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Risk Mapping and Mathematical Modelling:Assessment Tools for the Impact of Climate Change on Infectious Diseases

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Content

1. Abstract

There is now near undisputed scientific consensus that the rise in atmospheric concentration of greenhouse gases causes warming at the Earth's surface. Global warming will also have impacts on human health. We focus here on vector-borne infectious diseases because climatic variables are major determinants of the geographical distribution of the cold-blooded insect and tick species that can transmit viruses, bacteria and other microparasites to humans. The distribution of vectors is thus one important component of infection risk. We review the methods that have been developed in the past few years to determine and to model the distribution of species under actual and hypothetical environmental conditions and show how mathematical models have been used in this context.

Remote sensing technology offers progressively better environmental and climatic data which can be employed in conjunction with Geographic Information Systems (GIS) and spatial statistical techniques to determine the distribution of vector species under different scenarios. Mathematical models can help to elucidate many aspects of infectious disease dynamics. The available studies lead to the expectation that climate change affects the transmission dynamics of vector-borne infectious diseases. However, the details and the degree of these effects are very uncertain. In order to predict more reliably the effects of extreme climate variability or climate change on infectious disease dynamics more data on the interaction between ecological, epidemiological, economical and social processes are needed.

2. Risk mapping

2.2. Climate Change and Health

There is now near undisputed scientific consensus that the rise in atmospheric concentration of greenhouse gases causes warming at the Earth's surface. These changes will become progressively more apparent through increases in extremes of temperature and precipitation, loss of seasonal and permanent snow and ice cover and sea level rise. Weather and climate directly affect human physiology and thus human well-being, especially in extreme weather situations which fall outside of the range to which individuals in a region are adapted to. The effects of heat waves are the most obvious demonstration of this fact. Health outcomes of extreme climate variability or even climate change do, however, not exclusively depend on the direct exposure to weather- or climate-related hazards, but also on indirect effects through ecological, demographic and social factors.

Infectious diseases involve humans in a "mini-ecosystem" consisting of a few components: host, pathogen, environmental factors and in some systems vectors and non-human reservoir species as well. Vector-borne diseases offer a very good opportunity to study the potential impact of climate change on infectious diseases; this is because methods that have been developed to predict the distribution of species under new climatic conditions can be applied in a relative straightforward manner to insect and tick vectors of important infectious diseases.

2.3. Climate Change and Vector-Borne Infectious Diseases

The dynamics of most infectious diseases, if transmitted through blood eating vectors or not, are affected by climatic factors. In temperate latitudes, influenza mainly occurs in winters and outbreaks of cholera in India are apparently affected by the El Niño Southern Oscillation (ENSO). However, the mechanisms behind the climate-sensitivity of such diseases not relying on vectors for transmission are still hypothetical and are not yet supported by robust empirical evidence. For example, the strong seasonality of influenza in temperate latitudes could be caused by the effects of environmental factors on the virus during transmission (Lowen *et al.*, 2008) or by seasonal changes in the susceptibility of the host (Dowell and Ho, 2004). It is, therefore, not feasible at the moment to try to predict with any confidence the consequences of climate change on, for example, influenza.

The situation is very different for vector-borne diseases. Survival and reproduction rates of the cold-blooded insect and tick vectors of human pathogens are sensitive to variation in temperature and moisture. Furthermore, the development of the infectious agent within the vectors (extrinsic incubation) is also temperature-dependent. It is not only these direct links between biological and climatic parameters which make vector-borne diseases of special interest in the context of environmental and climate change. Until the early 20th century, vector-borne diseases were responsible for more deaths in humans than all other causes combined. These diseases prevented the settlement and development of large areas in the tropics, but also held back European countries like Italy. In the course of the 20th century, malaria was controlled in many areas of the world, but the ambitious goal of eradication failed and malaria still causes one million deaths and 300 million acute

illnesses per year worldwide. In many countries, especially in Sub-Saharan Africa, malaria was never under control and the situation is worsening. The continued presence, emergence and re-emergence of vector-borne diseases, the geographic spread of vector species such as the tiger mosquito *Aedes albopictus* and concerns about climate change have brought vector-borne diseases back into the limelight.

The dependence of biological parameters of vectors and pathogens on single climatic factors like temperature and moisture is often relatively straightforward, but to predict the outcome of complex climate change on the web of interactions between vector, pathogen and host – a web that is embedded into a social and economic system that co-determines health risks and outcomes – is certainly far from easy. Using new technologies of data acquisition and analysis, certain aspects can, however, be investigated. For most vector-borne diseases (some like plague and tularemia also do have non-vector-borne transmission pathways) there can be no transmission without vectors. The distribution of vectors thus is one measure of risk. In the context of climate change and biodiversity research new methods to determine and to model the distribution of species under actual and hypothetical conditions have been developed in the past few years and these methods are increasingly used to study the epidemiology of vector-borne diseases.

