Climate modelling can be used to forecast what is likely to happen in the future, to diseases for which climate drivers have been identified. Within such modelling, a number of different analytical or semi-analytical approaches can be taken. Also, multiple different environmental emissions scenarios, and sets of climate data observations, weather forecasts and climate projections can be utilised, all at various data resolutions and for numerous time windows. To make the outputs of the ENHanCE project most useful for agencies planning for changing disease distributions and incidences, the output scenarios need to be tailored to meet their needs. Within this position paper, different types of quantitative and qualitative risk assessment models were illustrated and reviewed so that attendees to our agency meeting would be able to identify the approaches most useful to them for future planning.

Whilst reading the position paper, the agencies were asked to think about the questions below.

- Have you any on-going or past interactions with the disease modelling community? What is your source of disease model information and expertise?
- Would the use of qualitative (disease X may be affected by climate change); semi-quantitative (disease X may spread northwards to UK by 2050); or quantitative (disease X will have the following distribution by 2050) approaches be most useful to your agency?
- If qualitative approaches would be best, would this be using expert opinion or objective measures within a formal risk assessment?
- If quantitative approaches would be best, would this be using statistical extrapolation, which assumes the relationship between disease occurrence and climate never changes; or biological, process-based models, in which the relationship between climate and disease can change, but which are invariably gross oversimplifications of the reality they are modelling?
- Are less complex models (which are more easily understood) or more complex models (which are less easily understood) most useful to you?
- Do you need estimations of future disease distribution, future disease incidence, future population at risk, future control effort required, within your work?

Following engagement with stakeholders, we feel within the ENHanCE project that when undertaking modelling of the impacts of climate change upon diseases we should:

- Initially use qualitative approaches to studying the effects of climate change upon multiple diseases, followed by more rigorous semi-quantitative and potentially quantitative approaches to study a limited number of diseases.
- Use a combination of initially objective measures followed by expert opinion within formal risk assessment.

- Use biological models to study the relationship between climate and disease as opposed to statistical extrapolation because, if they can be suitably parameterised and validated, they often provide a better understanding of the underlying processes driving changes in disease, and are therefore potentially more useful from the perspective of planning interventions and controls.

- Remember that as long as model assumptions are clearly communicated and models are clearly validated, it doesn’t matter how complex they become, though obviously Occam's razor should always be considered.

- Be aware that it is useful if estimations of disease parameters can be undertaken and presented within disease models, such as assessments of future disease distribution, future disease incidence, future population at risk and future control effort required.

**ENHanCE Position Paper #3**

1. **Quantitative risk assessment**

   a. **Statistical models**

Forecasting future trends in disease can be undertaken using simple statistical approaches, for instance time-series techniques such as quadratic equations or spectral density analysis (SDA) to deal with strong seasonality. These statistical approaches can be criticised because they assume that the relationship between climate and disease will remain unchanged into the future. Hay and others (2001) used rainfall measurements to predict future case numbers of people with *Plasmodium falciparum* malaria, which could be undertaken due to a clear relationship between rainfall and malaria cases at a particular site, following a three month time-lag (figure 1).

![Figure 1. Malaria cases and rainfall by month. (a) The bars are malaria cases and the black line rainfall totals. (b) Observed (blue bars) and predicted (black line) malaria cases based on a simple quadratic relationship between present cases (x) and rainfall (y) 3 months previously.](image-url)
Lake et al. (2009) also used a simple approach, fitting higher-order polynomials of time to de-trend disease-incidence data and examine the effects of temperature upon reported cases of food-borne illnesses, whilst taking into account further effects of travel and public holidays with their associated changes in eating habits.

In examining a more complicated site with stable malaria epidemiology, Hay et al. (2001) also used SDA to investigate the periodicity in *P. falciparum* malaria admissions and contemporaneous temperature and rainfall data, thus potentially separating the seasonal versus longer-term cycles driving admissions (figure 2).

Figure 2. (a) The monthly incidence (cases per 100,000) are shown in black. The dashed line shows a moving average of 61 months and the bold red line the stationary malaria incidence series (original value – moving average) on which SDA was performed. (b) The spectral density plot for malaria incidence. Annual and lesser frequencies account for 69.8% of the total variance in the time-series and super-annual frequencies, with a mean periodicity of approximately three years, account for 30.2%.

