

Effects of climate change on tularaemia disease activity in Sweden

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Tularaemia is a vector-borne infectious disease. A large majority of cases transmitted to humans by blood-feeding arthropods occur during the summer season and is linked to increased temperatures. Therefore, the effect of climate change is likely to have an effect on tularaemia transmission patterns in highly endemic areas of Sweden. In this report, we use simulated climate change scenario data and empirical data of temperatures critical to tularaemia transmission to forecast tularaemia outbreak activity. The five high-endemic counties: Dalarna, Gävleborg, Norrbotten, Värmland and Örebro represent only 14.6% of the total population of Sweden, but have recorded 40.1–81.1% of the number of annual human tularaemia in Sweden from 1997 until 2008. We project here earlier starts and a later termination of future tularaemia outbreaks for the time period 2010–2100. For five localised outbreak areas; Gagnef (Dalarna), Ljusdal (Gävleborg), Harads (Norrbotten), Karlstad (Värmland) and Örebro municipality (Örebro), the climate scenario suggests an approximately 2°C increase in monthly average summer temperatures leading to increases in outbreak durations ranging from 3.5 weeks (Harads) to 6.6 weeks (Karlstad) between 2010 and 2100. In contrast, an analysis of precipitation scenarios indicates fairly stable projected levels of precipitation during the summer months. Thus, there should not be an increased abundance of late summer mosquitoes that are believed to be main vectors for transmission to humans in these areas. In conclusion, the results indicate that the future climate changes will lead to an increased burden of tularaemia in high-endemic areas of Sweden during the coming decades.

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Since the first description in Sweden in the 1930s (1), tularaemia has occurred predominantly in some northern and central areas of the country but, recently, the disease has extended southwards resulting in a considerable number of human cases in emerging areas. In 2003, for example, 700 individuals were diagnosed with tularaemia and half of them were affected in areas south of the river Dalälven cutting across central Sweden from the mountains in the west to its draining areas in the Botnian Sea in the east (2). The large majority of humans that contract tularaemia get infected in late summer and autumn (3, 4). Tularaemia is a zoonotic, often vector-borne disease occurring in a wide range of mammals and caused by the intracellular bacterium *Francisella tularensis* (5). In Europe, the etiological agent is *F. tularensis* subsp. *holarctica* (Type B) that appears to have a strong

association with water since many humans report to have contracted disease around lakes and rivers. The precise relationship between water and the persistence and spread of *F. tularensis* is, however, not well characterised, much due to the fact that the bacterium is difficult to culture from water samples (6, 7). Its presence in water and sediments has been proven through inoculation of samples into laboratory animals, from which culturable bacteria subsequently have been isolated.

Worldwide, a wide range of arthropods has been identified in the transmission of tularaemia to mammalian hosts, including ticks, tabanid flies (horseflies and deerflies), fleas and mosquitoes (8). Subspecies *holarctica* is believed to be heavily dependent on transmission by ticks, mites, tabanid flies and mosquitoes. In central Europe, blood-feeding mites and ticks are believed to be

most important vectors for rodent transmission of *F. tularensis* and to maintain epizootic tularaemia foci (9). In particular, *Dermacentor reticulatus* has been implicated to play a significant role in transmission of *F. tularensis* among small mammals in Europe but it does not feed on humans. Only *Ixodes ricinus* is capable of transmitting tularaemia to humans but overall, tick-borne human cases appear to be infrequent in central and northern Europe. As human tularaemia vectors, tabanid flies and mosquitoes appear to be essential in northern Europe including Sweden (4). In Northern Scandinavia, ticks are rare while tularaemia is sometimes common. According to clinical data, the predominant route of transmission to humans in Sweden is through mosquito bites. Some 10 mosquito species have been found to be naturally infected but the exact roles of different species for the spread of tularaemia in Sweden and other Scandinavian countries are not known.

