# Epidemiology of Lyme borreliosis

A retrospective descriptive study

in Kronoberg County primary care, 2006-2020

Brendan Brouwer, ST-läkare allmänmedicin, Kronoberg

brendan.brouwer@kronoberg.se

Scientific Supervisor: Kim Ekblom MD, Ph.D.

Specialist in Clinical Chemistry and

Transfusion Medicine

# Abstract

### Background

Lyme Borreliosis (LB) is the most prevalent tick-transmitted infection in temperate areas of Europe, North America, and Asia. Its geographic distribution is increasing, and studies show that weather factors influence incidence rates.

The most recent study from southern Sweden was over 15 years ago and showed an incidence of 464 per 100 000 person-years. There has not been a study in Sweden in which data over 15 years has been investigated for incidence trends.

### Methods

This study is a retrospective descriptive study over a period of 15 years in Kronoberg County, located in southern Sweden. The study population was selected from two databases. One database has patient data from 2006 – 2014, and the other has aggregated data from 2015 – 2020. Patients with LB from primary care were selected. Incidences, trend analysis, linear and Poisson regression were calculated and performed. Sex, age, and geographical distribution were described and analyzed. Weather data was collected to investigate a possible correlation between weather trends and LB incidence.

### Results

A total of 16 878 patients were included. Incidence rates showed a trend in time with a coefficient of 1.047 ($p<0.001$) per year. The highest incidence was calculated in 2019 with 951 per 100 000 person-years. Western Kronoberg had a higher LB incidence, with a rate ratio of 1.306 ($p<0.001$). The incidence per age group increased with a maximum at 65-69 years. Females had a higher risk for LB than men, with a rate ratio of 1.238 ($p<0.001$). Weather trends showed a correlation with significance for summer temperature, rainfall, humidity, and winter days.

### Conclusions

This study showed an incidence trend of LB in Kronoberg County. Other significant variables included geographical distribution and sex. The highest incidence was found in the age group of 65-69 years. Correlation between incidence and weather trends was investigated but could not satisfactorily show a strong correlation.

# Table of contents

# Background

Lyme Borreliosis (LB) is the most prevalent tick-transmitted infection in temperate areas of Europe, North America, and Asia, and its geographic distribution is ever-increasing (1, 2).

In Europe, annual cases are increasing in some areas, and tick vectors are expanding their range to higher altitudes and latitudes, suggesting that LB will remain an important health concern in the coming decades, especially in light of economic, land use, and climate change predictions (3).

In a review from 2017, the highest reported incidences for LB in Europe were in southern Sweden, Blekinge County, with 464/100 000 person-years and the lowest in Italy of 0.001/100 000 person-years. The average incidence rate in Western Europe was reported as 22/100 000 person-years (4). In a systematic review from 2019, LB seems to be an increasing disease in most Western European countries, most pronounced in the northern and central parts. Although, increased awareness and testing cannot be excluded as reasons for this observed emergence (5).

There have been previous studies in southern Sweden. Showing that LB is highly endemic, almost every patient with erythema migrans (EM) seeks assistance through the national primary healthcare system. Most cases of EM appear during the summer vacation period when people can spend more time outdoors. The EM incidence rate is influenced by a climate favorable for human tick exposure and an abundance of host-seeking ticks (6, 7). Correlations have been found between summer-season variations in the EM incidence rate and three-monthly mean summer temperature, the number of winter days with temperatures below zero degrees Celsius, three-monthly mean summer precipitation and summer days with relative humidity above 86% (6). Another study showed that the risk of reinfection of LB was linked to the number of tick bites, sex, age, and geographical location (8).

LB is caused by some members of the spirochete group *Borrelia burgdorferi sensu lato*. Reservoir-competent animals include small mammals and certain species of birds. The vectors are ticks of the genus *Ixodes*. Over 10% of ticks in central Europe are infected with Lyme Borreliae. The risk of infection for humans is highest from May to September. The transmission of Lyme Borreliae occurs on average 24h after a blood meal (1, 9). Climate, host abundance, and social factors may explain the upsurge of epidemics transmitted by ticks to humans (10). EM, the early skin rash of LB, occurs in 80-90% of cases. It is an erythematous rash that gradually expands from the site of a tick bite and is not significantly raised or painful. Some patients may also have a systemic, flu-like illness without significant respiratory symptoms.

Another early manifestation is borrelial lymphocytoma. Late manifestations include neuro-borreliosis, acrodermatitis chronica atrophicans, Lyme carditis, and Lyme arthritis (1, 9).