2.4. Remote Sensing and GIS

Remote sensing with satellites has transformed the study of the environment. Remote sensing satellites provide continuous and synoptic measurements of the terrestrial and atmospheric environment. This ability to monitor the Earth's surface

at large spatial scales is particularly important in a situation where human-caused environmental change spans the entire globe. Earth-observing satellites like Ikonos, Landsat or SPOT provide images with resolutions between 1 and 120 m on 4 or 7 multispectral channels and 1 panchromatic channel. These satellites have a low repeat frequency (i.e. the frequency with which the same area is visited) with a period of 11-26 days. Orbiting oceanographic or atmospheric satellites have lower spatial resolution, as low as 1.1 km, but they produce 2 images per day of the entire Earth's surface. The NOAA-AVHRR (Advanced Very High Resolution Radiometer) series of satellites has produced more than 20 years of continuous observations. A new generation includes the Terra and Aqua satellites. Geostationary weather satellites, such as GOES and the Meteosat series, give spatial resolutions of 1-5 km and two images of the entire Earth half-disk each hour. There are, however, many potential complications, limitations and causes of error associated with satellite data that add noise to the data – sensor calibration, ground and atmospheric conditions or orbital and sensor degradation – and that require careful quality control and specific statistical techniques in the processing of data.

Well-documented and quality-controlled data provided by satellites can be used in several different ways that are pertinent for ecology and epidemiology. Remote sensing data are routinely employed to estimate the variety, type and extent of land cover in a region. Such land cover data describe the physiographical characteristics of the surface environment, which can range from bare rocks to lush tropical forests. Land cover classifications are usually derived by applying statistical clustering methods to multispectral remote sensing data. Land cover data and bioclimatic variables can be combined to predict the presence and absence of species (e.g. Cumming 2000). Ecosystem function over wide areas can also be estimated through

remote sensing data; net primary productivity (NPP, the production of organic compounds from carbon dioxide) is represented by the normalized difference vegetation index (NDVI). The properties of NDVI time-series can be summarized in a variety of ecologically relevant indices: the Integrated NDVI (INDVI, a measure of overall productivity), measures of variability and a range of phenological measures (for example dates of the beginning and the end of the growing season). Measurements of NDVI have proved to be helpful in studies that attempt to differentiate between natural variation in ecosystem function and variation arising from human activities (Pettorelli *et al.*, 2005). Remote sensing data have also provided convincing evidence that climate has changed rapidly: time series AVHRR data demonstrate that vegetation structure, primary productivity and growing season length have changed in the past 25 years (Zhou *et al.* 2001). The use of NDVI is not restricted to studies of plants. Various studies have coupled vegetation dynamics with biodiversity, animal species distributions, movement patterns of animals (e.g. migratory birds) and the performance of animal populations (reproduction or survival).

The vast amount of complex data that can be gained by remote (and ground-based) sensing requires special methods of data analysis and evaluation. Geographic Information Systems (GIS) are systems of hardware, software and procedures to make possible the management, manipulation, analysis, modeling, representation and display of georeferenced data. Originally, GIS were developed to solve complex problems regarding planning and management of resources. GIS have the capacity to store, retrieve, analyze, model and map large areas with huge volumes of spatial data. In a GIS, data are organized into layers or coverages of related data that can be analyzed and visualized thematically. Three general types of spatial analysis tasks

can be performed in GIS: visualization, exploratory data analysis, and model building. With its extensive data management and display capabilities, GIS offers much more than simple mapping as a means for visualization. Map overlay operations allow, for example, computing new values for locations based on multiple attributes or data "layers" and to identify and display locations that meet specific criteria. Exploratory spatial analysis allows the investigator to sift meaningfully through spatial data, identify "unusual" spatial patterns, and formulate hypotheses to guide future research. The quantity and diversity of spatial data in GIS can be overwhelming: exploratory methods help to make sense of data and address "what if" questions. Modeling, the final class of spatial analysis methods, includes procedures for testing hypotheses about the causes of disease and the nature and processes of disease transmission. Modeling involves the integration of GIS with standard statistical and epidemiologic methods. GIS can assist in generating data for input to epidemiologic models, displaying the results of statistical analysis, and modeling processes that occur over space.

