Potential effect of climate change on malaria transmission in Africa

Frank C Tanser, Brian Sharp, David le Sueur

Summary

Background Climate change is likely to affect transmission of vector-borne diseases such as malaria. We quantitatively estimated current malaria exposure and assessed the potential effect of projected climate scenarios on malaria transmission.

Methods We produced a spatiotemporally validated (against 3791 parasite surveys) model of *Plasmodium falciparum* malaria transmission in Africa. Using different climate scenarios from the Hadley Centre global climate model (HAD CM3) climate experiments, we projected the potential effect of climate change on transmission patterns.

Findings Our model showed sensitivity and specificity of 63% and 96%, respectively (within 1 month temporal accuracy), when compared with the parasite surveys. We estimate that on average there are $3\cdot1$ billion person-months of exposure (445 million people exposed) in Africa per year. The projected scenarios would estimate a 5–7% potential increase (mainly altitudinal) in malaria distribution with surprisingly little increase in the latitudinal extents of the disease by 2100. Of the overall potential increase (although transmission will decrease in some countries) of 16–28% in person-months of exposure (assuming a constant population), a large proportion will be seen in areas of existing transmission.

Interpretation The effect of projected climate change indicates that a prolonged transmission season is as important as geographical expansion in correct assessment of the effect of changes in transmission patterns. Our model constitutes a valid baseline against which climate scenarios can be assessed and interventions planned.

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D le Sueur died in March, 2002

Malaria Research Lead Programme, Medical Research Council, Overport, Durban, South Africa (F C Tanser PhD, B Sharp PhD, D le Sueur PhD); The Africa Centre for Health and Population Studies, Mtubatuba (F C Tanser PhD)

Correspondence to: Dr Frank Tanser, Malaria Research Lead Programme, Medical Research Council, PO Box 70380, Overport 4067, South Africa (e-mail: tanserf@mrc.ac.za)

Introduction

90% of malaria cases occur in Africa.1 In the past decade, the incidence of malaria has been escalating at an alarming rate. There is an increasing interest in the mapping and predictive modelling of the distribution, intensity, and seasonality of malaria transmission.2-Climate change is likely to have various effects on health, including changes in distribution and seasonal transmission of vector-borne diseases.7 The extent of these effects, however, continues to generate intense debate,8,9 especially in the projected effect of climate change on the global distribution of malaria, in which different approaches have resulted in widely varying estimates. A general issue facing all researchers has, however, been the absence of comprehensive, goodquality empirical data to validate the models used. The link between climate and malaria distribution has long been established. Sustained transmission depends on favourable environmental conditions for both vector and parasite. The effect of temperature on the duration of the sporogonic cycle of the malaria parasite and vector survival^{10,11} is particularly important.

Several methods have been used to estimate changes in the worldwide distribution of malaria in scenarios of global climate change. One approach relies on a biological model that predicts a large increase in global malaria potential. Some have criticised biological models on the basis that crucial parameters and their relations with environmental factors have not yet been quantified.14 Thus, biological models have used only a limited number of covariates, and doubts have been raised about the qualitative validity of some results.15 An alternative approach, based on a statistical model derived from the current malaria distribution projects little change in distribution.14 The use of current malaria distribution to derive the model resulted in areas that are climatically suitable for transmission but in which malaria has been eradicated (eg, northern parts of Australia), skewing the results. Generic disadvantages of worldwide or continent-wide statistically-driven models are that data sets used to statistically develop the models are often of uncertain accuracy, models are not easily reproducible (ie, results vary with training data and methods used), and the results are often applicable only to national or subregional scales. We use a large set of parasite surveys done throughout Africa to produce a spatiotemporally validated model of malaria transmission and project the effect of three climate scenarios by Hadley Centre global climate model (HadCM3) climate experiments.

Methods

Data

We used mean long-term monthly rainfall and temperature data as the basis for the seasonality model. The gridded surfaces were based on weather station data from 1920 to 1980 and have a spatial resolution of 0.05° .