No laboratory tests are required in the diagnosis of EM, which depends on a clinical evaluation and an assessment of tick exposure risk. All patients with symptomatic *B. burgdorferi* infection should be treated with appropriate antibiotics. Early treatment can prevent the risk of developing late-stage complications, but even patients with late-stage LB can benefit from antibiotics. Nevertheless, clinical recovery may be incomplete if severe tissue damage had occurred prior to treatment (1).

A study from the Netherlands showed a substantial disease burden of LB. However, most of this burden is caused by patients with Lyme-related persisting symptoms in which EM and disseminated LB have a more modest impact (11).

The ECDC reports that areas for further research include more data on the epidemiology of LB (1). Enhanced surveillance and implementation of a uniform definition of LB are necessary to optimize LB epidemiology evaluation, thereby enabling the development of accurate risk prediction models and preventive strategies (5). In addition, tick numbers and activity are increasing, leading to greater risks of infection (4), which further strengthens the need for enhanced surveillance and epidemiological research. An important feature is the data that shows a probable link between climate change and increased infections (2, 12). Furthermore, a study showed that a combination of mild winters and extended spring and autumn seasons was related to increases in tick density (12).

Studies have been done on LB epidemiology in southern Sweden, but the last study was almost 15 years ago (6-8, 13). However, there has not been a study in which data for 15 years has been investigated for incidence trends.

# Objectives

The main objective of this study is to investigate the incidence and trend of LB over 15 years in general practice in Kronoberg County, Sweden.

Secondary objectives are to further investigate LB's epidemiology regarding sex, age, geographical distribution and investigate a possible correlation between LB incidence and weather trends.

# Methods

## Study design

This study is a retrospective descriptive study over a period of 15 years, 2006-2020. In this study, two databases were used in which the first database covered 2006-2014 and the second database 2015-2020. The first database had patient data in which one-way encrypted identification numbers ensured confidentiality. The second database used aggregated data in which no patient-specific data is included.

## Setting

The study was conducted in Kronoberg County, centrally located in the southern part of Sweden, and covers an area of 8 423 km2. The county is considered sparsely populated in southern Sweden, with 23.9 inhabitants/km2, near the average for the whole country. Only three urban areas in Kronoberg have more than 10 000 inhabitants, and only seven have more than 3 000. 79% of people live in urban areas, compared to 86% in the whole of Sweden. Kronoberg County ranks the highest number of people outside urban areas in southern Sweden. The urban population increased 18%, and the population outside urban areas has decreased by 3% during the first decade of this century.

Kronoberg County is characterized by forests, which take up around 80 percent of the land. The rest is open land with lakes and rivers. The animal life is rich with respect to tick hosts. The climate is characterized as a warm, humid continental climate (14-16).

According to municipalities, the county can be divided into two halves, in which eastern and western Kronoberg County have a centrally located hospital in the larger urban areas. Dividing the municipalities into five in eastern and three in western Kronoberg, see figure 2 (17).

Eastern Kronoberg has a bigger population and more dense urban areas. Also, this part is closer to Blekinge County, in which previous studies showed high incidence rates (6).

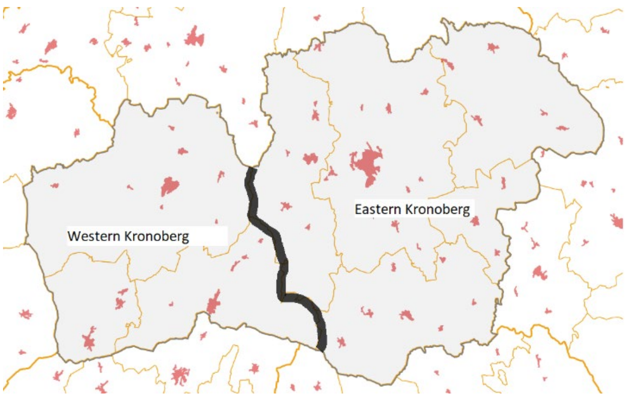


**Figure 1. Eastern and Western Kronoberg**

## Participants

The study population was selected from two databases, which use data from the electronic medical records system, Cambio Cosmic (Cambio Healthcare Systems Ab; Stockholm, Sweden), used in primary and secondary health care.