In view of this background, it is apparent that much research is required before a complete understanding of the epidemiology and the risk factors for human tularaemia outbreaks can be obtained. Thorough field and experimental research on the ecology of *F. tularensis*, its transmission routes to humans, and biotic and abiotic prerequisites for tularaemia outbreaks will be invaluable to create models for disease prediction. Before robust field and experimental data exists, it is still possible to develop statistical projections for the purpose based on existing knowledge of correlations between climate parameters and human tularaemia cases. One such attempt using a large-scale climate approach has been performed. Using the North Atlantic Oscillation (NAO) index representing the dominant mode of winter climate variability in the whole North Atlantic region, it was concluded that a low NAO-index indicating cold winters, and low water flow in rivers during the following summer was associated with high numbers of human cases of tularaemia in Sweden two years later (10). Considering the scarcity of studies, additional work seems warranted. There is precedence from other parts of the world that the current wealth of climate data and models of future climate conditions can be used as a foundation to predict future transmission patterns. For example, a recent study generated models based on historical data on tularaemia and plague from the USA that were consistent in relation to known climate changes over the period. The models were then used to forecast likely shifts in patterns of transmission over the next 50 years (11).

The present study aims to utilise regional climate change scenario data for Sweden and regional data on past human tularaemia infections to create a model that forecast the magnitude of future human outbreaks.

Materials and methods

Data on human tularaemia

Tularaemia in humans is a disease that is mandatory to report. The figures used here were based on annual numbers of human tularaemia cases reported to County Medical Officers for Communicable Diseases in all regions of Sweden and are available at the website of the Swedish Institute for Infectious Disease Control (<http://www.smittskyddsinstitutet.se>). Demographic data for Sweden year 2008 was obtained from Statistics Sweden available at <http://www.ssd.scb.se>.

Climate change scenario data

A 140-year model run of regional climate simulations for Sweden performed at the Rossby Center, SMHI, Sweden, was used (12). Scenario data for the period 2000–2100 using the regional climate model RCA3 and the Intergovernmental Panel on Climate Change (IPCC) Special Report on Emissions Scenario B2 was downloaded at <http://www.smhi.se>. The resolution was given as 50 × 50 km squares. The data was arranged to regions by use of the WGS84 coordinates for the square centres. A square with its centre coordinate within a regional border was assigned to that region.

Empirical data for deciding temperatures suitable for tularaemia transmission to humans

Reported date of disease onset for 379 individuals 1981–2007 in Dalarna County was obtained from the local County Medical Office and used for prediction of time and temperature ranges suitable for tularaemia transmission in Sweden. Outbreaks with five or more cases were used to determine the date for first and last case of the epidemic, respectively. For these time points, the average temperatures (± 3 days around the day of onset of disease) were used to determine the temperature critical for the start and the termination of an epidemic.

Visualisation of trends in climate change scenario data

At the regional level, monthly average values were calculated for temperature and precipitation using the corresponding 50 × 50 km squares. The data was smoothed by a non-parametric method for estimating local regression surfaces, loess smoother, with the span-parameter set to 0.75 for each variable and county and visualised using in-house S-Plus scripts (13).

Outbreak duration calculated from scenario data

For each year, geographical region and local outbreak area, the first and last human tularaemia case was predicted using scenario data as follows: The temperature profile of an area was obtained by linear interpolation of

monthly smoothed scenario mean temperatures from May to October. Time points for first and last case of an epidemic was predicted with the intersections of the temperature profile and the empirically determined temperatures critical for start and end of a human tularaemia epidemic. The duration of an epidemic was obtained as the estimated interval.

Results

The five investigated counties reported 40.1–81.1% of the total number of annual human tularaemia in Sweden 1997–2008 (Fig. 1A). The counties Dalarna, Gävleborg, Norrbotten, Värmland and Örebro contain 14.61% of the total population of Sweden (1,352,558/9,256,347 inhabitants) with annual tularaemia incidences per 100,000 inhabitants of 0.70–78.05 (Dalarna), 0.70–66.04 (Gävleborg), 0.38–20.82 (Norrbotten), 0–24.86 (Värmland) and 0–54.78 (Örebro) during the same time period. The geographical distribution of tularaemia within counties was uneven with a large fraction of disease reports from repeated outbreaks in more restricted geographical areas; namely, Gagnef and adjacent villages (Dalarna), Ljusdal (Gävleborg), Harads (Norrbotten), Karlstad (Värmland) and Örebro municipality (Örebro) (Fig. 1B).

