Predicting malaria epidemics in the Kenyan highlands using climate data: a tool for decision makers

While the underlying cause of malaria epidemics in the East African highlands remains a subject of debate, we argue that permissive climatic conditions in the normally cool highlands are required for the epidemics to occur. Analysis of climate data from East Africa suggested that, over the last decade, there has been an increase in the frequency and intensity of anomalies in the mean monthly maximum temperatures. We found an association between rainfall and unusually high maximum temperatures and the number of inpatient malaria cases 3-4 months later. A malaria epidemic prediction model was then constructed.

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During the last 13 years, malaria epidemics in western Kenya have spread from 3 to 15 districts, often taking the population by surprise. The epidemics are associated with high morbidity and mortality in all age groups, with prevalence of the disease rising from about 20% to about 60%. The case mortality in functional health facilities has been estimated as about 7.5%. The government's policy on malaria control is based on quick diagnosis and effective treatment; however, availability of sufficient manpower, drugs, other resources, and prompt interventions to prevent a potential epidemic are assumed. Quite often, the number of people infected is so high that the demand for drugs outstrips supplies, complicating management of the epidemic. Predicting when and where epidemics will occur is a major problem.

Climatic conditions in the highlands, such as temperature and rainfall, affect the development of mosquitoes and malaria parasites. Increasing temperature accelerates the rate of mosquito larval development, the frequency of blood feeding by adult females on humans, and reduces the time it takes the malaria parasites to mature in female mosquitoes. Increased rainfall creates additional breeding sites for mosquitoes, thus increasing their numbers. In generating a predictive model temperature and rainfall were taken as risk factors for malaria transmission. Temperature was transformed into a discrete exponential value and rainfall, into a discrete linear value. A fractional risk was then calculated from these values. Maximum transmission risk was demonstrated to have occurred four months before the peak of the malaria epidemics. The model's only data inputs are mean monthly rainfall and monthly maximum temperature.

Decision makers can use this tool to determine in which areas malaria epidemics are likely to occur and the severity of the epidemic, reducing uncertainties in decision-making and leading to better resource and disease management.

Predicting malaria epidemics

Epidemic malaria in the Kenya highlands is caused by *Plasmodium falciparum* species and transmitted by *Anopheles gambiae s.s.* and *Anopheles funestus* mosquitoes. Epidemics, in western Kenya, generally occur in areas at altitudes of between 1500-2200 meters above sea level, where the annual mean daily temperature varies between 18-22°C. Topographically, these areas consist of river valleys, hills, and plateaus. The valleys are well drained, unlike the plateaus which are not, and can provide permanent mosquito breeding sites. The epidemics

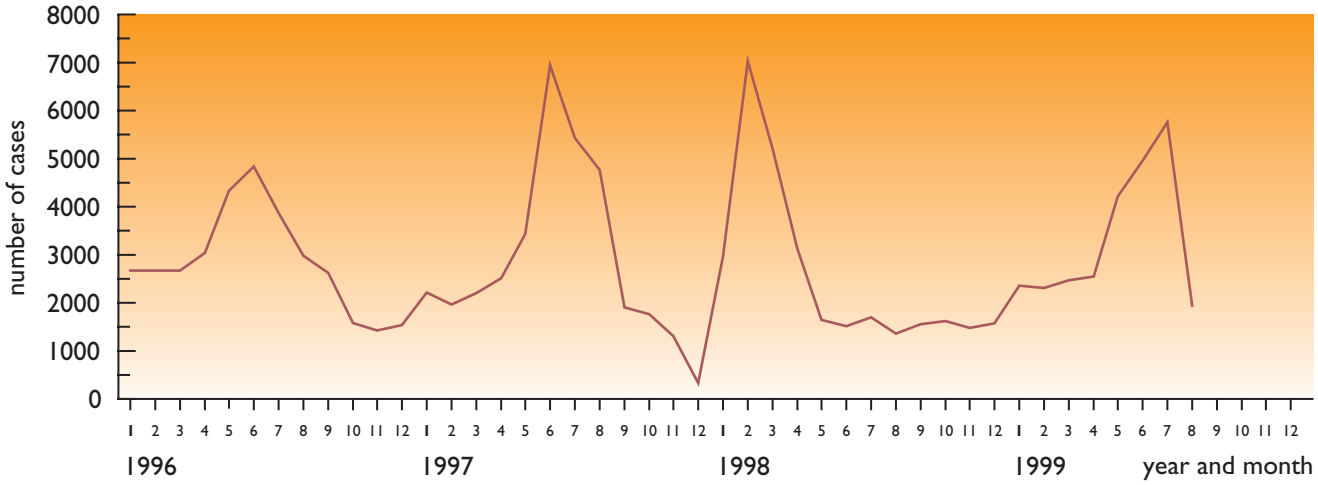

Figure 1 *Out-patient Department malaria cases in Kisii District Hospital, 1996-1999, Western Kenya.*

normally occur from May to August, following the long rains. However, during the 1997/98 El Niño, the epidemic occurred from January through March 1998, following unusually heavy rains (from October to December, 1997) caused by the El Niño weather.

