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Article *in* Tropical Medicine & International Health · March 2008

DOI: 10.1111/j.1365-3156.2007.01993.x · Source: PubMed

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Tropical Medicine and International Health doi:10.1111/j.1365-3156.2007.01993.x

VOLUME 13 NO 2 PP 218–228 FEBRUARY 2008

Effectiveness of malaria control during changing climate conditions in Eritrea, 1998–2003

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Summary

OBJECTIVE To assess the effectiveness of impregnated mosquito nets, indoor residual spraying and larval control relative to the impacts of climate variability in the decline of malaria cases in Eritrea.
METHODS Monthly data on clinical malaria cases by *subzoba* (district) in three *zoba*s (zones) of Eritrea for 1998–2003 were used in Poisson regression models to determine whether there is statistical evidence for reduction in cases by DDT, malathion, impregnated nets and larval control used over the period, while analysing the effects of satellite-derived climate variables in the same geographic areas.
RESULTS Both indoor residual spraying (with DDT or malathion) and impregnated nets were independently and significantly negatively associated with reduction in cases, as was larval control in one *zoba*. Malaria cases were significantly positively related to differences in current and previous months' vegetation (NDVI) anomalies. The relationship to rainfall differences 2 and 3 months previously was also significant, but the direction of the effect varied by *zoba*. Standardized regression coefficients indicated a greater effect of climate in the *zoba* with less intense malaria transmission.
CONCLUSION The results support the view that both indoor residual spraying and impregnated nets have been independently effective against malaria, and that larval control was also effective in one area. Thus climate, while significant, is not the only explanation for the recent decline in malaria cases in Eritrea. If appropriate statistical approaches are used, routine surveillance data from cases attending health facilities can be useful for assessing control programme success and providing estimates of the effectiveness of individual control measures. Effectiveness estimates suitable for use in cost-effectiveness analysis have been obtained.

keywords malaria, Eritrea, climate variability, control measures

Introduction

The burden of malaria, especially *Plasmodium falciparum*, remains very high: recent estimates of the annual number of clinical malaria cases worldwide range from 214 to 515 million (WHO 2002; Breman *et al.* 2004; Snow *et al.* 2005). In most of sub-Saharan Africa neither malaria morbidity nor mortality declined appreciably over the last 5–10 years (Snow *et al.* 2004), but malaria has declined in some African countries, including Eritrea (Nyarango *et al.* 2006) and South Africa (Barnes *et al.* 2005). Eritrea achieved an 80% reduction in malaria morbidity since 1999 and implemented a vigorous control programme comprising impregnated nets, indoor residual spraying, larval control, community health agents providing treatment and training on case management (Barat 2006; Nyarango *et al.* 2006).

Although randomized trials have provided evidence that malaria prevention and control activities may be effective, it has not been conclusively determined whether decreases in malaria are due to prevention and control activities or to variation in climate, or whether multiple control methods were necessary. Because a large prospective randomized trial to answer these questions is not feasible, we aimed to determine whether there is robust statistical evidence that malaria prevention and control activities have, in fact, reduced malaria rates and if so, by how much. We used a relatively conservative statistical approach that is designed to address potential biases and errors in imperfect clinical reporting data and filter out evidence for which causality cannot be assigned to correlation. At the expense of having a test that is biased towards the null hypothesis, the statistical specifications used reduce the potential for spurious detections. Impacts must be sufficiently large to easily distinguish themselves above the noise in the clinical data to yield significant results.

Nyarango *et al.* (2006) provided some evidence for the impact of the malaria control programme and climate in Eritrea using nationwide annual data. This paper extends this analysis using 6 years of monthly case data by *subzoba* (district) in conjunction with additional seasonally adjusted monthly climate data and detailed records of control programme activities.

Quantitative estimates of the impact of each control activity on malaria incidence are essential for cost-effectiveness studies. Although randomized trials of impregnated nets (ITNs) indicated that they could reduce malaria incidence by about half (Lengeler 2004), their effectiveness under field conditions and in combination with other methods is unclear. It is likely that vector control methods in addition to ITNs will be needed to make a significant dent in malaria transmission in Africa. Opinions are divided on whether elimination or treatment of larval habitats is a feasible or effective way to control malaria (Killeen *et al.* 2002). There is also debate about the extent to which indoor residual spraying, particularly with DDT, should be used (Curtis 2002). DDT spraying was reintroduced in South Africa in 2000 (Craig *et al.* 2004a) and has also been used together with synthetic pyrethroids in Zambian mining areas since 2000 (Sharp *et al.* 2002), where the incidence of malaria was reduced by 35% after 1 year of spraying. Some information is available from comparative trials of indoor residual spraying and ITNs (Goodman *et al.* 2001; Guyatt *et al.* 2002), but such trials are relatively rare (Curtis & Mnzava 2000) and do not consider mixtures of the two. In the absence of large prospective randomized trials of each intervention or combination of interventions, past observational data on malaria incidence can in some circumstances be used to assess the effectiveness of control measures (Over *et al.* 2004) provided that data on the control measures performed are available in the same geographic and time units as the malaria incidence data.

