Using climate to predict infectious disease epidemics

World Health Organization

Geneva 2005

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Communicable Diseases Surveillance and Response
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World Health Organization

Geneva
2005

WHO Library Cataloguing-in-Publication Data

Using climate to predict infectious disease epidemics / Communicable Diseases Surveillance and Response, Protection of the Human Environment, Roll Back Malaria.

1. Climate. 2. Disease outbreaks. 3. Forecasting. 4. Temperature. I. World Health Organization.

ISBN 92 4 159386 5 (NLM classification: WB 700)

Printed by the WHO Document Production Services, Geneva, Switzerland

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PREFACE

This document was written to provide guidance for the Department of Communicable Diseases Surveillance and Response (CSR), the Department of Protection of the Human Environment (PHE) and the Roll Back Malaria Department (RBM) on the potential of early warning systems (EWS) based on climate variations to enhance global surveillance and response to epidemic-prone diseases.

CSR has a unique mandate to lead international efforts to achieve global health security. Its strategy has three components: to improve preparedness of Member States by strengthening national surveillance and response systems; to contain known risks; and to respond to unexpected health events. PHE aims to achieve safe, sustainable and health-enhancing human environments, protected from biological, chemical and physical hazards and secure from the adverse effects of global and local environmental threats. Founded in 1998, RBM aims to halve the world's malaria burden by 2010. Its four main technical strategies are: prompt access to treatment, especially for young children; prevention and control of malaria in pregnant women; vector control; and prevention and containment of epidemics.

Knowledge of the interactions between climate and health dates back to the time of Aristotle (384–322 BC), but our understanding of this subject has recently progressed rapidly as technology has become more advanced. At the same time, our ability to forecast weather and climate (in terms of both accuracy and lead-times) has improved significantly in recent years. The increased accuracy of climate predictions, and improving understanding of interactions between weather and infectious disease, has motivated attempts to develop models to predict changes in the incidence of epidemic-prone infectious diseases. Such models are designed to provide early warning of impending epidemics which, if accurate, would be invaluable for epidemic preparedness and prevention.

This document evaluates the potential of climate-based disease early warning as a means of improving preparedness for, and response to, epidemics. On the basis of the history of the development of EWS to date, the authors develop a conceptual framework for constructing and evaluating climate-based EWS. They identify the climate-sensitive diseases of major public health importance and review the current state of the art in climate-based modelling of these diseases, as well as future requirements and recommendations.

This document lays the foundation for future development of EWS that capitalize on new knowledge about interactions between climate and infectious diseases, as well as improved capabilities for assessing vulnerability, monitoring the environment and climate and producing seasonal climate forecasts. It reviews the current state of development of EWS for a number of key infectious diseases. The last few years have seen rapid progress in research; many new studies have demonstrated significant associations between climate variability and infectious disease transmission, and have specifically highlighted the potential for developing climate-based EWS. To date, however, only limited experience of full operational application has been gained. For some diseases, such as malaria and Rift Valley fever (RVF), early warnings based on climatic conditions are beginning to be used in selected locations to alert ministries of health to the potential for increased risk of outbreaks and to improve epidemic preparedness, but coverage is patchy.

The document highlights the most important challenges that need to be overcome before the full potential of EWS can be realized. These include:

►developing and strengthening disease surveillance systems to produce the high-quality, long-term data needed for the development and testing of models;

►identifying and testing a range of climatic, environmental and socioeconomic indicators as potential co-variables in predictive models of infectious disease;

►developing standard terminology and criteria for evaluating the accuracy of such models;

►ensuring that modelling efforts are carried out in collaboration with the disease control community in order to make them directly relevant to specific response decisions and to the particular needs and constraints of policy-makers; and

►developing suitable frameworks for the rigorous epidemiological, institutional and economic evaluation of EWS that are implemented.

This joint CSR, PHE and RBM publication was prepared with the understanding that climate-based EWS, when fully developed, do have the potential to provide increased lead-times in which to implement epidemic prevention and/or control activities. Therefore their development should be encouraged, and both the positive and negative experiences of using such systems should be recorded and disseminated. It is only with experience that such systems will become useful operational tools.

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LIST OF ABBREVIATIONS

ADDS	Africa Data Dissemination Service
ARIMA	Autoregressive-moving average
AVHRR	See NOAA AVHRR
CCD	Cold cloud duration
CDC	Centers for Disease Control and Prevention, Atlanta, GA, USA
CDNA	Communicable Disease Network Australia
CIMSiM	Container Inhabiting Mosquito Simulation Model
CL	Cutaneous leishmaniasis
CPC	Climate Prediction Center
CSR	Department of Communicable Diseases Surveillance and Response
DALY	Disability-adjusted life years
DENSiM	Dengue simulation model
DEWS	Dengue early warning system(s)
DHF	Dengue haemorrhagic fever
EIR	Entomological inoculation rate
ENSO	El Niño Southern Oscillation
EUMETSAT	European Organisation for the Exploitation of Meteorological Satellites
EWS	Early warning systems
FAO	Food and Agriculture Organization of the United Nations
FEWS	Famine early warning systems
GIS	Geographical information systems
HMIS	Health management information system
IDSR	Integrated disease surveillance and response
JE	Japanese encephalitis
LST	Land surface temperature
MARA	Mapping Malaria Risk in Africa Project
MODIS	Moderate Resolution Imaging Spectroradiometer
MVE	Murray Valley encephalitis
NOAA AVHRR	National Oceanic and Atmospheric Administration Advanced Very High Resolution Radiometer
NDVI	Normalized Difference Vegetation Index
PHE	Department of Protection of the Human Environment
RBM	Roll Back Malaria
RFE	Rainfall Estimate (derived from remote sensing data)
RRV	Ross River virus
RVF	Rift Valley fever
SADC	Southern African Development Community
SD	Standard deviation
SLE	St Louis encephalitis
SSH	Sea surface height
SST	Sea surface temperature
STD	Sexually transmitted disease
TB	Tuberculosis
VL	Visceral leishmaniasis
WNV	West Nile virus

EXECUTIVE SUMMARY

It is commonly accepted that climate plays a role in the transmission of many infectious diseases, some of which are among the most important causes of mortality and morbidity in developing countries. Often these diseases occur as epidemics which may be triggered by variations in climatic conditions that favour higher transmission rates. With increasing demand for operational disease early warning systems (EWS), recent advances in the availability of climate and environmental data and increased use of geographical information systems (GIS) and remote sensing make EWS incorporating information on climate increasingly feasible from a technical point of view.

This report presents a framework for developing disease EWS. It then reviews the degree to which individual infectious diseases are sensitive to climate variability in order to identify those diseases for which climate-informed predictions offer the greatest potential for disease control. The report highlights that many of the most important infectious diseases, and particularly those transmitted by insects, are highly sensitive to climate variations. Subsequent sections review the current state of development of EWS for specific diseases and underline some of the most important requirements for converting them into operational decision-support systems.

Considerable research is currently being conducted to elucidate linkages between climate and epidemics. Of the 14 diseases meeting the defined criteria for potential for climate-informed EWS, few (African trypanosomiasis, leishmaniasis and yellow fever) are not associated with some sort of EWS research or development activity. For West Nile virus, an operational and effective warning system has been developed which relies solely on detection of viral activity, and it remains unclear whether the addition of climatic predictors would improve the predictive accuracy or lead-time. For the remaining diseases (cholera, malaria, meningitis, dengue, Japanese encephalitis, St Louis encephalitis, Rift Valley Fever, Murray Valley encephalitis, Ross River virus and influenza), research projects have demonstrated a temporal link between climatic factors and variations in disease rates. In some of these cases the power of climatic predictors to predict epidemics has been tested. In many of the early studies these tests were preliminary, based either on a very limited dataset or else they provided little description of the methods used. Most of the studies published in the last few years, however, have been both considerably more comprehensive in their consideration of climate and non-climatic effects, and more rigorous in terms of testing predictive accuracy.

The published literature to date, however, includes no full descriptions of climate-based EWS being used to influence disease control decisions.

This report suggests a number of likely explanations for this:

► affordable and accessible data and analytical tools have only recently become widespread, so that this field is at a relatively early stage of development and new studies are now being published at a rapid rate;

► as yet, there is no common consensus on good practice in building predictive models, or on assessing their accuracy and lead-times: as a consequence it is often difficult to judge the utility of existing models;

► most research projects have had relatively limited resources and therefore have not been tested in locations outside the original study area;

► many studies in this area focus solely on climatic factors and do not explicitly test other hypotheses that might explain variations in disease rates over time; and

► many studies are undertaken as “pure research”, therefore, neither the extent to which they address specific control decisions nor their potential utility for planning public health interventions is clear.

This report concludes that a number of steps could be taken to begin to address these issues. These include:

►Maintaining and strengthening disease surveillance systems for monitoring the incidence of epidemic diseases. High-quality data on the incidence of infection or disease, covering long periods, are essential for generating and refining models relating climate to infectious disease; lack of disease data is a more common limiting factor than lack of climate data. In some cases existing approaches to surveillance may generate disease data appropriate for use within an early warning system – in others it may be necessary to either modify existing systems or to build new ones. The introduction of computer hardware and software at appropriate levels within the surveillance system can facilitate timely collation and analysis of incoming disease data. Widespread introduction of GIS tools, for example, the WHO Healthmapper software, would enable surveillance data to be stored and accessed in a disaggregated form, allowing the detailed analysis of spatial and temporal disease distributions. Consideration should be given to integrating this type of monitoring into single systems (e.g. by combining disease and famine EWS) to facilitate data access and maximize comparability.

►Clarifying definitions of terminology and methods for assessing predictive accuracy. For instance, while the threshold value used to define an "epidemic" (i.e. number of cases in a specific population over a specified time) may vary depending on the disease and the local context, it should be clearly defined before the modelling process begins. The accuracy of the system should also be measured using standard epidemiological tools that provide an objective overall measure of model "skill", and are also directly relevant to control decisions (e.g. sensitivity, specificity, positive and negative predictive value). The accuracy of models for predicting incidences or rates could be measured as the root mean square error, or as correlation coefficients between observed and predicted case numbers. Assessments of predictive accuracy should always be made against independent data (i.e. using data not included in the original model-building process).

►Testing for non-climatic influences (e.g. population immunity, migration rates and drug resistance) on disease fluctuations is dependent on the availability of appropriate data. Distinguishing underlying trends from interannual variability should help to avoid disease variations being attributed incorrectly to climate. More importantly, in practical terms, incorporating the data available for non-climatic variables should lead to greater accuracy in predictive models.

►Early consideration of operational mechanisms. Including health policy-makers in all stages of system design (e.g. involving local control personnel in defining epidemic thresholds and in determining the most appropriate warning lead-time) should increase the likelihood that the system will be implemented effectively, and thereby increase its chances of having a positive impact on disease control. Discussions should relate to specific control decisions and consider local constraints (particularly on resources) on the implementation of the EWS. Discussions should also identify opportunities for implementation over wider areas (i.e. regions comprising several countries) with similar climate and disease conditions. Experience with famine EWS in the 1990s suggested that the effectiveness of predictions depended less on their accuracy than on political and operational factors.

►Making final recommendations on implementation of EWS on the basis of rigorous assessments of epidemiological impact and cost-effectiveness analysis. These should assess the value of collecting data on the various climatic and non-climatic influences in predicting the occurrence, timing and scale of epidemics. For example, in some situations adding climatic information to an early warning system may lead to only a small increase in predictive power and therefore in effectiveness of control; however, if sufficiently inexpensive and simple to collect, inclusion is justified. Economic evaluation of EWS should also take into account the opportunity costs involved in diverting scarce resources from areas with other epidemiological patterns (e.g. stable transmission) to epidemic-prone areas.

The research reviewed in this report demonstrates that that climate information can be used to improve epidemic prediction, and therefore has the potential to improve disease control. In order to make full use of this resource, however, it is necessary to carry out further operational development. The true value of climate-based early warning systems will come when they are fully integrated as one component in well-supported systems for infectious disease surveillance and response.

1. INTRODUCTION

The early identification of an epidemic of infectious disease is an important first step towards implementing effective interventions to control the disease and reduce the resulting mortality and morbidity in human populations. Usually, however, epidemics are well under way before the authorities are notified and epidemic control measures are put in place.

Because the geographical and seasonal distributions of many infectious diseases are linked inherently to the climate, the possibility of using climate parameters as predictive indicators in disease EWS has long been a focus of interest. During the 1990s especially, a number of factors led to increased activity in this field, including: significant advances in data availability, epidemiological modelling and information technology, and the implementation of successful EWS outside the health sector. In addition, convincing evidence that anthropogenic influences are causing the world's climate to change has provided an added incentive to improve understanding of climate–disease interactions. Projections indicate an approximate average global warming of 1.5–5.8 ºC during the twenty-first century, accompanied by an increase in the frequency of extreme and anomalous weather events such as heat-waves, floods and droughts (IPCC, 2001). If climatic changes occur as projected, it is likely that they will have significant impacts on the timing and severity of infectious disease epidemics in many locations.

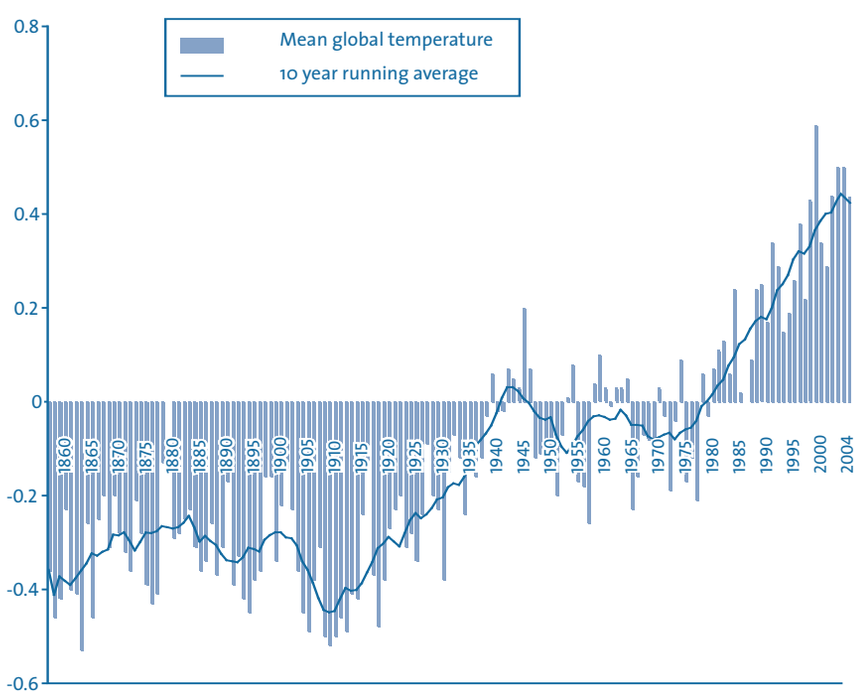

FIGURE 1: OBSERVED CHANGES IN GLOBAL AIR TEMPERATURE, 1850–2004, RELATIVE TO 1961–1990 CONDITIONS. BASED ON DATA FROM THE UNIVERSITY OF EAST ANGLIA CLIMATE RESEARCH UNIT, UK

A range of infectious (particularly vector-borne) diseases are geographically and temporally limited by variations in environmental variables such as temperature, humidity and rainfall, and vegetation and land-use patterns. The direct impact of climate on infectious diseases can occur by three principal pathways: effects on human behaviour; effects on the disease pathogen; and effects on the disease vector.

Human behaviour

Climate variability has direct influences on human behaviour (e.g. seasonal occupation, migration, winter–summer lifestyles), which in turn can have a significant impact on disease transmission patterns. The strong seasonal pattern of influenza infections in Europe, for example, is thought to reflect the increased tendency among humans to spend more time indoors during the winter months (Halstead, 1996). Conversely, the peak incidence of gastroenteritis in temperate developed countries during the summer months can be linked to changes in human behaviour (e.g. more picnics and meals cooked outside) associated with warmer temperatures (Altekruse et al., 1998).

Disease pathogens

For infectious diseases caused by a pathogen that develops outside the human host (i.e. in the environment or in an intermediate host or vector), climate factors can have a direct impact on the development of the pathogen. Most viruses, bacteria and parasites do not complete their development if the temperature is below a certain threshold (e.g. 18 ºC for the malaria parasite *Plasmodium falciparum* and 20 ºC for the Japanese encephalitis virus; Macdonald, 1957; Mellor & Leake, 2000). Increases in ambient temperature above this threshold will shorten the time needed for the development of the pathogen and increase reproduction rates, whereas temperatures in excess of the tolerance range of the pathogen may increase mortality rates.