	Variable	Threshold
Simulated effect		
Parasite development	Moving average	≥(19·5°C+yearly SD of
and vector survival	temperature	mean monthly temperature)
Frost	Minimum yearly	≥5°C
	temperature	
Availability of vector	Moving average	≥60 mm
breeding sites	rainfall	
Catalyst month	Moving average rainfall	At least 1 month ≥80 mm
Parasite reservoir	1 month interruption	Automatically assigned
(also simulated by	in transmission (as	transmission status
the differential	predicted by	
temperature	climate thresholds)	
threshold imposed)		

Table 1: Criteria used to calculate months suitable for P falciparum malaria transmission in Africa

The temperature data have SEs of 0.5° C and monthly mean precipitation data have errors of 10-30%.

The population data we used was an interpolated gridded surface 17 of resolution 0.042° with 1995 population estimates. Data were interpolated with a spatial interaction model that incorporated information about the location and size of major towns, transport infrastructures, and uninhabited areas. Overall, uncertainty in these population estimates is likely to be large, but remains within the usual range of error that is associated with census figures for developing countries.

We used B1 (low greenhouse gas emissions), A2a (medium-high emissions), and A1FI (high emissions) Intergovernmental Panel for Climate Change (IPCC) climate scenarios¹⁸ generated with the HadCM3 model.

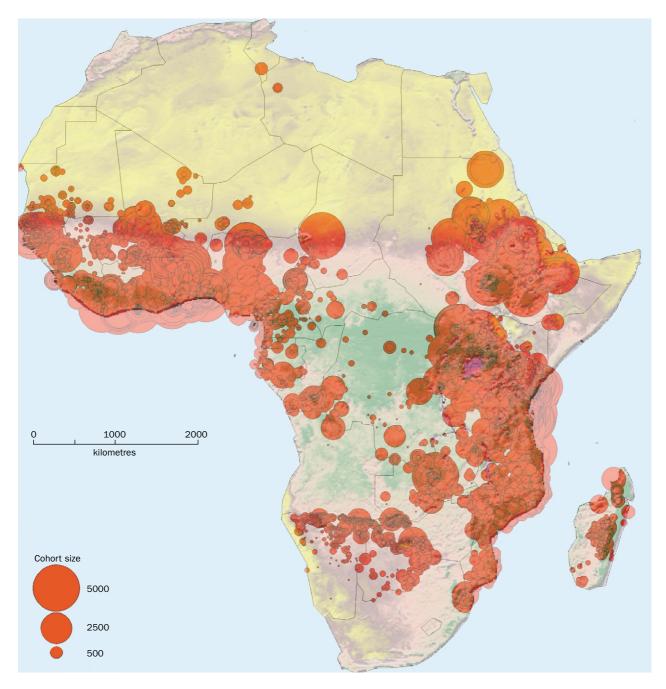


Figure 1: **Distribution of parasite survey sites in Africa** Surveys n=6284, total number of people tested n=1105596.