Multivariate regression models including for example, the effects of historical distributions of pathogens, land cover, agricultural factors and climate variables can be used to identify climatic drivers of pathogens. Future predictions of these can then be applied to contemporary disease data using future emissions scenarios and climate forecasts to give an illustration of how disease is likely to change. Rogers and Randolph (2000) used this two-step statistical approach to mapping vector-borne malaria: exploiting knowledge of present day malaria distribution to establish the climatic constraints currently affecting the pathogen, and then applying the results to future climate scenarios to predict future distribution (Figure 3). However, their modelling approach has been criticised because the data used was contemporary rather than historical malaria distribution data, and this may bias the model towards establishing multivariate relationships which are relatively inert to future climate change, as they were sampled from the centre of an ancestral malaria distribution.
Figure 3. The difference between the predicted distributions of malaria caused by *P. falciparum* currently, and in the future (modelled using the high scenario from the HadCM2 experiment). The gray hatching is the current global malaria map, also shown are areas where malaria is predicted to disappear (i.e., probability of occurrence decreases from >0.5 to <0.5) (in red) or invade (i.e., probability of occurrence increases from <0.5 to >0.5) (in green) by the 2050s in relation to the present.

Purse and others (2006) used a different technique within the modelling process, after ascertaining current and historical distributions of Bluetongue Virus (BTV) and its *Culicoides* vectors using an extensive literature review. They defined the relationship between present-day transmission of BTV and a variety of climate variables using discriminant analysis techniques, producing an estimation of the present-day climatic envelope of the virus (for instance Figure 4).

Figure 4. Bivariate scatter plot of annual phase of temperature versus annual minimum precipitation in grid-squares with present-day BTV transmission in Europe. Colours indicate whether transmission was due to indigenous European vectors or *C. imicola*; 95% ellipses are drawn around the scatter for each of these transmission categories.

This present day climatic envelope was then mapped for future climate (Figure 5). This technique, however, assumes that the climate envelope for the disease remains constant.
The identification of climate envelopes technique was further adapted by Purse and others (2007), when having used discriminant analysis, they thereafter quantified the overlap of BTV, its main southern European vector *C. imicola* and other Palearctic *Culicoides* vector species distributions in multivariate space. Multivariate environmental distances (Mahalanobis distances) between known areas of BTV and areas known to have the presence of vectors were defined by the predictor variables describing the climate envelopes (Figure 6).

Such measures of separation may indicate the relative importance of each vector species in disease transmission, because the distribution of any pathogen transmitted by several vectors is composed of subsets of the distribution of each of its vectors.

Ecological niche modelling can be used within the first stage of the statistical, climate modelling process, instead of multivariate techniques for example. It can be employed to develop spatial data by predicting the geographic range of a pathogen or vector, when some presence data (or presence and absence data) is available, taking into account other environmental determinants such as land use change, soil type, host population, temperature, precipitation, elevation and species’ locality data. Further climate modelling using contemporary disease data, future emissions scenarios and climate forecasts can then be undertaken. Such a technique was used to identify geographical areas of disease transmission risk, by forecasting the ecological niche of the vectors of Lyme disease in British Columbia (Figure 7) (Mak et al., 2010). Validation for such models can be undertaken by
dividing the original spatial presence data, into that to use within the model and some with which to test the model.

b. Biological, process-based models

Integrated, systems based mathematical models can also be used to estimate future trends in diseases in relation to global environmental change and human health. Such modelling builds on systems-orientated analyses, concentrating on the interactions and feedback mechanisms between different subsystems of the cause-effect chain, rather than focussing on each sub-system in isolation. However, feedback processes can amplify or dampen important aspects of the system, for instance acquired immunity would reduce the effects of an increased risk of malaria in endemic regions. Gaps in knowledge also devalue such models, because without good estimates of all parameters, weaknesses in models can be identified and revealed, and accumulation of uncertainties can be analysed and interpreted, uncertainties always being greater in more complex models. Model validation can also be difficult where little data has been collected, for instance in resource-limited countries.

