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Association between incidence of Lyme disease and spring-early summer season temperature changes in Hungary – 1998–2010

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Abstract

The increase of Lyme borreliosis (LB) can be expected due to climate change, while the distribution of the disease and annual activity of the vector and host animals depend on several factors of the environment. The presented study aimed to assess expressly the spring season temperature dependence on the incidence of LB in Hungary. The weekly LB data were obtained from the National Epidemiologic and Surveillance System for a period of 13 years – 1998–2010. Daily temperature data were derived from the European Climate Assessment and Dataset. The association was studied at national level, descriptive statistics and linear regression models were applied. A significant increasing trend was observed in the mean temperature of the analysed years (0.052 °C per year). The annual LB incidence doubled during the 13 year period. The incidence rates of the periods 1998–2001 and 2007–2010 were 11.1 resp. 17.0 per 100,000. The start of a steep increase in weekly LB incidence (0.1 per 100,000) shifted significantly by 3 weeks earlier, the start date of spring showed similar trend ($p=0.0041$). LB incidence increased more steadily in spring than in summer, with 79% of the increase being reported during weeks 15–28, with maximum rates of increase occurring in weeks 23–25. The trend was significant between the weeks 15–28. In the warmer years with 19.02 °C mean temperature in May and June, the LB incidence curve reached the annual peak 2–3 weeks earlier, and the descending phase of the curve started earlier than in the colder years with 17.06 °C of the same period.

Key words

Lyme borreliosis, Climate change, *Ixodes ricinus,* Indicator species, Pannonian biogeographical region

INTRODUCTION

For observing and detecting the effects of climate change one of the most adequate method is to use environment-sensitive indicator species. These indicator organisms can be used in different sectors of science, e.g. in agriculture, paleoecology, and also to observe and predict the changing environmental human health patterns [1]. The vector-borne diseases are sensitive to climatic conditions [2]. The environmental sensitivity of the onthogeny of *Ixodes* tick species makes these organisms one of the most suitable climate change indicators. Lyme borreliosis (LB), which is the most common and important vector-borne, tick-borne disease in the temperate areas of Europe, is a highly recommended environmental health indicator of climate change [3]. The tick, *Ixodes ricinus,* is the primary European vector of Lyme borreliosis spirochaetes to humans [4].

In the study area, Hungary, the main vector is *Ixodes ricinus* – castor bean tick [5, 6]. The first patients in Hungary with Lyme diseases were observed in 1984 [7]. Lyme is not the only important tick-borne disease in the Carpathian Basin: tick-borne encephalitis virus, *Anaplasma*, *Borrelia*, *Francisella*, *Rickettsia* and *Babesia* infections in *I. ricinus* ticks also exist in Hungary and in the neighbouring countries [8]. Rigó (2011) found that prevalence of the *Borrelia* pathogens is very low in field-collected ticks and in rodents in Hungary [9].

Due to climate change, the terrestrial climate becomes milder and tick vectors can spread towards the higher altitudes and latitudes, if the spread of host animals can follow these changes geographically and earlier springs are likely to affect many aspects of tick phenology [10]. It is very important to define the causes of this change to facilitate the mitigation process and to prepare for the future. In the past 20 years, studies have found an increasing incidence of Lyme disease in Europe. Increases have been seen in Poland, eastern Germany, Slovenia, Bulgaria, Norway, Finland, Belgium, Britain, and in the Netherlands [11]. In Sweden, the recent increasing prevalence of LB has been confirmed by serological tests [12]. The main vector *Ixodes ricinus* has been observed to appear at higher latitudes and altitudes during the last 50 years on the old continent [13]. In the neighbouring country, Slovakia, a significant increase in the incidence of early disseminated infection and late persistent infection of LB was observed from 1999–2008 [14]. Regarding the seasonality of LB, the highest incidence in Slovakia was recorded from April-June and from September-November. In the south-western part of New York State (USA) the increasing distribution of *Ixodes scapularis* – deer ticks – were seen from 1990–1996 [13]. According to a meta-analysis, the incidence, the prevalence, and the distribution of the infectious disease are projected to shift in a changing environment [15]. An American study has assessed that the number of LB cases has been influenced by annual changes in population densities of *Ixodes scapularis* and has a corresponding change in the risk of contact with infected ticks [16]. Previous studies have suggested that the impact of climate change on the spread of the European tick, *Ixodes ricinus*, has already had a noticeable effect [17].