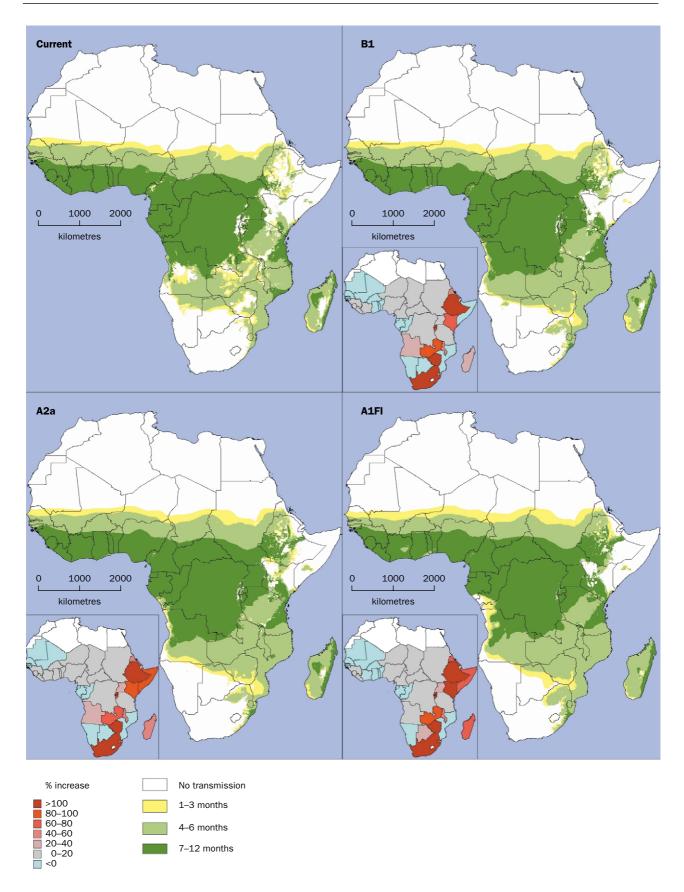


Figure 2: Estimated number of months suitable for *Plasmodium falciparum* malaria transmission, and change in person-months of exposure by country at present and by 2100 using three HadCM3 scenarios (B1, A2a, A1FI)

The scenarios project overall potential increases in person-months exposure by 2100 to be 16% (B1), 23% (A2a), and 28% (A1FI), respectively (constant population assumed).

	Change in annual rainfall (mm)†	Change in average temperature (°C)†	Area (km²)‡	Population exposure (millions)	PME (millions)	Proportion of increase in PME in areas of existing transmission (%)	
Current			15.24	444.722	3082-027		
2010-39							
B1	-35.8 (77)	1.1 (0.3)	15.70 (3.0%)	471.61 (6.0%)	3220.51 (4.5%)	32.3%	
A2a	2.0 (71)	1.3 (0.3)	15.80 (3.7%)	477.51 (7.4%)	3450.75 (12.0%)	65.8%	
A1FI	-16.8 (72)	1.3 (0.3)	15.52 (1.8%)	476.18 (7.1%)	3343.062 (8.5%)	51.7%	
2040-69	<u> </u>						
B1	-55.3 (94)	1.9 (0.5)	15.62 (2.5%)	483.72 (8.8%)	3325.30 (7.9%)	22.3%	
A2a	2.9 (101)	2.2 (0.5)	16.02 (5.1%)	495.15 (11.3%)	3626.50 (17.7%)	53.0%	
A1FI	-36.0 (139)	3.0 (0.7)	15.93 (4.5%)	507.13 (14.0%)	3619.00 (17.4%)	33.7%	
2070-99	_						
B1	-32.6 (99)	2.6 (0.6)	15.96 (4.7%)	502.67 (13.0%)	3559.42 (15.5%)	35.0%	
A2a	-18.0 (146)	3.3 (0.7)	16.20 (6.3%)	513.32 (15.4%)	3797.91 (23.2%)	41.5%	
A1FI	-38·2 (225)	5.3 (1.1)	16.33 (7.2%)	528.71 (18.9%)	3949.98 (28.2%)	27.6%	

PME=person-months of exposure. *Constant population assumed. †Mean (SD). ‡% increase shown in parentheses.

Table 2: Estimated P falciparum malaria exposure and transmission in Africa with the HadCM3 B1, A2a, and A1FI scenarios*

The climate scenarios differ in the concomitant increase in global mean temperature (under HadCM3) as a result of possible future political, economic, technical, and social developments affecting greenhouse gas emissions. For example, between 1990 and 2100, B1, A2a, and A1F1, project global increases of atmospheric CO₂ of 47%, 98%, and 126%, respectively.