Disease vectors

The geographical distribution and population dynamics of insect vectors are closely related to patterns of temperature, rainfall and humidity. A rise in temperature accelerates the metabolic rate of insects, increases egg production and increases the frequency of blood feeds (e.g. Detinova, 1962; Mellor & Leake, 2000). The influence of rainfall is also often significant, although it is less easy to predict. Rainfall has an indirect effect on vector longevity through its effect on humidity; relatively wet conditions create favourable insect habitats and thereby increase the geographical distribution and seasonal abundance of disease vectors. In other cases excess rainfall may have catastrophic effects on local vector populations if flooding washes away the breeding sites.

Integrating climate information into early warning systems

Many infectious diseases are known to have epidemic cycles which are unrelated to external drivers. Measles epidemics, for example, are cyclic, recurring in the population whenever the proportion of susceptible individuals reaches a suitable threshold. Other disease epidemics may result from a combination of intrinsic and extrinsic factors.

Even where linkages between disease and climate are relatively strong, other non-climatic factors may also have a significant impact on the timing and severity of disease outbreaks. One of the most important determinants of population vulnerability is the level of herd immunity, which is influenced by factors such as malnutrition, prevalence of human acquired immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), and previous exposure to infection. Various studies, for example, have presented evidence that even under suitable climate conditions, epidemics are likely to occur only if there is a sufficient proportion of non-immunes in the population (e.g. Shanks et al., 2000, on malaria in Western Kenya; Koelle et al., 2005, on cholera in Bangladesh). Human-related factors such as the status of control interventions, housing conditions, population movements and agricultural practices can also have a considerable impact on disease patterns, from the local (e.g. village) to wider spatial scales (e.g. between districts or provinces). For example, the prevalence of malaria and leishmaniasis can be strongly influenced by irrigation schemes and deforestation (Campbell-Lendrum et al., 2001; Guthmann et al., 2002).

Ideally, the importance of non-climatic factors should be assessed in comparison with that of climate variability in order to justify the development of climate-based EWS for infectious diseases. Where both climatic and non-climatic factors contribute significantly to predictive power, both should be incorporated into the early warning system model.

2. LESSONS FROM HISTORICAL EARLY WARNING SYSTEMS

The use of climate data for predicting outbreaks of infectious diseases dates back to work by Gill and others in India. Gill (1923) developed an early warning system for malaria based on rainfall, prevalence of enlarged spleens, economic conditions (as indicated by the price of food grains) and epidemic potential (the coefficient of variation of fever mortality during October for the period 1828–1921). A response mechanism also existed which could be initiated within time to avert the worst impact. The model itself was used to predict epidemics from 1921 to 1942 in 29 districts of the Punjab (India), although the author believed that warnings in the first two years were issued too late (both in late September when the malaria season occurs in October). A formal assessment of the model's predictions for 1923–1942 indicated that accuracy was significantly better than would have been obtained by chance (Swaroop, 1949). However, the model's accuracy is difficult to assess exactly as there is no indication of the number of epidemics correctly predicted. Another problem with this analysis is that there is no indication of how an epidemic was defined. Gill's approach demonstrates how an early warning system can be constructed from relatively few variables, although this method can be very demanding in terms of the number of observations required for each variable.

Rogers (1923, 1925, 1926) described associations between climatic variables such as temperature, rainfall, humidity and winds, and the incidence of diseases such as pneumonia, smallpox, leprosy and tuberculosis (TB) in India and elsewhere. Although Rogers' inferences were made based solely on visual comparisons of apparent correlations between climate and disease variables, rather than statistical tests, these studies highlighted the potential utility of long-term datasets. The leprosy data used, for example, represented 30 years of annual incidence data for the whole of India in combination with meteorological records from over 2000 sites (Rogers, 1923). On the basis of his conclusions, it was recommended that climatic variables be used for forecasting epidemics of TB, smallpox and pneumonia and for mapping the worldwide incidence of leprosy. However, such systems were never implemented on a large scale.

These historical studies demonstrate the usefulness of long-term historical or current datasets in predicting future patterns of disease. They also suggest that it is possible to develop an early warning system based on overall associations of climate variables with disease incidence, without necessarily requiring a complete knowledge of the effects of climate on all components of the disease transmission cycle.

The health sector is now in a much stronger position to explore the utility of EWS. Firstly, standardization of disease diagnosis and networked computerized reporting have the potential to allow accurate and rapid monitoring of disease incidence (although undermined by patchy and often deteriorating surveillance systems in many parts of the world). Secondly, a wide variety of environmental monitoring data from satellite and ground-based systems are easily accessible at no or low cost, facilitating the investigation of potential links to climate. Thirdly, advances in statistical and epidemiological modelling allow apparent associations to be tested explicitly, rather than relying on visual inspection.

Despite the renewed interest in EWS within the health sector, there has been little operational activity to date. This contrasts with other sectors: most notably the considerable research and development effort focused on the development of famine early warning systems (FEWS) following widespread famine in Africa in the early 1980s. A famine early warning system has been defined by Davies et al. (1991) as "a system of data collection to monitor people's access to food, in order to provide timely notice when a food crisis threatens and, thus, to elicit appropriate response".

FEWS operate at various geographical levels (Table 1); food availability is predicted using risk indicators such as market export prices, pest infestations, war and conflict, nutritional indices and climate and vegetation variables.

TABLE 1: EXAMPLES OF FAMINE EARLY WARNING SYSTEMS AND THEIR GEOGRAPHICAL COVERAGE

LEVEL	EARLY WARNING SYSTEM
Global	Global Information and Early Warning System (GIEWS)
Regional	Southern African Development Community (SADC)
	Comité Permanent Interetats de Lutte contre la Sécheresse dans le Sahel (CILSS)
National	USAID Famine Early Warning System Information Network (FEWS NET)
Sub-national	Save the Children Fund (SCF-UK), Darfur, Sudan
Local	Suivi Alimentaire Delta Seno (SADS), Mopti, Mali

A critical factor in Davies' definition of FEWS is the inclusion of an "appropriate response", which suggests that an early warning system should be part of a wider, integrated system designed to respond to a crisis. The importance of a response will be discussed below with particular reference to infectious diseases, but it is the phase following the early warning (i.e. mitigation and response), which has so far been crucial in determining the success of FEWS. The message from numerous studies is that EWS are of little use without the capacity to respond – i.e. the resources to react promptly and effectively must be included within the EWS. For instance, the 1990–1991 drought in southern Africa was the worst in the twentieth century, placing approximately 40 million people at risk of starvation. A major famine was averted both as a result of the South African Development Community (SADC) Regional early warning system warning in March 1991 of a substantial grain shortfall, and extensive national and international government involvement in ordering and delivering food imports.

Experience elsewhere has shown that where decisions are predicated on the basis of signs that a crisis is already under way, relief is not delivered on time – as was the case in Sudan and Chad in 1990–1991.

In addition, political issues can have a significant impact on the timing of the response. In Ethiopia, for example, early warning information from national systems was ignored for years because of political instability (Buchanan-Smith et al., 1995).

In various instances the success of the FEWS approach has been limited by a number of organizational problems, the implications of which should not be overlooked in the health sector. The following points should therefore be taken into consideration:

- Climate is only one of many determinants that could be included in an early warning system.
- Early warning of a crisis is no guarantee of prevention.
- Interest in preventing a crisis is part of a wider political, economic and social agenda. In many cases governments are not directly accountable to vulnerable populations.
- In most cases, the purpose of early warning is undermined as relief arrives too late due to poor organization at the donor and/or national level.

3. CONCEPTUAL FRAMEWORK FOR DEVELOPING CLIMATE-BASED EARLY WARNING SYSTEMS FOR INFECTIOUS DISEASES

Attempts to initiate development of EWS within a specific country should be preceded by a decision-making process to identify the principal disease(s) of interest. This will depend on the burden of various infectious diseases in the region and on levels of national and international funding available for disease-specific activities.

On the basis of an extensive literature review, the following framework for constructing climate-based infectious disease EWS is proposed (Figure 2). The framework comprises four preliminary phases, the early warning system itself, and the response and assessment phases.

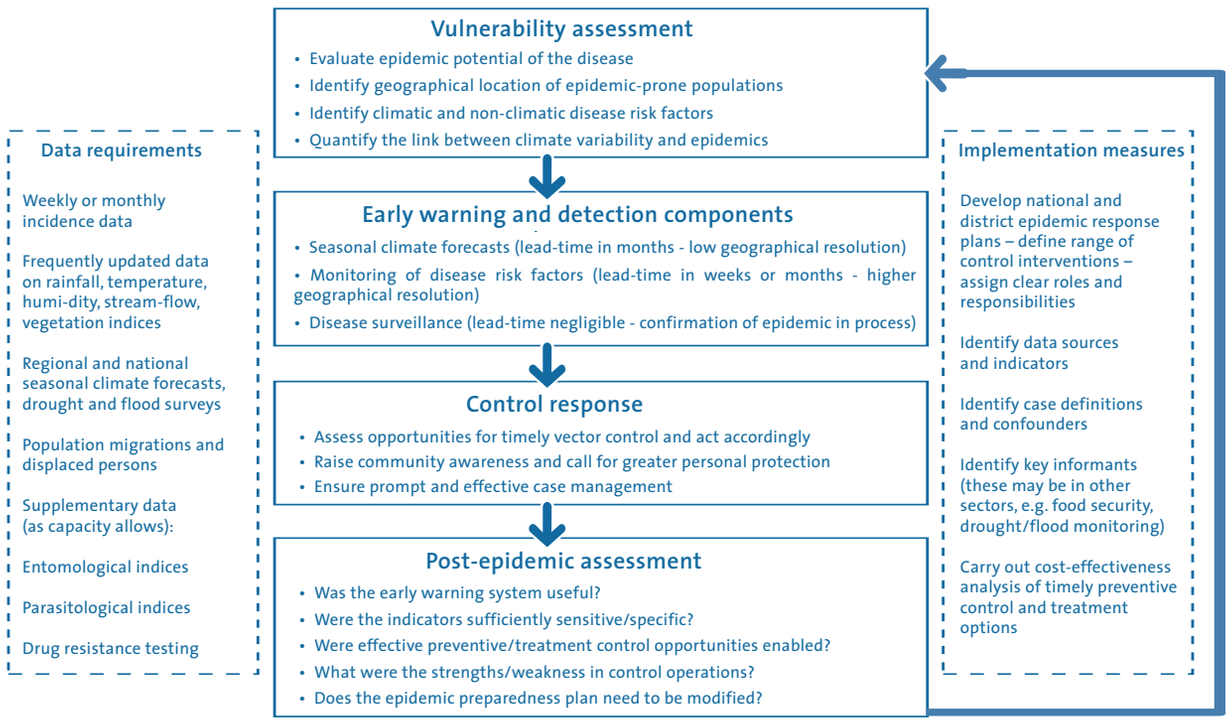

FIGURE 2: FRAMEWORK FOR DEVELOPING EARLY WARNING SYSTEMS FOR CLIMATE SENSITIVE DISEASES

3.1 Preliminary phases

3.1.1 Evaluating potential for epidemic transmission

An early warning system for an infectious disease should be developed only if the disease is epidemic-prone. An epidemic is defined by Last (2001) as:

the occurrence in a community or region of cases of an illness, specific health-related behaviour, or other health-related events clearly in excess of normal expectancy. The community or region and the period in which the cases occur are specified precisely. The number of cases indicating the presence of an epidemic varies according to the agent, size, and type of population exposed; previous experience or lack of exposure to the disease; and time and place of occurrence.

The term "outbreak" is also commonly used, and is defined by Last (2001) as "an epidemic limited to localized increase in the incidence of a disease, e.g. in a village, town or closed institution".

If it is assumed that outbreaks and epidemics differ only in the scale of their effects and not in their etiology, the concept of climate-based EWS will, in theory, be equally applicable to both.

In practice, however, because of the increased impact of local effects and random noise in the analysis of outbreaks in small areas (e.g. in particular villages), climate-supported EWS are most likely to be effective when the outbreaks occur in relatively larger areas (e.g. districts or provinces).

Generally, any disease that exhibits large interannual variability can be considered as epidemic. The transmission of many infectious diseases varies markedly by season. For example, the majority of influenza outbreaks in the northern hemisphere occur in mid- to late winter (WHO, 2000), whereas, even in areas where transmission is relatively stable, a peak in malaria transmission generally follows periods of heavy rain (Macdonald, 1957). Where disease is present in an area, fluctuations in its incidence are considered epidemics only if the number of cases exceeds a certain threshold. A variety of epidemic detection thresholds have been used in the past (e.g. WHO, 2004a), with different thresholds offering different advantages and disadvantages depending on the disease being considered and the nature of variability in its transmission (many algorithms are really only suitable for relatively rare events and their use in other contexts is questionable). Probably the most commonly used definition of an outbreak is a situation where reported disease cases exceed a threshold of 1.96 multiplied by the standard deviation of the mean for at least 2 weeks (Snacken et al., 1992). For influenza, the duration of an epidemic has also been defined as the number of weeks when virus has been isolated from at least 10% of samples (Snacken et al., 1992). In all cases, an epidemic is defined best by examining continuous long-term datasets; therefore setting up surveillance centres is an important preliminary requirement.

3.1.2 Identifying the geographical location of epidemic areas

Even if an infectious disease is widespread throughout a country or an entire region, geographically the risk of an epidemic is not equal at all locations and will reflect, inter alia, the distribution and behaviour of disease vectors and hosts. Geographical variation in risk of epidemics is widely acknowledged, but epidemic-prone areas are seldom defined formally. This is partly a result of the difficulties in defining epidemics, and partly of the lack of long-term surveillance data and the changing epidemiology of diseases over time. For example, malaria transmission in many lowland areas of Africa is often characterized as holoendemic, with year-round transmission, while neighbouring regions at higher altitude are considered to be epidemic-prone. In these areas, environmental conditions (presumably temperature) are on average less favourable, and transmission occurs in the form of epidemics only on occasions when changes in environmental conditions and/or population immunity create permissive conditions. However, the difficulties in characterization have been demonstrated by a study by Hay et al. (2002a) who found no evidence of greater instability in transmission in three study sites with altitudes over 1600 m, than occurred in low altitude areas.

When testing research hypotheses it is important to apply consistent definitions in order to identify epidemic areas. Conversely, in efforts to improve public health this may be less important than consideration of whether the pattern of transmission in a particular area is sufficiently different to require a qualitatively distinct type of operational response.

3.1.3 Identifying climatic and non-climatic disease risk factors

Also known as risk assessment or modelling, the phase of identifying climatic and non-climatic disease risk factors provides vital input to EWS development. Numerous studies have been undertaken to identify environmental risk factors, including climate (see section 5).

There are two principal approaches to modelling: statistical and biological. Statistical models are used to determine the direct statistical correlations between predictor variables (e.g. climate) and the outcome of interest (e.g. disease incidence). Biological models attempt to provide a mechanistic process in which the effects of climate on the population dynamics of pathogens and vectors are represented. The majority of past studies have used statistical modelling of locality-specific historical disease measures and/or vector distributions. Biological models potentially offer greater insights into the mechanisms driving variation in disease incidence, but require a more extensive understanding of the effects of climate on all aspects of pathogen and vector dynamics. As a result, such models have rarely been applied (e.g. Randolph & Rogers, 1997).

Whichever modelling approach is used, it is important to take non-climatic factors into account. These include indicators of the vulnerability of populations to disease outbreaks such as (in the case of malaria) low immunity, high prevalence of HIV, malnutrition, drug and insecticide resistance (WHO, 2001). Failure to incorporate such influences can lead either to variation in disease incidence being incorrectly attributed to climate effects and/or to poor predictive accuracy.

3.1.4 Quantifying the link between climate variability and disease outbreaks: constructing predictive models

The relationship between disease incidence and the climate factors identified in section 3.1.3 can be quantified in a statistical or biological model which may subsequently form the basis for future predictions of disease outbreaks. Before modelling can be initiated, however, it is necessary to ensure that both disease and explanatory data are available at appropriate spatial and temporal resolutions and for a sufficient time-frame.

Climate data for use in EWS are available in two basic forms: direct, ground-based measurements and surrogate measures derived by remote sensing. Ground-based data are usually measured at standard synoptic weather stations. Such data have the advantage of being accurate, direct measurements of meteorological conditions – but will be representative only of a small area in the vicinity of the station itself. If the area of interest does not contain meteorological stations, the use of ground-based data depends on appropriate extrapolation methods being applied to the data.