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OBJECTIVES

According to the VAHAVA Report [18], the most obvious consequences and the most likely predicted effects of climate change are the rising average and seasonal temperatures and extension of the growing season in Hungary. The scenarios are uncertain about the precipitation changes, and faunal and vegetation changes are even less known. The connections between the changing start, average temperature of spring season, and the changing character of LB seasons are one of the well-observable symptoms of the changing climate.

The aim of the presented study was to find correlations between Lyme disease incidence and a meteorological factor, namely, between the change of the spring-early summer weekly temperature and the weekly incidence of Lyme borreliosis. In the case of Hungary, it is an urgent task to define these factors and correlations in order to plan recommendations for policy makers to help with the elaboration of adaptation measures. LB can also be used as an indicator of climate change to help develop the necessary elaboration of adaptation measures.

MATERIALS AND METHOD

Climate and geography. The Hungarian climate is mainly continental with cold, humid winters and warm summers. The average annual temperature is about 10 °C, the summer temperatures are similar in all regions. The average altitude of Hungary is very homogenous, 68% of the country is lowland plain (78–200 meters), areas reaching heights of 300 meters or more cover less than 2% of the country, and only about 1% of the area of Hungary is located above sea level higher than 500 meters. The north-south extension of the country is slight, from 45°48’ latitude to 48°35’ – 268 km.

Data and statistics. The weekly incidence of LB data for 1998–2010 were retrieved from the National Epidemiologic and Surveillance System. Lyme borreliosis is a mandatory reportable disease from 1998 in Hungary. The diagnosis in our database may be based on 3 main criteria:

1) persons with typical ECM symptoms;
2) persons with late clinical manifestations (arthritis and/or cardiac, neurological disorders, late phase ECM);
3) persons with laboratory confirmed LB with or without symptoms by ELISA, western blot or VlsE lipoproteine IR6 antibody serological tests.

The ECM cases and late manifestations are not separated in the database.

The daily temperature data in 25 km grids are from the European Climate Assessment and Dataset [19]. Descriptive statistics were used, and the associations analysed by linear regression models using SPSS 10.0 software.

RESULTS

Temperature data. The yearly mean temperature showed a non-significant increasing trend of 0.04 °C per year according to the linear regression model during 1998–2010. In the summer, the increase was 0.043 °C per year, in spring it was 0.040 °C per year, in autumn the increase was the lowest – 0.036 °C per year, and was the highest in winter – 0.047 °C per year. According to the linear regression model, the mean temperature growth was 0.52 °C in summer during the analysed 13 years, from 20.83 °C – 21.35 °C. For the entire period, spring growth was 0.48 °C, autumn growth was 0.44 °C, and the increase of mean winter temperature reached 0.56 °C. The seasonal variability was the highest in winter – 3.44 °C, which was 3.6–4.4 times higher than that of the other seasons: spring – 0.898 °C, summer – 0.774 °C, autumn – 0.944 °C).