The data have a resolution of $3.75^{\circ} \times 2.5^{\circ}$ for three 30-year mean periods: 2020s, 2050s, and 2080s.¹⁹ The scenarios are presented in storylines, which represent mutually consistent characterisations of future states of the world during the 21st century, including demographic and economic development and associated changes in climate and sea level.¹⁸ The associated population and gross domestic product scenarios were not incorporated into the model. The settings are neither predictions nor forecasts of future conditions. Rather, they describe alternative plausible futures that conform to sets of circumstances or constraints within which they arise.²⁰ The true purpose of scenarios is to remove uncertainty by determining the possible ramifications of climate change along one or more plausible (but indeterminate) paths.²¹

Model

To derive the suitability criteria for the model, we extracted climatic data from 15 sites (in transmission settings ranging from holoendmic to malaria-free) for which published malaria seasonal profiles existed.² We systematically analysed site-specific climatic data to identify climatic thresholds to explain the observed seasonal profiles. All thresholds used were derived from published biological ranges affecting both vector and parasite development. The thresholds were refined with area-specific expert knowledge of the distribution and seasonality of the disease in Africa and historical published and unpublished maps for Kenya, Tanzania, Zimbabwe, Namibia, and South Africa, and clinical-case data for South Africa and Botswana.

Two monthly variables (moving average temperature and rainfall) and three yearly variables (minimum temperature, standard deviation of average monthly temperature, and existence of a catalyst month) constituted the basis of our model (table 1). Since a sporadic month of suitable climatic conditions is not adequate for malaria transmission, we used a 3-month moving average for variables such as rainfall and temperature. Thus, for March, values used were the average of January, February, and March. Once minimum temperatures approach freezing, African anopheline vector populations are radically reduced. ²² At a consistent temperature of 19·5°C, the duration of the sporogonic cycle of the *Plasmodium falciparum* parasite is

32 days with 4% of the total vector cohort surviving. We analysed stable and seasonal climatic profiles and showed that lower monthly temperatures can sustain transmission of malaria in stable malarious areas. These differences are a function of the annual variations in temperature. In seasonal areas (higher latitudes and altitudes) vector and parasite populations need to be fully regenerated after the cold winter months to facilitate transmission. In stable areas (lower latitudes and altitudes) temperatures hover around the threshold mark for much of the year, therefore lower temperatures can sustain transmission on account of the existing parasite reservoir.

Studies of anopheline mosquitoes have shown a close association between breeding site availability and precipitation.23 Additionally, rainfall is closely related to soil moisture status, an important factor in mosquito survival.11 However, a substantial lag can exist between a precipitation event and suitable soil moisture status being attained.3 Suitable vector breeding sites could occur in an area that has recorded a low (or no) rainfall for the current month on the strength of preceding precipitation events. Conversely, latent moisture values are likely to be reduced during a month of average rainfall but preceded by low rainfall conditions. For these reasons a 3-month moving average was also used for the rainfall data. This approach allows rainfall from the previous 2 months to contribute to a more accurate moisture-status estimate in the current month.

Our analysis of climatic profiles in both seasonal and stable malaria areas has shown the need for a catalyst month (unpublished data)—ie, a month of highly suitable rainfall conditions to provide adequate vector breeding sites and regenerate the vector population.

A predicted 1-month transmission interruption (eg, between two malaria seasons) was assigned transmission status on the strength of the climatic suitability of the bordering months and the existing parasite reservoir. The thresholds are designed to delimit high-probability malarious areas because the use of long-term mean data precludes the delimitation of occasional epidemic areas. All criteria had to be met for a pixel to be classed as malarious in a particular month.

Model validation

To independently validate the model both spatially and temporally, we analysed 6284 laboratory-confirmed parasite-ratio surveys, consisting of 1105 596 people tested, across Africa²⁴ obtained between 1929 and 1994 (figure 1). We selected surveys that were undertaken during 1 month and excluded those done in the same location during the same month to minimise potential

