The largest group of hunters in the European Union are from so-called 'Latin' countries (Greece, France, Spain, Portugal and Italy) and Ireland, where there are around 40 people for every hunter. In these countries hunting is an activity associated with rural people and lower income groups. In the UK and Austria hunting is enjoyed by around 1 in 60 people. The tradition is of a sporting approach, with pheasants and partridges the most sought after species. Germany and the Netherlands (referred to as the Continental 'north' by Dickson (2009)) have much lower levels of hunting with less than 1 hunter per 100 people. In these countries, hunting requires high income due to complex codes of conduct.

The hunting legislative frameworks can be quite restrictive, often requiring a permit, annual subscription and membership to an association (Table 7.4). European countries can be broadly split into those where the hunting right belongs to the landowner and those where wildlife belongs to the state. Hunting rights are often leased to hunters and hunting clubs. Hunting legislation is fairly uniformly strict across Europe, suggesting tradition is most important in shaping national enthusiasm for hunting.

7.3.2.4. Tradition, legislation and fashion

The tradition in a given country towards a particular outdoor activity will impact the legislation pertaining to the outdoor activity, or indeed the lack thereof. For instance in Finland and Sweden, there is no law allowing for M&B foraging and recreational usage of forests, because it is considered a right of the people based on tradition. Although the tradition is clearly stable through time, legislative changes can be responsible for trends in outdoor activity participation. In Italy, for instance, more restrictive rules and the availability of other outdoor activities have led to a declining demand in hunting (UN-ECE/FAO, 2000).

Given that the influence of tradition and legislation in shaping outdoor activity behaviour is fairly stable, other factors, such as fashion, might play a part in changes in the popularity of certain outdoor activities. For instance, the newly introduced outdoor activity of Nordic walking in Germany is fashionable and growing in popularity (Türk et al., 2004). Not all outdoor activities would be likely to increase in response to changes in fashion. For instance, people are unlikely to take up hunting, because it is a blood sport and not to everyone's taste (Dahles, 1993; Pardo and Prato, 2005). However, fashion can negatively affect hunting. Anti-hunting sentiment in The Netherlands has reduced participation in hunting (UN-ECE/FAO, 2000).

There has been a considerable increase in foraging for mushrooms in the UK, partly as a result of a recent trend for the activity. This is largely attributable to the changes in media coverage; celebrity chefs have received publicity for their advocacy of foraging (Tobin, 2010). John Wright, forager from wildfood.net thinks interest in foraging has shown a considerable increase due to celebrity chefs and the influence of survival specialists, such as Ray Mears (personal communication, 2010). However, some experienced foragers, such as Mrs. Tee who forages in the New Forest and provides a number of top restaurants, are more doubtful about the role of celebrity chefs have had in

popularising foraging (personal communication, 2010). Additionally a number of major newspapers have produced articles in recent years which promote the idea of foraging (Morris, 2002; Daoust, 2010; Jowit, 2010). This has resulted in some discussion of the negative impact on UK forests. The fashion for wild mushroom foraging has caused Epping Forest to implement a permit system, as hitherto there has been no way of monitoring commercial collection in the forest (Morris, 2002). 500 licenses are issued each year, which allow 1.5kg for personal consumption. A number of large-scale collectors are being prosecuted in some particularly targeted forests, e.g. New Forest, Epping Forest, around the North Downs and the Chilterns (Morris, 2002).

Overall, there are differences in the time spent in outdoor activities across European countries as a result of differences in social tradition and legislation. While productive exercise, including M&B foraging and hunting, is popular in the Baltic and Scandinavian countries, Western European countries show little enthusiasm for this activity. The highest average time spent in walking and hiking was seen in Slovenia, Italy, Poland and Germany, but enthusiasm for this activity is seen throughout Europe, likely as a result of the almost universal access to forest for recreational purposes. Next, an examination of the effect that

Table 7.2. Recreational access legislation across Europe**

Country	Law	Legislation	Public land accessible, 1000 ha (%)	Private land accessible, 1000 ha (%)
Austria	Forest Act, 1975	Anybody may enter the forest for recreation purposes and spend time there, but some forests can be excluded based on planting system. Some activities such as camping, driving or horse-riding may require permission from the owner.	682 (94.5)	3050 (95.0)
Czech Republic	Act on Forests, 1995	Individuals can enter forest at own risk, but are obliged to cause no damage and follow instructions of owner/tenant. Areas can be closed due to safety.	2091 (94.5)	418 (100.0)
Estonia	Forest Act of Estonia, 1998	If forests are not fenced or marked, entrance is permitted provided no disturbance is caused, the interests of the owner not harmed and their requirements are followed. Entrance can be suspended or permitted for protection of the ecosystem and safety.	1971 (99.6)	
Finland		Everyman's right, although no specific legislation covers this. Visitors cannot cause harm to the property or nature.	6466 (95.5)	15949 (99.7)
Germany	German Federal Forest Act 1975	Entering all kinds of forests for recreational purposes allowed at any time, everywhere and independently of ownership structures, with a few exceptions. Details can be regulated by forest laws of the Lander.	5762 (100.0)	4978 (100.0)
Hungary		Entrance to forest permitted for recreation and sport purposes, but not in protected or forest growth areas. Restrictions can be put in place if entrance endangers life or the assets of others.	1165 (99.7)	
Italy			3681 (99.8)	7155 (100.0)
Latvia *	Law on protection belts 1997	Free access to forests and coastal areas.	1674 (99.8)	

Country	Law	Legislation	Public land accessible, 1000 ha (%)	Private land accessible, 1000 ha (%)
Lithuania	Law on Forests 2001	Free access to visit forests, with the exception of environmentally protected areas and those less than 100m from owners home. Restrictions are possible to preserve forest resources of business or for forest cutting.	1654 (98.3)	359 (97.8)
Poland	Act Concerning Forests 1991	Access to all public forests permitted, but owners can limit access to private forest. Restrictions for young or experimental plots or if there is a risk to humans.	6783 (91.1)	0 (0)†
Slovakia	Forest Act 1993	Free access to Slovakian forest for recreational use, whilst remaining cautious and not disturbing the environment. Restrictions for forest protection or safety.	1079 (95.2)	864 (96.2)
Slovenia	The Law on Forests, 1993	Free public access to forests, but owners may limit access for reasons or protecting regeneration, wildlife or forest ecosystems.	342 (98.6)	819 (100.0)
Sweden		Do not disturb, do not destroy - no specific legislation.	6070 (98.7)	24112 (100.0)
Switzerland	Federal Law on Forests	Anyone can go to the forest whenever and wherever they like; there is a right of free access. Restrictions only if for forest protection or other public concerns.	850 (100.0)	384 (100.0)

**Based on Bauer et al.,(2004), * Based on Sievänen et al.,(2008), † Out of a possible 1493,000 ha

Table 7.3. Legislation affecting mushroom and berry foraging across Europe.