Climate variability is a significant factor in either helping or hindering malaria control. Seasonal and interannual climate variations have a large impact on malaria transmission (Craig *et al.* 2004b; Thomson *et al.* 2005). Interannual variability in rainfall accounted for approximately 50% of the interannual variation in slide-confirmed malaria incidence in Botswana (Thomson *et al.* 2005). Heavy rain in East Africa due to the 1997–98 El Niño event was associated with malaria epidemics in highland regions (Kilian *et al.* 1999) while periodic drought years reduced malaria risk in the Horn of Africa, including Eritrea and Ethiopia. It is therefore essential that climate information is taken into account when assessing control programme effectiveness. This has recently become easier to do with the availability of satellite-derived climate data sets covering Africa and the ability to extract such data according to administrative boundaries (Grover-Kopec *et al.* 2005).

In general, evaluation of progress in controlling malaria presents a significant challenge. Changes in childhood mortality (either malaria-specific or all-cause) can only be measured with infrequent representative large-scale demographic and health surveys, or at a few established longitudinal demographic surveillance sites (Korenromp *et al.* 2003, 2004b). Other suggested indicators such as anaemia (Korenromp *et al.* 2004a) require repeated invasive surveys of carefully selected samples of the population. More routinely available indicators of progress are needed.

In certain circumstances, health information system surveillance data from cases attending health facilities could provide information for assessing control programme success and for evaluating the effectiveness of control measures. It is well-known that such routine data systems included misdiagnosed cases and do not capture all cases occurring, but if chosen carefully they may present a sufficiently representative sample to assess changes over time. Our statistical specification is designed to be as robust as possible to biases in the health facility data. Location-specific and time invariant potential biases in reporting are removed by the analyses.

By using 'clinical malaria' cases in this analysis, we include an unknown proportion of other diseases that are diagnosed as malaria, although in Eritrea, the specificity of malaria diagnosis is likely to be higher than in more highly endemic countries. These other diseases may or may not respond to prevention and control activities and climate in the same way as malaria. If they do not, the use of clinical cases biases our approach towards the finding of no effect, leading to more conservative results. Although it is possible for biases in the malaria reporting to lead to spurious detections of impacts, these biases would have to be structured according to highly idiosyncratic patterns to drive the statistical analysis to produce erroneously significant climate or control programme impacts.

Eritrea is divided into six main administrative zones (*zoba*s) and 58 smaller districts (*subzoba*s, Figure 1). Each *zoba* has several malaria control personnel including a

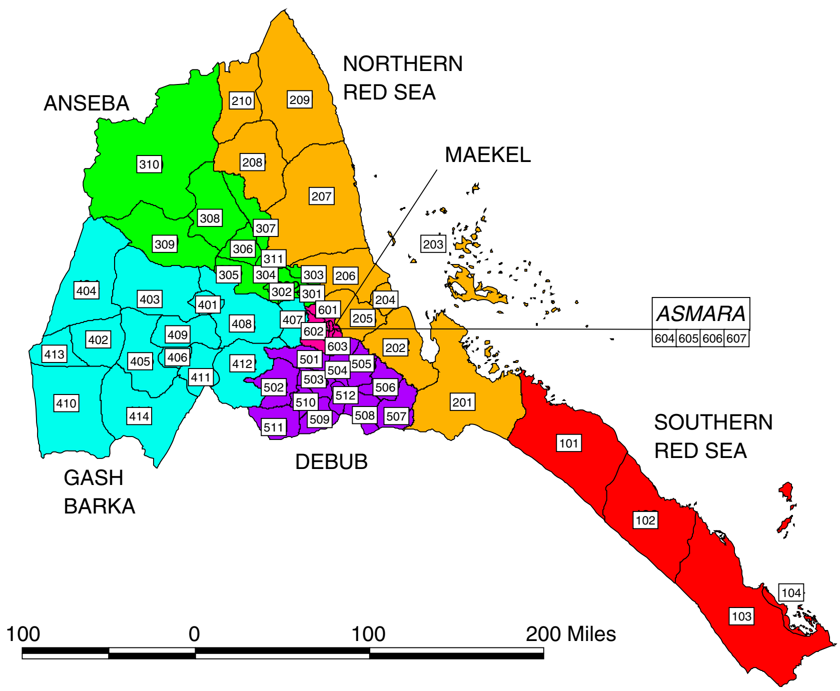

Figure 1 *Zoba*s and *subzoba*s of Eritrea. *Subzoba*s numbered according to the National Health Management Information System.

zoba malaria coordinator who decides, together with the National Malaria Control Programme, on planning and policies such as location and timing of spraying and/or larval control, and method of impregnated net distribution. The National Malaria Control Programme coordinates the supply of insecticides and nets to the *zoba*s, conducts training activities and operational research, and compiles data on the malaria situation at regular intervals.

The country is situated towards the northern margin of malaria transmission in Africa, but has a complex malaria endemicity due to two distinct rainfall patterns and large variations in altitude. The overall endemicity is quite low; in 1999–2000 the prevalence was 2.2% overall (Sintasath *et al.* 2005), although prevalence by village varied from 0% to 30%. The majority of cases occur in children over 5 years old and in adults.

