Increased incidence of Lyme borreliosis in southern Sweden following mild winters and during warm humid summers

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Abstract:

The aim of the present study was to investigate the long-term incidence rate of Lyme borreliosis and, additionally, to determine whether a correliation exists between climatic factors and summer-season variations in the incidence of Lyme borreliosis. Climatic variability acts directly on tick population dynamics and indirectly on human exposure to Lyme borreliosis spirochetes. In this study, conducted in primary health care clinics in south-eastern Sweden, electronic patient records from 1997–2003 were searched for those that fulfilled the criteria for erythema migrans. Using a multilevel Poisson regression model, the influence of various climatic factors on the summer-season variations in the incidence of erythema migrans were studied. The mean annual incidence rate was 464 cases of erythema migrans per 100,000 inhabitants. The incidence rate was significantly higher in women than men, 505 and 423 cases per 100,000 inhabitants respectively ($p<0.001$). The summer-season variations in the erythema migrans incidence rate correlated with the monthly mean summer temperatures (incidence rate ratio 1.12, $p<0.001$), the number of winter days with temperatures below 0ºC (incidence rate ratio 0.97; $p<0.001$), the monthly mean summer precipitation (incidence rate ratio 0.92; $p<0.05$), and the number of summer days with relative humidity above 86% (incidence rate ratio 1.04; $p<0.05$). In conclusion, Lyme borreliosis is highly endemic in southeastern Sweden. The climate in this area, which is favourable not only for human tick exposure but also for the abundance of host-seeking ticks, influences the summer-season variations in incidence of Lyme borreliosis.

Introduction

In Europe, Lyme borreliosis (LB) is caused by the spirochetes *B. burgdorferi* sensu lato i.e; *B. afzelii*, *B. garinii* and *B. burgdorferi* sensu stricto, all of which are transmitted by the tick *Ixodes ricinus.* The prevalence of *B. burgdorferi* sensu lato spirochetes in *I. ricinus* ticks is reported to range from 6 to 13% in nymphs and from 15 to 36% in adult females [1]. The nondisseminated cutaneous form, erythema migrans (EM), is the most frequent clinical manifestation of LB, representing over 70% of the cases diagnosed in southern Sweden [2]. In a study in this area, 94% of EM skin isolates were *B. afelii* strains and 6% were *B. garinii* strains [3], while in a Finnish study on the island of Åland, 66% of the EM were *B. afzelii* strains and 33% *B. garinii* strains [4].

There are indications that the incidence of LB is increasing in this area of Sweden. In 1992, 164 cases of LB were reported in the county of Blekinge in southern Sweden [2], and in 1997, 459 cases were reported [5].

Studies show that risk factors for human exposure to ticks and tick-borne diseases depend on tick abundance and the prevalence of infected ticks [1, 6-10]. Climate has an influence on tick abundance, and ambient conditions such as air temperature and humidity affect seasonal tick activity [11-13]. Mild winters, early springs, warm summers, and warm autumns with a high relative humidity seem to increase tick abundance and the risk of tick-borne infections [9, 14-16].

The aim of the present study was to investigate the long-term incidence of EM. In addition, we wanted to study correlations between climatic factors and the summer-season variations in the incidence of EM.

Materials and methods

Study area and population

The study area, Blekinge County, is located in the southeastern part of Sweden and covers an area of 2,941 km². It is characterized by long coastlines along the Baltic Sea and an extensive archipelago. Seventy-five percent of the area is covered by deciduous woodlands and pine and mixed forests. The rest of the area is open land and moors with numerous small lakes and rivers. The climate is characterized as ”warm temperate”, with mild winters. Mean temperatures above –3ºC in winter and around 15ºC in summer. Precipitation varies between 500 and 700 mm per year. The county has a rich animal life, especially with respect to tick hosts such as birds, rodents, deer and elk.

About 150,000 individuals live in Blekinge County; of whom 123,495 (61,712 women; 61,783 men) receive care through the national primary health care system. During the study period, the change in population size, at less than 0.2% was considered negligible.

Study design

In this retrospective study, we used the electronic patient record systems Swedestar and PAS-ORIGO to search for all medical records of patients diagnosed with EM attending primary health care clinics and the Department of Infectious Diseases at Blekinge County Hospital. The study period covered 6 years 1997–2002.