El Niño Southern Oscillation (ENSO) and disease outbreaks

The ENSO phenomenon, which originates from anomalous sea surface temperatures in the Eastern Tropical Pacific Ocean, tends to cause excess rainfall in some parts of the tropics and droughts in others. A number of disease outbreaks such as malaria, dengue and cholera have been associated with ENSO in endemic regions[1]. In Venezuela, malaria mortality and morbidity have been reported to increase by 36.5% in the years following recognized El Niño events[2] . In the Northeast region of the Punjab, malaria epidemics increased five-fold in the year following the El Niño and in Sri Lanka the risk of malaria epidemics increases four-fold during an El Niño year. In the Punjab, epidemics are associated with above normal precipitation while in Sri Lanka with below normal precipitation[3]. Recently, a number of research groups have pioneered the use of models to predict individual El Niño events and their effects on weather patterns throughout the world. Such models can be useful in predicting the probability of disease outbreaks in endemic areas, providing improved opportunities for taking preventative measures.

Although climate factors can increase malaria transmission, the outcome of the clinical disease depends on the level of immunity of the infected person, how early the disease is treated, and the effectiveness of the antimalarial drugs.

Currently, in western Kenya, 15 districts, compared to 3 in 1988, are under constant threat of the epidemics[4]. Although there is greater frequency of epidemics in some districts, such as Kisii and Nandi, predicting when and where the outbreaks will occur, has, so far, been a matter of guesswork.

A climate-based model of transmission intensity for estimating the proportion of Kenya's population exposed to different epidemiological conditions has been developed[5]. However, this model only provides information on the estimated annual morbidity and mortality burden of malaria among Kenyan children. It has been shown, using remotely sensed data, that the normalized difference vegetation index (NDVI) has the potential for predicting malaria transmission in Kenya[6]. In another model, key malaria transmission factors such as vector biting and entomological inoculation rates can be estimated using soil moisture in western Kenya[7]. None of these models has been used to predict malaria outbreaks in the highlands. However, it has been demonstrated that in Kenya, a combination of satellite derived data, such as NDVI, and sea surface temperature anomalies in the Pacific and the Indian Oceans can be used to forecast the Rift Valley Fever outbreaks up to five months in advance[8].

Currently, there is no clear definition of a malaria epidemic, posing serious operational implications for disease control. Epidemics usually require emergency measures that must be implemented as promptly as possible in order to be effective. However, a declara-

tion of an emergency, generally based on the inability of normal medical services to cope with demands following outbreaks, such as an epidemic, must be made.

The development of parasites in the mosquitoes, which is part of the malaria transmission cycle, is very sensitive to external temperatures. The rate of larval development (and subsequent increase in the size of mosquito populations) is also dependent upon water temperatures and the quantity and quality of breeding sites.

Expressing malaria transmission in mathematical terms: the vectorial capacity

The transmission of malaria has been described in mathematical terms as the vectorial capacity, the number of new mosquito infections daily that arise from one infected individual in a non-immune population if all the biting mosquitoes become infected[9,10,11].

$$C = \frac{Ma^2p^n}{-\log_e p} \qquad \text{Eq. 1}$$

- **C** = vectorial capacity
- **Ma** = composite index of the daily mosquito man-biting rate
- **a** = daily mosquito man biting habit, how often the mosquito feeds on man in a day (24 hours)
- **p** = probability of the vector surviving through 1 day (24 hours)
- **n** = parasite's extrinsic incubation period – the duration it takes the parasite to develop, mature and become infectious in the mosquito

$$a = \frac{HBI}{b} \qquad \text{Eq. 2}$$

- **HBI** = Human blood Index
- **b** = interval between blood means in days

All of the above transmission parameters are affected by temperature. For example, as the temperature increases, the female mosquito feeds on blood more frequently, reducing b and increasing a (Eq. 2). Moreover, the interval between blood meals has exponential effects on the parasite's survival rate (Eq. 3) and on Eq 1, so that C, the vectorial capacity (Eq. 1) is sensitive to the changes in the vector's blood feeding frequency[12].

The probability of the vector surviving one day (24 hours) p:

$$p = P^{1/b} \qquad \text{Eq. 3}$$

P equals the proportion of females that have laid eggs or the parity rate and a function of the daily survival probability of **p**. Changes in the probability of survival, **p**, has a large effect on **C** as **p** is raised to the power *n* in the numerator and as a log in the denominator in Eq. 1.

The parasite's extrinsic incubation period, n, is a function of temperature:

$$n = \frac{T}{t - t_{min}} \qquad \text{Eq. 4}$$

where **T** is the constant (thermal sum), 111, for *P. falciparum*, **t** is the actual mean temperature and t_{min} 16.5-18°C (temperature in degrees centigrade) during the incubation period, n.
Because *n* has an exponential effect on C, small changes in temperature will have a great effect on malaria transmission.

Although the vectorial capacity equation is a powerful tool for simulating malaria transmission, it is very difficult to obtain the required parameters with the necessary degree of precision. For this reason, a simpler climate based method was required to simulate and forecast malaria transmission using easily obtainable data. In order to develop such a method, the behavior of malaria transmission was first studied, using published data as inputs for the vectorial capacity equation.