	Person-months of exposure (millions)				Population exposure (millions)				
	Current	B1 (%)	A2a (%)	A1FI (%)	Current	B1 (%)	A2a (%)	A1FI (%)	
Country									
Algeria	0			∞*	0			∞†	
Angola	42.791	35.4	31.2	16.4	8.049	11.2	5.8	0.8	
Benin	44.906	-12.9	7.8	-10.9	5.409	0	0	0	
Botswana	1.360	-28.6	-28.9	36	0.382	-21.5	-15.7	58.6	
Burkina Faso	56.592	-1.6	5	-3.7	10.479	0	0	0	
Burundi	24.194	93.6	97.3	117.5	3.738	51.3	56.5	62	
Cameroon	103.665	8.9	17.6	16.8	12.682	2.5	3.2	3.6	
Central African Republic	28.091	1.1	17.5	15.8	3.273	0	0	0	
Chad .	29.314	4.5	9.9	16.9	5.958	2.3	3.9	4.5	
Congo	22.603	-9.5	-19.4	-54.6	2.593	0	0	-29.2	
Democratic Republic of Congo		8.3	10.4	7.2	40-464	7.7	8.3	9.1	
Equatorial Guinea	4.597	-5.1	-3.8	-12.7	0.391	1.8	1.8	1.8	
Eritrea	5.462	53	59.3	64	1.921	22.7	23.1	26.2	
Ethiopia	85.807	149.3	231.1	349.3	22.551	78-1	92.1	122.3	
Gabon	10.424	-2.3	-3.8	-8	1.032	0.1	0.1	-1.9	
Gambia	5.555	0	0	-0.3	1.111	0	0	0	
Ghana	157.591	-2.6	2.1	-4.8	17.338	Ö	Ö	Ö	
Guinea	56.524	2.9	6.4	4.7	7.346	Ö	Ö	Ö	
Guinea Bissau	6.469	-0·7	-2.3	-10·7	1.064	Ö	Ö	Ö	
vorv Coast	132.988	8.3	9.4	-5·1	13.692	Ö	0	0	
Kenya	111.214	69.7	93.6	124.1	14.496	49.1	58.8	73·1	
_esotho	0			∞‡	0			∞§	
_iberia	23.835	6.9	6.9	∞ + 6⋅8	2.123	0	0	~g 0	
Malawi	36.616	42	40.7	52.8	8.323	15·7	15.9	16·2	
vialawi Mali	48.971	-5·4	-5·4	-14·2	9.968	0.2	0.6	-1.1	
Mauritania	2.431	-45·4	-56.2	-87·1	0.791	-44	-54.7	-86.6	
Mauritius	59.341	35.8	47·9	-67·1	9.179	-44 36	-34·7 42·4	52·6	
Mozambique	99.075	-7·3	-7·9	-4·7	16.968	1.4	1.5	1.6	
Namibia	3.485	-43·8	-81	-81·9	0.919	-40·8	-79·2	-81·2	
	33.352	-43·6 2	-61 5·6	3.3	8·787	-40·8 0·5	0.6	-81·2 0·7	
Niger Nigeria	834.941	∠ 0·5	6	5·3 6·4	111.710	0.5	0.6	0.7	
•						70·8	86·5	107·3	
Rwanda	18.333	103·8 –6·6	122·5 −10·2	171∙3 –24∙7	2.435		-4·9		
Senegal	34·885 38·206	–6·6 6	-10·2 8·2	-24·7 8·5	8·306 4·194	–3⋅8 0	-4·9 0	–10·5 0	
Sierra Leone Somalia	38·206 2·036	-43·3	8·2 90·2	8·5 78·6	4·194 0·553	-14·1	0 76·5	0 54·1	
South Africa	28.296	164.7	237	377	7.606	124.3	188.6	247	
Sudan	80.011	4.8	6.6	8.2	17.908	5.1	0.5	1.7	
Swaziland	2.441	56	68-2	99.6	0.583	31.6	37	47	
Tanzania -	178.642	11.6	12.9	19.2	26.501	9.1	10.7	12.7	
Годо	33.000	-19.9	3.7	-16·1	4.085	0	0	0	
Jganda	174.167	14.2	20.1	28.8	17.302	8.1	9.4	13	
Zambia	24.827	81.1	77.2	82.9	7.190	12.4	12.4	12.4	
Zimbabwe	20.015	152-2	149-2	156.8	5.322	106⋅8	108.9	109-3	
Total	3.082.027	15.5	23.2	28.2	444.722	13.0	15.4	18.9	

Table 3: Estimated P falciparum malaria population exposure in Africa with the HadCM3 B1, A2a, and A1FI climate scenarios*

bias caused by excessive spatiotemporal clustering. We superimposed the remaining 3791 surveys on the resulting seasonality maps (derived from the model) and calculated the sensitivity and specificity of the model (to within a month's temporal accuracy). Respective sensitivity/specificity was defined as the proportion of surveys in which malaria occurrence/non-occurrence is correctly predicted by the model to within a month.