The first database covered only primary care data from 2006 to 2014 and contained data on diagnosis, diagnosis text, sex, age, and municipality (18). Aggregated patient record system data formed the second database from Kronoberg County and included the same variables as the first database for 2016 to 2020. Patients were not counted per visit to health care provider but once per year. Data from 2015 was not collected completely, although this data from 2015 was partly collected before starting this study and included data for coding for diagnoses, sex, and age but not municipality and diagnosis text.

From the data of these two databases, patients from primary care were selected. Then, further selections were made by diagnostic coding with ICD-10. In the ICD-10 coding system, A69.2 is used for any Borrelia infection.

The main diagnosis in primary care is EM. To verify the number of patients with non-EM borreliosis, control of the diagnosis text was done to evaluate the amount of non-EM borreliosis.

## Method and measurements

Concerning the objectives of this study, the main measurements were descriptive and looked at the amount of LB diagnoses to see if there was a possible trend. The incidence per year was calculated by dividing the amount of LB diagnoses in a year by the county's population of that year. The trend was analyzed with linear regression.

For the secondary objectives, descriptive statistics were done to describe patient characteristics such as age, sex, and the municipality of primary health care centers.

This data was further analyzed to see if there were any statistical differences between these characteristics, using Poisson regression. In Poisson regression the exponents of coefficients are equal to the incidence rate ratio (relative risk or RR).

The population data from Kronoberg County and its eight municipalities were gathered from the Swedish SCB (Statistics Sweden) (15). The municipalities were divided into western and eastern Kronoberg.

Weather data was collected from the meteorological institute of Sweden (19). In the larger urban areas, data from two stations were used to represent eastern and western Kronoberg. Summer data was retrieved for mean temperature and rainfall per month and number of days with humidity over 86%. In addition, because of the vector's life cycle, winter data was gathered for days under 0 degrees Celsius up to the 2 winters preceding the summer of that year. This data was used to investigate possible correlations between weather trends and LB incidence by using Poisson regression.

The data were analyzed with IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

## Ethics

Database 1: Ethical approval was obtained from the Regional Ethical Review Board in Linköping, Sweden (Dnr 2014/121-31).

Database 2: According to Swedish law, no ethical approval was needed for Database 2.

# Results

We collected 16 878 patients with LB diagnoses during 2006-2020 at primary care health centers, shown in figure 2. Table 1 shows the patient characteristics.

From database 2, 2016-2020, total patients in Kronoberg county with A692 code were 7 592, and 7 400 for primary care. Indicating that only 192 patients, 2.5%, were diagnosed in secondary care.

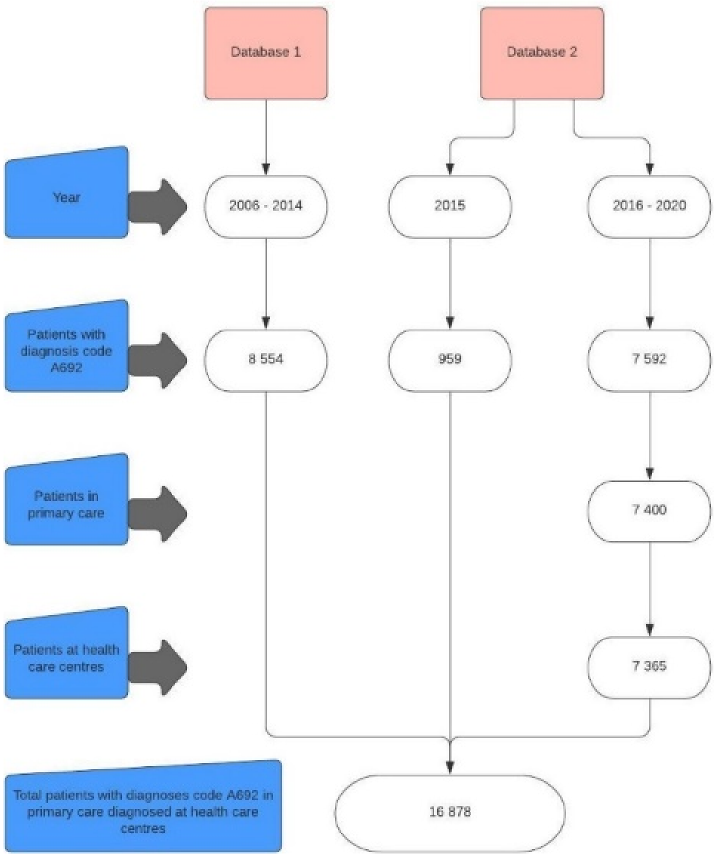


**Figure 2. Flowchart collection of patients**

**Table 1. Patient characteristics**

| *Characteristics* | *Amount (N = 16 878)* |
|---|---|
| *Male* | 7 652 (45) |
| *Female* | 9 226 (55) |
| **Age-yr** | |
| *Median (interquartile range)* | 58 (42-68) |
| *Mean* | 53 |
| **Municipality-nr. (%)** | |
| *Eastern* | 10 504* (66%) |
| *Western* | 5 416* (34%) |