GIS has been used in epidemiological research in all these three ways. The most basic application involves mapping the incidence/prevalence of a disease over some geographic area and to perform descriptive spatial statistics (Kleinschmidt *et al.*, 2000; Pfeiffer *et al.*, 2008). Procedures for weighing and overlaying maps have been used to model the risk of Lyme disease (Glass *et al.*, 1995). The goal of other studies is to investigate if any relationship exists between disease incidence/prevalence and a range of environmental or demographic data; such studies are focused on past trends and present situation. A number of studies are future-oriented and focus on predicting prospective risk (Schröder *et al.*, 2007) and the production of risk maps is a central goal of such studies.

2.4. Risk Maps

For both infectious and non-infectious diseases, spatial and spatio-temporal proximity to some "source" are relevant for the understanding of epidemiological patterns. The transmission of viruses or bacteria between a susceptible and an infectious person is generally far more likely if they are close to each other. This is also true for most vector-borne diseases as the vectors usually do not move over large distances. In the case of non-communicable diseases, the proximity to environmental risk factors may be important.

The construction of reliable risk maps is a fundamental objective of epidemiology. Mapping of diseases to stimulate the formulation of causal hypotheses has a long history. Dot maps were already used in the 18th century to show the spatial distribution of cases; later, diffusion maps were employed to illustrate the spread of epidemics. Increasing knowledge on the exposure status of individuals allowed more quantitative estimates of risk and its spatial variation. The increased availability of epidemiological and environmental data and the advent of Geographic Information Systems have turned risk maps into an important tool for early warning, for planning efficient control measures, for subsequent evaluation and for optimizing the allocation of limited resources.

The combination of spatially referenced environmental parameters and geo-referenced records of vector occurrence can be turned into risk maps by using several different techniques. Spline and kriging are two methods for interpolating and predicting spatial data and these techniques have been used in spatial epidemiology

(e.g. Kleinschmidt *et al.*, 2000). The past few years have also witnessed the increased use of ecological niche modeling (ENM) in the context of particularly biodiversity and climate change research, but also in epidemiology (Guisan and Thuiller, 2005; Peterson, 2006; Moffett *et al.*, 2007; Benedict *et al.*, 2007). The ecological niche of a species is the set of conditions under which the species can maintain populations without immigration of individuals from other areas; the fundamental niche describes under which conditions a species can potentially occur, whereas the realized niche describes the actual habitat types in which the species occurs. Based on geo-referenced presence data, bioclimatic parameters and other ecologically relevant data it is possible to construct an "environmental envelope" for a species. Several computational techniques are used to produce ENMs; the two most reliable and widely employed are genetic algorithms (GARP, Genetic Algorithm for Rule-Set Prediction) and maximum entropy modeling (Maxent). GARP predicts simple absence or presence of a species, whereas Maxent calculates relative probabilities of occurrence and thus allows a more nuanced risk assessment.

Vector-borne diseases offer excellent case studies for the construction of risk maps. Without competent vectors there can be no disease transmission. Mapping the fundamental niche of vector species thus identifies the regions, where the conditions for the existence of the species in question currently prevail or will prevail in the future if a certain scenario of climate change will be realized. A number of studies have shown promising results. Moffett *et al.* (2007) have produced a global risk map for malaria using ENM. The methods to produce risk maps are computationally intensive. For example, Moffett *et al.* (2007) include the following 21 environmental parameters into their maximum entropy model: annual mean temperature, mean diurnal range, isothermality (mean diurnal range/temperature annual range),

temperature seasonality, maximum temperature of warmest month, minimum temperature of coldest month, temperature annual range, mean temperature of wettest quarter, mean temperature of driest quarter, mean temperature of warmest quarter, mean temperature of coldest quarter, annual precipitation, precipitation of wettest month, precipitation of driest month, precipitation seasonality, precipitation of wettest quarter, precipitation of driest quarter, precipitation of warmest quarter, precipitation of coldest quarter, altitude and land cover. Peterson *et al.* (2005) use seven GIS coverages (elevation, slope, aspect, topographic index and three NDVI-based indices) and GARP to model the temporal dynamics of dengue mosquitoes in Mexico; their predictions of monthly mosquito activity coincide significantly with human cases of dengue. The study by Benedict *et al.* (2007) uses ecological niche modeling to evaluate the global risk of spread of the tiger mosquito *Aedes albopictus*.

Risk maps based on arthropod vector data are a first important step, but they need to be complemented with more detailed information on vector species and with epidemiological data on hosts (Eisen and Eisen, 2008). Risk maps are often based on records of vector presence; however, for maintenance or spread of a pathogen, abundance of infected vectors has to be above a threshold and distribution models do not provide this kind of information. Modeling therefore becomes an important aspect in the construction of reliable risk maps; models cannot easily predict vector abundance either, but in the interplay of predictions on occurrence and observed data on abundance, models can help to deliver a more reliable risk assessment. A further potential limit on the predictive capacity of risk maps are complex interactions with resident competitors and potential microevolutionary, genetic responses of vectors when invading new habitats that never are exactly alike the original habitats. For example, larval competition from invaders can increase the vectorial capacity of the

adults of resident mosquito species (Bevins 2008). In mosquitoes and many other organisms, genetic change with respect to changing photoperiod – and not changing temperature – when invading new habitats has been demonstrated (Bradshaw and Holzapfel 2006).