Projecting the effect of climate change

Following standard practice, we interpolated the future climate scenario surfaces¹⁹ to the resolution of the long-term mean data (1920–80) using a bilinear interpolation. We superimposed the change data from the HadCM3 experiments onto the long-term mean data to calculate projections for future periods. We also superimposed gridded population data¹⁷ on the resulting maps to calculate potential person-months of exposure under current and future climatic conditions. To isolate the effects of climate change we assumed a constant population over the century and did not attempt to incorporate population projections into the future estimates. We used person-months of risk as the main

outcome measure for assessment of the overall potential effects of the climate scenarios on malaria transmission. The measure combines both spatial and temporal aspects of population exposure.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, writing of the manuscript, or interpretation of results.

Results

Our seasonality model estimates that on average there are 3·1 billion person-months of exposure to malaria (445 million people exposed) in Africa every year (table 2). The spatial and temporal validation of the predicted current malaria distribution (figure 2) was undertaken with positive (n=3199) and negative (n=592) parasite surveys of 1 month duration. The model showed a sensitivity (ie, the ability of the model to accurately predict areas of transmission to within a month) of 63% (95% CI 61–65) and a temporal sensitivity (the ability to accurately predict malaria occurrence in any month) of 90% (89–91). A specificity within 1-month temporal

accuracy of 96% (91–100) was obtained. The specificity is remarkable because malaria surveys are usually done in areas and during times of the year when malaria cases are expected or have been recorded previously. Similarly, the sensitivity is derived using some surveys done during epidemic years and in areas with permanent breeding sites. When interannual and small area variation and effect of vector control and resolution of data used is taken into account, the overall accuracy of the model is good.

By 2100, the model estimates a potential continental increase of 16-28% in person-months of exposure across all three scenarios (table 2). This rise is coupled with a 5-7% (mainly altitudinal) increase in distribution with surprisingly little change in the latitudinal extents of the disease. The only substantial latitudinal extension (across all scenarios) is seen in a region in the Limpopo Province of South Africa, which is prone to occasional epidemics (figure 2). The potential effect of climate change in areas of existing transmission is noticeable, with 28-42% of new person-months of exposure towards the end of the 21st century arising in areas presently suitable for the disease (table 2). This result is due to the increase in the length of transmission season in these areas. The B1 scenario shows the least increase in person-months of exposure across all periods because of reductions in rainfall and smallest rises in average temperature. The highest increase in personmonths of exposure during the 2020s and 2050s shown by the A2a scenario is a result of the combined effect of slight increase in rainfall and large rise in temperature, and emphasises the importance of rainfall in malaria transmission. The A1FI scenario shows the highest increase in person-months of exposure by 2100, in which the largest rise in temperature is coupled with a moderate reduction in rainfall. This scenario shows the smallest increase in distribution in the 2020s as a result of most of the projected changes in transmission taking place in populous areas of existing transmission, as an extension of the malaria season.

Countries with large areas that are close to the climatic thresholds needed for transmission show large potential increases across all scenarios. Ethiopia, Zimbabwe, and South Africa are projected by all scenarios to show increases of more than 100% in person-months of exposure towards the end of the 21st century (table 3). This effect would result from the projected potential increase in highland malaria in Zimbabwe and Ethiopia, and the rises in distribution and season length for South Africa. A host of countries in West Africa (eg, Mali, Ghana, and Burkina Faso), and Namibia and Mozambique in southern Africa are projected by all settings to show a fall in person-months of exposure because of the drier climate in these areas. Regions where rainfall is the limiting factor are especially prone to epidemics. The catastrophic malaria epidemic in Ethiopia in 1958, for example, was largely associated with unusually high rainfall over a long time.