*: Does not include 2015

To verify the amount of non-EM LB, we went through the diagnoses text of both databases 1 and 2 but not including 2015. In both databases, patients with diagnosis text which were other than the standard diagnosis text or were changed to another text which was non-EM or unclear were counted. Database 1 counted 149 patients, which equals 1.75%. Database 2, excluding 2015, counted 79 patients, which equals 1.07%. The most common diagnoses text in descending order is post-borreliosis, neuroborreliosis, acrodermatitis, borrelial lymphocytoma, and Lyme arthritis.

Incidence rates were calculated for Kronoberg county and eastern/western, which are shown in figure 3. However, as described previously, the data from 2015 did not include municipality and could therefore not be included in the incidence rates for eastern/western Kronoberg.

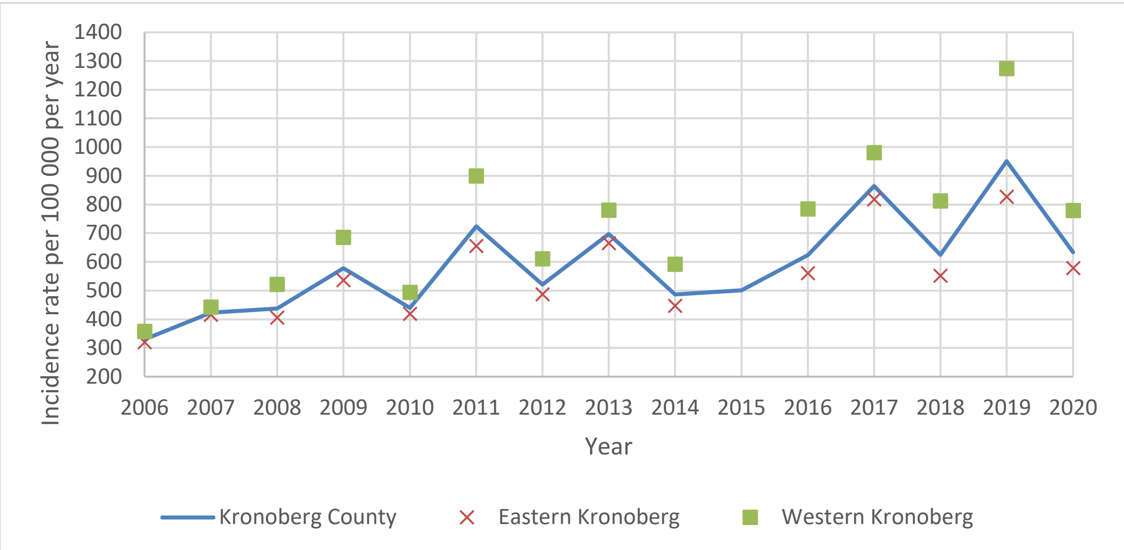


**Figure 3. LB incidence rates per 100 000 inhabitants per year in Kronoberg County 2006-2020. Also showing data for Eastern and Western Kronoberg respectively, where data is missing for 2015.**

Linear regression has been done to investigate if there is a correlation between time in years and incidence rates during 2006-2020. Figure 4 shows the linear regression and trend line with $R^2$ being 0.49 (p=0.004).