Trends of LB incidence. In the period 1998–2010 in Hungary, the average annual incidence rate of Lyme borreliosis was 13.57 (SD=3.82) per 100,000. The year of the lowest incidence rate, 9.47 per 100,000, was recorded in 2007, and the highest incidence rate, 23.04 per 100,000, was recorded in 2010. The cumulative incidence rate was 176.47 per 100,000. The rates of lowest incidence were observed in the following 3 years, sorted by descending order: 1998, 1999, and 2007, respectively; the highest incidence rates were recorded in 2009, 2008, and 2010, sorted in the same way. When the studied years were grouped into 3 periods: 1998–2001, 2002–2005 and 2006–2010, the average incidence rates per 100,000 were as follows: 11.18, 12.85, 16.06, showing an increase of 15% and 43.6% compared to the first period. Figure 1 shows the change of annual Lyme disease incidence between 1998 and 2010. An annual significant growth rate of 0.71 per 100,000 was observed (p=0.0049). The SD for the entire 13 years was 3.84. According to the fitted linear trend, the expected incidence of the year 2007 was 15.18. The expected incidences of 2007 (9.47/100,000) negatively, and in the case of the year 2010 (23.04 per 100,000), positively differed from the standard deviation of the points belonging to the trend.

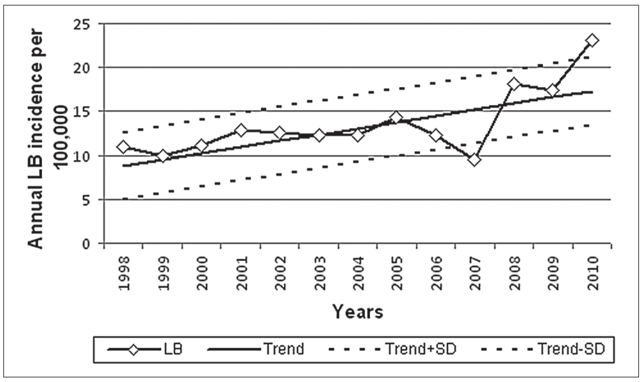

Figure 1. Annual Lyme disease incidence rate per 100,000 in Hungary (1998–2010).

The observed incidence rate for 2010 (23.04 per 100,000) was opposite to that expected (17.32 per 100,000), falling out of the range of the standard deviation.

Association between LB incidence and temperature. Analysing the association between the mean weekly temperatures and LB incidence we observed the lowest weekly incidence rates in winter (the mean incidence in the 8th week, in February, were 0.02 per 100,000). The highest incidence rates occurred in summer, mainly in July in the 24th week, with a mean incidence of 0.83 per 100,000.

Using polynomial regression model (2rd degree), a strong relationship was found between weekly Lyme incidences and weekly temperatures of weeks 1–23 (in the ascendant phase of the seasonal Lyme incidence curve). The R^2 value fluctuated between 0.8823 (1998) and 0.5878 (2007). The average of the R^2 was 0.7764.

Observations showed that the LB incidence rate started to increase rapidly after reaching the weekly rate of 0.1 per 100,000, when the weekly mean temperature was around 10 °C. The peak period of the weekly LB incidences of the 13 years was observed at weeks 23–28, followed by the highest weekly mean temperatures recorded at weeks 28–29. The increase of the incidence rate was more intensive from weeks 16–2; the decreasing phase started from week 28. In each week between weeks 23–28, LB incidence rates exceeded 0.7 per 100,000; the mean of these values was 0.76 per 100,000. To the contrary, the mean incidence of the preceding and following 5 weeks was much lower (0.45 per 100,000 resp. 0.58 per 100,000) (Fig. 2).

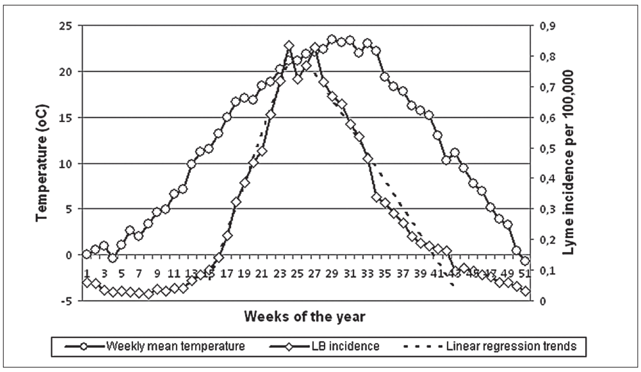

Figure 2. Weekly mean temperature and LB incidence rate and linear regression trend of the increasing and decreasing part of annual LB incidence curve in Hungary (1998–2010).