Computer simulations of the effects of temperature on the extrinsic incubation period and the vectorial capacity for *An. gambiae*

All simulations were performed using the spreadsheet program, Quattro Pro 8. Perhaps the most important effect of temperature on malaria transmission in the highlands is the change in the extrinsic incubation period

Table 1 Effect of temperature on duration of development and maturation of *Plasmodium falciparum* parasites.

scenario[1]	mean monthly temp °C	Ma[2]	HBI[3]	biting cycle rate (a)	daily feeding	Parity (P)	extrinsic incubation period (x)	daily survival rate (p)	-ln p[4]	density X 1 $(Ma^2 p^x)/-\ln p$	density x2 $(Ma^2 p^x)/-\ln p$
1	17	4	0.95	4	0.24	0.75	111.0	0.93	0.07	0.00	0.01
2	19	6	0.95	3.20	0.30	0.75	37.0	0.91	0.09	0.71	1.42
3	21	8	0.95	2.67	0.36	0.75	22.2	0.90	0.11	2.41	4.82
4	23	10	0.95	2.29	0.42	0.75	15.9	0.88	0.13	4.49	8.98
5	25	12	0.95	2.00	0.48	0.75	12.3	0.87	0.14	6.72	13.45

1 Each scenario consists of a specific temperature, man-biting rate, and daily blood feeding rate
2 Ma = daily man biting rate measured by counting the number of female mosquitoes biting man throughout the night.
3 HBI = The proportion of female mosquitoes of a specific species that take their blood meals on man
4 -nl p = the negative natural log of the daily survival rate

n, of *Plasmodium falciparum* in the vectors. The extrinsic incubation period is the duration of time it takes the parasite to develop into a mature and infective stage.

Equation 4 was used to calculate and simulate the effects of temperature on the extrinsic incubation period. The annual mean temperatures at the altitude of 2000 m in western Kenya (18°C) is very close to the minimum temperature (16°C) required for transmission of *P. falciparum* malaria.

Data on parity rates (P) and man-biting rates (Ma) were estimated from our internal data for the local highland sites in western Kenya where mean temperatures range from 17-25°C. (Centre for Vector Biology and Control Research unpublished data). It was assumed that the parous rate within this temperature range

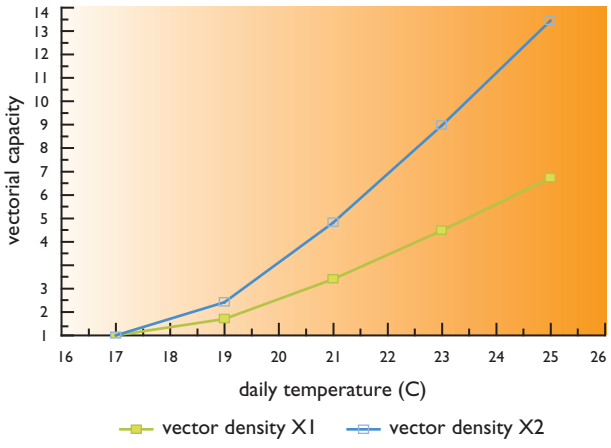

Figure 2 *Effects of temperature and doubling vector density on vectorial capacity.*

was constant. The temperature dependent durations of the gonotrophic period (time, in days, between blood meals) were calculated for each temperature[12]. From these parameters the vectorial capacity at each temperature was calculated and graphed.

Development of a temperature and rainfall based malaria epidemic prediction model

Long-term temperature data in the East African region covering the western Kenya highlands were obtained from the International Research Institute for Climate Prediction (IRI) website data bases,

NOAA NCEP-NCAR: NCEP/NCAR Reanalysis Project,
http://ingrid.ldeo.columbia.edu/SOURCES/.NOAA/.NCEP-NCAR/.

Maximum and minimum temperature data from January 1970 - June 2000 for the grid 33.75E-39E, 2.8N-2.8S was down-loaded and plotted to show long-term trends in anomalies and to detect association, if any, between the trends in monthly mean maximum and minimum temperatures and recent malaria epidemics in the East African highlands.

The relationship between rainfall and man biting rates is complex and not yet understood. To study the effects of increased rainfall, we chose a simple, feasible scenario where, due to the creation of extra breeding sites (and therefore, an increase in the number of biting adult mosquitoes), the value of man-biting rates were doubled by rainfall.

Modeling malaria transmission and construction of an epidemic forecasting model

Field and hospital malaria data were collected in Kakamega district at an altitude of about 1500 m above