Country	Access legislation†	Access law†	Notes†	Significant importance? ††	Quantity of Mushrooms (tons)‡	Quantity of Berries (tons)‡
Austria	Austrian Forest Act 1975 and Amendments	Collection of less than 2kg allowed. It is an offence to collect for profit or take part in collection events.		No		
Czech Republic	Act on Forests 1995	Entitled to collect for own needs without damaging environment or livestock grazing.	No selling allowed.		23900*	22700*
Estonia	Forest Act of Estonia 1998	Right to gather, no separation of private and commercial usage.	If owner incurs expenses to increase NWFP right to charge 3rd parties to gather.		4130	8043
Finland	Penal Code	Everyman's rights		Yes M & B	6000*	40000*
Germany		Given at Lander level. Generally law demands forest must not be damaged, picking in small amounts allowed in some states and must be tolerated by owner without fee.	Commercial/organized picking requires permission and possible remuneration.	No		
Hungary	Act on forests and protection of Forests 1996	Collection of mushrooms and fruits not exceeding personal needs allowed in state-owned forests.		No B, Yes M		
Italy§		Governmental bodies sell permits for permission of collection for mushrooms, but free access for fruits and berries.	Some national provisions applying to mushrooms, medicinal plants and truffles. Regional laws given wide discretion.	Yes M, No B	2413	496

Country	Access legislation†	Access law†	Notes†	Significant importance?††	Quantity of Mushrooms (tons)‡	Quantity of Berries (tons)‡
Latvia §§		Everyman's rights.				
Lithuania	Law on Forests 2001	Gathering allowed.	Prohibition and restriction allowed for determined reasons.	Yes M & B	3026	4328
Poland	The Act concerning Forests 1991	Gathering allowed for personal and commercial needs; commercial needs require a contract.	Functionally no contract needed.	Yes M & B	940	5683
Slovakia	Forest Act, 1993	Gathering for private needs in State forests.				6301
Slovenia	Law on Forests 1993	Gathering allowed unless it threatens species/function.	Owner can stop/limit collection if fruit trees cultivated.		800	600
Sweden	Forestry Act 1979	Everyman's rights.			8500*	20700*
Switzerland		No damage to forests allowed but no specific laws.	Cantonal legislation may complement federal.	Yes M, No B	735	

†Largely based on Bauer et al., (2004), †† (Seeland and Staniszewski, 2006), ‡(UN-ECE/FAO, 2000)

§(Mantau et al., 2001), §§(Arkuszewska et al., 2006), *Estimate of personal use, whereas others are only commercial productions,

Table 7.4. Hunting legislation and the ratio of the number of hunters to the total population size across European countries.*

Country	Hunters : population	Individual requirements	Obtaining land to hunt
Austria	1:70	Holders of permits must be members of Landesjagdverbände.	Revier system applies, whereby hunting restricted to the person entitled to hunt in each Revier. Hunting right belongs to landowner, but to exercise it must have private hunting entitlement (generally granted to landowners with more than 115ha of unbroken area). If landowner has permit can hunt themselves, otherwise must have land hunted and managed by another authorised person. If no private hunting entitlement, areas pooled together and leased out. Renters must have annual permit, which has been held for last 3 years.
Finland	1:17	Hunting permit required, which is subject to passing a written test.	Hunting rights belong to landowner. Landowner leases hunting right to third party. On State owned land, Finnish Forest and Park Service leases small land to a local hunting associations, larger areas utilise a licence system. Permits are for 1-7 days and subject to quotas.
Germany	1:240	Hunter must pass an exam to obtain first licence. There is an annual fee for a licence.	Hunting rights belong to the landowner. Uses a Revier, or hunting estate system, whereby hunting is only allowed in certain areas. Hunting rights are leased to a third party, but leasers must have a German annual hunting permit and must have had it for last 3 years.
Italy	1:60		Game belongs to the State and sells licences for hunting (Pettenella et al., 2005). Hunting licences can also be sold to hunting enterprises.
Hungary	1:180	Compulsory permit. Theory and practice examination.	Hunting rights belong to the State. Rights can be transferred to hunting clubs by renting territories. 83% land hunted by clubs, 17% retained by authorities.

Country	Hunters : population	Individual requirements	Obtaining land to hunt
Latvia	1:92	Annual licence required after passing exams.	Hunting rights belong to landowner. Hunting events announced to State Forest Service.
Poland	1:380	Hunters must be members of the Polish Hunters' Association. Permits available if passed an exam and one year hunting apprenticeship. Annual subscription fee.	Game living in the wild belongs to the State. Hunting territories are rented to clubs for a ten year period (there are 5250 in Poland). Clubs pay for game rearing, protection, lease and game damage.
Sweden	1:31	Individual must pay annual fees paid to hunt (300 SEK, around \$30 in 2003/4). Hunters must pass a proficiency test.	Hunting rights belong to landowner.
Switzerland	1:230	Test is undertaken for permit, right to hunt applied for in each canton**	Reviersystem in 9 northern cantons where land is leased for hunting rights, patents elsewhere that allow hunting throughout the canton. Hunting is forbidden in Geneva**

* Reference: Federation of Associations for Hunting and Conservation of the EU country reports, available from <http://www.face.eu/>, unless otherwise stated. ** Reference: <http://www.bafu.admin.ch/jagd-fischerei/07833/07883/index.html?lang=de>, http://www.admin.ch/ch/d/sr/922_0/a3.html

7.3.3. Is foraging for mushrooms and berries an opportunistic or planned exercise?

Foraging for M&B could be opportunistic, as a by-product of other outdoor activities such as walking, or it could be the main reason to visit forests. Opportunistic and planned foraging behaviour may differ in protection against ticks (e.g. vaccination and protective clothing) and may respond to different external factors, such as economic and weather factors.