The slope of the linear regression line of the increasing LB weekly incidence phase was +8.28 ($p<0.0001$) between the first week, with LB incidence of 0.1 per 100,000 (usually from week 16) to the first week, when the incidence was greater than 0.8 per 100,000 (this usually occurred during week 24). The slope of the fitted linear regression line of the decreasing weekly LB incidence phase was –4.41 ($p<0.0001$) between the last week, with an incidence of 0.8 per 100,000 (usually from week 28) to the last week, when the incidence decreased to 0.1 per 100,000 (usually recorded in week 43). Accordingly, the absolute value of the slope of the increasing spring-early summer phase was 1.88 times greater than that of the late summer-autumn decreasing phase (Fig. 2). A secondary autumn peak of incidence was not observed.

These observations show that the incidence rate of 0.1 per 100,000 is a good indicator of the onset of the LB season, and usually coincides with the first stable spring week with a mean temperature of 10 °C, not followed by a week with mean temperature less than 7 °C.

During 1998–2010, this indicator day of the onset of spring shifted from day 113 to day 89 day of the year, defined by the linear regression model ($p=0.0041$), meaning a shift of 24 days (Fig. 3). The last spring day with a minimum temperature below 0 °C shifted from day 68 to day 55 by the linear regression. Only the year 2005 fell out of the 1 SD interval.

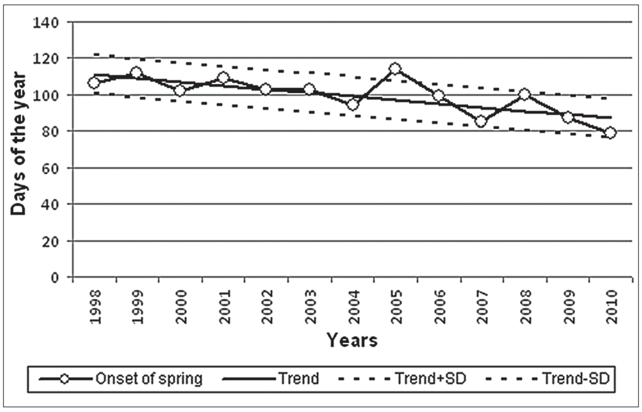

Figure 3. Change on the first day with 10 °C mean temperature followed by days with mean temperature warmer than 8°C (used as the onset of spring) in Hungary (1998–2010).

During the 13 years analysed, the onset of the LB season shifted from week 17 to week 13 (Fig. 4). A trend of -2.4 days per year was observed ($p=0.0144$). According to the linear trend, the expected start of the LB season for the years 2001 and 2008 fell out of the 1 SD interval.

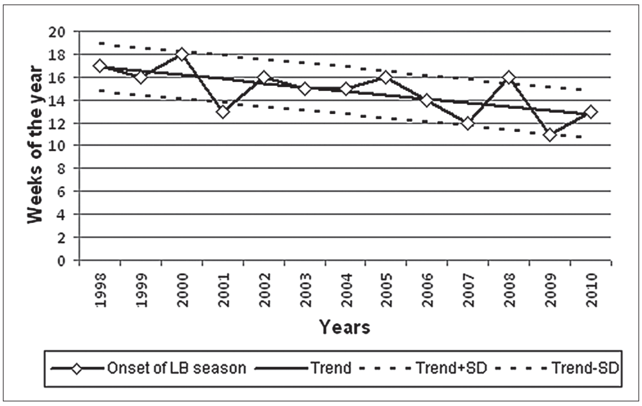

Figure 4. Change in the first week with LB incidence rate exceeding 0.1 per 100,000 in Hungary (1998–2010).