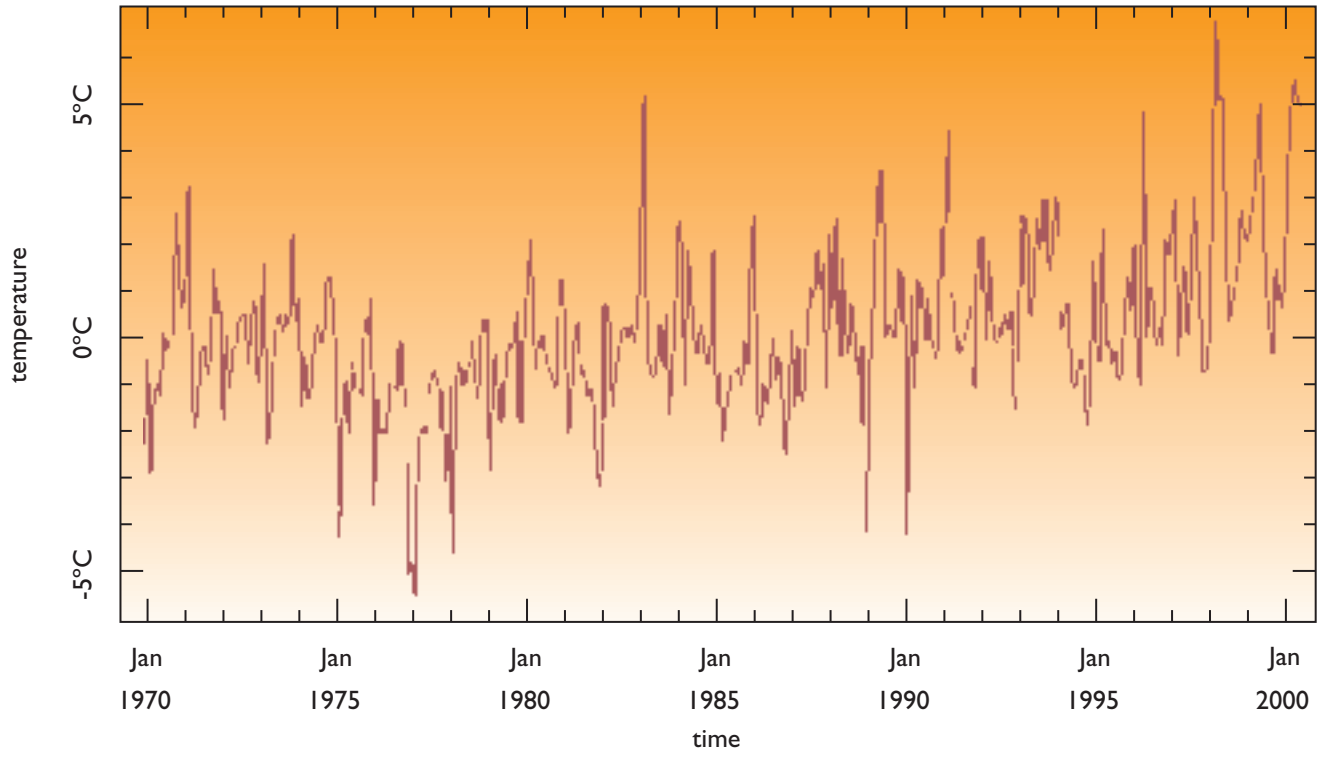

Figure 3 *Mean monthly maximum temperature anomalies for the grid 33.7-38.5E and 2.9S-2.9N covering western Kenya and Uganda.*

sea level. Entomological data were obtained between February 1998 and February 1999, in 9 sentinel houses. Parasitological data were collected in two schools in the same area (data not included in this analysis). Data on the proportion of in-patient malaria cases out of all in-patient admissions were obtained from Mukumu Mission Hospital in Kakamega for the period 1997-1999. The total number of hospital admissions is used as the denominator in the determination of changes in seasonal trends in malaria admissions. The hospital has a good diagnostic laboratory and computerized records. The annual mean proportion of malaria cases out of the total in-patient cases was calculated and used to determine the monthly anomaly (incidence) of malaria cases.

In order to determine whether there had been any departures in monthly mean maximum and minimum temperatures and in the monthly proportion of malaria cases, monthly values of these parameters obtained during the study period were compared to long-term mean values. The difference between long term values and current values has been referred as anomalies and can have positive or negative values.

Rainfall and temperature data were officially obtained from the Kenya Meteorological Department for the Kakamega Meteorological Station. Anomalies in mean monthly maximum and minimum temperatures and rainfall were calculated for the Kakamega station from a 25-year climatology (1975-2000). We had shown in earlier work[13] that *An. gambiae* in western Kenya required a mean of 150 mm rainfall per month for the population to increase significantly. This value was taken as the threshold value required for significant change in malaria transmission.

It has been shown that temperature has an exponential effect on parasite development in the female mosquito; therefore, small increases in ambient temperature of the mosquito habitat have large effects on the acceleration of parasite development. The effect of temperature is greatest on transmission at lower temperature (17-21°C); thereafter, the rate of reduction on the period of the development and maturity of the parasites is low[14].

Our laboratory experiments, where temperature and humidity were equivalent to those of local village houses, indicated that the average lifespan of the female *An. gambiae* mosquito is 18 days (Hidde *et al* unpublished report). Therefore, the malaria parasites would have to mature in the majority of the mosquitoes before 18 days in order to be transmitted. However, 20% of the laboratory bred mosquitoes survived for 25 days. This means that transmission for the majority of the mosquitoes, which survive for only 18 days, can only take place at