However, risk maps still can play an important role. It will be difficult to estimate *absolute* risks unless very good information on vector abundance and habitat structure is already available; estimation of *relative* risks in different regions appears, though, to be a realistic outlook for a number of vector-borne diseases.

3. Mathematical Modelling

In recent years, there has been a growing awareness of the risks to human health posed by anthropogenic global environmental change. Changes in the pattern of infectious diseases may be one of the most noticeable risks (IPCC 2007). Numerous research challenges are associated with exploring the impact of temporal and spatial variations of climate as well as that of global climate change on the transmission dynamics of infectious diseases.

Public health scientists face the task of estimating via interdisciplinary collaborations, the future health impacts of projected scenarios of climatic-environmental conditions. Mathematical models have been used to exploring the potential effects of climate and ecological changes on the dynamics of diseases. For example, models have been employed to estimate how climatic changes would affect the potential geographic range of vector-borne infectious diseases.

3.1. Climate Change

Climate is the average weather, described in terms of the mean and other statistical quantities that measure the variability over a period of time and possibly over a certain geographical region (IPCC 1996). Climate factors that are usually measured are long-term averages and natural variability in meteorological variables such as temperature, precipitation, humidity. Climate change is defined as a statistically significant variation in either the mean state of the climate or in its variability, persisting for an extended period (IPCC, 2001). Climate change may occur due to natural internal processes or external forces. The latter include the anthropogenic components of climate change.

Computerized General Circulation Models (GCMs) have been used to estimate and quantify the magnitude and extent of climate change on global and regional levels. The results, however, from different GCMs with respect to changes at more detailed levels than global temperature are highly divergent and debatable.

Depending on how changes of a few degrees in global average temperature are realized they appear to produce dramatic effects. Because of the enormous uncertainties about regional and local effects regarding the amount and the direction of change, it is difficult to predict the effects of human-induced climate change. But by exploring the health implications of hypothesized climate changes one can gain useful insights also with respect to how these effects might be avoided.

3.2. Tools for exploring the climate-disease linkage

There is a wide range of possible approaches which can be used to understand the association between climate and infectious diseases. Epigrammatically, they include observational and experimental studies, mathematical modelling, risk mapping and assessment and surveillance. We focus here on the mathematical modelling approaches.

Several models have been developed to capture the complex dynamics that govern the interaction of vector species transmission and meteorological factors. The purpose of these models was to link the presence of the vector with a number of climate parameters and then to project the effects of extreme climate variability or even climate change on vector distribution. Within this context a distinction between so called biological process-based versus so called statistical data-based models has been suggested and used.

Models of biological processes are models by which certain parameters, e.g., temperature affects mosquito development, feeding frequency and longevity and the incubation period of the malarial parasite in the mosquito. Models of processes have in cases with insufficient surveillance data enormous heuristic value.

Some biological modelling of the potential impact of climate variables, primarily temperature increases, e.g., on malaria as done on a global scale projected net increases in the geographic area and season for potential malaria transmission (Martens *et al.* 1999). It is possible that small increases in minimum temperature in cooler regions may disproportionately increase malaria transmission (Lindsay and Birley 1996; McMichael *et al.* 2001). It is difficult to extrapolate the data from these global malaria-climate models (Lindsay and Birley 1996) from the situation in Africa

(Lindsay and Martens 1998) or from El Nino-malaria studies conducted in South America, where a relationship between the incidence of malaria in Colombia and the occurrence of the El Nino Southern Oscillation was shown (Bouma *et al*. 1997), to other places.

Bradley (1993) estimated temperature sensitivity of factors driving R_0 the basic reproduction number, which is defined as the number of new cases of a disease that will arise from one current case when introduced into a non-immune host population during a single transmission cycle (Anderson and May 1992). He found that changes in the extrinsic cycle of the Plasmodium protozoan could raise R_0 in many currently non-malarious areas to a point where malaria might take hold. In another approach Jetten and co-workers (Jetten and Takken 1994; Jetten *et al*. 1996) predicted that infections in southern Europe could increase dramatically, using a simulation model which included anopheline physiology and climate-change scenarios. A study by Sellers *et al*. (1990) analysed wind trajectories as a weather parameter and investigated their impact on eastern equine encephalitis in the USA. Their study indicated that mosquitoes potentially infected with eastern equine encephalitis virus could be carried by storm fronts from North Carolina northeast-ward as far as upstate New York from western Kentucky to Michigan. Using a dengue fever simulation model, Jetten and Focks (1997) projected that increasing temperature would increase the length of transmission season in temperate regions. They examined the critical mosquito density for dengue fever and related it to temperature change to quantify the influence of global warming on the intensity and distribution of dengue. Patz *et al*. (1998) applied the same simulation model to future climate scenarios generated from general circulation models (GCMs). Fock *et al*. (1993, 1995) developed a weather-driven model to simulate life-table information for Aedes aegypti