Comparing the weekly incidences of LB between 1998–2001 and 2007–2010, a shift of 3 weeks was observed in the onset of the annual LB seasons (using the first week with 0.1 per 100,000 incidence rate as the start of the LB season). The peak of the weekly incidence showed a similar change; it shifted 2–3 weeks earlier in the spring during the later observational period, and reached a higher maximum. Further, the LB incidence curves of the periods of 1998–2001 were compared to that of 2007–2010. 47% of the annual cases (5.26 per 100,000) occurred between weeks 15–28 in the period of 1998–2001, and 58% of the cases (9.85 per 100,000) were recorded in the same weeks in the period 2007–2010. The total annual difference of LB incidence rate was 5.81 per 100,000 between the 2 periods (1998–2001 vs. 2007–2010), the difference between the number of cases of between weeks 15–28 was 5.26 per 100,000; thus, 79% of the difference occurred during weeks 15–28.

Trends of incidence rate for every week during the 13 years was examined, and proved to be 0.07 per 100,000 per year; the total growth was 0.8 per 100,000 during the 13 year period (Fig. 5). By using the linear regression coefficients of each week, the profile of the weekly coefficients of LB incidence

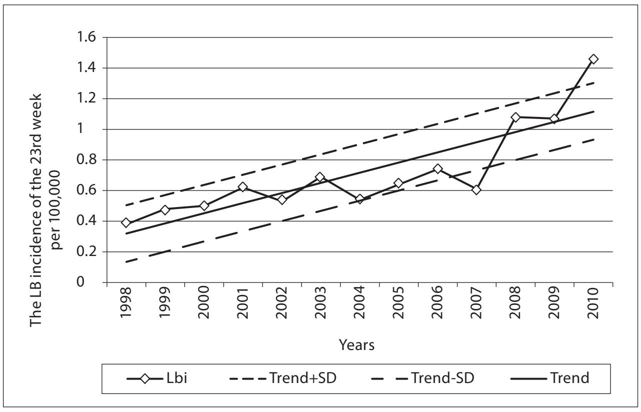

Figure 5. Trend of LB incidence rate per 100,000 at week 23 in Hungary (1998–2010).

could be determined. From weeks 15–28, the increasing trend was significant and the maximum growth occurred between weeks 23–25 (linear coefficient at week 23 was 6.64, p=0.0002). The curve of linear regression coefficients runs parallel with the curve of incidence until week 24; after that, the former curve drops several weeks earlier (Fig. 6).

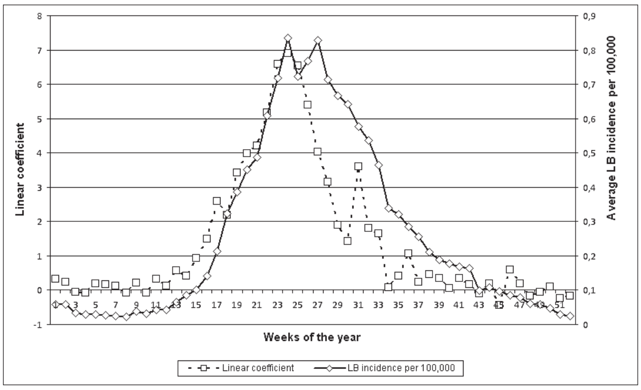

Figure 6. Weekly mean LB incidence for 13 years and linear coefficients of weekly LB incidence of the 13 years.

Assuming that the temperature in May and June is very important in the life cycle of ticks, the association between LB incidence and the mean temperature of these months was studied. The LB seasons were divided into 2 groups according to positive (years 2000, 2002, 2003, 2007, 2008) or negative (years 1998, 1999, 2001, 2004, 2005, 2006, 2009, 2010) deviation from the mean temperatures of May and June for the 13 year period. In the warmer years, the mean temperature for May and June was 19.02 °C, and in the colder years – 17.06 °C; therefore there was observed a 1.96 °C difference between the late spring and early summer mean temperatures of colder and warmer years. In the years with a warmer late spring-early summer, the LB incidence curve reached the annual maximum point 2–3 weeks earlier, and the descending phase of the curve started earlier (Fig. 7).