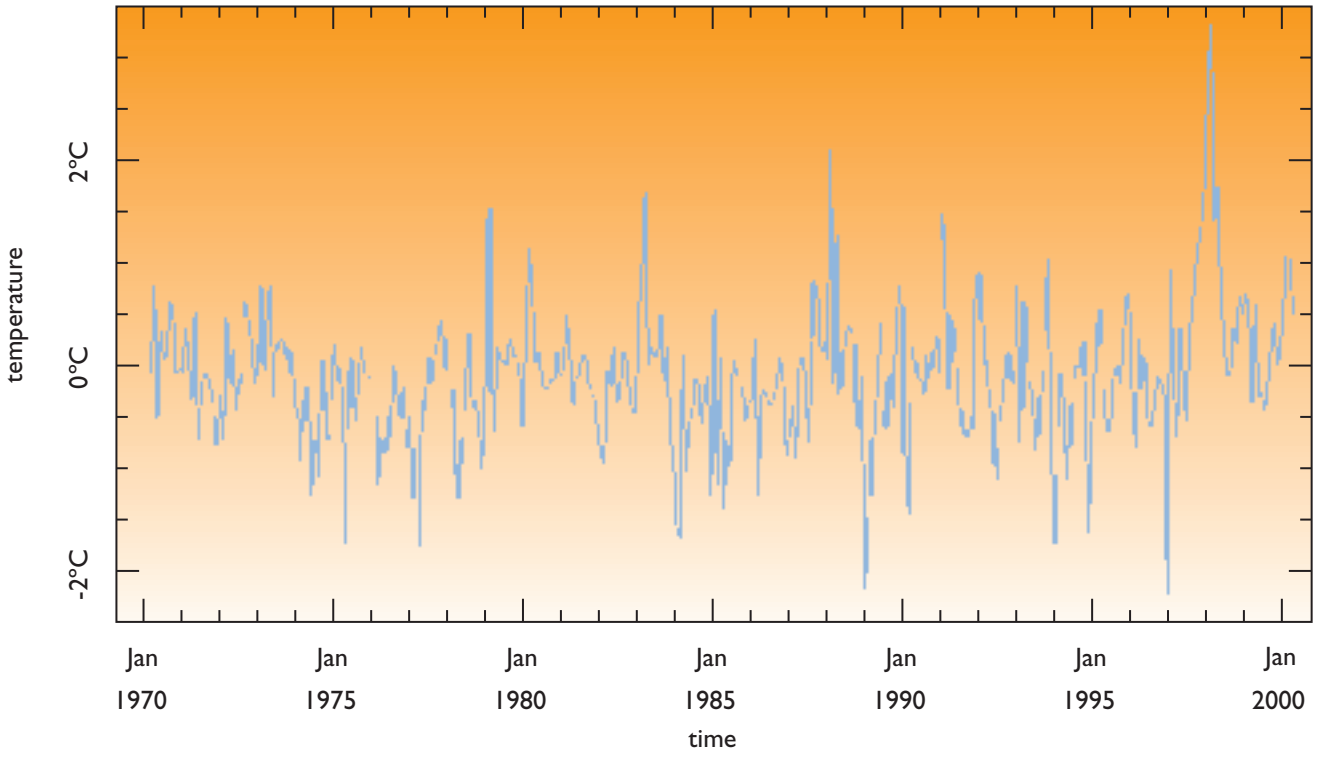

Figure 4 *Mean monthly minimum temperature anomalies for the grid 33.7-38.5E and 2.9S-2.9N covering western Kenya and Uganda.*

an ambient mean temperature of 23°C when it takes the parasites 16 days to mature. At 27°C, the parasites require only 10 days to become infectious. In western Kenya, nighttime temperatures inside village houses, where mosquitoes spend most of the time resting, are generally two to three degrees warmer than outdoor ambient temperatures (Sander personal communication). The assumption was made based on our unpublished data, that the *An. gambiae* blood-feeding habit and host choice is not a function of temperature. Parity was assumed to be constant at all temperatures.

Figure 2 shows that below a mean daily temperature of 18°C, very little transmission of malaria can occur, even if the number of vectors is doubled. However, at 21°C, each infected person can generate 2.41 new infections in mosquitoes and, if the mosquito density is doubled, the number of new mosquito infections is 4.82. Assuming that rainfall increases the number of breeding sites (and the number of malaria vectors), then rainfall has a linear effect on vectorial capacity.

Evidence of recent changes in temperature anomalies in parts of Western Kenya and Uganda

Anomalies of ≥ 3°C in western Kenya at altitudes of 1500-2000 meters have the potential to precipitate increased malaria transmission provided there is sufficient rainfall. This was confirmed by the data from Kakamega (Fig 5). From 1970-80, these conditions occurred only once, and from 1981-90 twice. From 1991 to 2000, there were six such events, with the highest anomaly recorded in 1998. These events are consistent with the past malaria outbreaks.

Minimum temperatures are less variable than the maximum temperature (see in Figures 3 and 4). Between 1970 and 1980, there was only one event with anomalies > 1°C, 1981-1990, three, and 1991-2000, four. The greatest positive anomaly, about 3°C, was recorded in 1998 during the El Niño.

Occurrence of positive anomalies in the maximum temperatures followed by rainfall may support a large malaria epidemic.