An analysis of summer temperatures was performed under the assumption that late summer epidemics of tularaemia in Sweden require temperatures critical for replication of the infectious agent and dispersal by blood-feeding arthropods. Temperature scenarios projected for the five tularaemia hotspot areas showed an increase in average monthly summer temperatures during the period 2010–2100 (Fig. 2). The analysis suggests that a critical

time point for the start of a summer epidemic will occur earlier in the future. Simultaneously, a temperature-dependent termination of a summer epidemic will be displaced to a later time point. This overall scenario is similarly projected for all five endemic areas. The scenario suggests an approximately 2°C increase in monthly average summer temperatures during the years 2010–2100. Then, an analysis of projected summer precipitation was performed under the assumption that vector abundance in late summer (mainly flood mosquitoes) will be dependent on local spring and summer rains. The precipitation analysis showed a fairly stable projected level of precipitation during the summer months (Fig. 3). A slight increase was projected for late October, an effect that will be much more pronounced during winter months according to the used climate scenario (data not shown). Projections of temperature and precipitation changes were also performed at the regional scale for Dalarna, Gävleborg, Norrbotten, Värmland and Örebro, and very similar trends were obtained at this larger geographical scale (data not shown).

A projected temperature-dependent increase in duration of human tularaemia epidemics for five tularaemia high-endemic areas is shown in Fig. 4. An analysis of the projected displacement in time of temperatures critical to the start and termination of human tularaemia outbreaks suggests that the effects may be pronounced. The projection indicates increases in outbreak durations as follows: 3.5 weeks (for Harads), 4.9 (Örebro), 5.5 (Ljusdal), 6.0 (Gagnef) and 6.6 (Karlstad) during the time period 2010–2100.

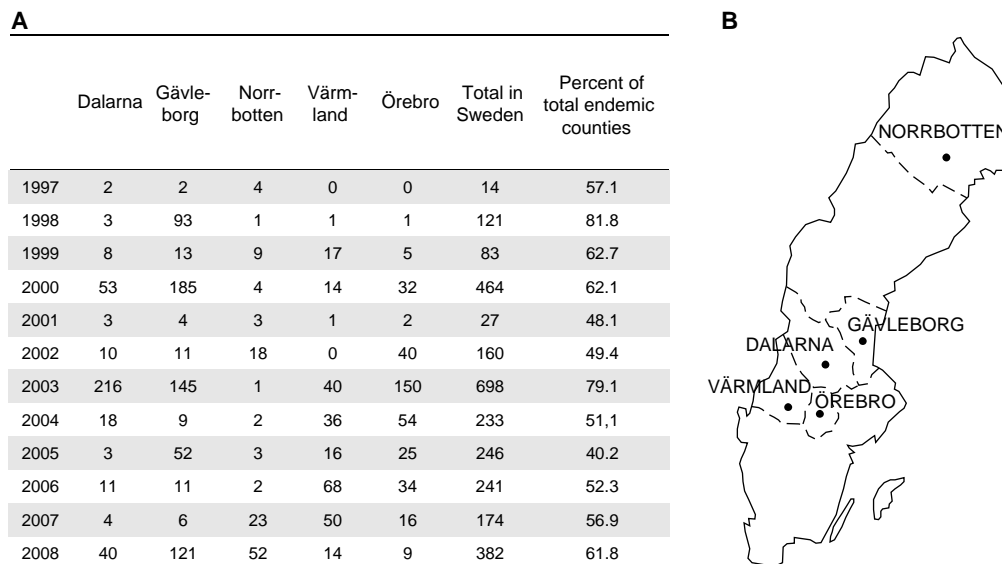


Fig. 1. Number of human tularaemia infections in Sweden 1997–2008. Panel A shows the number of individuals for each of five high-endemic counties. Panel B shows the geographic locations of the five counties and the five black dots indicate localised outbreak areas within the respective counties. The indicated areas are the following: Harads (Norrbotten), Ljusdal (Gävleborg), Gagnef (Dalarna), Karlstad (Värmland) and Örebro municipality (Örebro).