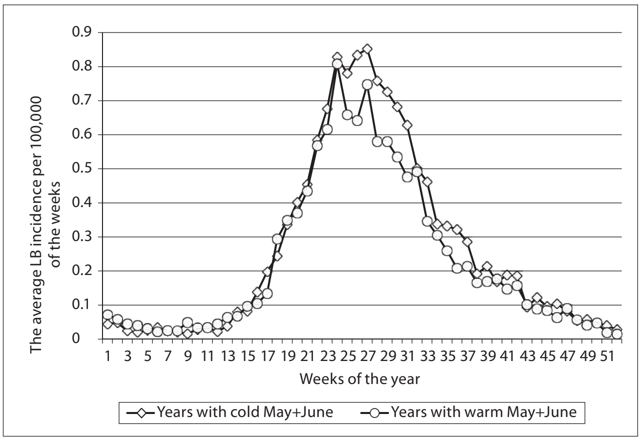

Figure 7. Weekly LB incidences divided into 2 groups according to positive or negative deviation from mean temperature in May-June for the 13 year period.

DISCUSSION

According to the presented results and observations, the LB incidence showed a significant increasing trend in Hungary during 1998–2010, with an incidence rate of 0.71 per 100,000 per year. The greatest annual LB incidences were reported in the last 3 years, when a continuous increase was observed in Hungary. The annual LB incidence even doubled during the relatively short observation period of 13 years. This studied period may be sufficient to find significant correlation between Lyme incidence and climatic factors, as supported by the findings of Bennet et al. (2006), based on the analysis of 8 years' data between 1997–2003 [20]. The onset of the LB season shifted 3–4 weeks earlier, and the peak of the weekly LB incidence showed a shift of 2–3 weeks earlier in the calendar year. The decrease of the weekly LB incidence also started earlier by 2–3 weeks. The start of the LB season correlated with a similar change in the onset of spring by 3.5 weeks. A non-significant increasing trend was observed in the mean temperature of all seasons. It is possible that the increasing trend of temperature and the earlier onset of spring are related to the increasing annual LB incidence and the earlier start of LB season.

The rising phase of the LB cases occurred from March-June, which is consistent with the observations of Hornok in Hungary who found that the activity of the *I. ricinus* nymphs was the greatest in the same period [6].

By using linear regression analysis to determine the trend of LB incidence of each week during the 13 years, an increasing trend was observed from weeks 15 – 28. 79% of the growth of LB incidence occurred during these weeks in the later period of 2007–2010. The presented findings are in accordance with the statement of the IPCC 4th Assessment Report [7] stating that the recent climate change may affect the abundance, seasonality and geographical distribution of vector-borne diseases. This study is the first to attempt to find a correlation between the changing temperature and LB incidences in Hungary.

In Hungary, the average LB incidence rate was only 13.57 per 100,000 per year during 1998–2010, while in the neighbouring country, Slovenia, during the past decade the incidence of the disease has been more than 100 per 100,000 [21]. It is very likely that LB is underreported in Hungary; however the difference in forest cover is not comparable between Hungary and Slovenia. In Hungary, the forestation is only 19.2% [22], whereas in Slovenia – 58.5% [23], and forests are the greatest habitats for ticks.

The polynomial regression model showed a strong relationship between weekly temperature and weekly Lyme incidence from weeks 1–23 (from start to the peak phase of LB incidence), the temperature determined the Lyme incidence by 77,64% in the first half of the season. This observation can be explained by the relatively high soil moisture of the spring season. From these results it can be concluded that in the increasing phase of the Lyme season, temperature is the most important climatic factor explaining the observed values of Lyme incidence.