If people have the skills to forage, any trip to the forest, even if for an alternative purpose such as walking the dog, could have the additional benefit of allowing foraging. In Finland, 73.2% of the population have the skills for mushroom foraging, but elsewhere very few people have the necessary skills or knowledge. To highlight this, the number of calls regarding mushroom poisonings to the National Poisons Information Service has increased in the UK in recent years; in 2008 there were 147 calls, in 2009 123 calls and in 2010, 209 calls.

The proportion of people visiting forests for the sole purpose of foraging, versus those visiting for foraging combined with other activities, will give insight into the extent to which foraging is an opportunistic activity. In 2004, a survey in Poland reported that a significant proportion of the population (41.1%) visited forests for non-wood forest product (NWFP) collection only, and a further 45.7% stated that they visited forests for both NWFP and recreation (Barszcz, 2006). The proportions that visit for both purposes vary with the size of the municipality. In small villages (up to 500 residents) we see almost 50% of the population visit solely for foraging, while in towns with populations of more than 100,000, only 20% visit solely for foraging and over 50% visit for foraging and recreation.

In Latvia, 33% of the population enter forests to collect mushrooms and berries (Sumilo et al., 2008a). A further 29% state that they enter forests to forage while enjoying

recreation or walking.

In the Czech Republic, short term recreation is the primary reason for visiting a forest (42.5%) and foraging for NWFP is second (29%) (Šišák, 1998). However, two thirds of the population collected NWFPs, suggesting they are foraging while on trips for other purposes. A significant amount of time is spent foraging, with 10.3% spending over 50 hours a year foraging, a further 18.6% spending 20 - 50 hours and 15.4% spending 10 - 20 hours (Šišák, 2000).

Where people have the skills to forage, are permitted to forage and regularly visit forest environments, a large proportion of foraging activity is likely to be opportunistic. This is the situation in Finland, Latvia and the Czech Republic. In Poland, the effect of town size supports this idea; in small villages, which are more likely to be rural, foraging can occur regularly and with less prior planning, perhaps when a crop is particularly good, and people visit forest specifically for this reason more often.

However, opportunistic foraging is not universal to Europe. In Italy, there is a strong legislative system that requires a permit to forage. This has the effect of making people plan trips to forage often a long time in advance. In Italy, trips for M&B foraging had a fairly long duration time; the total number of hours spent in forests for mushroom foraging was fourth to walking excursions, walking with no purpose and long stay in forest (Scrinzi et al., 1994). Relevant to exposure to TBE, people undertaking foraging for mushrooms are more likely to go off the path than in all other activities, except fishing. 60% of people go off-path when foraging for mushrooms, compared with 24% in walking excursions and 18% in walking without a purpose.

7.3.4. How does weather affect the crop of mushrooms and berries?

In Finland, mushroom picking decreased when the crop was poor (Sievänen et al., 2004). This suggests people are responsive to years of high crop, which is in line with the idea that foraging is opportunistic in some countries. Warm and rainy weather in the

autumn, without very high summer temperatures, appears to promote mushroom abundance. In Norway, mushroom abundance was found to be significantly correlated to cloud cover and rainfall, which is likely to be related to humidity at ground level (Dahl et al., 2008). Hot summers and frosty autumns limited mushroom yields in Karelia, and ideal mushroom weather would appear to be rainy warm weather from May to August and dry autumns without early frosts (Shubin, 1993). Mushroom productivity in Switzerland was positively correlated with rainfall between June and October until around 550mm when the relationship plateaued (Straatsma et al., 2001). The timing of fruit body production was negatively correlated with July and August temperatures; high temperatures impede fruiting. While warm and rainy weather in the autumn, without very high summer temperatures appears to favour mushroom growth, the effect of weather on wild berry crops is unknown.

The role of weather in the crop of wild forest products, and the importance of opportunistic foraging in Central and Eastern Europe and Scandinavia, support the supposition that unusual weather patterns can promote foraging and therefore exposure to ticks in some areas of Europe. This was borne out in 2006 when a bumper mushroom crop promoted foraging and a spike in TBE was consequently observed (Daniel et al., 2008). In those areas with limited foraging, for instance because of restrictive legislation (e.g. in Italy) or lack of skills (e.g. in the UK), it seems unlikely that bumper crops would promote foraging, and therefore increase exposure to ticks.

7.3.5. What impact does weather have on walking, hiking and other outdoor activities?

Aside from the impact of weather patterns on the M&B crop, weather is likely to have an additional effect on recreational outdoor activity, as people are encouraged to go outdoors by favourable weather patterns. A link between the weather and outdoor activities was identified using entrance data at Lobau in the Danube National Park, Austria

(Ploner and Brandenburg, 2003). Sunshine was positively correlated and precipitation negatively correlated with both the total number of visitors and the number of hikers.

In an urban forest in Stuttgart, the number of visitors was monitored for a year, along with the date, day of the week and the weather conditions (classed as sunny, cloudy or rainy) (Janowsky and Becker, 2003). The weather situation was significantly related to the number of visitors. The highest numbers of visitors were seen on sunny days (Janowsky and Becker, 2003).

Aside from visits to outdoor areas, general exercise behaviour is also influenced by weather. In a study in Canada, temperature was positively associated with the daily number of steps taken by participants, after the day and month were accounted for, with an increase in 290 steps per 10°C for an individual taking around 10,000 steps/day (Chan et al., 2006). A negative relationship is observed between the number of steps taken by participants and rainfall, snow on the ground and maximum wind speed.

Information from studies on visits to outdoor recreation areas and on exercise in general suggest that warm temperatures, high sunshine, and low rainfall promote human outdoor recreational activity levels. However, this relationship cannot be extended to promotion of outdoor activities undertaken to produce an income, where the pervasive weather patterns are less likely to limit the desire to go outdoors.

7.3.6. Is mushroom and berry picking a response to poverty? And who is likely to respond to poverty by increasing foraging?