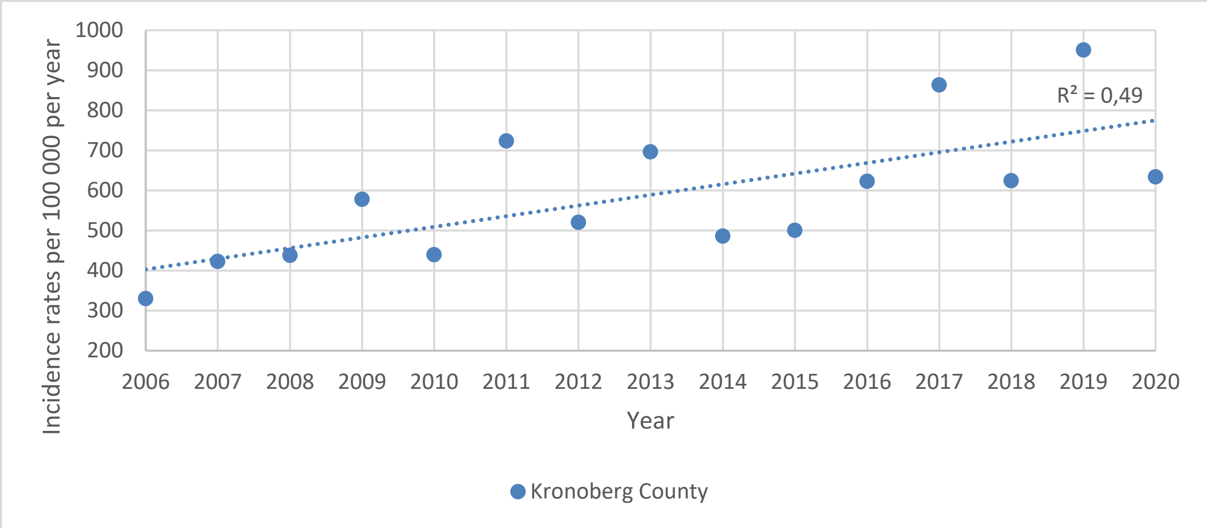


**Figure 4. Linear regression of LB incidence trend, Kronoberg County 2006-2020**

Poisson regression was used in SPSS and is shown in table 2 with the total of A69.2 diagnoses as the dependent factor. There was a significant association between time and eastern/western Kronoberg, with western Kronoberg having a 1.306 rate ratio and time in years 1.047 rate ratio for LB.

**Table 2. Poisson regression: Year and Eastern/Western Kronoberg, dependent value total LB diagnoses**

| *Parameter* | *RR* | *95% Wald Confidence interval for RR* | |
|---|---|---|---|
| | | *Lower* | *Upper* |
| *Eastern* | Ref. | N.A. | N.A. |
| *Western* | 1.306* | 1.264 | 1.350 |
| *Year* | 1.047* | 1.044 | 1.051 |

* = Significance (p<0.001)

N.A. = Not applicable

Ref. = Reference
RR = Risk ratio (relative risk)

The total diagnoses per month from 2006-2020 were summed up, and the distribution is shown in figure 5. Most diagnoses are registered around summer and early fall.