The use of satellite remote sensing data obviates the need for interpolation, as measurements are taken repeatedly for all locations. Raw remote sensing data can be transformed to provide a number of indices that constitute proxies for standard meteorological variables (Hay et al., 1996; Hay & Lennon, 1999). Since 1981, data from the Advanced Very High Resolution Radiometer (AVHRR) sensor on board National Oceanic and Atmospheric Administration (NOAA) satellites, for example, have provided daily estimates of land surface temperature (LST), and vegetation status

(greenness), typically at a spatial resolution of 8 km. A more recent sensor, NASA's Moderate Resolution Imaging Spectroradiometer (MODIS) also provides information on LST and vegetation status, but at a much improved spatial resolution (250–1000 m). For rainfall, Meteosat, a geostationary satellite operated by the European Organisation for the Exploitation of Meteorological Satellites (EUMETSAT), provides information on cloud-top temperatures that has been used to construct a proxy variable for rainfall (cold cloud duration or CCD). For Africa, NOAA's Climate Prediction Center (CPC) produces 10-day rainfall estimates (RFE) based on a combination of CCD, interpolated ground-measurements, orographical models and, more recently, inputs from microwave sensors. RFE and Normalized Difference Vegetation Index (NDVI) data are disseminated free of charge through the Africa Data Dissemination Service.[1] Software for extracting and analysing these data for specific localities (WinDisp) is also available as freeware. CCD data go back to 1988, although CPC rainfall estimates are available only from 1995.

Satellite-derived climate information is increasingly accessible, and can be combined with other sources of epidemiological data to provide information that is directly relevant to disease control services. For example, near real-time data on rainfall anomalies can be overlaid on maps of zones with malaria epidemic potential, to provide rapid identification of areas at elevated risk of malaria (Figure 3).

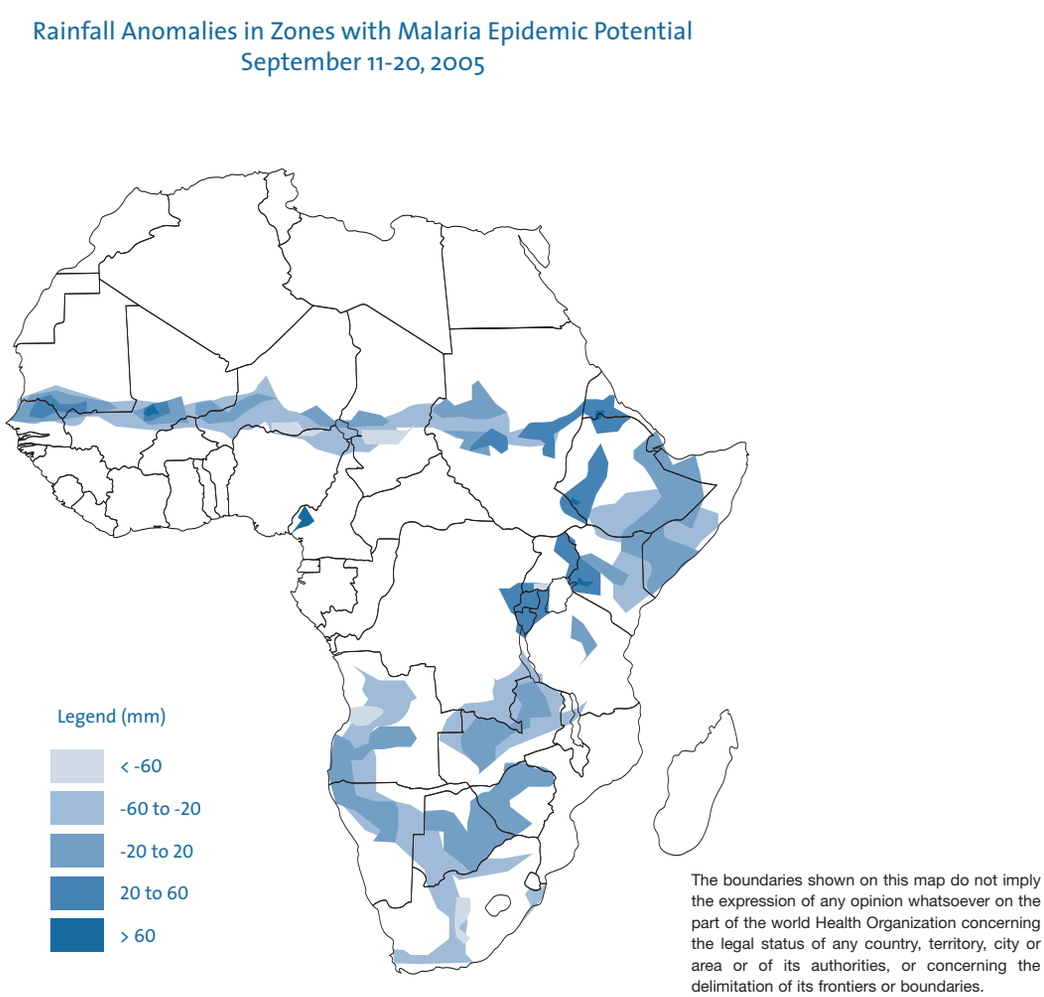

FIGURE 3: REDRAWN FROM INTERACTIVE, NEAR REAL-TIME (UPDATED EVERY 10 DAY) MAPS DESCRIBING RAINFALL ANOMALIES OVERLAID ON ZONES WITH MALARIA EPIDEMIC POTENTIAL IN AFRICA; AVAILABLE AT: HTTP://IGSKMNCNWB015.CR.USGS.GOV/ADDS/

[1]http://igskmncnwb015.cr.usgs.gov/adds/index.php

The analytical process involved in quantifying climate–disease links can be separated into five main steps:

1. Fitting trend lines and sine–cosine waves (or similar) to remove long-term trends and potentially non-climatic seasonal variation from outcome and predictor variables.
2. Testing, by parametric or non-parametric means, for correlations between climate variability and variability in the outcome variable.
3. Using cross-validation techniques to test the robustness of the model.
4. Using the derived equations to make predictions for subsequent time points not included in the original model.
5. Measuring levels of agreement between predictors and outcomes.

Numerous attempts have been made to quantify the relationship between climate parameters and the occurrence of infectious diseases and/or their vectors in order to predict geographical and temporal patterns of disease (see sections 2 and 5). Although many of these predictions allow us to map disease and vector ranges, the majority are not EWS, either because they aim to make spatial rather than temporal predictions (i.e. predict disease rates in locations that have not previously been surveyed), or because they are used to explore possible effects of long-term changes in climate over decades, rather than during the next few weeks or months.

The specific analytical methods and the associated measures of accuracy used for EWS depend on the specific purpose. For example, one major aim of EWS is to predict the likelihood of an epidemic (i.e. whether a pre-defined threshold of incidence will be exceeded). For this purpose it is appropriate to use techniques for predicting a binary outcome, such as logistic regression or discriminant analysis, with climatic and non-climatic data as the predictor variables and the occurrence or non-occurrence of an epidemic as the outcome. Various measurements can be used to assess different aspects of predictive accuracy. For example, overall accuracy may be assessed using kappa statistics, a measure of increased predictive accuracy above that expected by chance alone (Brooker et al., 2002). Other measures may be more directly relevant to control decisions; these include the overall proportion of correct predictions, the sensitivity (proportion of epidemics correctly predicted), specificity (proportion of non-epidemics correctly predicted), positive predictive value (proportion of predictions of an epidemic that were correct) and negative predictive value (proportion of predictions of non-epidemics that were correct).

Another major aim of an early warning system is to predict the size of an impending epidemic. In this case, it is appropriate to use regression techniques with a continuous outcome, such as traditional linear and non-linear regression, or more complex regression techniques such as ARIMA (autoregressive-moving average) models that incorporate trends and temporal autocorrelation into a single model. In this case, predictive accuracy can be represented by comparing the magnitude of the observed with that of the predicted epidemic, using the root mean square error, or as the proportion of variance in case numbers explained by the predictive model (e.g. Abeku et al., 2002; Thomson et al., 2005).

Cross-validation techniques can be used to assess the robustness of the fitted model, but in all cases, the accuracy of predictions produced by the model should be assessed against independent data (i.e. data not included in the original model- building process) to give an accurate replication of an attempt to predict a future epidemic. Using the same data both to build and test a model will tend to exaggerate its predictive accuracy.

3.2 Early warning systems

In many cases the term “early warning” may be confined to the information that can be obtained from climate and environmental monitoring alone. For this report we adopt a more inclusive definition of early warning which includes both active disease surveillance for the early detection of epidemics and a defined system of epidemic response (or, more specifically, a set of pre-determined responses which are linked explicitly to warnings generated by the EWS).

3.2.1 Disease surveillance

Disease surveillance provides a means of monitoring disease incidence over time and, depending on the nature of the system, may be an appropriate instrument for detecting unusual patterns among incidence data. Surveillance provides a means of detecting rather than predicting the

onset of an epidemic (there is therefore no lead-time as such). However, disease surveillance may be considered to provide early warning of an epidemic when collected and analysed routinely on a weekly basis, because crossing an epidemic threshold may provide 2–4 weeks warning of the peak of the epidemic. In this way a properly designed surveillance system should bring forward significantly the point of intervention, thereby increasing the chances of such intervention assisting in disease control. As a means of validating disease predictions produced by climate-based models, surveillance data constitute an integral part of any fully-fledged early warning system. In most cases, the existence of accurate, validated predictive models depends on the availability of historical surveillance data.

An important first step in EWS development at the national level is to assess current approaches to disease surveillance and the quality, quantity and completeness of associated disease data. In many cases – and especially for diseases that are subject to compulsory notification in well-resourced health systems – existing disease data may be suitable for model development and the system itself quite appropriate for early detection of an epidemic. In other situations, existing systems may need extensive modification, either in the way in which disease data are collected (e.g. diagnostics), or in the manner in which data from individual health facilities are collected, aggregated and communicated to higher levels in the health system. Standard health management information system (HMIS) data, for example, commonly aggregate data from individual facilities to the extent that localized disease outbreaks may be obscured. Many standard surveillance approaches may also lack sufficient temporal resolution for the detection of epidemics, especially where data are reported monthly.

Where appropriate disease surveillance systems are in place, tracking disease incidence on a weekly basis with reference to expected normal levels of incidence can indicate the onset of an epidemic and (where surveillance data include information on the location of cases) provide information about its geographical extent. However, aberrations in surveillance data indicating abnormal levels of disease transmission should be investigated before large-scale interventions aimed at epidemic control are implemented. Such aberrations may constitute artefacts within the surveillance system (e.g. resulting from changes in diagnostic practices or shifts in the levels of usage of individual health facilities by the general public) and may not reflect changes in levels of disease transmission. It should also be borne in mind that there is no single, standard approach available for detecting aberrations (i.e. outbreaks) on the basis of surveillance data. A number of detection algorithms have been proposed (for example, Abeku, 2002; Hay et al. 2003; Teklehaimanot et al., 2004a) and the sensitivity and specificity of each will vary depending on the nature of the temporal distribution of cases associated with each disease type. Similarly, a number of concerns regarding how best to construct a “reference” disease baseline require further exploration, on a case-by-case basis. For example, what is the minimum number of years of data required to develop a reliable baseline? Should the baseline lengthen with each year of new data, or should older data be discarded? Should data from known epidemic years be omitted from the baseline calculation? These and other issues await further clarification through empirical field-testing (Abeku et al., 2004a).

3.2.2 Monitoring disease risk factors

As described in section 1.2, a range of weather-monitoring datasets is available from earth observation satellites. These (and basic software for the display and extraction of data) are available free of charge but funds may need to be secured for purchasing the GIS software capable of more advanced geographical processes and analysis.

At this stage it is also important to assess vulnerability indicators such as herd immunity, prevalence of HIV, malnutrition and drug resistance. As will be discussed below, these are difficult to monitor accurately, as this would require a large staff and well-organized surveillance systems.

There are several vector-related risk factors for vector-borne diseases. These include local vector species composition and the human blood index (i.e. the tendency to bite humans). It has been suggested that data from monitoring vector densities may be sufficient to forecast changes in malaria transmission (Lindblade et al., 2000), with densities exceeding an “epidemic threshold” indicating a potential epidemic. Alternatively, measures of intensity of malaria transmission such as the entomological inoculation rate (EIR – the product of the infection rate in vectors and the biting rate on humans) have been used to assess spatial variation in risk of malaria transmission in Africa (Snow et al., 1999; Hay et al., 2000b) and could theoretically be monitored as indicators of potential epidemics. Unfortunately, in most cases, monitoring both EIR and vector densities is too expensive to be feasible (Thomson & Connor, 2001). In addition, the quantitative relationships

between these variables and the probability and intensity of epidemics are still at the research stage. To our knowledge, there are no published examples of such a system being put into operation.

3.2.3 Model forecasts

Modelled disease forecasts can be based on relationships between disease and correlated variables to predict risk in both surveyed and unsurveyed areas. Inputs for such predictions can come from either direct monitoring of known risk factors (e.g. using rainfall measurements in one month to predict the probability of an epidemic of mosquito-borne disease in the next few months) or forecasting based on predictions of these risk factors (i.e. seasonal climate forecasts). The choice will depend on the relative importance of accuracy (usually maximized by using direct observations of risk factors) and lead-time (maximized by predictions of risk factors).

Likely predictor climatic variables include temperature, rainfall and the El Niño Southern Oscillation (ENSO), data on all of which are readily available. Climate-based predictions of disease variability require projections of climate events. It is possible to predict weather relatively accurately up to a week ahead using complex atmospheric models (Palmer & Anderson, 1994). In some regions and under some existing climate conditions, climatic conditions can be predicted for up to several months ahead (from similar models). In particular, there has been considerable interest in predicting the interannual variations of the atmosphere–ocean system, such as the onset, development and breakdown of the ENSO. ENSO is a periodic appearance of warm and cool sea surface water in the central and eastern Pacific Ocean (Wang et al., 1999). ENSO events are associated with an increased probability of drought in some areas and excess rainfall in others, together with temperature increases in many regions. In the tropics, variability in the ocean-atmosphere associated with ENSO can be predicted with a lead-time of several seasons (Palmer and Anderson, 1994). In Asia and South American regions, there is evidence that ENSO events have an intensifying effect on seasonal transmission of malaria, including epidemics (Kovats et al., 2003).

The first successful computer models of the atmosphere–ocean interactions associated with ENSO were developed in the 1980s. Since that time increasingly sophisticated and realistic computer models have been developed in support of seasonal climate prediction. Seasonal forecasts of some of these climate variables are available for specific regions of the world.[2] Forecast lead-times vary for different climate parameters, from 1 to 4 months for rainfall in Africa to a year or more for the strength of an ENSO event. Although these forecasts allow relatively long potential lead-times, which can be particularly useful for gathering the resources necessary for control measures, forecasting climate introduces an additional source of uncertainty into the prediction of epidemics. In addition, climate forecasts are not available for all regions and seasons and their low spatial resolution means that any epidemic warnings generated will be on a relatively coarse geographical scale.

The EWS options presented above demonstrate a trade-off between warning time and specificity. In each case, the precision of predictions depends on how disease and climate indicators are selected – are they long-term projections or short-term active observations? The important question of whether predictions should be relatively general one-year forecasts or more precise predictions for the following week depends mostly on the public health requirements. It has been suggested that epidemic forecasting is most useful to health services when case numbers are predicted two to six months ahead, allowing time for tactical decision-making (Myers et al., 2000).

The hierarchical systems proposed below for malaria EWS in Africa (Cox et al., 1999; WHO, 2001) take account of all the different ranges of forecasts which can be developed to suit the various needs of the health sector:

[2]e.g. NOAA Climate Prediction Center information at http://www.cpc.ncep.noaa.gov/products

Assessments of population vulnerability to potential epidemics.

- Long-range predictions of epidemic risk based on seasonal climate forecasts. The resulting risk assessments will cover wide areas and typically have lead-times between four and nine months. Such forecasts are relevant only in certain regions and in certain seasons.
- Short-range predictions of changes in epidemic risk based on active monitoring of risk factors (e.g. temperature and rainfall). Geographical resolution is much more specific and lead-times can be measured in weeks rather than months.
- Early detection of epidemics using disease surveillance. There is no lead-time for the onset of an epidemic per se, but this approach provides specific information on timing and location of an epidemic.

3.3 Response phase

Appropriate forms of response to an epidemic will be geographically and disease-specific and may consist of either chemo-therapeutic or vector control measures, or a combination of both. Ultimately, responsibility for organizing relief or other measures necessary to contain an epidemic lies with national governments or nongovernmental bodies. Ideally the response to an epidemic warning should follow a preparedness plan that has been developed through an integrated multisectoral approach (FEWS, 2000). The majority of outbreaks of infectious disease occur in developing countries where national financial, material and human resources are (usually) extremely limited. An effective response may therefore require the extensive involvement of international organizations.