NWFP collection is a recognised method of poverty alleviation, either as a safety net in times of faltering income, or to reduce the overall level of poverty by supplementing other sources of income (Belcher, 2005). The value of these products can be substantial; in the Czech Republic the market value of collected mushrooms and berries was estimated at around 2.9 billion CZK per year, equivalent to around \$160 million at the 2011 exchange rate (Šišák, 2006).

Historical data of wild berry utilization in Finland since 1860 demonstrate the influence of economic change on foraging levels (Kangas, 2001). Quantities picked have increased in line with population changes and with peaks in times of national trouble, such as the Second World War. Since the 1950s, rising living standards have caused a decline in picking. Present levels are maintained through recreational foraging, not for subsistence. For instance, collection is seen “not as a necessity in Finnish household’s food economy but [M&B] are rather luxury goods of more highly educated Finns” (Sievänen et al., 2004).

Economic gain is an important incentive for foraging in Poland, where a significant proportion of the collected NWFP are sold (Barszcz, 2006). For mushrooms, 97.8% of households used the product for family needs, 13.5% for sale in purchasing centres, 12.4% for sale on marketplaces and 10.8% for sale by the road. When asked what might increase the amount of NWFP they harvested, 46.5% of respondents answered worse financial status of family and 19.8% answered higher income from NWFP sale. Conversely, when asked what might decrease harvest size, 37.8% blamed lower frutification, 11.8% identified lower income and 9.5% the better financial status of the family. This suggests that people turn to NWFP collection in times of poverty, but if these financially straitened times are resolved they are less likely to stop foraging. Foraging provides a substantial proportion of the total income to those who utilise it. In the families interviewed, the sale of NWFP accounted for 17.8% of yearly income and 27.7% of summer income. This income is used for necessary items: 42.8% state they use the income for food, 24.6% use the income to buy clothes and 20.1% use the income to pay for school.

A separate survey in Poland of women living in small villages, hamlets and towns in, or near, large expanses of forest showed that more than 66% were living below the social minimum income (Nowacka, 2009). It was found that in this group, 70% picked mushrooms for their own use and 35% collected for sale. Collection of forest fruits was seen in 64% of the group and 45% sold the produce. More than 67% of respondents stated

that the advantages flowing from living in close proximity to forest were very big.

As in Poland, in Latvia foraging is associated with low economic status. Latvian collectors are more likely to have a low income, as well as being female, older, living rurally and with low educational status, suggesting that foraging is not just for recreational purposes (Sumilo et al., 2008a).

An investigation into alternative sources of income for farmers in rural Russia (Perm and Ivanovo Oblast) surveyed 800 families in autumn 2006 (Lerman et al., 2008). The survey showed 7% of income is earned from self-employment activities; 60% of which is from picking and selling of wild mushrooms and berries, but also some fishing, hunting, commerce and provision of services. 18% of the families reported this as a source of income.

In contrast with Poland, Russia and Latvia, only 12% of the public surveyed in the Czech Republic stated the reason for foraging was saving money or increasing family income (Šišák, 2006). People commonly think that their own collected products are of higher quality than those sold in the markets, so collection is still predominantly for one's own needs. A decrease in collection in 1996 was thought to be due to worsening socio-economic circumstances (Šišák, 1997).

Similarly, the recreational element in Finland is reflected in the characteristics of foragers. In Finland, a berry forager is more likely to be female, over 64 years old, living in a small town and of low educational status but with no significant difference in income (Pouta et al., 2006). In a logistic regression model of factors that influence participation rate in wild berry foraging, rural people are more likely to forage (Pouta et al., 2006). However, a significant interaction between the size of the municipality in which a person lives and access to a vacation residence, also suggests that the difference in participation among rural people compared to urban inhabitants is removed if the urban person has access to a vacation residence. Furthermore, household use of berries accounts for 73% of

foraging in Finland, with the remainder sold. Only around 5% of households forage for commercial purposes (Saastamoinen et al., 2000).

However, there is still considered to be potential for the development of poor Finnish regions using income from NWFP collection, largely berry foraging, although relative importance is by no means as great as in some developing countries (Kangas, 2001). Any income derived from berry foraging in Finland benefits from being tax-free (Kangas, 2001). 'Most of the income generated from foraging is distributed to the sparsely populated eastern and northern regions of the country which suffer from high unemployment, rural-urban migration and a slim economic base' (Kangas, 2001). Survey data and modelling suggested that unemployment and the municipality of residence were significant in predicting the income received from foraging, with the highest foraging participation rate and income in the municipality with lowest average income, highest unemployment rate and the highest rate of emigration (Kangas, 2001).

In Poland, Latvia and Russia, and perhaps also in Lithuania and the most rurally deprived areas of Finland, where foraging is for commercial gain, the effect of declining economic status could increase foraging patterns, which could be associated with increases in TBE. This would appear to have been the case in 2009 when an economic downturn, caused by the recession appeared to increase foraging for M&B, and subsequently a spike in TBE was observed in Latvia, Lithuania and Poland (Godfrey and Randolph, 2011). In contrast, in those places where foraging is recreational, such as the Czech Republic and most of Finland, decline in socioeconomic status is likely to have no (or even negative) impact on foraging, and therefore on the risk of TBE infection.

7.3.7. Do individual socioeconomic factors impact on outdoor activities, such as walking and hiking?

Economic factors could also influence recreational outdoor activities such as walking and hiking. To understand the possible effects, the relationship between these activities and socioeconomic variables will be examined using HETUS data. Across various European countries, retired and unemployed people spend the greatest amount of time in hiking or walking (Fig. 7.3). The exceptions are Latvia and Lithuania where the ‘on-leave’ group show the greatest time spent in walking and hiking. Full-time employed people show low time spent in walking or hiking.