The peak of the annual LB incidence always occurs 1–3 weeks earlier than the peak of the annual temperature. It is very important to note that the difference between the start the increase of LB incidence and the onset of spring may be more than the observed difference of 2–3 weeks, due to the lag between the tick bite and the appearance of erythema. This lag is usually between 1–3 weeks, in most cases not more than 1 week. Nevertheless, based on the presented analysis, the coincidence is good between the onset of the LB disease season and that of a stable 10 °C or higher daily temperature. This result is in accordance with literature describing the threshold temperature of questing (food-seeking) tick activity being at 7–8 °C. The lag between the start of the annual tick season and the observation of the first new primary cases would be approximately not more than 2 weeks in spring [24]. Perret et al. found that when the 5-day average of the daily maximal temperature was above 7 °C tick questing activity was always observed [25]. On the other hand, ticks were always collected when the temperature reached or exceeded 10.5 °C, and at temperatures ranging between 6.6 °C–8 °C questing ticks were only occasionally collected. Based on this literature data, this period is considered as the start of the activity of Ixodidae ticks.

In Europe, the start of spring shifted 2 weeks earlier during the calendar year, and the vegetation period became longer by 2 weeks between 1980–2001 [26]. From 1960–1995, the vegetation period shifted 12 days earlier between the latitudes 45–70 °N [7]. In the presented study, the 24-day shift in the start of spring during the 13 years seemed to be an overestimation, the length of the analysed period may explain the observed changes; however, this might be an actual trend.

In contrast, Randolph (2004) warned that climate change is not necessarily the only cause of the emergence of tick borne diseases, the changing socio-political environment and habitat structure in the former socialist countries are also important factors of the changes well [27].

In Hungary, the highest incidence was observed at the turn of June-July, but in Estonia, for example, the annual LB curve reached its maximum incidence in August, due to the different climatic conditions [13]. The annual LB incidence curve can be further analysed according to the symptoms of the disease as carried out in the USA [28]. North-American studies have observed an increasing trend of *Ixodes ricinus* abundance and the incidence of tick-borne diseases, such as Tick Borne Encephalitis and Lyme borreliosis diseases. The environmental needs of the North-American relative of *Ixodes ricinus* (*I. scapularis*) are very similar to those of the European species. Therefore, these models can be useful tools to develop local prediction models [29].

The increasing trend of LB incidence was steady during the 13-year period in Hungary, except for the irregular years of 2007 and 2010. In 2007, the most severe heat wave in the history of Hungarian meteorological observations was recorded. In Budapest, the daily mean temperature was more than 30 °C for 5 days, and the mean daily temperature reached 27 °C for more than a week. In 2010, the summer was unusually wet, and the annual LB incidence was significantly higher than the expected value. Retrospective studies showed that hot summers could modify the dynamics of the activity of ticks, and the active life-stage of the vectors could expand to a longer duration [30]. The activity of ticks during hot summer days is restricted to morning and late-afternoon hours [24]. In the case of the extreme hot weather in July of 2007 in Hungary, it is probable that the weather conditions caused very similar avoidance behaviour for people and ticks, which reduced the possibility of human infection. On the contrary, Šumilo et al. found [31] that hot, sunny, summer weather and holiday times make an additional risk on human infection by compelling people to take journeys in nature.

The extreme hot summers and heat waves may moderate the effect of the climate change, as in the case of the Hungarian heat wave in 2007, but one single event is not sufficient to assess the effect. May and June are very important months in the life-cycle of ticks. During these months, the vegetation has the most intensive development and the amount of tick metamorphosis and egg laying activity is the highest. In the presented study, the LB seasons were divided into two groups according to positive or negative deviation of the years from the mean temperature of May and June. In the case of the warmer late spring-early summer years, the LB curve reached the annual peak 2–3 weeks earlier, and the descending phase of the curve also started earlier.