The annual and monthly incidence rates of EM were studied. The influence of climate on the EM incidence rate was studied relative to the summer seasons, since over three-quarters of the cases and the greatest variations in the EM incidence rate occurred during 1 June to 30 September. The influences of general climatic factors such as temperature, precipitation and relative humidity on the EM incidence rate during the summer seasons were studied. Additionally, the influence of certain climatic thresholds on the EM summer incidence rate relative to earlier published data of climatic influence on *I. ricinus* tick abundance and tick activity were studied. Only thresholds applicable to the prevailing climate in the area were used in the present study. The temperature threshold for tick host seeking activity is a weekly mean maximum temperature >7ºC [17-21]. The tick can actively seek a host at levels of relative humidity above 86%; below this threshold, the tick climbs down to lower vegetation in order to rehydrate [22]. Cold winter days with temperatures below 0ºC can negatively influence tick abundance by reducing the survival of the ticks and their hosts (Jeremy Gray, personal communication, September 15, 2005). This outcome could affect tick abundance in the following 2 years, since the tick lives 3 years, with larvae and nymphs as the host-seeking stages.

Climate data were correlated 14 days before the diagnosis of the EM cases, which represents the incubation period from tick bite to diagnosis. Winter temperatures were measured from 1 December to the last of February each year (Table 1).

Case definitions

To identify cases of EM, the electronic patient records were searched by diagnosis. For inclusion in the study , the electronic patient records had to contain the following: information indicating that the EM was preceded by a probable tick bite; a description of the clinical appearance and size of the lesion which had to reach at least 5 cm in diameter; and verification that antibiotics had been prescribed. The cases included fulfilled the surveillance criteria set forth by the Centers for Disease Control and Prevention (CDC) [23].

Climate definitions

Climate information on temperature, relative humidity, and precipitation were obtained from the Swedish Meteorological and Hydrological Institute. The data were measured 1.5 m above ground level in Ronneby/Bredåkra, which is located in the middle of Blekinge County.

Temperature was measured in degrees Celsius, relative humidity in percent, and precipitation in millimetres.

Statistical methods

In all studies, *p*-values were 'two-tailed' and a *p*-value <0.05 was considered significant. Student's *t*-test was used when comparing normally distributed continuous data. The chi-square test was used when comparing categorical data and the Mann-Whitney U-test when comparing nonparametric continuous data. Analyses were performed using the SPSS statistical computer software, version 11.0 (SPSS, Chicago, IL, USA).

To analyse ”count data”, multilevel analysis using multiple Poisson regression analysis was done to evaluate the effect of a particular climatic factor after adjusting for other climatic factors [24]. To examine the extent to which individual and climatic characteristics explain the variability in the summer incidence rate of EM, we used a two-level model with a random intercept, with individuals at the first level and municipalities in the Blekinge County at the second level. The associations between the variables studied were expressed as incidence rate ratios (IRR) (95 percent confidence intervals [CIs]) in the fixed-effects part of the model. MLwiN software, version 2.0 [25], was used to perform the analyses. Parameters were estimated by using iterative generalized least squares. The use of restricted iterative generalized least squares gave very similar results.

Ethical considerations

The study was approved by the Ethics Committee at Lund University. These experiments complied with the current laws in Sweden.

Results

We identified 3437 cases (1869 women, 1567 men) that met the criteria for EM. The annual mean incidence rate of EM was 464 cases of EM per 100,000 inhabitants. There were considerable variations in the incidence during the study period: 1999 had the lowest incidence, at 264/100,000, while 2000 had the highest incidence, at 664/100,000 (Fig. 1).

The mean age of women was 51.7 years (standard deviation [SD] =19.8 years, range 0.7–92.0 years) and of the men, 46.9 years (SD= 20.4 years, range 1.0–90.0 years) (p<0.001).

Significantly more women than men were affected (505 and 423 cases per 100,000 inhabitants, p<0.001). Among women, the incidence of EM was highest in those aged 65–69 years, with a prominent peak of 1174/100,000 seen in the incidence curve. The incidence was higher in women over 40 years than in men of the same age (Fig. 2).