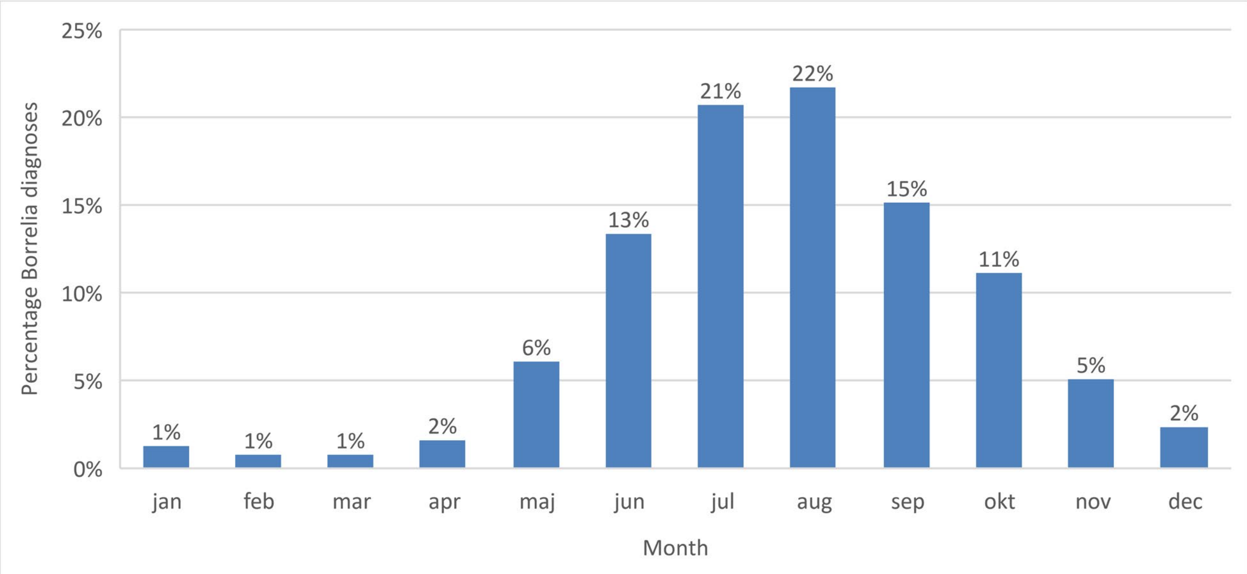


**Figure 5. Distribution of LB diagnoses per month in percentages, during 2006-2020, Kronoberg County**

The distribution of diagnoses in age groups was calculated for each database and summed up. The distribution of age groups for all inhabitants in Kronoberg county per year was collected from the national statistical bureau and summed up in 5-year age groups during 2006-2020. The amount of LB in the same age groups was collected from the two databases during the same years. We calculated the incidence rates per age group and are shown in figure 6. Incidence in age groups up to 65-69 years, after which it declined more rapidly.

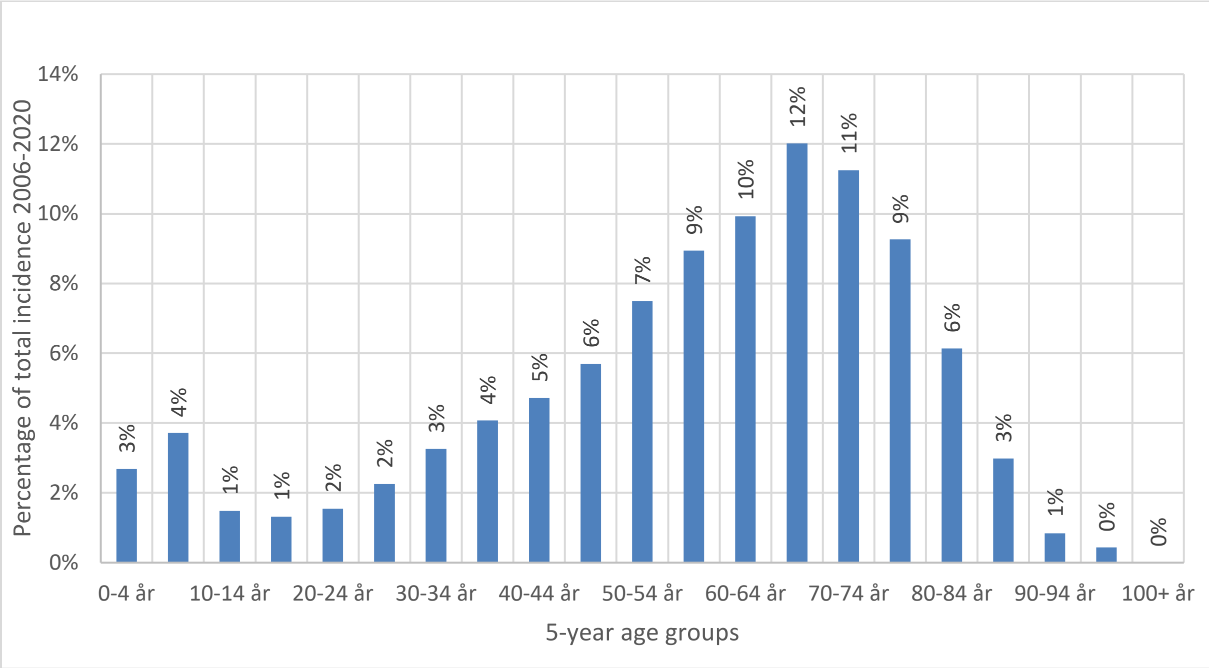


**Figure 6. Distribution of LB incidence in percentages per 5-year age groups, 2006-2020, Kronoberg County**

Incidence per sex per year was calculated and plotted in figure 7, showing that females had higher incidences than men.