3.4 Assessment/evaluation phase

After the onset of an epidemic (preferably during the response phase), the early warning system should be evaluated technically in consultation with end-users. Questions that need to be addressed include the following:

- How easy is the system to use?
- Are the predictions accurate enough to make a useful contribution to planning responses to the disease? (See below.)
- Is the system cost-effective and could resources have been used more effectively?

Despite many attempts to develop EWS for infectious diseases (and other areas), to our knowledge there are no generally agreed criteria or practical guidelines for assessing the accuracy of EWS. This report suggests the development of flexible rather than prescriptive guidelines for determining appropriate measures and acceptable levels of predictive accuracy, as these are likely to vary between diseases and situations. In all cases, early communication between researchers and end-users should increase the chances that the early warning system is both sufficiently accurate and timely to improve control decisions.

There are two separate principal aims of an early warning system:

1. To identify whether an epidemic will occur within a specific population, according to a pre-defined threshold of cases.

2. To predict the number of cases that will occur within a defined period of time.

The relative importance of the two aims will depend on the control decisions to be taken and the degree of interannual variation in disease. For example, for diseases which are absent from the human population for long periods and then occur in explosive epidemics, early detection and/or predictions of the probability of an epidemic may be more important than predictions of epidemic size. Assessments should be performed as “value-of-information” assessments; i.e. it should be determined whether collection and analysis of climate data adds sufficient predictive power, or if allocating the funds to collection of other information has a greater effect on predictive power.

4. IDENTIFYING CANDIDATE DISEASES FOR EARLY WARNING SYSTEMS

As described in the preceding sections, a number of preliminary steps are necessary to assess the viability of climate-based EWS for a given disease. Table 2 has been constructed by following each of the preliminary steps presented in the framework proposed above. It comprises a list of the most important infectious diseases, using the global burden of disease classification system, in descending order of number of disability-adjusted life years (DALYs) lost annually (WHO, 2004b). Each disease has been assessed for inclusion in this review according to its associated disease burden, evidence of interannual variability and climate sensitivity.

Table 2 indicates that the evidence for climate sensitivity of a range of epidemic-prone infectious diseases varies both in terms of the number of studies undertaken and the rigour with which apparent associations have been tested. While many relationships between climate and disease have been well investigated, some apparent links still lack solid statistical support. On the basis of the evidence presented in the table, the following diseases have been selected for further examination in this report:

- cholera
- malaria
- meningococcal meningitis
- dengue/dengue haemorrhagic fever (DHF)
- yellow fever
- Japanese (JE) and St Louis encephalitis (SLE)
- rift valley fever (RVF)
- leishmaniasis
- African trypanosomiasis
- West Nile virus (WNV)
- Murray Valley encephalitis (MVE) and Ross River virus (RRV).
- Influenza

Other diseases are not considered here, either because they have relatively weak interannual variability (including non-cholera diarrhoea, intestinal nematode infections, schistosomiasis, lymphatic filariasis, Chagas disease and Lyme disease), or because their interannual variability is unlikely to be strongly related to climate (the various directly transmitted diseases grouped together as ”childhood cluster”, sexually transmitted diseases and tuberculosis). Further details on reasons for inclusion are given in (WHO, 2004c).

TABLE 2: COMMON COMMUNICABLE DISEASES, THEIR DISTRIBUTION, EPIDEMIC POTENTIAL AND SENSITIVITY TO CLIMATE

Disease	Global burden (1000 DALYs)	Transmission	Distribution	Evidence for interannual variability	Climate–epidemic link	Strength of temporal climate sensitivity	Climate–epidemic relationship quantified?
STDs (including HIV)	95 805	Sexually transmitted	Worldwide	*	No published evidence for climate link.	–	✗
Influenza	94 603 (all respiratory infections – only a fraction due to influenza)	Air-borne transmission	Worldwide	* * * * *	Decreases in temperature (winter) associated with epidemics. A range of human-related factors are more significant.	++	✓
Diarrhoeal diseases	61 966 (incl. cholera)	Food- and water-borne transmission	Worldwide	* * *	Increases in temperature and decreases in rainfall associated with epidemics. Sanitation and human behaviour are probably more important.	++	✗
Cholera	(see diarrhoeal diseases)	Food- and water-borne transmission	Africa, Asia, Russian Federation South America	* * * * *	Increases in sea and air temperatures as well as El Niño events associated with epidemics. Sanitation and human behaviour are also important.	+++++	✓
Childhood diseases	41 480	Transmitted by person-to-person contact	Worldwide	* * * *	No published evidence for climate link.	–	✗
Malaria	46 486	Transmitted by the bite of female *Anopheles* mosquitoes	Currently endemic in > 100 countries throughout the tropics and subtropics and some temperate areas	* * * * *	Changes in temperature and rainfall associated with epidemics. Many other locally relevant factors including vector characteristics, immunity, population movements, drug resistance, environmental changes etc.	+++++	✓
Tuberculosis	34 736	Air-borne transmission	Worldwide	* *	No published evidence for climate link.	–	✗

Disease	Global burden (1000 DALYs)	Transmission	Distribution	Evidence for interannual variability	Climate–epidemic link	Strength of temporal climate sensitivity	Climate–epidemic relationship quantified?
Meningococcal meningitis	6 192 (all meningitis)	Air-borne transmission	Worldwide	* * * *	Increases in temperature and decreases in humidity associated with epidemics.	+++	✓
Lymphatic filariasis	5 777	Transmitted by the bite of female *Culex, Anopheles, Aedes* and *Mansonia* mosquitoes	Africa, India, South America, South Asia and Pacific Islands	–	Temperature and rainfall determine the geographical distribution of vectors and disease.	++	✗
Intestinal nematodes	2 951	Soil and faecal–oral route transmission	Worldwide	–	Increases in temperature and soil humidity and changes in soil type can affect transmission and geographical distribution.	+	✗
Leishmaniasis	2 090	Transmitted by the bite of female phlebotomine sand flies	Africa, central Asia, Europe, India, South America	* *	Increases in temperature and rainfall associated with epidemics.	+++	✗
Schistosomiasis	1 702	Water-borne transmission involving intermediate snail host	Africa, east Asia, South America	*	Increases in temperature and rainfall can affect seasonal transmission and geographical distribution.	+	✗
African trypanosomiasis	1 525	Transmitted by the bite of male and female tsetse flies, *Glossina* spp.	Sub-Saharan Africa	* * *	Changes in temperature and rainfall may be linked to epidemics. Cattle density and vegetation patterns also are relevant factors.	++	✗
Trachoma	2 329	Transmitted by person-to-person contact and flies	Africa, Asia, east Europe, South America	–	Flies (especially *Musca sorbens*) are important for transmission in many parts of the world. *M. sorbens* has an optimal temperature and humidity range.	–	✗

Disease	Global burden (1000 DALYs)	Transmission	Distribution	Evidence for interannual variability	Climate–epidemic link	Strength of temporal climate sensitivity	Climate–epidemic relationship quantified?
Onchocerciasis	484	Transmitted by female simuliid blackflies	Africa, south-west Asia, South America	*	Evidence for climate effects on spatial distribution and seasonal vector biting rates, but not temporal variation in disease.	–	✗
Chagas disease (American trypanosomiasis)	667	Transmitted by blood-feeding male and female reduviid bugs	South and central America	*	Presence of bugs associated with high temperatures, low humidity and specific vegetation types.	+	✗
Dengue	616	Transmitted by the bite of female *Aedes* mosquitoes	Africa, Europe, South America, south-east Asia, western Pacific	* * * *	High temperature, humidity and rainfall associated with epidemics in some areas. Non-climatic factors also have an important impact.	+++	✓
Japanese encephalitis	709	Transmitted by the bite of female *Culex* and *Aedes* mosquitoes	South-east Asia	* * *	High temperature and heavy rains associated with epidemics. Reservoir animal factors are also important.	+++	✗
St Louis encephalitis	NA	Transmitted by the bite of female *Culex* and *Aedes* mosquitoes	North and South America	* * *	High temperature and heavy rain associated with epidemic. Reservoir animal factors are also important.	+++	✓
Rift Valley fever	unquantified	Transmitted by the bite of female culicine mosquitoes	Sub-Saharan Africa	* * *	Heavy rains associated with onset of epidemic. Cold weather associated with end of epidemic. Reservoir animal factors are also important.	+++	✓
West Nile virus	unquantified	Transmitted by the bite of female culicine mosquitoes	Africa, central Asia, south-west Asia, Europe	* * *	High temperatures and heavy precipitation associated with onset of epidemic.Non-climatic factors may have more important impact.	++	✗

Disease	Global burden (1000 DALYs)	Transmission	Distribution	Evidence for interannual variability	Climate–epidemic link	Strength of temporal climate sensitivity	Climate–epidemic relationship quantified?
Ross River virus	unquantified	Transmitted by the bite of female culicine mosquitoes	Australia and Pacific islands	* *	High temperature and heavy precipitation associated with onset of epidemic. Host immune factors and reservoir animals are also important factors.	+++	✓
Murray Valley fever	unquantified	Transmitted by the bite of female *Culex* mosquitoes	Australia	* *	Heavy rains and below average atmospheric pressure associated with epidemics.	+++	✓
Lyme disease	unquantified	Transmitted by ixodid ticks	Asia, Europe and North America	*	Temperature and vegetation patterns associated with distribution of vectors and disease.	+	✗
Yellow fever	unquantified	Transmitted by the bite of female *Aedes* and *Haemagogus* mosquitoes	Africa, South and central America	* * * *	High temperature and heavy rain associated with epidemic. Intrinsic population factors are also important.	++	✗

[a] Estimates for 2002: source WHO (2004b).

* very weak variability;
* * some variability;
* * * moderate variability;
* * * * strong variability;
* * * * * very strong variability.

+ climate link is very weak;
++ climate plays a moderate role;
+++ climate plays a significant role;
++++climate is an important factor;
+++++climate is the primary factor in determining at least some epidemics, and the strength of the association between climate and disease outbreaks has been assessed on the basis of published quantitative (statistical) rather than anecdotal evidence.

5. CLIMATE-BASED EARLY WARNING SYSTEMS FOR INFECTIOUS DISEASES

This section presents an overview of the diseases highlighted in section 4 with respect to their climate sensitivity and the existence of or potential for the development of EWS following the framework previously presented. On the basis of a literature review, each disease is assessed according to the progress made – i.e. which steps of the proposed framework have so far been completed successfully.

5.1 Cholera

Cholera is a bacterial infection that causes both local outbreaks and worldwide pandemics, of which the current, and longest-running, began in 1961 (Colwell & Patz, 1998). Regional epidemics occur seasonally and are associated with periods of excessive rainfall, warm temperatures and increases in plankton populations (Colwell & Patz, 1998; Shope, 1991; Lipp et al., 2002).

The strong, well-studied link between cholera epidemics and fluctuations in climate, suggests that there is potential for constructing climate-based EWS for this disease. Cholera was the first disease for which surveillance and reporting was initiated on a large scale (WHO, 2000). Due to its high impact (Table 2) it is one of three diseases currently reportable under the International Health Regulations (IHR) of 1969, which state that the first cases of cholera (both indigenous and imported) should be reported to WHO within 24 hours. Weekly notifications of these reports are published in WHO's Weekly Epidemiological Records which are freely available.3 Annual numbers of cases and the number of deaths reported to WHO (with substantial gaps) are available for Africa, the Americas and Europe from 1970 onwards and for Asia from 1949. In 1998, 74 countries reported annual figures for cholera cases and deaths.

It has been suggested that epidemics of cholera might be predicted by monitoring or forecasting the seasonal abundance of zooplankton in aquatic environments using remotely sensed vegetation images (Colwell, 1996; Lobitz et al., 2000). Colwell (1996) suggested a positive relationship between the monthly abundance of *Vibrio cholerae* and the abundance of copepods in ponds in Bangladesh and presented graphical evidence that cholera cases occurred following rises in sea surface temperature (SST). Lobitz et al. (2000) used weekly 1-km resolution NOAA AVHRR data for SST and sea surface height (SSH) in combination with weekly cholera cases in Bangladesh and found a significant correlation between cycles of cholera cases and SST during 1992, 1994 and 1995, but did not attempt to construct a predictive model.

In the last few years, several studies have been undertaken that could form the basis of future operational EWS. Studies have shown correlations between climatic and other environmental conditions and the presence of *V. cholerae* in North American waters (Louis et al., 2003), and the incidence of cholera in Peru (Gil et al., 2004). The most detailed analyses are of long climate–cholera time series in Bangladesh. These have demonstrated a link between cholera incidence and the ENSO that has become stronger as the ENSO signal has intensified in recent decades (Rodo et al., 2002). More recently, Koelle et al. (2005) explicitly measured the separate and interacting contributions of climatic and non-climatic factors A range of climate variables with different lead-times (over seven years, for monsoon rains and Brahmaputra river discharge; less than seven years, for flood extent in Bangladesh, SSTs in the Bay of Bengal and the ENSO) were shown to influence cholera transmission rates. The study also modelled the build-up of herd immunity, resulting in "refractory periods" during which there are relatively few susceptibles in the population, and climate-driven increases in transmission rates do not result in large outbreaks of human disease.

While these studies strengthen the theoretical basis for cholera EWS, there remain several challenges to developing operational decision-support systems in any region. The most important are the need to incorporate real-time monitoring of climate conditions, the maintenance and enhancement of disease surveillance systems which underpin the models of susceptibility, and involvement of disease control personnel to clarify operational conditions (i.e. identifying relevant control decisions, suitable lead-times and accuracy levels, and resource implications). The greatest challenges are in cholera-prone regions in Africa, where the relative weakness in disease surveillance and reporting systems hampers detection and control of cholera epidemics, and as a side-effect, make it difficult to obtain the long-term linked datasets on climate and disease that are necessary to develop EWS.

5.2 Malaria

Malaria is the most important vector-borne disease in the world today, causing more than one million deaths worldwide annually, over 80% of which occur in sub-Saharan Africa (WHO/UNICEF, 2005). It is a disease of tropical and temperate countries between the latitudinal limits of northern Korea and southern Africa with prevalence generally increasing towards the equator. Epidemic malaria is a particular cause for concern and affects all age groups among immunologically vulnerable populations (Kiszewski & Teklehaimanot, 2004). It is estimated that epidemic malaria may cause 12–25% of malaria deaths worldwide (Worrall et al., 2004).

Outbreaks often occur following periods of increased rain and/or temperature. It is thought that this is primarily the result of positive effects on vector breeding (e.g Kilian et al., 1999), development rates (e.g Jetten & Takken, 1994), parasite sporogony and vector survival (MacDonald, 1957) and ultimately EIRs. The impact of epidemics is particularly severe when they follow prolonged periods of drought and famine.

The early detection, containment and prevention of malaria epidemics constitutes one of the four main elements of WHO's global malaria control strategy.[4] During the past 20 years, a few countries have begun to develop EWS which use climatic indicators of transmission risk. Progress towards operational systems has been limited, however, because of poor intersectoral collaboration and lack of evidence of the cost-effectiveness of malaria EWS. WHO has supported the development of malaria EWS by establishing a technical support network together with a framework that defines generic concepts, identifies early warning and detection indicators with the potential to predict the timing and severity of malaria epidemics, and outlines how these can be related to control decisions (WHO, 2001; WHO, 2002; WHO, 2004a).

Quantitative spatial models of the relationship between malaria and climatic factors have often been used for geographical mapping of disease risk, with an overwhelming focus on Africa (e.g. Craig et al., 1999; Snow et al., 1999; Kleinschmidt et al., 2000, 2001). Such risk mapping is a useful preliminary stage, as it can be used to differentiate areas that experience epidemic or highly seasonal transmission from those with more stable transmission patterns where EWS are likely to be less useful. It can also be used to explore those areas where predicted global climate change is most likely to be reflected in changing patterns of malaria transmission (Tanser et al., 2003; Thomas et al., 2004).

Monitoring of malaria cases can be used in the early detection of an epidemic if collection and notification are timely (i.e. weekly). There are functioning weekly notification systems from sentinel sites in Kenya, Madagascar, Uganda and Zimbabwe (Cox et al. 1999; WHO 2001). Computerized collection and organization of surveillance of data has begun in Niger and is proposed elsewhere (WHO, 2001). Eight African countries (Eritrea, Ethiopia, Kenya, Mali, Niger, Senegal, Uganda and Zambia) have also included EWS with climate and vulnerability monitoring in their application to the Global Fund to Fight AIDS, Tuberculosis and Malaria. However, in most epidemic regions there is as yet a lack of regular surveillance that could result in an appropriate response.