and a dengue simulation model. Both approaches focused on vector dynamics and have been parameterised with field data with a view toward informing the design of vector control strategies. They validated the dengue model in some places, where the model accurately predicted actual disease incidence.

Several studies focused on the impact of future climate change on the transmission dynamics of malaria (Haile 1989; Martin and Lefebvre 1995; Martens *et al.* 1995; Lindsay and Martens 1998; Martens 1998; Martens *et al.* 1999). Some climate change scenarios presented in those studies and run specifically for the USA showed little change in malarial transmission risk in the USA (Haile 1989). However, in general most of their scenarios predict that spread of malaria into northern latitudes such as central and northern Europe and North America, where there is no acquired immunity, would be detrimental (Martin and Lefebvre 1995; Martens *et al.* 1995; Lindsay 1998; Martens 1998; Martens *et al.*1999). Martens *et al.* (1995) considered mosquito survival probabilities, biting frequency, and extrinsic incubation period, and developed a model for the epidemic potential for *Plasmodium vivax* and *Plasmodium falciparum* as a function of temperature. They utilized this information in conjunction with temperature projections from a GCM to estimate how worldwide malaria distributions might change. Martin and Lefebvre (1995) developed a Malaria-Potential-Occurrence-Zone (MOZ) model. This model was combined with 5 GCMs (General Circulation Models) to estimate the changes in malaria risk based on moisture and minimum and maximum temperatures required for parasite development. This model corresponded fairly well with the distribution of malaria in the past, after allowing for areas where malaria had been eradicated. An important conclusion of this modelling exercise was that all simulation runs showed an increase

in seasonal (unstable) malaria transmission, under climate change, at the expense of perennial (stable) transmission.

Both studies predicted that the strongest increases in malaria would be at the borders of endemic areas and at higher altitudes. In another study Martens (1995) attempted to quantify mitigation efforts by developing an index to measure the sustainability of malaria spread. This index incorporated as major components, rate of temperature change, change in the disease burden on human populations, and economic factors, measured by the ratio of the gross national product growth to the rate of population growth. Although the areas of low endemicity showed the greatest increase in disability-adjusted life-years lost per year, the greatest disease burden still lay in poor tropical countries where *Plasmodium falciparum* is most prevalent and mitigation efforts are mostly inadequate. These studies concluded that even a slow rise in temperature could cause permanent malaria to expand to higher altitudes in the tropics and subtropics. Moreover, they predict that seasonal malaria could be found in some temperate regions as far as north as northern Europe.

An integrated, process-based model to estimate climate change impacts on malaria (that is part of the MIASMA modelling framework) has been developed by Martens and colleagues (Martens *et al.* 1995). This model differs from the others in that it takes a broad approach in linking GCM-based climate change scenarios with a module that uses the formula for the basic reproduction number (R_0) to calculate the 'transmission or epidemic potential' of a malaria mosquito population. That goes back to classical epidemiological models of infectious disease. Model variables within R_0 which are sensitive to temperature include: mosquito density, feeding frequency, survival, and extrinsic incubation period. The extrinsic incubation period (i.e., the

development of the parasite in the mosquito) is particularly important. The minimum temperature for parasite development is the limiting factor for malaria transmission in many areas.

A global model for malaria transmission was used by van Lieshout *et al.* (2004) to estimate the population at risk in areas where climate conditions are suitable for malaria transmission. The model provides a way to describe vulnerability to the potential impacts of climate change. Simulations are driven by the IPCC scenarios. For countries with currently limited capacity to control the disease, the model estimates additional populations at risk by 2080. The model results are sensitive to the spatial distribution of precipitation projections and population growth in the areas where there is a new risk due to climate change.

In another study El Nino events were linked to variability in malarial incidence in Colombia and Venezuela (Bouma *et al.* 1997). Craig *et al.* (1999) developed a simple climate-based distribution model of malaria transmission in Sub-Saharan Africa based on biological constraints of climate on parasite and vector development. This kind of initial approaches provide the numerical basis for further refinement and prediction of the impact of climate change on transmission.