Determining the relationship between hospitalized malaria cases and maximum temperature anomalies in western Kenya

Trends in the maximum and minimum temperature anomalies suggest that the mean of the two temperatures is not a suitable indicator of temperature effects on malaria transmission. The data indicate that when the maximum temperatures are rising and minimum temperatures are falling, resulting mean temperature values conceal the epidemic related signal seen in the maximum temperatures. It should be noted that during the

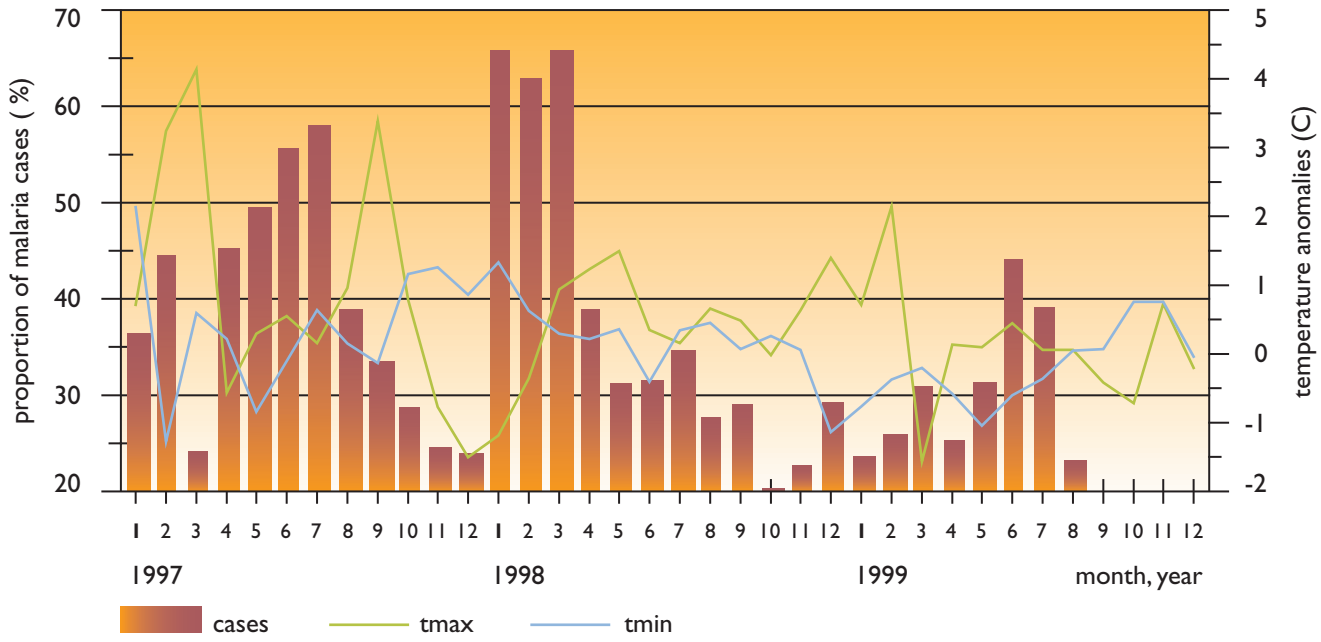

Figure 5 *Maximum and minimum temperature anomalies in Kakamega and the proportion of malaria cases in Mukumu Hospital, 1997-1998.*

1997/8 El Niño event, there were more than the usual proportion of malaria cases hospitalized at Mukumu hospital because the neighboring hospital was not fully operational due to striking medical staff.

Epidemic prediction model

The above information suggested that anomalies in the mean monthly maximum temperatures were a significant risk factor for malaria outbreaks. Furthermore, we had earlier observed that a minimum of monthly mean rainfall of 150 mm was required for a significant increase in the population of *An. gambiae*, the major vector of malaria. Consequently the two meteorological parameters, i.e. maximum temperature anomalies and rainfall were used as key risk factors for malaria outbreaks. Figure 2 displays the exponential effect of temperature on malaria transmission. Rainfall has a linear effect. To construct the model, the additive value of the two risk factors was expressed as a fraction of a predetermined maximum value. To simplify the calculation and remove "noise" from the signal, the temperature and rainfall data were transformed from continuous variables into discrete values. Transformed temperature values were squared to create an exponential effect. The mathematical expression representing the epidemic risk is shown in Equation 5.

$$ER = \frac{T^i + R^i}{T^m + R^m} \times 100 \qquad \text{Eq. 5}$$

- ER = the epidemic risk, expressed a percent
- T^i = transformed mean monthly maximum temperature anomaly
- R^i = transformed mean monthly rainfall above 150 mm threshold for An. gambiae
- T^m = the maximum intensity index for the transformed mean monthly temperature anomaly
- R^m = the maximum intensity index for the transformed mean monthly rainfall

Negative index values are assigned to rainfall above 300 mm per month as such rainfall causes flashing of larvae and consequent reduction in the rate of transmission. ER above 50%, as seen in figure 7, indicates a high risk for an epidemic.

Examples of data transformation

Temperature data filters

Programmable stepwise logic statements (filters) have been used to demonstrate the transformation. These statements can be constructed into a single logic formula to perform automatic calculations in a spreadsheet program.

Calculation of anomalies in monthly mean maximum temperatures

The mean maximum temperatures for each month are calculated for a period of 25 to 30 years.

These values are described as the climatology of the area. The mean maximum temperature of the month of interest is then subtracted from the long-term mean and this is the maximum temperature anomaly.