Discussion

We have produced a spatiotemporally validated malaria transmission model for Africa and projected changes in transmission patterns in differing climate scenarios. Our findings have important implications for malaria control in Africa since both the duration and timing of malaria transmission season are important to inform efforts in malaria control. The duration of the season will affect the dynamics of transmission, with longer seasons allowing heightened transmission and high levels of infection in the population. Short periods of exposure are linked with a waning immune response and fatal outcomes.

The potential increase of 16–28% in person-months of exposure in Africa by 2100 (on the assumption that future climates fall within simulated ranges) should be of concern because social conditions are likely to facilitate this rise in most countries in view of the inadequate health infrastructure, deteriorating malaria control programmes, possible link between the HIV/AIDS and malaria,²⁵ and overall human landscape of the continent.

The basis for our model is climatic, and thus has some limitations. For example, areas such as the Limpopo valley (the border between South Africa and Zimbabwe) that are adjacent to perennial water reservoirs might fail to meet the necessary monthly rainfall threshold, but could still provide good breeding grounds for vectors. We did not take local demographic and socioeconomic circumstances into account nor make provision for the effect of malaria control on transmission. The inability of global circulation models to accurately predict the current climate from retrospective data,26 has led to a debate about their application. As our understanding of global climate dynamics increases and models are increasingly able to handle this complexity, projections of the probable response of the climate system to any scenario are likely to improve and the model will constitute a valid baseline for assessment.

The resurgence of highland malaria cannot necessarily be attributed to recent climate change. Malaria is a complex disease that is affected by a range of factors in addition to climate—a recent analysis of four highland sites in Africa where large increases in malaria cases were noted showed no large climatic change during resurgence or the last century.27 Some of these cases were attributed to factors such as drug resistance, breakdown of control programmes, and land-use change (although doubts have been raised about the suitability of the data used in the analysis²⁸). However, climate provides the framework within which transmission is possible and other factors (except those that determine the availability of breeding sites-irrigation, construction of dams, or removal of potential breeding sites) can affect malaria transmission only in spatio-temporal zones that are climatically suitable.

With adequate funding, technology, and commitment, WHO's Roll-Back Malaria campaign will endeavour to halve deaths related to Plasmodium falciparum by 2010.29 The organisation recognised the need to improve understanding of how climate-related and other ecological factors affect the spread and severity of malaria.30 We believe that transmission maps generated by our model could form an integral component of this strategy. Our model has achieved a good accuracy and is validated against empirical data. Our work is an important first step towards a model of intensity of transmission and constitutes a valid baseline against which interventions can be planned and climate change projections evaluated. Such a baseline is essential if we are to put the theory of the effect of climate change on vector-borne diseases into practice.

Contributors

The corresponding author had full access to all data used in the study and had the final responsibility for the decision to submit for publication. F Tanser developed the malaria seasonality model and was responsible for all GIS and statistical analysis, and writing of the manuscript. B Sharp critiqued all versions of the model and assisted in writing the manuscript. D le Sueur conceived the MARA project and was responsible for the initial seasonality model concept. He gave input into the research at all stages of its development and assisted in the writing of the manuscript.

Conflict of interest statement None declared.