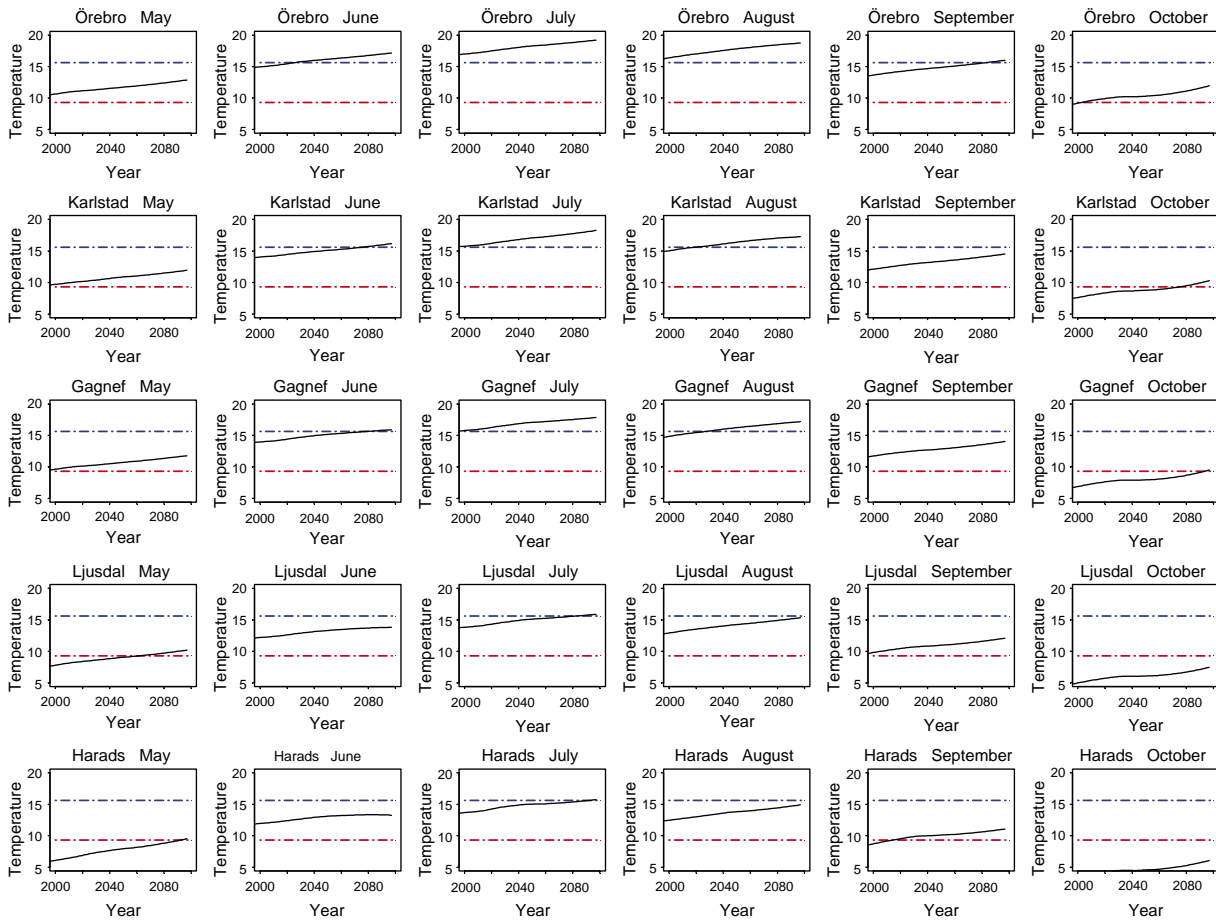


Fig. 2. Projected monthly average temperatures (°C) for the period 2000–2100. The projections (black lines) for the localised outbreak areas Örebro, Karlstad, Gagnef, Ljusdal and Harads are based on the IPCC climate scenario B2. The permissive thresholds for transmission, for the start of epidemic (blue) and termination of epidemic (red), are estimated from empirical data from Dalarna.

Discussion

Tularaemia is a disease which occurs only in the Northern hemisphere and in most countries presenting as isolated cases. However, in a few countries there exist regions where tularaemia has been endemic for many decades, most notably in Sweden, Finland and Russia (14). In Sweden, it is well known that certain regions have been affected since the 1930’s and with such high incidences that has become a public health problem. The most notable examples in this regard are the county of Ljusdal along the river Ljusnan in Gävleborg and a few counties and villages, e.g. Gagnef, along the river Västerdalälven in Dalarna. The existing data on tularaemia cases in Sweden, even when going back many decades, demonstrate that an absolute majority have occurred during a narrow span of the year, commencing in late July and terminating in mid-September, sometimes during an even more narrow time span (15). Thus, the seasonality unequivocally demonstrates that a number of climate factors must be intimately linked to the outbreaks. The most obvious factor is temperature, since the seasonal changes in Sweden are very marked and the periods of the

outbreaks are characterised by much higher temperatures than those during the remainder of the year. Although our knowledge is incomplete as to why there is such strong association with temperature, there are many temperature-affected parameters that are intimately linked to the transmission, such as precipitation, water temperatures and abundance of blood-feeding arthropods, e.g. mosquitoes, which may transfer disease to humans.