T = temperature anomaly
T^z = transformed data (discrete values)
T^2 = exponential temperature

If $T \geq 0$, then $T^z = 0$ $T^2 = 0$
If $0 < T < 1$, then $T^z = 1$ $T^2 = 1$
If $1 \geq T < 2$, then $T^z = 2$ $T^2 = 4$
If $2 \geq T < 3$, then $T^z = 3$ $T^2 = 9$
If $3 \geq T < 4$, then $T^z = 4$ $T^2 = 16$
If $4 \geq T < 5$, then $T^z = 5$ $T^2 = 25$

Rainfall data filter

R = Mean monthly rainfall,
R^Z = transformed data.

If $R < 150$, then $R Z = 0$
If $150 \geq R < 175$, then $R^Z = 1$
If $175 \geq R < 200$, then $R^Z = 2$
If $200 \geq R < 225$, then $R^Z = 3$
If $225 \geq R < 250$, then $R^Z = 4$
If $250 \geq R < 275$, then $R^Z = 5$
If $275 \geq R < 300$, then $R^Z = 6$
If $R > 300$, then $R^Z = -6$

The maximum risk value for maximum temperature anomaly was taken as 5.5°C and for rainfall 320 mm per month.

The epidemic risk (ER) index was calculated, for the study site, (using Eq. 5) using data obtained from the Kakamega meteorological station (1997-99). A correlation, with lag effects, of the monthly ER was calculated for monthly incidence of malaria cases, using the Mukumu Hospital data. The highest correlation ($r^2 = 0.26$) was obtained with a lag of 4 months. This analysis indicated that there is a significant correlation between the ER and the incidence of malaria cases.

The ER was plotted against the malaria case anomalies and as shown in Fig 7. In all cases, the peak of the ER appeared four months before the peak of the malaria cases. The model was able to predict both El Niño and non-El Niño malaria outbreaks. There were no false predictions, suggesting that the model has both high specificity and sensitivity.

For operational purposes, we have defined an epidemic as incidence of inpatient malaria cases 15% above the annual mean value. The mean value used was obtained for the period January 1996 to December 1999, a period that included epidemic and non-epidemic years. The threshold-risk for decision-making is an ER value of 50 % which occurs 3-4 months before the epidemic reaches the peak.

The regression equation in Fig.6 showing the relationship between the monthly malaria case incidence (MCI) and the monthly percent epidemic risk (PER) (y

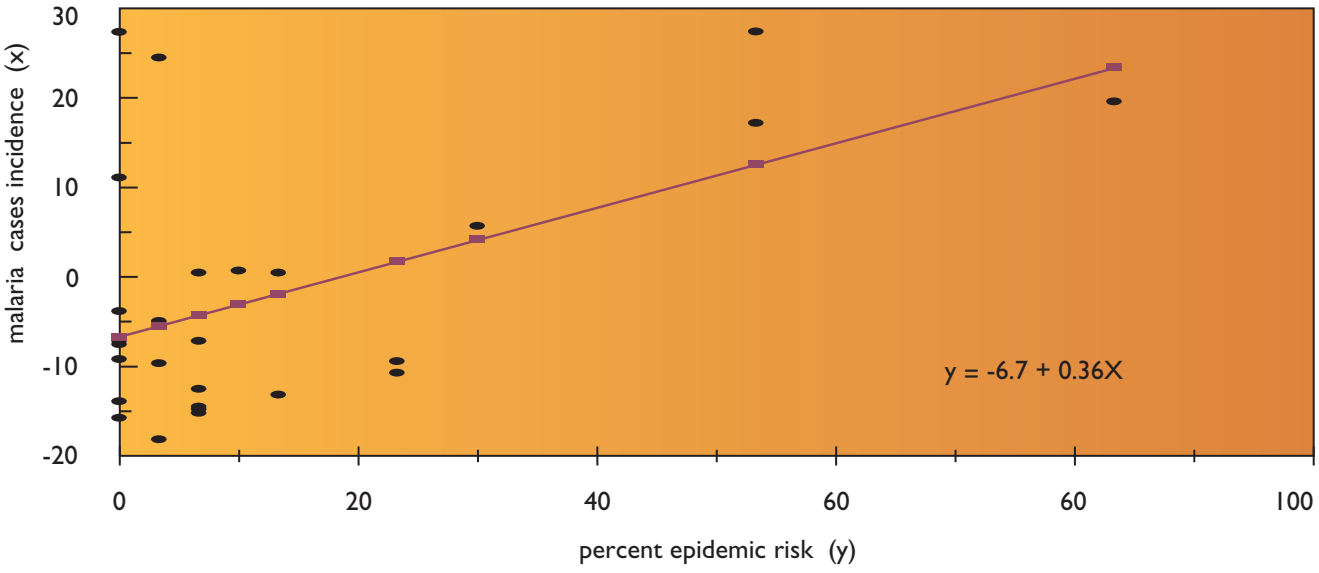

Figure 6 *Correlation between epidemic risk and the incidence of inpatient malaria cases in Mukumu Hospital. The dots indicate the observed malaria incidence and the line represents the predicted incidence.*