Cases occurred throughout the year. However, youths under 15 years of age were affected by EM earlier in the year, i.e. in July, compared with individuals 15 years and older, who were affected primarily in August (p=0.021) (Fig. 3). Both women and men were affected by EM primarily in August (p=0.61).

Overall, 47% of the cases appeared in July and August. The greatest variations in the EM incidence rate were also observed during these months, which in large part explained the seasonal variations in EM incidence rate.

In a multilevel analysis using the Poisson regression model, the correlations between the summer-season EM incidence rate and climatic data were studied. The summer seasons, 1 June to 30 September, 1997–2002, included 76% of the cases and the greatest variations in EM incidence rate. The monthly mean temperatures (IRR 1.12; 95% CI 1.08–1.16; p<0.001) and the number of days during the winter with mean temperatures below 0ºC (IRR 0.97; 95% CI 0.97–0.98; p<0.001) correlated with the EM incidence rate during the period studied. In addition, the EM incidence rate correlated negatively with mean monthly precipitation (IRR

0.92; 95% CI 0.84–0.99; p<0.05), and positively with the number of days with relative humidity levels above 86% (IRR 1.04; 95% CI 1.00–1.06; p<0.05). Additionally, in this model the incidence rate was lower in men than in women (IRR 0.86; 95% CI 0.76–0.96, p<0.05). The incidence rate was 47% higher in individuals aged 15–64 (IRR 1.47; 95% CI 1.25–1.72; p<0.001) and 94% higher in individuals over 65 years (IRR 1.94; 95% CI 1.64–2.30; p<0.001) compared with youths under 15 years of age (Table 2). The variance between the municipalities was 0.64, with a standard error of 0.5.

Discussion

LB is highly endemic in Blekinge County, Sweden with an annual mean EM incidence rate of 464 cases per 100,000 inhabitants. This figure, however, is conservative, since 14% of the electronic patient records from the primary health care system lacked a definite diagnosis and thus some cases of EM could have been missed. A total 98.3% of the EM cases were treated in primary health care clinics, which confirms that EM cases in Sweden are addressed primarily by the national primary health care system.

There was a great variability and a general increase in the seasonal incidence rate of EM during the study period. The population has been stable during the whole study period, and therefore the great variations in the EM incidence rate cannot be attributed to population changes. The highest incidence rates were observed in 2000 and 2002, and the incidence rate more than doubled between 1999 and 2000 (Fig. 1). Interestingly, in the UK the number of LB cases also doubled during the same period, from 150 to 300 cases per 100,000 population per year [26, 27].

We studied climatic factors that may have influenced the summer-season variations in the EM incidence rate. The number of EM cases depends on many factors, including human exposure to ticks, tick–host relationships and tick abundance. To directly measure the tick or host abundance on a large scale is difficult; instead we correlated climatic data with the incidence of EM. In the literature, certain climatic thresholds have been described as influencing tick activity and the abundance of ticks and hosts. We also studied the influence of climate from a more general perspective, not categorizing data according to thresholds, but instead using continuous data from monthly mean temperatures, relative humidity, and precipitation. We found a strong positive correlation between the monthly mean incidence rate of EM and the monthly mean temperature during June, July, August and September. An increase in the mean monthly summer temperature by 1ºC increased the incidence rate of EM by 12%. Thus, the warmer the weather, the higher the probability of an increased number of cases. This effect is probably mostly the result of an increase in human exposure to ticks, since no positive correlations between summer air temperature and host-seeking activity for nymphs and adults have been observed [17–21]. In a German study, an increase in the incidence of tick-borne encephalitis was observed during warmer summers, an effect attributed to increased human exposure to outdoor activities [28]. We found no studies that correlated climatic factors with the amount of time humans spend outdoors, but undoubtedly humans dress more lightly during the summer, thus increasing the risk of attracting tick bites.

In this study there was also a strong correlation between milder climate during the winter and the EM incidence rate; a decrease by 1 day of the number of winter days with temperature below 0ºC increased the incidence rate of EM by 3% the following summer season. This result is interpreted as an effect on the survival of ticks and their hosts. The findings are in accordance with studies performed by Lindgren et al. [14,15], who concluded that a warmer climate with milder winters and earlier arrival of spring was related to an increased tick density and an increased number of tick-borne encephalitis cases in Sweden.