In view of the predicted highly significant temperature increases by all existing climate models, we therefore postulated that these increases will coincide with extended annual time spans for tularaemia outbreaks. To this end, we simulated future changes in temperature and precipitation for today’s endemic areas, Karlstad, Örebro, Gagnef, Ljusdal and Harads. Our analysis demonstrates that there will be much longer time spans with temperatures allowing tularaemia outbreaks in the coming decades (Fig. 4). The model predicted that the extension to some extent will be dependent on the geographical location. The most pronounced increases will be in the areas of Karlstad and Gagnef followed by Ljusdal (Fig. 1B and 4). Measured as a

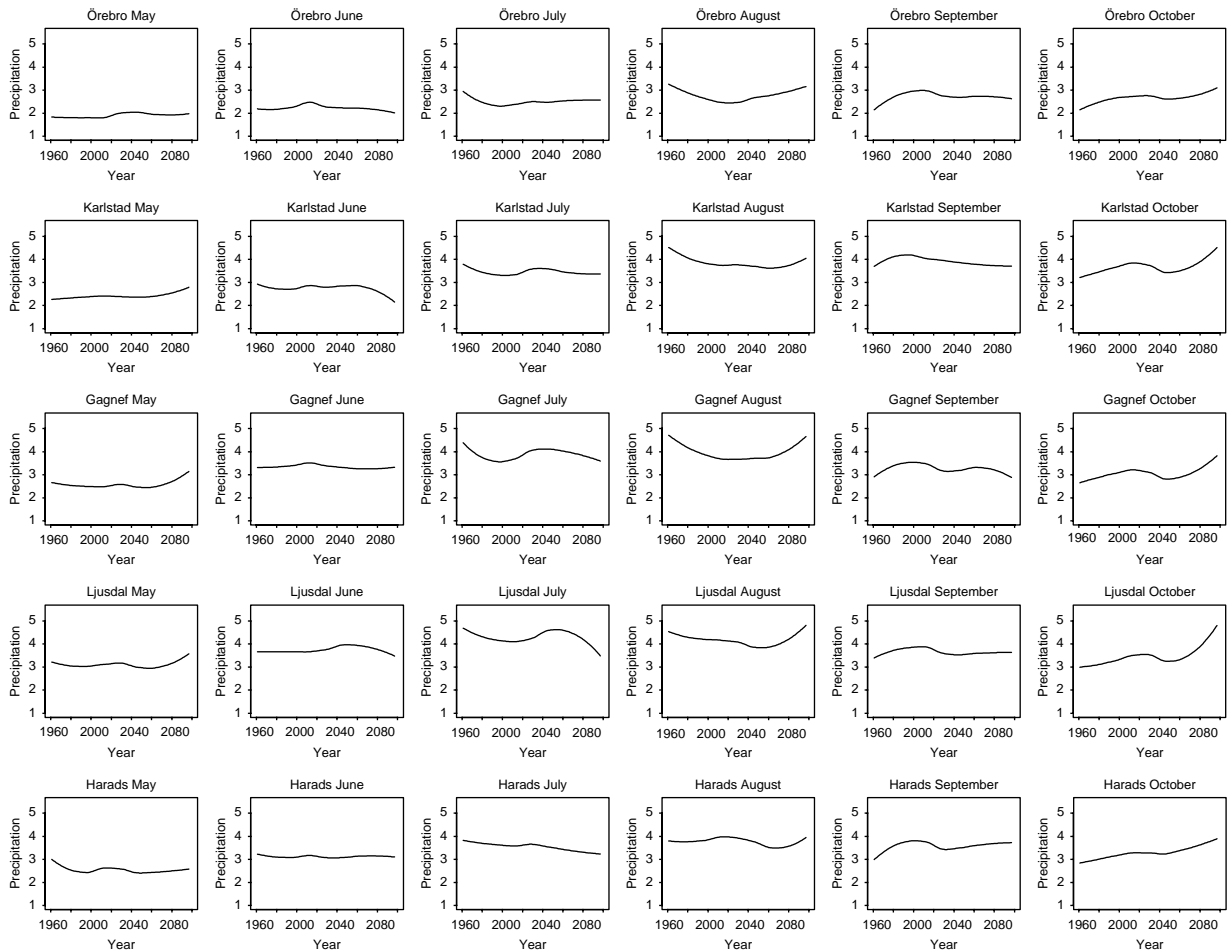


Fig. 3. Projected monthly average precipitation (mm/day) for the period 2000–2100. The projections (black lines) for the localised outbreak areas Örebro, Karlstad, Gagnef, Ljusdal and Harads are based on the IPCC climate scenario B2.