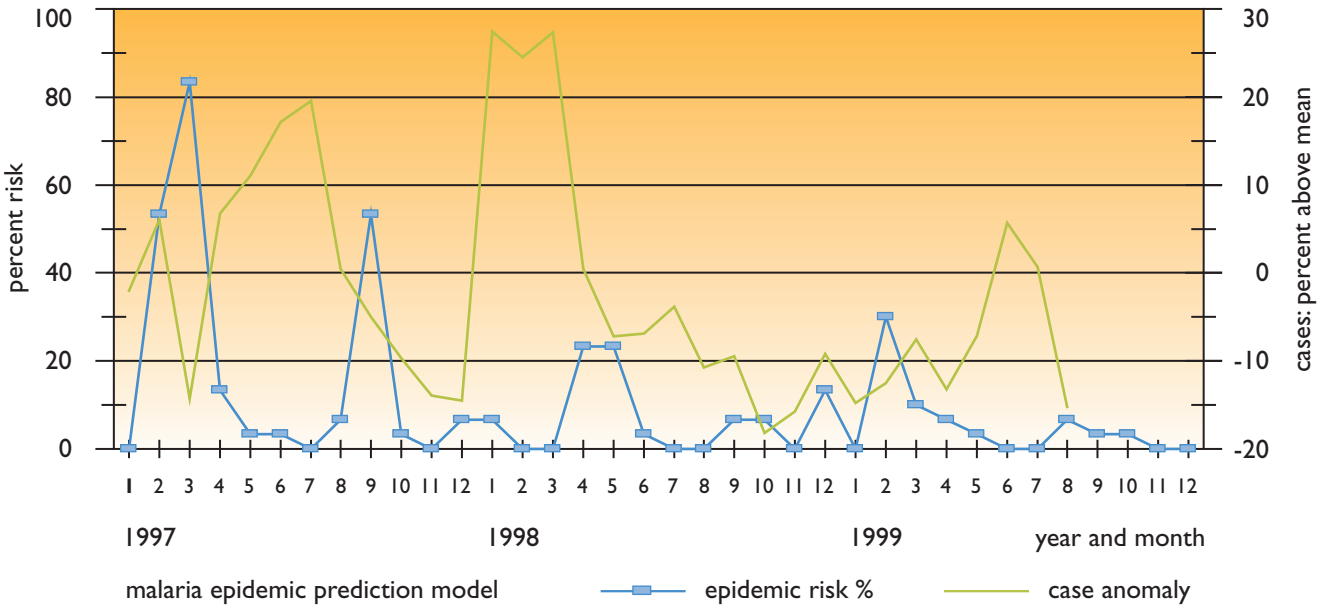

Figure 7 *Malaria epidemic risk; percent of malaria cases above the annual mean inpatient malaria cases in Mukumu Hospital*

= -6.7+0.36X, where y is the MCI and X is PER) can be used to estimate the size on the malaria epidemic. In this equation, X is equal to ER in equation 5. Furthermore the regression equation can be used to estimate specific outcomes of malaria case incidence with given temperature anomalies and amounts of rain by substituting the right side of equation 5 for X.

Application and further development of the model

The malaria epidemic prediction model meets the criteria of a simple malaria epidemic prediction model needing no special equipment or skills and so can be used by existing health personnel using readily available temperature and rainfall data of the meteorological department stations throughout the country. With centralization of data analysis and automation we envision that decision makers will receive warnings of impending epidemics within a few days following generation of data.

Although this system was developed using data collected at 1500 m, we believe that it can be adapted so as to predict epidemics in malaria endemic areas at higher altitudes; if the mean annual temperature is ≥ 18°C, anomalies of ≥ 3°C would be expected to precipitate malaria outbreaks as long as the mean monthly rainfall is greater than 150 mm. Further, the size of the forecasted epidemic can be estimated on the strength of the ER signal.

In the future, the lead-time between the predction and the epidemic may be increased using sea surface temperature anomalies (SSTA) of the Indian and the Pacific Oceans. However, the SSTA data may not be readily available at the district level and it may not be site specific.

Most vector borne diseases are sensitive to climate change and variability. Some, such as malaria and dengue, are more sensitive than others, such as trypanosomiasis or schistosomiasis. However, we speculate that our model may be adaptable for prediction of other diseases.

Temperature trends and malaria epidemics

Our data indicate that the use of the mean monthly temperatures may be insensitive for the detection of anomalies that are associated with malaria epidemics. This could lead to a failure in identifying an association between temperature change and malaria transmission.

Historically, malaria epidemics in Kenya occurred in the mid 1930s to 1940s and then again, from 1988 to the present. During these periods, increases in the mean temperatures were observed in the African region [15] and, they could be translated into significant positive anomalies in the maximum, and perhaps, even in minimum temperatures. In the 1930's to1940's, the problem of drug resistance or deforestation in western Kenya may not have been significant so the epidemics could possibly be explained by changes in the climate. It is notable that the areas affected by the epidemics at that time were largely occupied by pastrolists and there was little land-use change. Whereas, there was only one extreme event between 1970-1980, there were six such events between 1990 and 2000. Moreover, the

magnitude of the extreme events is increasing, a worrisome trend that can only intensify the frequency of malaria epidemics.

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Keywords Malaria, epidemic, prediction, model, climate

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