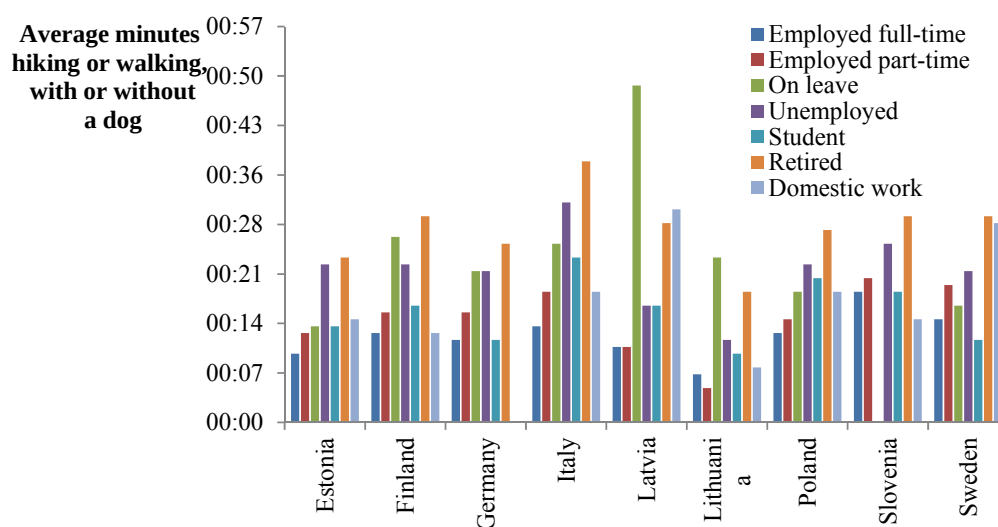


Figure 7.3. Time spent in hiking or walking, with or without a dog, across employment groups.

There appears to be no consistent effect of income on time spent in walking and hiking in each European country (Fig. 7.4). In Latvia and Slovenia, time spent in walking and hiking increases with income, in Sweden it decreases with income and in Estonia, Finland, Germany and Poland there is no trend. However, the effect of income on lifestyle is likely to be quite disparate across the countries considered, depending on the average income, cost of living and benefits for low-earning people.

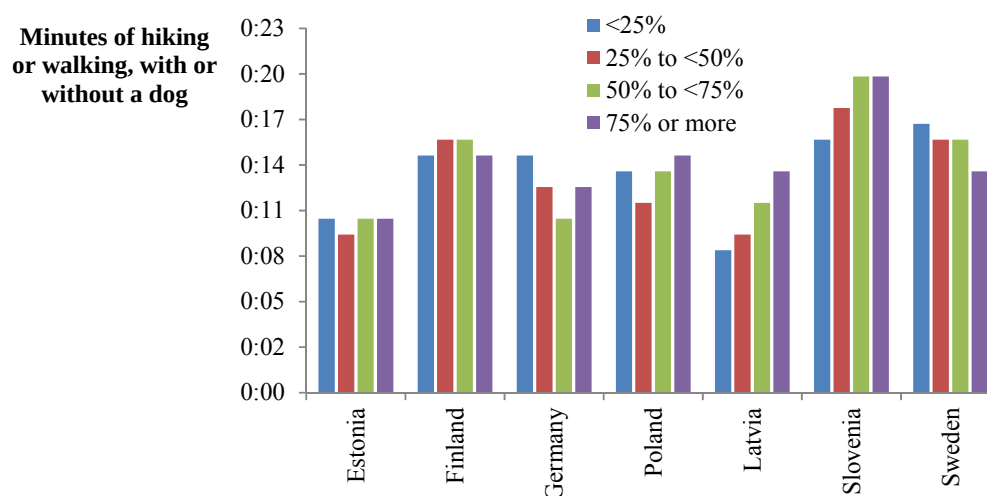


Figure 7.4. The minimal effect of income (divided into quartiles of mean levels) on time (minutes per day) spent walking and hiking.

When comparing a range of disparate countries, there are no clear effects of income, suggesting that in those countries where exposure to TBD is recreational, a change in income would have no consistent impact on exposure to the disease. Occupation is, however, an important determinant of the time spent in walking and hiking. Changes in an individual's occupation could therefore have an important effect on the average time spent in walking and hiking.

7.4. Conclusion

There are considerable differences in the nature of outdoor activities across Europe. Permits are required for hunting in most places, while mushroom and berry foraging is usually only permitted for personal consumption; consequently productive exercise is less popular than other forms of outdoor activity across Europe. Societal tradition and legislation dictates that the Baltic States and Scandinavian countries are most enthusiastic about productive exercise activities. There is near universal access to public and private forest for recreational walking and hiking throughout Europe. Within Europe, people in the Baltic States spend the least time in walking and hiking, compared with people in Germany, Slovenia, Italy and Poland who spend the greatest time comparatively.

Outdoor activities do not, of course, have to be uniform across the countries with TBD. The heterogeneities can, in fact, shed light on the external factors that contribute to the incidence of TBD. For instance in 2009, the upsurge in TBE triggered by an increase in unemployment was seen only in Poland, Latvia and Lithuania (Godfrey and Randolph, 2011). The mechanism therefore had to be local to these countries and in some way link economic wellbeing with TBE exposure. M&B foraging, a common activity in these countries provides one such necessary link amongst three suggested mechanisms. M&B foraging is a source of poverty alleviation and data from Poland show that people do indeed increase foraging in times of economic stress. In other areas that suffered an upsurge in unemployment (for instance Finland and Czech Republic), foraging is not linked to poverty alleviation but to recreation. Although unemployment is associated with more time spent in recreational outdoor activities, such as walking and hiking, in this case no effect on TBE incidence was seen.

Empirical evidence suggests there is a strong relationship between recreational outdoor activities, such as walking and hiking, and weather. The impact of this was observed in 2006, when a spike in TBE coincided with unusual weather patterns. This unusual weather did not appear to cause any systematic increase in the number of ticks actively questing across Europe. Instead, the weather was linked to both an abundant crop of mushrooms (Daniel et al., 2008) and favourable weather for outdoor recreational activity (Randolph et al., 2008). This spike was observed across Eastern and Western Europe, but potentially with different mechanisms, with the mushroom crop attractive in countries with a strong tradition for foraging (e.g. Czech Republic) and increased walking, hiking and other outdoor activities, attractive in other parts of Europe.

It would seem possible that years of either particularly good or particularly bad M&B crops could both influence TBD incidence. Good crops, plus the opportunistic foraging that is seen in some countries of Europe, could increase TBE incidence on a yearly basis.