relative increase compared with current permissive transmission periods, the projected increase is largest for the area of Ljusdal. Our analyses suggest a two-fold increase of the period suitable for tularaemia transmission in Ljusdal with a following increase of the disease burden. In this study, we chose to use Rossby centre climate simulation data (12) which are based on the climate change scenario B2 prepared by the IPCC (16). The decision to use the B2 scenario meant that our projections are conservative as it assumes lower CO₂ concentrations, a smaller human population, lower energy consumption and less change in land use as compared with another frequently used scenario, named A2. The use of the less conservative scenario A2 for this study would have produced more pronounced climate change effects including greater and more rapid temperature increases.

In contrast to previous studies using the NAO-index which models very large geographical scale climate changes (10, 17), we selected to use a regional simulation model with a resolution of only 50 × 50 km. A smaller geographical scale approach to climate change seems

warranted in attempts to forecast tularaemia outbreaks since the disease is known to be highly localised. Both past (18) and more recent research have suggested that tularaemia is included among the diseases that display a pronounced ‘natural nidality’ (nidus means nest, home or habitat). Such nidi could be as large as a landscape zone, such as the flat land adjacent to a river, or as small as a single rodent burrow (‘a microfocus’). Permanent foci (‘elementary foci’) are present where there is an environmental reservoir of an infectious agent. The maintenance of several vector-borne infections, such as plague and tick-borne encephalitis appear to be best explained by natural nidality (19). In a recent field survey on Martha’s Vineyard, Massachusetts, ticks infected by *F. tularensis* were found in a natural microfocus with a diameter of only a few hundred metres where the agent of tularaemia stably persisted for a period of four years (20). Similarly, previous studies of human infections in Ljusdal (Gävleborg) and in villages along Västerdalälven (Dalarna) in Sweden have shown that the same genotype of *F. tularensis* overwinters between outbreaks within geographical scales of 50 km