We also found a significant negative correlation with the mean monthly precipitation and the EM incidence rate; an increase of the mean monthly summer precipitation by 1 mm decreased the EM summer incidence rate by 8%. This finding might be explained by two factors: decreased human tick exposure because of less time spent outdoors, and the use of rain garments, which provide more coverage. A study in the UK identified a negative effect of rain on the attachment rate of ticks to humans [7]. The result could also be explained by an impairment of the host-seeking ability in ticks; the dampness may inhibit their ability to climb vegetation when seeking a host (Jeremy Gray, personal communication, September 15, 2005).

Furthermore, the number of days with levels of relative humidity above 86% also correlated positively with the incidence rate of EM. An increase by 1 day in the number of days with relative humidity above 86% increased the EM incidence rate by 4%. This is interpreted as having a direct effect on ticks, as earlier studies have shown that the host-seeking activity of *I. ricinus* depends on the relative humidity [12], and others have shown that below a relative humidity threshold of 86%, the tick dehydrates and cannot continuously seek a host [22].

The lowest incidence rate occurred in 1999, a year that was preceeded by a cold winter with many days below 0ºC (*n*=42 days) and that had few summer days with relative humidity above 86%, (*n*=7.0 days). The highest incidence rates occurred in 2000 and 2002. In 2000 the preceeding winter was mild, with few days below 0ºC, (*n*=27 days), and the summer had many days with relative humidity above 86%, (*n*=11.3 days). In 2002 there were low amounts of summer precipitation, a mean daily precipitation of 1.5 mm, a mild winter with few days below 0ºC, (*n*=31 days), and a high mean temperature 16.9 ºC. Cases occurred all year around. This may have been due not only to patient delay in seeking treatment but also to the mild winters. For example, during the year with the mildest winter, 2000, the highest number of cases were observed from January to March.

The seasonal activity of the *I. ricinus* nymphs and adults peaks from March to May, and from August to October, respectively [1, 17, 18, 29]; thus peaks in the incidence rate of LB would be expected in April/June and in September/November. Yet in this study, in almost half of the cases the onset of disease occurred in July and August; consequently, on the basis of the incubation period, subjects were exposed to tick bites in June and July. This is supported by a recent study in Blekinge County, where most individuals were bitten by ticks during the Swedish vacation months June and July [30]. The fact that the majority of the EM cases occurs after a period when the numbers of host-seeking ticks drops strongly points to the influence of increased human outdoor activity (Fig 3). Thus, human exposure to ticks has a stronger influence on the EM incidence rate than the seasonal feeding activity of the nymphal *I. ricinus.*

The bimodal distribution seen in this study has been reported in other work from the USA and France [31–33]. In this study, as in a former study from southern Sweden [2], the incidence rate was highest in middle-aged and elderly women, with incidence peaking among women aged 65–69 years. Our finding that women are affected by EM to a higher extent than men is supported by earlier studies in Europe [34, 35] but not in the USA [31, 36, 37].

Further studies are needed to explain the gender differences between EM incidence rates in Europe and the USA. Exposure to outdoor activities may explain the differences between Swedish women and their American counterparts, although differences in genospecies, as well as differences in immunological characteristics, may also affect gender differently in Europe and the USA. In collaboration with the University of Linköping, a study of reinfected Swedish patients with EM has indicated that the type 1 immune response is less intense in postmenopausal females than in males [38]. The type 1 cell-mediated immune response is important in eradicating the spirochete in humans [39]. Thus postmenopausal women may be more susceptible to spirochetal infections.

In conclusion, LB is highly endemic in Blekinge County, and almost every patient with EM seeks assistance through the national primary health care system. Most cases of EM appear during the vacation period, when people have the opportunity to spend more time outdoors. The EM incidence rate was influenced by climate favourable not only for human tick exposure but also for an abundance of host-seeking ticks.

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Table 1. Description of the climatic variables included in the multilevel Poisson regression model.