Disease surveillance for early detection of malaria epidemics has been used in Thailand where deviations from seasonal averages were used to detect outbreaks (i.e. where monthly case numbers exceed the long-term mean plus two standard deviations). This approach detected 228 out of 237 epidemics in 114 districts from 1973–1981 (Cullen et al., 1984). Several studies have tested alternative algorithms for triggering alerts, based either on comparisons with past records or rates of changes in numbers of cases (Abeku et al., 2002; Hay et al., 2002b; Teklehaimanot et al., 2004a; Negash et al., 2005). This work suggests that, in general, relatively simple methods based on departures from the long-term average have an accuracy comparable to or better than more complex measures. These studies are also beginning to clarify the most useful criteria for assessing accuracy, incorporating both sensitivity and specificity (in recognition of the problem of raising false alarms).

For complex emergencies and for settings where no historical data are available for comparison, a "clustering of severe cases and deaths" should raise an alarm. Another method suggested for defining a threshold is a doubling of cases compared to the previous week, adjusted for fluctuations in clinic attendance due to external factors.

As outlined in section 3, early detection of malaria epidemics can potentially be supplemented by prediction. Monitoring data on the various risk factors (e.g. temperature and precipitation measurements from remotely sensed images and ground-based meteorological measurements) can be used as input to mathematical and/or statistical models, based on correlations between

[4] http://www.who.int/malaria

risk factors and disease rates in the past. Currently there are several constraints on the use of this approach for malaria. Firstly there is a paucity of long-term disease datasets for model construction. Those time-series data that are available often consist of clinically-diagnosed rather than laboratory-diagnosed incidence. The most extensive collection of data has been undertaken by the Malaria Risk in Africa (MARA) project, which has established a database for various malariometric indicators in Africa.[5] Elsewhere in Africa – in Botswana, Ethiopia, Kenya, Madagascar, South Africa, Uganda and Zimbabwe – individual studies have collated retrospective data, but large gaps still exist for regions where populations at risk of epidemics are relatively large. Outside Africa, extensive historical datasets (with gaps) are also available for Europe (Kuhn, 2002) and India. However, these datasets lack continuous long time-series at high temporal resolution and therefore have been used principally for mapping geographical variation in risk (e.g. Craig et al., 1999) or investigating relatively long-term trends (Kuhn et al., 2003), rather than for the prediction of epidemics on a seasonal or interannual basis.

In addition, non-climatic risk factors such as population immunity, food security and reductions in control activities are known to have a strong influence on the potential occurrence of an epidemic, but are often hard to quantify (e.g. Thomson & Connor, 2001; Lindblade et al., 2000).

As for cholera, recent research studies have begun to provide a solid theoretical basis for assembling and testing climate-based malaria EWS in many locations in Africa. For example, studies in Ethiopia have demonstrated that malaria epidemics are more common following periods of high minimum temperatures (Abeku et al., 2003), and that the fit of a predictive model was improved by including data on minimum temperature and rainfall over the preceding one to three months, as well as previous incidence of *P. falciparum* infections, to reflect population immunity (Abeku et al., 2004a). Retrospective analysis in Botswana has also demonstrated that the inclusion of both climatic (rainfall and SSTs) and non-climatic variables (occurrence of control policy interventions) improve the fit of a model for interannual variations in log malaria incidence (Thomson et al., 2005).

These types of analyses have been used to test the potential accuracy and public health benefits of EWS. Studies in the Ethiopian highlands have shown that a prediction algorithm based on biologically plausible relationships between temperature and rainfall data and malaria has a performance comparable to that of systems based entirely on early detection of changing patterns of cases, with a slight reduction in predictive accuracy offsetting longer lead-times (Teklehaimanot et al. 2004b,c). These studies highlight the variations in the effectiveness of the models between districts with different climate characteristics: they are more effective in colder areas.

Advances in the analysis of the effects of climate and other determinants of variations in malaria incidence have prompted more serious consideration of operational feasibility, including the availability and reliability of climate and health surveillance data. Hay et al. (2002b, 2003) reviewed experience with a malaria emergency in four districts in western Kenya in 2002. They concluded that whereas early detection of the epidemic through case monitoring would not have been possible, due to the weakness of the surveillance system, the epidemic could have been predicted on the basis of rainfall data available in the previous month.

Significant relationships between fluctuations of SST (associated with ENSO) and malaria cases or mortality rates have been demonstrated in South America (Barrera et al., 1999; Bouma et al., 1997; Bouma & Dye, 1997; Poveda et al., 2001), Asia (Bouma et al., 1996; Bouma & van der Kaay, 1996) and Africa (Bouma, 2003; Thomson, 2005). These associations offer the possibility of seasonal forecasting in some regions and in some seasons. For example Hay et al. (2003) noted that that seasonal rainfall forecasts were too unreliable to predict an epidemic in Kenya following the main rainy season. However, Thomson et al. (2003) pointed out that although seasonal forecasts for the main Kenyan rainy season have limited skill above that expected by chance, the short rains from October to December are highly predictive, and that seasonal forecasting remains a promising tool for epidemics associated with the short rains, e.g. that which occurred in Wajir, Kenya in 1998 (Brown et al., 1998).

To summarize the situation for malaria; advances in satellite imagery and GIS, including more timely and accessible provision of important environmental data sources, e.g. (Grover-Kopec et al., 2005) should provide sufficient environmental data to build satisfactory models of malaria transmission (Thomson & Connor, 2001; Rogers et al., 2002). High-resolution long-term malaria datasets remain rare, but detailed analyses have now been carried out in a series of locations. These studies have significantly improved our understanding of the relationship between climate variations, other determinants of population vulnerability and malaria epidemics, so that existing

[5]http://www.mara.org.za/

predictive models may be sufficiently accurate and timely for operational use. Several countries (e.g. Botswana and Swaziland) are reported to be using climate indicators to support control decisions on the ground (WHO, 2004a), but these have not been documented in detail.

At the research level, further progress towards accurate predictive models is likely to come from using a wider range of long-term datasets to quantify the links between climatic and non-climatic factors and interannual variability in numbers of malaria cases and/or deaths. Although most easily-accessible datasets have already been investigated, there are non-computerized surveillance records in Africa, Asia and potentially elsewhere, that could add to the evidence base relating variations in climate to malaria incidence.

Additional steps are necessary if the results of research on EWS are to be fully implemented in control activities in the field. As for other diseases, these steps include strengthening of reporting systems to promote early detection of epidemics, and better definition of the control responses that should follow an epidemic warning. For example, it may be important to differentiate between simply scaling up current control activities (Hay et al., 2003), as compared to a qualitatively different response, such as shifting to a different control intervention or treatment regime. Demand-driven approaches, including disease control personnel from the earliest stages, are most likely to result in usable predictions and to be sustainable over time (Abeku et al., 2004b). Operational systems will also need to be sufficiently flexible to take account of both the observed spatial variation in climate–malaria relationships, as well as long-term trends in both mean climate conditions and long-term climate variability, already noted in specific locations in Africa (Hay et al., 2002c; Zhou et al., 2004; Hay et al., 2005; Zhou et al., 2005). They should also use opportunities to share knowledge and, where practical and cost-effective, implement regional programmes across several countries that share similar climate characteristics and vulnerabilities (DaSilva et al., 2004; Thomson et al., 2005). Finally, although the main aim of these systems is to support control decisions on the ground, it is also important to document these approaches fully in the scientific literature, so that both scientific and practical lessons can be learned not only from experience with malaria EWS in different locations, but also from EWS for other infectious diseases.

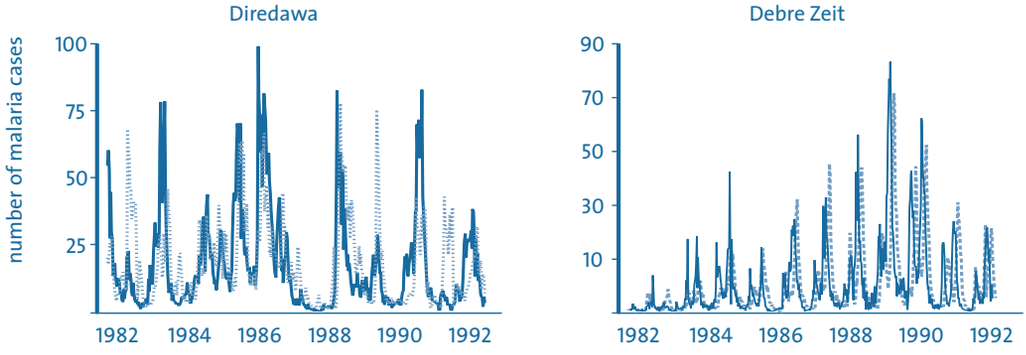

FIGURE 4: OBSERVED (SOLID LINES) AND PREDICTED (DOTTED LINES) NUMBER OF MALARIA CASES IN DIREDAWA (HOT), AND DEBRE ZEIT (COLD) SITES IN ETHIOPIA. FIGURE REPRODUCED WITH PERMISION FROM TEKLEHAIMANOT ET AL. (2004C).

5.3 Meningococcal meningitis

Meningococcal meningitis is an air-borne bacterial disease which shows a highly seasonal and epidemic pattern in sub-Saharan Africa.

There is accumulating evidence that climate, as well as human-related factors, such as vaccination programmes, helps to determine the spatial extent, timing and intensity of meningitis epidemics in situations where outbreaks occur during the hot, dry season and decline when the rainy season begins (Colwell & Patz, 1998; Molesworth et al. 2002).

In 1998, a total of 98 countries regularly reported meningitis cases to WHO (WHO, 2000). Since 1997, countries in the African meningitis belt have undertaken weekly surveillance of disease activity during the meningitis season and have provided total annual case numbers to WHO as input for the International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control. In addition, various nongovernmental organizations in vulnerable areas regularly supply information on meningitis outbreaks.

For modelling purposes, WHO holds non-continuous annual data on meningitis cases from 1966 onwards from reporting countries as well as the (more or less continuous) weekly reports from countries in the African meningitis belt. Although reporting differences mean that the data are not always completely reliable, they do allow testing of potential correlations with climate variables at low resolution.

The association between meningococcal meningitis and climate has been noted since the early 1900s. Low absolute humidity and increasing intensity of the Harmattan wind were correlated with a rise in the numbers of meningococcal meningitis cases during an epidemic in Nigeria (Greenwood et al., 1984), and with more general temporal variability in cases in Benin (Besancenot et al., 1997).

Climate–meningitis links have begun to be investigated in a more systematic manner, to provide information of relevance to control programmes. Cheesbrough et al. (1995) reviewed geographical locations of epidemics and found that outbreaks were concentrated within a zone where absolute humidity remained below 10 g/m^3 throughout the year. These associations have been used to produce maps of areas that are at risk (Molesworth et al., 2002; Molesworth et al., 2003). In addition, a recent study has demonstrated that the onset of meningococcal meningitis epidemics in Mali over the period 1994–2002 was closely correlated with the timing of maximum values of the regional Harmattan wind index. The correlations describe only the timing of the seasonal onset of the epidemics. There is, as yet, no evidence that they can be used to predict either the occurrence or size of the epidemics (Sultan et al., 2005).

Although promising, this study is based on a relatively short time-series, and there is a need to investigate these associations further, possibly using:

- annual data collected worldwide from 1966 onwards; and
- weekly data from the meningitis belt from 1997 onwards, including data from countries other than Mali.

If these analyses continue to support a strong association, this would provide a robust basis for considering operational aspects of an early warning system, in collaboration with local and regional control personnel. As for all other diseases, strengthening of surveillance is essential to further develop and test predictive models and, more importantly, to support control responses.

5.4 Dengue/dengue haemorrhagic fever

Dengue epidemics in urban areas are due to transmission by *Aedes aegypti* and can affect up to 70–80% of the population (Gubler & Trent, 1993). There has been considerable discussion of the development of dengue EWS because of its comparatively high impact in epidemic and endemic areas.

Passive surveillance of dengue and DHF cases is currently undertaken in most endemic countries (Gubler, 1989). The WHO-managed DengueNet is a system for global surveillance of dengue and DHF which collects and analyses case data reported by participating partners. The data can be entered directly and accessed via the Internet.[6]

The quality of data on dengue, and the degree of reporting to the national or international level, varies between countries. For example, in the USA, dengue cases are reported to the Centers for

[6]http://gamapserver.who.int/GlobalAtlas/home.asp

Disease Prevention and Control (CDC) and data distributed by the VECTOR list server (Gubler et al., 2001). Many developing countries report dengue cases, but diagnosis is generally based on clinical criteria only, without serological confirmation. This introduces the possibility of both noise and bias in temporal relationships, as suspect cases may be more likely to be classified as dengue during what is generally considered to be the dengue season, or during a known dengue epidemic. Cases of DHF are much more likely to be serologically confirmed, and data on DHF may therefore be considered as more reliable. There is, however, the additional complication that the chances of developing DHF are strongly influenced by previous exposure to the four dengue virus serotypes (Halstead, 1988). This means that it may be particularly important to include the effects of population immunity together with climatic effects in building a predictive model.

Historically, outbreaks of dengue and DHF have characteristically been associated with the direct and indirect effects of high rainfall as well as elevated temperatures and humidity (Gubler et al., 2001) on pathogen and vector biology. Hales et al. (1999) suggested a positive relationship between monthly dengue incidence and temperature and rainfall in the south Pacific. In contrast, Hay et al. (2000a) analysed monthly time series of DHF in Bangkok together with mean monthly temperature and precipitation and found that the interannual periodicity of dengue was not matched by similar periodic cycles in temperature and rainfall. The authors concluded that intrinsic factors such as population immunity were more likely than climate to be the driving factors behind the epidemics.

A study in Barbados has documented a correlation between the incidence of dengue in a specific parish from 1995–2000, and a range of climate variables, with lags from 7–16 weeks (Depradine & Lovell, 2004). The strongest correlations were with vapour pressure (or absolute humidity, reflecting both temperature and precipitation), consistent with analyses of global patterns of dengue distribution (Hales et al., 2002). The study did not differentiate between climate–disease correlations within the seasonal cycle, and interannual variability, i.e. the ability to predict years with unusually high transmission has not been directly tested.

Two recent studies of DHF in Thailand during the period 1983–1997 demonstrate the complex spatio-temporal dynamics of dengue transmission. Cummings et al. (2004) characterized travelling waves of DHF radiating out from Bangkok, whereas Cazelles et al. (2005) showed a significant, but transient, correlation between El Niño and DHF, that is evident only for the period 1986–1992. Neither study attempted to produce an early warning system, but they make clear that such systems are only likely to have a useful level of accuracy if they take realistic account of both climatic and non-climatic factors, including the time-course of epidemic spread from one region to another, and population immunity (Gubler et al., 2001).

Dengue surveillance data have begun to be used to develop EWS, in some cases in combination with climate information. A relatively basic system, the dengue early warning system (DEWS) is based on a malaria EWS, where simple comparisons of the monthly observed number of cases and the epidemic threshold (mean + 2 SD, as above) provides information on the onset of an epidemic (Cullen et al., 1984). DEWS uses data from Bangkok and the four main regions of Thailand in combination with remotely sensed environmental data to identify vulnerable areas. Forecasts are made on the basis of time-series analysis of past case numbers, but although the model accurately describes historical epidemics, as yet it is unable to describe epidemic cycles (Myers et al., 2000).

A more complicated two-part model has been developed to predict various parameters of the dengue transmission cycle (Focks et al., 1993). The model consists of the Container Inhabiting Mosquito Simulation Model (CIMSiM) (mosquito) and the Dengue Simulation Model (DENSiM) (dengue) and estimates mosquito density and survival as well as the prevalence and incidence of dengue in a human population, according to site-specific variables such as microclimate. Model simulations have been shown to provide a good description of temporal variations in mosquito population dynamics in Bangkok and New Orleans, and of the seasonal pattern of transmission during an epidemic in Honduras (Focks et al., 1993; Focks et al., 1995). This model represents a full biological approach to an early warning system, and requires specific information on a range of parameters such as mosquito breeding, population density, virus serotypes and vertebrate hosts. Such monitoring may be too costly and time consuming for use in developing countries. Also, there has as yet been no attempt to predict deviations from the seasonal pattern (i.e. epidemics).

A version of the model, driven by sea surface temperatures, the El Niño Southern Oscillation Index and previous case numbers, is reported to be in use for epidemic prediction in Indonesia and Viet Nam, but has yet to be fully documented.