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References

- 1 WHO. The world health report 1999: making a difference. Geneva: World Health Organization, 1999.
- 2 Craig MH, Snow RW, le Sueur D. A climate-based distribution model of malaria transmission in sub-Saharan Africa. *Parasitol Today* 1999; 15: 105–11.
- 3 Hay SI, Snow RW, Rogers DJ. Predicting malaria seasons in Kenya using multitemporal meteorological satellite sensor data. Trans R Soc Trop Med Hyg 1998; 92: 12–20.
- 4 Kleinschmidt I, Bagayoko M, Clarke GP, Craig M, Le Sueur D. A spatial statistical approach to malaria mapping. *Int J Epidemiol* 2000; 29: 355-61
- 5 Rogers DJ, Randolph SE, Snow RW, Hay SI. Satellite imagery in the study and forecast of malaria. *Nature* 2002; 415: 710–15.
- 6 Snow RW, Gouws E, Omumbo J, et al. Models to predict the intensity of *Plasmodium falciparum* transmission: applications to the burden of disease in Kenya. *Trans R Soc Trop Med Hyg* 1998; 92: 601–06
- 7 McMichael A, Githeko A. Human Health. In: McCarthy J, Canziani O, Leary N, Dokken D, White K, eds. Climate change 2001: Impacts, Adaptation, and Vulnerability—contribution of Working Group II to the Third Assessment Report of the Intergovernmental Panel on Climate Change. New York: Cambridge University Press, 2001: 451–85.
- 8 Lindsay SW, Martens P. Malaria in the African highlands: past, present and future. Bull World Health Organ 1998; 76: 33–45.
- 9 Reiter P. Global-warming and vector-borne disease in temperate regions and at high altitude. *Lancet* 1998; 351: 839–40.
- 10 Onori E, Grab B. Indicators for the forecasting of malaria epidemics. Bull World Health Organ 1980; 58: 91–98.
- 11 Molineaux L. Malaria: principles and practice of malariology: Churchill Livingstone, 1988: 919–98.
- 12 Martens P, Niessen LW, Rotmans J, Jetten TH, McMichael AJ.

- Potential impact of global climate change on malaria risk. *Environ Health Perspect* 1995; **103:** 458–64.
- 13 Martens P, Kovats RS, Nijhof S, et al. Climate change and future populations at risk of malaria. *Global Environmental Change* 1999; 9 (Special issue): 89—107.
- 14 Rogers DJ, Randolph SE. The global spread of malaria in a future, warmer world. *Science* 2000; 289: 1763–66.
- 15 Reiter P. From Shakespeare to Defoe: malaria in England in the little ice age. *Emerg Infect Dis* 2000; **6:** 1–11.
- 16 Hutchinson MF, Nix HA, McMahan JP, Ord KD. Africa A topographic and climatic database, CD-ROM (1): Centre for Resource and Environmental Studies, Australian National University, 1995.
- 17 Deichmann U. Africa population database: National Centre for Geographic Information and Analysis and United Nations Environment Programme, World Resources Institute, http://grid2.cr.usgs., 1996.
- 18 Nakicenovic N. Special report on emissions scenarios: a special report of working Group III of the Intergovernmental Panel on Climate Change. New York: Cambridge University Press, 2000.
- 19 Johns T, Ingram W, Johnson C, et al. Anthropogenic climate change for 1860 to 2100 simulated with the HadCM3 model under updated emissions scenarios. Clim Dynam 2003; 20: 583–612.
- 20 Hammond A. Which world? Washington DC: Island Press, 1996.
- 21 Fisher RW. Future energy use. Future Research Quarterly 1996; 31: 43–47.
- 22 Stuckenberg BR. Effective temperature as an ecological factor in Southern Africa. Zool Afr 1969: 145–97.
- 23 Sloof R. Field observations on the biting activity of Anopheles koliensis Owen. Trop Geogr Med 1961: 67–76.
- 24 MARA. Towards an atlas of malaria risk in Africa: first technical report of the MARA/ARMA collaboration. Durban, 1998.
- 25 Whitworth J, Morgan D, Quigley M, et al. Effect of HIV-1 and increasing immunosuppression on malaria parasitaemia and clinical episodes in adults in rural Uganda: a cohort study. *Lancet* 2000; 356: 1051–56.
- 26 Barnett TP. Comparison of near-surface air temperature variability in 11 coupled global climate models. *J Climate* 1999; **12:** 511–18.
- 27 Hay SI, Cox J, Rogers DJ, et al. Climate change and the resurgence of malaria in the East African highlands. *Nature* 2002; **415:** 905–09.
- 28 Patz J, Hulme M, Rosenzweig C, et al. Climate change: regional warming and malaria resurgence. *Nature* 2002; **420**: 627–28.
- 29 Nabarro DN, Tayler EM. The roll back malaria campaign. Science 1998; 280: 2067–68.
- 30 WHO. A global strategy for malaria control. Geneva: World Health Organization, 1993.