Climate variable:	Explanation:	Range:	Mean:	Median	SD:
Mean temp.[A]	mean monthly temperature (ºC)	11.2–19.4	15.2		2.2
Mean RH [A]	mean monthly relative humidity (RH, %)	67.9–90.4	79.4		4.5
Mean precip.[A]	mean monthly value of daily precipitation (mm)	0.0–3.9	1.9		0.9
No. days RH > 86% [A]	number of days with relative humidity > 86%	0–26		8.0	5.6
No. winter days < 0ºC [B]	number of winter days with average temperature <0ºC	20–47		35.5	9.4
No. winter days < 0ºC, (t-1)[B]	number of winter days with average temperature <0ºC, previous year	20–72		41.0	16.6

SD standard deviation

[A] Climate data were collected 14 days before the EM cases, which represents the approximate mean incubation period from tick bite to diagnosis. EM cases were diagnosed 1 June through 30 September.

[B] Winter temperatures were measured from 1 December to the last of February each year.

Table 2. Variables included in the multilevel Poisson regression model that influenced fluctuations in the LB incidence rate from 1 June through 30 September 1997-2002 in southern Sweden.

Parameter	IRR	95% CI	*p*-value
Gender:			
Female	Reference		
Male	0.86	0.76–0.96	<0.05
Age:			
0–14 years	Reference		
15–64 years	1.47	1.25–1.72	<0.001
65– years	1.94	1.64–2.3	<0.001
Climate:			
Mean temp.	1.12	1.08–1.16	<0.001
Mean RH	0.98	0.94–1.02	ns
Mean precip.	0.92	0.84–0.99	<0.05
No. days RH > 86%	1.04	1.00–1.06	<0.05
No. winter days < 0ºC	0.97	0.97–0.98	<0.001
No. winter days < 0ºC (t-1)	1.00	0.99–1.01	ns

Fig. 1. Annual incidence of erythema migrans per 100,000 inhabitants in Blekinge County.