There have been similar modelling approaches in which the climate change impact on the transmission dynamics of tick-borne disease and rodent-borne disease were explored and demonstrated (Haile 1989; Amerasihge *et al.* 1993; Mount *et al.* 1993; Glass *et al.* 1994; Wilson 1998). They also indicate to, e.g., a correlation between Lyme disease tick density and rainfall and elevation (Amerasinghe *et al.* 1993) or tick abundance was predicted by land use, land cover, soil type, elevation, and the timing, duration, and rate of change in temperature and moisture [Mount *et al* 1993; Glass *et al.* 1994; Wilson 1998).

It should be pointed out that most of the above models, especially those dealing with malaria, are primarily driven by temperature. Temperature is certainly a major impact factor for the transmission of vector borne infectious diseases like malaria but not the only one. Nevertheless, the studies by Martens *et al.* (1995) and Martens (1995) point in the right direction of research and can be viewed as integrative studies. Besides that, many of the above studies mainly project potential epidemic malaria transmission and can be considered rather as sensitivity analyses than as modelling approaches. These models are not fully parameterised and therefore they cannot be used for regional prediction.

Statistical data-based models: Another modelling approach within this context is the one suggested by Rogers and Randolph (2000). These authors explored the effects of global climate change on the future incidence of cerebral malaria using a two-step multivariate statistical approach. First, they used maximum-likelihood methods to map present day malaria distributions by determining the key climate variables associated with the presence or absence of disease. Then, these results were used to predict the worldwide distribution of cerebral malaria in the year 2050, based on a widely accepted GCM scenario. This predicted that changes in the distribution of Plasmodium falciparum will largely be restricted to the tropics and sub-tropics, with just as many people being freed of the risk of infection as being newly exposed. Based on the current distribution of malaria they could empirically establish how the disease is currently constrained by the means and covariances of meteorological factors, like temperature precipitation, and humidity. However, using current distribution limits in the estimate yields a biased estimation of the multivariate relationship between climatic variables and malaria occurrence since the lower

temperature range in temperate zones would have been treated as non-receptive to malaria.

An example of another empirical statistical model is the CLIMEX model. This model, developed by Sutherst and co-workers (Sutherst *et al*. 1995; Sutherst 1998), maps the translocation of species between different areas as they respond to climate change. The assessment was based on an 'ecoclimatic index' governed largely by the temperature and moisture requirements of the malaria mosquito. CLIMEX analyses conducted in Australia indicate that the indigenous vector of malaria would be able to expand its range 330 km south under one typical scenario of climate change. However, these studies clearly cannot include all factors which affect species distributions. For example, local geographical barriers and interaction/competition between species are important factors which determine whether species colonise the full extent of suitable habitat (Davis *et al*. 1998). Assessments may also include additional dynamic population (process-based) models (e.g., DYMEX).

In a model based on the mapping malaria risk in Africa project (MARA) Tanser *et al*. (2003) produces a spatiotemporally validated approach of Plasmodium falciparum in Africa. Using different climate scenarios they projected the potential effect of climate change on transmission patterns. Their results indicate that there will be an increase in person-months of exposure for stable malaria transmission as well as an increase in altitudinal distribution of malaria. Ebi and colleagues obtained similar results with respect to the malaria distribution due to climate change (Ebi *et al*. 2005). However, using similar methods, results from other studies point to a much weaker impact of climate change on malaria distribution indicating that the issue if far from being resolved (Thomas *et al*. 2004).

All of the examples discussed above have their specific advantages and disadvantages. For example, the model developed by Rogers and Randolph incorporates information about the current social, economic, technological modulation of malaria transmission. It assumes that those contextual factors will apply in future in unchanged fashion. This adds an important, though speculative, element of multivariate realism to the modelling - but the model thereby addresses a qualitatively different question from the biological model. The biological model of e.g. Martens and colleagues (Martens 1998) assume that there are known and generalisable biologically-mediated relationships. Also, this modelling is only making a start to include the horizontal integration of social, economic and technical change. The statistical model is based on socio-economically censored data. It derives its basic equation from the existing (constrained) distribution of malaria in today's world and climatic conditions, and foregoes much information on the malaria/climate relationship within the temperate-zone climatic range. Yet this range is likely to be considerably important in relation to the marginal spread of malaria under future climate change.

Randolph and Rogers (2000) tried to predict the future distribution of tick-borne encephalitis virus in Europe. Both studies make predictions that run against the conventional wisdom. At the same time they use multivariate statistical methods that incorporate predicted changes not only in temperature, which is the main meteorological factor that has been used by biological models, but also rainfall, humidity, and their interactions. Thus, they appear to be able to capture more of the constraints on parasite transmission and development.