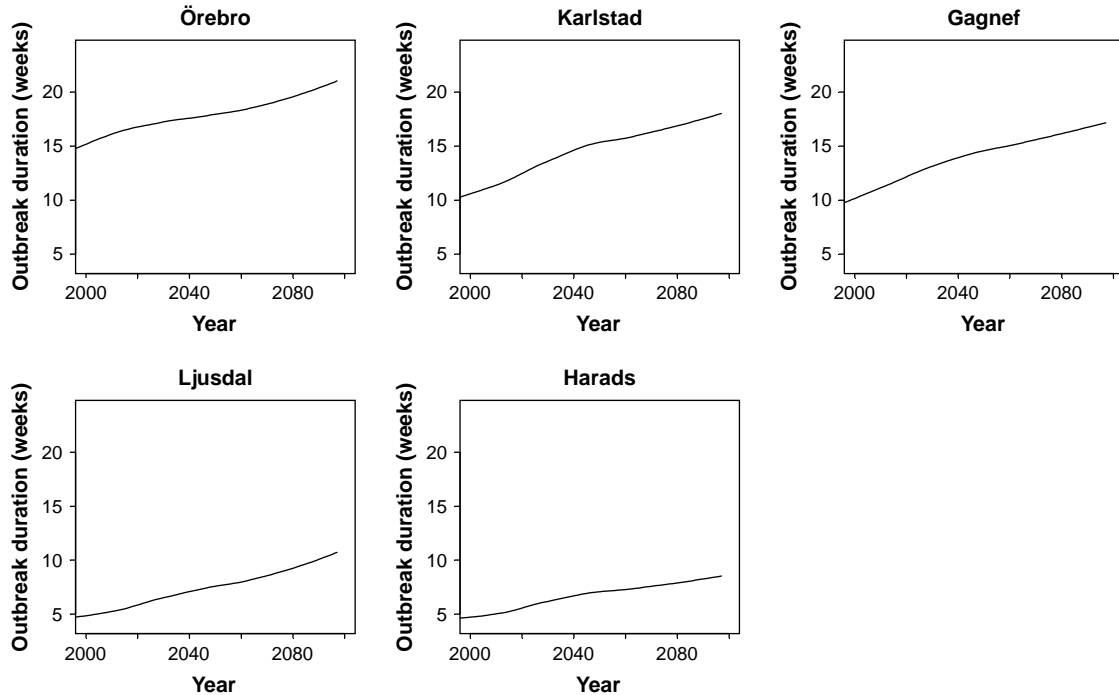


Fig. 4. Projected outbreak duration (in weeks) for the period 2000–2100. The projections for the localised outbreak areas Örebro, Karlstad, Gagnef, Ljusdal and Harads are based on the IPCC climate scenario B2.

and cause infections in humans for a time period of more than 17 years (21, 22). Collectively, these results strongly suggest that local climate parameters in tularaemia high-endemic areas should be better for forecasting outbreak activity than global scale climate parameters.

The analysis indicated only marginal changes in the precipitation, albeit changes will occur during the middle of the modelled period (Fig. 3). In an ongoing eco-epidemiological project, we have postulated that *F. tularensis* has an enzootic life cycle in Sweden. Its natural habitat is predicted to be wetlands and natural waters, where the organism constitutes a natural part of the microbial food web in interplay with protozoa and biofilms. Mosquitoes would become infected already during their larval stages in water and thus constitute the link between the aquatic and the terrestrial environments. In our hypothesis, rodents and lagomorphs are dead-end hosts for *F. tularensis* and rarely disseminate tularaemia to other animals and to humans and only by direct contact. A change of environmental factors, such as an increased abundance of nutrient-rich wetlands in close proximity to populated areas, is predicted to be an important factor for the incidence and magnitude of tularaemia outbreaks. Thus, if the hypothesis is true, then precipitation during the summer months will be an important factor affecting the occurrence of late summer mosquitoes and thereby the transmission of tularaemia. Our current findings indicated, however, that changes in precipitation in the tularaemia hotspot areas will be subtle and therefore

should not be decisive for the future outbreaks of tularaemia. Still, this prediction has a number of caveats. First, the role of precipitation for mosquito abundance may be complex, so projections based on overall precipitation may be too simplistic. Additional parameters probably influence the mosquito abundance considerably, e.g. forerunner wetness, soil type, and rates of evaporation and transpiration. Moreover, excessive rainfall can decimate some mosquito populations by flushing larval habitats or antecedent drought may reduce competitor species of mosquito larva leading to elevated rates of mosquito production (23). The proportion of mosquitoes that are infectious may also be variable and reflect the distance from their breeding habitats and the age structures of mosquito populations (24). Thus, a detailed and comprehensive modelling of mosquito populations in the future will require more sophisticated models. Finally, the exact relationship between the occurrence of specific mosquito species and transmission of tularaemia needs to be clarified.

Apart from climate-driven changes in ecology, like replication habitats for *F. tularensis* and blood-feeding disease vectors, it will also be important to determine how humans adapt to a warmer climate. These issues should be addressed in future research on forecasting the human burden of vector-borne infectious diseases including tularaemia. It is likely that human responses to climate change, e.g. changes in residential patterns in proximity to active disease transmission areas, in the period of time spent

outdoors versus indoors and in the extent of restoration of wetlands and the future use of irrigation, affect the burden of vector-borne diseases as much as ecological changes.

Considering the increasing temperatures during the coming decades, inevitable changes in the flora and fauna will result and most likely this will affect the geographical distribution of tularaemia. Currently, we are lacking the detailed information required to identify the denominators of hotspot regions. Since these regions encounter very high incidences of tularaemia, it may be warranted to implement local surveillance systems and preventive health measures such as vaccination of the populations. Therefore, the development of models to precisely identify regions at risk to become tularaemia hotspots will be of high priority. The current model is a first step in the development of the required, more sophisticated future models. Even the current simplistic model unambiguously indicates that the future climate changes will lead to an increased burden of tularaemia in Sweden during the coming decades and in view of this, additional research will be required to more specifically understand the prerequisites of tularaemia outbreaks, enabling the development of sophisticated models that can forecast risks of local outbreaks so appropriate preventive actions can be undertaken.

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