Using the extensive dengue database from Puerto Rico, Schreiber (2001) developed a model to predict dengue cases with two-week intervals and a three-week lead-time. The model uses a quantified relationship between dengue cases and daily temperatures, precipitation and water budget to make predictions. Although this approach is promising, the predictive power is very low for epidemic years (the definition of which also is unclear). Additionally, the authors do not indicate whether the assessment was made on independent data (i.e. data not included in the model).

In light of the above, the most important next steps for the establishment of a climate-based dengue early warning system are to:

- properly identify and quantify the relationship between climatic factors and the occurrence of dengue epidemics in vulnerable locations above that explained by other variables; and
- ensure that local surveillance centres are maintained and expanded to facilitate case reporting at regular intervals (weekly or monthly). If possible, active case detection should be employed.

5.5 African trypanosomiasis

African trypanosomiasis (sleeping sickness) is caused by two subspecies of the protozoan parasite *Trypanosoma brucei*, transmitted via the bite of tsetse flies in large areas of sub-Saharan Africa. Infections are fatal if left untreated. During the twentieth century there were three severe epidemics of African trypanosomiasis; the (third began in the 1970s and is still continuing. In endemic countries, systematic population (screening is currently undertaken for the Gambian form of trypanosomiasis (i.e. the nonepidemic (form of disease).

There has recently been much interest in analysing the relationship between spatial patterns of African trypanosomiasis and climatic factors (Rogers, 2000), with particular focus on constructing predictive maps of the distribution and abundance of tsetse flies for future control purposes (e.g. Rogers et al., 1996; Robinson, 1998; Hendrickx et al., 1999). Past studies have suggested a link between temperature and vegetation and the distribution of tsetse flies in Africa (e.g. Brightwell et al., 1992; Rogers & Williams, 1994; Robinson et al., 1997). Rogers (2000) reported a significant correlation between monthly cases of sleeping sickness and Land Surface Temperature LST in Uganda. It is also likely that rainfall patterns may be related to temporal distribution of disease. However, because of the strong association between infections in cattle and humans (e.g. Rogers, 2000; Fevre et al., 2001) and other non-climatic factors such as population movements, deforestation and drug resistance, the exact role of climate in epidemics of sleeping sickness remains unclear.

Although there are extensive national datasets on the annual prevalence of rhodesiense trypanosomiasis in individual African countries, these are not reported automatically to WHO. Generally, these data date back to the beginning of the twentieth century but it is expected that they contain large gaps: in Uganda, for example, no data are available for 1970–1975 (WHO, 2000). In order to assess the quality of these data, it will first be necessary to inspect national databases.

At present there is no clear link between climate and interannual variability in the numbers of cases of sleeping sickness. However, existing WHO and national datasets from the early twentieth century should be used as a basis on which to undertake a rigorous investigation of any potential link between climatic variables, non-climate factors (such as cattle density and environmental modifications) and epidemics of sleeping sickness. The results of such analyses would indicate whether there is any potential to develop and test climate-based warning systems.

5.6 Yellow fever

Yellow fever is a zoonotic viral disease which is transmitted by a variety of mosquito species in forest areas, and by *Aedes aegypti* in urban settings in Africa and South America. There has been a resurgence of yellow fever in Africa in recent decades. There is also increasing concern that the occasional outbreaks of yellow fever from forest sources in South America could lead to more widespread epidemics in the many urban areas where *Aedes* aegypti densities are now very high, and vaccination rates very low (Gubler, 2004).

Yellow fever is reportable to WHO under the International Health Regulations. Annual reports of cases and deaths date back to 1948, although it is thought that only a small proportion of cases are reported (WHO, 2000). In 1998, only 10 out of a total of approximately 40 epidemic countries reported yellow fever cases and deaths to WHO.

Despite the current lack of quantitative evidence to support the role of climate in driving yellow fever epidemics, there is a biologically plausible link supported by some anecdotal evidence. The development of *Aedes aegypti* as well as the extrinsic incubation period of the yellow fever virus is highly dependent on temperature (Shope, 1991) but the importance of temperature fluctuations in the interannual variation of disease is unclear (Reiter, 2001). Vasconcelos et al. (2001) suggested that an increase in temperatures and rainfall in Brazil, may have contributed significantly to the epidemic in 2000. The role of rainfall in yellow fever epidemics remains unquantified, but increases in precipitation are thought to be the principal driving factor behind epidemics by increasing the number of mosquito breeding sites (Reiter, 2001).

The extensive historical dataset could be used to test possible links between climatic conditions and yellow fever outbreaks in a more rigorous manner. Where other potential predictive data are available (e.g. from monitoring mosquito abundances in many affected urban areas of Africa and South America, and infection rates in sylvatic monkeys) they should be included in statistical models.

5.7 Japanese encephalitis and St Louis encephalitis

Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia with 30 000–50 000 cases reported annually.[7] The disease is transmitted by *Culex* mosquitoes among water birds, with pigs acting as amplifying reservoirs, and humans as dead-end hosts.

JE causes severe epidemics which are highly seasonal, occurring during the monsoon season when temperatures reach 30 °C or above (Mellor & Leake, 2000). Rao et al. (2000) observed that the number of cases of JE in India peaked as temperature and rainfall increased, whereas epidemics in China have been shown to be associated with particular phases of the rice cultivation cycle (Okuno et al. 1975).

To date, the only early warning system for JE is based on passive surveillance of human cases which are reported to national reference laboratories in endemic countries. To our knowledge, the most extensive long-term datasets of cases exist in Japan and Thailand (IDSC, 2002). A quantitative model has been developed to predict JE epidemics in Thailand using remotely sensed vegetation, rainfall and temperature (Suwannee et al., 1997). It was estimated that increases in rainfall and temperature, of 10% and 20%, respectively, would increase the expected number of JE cases by 2–5% above the annual mean. However, no attempt was made to predict future interannual variation in JE. Existing long-term datasets on JE from Thailand and Japan could potentially be used to build statistical models to quantify the role of climate. In addition, the efficient monitoring programmes already running in some areas could be expanded to include other endemic countries with less developed programmes (e.g. China and India for JE).

St Louis encephalitis (SLE) is transmitted by *Culex* mosquitoes and normally circulates in wild birds, but also causes occasional outbreaks in humans. Before an SLE epidemic, the number of virus-infected mosquitoes increases through amplification, resulting in a rapid increase in the number of infected birds and humans (Day & Stark, 2000).

Surveillance of SLE in north and South America is part of the CDC arbovirus surveillance programme[8] which consists of monitoring vector abundance, surveillance of sentinel chickens and monitoring of human cases. In Florida, a state-wide sentinel chicken arbovirus surveillance system has been in place since 1978 (Day, 2001). Human cases are detected by active surveillance either weekly or monthly. Bird monitoring is generally considered to be successful in providing warnings a few weeks in advance of an epidemic, sufficient to initiate control responses (Day, 2001).

It has been proposed, however, that certain biotic and abiotic conditions favour early-season virus amplification and transmission. For instance, an increase in temperature favours the development of mosquitoes and virus incubation (Hurlbut, 1973). The 1999 outbreak in New York City occurred during the hottest and driest summer on record (Day, 2001).

Studies in a single county in Florida have also investigated the links between land-surface wetness, and SLE virus infections in chickens (a known marker for SLE virus risk to humans) (Shaman et al., 2004a,b). The analyses demonstrate that SLE virus infection rates measured in chickens are correlated with drought conditions 8–17 weeks earlier (hypothesized to bring vectors and hosts into more frequent contact, amplifying the transmission cycle), and, for some infection measures and time intervals, with high levels of surface wetting (probably associated with high mosquito densities) immediately before the infection measures are taken. These relationships have been used to generate a predictive model based on the 8–17-week lag between drought

[7] http://www.cdc.gov/ncidod/dvbid/jencephalitis/index.htm

[8] http://www.cdc.gov/ncidod/dvbid

conditions and transmission risk, which has been shown to be significantly more accurate than would be expected by chance, when assessed against retrospective data. The forecast probabilities reflect the observed probability of epidemic transmission, and are relatively low, i.e. in the range 0–0.2, suggesting that the model can predict above or below-average risk of a relatively low-probability event, rather than giving a definitive prediction that an epidemic is likely.

The most important next stage is likely to be an evaluation of how the predictions from the climate-based model can be used most efficiently to complement the more accurate but less timely information currently available from bird monitoring.

5.8 Rift Valley fever

Rift Valley fever (RVF) is a zoonotic disease which is transmitted by female culicine mosquitoes and causes occasional serious outbreaks in humans. The disease affects both livestock and humans, and therefore has both economic and public health implications. Its transmission is complex but major RVF events have been associated with extensive flooding, caused by major climate anomalies or the construction of dams, which result in the production of massive populations of primary and secondary vectors (including *Aedes, Culex and Anopheles*). Outbreaks in recent years have been accompanied by bans on livestock trade between the Greater Horn of Africa and the Middle East which have cost the Greater Horn of Africa US$ 300–500 million annually. Where the disease has spread to the human population, many hundreds of deaths have occurred (e.g. in Yemen in 2000).

Throughout history, these epidemics have been associated with above average rainfall and temperatures, but until the late 1980s this link was based mainly on observations and anecdotal evidence. Improvements in disease databases and environmental data have raised interest in developing EWS for this disease.

In Kenya, the RVF activity database has facilitated initial risk-mapping studies. The database contains monthly information on clinical RVF cases, infected mosquitoes, and antibodies in humans and animals dating back to 1950 (Linthicum et al., 1999; Anyamba et al., 2002). A similar database exists in Zimbabwe (with gaps from the mid 1950s to the early 1990s), but information about the maintenance of this database is not available.

Davies et al. (1985) demonstrated the importance of climate anomalies in the occurrence of RVF epidemics in Kenya. Subsequent studies by Linthicum and colleagues indicated the potential for NDVI and SST monitoring in predicting epidemics. The main limitation of this model is that it was not validated independently (i.e. the epidemics predicted were included in the model), and that a large number of environmental variables (Atlantic and Indian Ocean SSTs and NDVI) were used to predict just three epidemics between 1982 and 1998. There is also no information on how an epidemic was defined. Although this approach is promising, the predictive power of the model should now be assessed on its ability to forecast future epidemics.

The CDC in the United States has established RVF International Programmes in eastern and southern Africa with the aims of:

- assessing the relative importance of climatic and environmental factors on RVF transmission; and
- constructing an environmentally-driven model to predict future RVF activity in these areas.

These programmes are designed to use recent Landsat satellite images as well as historical climate and vegetation data from the FEWS database.[9]

In West Africa, a regional early warning system for the surveillance of RVF was established and has been in operation since 2000 (Thonnon et al., 1999). This system is based on the seasonal monitoring of sentinel flocks of small ruminants located in high-risk areas combined with the collection of near-real-time climatic data provided by satellite imagery as well as the result of a three-month climate forecast delivered at the onset of the rainy season (Thiongane & Martin, 2003).

The development of EWS for RVF is at an early stage. Further progress could be made by ensuring that surveillance of RVF activity is maintained in Kenya and Zimbabwe, and expanded to South Africa (where RVF research has been strong for many decades). In addition, it is important to assess the value of surveillance of sentinel animals (lambs) to provide warning of an epidemic (see St Louis encephalitis), and test the ability of the Linthicum model, using SST and NDVI, to predict

[9]http://edcintl.cr.usgs.gov/riftvalley.html.

historical epidemics outside Kenya, and to predict epidemics within Kenya that were not included in the model-building process.

5.9 Leishmaniasis

Leishmaniasis is caused by a protozoan parasite which is transmitted by the bite of phlebotomine sand flies. Visceral leishmaniasis (VL) is epidemic in certain areas, for example, large areas of north Africa, southwest Asia and South America (e.g. Seaman et al., 1996; Sundar et al., 2000; Werneck et al., 2002)

Outbreaks of VL have been associated with population movements (Mansour et al., 1989), environmental modifications such as dam constructions and deforestation (Molyneux, 1997) and changes in the availability of zoonotic reservoirs. Climatic factors are thought to have been responsible for outbreaks in Sudan in 1985 and 1986 where heavy rains favoured sand fly breeding (Elsafi et al., 1991). Franke et al. (2002) demonstrated a positive relationship between the incidence of VL and ENSO in Brazil. In Turkmenistan, Neronov & Malkhazova (1999) suggested a significant positive relationship between the incidence of zoonotic CL, soil moisture and temperatures. Broutet et al. (1994) concluded that epidemics of CL in Brazil between 1986 and 1990 may have been attributable to climatic factors. In addition, the seasonal abundance of sand flies in south-west Asia has been shown to be dependent on temperature and humidity (Cross & Hyams, 1996; Cross et al., 1996).

The worldwide increase in prevalence of VL over the past 20 years has caused a renewed interest in disease surveillance that has generated considerable datasets useful for modelling purposes. In Europe, this increase has been attributed mainly to the increase in HIV. VL is notifiable in 33 out of 88 endemic countries and, since 1994, WHO has received annual data from 13 countries, most of which are in Europe (WHO, 2000). Surveillance for CL, and VL in tropical countries, is patchy and the existence of full datasets is questionable. There have been no documented attempts to develop climate-based EWS.

This situation could be addressed by quantifying the role of the climate in the interannual variation in VL using the existing datasets from southern and eastern Europe, and the output from these models, to predict epidemics of both human and canine VL in selected areas of the Mediterranean. It is also important to strengthen surveillance in other areas subject to epidemics, particularly for VL in south Asia, east Africa and South America, and for CL in Asia. In these areas, it would be useful to identify possible long-term datasets which could be used to quantify climate–epidemic links.

5.10 West Nile virus

West Nile virus (WNV) is a zoonotic arbovirus which is transmitted by culicine mosquitoes, including urban *Culex* species, and sometimes produces illness in humans. While WNV does not cause a burden of disease comparable to that of many other arthropod-borne infections, it has received intense attention because of the epidemic that began in the USA in 1999, and has since spread to Canada, the Caribbean and Latin America, resulting in over 7000 cases of neuroinvasive disease (Hayes, 2005; Hayes & Gubler, 2005).

Although there has been much debate about the role of climate changes in the emergence of WNV in North America (Epstein, 2000; Reiter, 2000; Epstein, 2001), the relative importance of direct climate influences, as opposed to factors such as the availability of mosquito breeding sites and avian hosts, remains a matter of speculation.

Since the first outbreak in 1999, surveillance of WNV in the United States has become highly efficient. A total of 49 states, five cities (e.g. New York) and the District of Columbia have initiated special WNV surveillance programmes which include active monitoring of dead or ill birds, active surveillance of mosquitoes and passive detection of human cases (CDC, 2001). Virus activity is reported regularly by state health departments of the CDC from which data are freely available via the Internet. Reports of infected birds, mosquitoes, humans and horses are accumulated at state level and used to produce retrospective maps of disease occurrence (Figure 5).

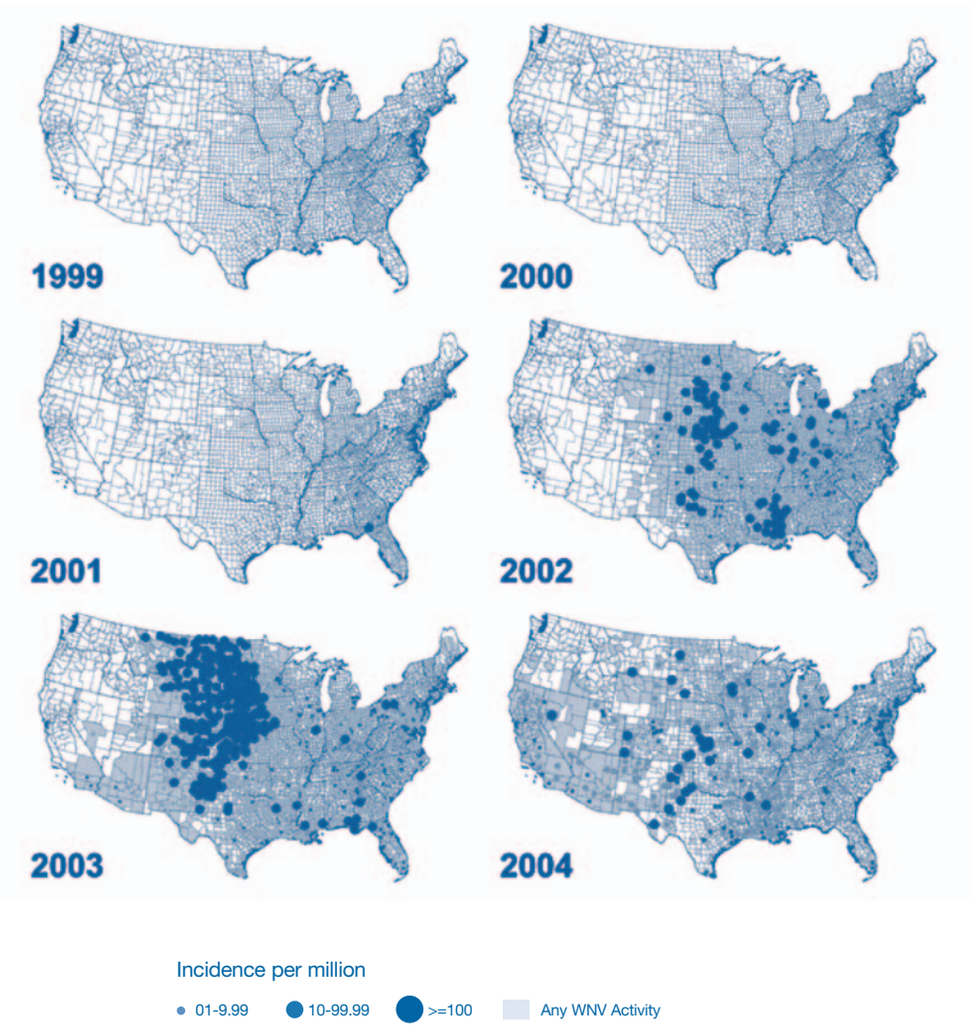

FIGURE 5: REPORTS OF WEST NILE VIRUS ACTIVITY FROM 1999–2004. REPRODUCED WITH PERMISSION FROM HAYES (2005).