However, in areas where foraging is a method of poverty alleviation, a poor crop may require a greater investment of effort to collect the necessary amount of product, thus increasing the risk of tick bites. It would be predicted that in these years, in a few Eastern European countries, TBD could also demonstrate a spike, although such occasions have not yet been identified. It remains to be seen what effect the weather has on berry crops, which would be particularly important to Scandinavian countries where berry foraging is very popular.

In years with particularly abrupt changes in tick-borne disease incidence, a potential human effect should be considered. Tick populations can react to anomalous weather patterns given the high potential reproductive rate of ticks, but population change is likely to require a lead-in time of several months or even years before changes are observed. However, if unusual weather is immediately met by unusual TBD patterns, as it was for TBE in 2006, then human exposure has to be considered as the mechanism. Similarly, if there are no unusual weather trends but changes in social circumstances, this could still influence TBD through changing human exposure.

CHAPTER 8. DISCUSSION AND CONCLUSIONS

8.1. Introduction

Tick-borne encephalitis is just one of many examples of emergent vector-borne zoonoses that have been observed throughout the world over the past few decades. Despite some being vectored by insects and others by ticks, which differ markedly in their biology and therefore dynamic performance as vectors, certain similarities in the underlying causal factors for emergence are becoming apparent. In particular, the importance of human factors acting in concert with environmental changes has been recognised. This unifying framework has been illustrated in the present study by new analyses of the TBE system in western Europe, with explicit comparisons to previous results from Central and Eastern Europe.

Across the majority of endemic countries in Europe, the incidence of TBE has increased (the exceptions being Hungary and Austria) (Suss, 2008). TBE endemic countries can be broadly split into two groups: (a) Central and Eastern European countries that experienced a step increase in TBE incidence in around 1993; and (b) Western European countries that have experienced a much slower, steadier increase over several decades. Hungary is exceptional in showing a step decrease in TBE incidence in 1997, despite a spread in TBE further eastward within the country. Although the underlying causes have not been analysed in full, there is suggestive evidence that the changes in the public health system in Hungary, particularly passing the costs of diagnosis to the patient, were responsible (S.E.Randolph, pers. comm.). In Austria, an extensive vaccination programme, with coverage increasing from around 6% in 1980 to 86% in 2001 led to the dramatic decline in TBE case numbers (Kunz, 2003).

In the Baltic States and other previously communist countries, changes resulting from the fall of communism acted synergistically to promote both the survival of TBEV

infected ticks and greater interaction between ticks and humans. Concomitant with changes in temperature, there were changes in abiotic and biotic factors and the human circumstances that promote exposure to ticks. The situation in Central and Eastern Europe demonstrates that a variety of factors (abiotic, biotic and social) can influence the complex TBE system in time and space.

In Western Europe, the increase in TBE incidence has been steady in countries including Italy, Switzerland, Germany, Finland and Sweden. The work of this DPhil addresses why these changes have occurred in Western Europe, and how this compares to the TBE situation in Central and Eastern Europe.

8.2. Climate change

In 1989, there was a step change in temperature in the second dekad in April in the Baltic States, which pushed temperatures during this ten-day period consistently over 10°C (Sumilo et al., 2007). There is no evidence that this increased the rate of spring warming but the onset of synchronous activity by larvae or nymphs and therefore of TBEV transmission could have advanced by ten days. This may, however, have no impact on the transmission potential (the R_0 value) *per se*, and heterogeneities in the degree and timing of the increase in TBE incidence across the countries of Latvia, Lithuania and Estonia show that the virtually uniform changes in temperature cannot account for all the changes in incidence of TBE (Sumilo et al., 2007).

Testing the effect of climate change on vector-borne diseases, such as TBE, involves the identification of the right change at the right place and at the right time (Randolph, 2004a). In Switzerland, the environment of areas with TBE since the 1980s and areas that developed endemicity more recently became more similar between 2001 and 2009. However, no increase in the rate of spring warming was observed in Switzerland, which is considered to be one important climatic condition for TBE endemism. In both Switzerland and Germany increases in the temperature in April, May and June were seen. This could

have increased the resident tick population through an increase in the development rate of ticks between life-stages (Dobson and Randolph, 2011), but satellite modelling suggests warming may also decrease tick survival through moisture stress (Randolph, 2000).

Although it remains untested, the temperature changes could also have modified the tick-human exposure rate through shifts in the seasonality of tick and human activity. The season of tick bites in Switzerland is typically delayed compared with the season of questing ticks, which has been attributed to the usual season of human outdoor exposure. Consequently peak tick bites are observed in the months of highest coincidence between questing tick availability and human exposure. If temperature changes promoted a shift to align the seasons of questing ticks and human exposure more closely, through a more marked advancement in the onset of human activity than of tick activity, an increase in TBE incidence would be observed. The emergent testable hypothesis is therefore that tick abundance and/or tick-human exposure have increased with rises in April, May and June temperature.

Despite the initial hysteria about a link between climate change and changing vector-borne disease epidemiology, strong evidence has not been forthcoming. Indeed, the existing evidence for other causal factors (such as changes in land use) is rather more convincing (Kilpatrick and Randolph, In press). Claimed as the most persuasive example of climate change causing the emergence of vector-borne disease is bluetongue, a viral disease of ruminants, in Southern Europe. Even so, the match between climate change and places where bluetongue has emerged has never been tested, beyond the general coincidence of a rise in winter temperature and the northward spread of the main vector species *Culicoides imicola* so that it overlapped in space and time with other indigenous virus-competent *Culicoides* species (Purse et al., 2005). Other biotic, sociological and agricultural factors were discounted as they did not match the observed spatial and temporal changes in the disease epidemiology. This cannot be stated for TBE in Western

Europe, nor is it the case for other vector-borne diseases such as malaria (Hay et al., 2002; Chaves et al., 2012), dengue (Gubler and Clark, 1995) and Crimean-Congo haemorrhagic fever (CCHF) (Ergonul, 2006).

8.3. Vertebrates, pesticides and land use

Coincident with changes in temperature, changes in vertebrate abundance and habitat suitability occurred. These changes could have combined to provide an improved environment for ticks in Germany and Switzerland, and as will be seen, similar changes have occurred throughout Western Europe.