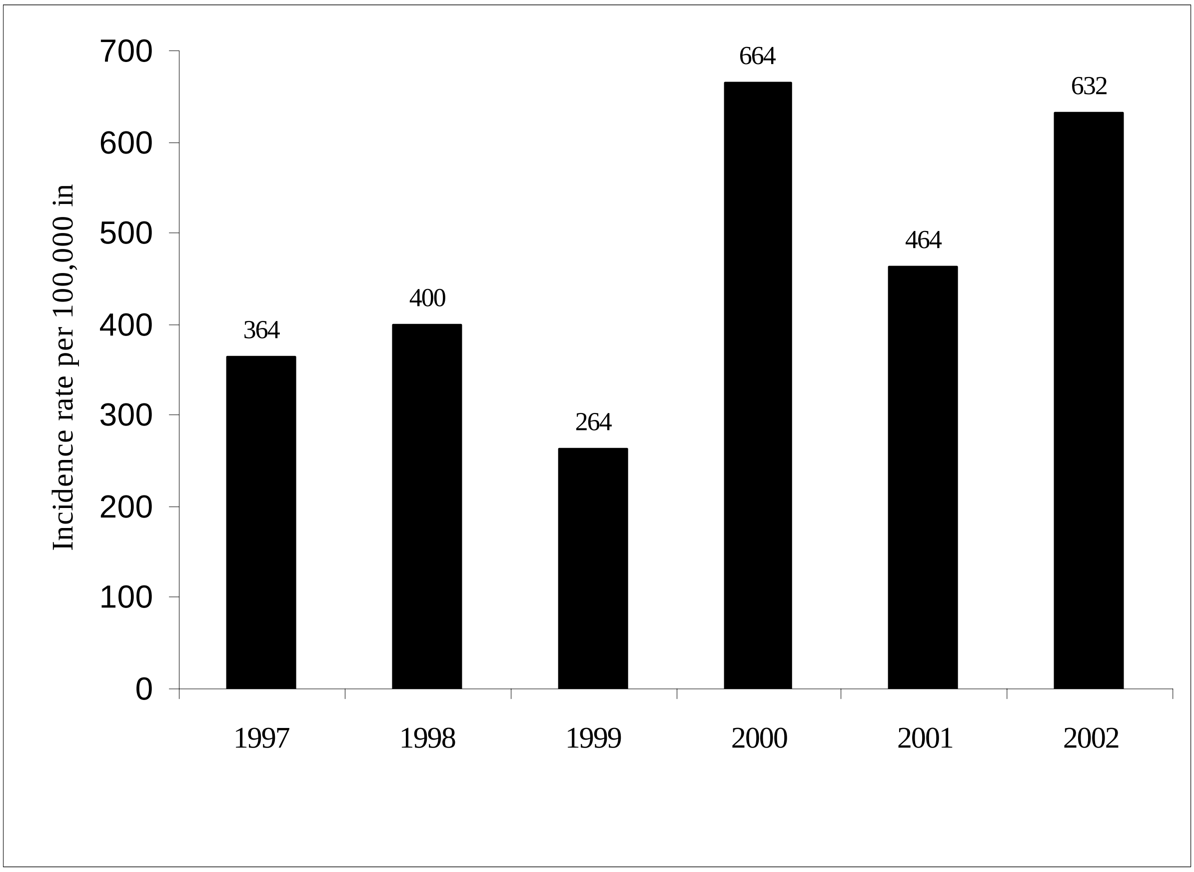


Fig. 2. Incidence of erythema migrans in women and men in different age groups 1997–2002.