This observation can be explain if it is note that the maximum activity of the nymph life-stage occurs during late spring and early summer in the temperate climatic zone. In the case of a vector-borne disease in general, higher temperatures accelerate the development of individual ticks, the ovulation and the metamorphosis, and increase the population density and abundance. According to a US study, the inter-annual variation in entomological risk of exposure to Lyme disease correlates positively with prior abundance of key hosts (deer, rodents) for the immature stages of the tick vector and with their critical food resources [32]. The earlier onset of spring and a longer vegetation period is favourable for the ticks, and in accordance with the presented results, these changes enhance the LB incidence. These results support the findings in the literature that in Central Europe, due to climate change, the seasonal activity, as well as the modification of the annual biological activity of ticks, will change significantly [22].

Due to technical problems with the sensitivity of the tests and personal diagnostic difficulties (LB is a great imitator of other cardial, neurological, and other diseases), last but not least, the relatively late first isolation of the pathogen [33], as well as the discovery of the connection between the pathogen and the clinical manifestations [34], the real cumulative prevalence of the disease could be 10% of the full population (approx. 1 million people) in Hungary according to Bozsik [35].

The presented analysis pose some problems that could be difficult to solve. First, the incubation period of LB from infection to onset of the primary symptoms is usually 1–2 weeks. Ideally, the most likely date of infection, i.e. exact time of tick bite, should be determined. If the primary cases are separated from the secondary ones, the weekly incidence of primary cases could be statistically determined. Unfortunately, medical doctors often neglect to fill in the questions concerning the circumstances of the beginning of the disease. Consequently, the early localized infections cannot be separated from the early disseminated infections and late persistent infections; therefore the incidence of primary LB cases may be underestimated. A period of 13 years is a very short time to recognize a possibly existing long-term natural fluctuation such as the changing tick population density, or infection patterns with *Borrelia burgdorferi*.

The weekly incidence depends on several additional factors; for example, the behaviour of people, and the rate of infected ticks, host animals, etc. Another shortcoming of this study is the uncertainty of the reporting system, which may modify the association between temperature and the weekly incidence of LB. Another important problem is that the bias cannot be determined due to changes in laboratory testing. The diagnostic activity, the knowledge of medical doctors and reporting habits may have also changed.

The main impact of climate change on ticks may be a change of their abundance and population, the rate of their LB infection level and the changing trend of their seasonal behaviour and life-cycle, but the changing incidences of the disease are known. These problems should be kept in mind in the evaluation of the association between the increasing trend of LB incidence and the similar trend in the length of the vegetation season. It may be suppose that a systematic error due to improving laboratory detection or a strict reporting discipline, would affect homogenously the approximate LB incidence every week during the year. It would be difficult to explain the observed significant increasing trend between weeks 15–28, which correlates well with the shift of the vegetation period and can also explain 79% of the increasing annual LB incidence.

The daily mean temperature data on country level was used. Due to the relatively homogenous geographic circumstances of Hungary, the aggregated temperature data can characterize the different parts of the country. The associations can be further studied on a regional level when the effect of the changing ecological habitat and abundance of the vector and host of the disease can be taken into consideration. In the southern part of Europe, summers will become warmer and drier;,thus, climate change will likely affect the abundance and seasonal activity of the ticks more than in northern Europe where the geographical extension may show a greater change [15].

CONCLUSIONS

The presented reporting system offers a possibility to study the basic associations between climatic and meteorological conditions and LB. In spite of the possible bias of the notification system, our results support the hypothesis that association exists between the changing weekly temperature and LB incidence. Further studies are needed to clarify more precise associations. It would be useful to carry out a regional analysis in Hungary to search for differences of LB incidences between the counties with different climates. It is also desirable to know the proportion of the early and the later infections. Based on the associations, they may predict the future changes in the annual distribution of the incidence in relation to climate change.

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