Roe deer abundance has increased in many European countries (Burbaite and Csanyi, 2009), resulting from a number of human-induced changes in the system. Changes in management to protect deer from poaching, limit the hunting bag and provide supplementary feeding have all supported growing deer populations, especially when coupled with the removal of all major predators (Fuller and Gill, 2001). Increased popularity of winter cereal growth provides all-year feeding (Fuller and Gill, 2001). Favourable land-use changes to provide more forest and woodland area, and a reduction in extensive grazing of livestock on lowland woodlands, have also contributed to large increases in the roe deer population (Cederlund et al., 1998).

While roe deer abundance generally increased in the two countries studied here, not all the changes in abundance were accompanied by changes in TBE in Germany. Nor are increases in roe deer abundance always observed where TBE has increased in Switzerland. Roe deer population changes alone cannot explain all changes in TBE incidence, but they might contribute to a greater explanation. Evidence from Sweden supports the role of roe deer in changing TBE incidence; during the late 1970s and 1980s, a bout of sarcoptic mange decimated the fox population, an important predator of deer fawns (Lindstrom et al., 1994) and a TBE rise was first observed in 1984 (Randolph and EDEN-TBD Sub-Project Team, 2010). In 2010, roe deer population crashes, due to severe winter weather,

precipitated an increase in TBE cases through a switch of feeding ticks from deer to abundant and virus-competent rodents (Jaenson et al., 2012a). If this is the case, we might expect a crash in TBE cases in Sweden in the coming years, as the main reproductive host of ticks is less available. Similarly, in Italy, roe deer abundance has been linked to the emergence of TBE (Rizzoli et al., 2009).

Boar abundance has also increased in both Germany and Switzerland, but the effect of boar on TBE is yet to be tested, and field studies on the role of boar in the tick lifecycle are needed. If boar are a significant host of ticks, the substantial changes in population size that have been seen across Europe (Saez-Royuela and Telleria, 1986) could be important to the changing TBE incidence. Similar to the situation with deer, the increases in boar abundance and range are thought to relate to an increase in cereal, in this case maize, production (Geisser and Reyer, 2005).

The decline in pesticide use observed in Germany prior to the 1992 step increase in TBE may have contributed to an inadvertent improvement in the environment to support ticks, and therefore TBE. Pesticide use has declined since around the mid-1980s in many European countries. In 1985 EU policy was reformed for the first time to include measures which ensured environmental protection and provided national aid in environmentally sensitive areas (Kleijn and Sutherland, 2003). In 1993, the Fifth Environmental Action Plan was introduced across Europe, reinforcing the need to reduce pesticide use across Europe (CEC, 1992; European Union, 2012). Reductions in pesticide use were also attributable to the increased availability of low application products reducing the required amount to control the pests. Furthermore, a combination of product price decreases following the reform of the Common Agricultural Policy in 1992 and EU accession of Austria, Finland and Sweden in 1995, and voluntary set-aside programmes reduced pesticide use (Wossink and Feitshans, 2000).

Although only marginal changes in land cover and land use patterns were observed

in Germany, the reduction in pesticide use potentially indicates a broader change in the attitude towards land use. Other Common Agricultural Policies, such as set aside schemes, which covered 6.4 million ha in Europe in 1993/94 (Sotherton, 1998), could have further permitted an improvement in habitat for both ticks and their rodent hosts. For instance, in Poland larger populations of yellow-necked mice were supported by set-aside land than agricultural land, although no change in the population of bank voles was observed (Kozakiewicz and Kozakiewicz, 2008).

Changes in agricultural and hunting policy have therefore precipitated improvements in the environment for ticks through increases in vertebrate abundance and habitat suitability. Although the causes are different, this resembles changes in the environmental situation in the Baltic States after the fall of the Soviet Union. During this period, the organisation of farming changed in the Baltic States from predominantly large-scale, industrial farms, to small, privately owned enterprises (Sumilo et al., 2008b). This decreased the intensity of land use and resulted in the abandonment of agricultural land, increasing the suitability of the land to support ticks and their rodent hosts (Pupila and Bergmanis, 2006). Concurrently, reductions in pesticide use and pollutants, and an increase in large mammal abundance, such as deer and boar, occurred.

More broadly, emergence in other vector-borne diseases demonstrates similarities, with land-use and vertebrate abundance being key to changes in incidence. In America, reforestation promoted the reintroduction of white-tailed deer in the mid-20th Century, and consequently the tick vector for Lyme disease, *Ixodes scapularis* (Barbour and Fish, 1993). Despite deer densities recently becoming stable, Lyme disease cases have continued to increase (Levi et al., 2012). This may be a result of the expansion of coyote populations, as this depressed competing fox populations, and foxes are an efficient predator of small mammals (Levi et al., 2012). Similarly, both the initial outbreak of CCHF in 1944 in Crimea and subsequent epidemics in Turkey since 2002, have been characterised by the

displacement of normal agricultural and hunting activities by war or political uncertainty, which provided an environment for tick proliferation (Ergonul, 2006). When humans came into contact with this changed environment, an epidemic occurred (Ergonul, 2006).

Environmental changes as a result of war (CCHF in Crimea), political uncertainty (TBE in Eastern Europe, CCHF in Turkey) or changes in environmental policy (TBE in Western Europe, mid-20th Century in Lyme disease in America) have inadvertently provided environments more suitable for ticks to thrive, thus contributing to disease emergence.

8.4. Human exposure

Of course, TBE, as a vector-borne disease, is a product of both the enzootic cycle and the exposure between the vector and humans. Although there was evidently no increase in time spent by humans in outdoor activities in Italy, Germany or Austria between 1990 and 2000, an increase prior to 1990 may well have occurred. Time spent in outdoor activities was observed to have increased in America between 1965 and 1990 (Siikamäki, 2009), and surveys in Sweden and Denmark suggest a similar change may have occurred in Europe (Lindhagen and Hornsten, 2000; Jensen and Koch, 2004). This increase before 1990 could still have contributed to changes in TBE incidence. A possible scenario is that increased TBE incidence before 1990 might reflect increased human exposure, while after 1990 further increases in incidence might reflect changes in the enzootic system against the continuing relatively high levels of human outdoor activities, compared to 1970. Outdoor activities such as walking and hiking are popular recreational activities across Europe, partially because of the almost universal access to public and private land for recreational purposes. On average people spend between ten (in Lithuania) and 20 minutes (in Slovenia) walking and hiking per day. Daily participation varies between 10% (in Hungary) and 28% (in Sweden and Finland).