Many of the biological models studying changes in disease distribution are based on the equation describing the transmission potential of a pathogen, the basic reproduction ratio \( R_0 \); the average number of secondary infections produced when a single infected individual is introduced into a susceptible population, when no control measures are taken. The main components of this equation for vector-borne disease are the human-biting rate of the vector, human susceptibility, the susceptibility of the vector to the pathogen, the daily survival probability of the vector and the incubation period of the pathogen inside the vector. A re-arranged form of the \( R_0 \) equation is used to define the transmission potential of the pathogen, which can then be utilised to estimate the effect on pathogen transmission potential of a change in climate variables, which are defined from future climate model simulations. An improved version of this methodology was used to describe malaria by Martens and others (1999) (for instance Figure 8).
Their model included continental-scale estimates of the distribution of 18 main malaria vectors, species-specific relationships between temperature and transmission dynamics, and a more realistic approach regarding malaria endemicity to explore changes in populations at various degrees of malaria risk (for example the risk of epidemics vs. year-round transmission). The model was validated at country and regional level, and also using a time series of malaria cases in Colombia. Several of the variables included within the model could not be quantified and were set to one in the equations, however, which could over-estimate transmission potential in areas where $R_0$ is less than one.

In investigating whether a former malaria region could once more support transmission of the pathogens, Schröder and Schmidt (2008) modelled the potential of temperature-induced malaria transmission also according to the $R_0$ equation. By correlating the geographical distribution of malaria vectors and their incidences with habitat characteristics and their life stages, they examined potential effects on the seasonal transmission window of malaria due to ongoing and predicted climatic changes. Initially, they mapped vector presences using Geographical Information Systems (GIS) and supplementary data from archives, and then computed the lengths of the seasonal transmission window using temperature values (lower development thresholds, the optimum temperatures, and the upper limits above which no further progress is possible). Air temperature measures were integrated into GIS software and transformed into surface data using geo-statistics, and the resulting temperature maps were updated according climate change scenarios to be used as input for the calculation of $R_0$.

2. **Qualitative risk assessment**

Qualitative risk assessment methodologies can also be employed to try and identify what will happen to diseases with climate change. For instance, expert panel consultation can be utilised to identify the climatic drivers of pathogens, and to distinguish the ways in which surveillance activities can be focussed for best effect (Straetemans, 2008).

Expert panel prioritization was also used by Dufour et al. (2008), who identified the diseases whose incidence or geographical distribution could be affected by climate change, and then evaluated the risk of this happening in each. Identification of diseases was based upon: risks associated with arthropod vectors, molluscs, wild vertebrates, and other risks (for instance climate related changes in human behaviour). First, the mode of transmission of diseases was examined in order to exclude them from the above-mentioned four categories of risk or classify them into one of the categories. After this, more detailed analysis was undertaken using bibliographic data, which included
information on mode of transmission, susceptible species and epidemiological status in France and the rest of the world. The group of experts then identified and estimated qualitatively the risks and possible evolution factors associated with global warming based upon the bibliography, including impacts such as: the health impact for the animal, the impact of zoonoses on public health, and the collective economic impact for animals. This methodology also allowed the comparison of specific measures used against individual diseases, for instance particular surveillance measures that cannot be recommended for too large a number of diseases because they are too cumbersome and costly. It focuses discussion on the scientific data rather than the method used, however this limits the subjectivity of the qualitative evaluation, which is further influenced by the personality of the individual experts. Pooling of bibliographic information and following up with a group discussion does reduce such subjectivity, without eliminating it altogether. The technique suffers from a further limitation in that it is difficult for the expert group to decide on one of the five possible risk categories for whether a disease is likely to be affected by global warming (zero, negligible, low, moderate, high), although the qualitative assessment for each disease was not ‘absolute’ but ‘relative’.

Semenza and Menne (2009) also used expert opinion within workshops along with an extensive literature review, to evaluate infections acquired through various routes in view of a changing climate in Europe. They undertook searches in the bibliographic database PubMed, using different search strategies which combined the concepts of climate change, climate variability and specific infectious diseases which fitted into European Centre for Disease Prevention and Control programmes: food and water-borne diseases, vector-borne diseases, invasive bacterial infections, influenza, tuberculosis, and vaccine preventable diseases. The expert opinion workshops involved scientists and public health practitioners, and included findings from past and ongoing European-Community funded research projects and disease networks. Their aim was to review the diseases likely to be affected by climate change and propose the building of an integrated network to connect epidemic intelligence and infectious disease surveillance with meteorological, entomological, water quality, remote sensing and other data.