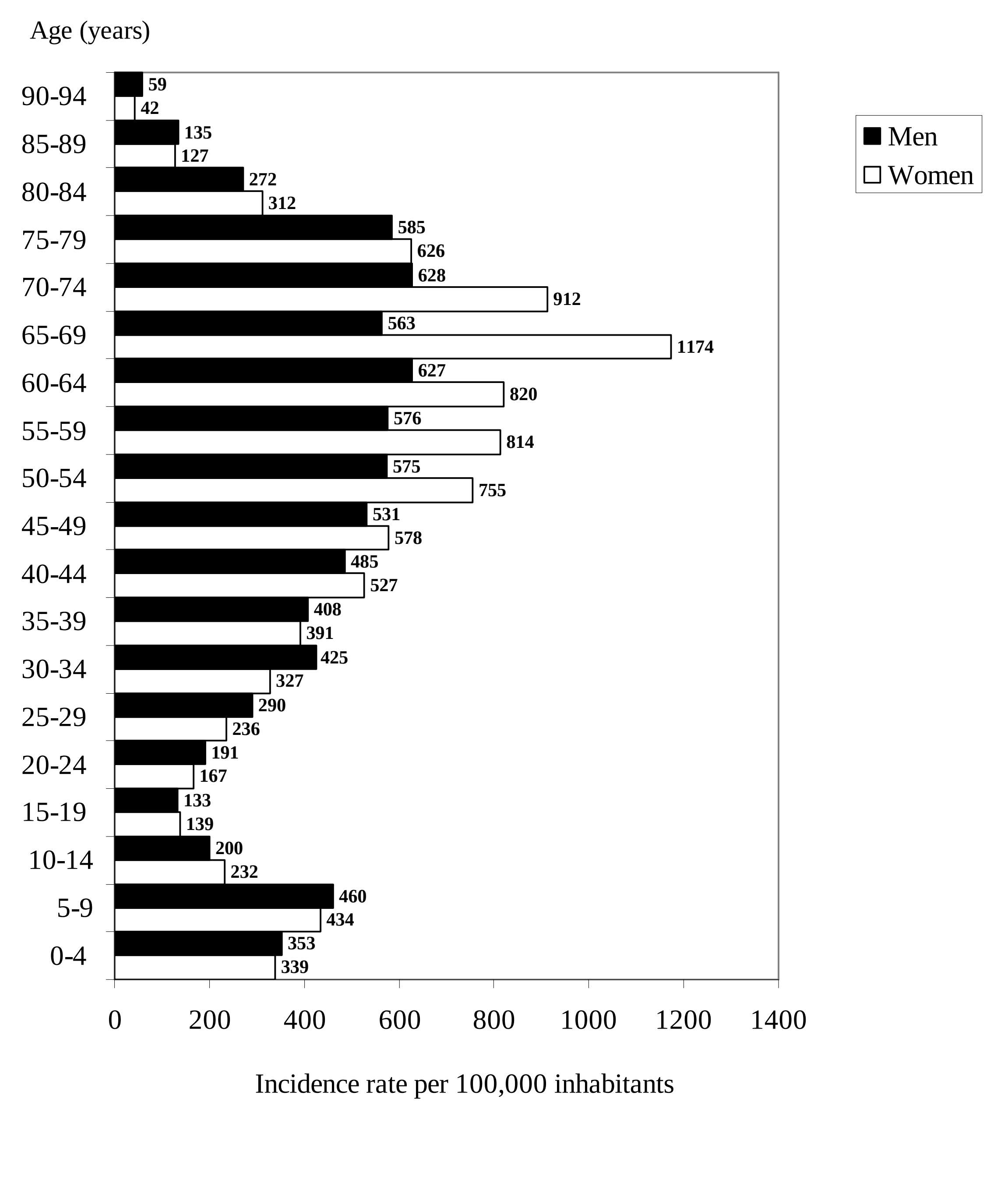
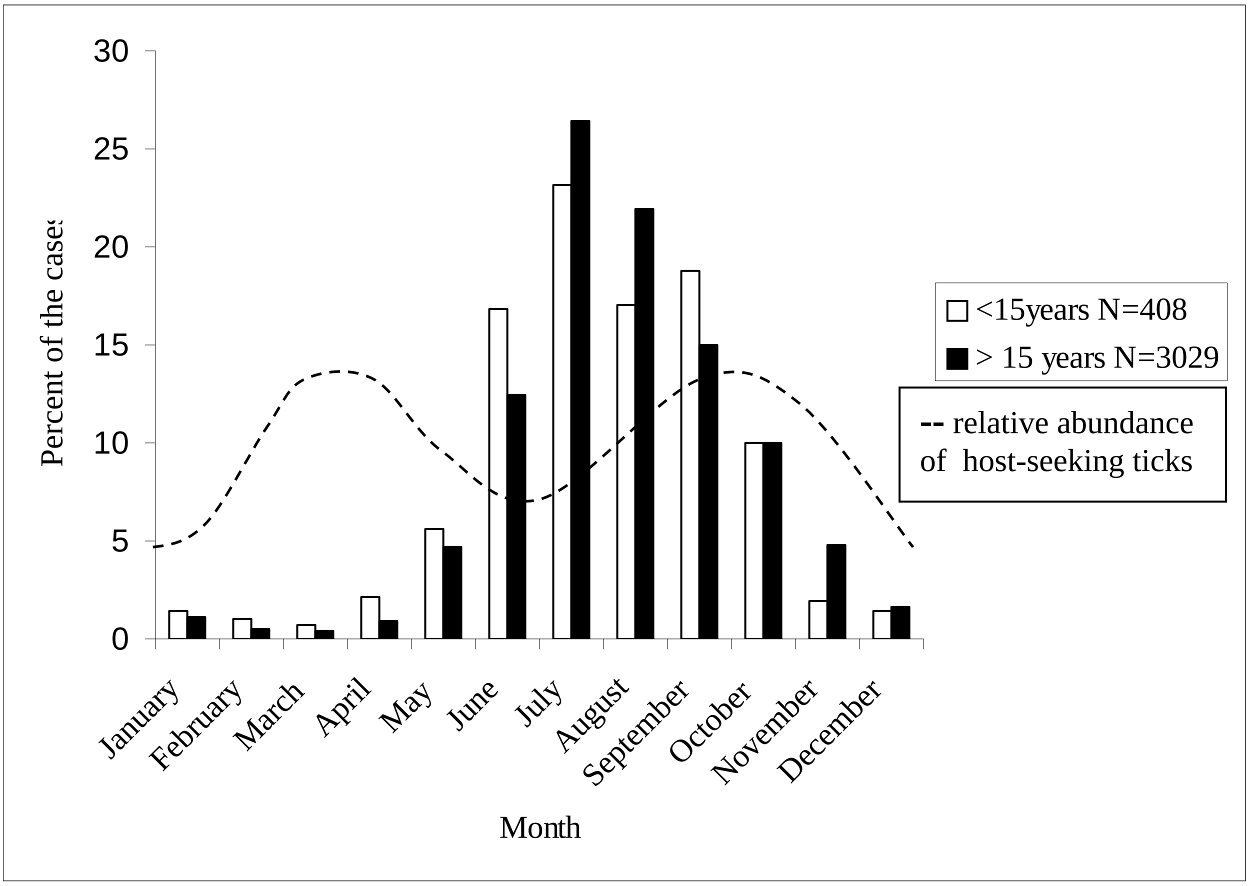


Fig. 3. Month of affliction with erythema migrans for individuals < 15 years compared with individuals ≥15 years, and the relative abundance of host-seeking ticks.



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