Spikes in weekly tick bites in Switzerland were shown in this study to be a result of

unusually warm, sunny weather with low rainfall and humidity. This weather is associated with increased outdoor recreational activity, such as walking and hiking. This weekly relationship between weather, outdoor behaviour and tick bites, was taken to an extreme in 2006 when unusually favourable summer and autumn weather promoted human outdoor exposure to the extent that a spike in TBE cases was observed in several western and central European countries, including Switzerland and Germany (Randolph et al., 2008). The increased outdoor activity was partially due to an unusually high mushroom yield favouring outdoor foraging in the Czech Republic (Daniel et al., 2008), and probably other central and eastern European countries, where foraging is an important pastime.

The effect of human behaviour in shaping the dynamics of TBE is particularly magnified because the vector (the tick) is relatively sedentary, relying on host activity for contact, but human activity is also important for other zoonotic diseases. Puumala virus, a species of hantavirus, is transmitted through contact with rodent excretions. Human cases are therefore associated with the proportion of the population that are hunters and negatively associated with income, and is found predominantly in areas with high numbers of forest workers and farmers (Linard et al., 2007). Occupational exposure is also found to be important to schistosomiasis infection in China, where fishing is associated with infection (Ross et al., 1998a) and in Guinea, where rice culture and tending of pirogue jetties in mangroves is associated with trypanosomiasis (Courtin et al., 2010).

Although little empirical work on the importance of human exposure to insect-borne diseases has been undertaken, modelling has hinted at the potential value of this approach. For instance, stochastic modelling demonstrated the importance of human dispersal in driving dengue epidemics, rather than mosquito movement (Barmak et al., 2011). Additionally a model accounting for exposure to dengue in just the home environment had a lower R_0 value than models that accounted for other areas of exposure, such as work (Stoddard et al., 2009). It was found that key dengue infection sites are not necessarily

those with the highest vector abundance and consequently variation in exposure could be more important to risk of disease than vector density (Stoddard et al., 2009).

Human mobility undeniably influences disease dynamics and this relationship can even be observed at continental levels. International travel and trade patterns contribute to the introduction of diseases to new countries. For instance, an epidemic of dengue fever in Hawaii resulted from infected people arriving from Tahiti (Reiter et al., 2006).

Additionally, *Aedes albopictus* was introduced to the United States through used tyres imported from Japan (Hawley et al., 1987) and separately to Hawaii through mosquitoes located on aircraft from the United States (Kilpatrick et al., 2004).

8.5. Socioeconomic status and exposure

Risk of TBE infection increases with both economic wealth and poverty (Kilpatrick and Randolph, In press). Time-use data provides a mechanism for this; in Germany, total time in outdoor activities is associated with unemployment and high income. In Belgium, Lyme disease was positively correlated with income, supposedly due to an association with large homes near woodlands where the ticks and their hosts are located (Linard et al., 2007). It seems likely, however, that both exposure activity levels and the geographical situation of people with a high income contribute to high levels of tick-borne diseases.

Unemployment was positively associated with TBE incidence in Germany. The mechanism for this positive association may simply be that unemployed people spend more time in outdoor activities that expose them to TBE-infected ticks than do people in employment. Similarly, TBE in Latvia was negatively associated with the proportion of the population in a parish who have an economic activity and with high levels of education (Vanwambeke et al., 2011). Poverty in Latvia is associated with increased exposure to ticks through mushroom and berry foraging and a decreased likelihood of being vaccinated against TBE (Sumilo et al., 2008a).

Mushroom and berry foraging is a particularly popular activity for raising extra

income in Poland, Latvia and Lithuania. Correspondingly, in times of economic downturn outdoor activity patterns may be predicted to rise and cause an increase in TBE; this was observed in 2009, when these three countries experienced a spike in TBE case numbers apparently in response to the economic downturn (Godfrey and Randolph, 2011). Other vector-borne diseases have also increased as a result of economic downturn. For example, due to the downturn in the housing market in the United States in 2007, many mortgages defaulted, homes were foreclosed, and swimming pools were neglected, which provided the ideal mosquito breeding habitat, and subsequently a spike in West Nile virus in Kern County, California (Reisen et al., 2009). The TBE situation also has parallels to the rises in deaths due to alcohol abuse and suicide following economic downturn, as the mechanism is a change in human behaviour (Stuckler et al., 2009).

TBE and Lyme Borreliosis risk is therefore associated with both poverty and wealth. Links between poverty and vector-borne diseases can also be seen in malaria (Worrall et al., 2005) and dengue fever (Reiter et al., 2003), but the relationship with wealth is particularly unusual.

8.6. The need for a holistic approach

As has been promoted before (Wilcox and Colwell, 2005), this work supports a holistic approach to examinations of emergent disease, including assessment of public health systems, environmental, climate and social change.

It would appear that the emergence of TBE in Western Europe was the product of an inadvertent improvement of the tick environment through human-induced changes in vertebrate abundance and habitat suitability, coupled with changes in temperature. Notwithstanding that no increase in human outdoor exposure has been observed since 1990, the increase in human outdoor activities between the 1970s and 1990s means that today people are often exposed to ticks. Human exposure patterns are as important as changes in the enzootic cycle in shaping the incidence of TBE, not only in the overall trend

but also in modifying the weekly, seasonal (as seen in tick bites) and yearly patterns (as seen in 2006 and 2009) of tick hazard into the observed incidence.

This situation is comparable to that seen in most Central and Eastern European countries in 1993, where a variety of environmental and human factors changed as a result of the fall of communism. Of course, the change has not been as sudden in Western Europe, but the same pattern of changes across a causal network of factors that can influence TBE has occurred.

A detailed analysis has been provided on the environmental and sociological determinants of TBE in Western Europe and it has been demonstrated that human exposure patterns, coupled with human-induced changes in the environment and temperature change may have all contributed to the increases in TBE incidence. This is not a complete quantitative solution, but instead a qualitative framework that explains the changes in TBE incidence and distribution across Western Europe.

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