A risk-based assessment framework may represent a semi-quantitative approach to screen for any unexpected organism that might have a higher likelihood of emerging as a result of climate change and to identify endemic pathogens and vectors that might be affected. Gale and others (2010, 2009, 2008) used such an approach, employing expert opinion (modified Delphi technique) on a top-down list of diseases; integrating within their framework, the identification of those factors through which climate change could affect livestock diseases. These included the molecular biology of the pathogen, the vectors, farming practice and land use, zoological and environmental factors together with the establishment of new microhabitats. The framework contained modules comprising: routes to and within GB (imported livestock, germplasm, animal feeds, meat and meat products, pets, vectors, wild animals and persons), molecular biology of the pathogen itself, host reservoirs, vector route, degree of animal contact and movement, and environmental routes (Figure 9). Each virus-specific questionnaire was divided into five parts which asked for background information on the expert, and through the different parts, then explored the modules of the framework, relating to the virus both currently, and predicted in the 2080s after climate change. Three consequences of climate change were considered, namely risk of incursion given exposure, risk of spread within the EU given incursion, and risk of becoming endemic in the EU given incursion. Each expert completed the same questionnaire twice; the first prior to the workshop and the second afterwards, without reference to
their answers from the first questionnaire. Only data from the second questionnaire were used in the risk assessment. The expertise of the experts was weighted according to their respective background, giving a weighted distribution of the overall risk of knowledge for each specific disease. This was then used, within sensitivity analysis, to investigate the impact of the weighting scheme on the results.

Largely descriptive investigation can also help identify contemporary changes in disease incidence. This can include a combination of literature review, questionnaires sent to public and private laboratories and clinics and some parasitological testing of samples, and comparison of historical and current available data on the pathogen and relevant vectors (Oranto et al., 2009).

**References**


Figure 9. Risk pathway for the risk of vector-borne livestock disease incursion, spread and becoming endemic in the EU.
<table>
<thead>
<tr>
<th>Questions</th>
<th>Answers</th>
<th>Do you need estimations of future disease distribution, future disease incidence, future population at risk, future control effort required, within your work?</th>
</tr>
</thead>
</table>
| Have you any on-going or past interactions with the disease modelling community? What is you source of disease model information and expertise? | No 35%  
All approaches 36%  
No preference 28%  
Either, depending on scenario 54%  
Either 45%  
All 70% | No 35%  
All approaches 36%  
No preference 28%  
Either, depending on scenario 54%  
Either 45%  
All 70% |
| Would the use of qualitative; semi-quantitative; or quantitative approaches be most useful to your agency? | Yes – Internal only 10%  
Don’t know 18%  
Formal risk assessment 36%  
Biological 36%  
Less complex 20%  
Future disease distribution and population at risk 15% | Yes – Internal only 10%  
Don’t know 18%  
Formal risk assessment 36%  
Biological 36%  
Less complex 20%  
Future disease distribution and population at risk 15% |
| If qualitative approaches would be best, would this be using expert opinion or objective measures within a formal risk assessment? | Yes – Internal and external 45%  
Semi-quantitative 18%  
Both 18%  
More complex 35%  
Future Disease 15% | Yes – Internal and external 45%  
Semi-quantitative 18%  
Both 18%  
More complex 35%  
Future Disease 15% |
| If quantitative approaches would be best, would this be using statistical extrapolation; or biological, process-based models? | Qualitative 18%  
Expert Opinion 18%  
Statistical 10% | Qualitative 18%  
Expert Opinion 18%  
Statistical 10% |
| Are less complex models (which are more easily understood) or more complex models (which are less easily understood) most useful to you? | Qualitative and semi-quantitative 10% | Qualitative and semi-quantitative 10% |
Have you any on-going or past interactions with the disease modelling community? What is your source of disease model information and expertise?

- No: 35%
- Yes – Internal only: 10%
- Yes – Internal and external: 45%
- Yes – External only: 10%

Would the use of qualitative; semi-quantitative; or quantitative approaches be most useful to your agency?

- All approaches: 36%
- Semi-quantitative: 18%
- Qualitative: 18%
- Qualitative and semi-quantitative: 10%
- Don't know: 18%
If qualitative approaches would be best, would this be using expert opinion or objective measures within a formal risk assessment?

- Formal risk assessment: 36%
- No preference: 28%
- Both: 18%
- Expert Opinion: 18%

If quantitative approaches would be best, would this be using statistical extrapolation; or biological, process-based models?

- Either, depending on scenario: 54%
- Biological: 36%
- Statistical: 10%
Are less complex models (which are more easily understood) or more complex models (which are less easily understood) most useful to you?

- More complex: 35%
- Less complex: 20%
- Either: 45%

Do you need estimations of future disease distribution, future disease incidence, future population at risk, future control effort required, within your work?

- Future Disease: 15%
- Future disease distribution and population at risk: 15%
- All: 70%