To date, no climate-based EWS have been developed for WNV mainly because the link between climate and WNV epidemics remains unquantified. Instead there has been much focus on predicting outbreaks using surveillance of animal hosts. Eidson et al. (2001) evaluated a system of dead bird surveillance as an early warning system for WNV in the state of New York. They found that reports of dead birds preceded confirmation of viral activity in humans by at least three months. In 2000, a system based on dead bird surveillance (both sightings and laboratory testing of birds) provided temporal and geographical early warning of virus activity before the first cases of infection in humans (Eidson et al., 2001).

The emphasis on animal surveillance so far has provided encouraging results, but it is not clear whether climate-based models would improve predictive accuracy. However, the extensive data collected in North America show continuous monthly trends in virus activity and can be combined easily with low (state-level) resolution climate and vegetation data to test for possible associations. This analysis could be used to identify the climatic risk factors that should be monitored to make predictions about coming outbreaks. As for other diseases, if climate variables are shown to be important they should be incorporated into predictive models, and their precision and economic costs compared with those of predictions from bird surveillance alone. Again, as with many other diseases, current surveillance programmes could be expanded to other epidemic-prone areas, such as North Africa, Asia and southern Europe.

5.11 Ross River virus and Murray Valley encephalitis

Ross River virus (RRV) is an enzootic arthritic infection transmitted by *Aedes and Culex* mosquitoes with occasional spill-over to humans following virus amplification in reservoir hosts. Epidemics of RRV occur mainly in southern Australia (Hales & Hearnden, 1999) and are typically initiated in early summer.

RRV is the most important arbovirus in Australia and there has therefore been significant regional interest in both surveillance and prediction of epidemics of this disease. Since 1991, RRV has been a notifiable disease in all Australian states and territories, from which monthly and annual cases are reported directly to the Communicable Diseases Network Australia (CDNA). The CDNA now possesses annual and monthly data at national and state level from 1991 to the present, and these data are freely available on the Internet.[10] These data serve partly as an early warning system in their own right, but also allow investigations of any associations between climate and the incidence of the disease. Tong & Hu (2001) have shown significant correlations between climate variables (relative humidity and precipitation) and the incidence of RRV in Cairns at various subsequent time points. Similar notification data have provided the basis for the development of early warning models, based on rainfall, for south-eastern Australia (Woodruff et al., 2002). The models were constructed for early and late season and predicted 62–96% occurrence/non-occurrence of epidemics in 38 districts, with non-epidemics predicted more successfully than epidemics. This shortcoming is most likely the result of the lack of data (because of passive disease surveillance) and the non-inclusion of host-related factors such as virus population dynamics (Woodruff et al., 2002).

A series of more recent studies have shown that RRV is also associated with climate (particularly rainfall) in other regions of Australia, but the link, especially with ENSO, is less strong (Kelly-Hope et al., 2004a,b,c).

Murray Valley encephalitis (MVE) is caused by a flavivirus related to JE, which is transmitted by *Culex* mosquitoes in Australia. MVE is also a notifiable disease in Australia and monthly and annual case numbers are reported to the CDNA at state and national level. However, this disease became separately notifiable only in January 2001 and therefore the reliability of data collected before this date may be questionable. This has meant that investigation of the potential impact of climate on the interannual variability of MVE has lagged behind that for RRV. As for other vector-borne diseases both climate and other determinants, such as mammalian host and mosquito factors, also play a crucial role in transmission (Kay, 1980).

Nicholls (1986) suggested that regional climate indices could be used for predicting MVE epidemics (with a lead-time of weeks rather than months) but made no attempt to develop a predictive model. Broom et al. (2003) showed a correlation between rainfall and MVE activity in Western Australia, but concluded that mammalian host and mosquito factors are also important determinants.

Clear climatic influences, coupled with relatively long-term, reliable datasets, suggest that RRV and MVE are strong potential candidates for the development of climate-based EWS, which would have stronger predictive power in some regions than in others. Progress towards implementation could be made through:

- expanding the RRV model to include non-climatic factors and assessing whether this improves its ability to predict epidemics;
- adapting RRV models to take account of different epidemiologies in different regions of Australia;
- developing a similar model, initially based on regional climate indices, to predict epidemics of MVE using existing data from 1991 onwards; and
- improving surveillance of RRV particularly in the affected southern states of Australia, continuing the separate surveillance of MRV to establish a longer running dataset, and if feasible, changing from passive case detection to active surveillance.

[10]http://www.who.int/emc/diseases/leish/leisdis1.html

5.12 Influenza

Influenza is caused by a range of viral pathogens, directly transmitted between humans. Highly epidemic and local outbreaks or pandemics occur as a result of changes in the viral antigenic proteins. Although influenza epidemics are associated with winter and thus lower temperatures (Fleming & Cohen, 1996; Lina et al., 1996), non-climatic factors such as virus type, vaccination programmes and human behaviour are generally considered to be more closely related to epidemics. Existing EWS therefore rely on the constant monitoring of virus activity in humans and animals (WHO, 2000).

National monitoring systems exist in many countries, and contribute to wider international initiatives. For example, the European Influenza Surveillance Scheme, a collaboration of eight European networks, collects information on, among other things, the number of influenza encounters per general practitioner, identification of viruses isolated from patients, and mortality (Snacken et al., 1992). These data are assessed in comparison to the epidemic threshold discussed above, and previous background rates of influenza (Fleming & Cohen, 1996) in order to provide early warning of an outbreak.

Such regional initiatives contribute to the international network for influenza surveillance, established by WHO in 1948. It now consists of 110 National Influenza Centres in 83 countries and four WHO Collaborating Centres for Virus Reference and Research. The network is complemented by a web-based database (FluNet) in which weekly reports of influenza activity in each location are entered. Results from the network are reviewed by WHO in February and September in order to assess the likelihood of an influenza epidemic and make recommendations to vaccination manufacturers about the antigenic strain likely to be prevalent in the following year. This system has operated for more than 50 years and is generally considered to be successful (WHO, 2000) although there have been no formal assessments of the accuracy of epidemic prediction.

There is a possibility that the existing systems could be improved by including weather data. Recent studies in France and the USA indicate that the impact of influenza epidemics in terms of morbidity and mortality is influenced not only by the type of serotype circulating both nationally and internationally (Viboud, et al., 2004), but also by climatic conditions associated with El Niño; more severe impacts are significantly associated with colder conditions (Flahault et al., 2004; Viboud et al., 2004). Further work would be necessary to explore the extent to which incorporation of weather data could improve predictions of the occurrence and size of outbreaks of influenza with sufficient accuracy and lead-times to be able to improve control decisions.

The existing system of influenza surveillance and early warning is a useful example of how similar systems could be set up for other infectious diseases. Indeed, it is feasible to envisage a scenario where these influenza centres could be equipped to monitor other infectious diseases in the region: for instance, the National Center for Infectious Diseases Surveillance Resources established by the CDC in Atlanta, GA, USA, Public Health Laboratory Services in the United Kingdom and Agence Française de Sécurité Sanitaire des Aliments in France. However, the WHO influenza network suffers from a lack of geographical coverage, and could be expanded.

TABLE 3: CURRENT STATE OF KNOWLEDGE AND RESEARCH RECOMMENDATIONS FOR IMPROVING EARLY WARNING SYSTEMS FOR IMPORTANT CLIMATE SENSITIVE DESEASES.

Disease	Current areas of interest	Data availability	Early warning systems (EWS)	Lead- time	Key variables of interest	Proposed actions
Influenza	Worldwide	Ongoing surveillance (weekly) Historical data 1948–	1. Active disease surveillance in 83 countries. Separate system in Europe 2. Documented climate effects	1. Weeks 2. Months	Virus type and subtype, SST, ENSO, temperature	Improve surveillance in Africa and central Asia Test advantages of including climate variables
Cholera	Asia, South America	Ongoing surveillance (weekly) Historical data 1949–	1. Passive disease surveillance in 74 countries 2. climate/population vulnerability model developed	1. Weeks 2. Months	Zooplankton abundance, SST, ENSO, human factors, socioeconomic variables	Maintain and improve surveillance (esp. Africa) Operational testing of Bangladesh and Peru predictive models Quantify the role of climate in Africa
Malaria	Asia, sub-Saharan Africa, South America	Ongoing weekly surveillance through sentinel sites and/or as part of IDSR in many epidemic-prone countries Historical datasets (Africa, Europe, India, South America)	1. Passive disease surveillance 2. Model-based EWS development in several countries 3. Africa – rainfall anomaly maps for zones with epidemic potential every 10 days available through ADDS and RBM websites since 2002	1. Weeks 2. Months 3. Months	Temperature, rainfall, ENSO, EIR, vector abundance, population immunity, control activities	Maintain and extend surveillance Further test predictive models Link predictions to operational decisions
Meningococcal meningitis	Sub-Saharan Africa	Ongoing surveillance (weekly) Historical data 1966–	1. Passive disease surveillance 2. Potential early warning based on wind index	1. Weeks 2. Months	Humidity, socioeconomic variables vaccination coverage	Maintain and improve surveillance Refine predictive models, including for epidemic size

Disease	Current areas of interest	Data availability	Early warning systems (EWS)	Lead- time	Key variables of interest	Proposed actions
Leishmaniasis	South and east Europe	Ongoing surveillance (monthly/annually) Historical data 1994–	Passive disease surveillance but no warning	NA	Temperature, precipitation, soil humidity, vegetation, HIV, socioeconomy	Quantify role of climate Improve surveillance in tropics Identify long-term datasets from tropics
African trypanosomiasis	Sub-Saharan Africa	Population screening (for non-epidemic form of disease) Historical datasets 1900–	No warning	NA	Temperature, precipitation, vegetation, reservoir animals	Quantify role of climate Improve surveillance Construct predictive models
Dengue/Dengue haemorrhagic fever	South America, North America, Thailand	Ongoing surveillance in all areas, but data quality (active versus passive detection) and timing vary greatly	1. Active disease surveillance in Puerto Rico 2. Effects of climate and population immunity quantified in several countries	1. Weeks 2. 6–12 months	Dengue seroprevalence, socioeconomy, virus type, precipitation, temperature and humidity	Maintain and improve surveillance Construct and test predictive models
Japanese encephalitis	Japan, Thailand	Ongoing surveillance (monthly/annually) Historical data	1. Passive disease surveillance 2. Predictive model	1. Weeks 2. Months	Temperature, rainfall, reservoir animals	Quantify role of climate Maintain, improve and extend surveillance Construct predictive models
St Louis encephalitis	North America	Ongoing surveillance in all US states Historical data 1978 –	1. Surveillance of bird infections 2. Surveillance of mosquito abundance and infection 3. Active surveillance of human cases 4. Climate-based prediction developed in one site	1. Weeks 2. Weeks 3. Weeks 4. Months	Bird infections, temperature, rainfall	Operational testing of predictive models for US Set up surveillance in South America
Rift Valley fever (RVF)	Kenya, Zimbabwe	Historical (non-complete) disease data 1950–1998	None confirmed (possibly disease surveillance)	Weeks	RVF activity, ENSO years, vegetation, rainfall and temperature	Ensure that surveillance is maintained Set up sentinel animal surveillance
West Nile virus	North America	Virus surveillance (passive) in birds and humans in North America	1. Surveillance of dead birds and infected mosquitoes 2. Surveillance of human cases	1.Weeks 2. Weeks	Dead birds	Quantify link between climate and disease outbreaks in US Set up surveillance in Europe and Asia

Disease	Current areas of interest	Data availability	Early warning systems (EWS)	Lead- time	Key variables of interest	Proposed actions
Murray Valley encephalitis	Australia	Ongoing surveillance in all states. Historical data 1991–	1. Passive disease surveillance 2. Quantification of effect of rainfall	Weeks	Atmospheric pressure, reservoir animals	Maintain and improve surveillance Construct and test predictive model
Ross River virus	Australia and Pacific islands	Ongoing surveillance in all states. Historical data 1991–	1. Passive disease surveillance 2. Predictive models in different ecological zones	1. Weeks 2. Months	Rainfall, virus dynamics, reservoir animals	Expand model and try to predict future epidemics in different zones Maintain and improve surveillance (active) Quantify role of other factors
Yellow fever	Africa and South America	Ongoing surveillance in at least 10 countries Historical data from 1948	Disease surveillance	Weeks	Temperature, rainfall, vector abundance and breeding, socio-economy, vaccination coverage	Quantify role of climate Maintain and improve surveillance Set up animal surveillance

HIV, Human immunodeficiency virus; ENSO, El Niño/Southern Oscillation; NA, not applicable.

IDSR, Integrated disease surveillance and response; ADDS, Africa Data Dissemination Service; RBM, Roll Back Malaria, SST, sea surface temperature; ENSO, El Niño Southern Oscillation; EIR, entomological inoculation rate.

6. GENERAL DISCUSSION AND CONCLUSIONS

It is generally accepted that the transmission of many infectious diseases is affected by climatic conditions. Diseases caused by pathogens which spend part of their life cycle outside human, or other warm-blooded, hosts are particularly climate-sensitive. Some of these diseases are among the most important global causes of mortality and morbidity, particularly in poorer populations in developing countries. In many environments, these diseases occur as epidemics, triggered in some instances by changes in climatic conditions favouring higher transmission rates.

Efforts to develop climate-based disease EWS date back to the work of Gill and co-workers in India in the 1920s (Gill, 1921). Interest in EWS has been rekindled in recent years, partly reflecting increasing levels of concern over the possible future impacts of climate change on human society. At the same time, climate and other environmental data have become widely available and relatively inexpensive, as have GIS and other tools required to link these observations with disease data. There is, therefore, clear justification for investigating the potential of climate-based EWS to allow advance planning of control interventions. The case for such EWS has been made repeatedly in review papers, particularly in the context of malaria.

In this report, we have reviewed the degree to which important infectious diseases are sensitive to climate variations, and used this information as a basis for identifying diseases for which climate may be most usefully incorporated into EWS. We have adapted existing work on malaria to form a generalized framework for developing EWS for infectious diseases. Subsequently we reviewed the extent to which existing systems provide accurate advance warnings of the likelihood and size of epidemics, which are useful in making control decisions.

This review showed that there is considerable research activity in this area. Of the diseases that meet our criteria for having the potential for climate-based EWS, there are only a few (African trypanosomiasis, leishmaniasis and yellow fever) for which there are no reports of an EWS being developed. For others (West Nile virus in the United States, and influenza) there are already operational and effective warning systems, but these currently rely solely on rapid detection of virus activity. It is possible that climatic predictors may improve predictive accuracy or the lead-times associated with these systems, but this awaits further investigation. For the remaining diseases (cholera, malaria, meningitis, dengue, Japanese encephalitis, Rift Valley fever, St Louis encephalitis, Murray Valley encephalitis and Ross River virus) research projects have demonstrated a temporal link between climatic factors and variation in disease rates. In some of these projects the power to predict epidemics has already been tested. In many of the early studies these tests were preliminary, based either on a very limited dataset, or providing little description of the methods used. Most of the studies published in the last few years, however, have been much more comprehensive in their consideration of both climate and non-climatic effects, and more rigorous in terms of testing predictive accuracy.

The degree to which these promising research findings have been converted into operational action remains unclear. Several reports indicate that climate-based systems are already being used to influence control decisions, for example for malaria in southern and eastern Africa. As yet, however, these have not been fully documented in the literature.