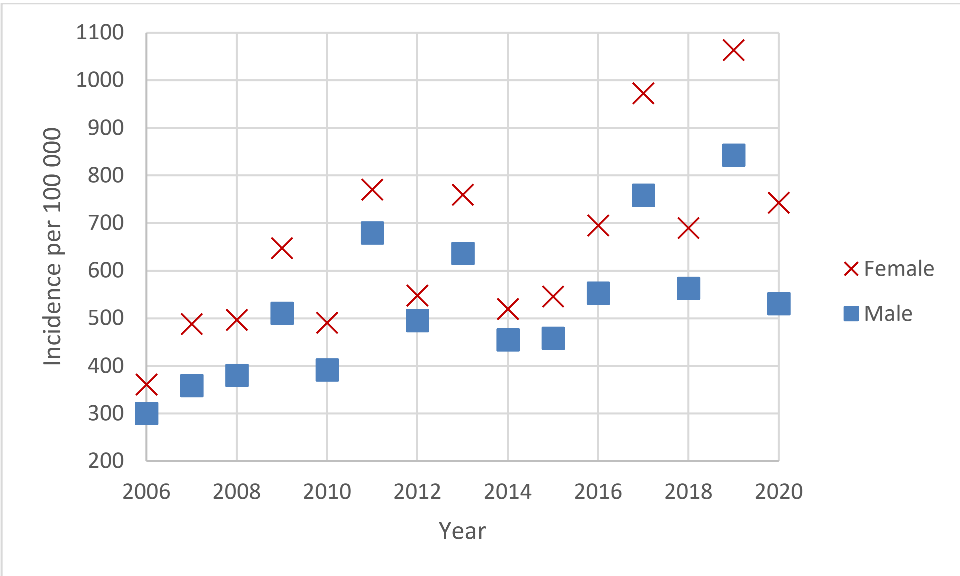


**Figure 7. Incidence per sex per 100 000 per year**

Poisson regression was done with sex and year as parameters (Table 3). Females had a significant rate ratio by 1.238.

**Table 3. Poisson regression: Sex and Year, dependent value total LB diagnoses**

| *Parameter* | *RR* | *95% Wald Confidence interval for RR* | |
|---|---|---|---|
| | | *Lower* | *Upper* |
| *Male* | Ref. | N.A. | N.A. |
| *Female* | 1.238* | 1.201 | 1.276 |
| *Year* | 1.046* | 1.043 | 1.050 |

* = Significance ($p<0.001$)

N.A. = Not applicable

Ref.= Reference
RR = Risk ratio (relative risk)

Poisson regression using weather data, year, and eastern/western Kronoberg was done and is shown in table 4. A significant association was found for all variables, but the RR is very small for all but eastern/western, year, and mean summer temperature. Mean temperature against time was plotted (Figure 8) and no clear trend was found during 2006-2020.

**Table 4. Poisson regression: Year, Eastern/Western Kronoberg and Weather data, dependent value total LB diagnoses**

| *Parameter* | *RR* | *95% Wald Confidence interval for RR* | |
|---|---|---|---|
| | | *Lower* | *Upper* |
| *Eastern* | Ref. | N.A. | N.A. |
| *Western* | 1.341* | 1.289 | 1.394 |
| *Year* | 1.074* | 1.068 | 1.080 |
| *Mean summer temperature (°C)* | 0.927* | 0.905 | 0.950 |
| *Winter days under 0 degrees* | 1.009* | 1.008 | 1.010 |
| *Winter days, t – 1 year* | 0.998† | 0.997 | 1.000 |
| *Winter days, t – 2 years* | 1.004* | 1.003 | 1.005 |
| *Mean rainfall (mm)* | 1.006* | 1.005 | 1.007 |
| *Days with humidity over 86%* | 0.987* | 0.982 | 0.991 |

* = Significance ($p<0.001$)

† = Significance ($p<0.05$)

N.A. = Not applicable

Ref.= Reference

RR = Risk ratio (relative risk)