But these models are far from being "perfect". For instance, they do not allow the parasites to evolve in response to changing selection pressures. It is possible, for

example, that reduced opportunities for transmission of non-systemic infections of tick-borne encephalitis between co-feeding ticks might lead to the evolution of alternative transmission routes or to changes in virulence. In addition statistical models tell us nothing about the mechanisms involved in those dynamic processes of interaction between spread of disease and climate change and their features. However, models of this type will be useful in identifying areas where vector-borne diseases are likely to alter or expand their distributions. Therefore, as already mentioned above they have their fully justifiable use. Models of data in cases with limited understanding of the transmission biology but with the availability of data are very useful.

In a statistical modelling approach based on vapour pressure as a measure for humidity Hales *et al.* (2002) assessed changes in the geographical limits of dengue fever transmission and the number of people at risk of dengue by incorporation future climate change and human population projections into the model. They found that climate change is likely to increase the area of land with climate suitable for dengue fever transmission and that a large proportion of the human population would be put at risk.

Another approach dealing with the association of cholera dynamics and the El-Nino-Southern oscillation used time series analysis due to lack of information that could be used to specify an appropriate model of process for the ENSO effect (Pasqual *et al* 2000).

The current infectious disease models do not do well at predicting future incidence of disease because they lack an adequate characterization of the feedback effects between weather-related changes in the ecology and the spread of infected vectors and disease. Although no model can accurately simulate real life, models are useful in

conceptualising dynamic processes and their outcomes. Well-conceptualised models help identify key knowledge gaps and guide empirical studies that ultimately will lead to improved models. At present, long-term regional weather and ecologic predictions still remain major barriers to predicting future changes in vector borne disease risk.

Both approaches are necessary and should be considered complementary. Combination of both provides higher predictive value. Although a good biological model is preferable to a statistical one, there are dangers in applying biological models before we understand the biology. Therefore, problems of this kind should be tackled by using all mathematical tools available and combine them to be able to extract the maximum information possible and make reliable predictions.

3.3. The role of Geographic Information Systems and Remote Sensing

The development of new technologies has helped to significantly improve surveillance and lead to the emergence of new modelling approaches. This type of modelling incorporates the effects of space, e.g., diffusion models or networks. Strongly linked to that is the employment of Geographic Information Systems (GIS). GIS are powerful automated systems for the capture, storage, retrieval, analysis, and display of spatial data. The enormous possibilities of the Geographic Information Systems should be exploited with respect to evaluating spatial data. It is obvious that besides the time component including the spatial component in a way offered by GIS opens new possibilities in evaluating epidemiological data. GIS can be used for identification of environmental factors that affect the patterns of disease risk and transmission. Using

remotely sensed data and GIS technologies one could develop predictive models of vector population dynamics and disease transmission.

Modelling involves the integration of GIS with standard epidemiologic methods. GIS can assist in generating data for modelling processes that occur over space. GIS models, for example, can express relationships or flows between people and places. Spatial interaction and spatial diffusion models are of particular relevance to the study of emerging diseases.

Spatial interaction models analyze and predict the movements of people, information, and goods from place to place. The flows of people between rural areas, villages, cities and countries are all forms of spatial interaction that are central to disease transmission. By accurately modelling these flows, it is possible to identify areas most at risk for disease transmission. Given actual flow data, one can estimate values that show the effects of distance and population size (or other factors) on interaction. The models can then be used to predict spatial interaction patterns elsewhere.

Another important approach is spatial diffusion models, which analyze and predict the spread of phenomena over space and time and have been widely used in understanding spatial diffusion of disease. Such models are quite similar to spatial interaction models except that they have an explicit temporal dimension. By incorporating time and space, along with basic epidemiologic concepts, the models can predict how diseases spread, spatially and temporally, from infected to susceptible people in an area and aid in understanding the emergence of infectious diseases.

With respect to the impact of climate on the transmission dynamics of malaria the availability, for instance, of a complete geographical information system including a digitized topographic map with key ecological information such as the temporal-

spatial pattern of surface water would be of major assistance. The ground map and the ground climate measurements are complemented with remote sensing data: temperature, moisture, normalized vegetation index. Using these GIS tools it is expected to receive high quality information about ecological factors.

New technologies such as remote sensing via satellites could be also extremely useful in collecting data for detection of pathogens by indirect measurements that could help to understand the linkage between climate and infectious diseases. Remote sensing could be employed in gathering data needed to develop prediction models for several infectious diseases. An interesting example is presented by Lobitz *et al.* (2000). They used satellite data to monitor the timing and spread of cholera. Public domain remote sensing data like sea surface temperature and sea surface height were compared directly with cholera case data in Bangladesh. The data indicated that cholera epidemics are climate-linked. For instance, based on this data, sea surface temperature shows as annual cycle similar to the cholera case data. Using this kind of data, predictive models could provide early warning of conditions associated with cholera outbreaks.