There are a number of likely explanations for why such systems are not widely used and reported. Firstly, affordable and accessible data and analytical tools have become widely available only recently so that the field is at a relatively early stage of development, and a rapid increase in published studies has been seen only in the last 2–3 years. Secondly, as few studies have as yet been published there is no clear consensus on either the general criteria or specific measures for assessing predictive accuracy. Consequently it is difficult to judge the utility of existing systems. Thirdly, most research projects have been carried out on relatively limited resources and therefore have not been tested in locations outside the original study area. Fourthly, many studies in this area have focused solely on climate factors and only more sophisticated recent studies have integrated climate and non-climatic effects. Finally, research studies are often not well-connected to control practice. Many of the studies that are reported in the scientific literature have been undertaken as pure research, and it is not clear to what extent they address specific control decisions or are of use to health policy-makers. In contrast, disease control personnel may use climate information either in an informal manner (e.g. increased expectation of risk of mosquito-borne disease following rains), or as part of a full predictive model, without documenting the experience for a wider audience.

There are several possible ways of helping to address these issues. Perhaps the most urgent is

the need to maintain and strengthen systems for reporting incidence of epidemic diseases. High-quality, long-term disease data are essential for generating models relating climate to infectious disease. It is probably true to say that development of EWS for some diseases has stalled because of a shortage of suitable epidemiological data. More commonly, disease–climate modelling has been restricted to discrete datasets obtained from relatively small areas. These exercises are useful for exploring methodological issues and in many cases have produced promising results, but it is now becoming clear that it in order to generalize these models to other areas, they often have to be adapted on the basis of local climate–disease relationships. The implications of this are that before EWS can be widely tested or applied, it will usually be necessary to bolster existing disease surveillance systems. In some cases there may be a need to begin this process from scratch – in others, viable systems may exist but require modification to ensure timely transfer of data from the point of collection to the point of analysis. For diseases such as malaria, which often are diagnosed clinically, further work needs to be carried out to determine the extent to which quality of diagnosis affects our ability to recognize (and predict) epidemics (WHO/UNICEF, 2005). Important progress could be made through better integration of health surveillance data with monitoring of other factors that contribute to vulnerability, such as on changes in land-use and other ecological conditions, food availability, and (for zoonoses) infections in wild and domestic animals.

It is important for any early warning system to test for non-climatic influences (e.g. the effects of population immunity, migration rates or drug resistance) on variations in disease rates. Thorough testing of alternative explanatory factors should avoid incorrectly attributing disease variations to climate. More importantly in practical terms, a series of papers published in the past 2–3 years have demonstrated that measurements of all relevant factors for which data are available allows the generation of more accurate predictive models.

There is a need for a better common understanding of the terminology and methods used for assessing predictive accuracy. This is partly a case of determining relatively straightforward “best practice” approaches. For example, if the aim of an early warning system is to predict epidemic versus non-epidemic time periods, the definition of an epidemic (i.e. number of cases in a specific population over a specified time) should be determined before the modelling process is carried out. In addition, model accuracy should be assessed against independent data (i.e. data not included in the original model building process) to give an accurate replication of an attempt to predict a future epidemic.

Recent studies have proposed a wide range of measures for assessing predictive accuracy. There is also a need for further discussion, if not to set definitive guidelines, on which are most appropriate for different purposes. For example, measures such as overall proportion of correct predictions, kappa statistics, Brier forecast scores, correlation coefficients between observed and predicted case numbers, and root mean square errors, have all been proposed as overall measures of accuracy in predicting the occurrence or size of epidemics, but their relative merits have not been systematically reviewed.

Other measures such as sensitivity, specificity, positive and negative predictive value (for epidemic occurrence), and potentially preventable cases (for epidemic size), provide additional information that may be more directly relevant to control programmes. These measures relate directly to the questions that are of relevance to those who make the decisions on control measures. Such questions include: What are the chances that we will fail to predict an epidemic, and how many lives would be lost? and: What are the chances of sounding a false alarm, thereby wasting resources and undermining public trust?

As research into EWS moves beyond the pure research stage, it becomes increasingly important to include health policy-makers in all stages of system design. For example, local disease control personnel should be involved in defining an epidemic and in determining the most appropriate lead-times over which predictive accuracy should be assessed (e.g. whether it is more important to have an accurate prediction with a lead-time of 1–2 weeks, or a more uncertain prediction with a lead-time of several months). These discussions should take place in relation to specific control decisions, and consider local (particularly resource) constraints on the implementation of the EWS. Experience with the famine early warning system in the 1990s showed that its effectiveness depended less on the accuracy of warnings than on political factors. This is beginning to be taken into account for operational epidemic malaria prevention and control in Southern Africa (DaSilva, et al., 2004) and is being considered for other regions.

Ideally, the final decision on whether an early warning system should be implemented should be made on the basis of a cost-effectiveness analysis. This should measure the value of collecting data on the various climatic and non-climatic influences, both in terms of predicting the occurrence and size of epidemics and increasing the effective use of control resources. In some situations, for example, adding climatic information to an early warning system may lead only to a small increase in predictive power and therefore in the cost-effectiveness of control: however it may be sufficiently cheap and simple to collect to justify its inclusion.

In conclusion; the amount, accessibility and affordability of climate data has increased dramatically in recent decades. The challenge now is to use this information as effectively as possible as a resource to improve human lives. Including climate information into early warning systems can potentially make a significant contribution to reducing the burden of epidemic diseases. To make full use of this resource, however, it is necessary not only to continue to improve access to climate information and refine analytical methods. More fundamentally, it depends on integrating early warning systems as just one component in well-supported systems for infectious disease surveillance and response.

ACKNOWLEDGEMENTS

Thanks are due to Madeleine Thomson and Steven Connor for review comments and contributions to the report content, to Fiona Gore for review comments and for preparing the glossary, to Tarekegn Akebu, David Bradley, Simon Brooker, Charles Delacollette, Sari Kovats, Mary Marimootoo, Michael Nathan, Dirk Pfeiffer, Aafje Rietveld and Paul Wilkinson for review comments, to Ned Hayes and Hailay Teklahaimanot for providing permission and data for redrawing figures, and to Susan Kaplan and Jo Woodhead for editing of the text

GLOSSARY

African trypanosomiasis: see Trypanosomiasis.

Chagas Disease: see Trypanosomiasis.

Cholera: Acute infection with the bacterium *Vibrio cholerae*, characterized by severe diarrhoea and vomiting, often leading to dehydration, electrolyte imbalances, and, if untreated, to death. Spread by water and food contaminated with the faeces of infected persons, it is endemic in some parts of the world and frequently occurs following natural disasters. It is treated with antibiotics and electrolyte replacement; a vaccine is available.

Climate: A measure of the expected atmospheric conditions at a particular location over a particular period (e.g. month or season), based on statistics built up from observations over many years (as distinct from weather, see below).

Cutaneous leishmaniasis (CL): Cutaneous form of leishmaniasis, a skin disorder caused by Leishmania parasites; it is characterized by ulcerative skin lesions. Treatment usually involves the use of antimony preparations.

Cross-validation: Statistical techniques in which part of a dataset is used to build a predictive model, the accuracy of which is then tested against the remaining observations.

DALY: A disability-adjusted life year is an indicator of life expectancy combining mortality and morbidity into one summary measure of population health to account for the number of years lost to premature death, or to living in a state of less than optimum health.

Dengue: Viral disease, transmitted by *Aedes* sp. mosquitoes mostly in tropical and subtropical areas; it is marked by fever, muscle and joint pain, headache, and rash. Symptoms recur after a brief interval and the patient may require some time to recover.

Dengue haemorrhagic fever (DHF): DHF is characterized by a breakdown of the blood-clotting mechanism with internal bleeding.

Endemic: Indigenous (native) to a given population or area; occurring frequently in a given group or community, especially pertinent to a disease.

El Niño Southern Oscillation (ENSO): ENSO is a periodic appearance of warm and cool sea surface water in the central and eastern Pacific Ocean. It is the most prominent known source of interannual variability in weather and climate around the world. ENSO events are associated with increased probability of drought in some areas and excess rainfall in others, together with temperature increases in many regions. The ENSO occurs on a quasi-periodic (~3–8 year) timescale.

Epidemic: The occurrence in a community or region of cases of an illness, specific health-related behaviour, or other health-related events clearly in excess of normal expectancy.

Early detection: Detection of changes in disease transmission, usually based on data from an active or passive disease surveillance system. Early detection systems usually include a set of pre-defined rules, e.g. thresholds of case numbers that must be exceeded for an epidemic to be declared and responses to be initiated.

Early warning: Warnings based on biologically and statistically important predictors of changes in disease transmission. These can be either measurements of these factors (e.g. rainfall data), or predictions in advance of their occurrence (e.g. seasonal forecasts of temperature and rainfall based on ENSO). Both early detection and early warning systems include consideration of operational conditions and responses.

Encephalitis: Inflammation of the brain, usually due to viral infection but sometimes occurring as a complication of another infection (e.g. influenza or measles) or resulting from poisoning. Symptoms include headache, drowsiness, neck pain, nausea, and fever, followed sometimes by neurological disturbances such as seizures, paralysis and personality changes. The outcome depends on the cause, extent of the brain inflammation, and general condition of the patient.

Etiology: The scientific study of the causes of disease.

Holoendemic: Areas that are subject to high and relatively stable transmission rates of an infectious disease (usually malaria).

Incidence: Number of times an event (e.g. an infection) occurs in a given period of time. Usually expressed as numbers of cases, per year, per capita of a defined population.

Influenza: Acute, contagious, viral infection of the respiratory tract. Several strains of the virus have been identified and new strains emerge at intervals, often named for the geographical region in which they are first discovered (e.g. Asian flu).

Japanese encephalitis: Disease caused by a flavivirus, transmitted from domestic pigs and wild birds via the bite of *Culex* mosquitoes in south-eastern Asia and the western Pacific. It causes severe rigours, fever, headache and malaise and may last for a period between one and six days. Infection may lead to involvement of the nervous system, resulting in deafness, emotional lability and hemiparesis, mental retardation and coma. It can be fatal, particularly in children.

Leishmaniasis: Infection, most common in warm climates, with protozoa of the genus Leishmania; it occurs in two forms: visceral (see Visceral leishmaniasis or Kala-azar) and cutaneous (see Cutaneous leishmaniasis), affecting skin tissues.

Leprosy: Chronic, communicable disease, caused by *Mycobacterium leprae*, that is widespread throughout the world, chiefly in tropical and subtropical regions.

Lyme disease: A disease caused by a spirochaete, *Borrelia burgdorferi*, and transmitted by certain ticks of the genus *Ixodes*. Following a 3–32-day incubation period, a slowly extending red rash develops in approximately 75% of cases. Intermittent systemic symptoms include fever, malaise, headache and neck stiffness, and muscle and joint pains. Later, 60% of patients suffer intermittent attacks of arthritis, especially of the knees, each attack lasting several months and recurring over several years.

Malaria: A potentially life-threatening disease common in many tropical and subtropical areas. It is caused by four related species of the protozoan parasite *Plasmodium: Plasmodium falciparum*, *P. vivax, P. ovale and P. malariae*. It is transmitted from human to human through the bite of an infected *Anopheles* mosquito. The most severe form is caused by *P. falciparum*, in which clinical features are variable but include fever, chills, headache, muscular aching and weakness, vomiting, cough, diarrhoea and abdominal pain; other symptoms related to organ failure may supervene, such as acute renal failure, generalized convulsions, and circulatory collapse, followed by coma and death.

Measles: Acute, contagious, viral disease, occurring primarily in children who have not been immunized and involving the respiratory tract and a spreading rash. Highly contagious, measles is spread by direct contact with droplets from the nose, mouth or throat of infected people.

Meningitis: An inflammation of the meninges due to infection by viruses or bacteria or fungi. Meningitis causes an intense headache, fever, loss of appetite, intolerance to light and sound, rigidity of muscles, especially those in the neck, and in severe cases convulsions, vomiting and delirium leading to death. Meningococcal meningitis is caused by bacterial infection. In this form, the symptoms appear suddenly and the bacteria can cause widespread meningococcal infection culminating in meningococcal septicaemia, with a characteristic purple haemorrhagic rash anywhere on the body.

Murray Valley encephalitis: Disease caused by a flavivirus endemic to northern Australia and Papua New Guinea. The virus is maintained in a bird–mosquito–bird cycle, with occasional infections of humans. Most infections do not cause clinical symptoms. Where symptoms do occur, they include fever, together with seizures, nausea and diarrhoea in children, and headaches, lethargy and confusion in adults. A significant proportion of those who develop the illness either suffer permanent neurological damage or die.

Outbreak: An epidemic limited to a localized increase in the incidence of a disease, e.g. in a village, town or closed institution.

Pandemic: Widespread epidemic, occurring throughout a country or geographical area or worldwide.

Pertussis: Acute, contagious, respiratory disease, occurring most commonly in non-immunized young children and characterized by attacks of coughing ending in inspiration with a loud whooping sound. It is caused by *Bordetella pertussis* bacteria; it is transmitted directly (by contact with infectious particles spread by coughing or sneezing) or indirectly (through contaminated articles).

Pneumonia: Inflammation of the lungs, usually caused by infection with bacteria (esp. Pneumococcus), viruses, fungi or rickettsiae. Symptoms include fever, chills, headache, cough, chest pain, and, as the disease progresses, difficult and painful breathing, production of thick, purulent sputum, rapid pulse, and sometimes gastrointestinal complications.

Poliomyelitis: Infectious disease that affects the central nervous system. It is caused by the poliovirus and was once epidemic in many parts of the world, but is now largely prevented by vaccination with Salk or Sabin vaccines.

Prevalence: In epidemiology, the number of occurrences of a disease or event in a given population; it is usually expressed as a ratio, the number of events occurring per the number of units in the population at risk for the occurrence.

Rift Valley fever (RVF): Self-limiting, usually short-lived viral infection that occurs in Africa; it is transmitted by mosquitoes or by handling infected animals; symptoms include fever, malaise, headache and photophobia.

Ross River fever or virus (RRV): A viral disease caused by an alphavirus transmitted by mosquitoes. Various vertebrates can be infected, and wild rodents may be reservoirs of the infection. The virus can cause epidemics of polyarthritis and skin rashes (macules and papules). It occurs in Australia and the western Pacific Region.

Smallpox: Highly contagious viral disease, characterized by fever, weakness, and a pustular rash that may result in permanent scarring.

St Louis encephalitis: Viral disease, transmitted from infected birds to humans via the bite of mosquitoes of the genus *Culex*. This disease occurs mainly in the United States; occasional cases have been reported from Canada and Mexico. The majority of infections result in mild illness, with symptoms including fever and headache. When infection is more severe the person may experience headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, occasional convulsions and spastic paralysis. Fatality rates range from 3–30%.

Trypanosomiasis: Any disease caused by the presence of parasitic protozoans of the genus *Trypanosoma*. The two most important diseases are Chagas disease (South American trypanosomiasis) and sleeping sickness (African trypanosomiasis).

Tsetse fly: The insect that carries the parasites that cause African trypanosomiasis.

Tuberculosis (TB): Chronic infection with the bacterium *Mycobacterium tuberculosis*, transmitted by inhalation or ingestion of droplets; it usually affects the lungs but may also affect other organs. Early symptoms include fever, loss of appetite, fatigue, and vague chest pain; later, night sweats, difficulty in breathing, production of purulent sputum and signs of severe lung involvement occur.

Visceral leishmaniasis (VL) or Kala-azar: Visceral form of leishmaniasis. Occurring mainly in warm regions of Asia, Africa, Central and South America, and parts of the Mediterranean area, it is caused by the protozoan *Leishmania donovani* or *Leishmania infantum*, transmitted by the bite of a sand fly. Symptoms include anaemia, enlarged spleen and liver, fever and loss of weight.

Weather: Observed atmospheric conditions at a particular location at a particular time (as distinct from climate, above).

West Nile virus (WNV): A viral disease caused by the West Nile virus (a flavivirus), which is spread by the *Culex pipiens* mosquito. It causes encephalitis, with influenza-like symptoms, enlarged lymph nodes, and a bright red rash on the chest and abdomen. In patients with a weakened immune system, it can progress to convulsions, coma and paralysis.

Yellow fever: Viral disease, transmitted by mosquitoes, chiefly female *Aedes aegypti* mosquitoes, found in tropical Africa and northern South America. Symptoms include fever, headache, pains in the back and limbs, reduced urine output, jaundice, and degeneration of liver and kidney tissue. There is no specific treatment, but the disease can be prevented by vaccination; recovery from one attack usually confers subsequent immunity.

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ISBN 92 4 159386 5