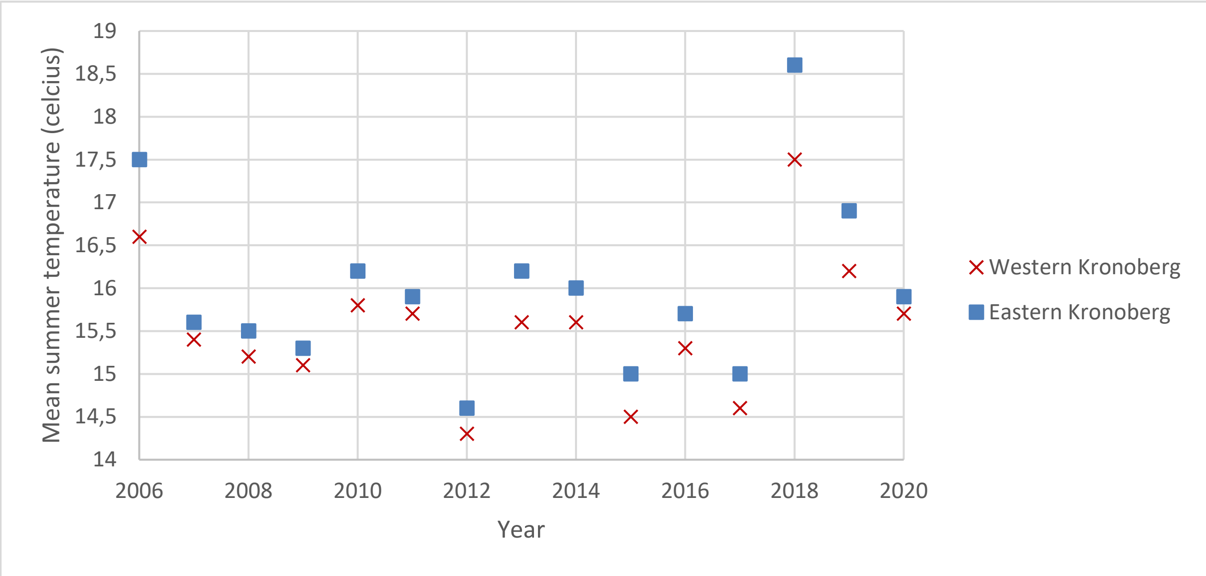


**Figure 8. Mean summer temperature per year, eastern/western Kronoberg**

# Discussion

The present study showed that incidence rates of LB increased in Kronoberg County and had a significant trend in time during 2006 - 2020. This study is the first in southern Sweden with a more extended period of time and the first done in Kronoberg county. Previous studies examined Southern Sweden and Blekinge County, which borders the southeast (1, 2). Our findings show even higher incidence rates, most likely due to the incidence trend and that the other studies were performed a long time ago.

Western Kronoberg had significantly higher incidence rates, although previous studies showed high incidence rates southeast of Kronoberg (1, 2). Differences in population distribution, forested areas, time spent outdoors, vacation destinations during summer, and cultural differences might be investigated in future studies.

The incidence per age group was highest at 65-69 years, and females had a significantly higher risk. These findings are also seen in other studies in Sweden and Europe (1, 2).

Weather factors were studied as a secondary objective and showed a significant correlation, though weak for most parameters. Summer temperature had a little stronger correlation, followed by humidity. The findings suggest that incidence decreases with increased temperature and humidity. A previous study showed just the opposite (1, 2). There was no clear temperature trend through the years, and weather trends are difficult to assess in this study. Therefore, the correlation could be unreliable, and a more extended time would be necessary to investigate possible trends. In a previous study, there was a more precise correlation between these weather variables in which weather was directly coupled to the diagnosis (1, 2). In that study, climate data were correlated 14 days before the diagnosis of the EM cases. In our study, data was partially aggregated and could therefore not be correlated in the same way.

The main strength of this study is the length of time included in which a significant incidence trend was found. Other strengths are the sample size and the inclusion coverage of the patient population.

There had not been an epidemiological study in Kronoberg County before, and other epidemiological studies in southern Sweden had been done more than a decade ago. Regarding the weather data, it shows interesting findings which differ from previous studies. Although the strengths of these correlations are not strong, it proposes interesting hypotheses which will need to be studied further.

A limitation in this study was the combination of two different databases in which one only had aggregated data. Aggregation of data might result in counting the patient more than once if health care visits were near the end of the year and could potentially lead to over-diagnosing, though this amount is thought to be minimal as EM is diagnosed clinically and therefore does not need multiple health care visits. In addition, the diagnosis code from the ICD system uses A69.2 as the only code for all types of LB, which hinders differentiating. Because this study focused on primary health care, the most important manifestation is EM which is primarily diagnosed clinically in primary health care, and in this study, the amount of non-EM diagnoses was also checked. Furthermore, a small number of people with EM might not seek health care, and 10-20% of LB infections do not present with EM, which leads to underdiagnoses.

Further limitations are that database 2 included 2015 data but was incomplete concerning municipality. This database uses data from the last 5 years, and the collection of data was only partially done before the system shifted a year. Though this was only one year, it would not affect the primary objective and presumably would not affect the overall outcome for the secondary objectives.

Generalizing the results of the study to neighboring counties or even countries could be difficult. For example, our data is based on one county in southern Sweden with a specific climate, geography, population, and population density. To try to generalize even further could prove to be even more difficult because of the particular type of tick and borrelia species present.

# Conclusion

Kronoberg County had a significant positive incidence trend of LB, higher incidences in females, and an increasing incidence with age, highest at 65-69 years.

Weather trends and incidence of LB showed a significant correlation, though weak.

## Disclosures

Brendan Brouwer is employed by and receives salary from Kronoberg County. No grants or financing has been given to this study.

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