The spatial occurrence of vector-borne diseases can be predicted from environmental factors impacting the vector or pathogen and the risk of exposure (Gu and Novak 2006, Rotela *et al.* 2007). There are already several local or regional GIS-based predictive spatial risk models in place in particular in the US (Estrada-Pena 2002, Eisen *et al.* 2006, Eisen *et al.* 2006, 2007, Wimberly *et al.* 2008). Mapping spatial patterns of human risk of exposure to vector-borne disease agents is of major importance for understanding the disease distribution and for the implementation of control measures. Using epidemiological data one can model spatial risk of human

exposure to vector-borne pathogens and thus identify human contact with the disease pathogen (Rotela *et al.* 2007).

4. Research needs

Extreme climatic variability and climate change is very likely to affect the transmission dynamics of infectious diseases, in particular vector-borne diseases. We know very little about the interactions of weather variables and the diseases they affect. More information is essential on how zoonoses persist in nature and what triggers their amplification and initiation of secondary cycles that increase the risk of human infection. To determine the role of climate or weather and the long-term climate trends we need to understand more on pathogens persistence and what triggers amplification. Multi-disciplinary research on diseases in their natural habitats is important to identify better the effect of weather on the natural maintenance cycles, disease incidence and epidemic potential. Mathematical models could in a first approach investigate the direct effects of:

1) climate change on ecologic changes such as biodiversity loss, community relocation, nutrient cycle changes.

2) climate change on sociological changes such as migration, nutrition, sanitation, population/economy.

3) climate change on changes in transmission biology such as vector dynamics (migration, breeding, physiology, behaviour) or pathogen dynamics (reproduction, transmissibility, virulence).

4) indirect interactions between ecological, epidemiological and sociological changes

To do so, more precise modelling data are necessary and therefore epidemiological surveillance at all levels of the health system is essential.

Information to address the health impacts of extreme climate variability or even climate changes is almost non-existent. The little available information comes from epidemic studies where the researchers focus on one event and collect data for a short period of time. More complete, detailed, long-term data sets are necessary. The complicated associations between climate and infectious diseases make essential the identification of model systems or diseases, which would enable the collection of long-term qualitatively valuable data sets. A sustained funding to ensure long term research on this issue is equally necessary.

Until now the few approaches that have made use of global circulation models to assess the impact of climate change on infectious diseases indicate that it is likely that warming trends and other changes could affect vector borne diseases. However, the details and the degree of these effects are extremely uncertain. We also do not know how projected climate change would affect the complex ecosystems required to maintain disease. More research on the natural transmission cycles of these pathogens is necessary. Future assessments that incorporate climate change scenario-based analyses demand the integration of local demographic and environmental factors. They are essential in guiding comprehensive, long-term preventive public health interventions.

5. Conclusions

Powerful empirical and theoretical methods are available to study the ecological consequences of extreme climate variability and climate change. Organisms that cause diseases of humans and animals are part of every ecosystem, but disease dynamics has mainly been studied using mathematical models that do not explicitly take complex and spatially explicit environmental information into account and focus on the temporal aspects of disease spread. Many lines of evidence suggest that climate change will have an impact on the geographical distribution of many insect and tick vectors of human diseases. There is therefore a strong need to overcome the traditional division between the spatial analysis of the environment and the temporal analysis of disease dynamics. Data derived from remote sensing technology, spatial statistics and numerical methods, mathematical models and also economic and social data need to be combined in order to provide more reliable predictions on infectious disease risks in new environmental circumstances.

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European Commission

Abstract
There is now near undisputed scientific consensus that the rise in atmospheric concentration of greenhouse gases causes warming at the Earth's surface. Global warming will also have impacts on human health. We focus here on vector-borne infectious diseases because climatic variables are major determinants of the geographical distribution of the cold-blooded insect and tick species that can transmit viruses, bacteria and other microparasites to humans. The distribution of vectors is thus one important component of infection risk. We review the methods that have been developed in the past few years to determine and to model the distribution of species under actual and hypothetical environmental conditions and show how mathematical models have been used in this context.
Remote sensing technology offers progressively better environmental and climatic data which can be employed in conjunction with Geographic Information Systems (GIS) and spatial statistical techniques to determine the distribution of vector species under different scenarios. Mathematical models can help to elucidate many aspects of infectious disease dynamics. The available studies lead to the expectation that climate change affects the transmission dynamics of vector-borne infectious diseases. However, the details and the degree of these effects are very uncertain. In order to predict more reliably the effects of extreme climate variability or climate change on infectious disease dynamics more data on the interaction between ecological, epidemiological, economical and social processes are needed.

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