In 1998 Eritrea introduced a new National Health Management Information System (NHMIS) based on monthly reporting of diagnoses from each health facility. A data set of clinical malaria cases extracted from this system, coupled with records kept by the National Malaria Control Programme for 1996 and 1997, was used to stratify malaria incidence throughout the country by *subzoba* (Ceccato *et al.* 2007). In this paper, we used a version of this data set together with additional information on control activities and climate to investigate the relative impacts of climate and different control methods on malaria incidence.

Methods

Data sources

The numbers of clinical malaria cases were extracted from the National Health Management Information System (NHMIS) Access database by month and health facility for the years 1998–2003. The National Malaria Control Programme (NMCP) provided similar data for the years 1996 and 1997. Hospitals, mini-hospitals, health centres and health stations were included. The first three types of health facility record data by ICD-9 code, while health stations complete a different form listing case numbers by clinical diagnoses.

The data set from the 325 health facilities which existed at the start of the time period was restricted to 242 sites by exclusion of national referral hospitals, private doctors, worksite clinics, maternal and child health clinics, and ophthalmic clinics, as these health facilities were not representative of the local area, had frequent interruptions in reporting or did not exist throughout the period of study. Three defunct facilities without reports over the period were also excluded. Because the availability of malaria diagnostic tests (microscopy and rapid tests) was poor and changed over time, we use clinically diagnosed cases of malaria, as determined by the appropriate ICD-9 codes and clinical diagnosis definitions. Thus the data consist of a representative sub-sample over space and time of the number of clinical malaria cases seen at health facilities in the country, rather than an exhaustive number of confirmed cases. For this analysis, we also excluded cases treated by the large network of community health agents as they only work part of each year and are likely to have a lower positive predictive value for malaria.

Malaria cases were summed over both age-groups (under and over 5 years) by *subzoba* (one to nine facilities per *subzoba*) and month. The numbers of cases of all diseases for the same health facilities were similarly extracted and summed, in order to provide a check that a report had been received if the number of malaria cases was reported as zero. If no report was received, the number of malaria cases was changed from zero to missing. The data set used here differs from that of Ceccato *et al.* (2007), in that missing values were not imputed in this analysis.

Administrative (*subzoba* and *zoba*) boundary files were obtained from the National Statistics and Evaluation office, Asmara, Eritrea, and visualized in ArcView 3.3. Climate information was extracted by *subzoba* boundary from the data library at the International Research Institute for Climate and Society (IRI).

Rainfall estimates were obtained from the Climate Prediction Center Merged Analysis of Precipitation (CMAP) version 0407, available from 1979 to date. CMAP is a data set of rainfall estimates in a 2.5×2.5 degree grid, constructed from five kinds of satellite estimates of precipitation. It is calibrated against available gauge data and undergoes dynamical model estimates (reanalyses) by the National Centers for Environmental Prediction (http://www.cpc.ncep.noaa.gov/products/global_precip/html/wpage.cmap.html). The data are expressed as daily averages (mm per day) for each month and were summed to provide monthly data.

Normalized Difference Vegetation Index (NDVI) is a satellite-derived measure of vegetation biomass and conditions. NDVI values vary between −1.00 and 1.00; the higher the NDVI value, the denser or healthier the green vegetation. NDVI estimates from NOAA-AVHRR satellite sensors were used, as unlike other possible sources from different satellites, they have an historical data series (July 1981 to present) overlapping with the current study. NDVI data are available for 10-day periods (dekads). We used the maximum value of the three dekads. The NOAA-AVHRR NDVI version 'e' product was retrieved from the USGS ADDS website (http://igskmncnwb015.cr.usgs.gov/adds/) and made available via the IRI data library website (http://iridl.ldeo.columbia.edu/SOURCES/.USGS/.ADDS/.NDVI/.NDVIe/.dekadal/.maximum/.NDVI/).

Information about the malaria control interventions performed over the study period was gathered from NMCP monthly reports and/or from paper records kept at the *zoba* malaria control offices. Adequate monthly records existed by *subzoba* for three *zobas*: Gash Barka, Anseba and Northern Red Sea. Of the other three *zobas*, only Debub has a significant amount of malaria. Amounts of DDT and malathion sprayed by *subzoba* were compiled from the spray locality record forms, and quantified in kg of each chemical. The number of people covered by spraying of their houses was also available for each locality. The amounts of DDT and malathion used to treat one house were similar (approximately 267 g DDT and 400 g of malathion, based on 100 m^2 per house).

Numbers of new impregnated mosquito nets distributed, and old nets reimpregnated, by *subzoba*, were obtained from the monthly report forms at the *zoba* malaria offices. Larval control activities were quantified by the number of breeding sites either eliminated or treated chemically with temephos (Abate), *Bacillus thuringiensis israelensis* (BTI) or *Bacillus sphaericus* (BS). Records were not comprehensive enough to allow quantification of larval control by the amount of chemical applied.

To allow for the persistence of insecticides after application, the amount of DDT used and number of treated nets were depreciated by 20% per month as described in Over *et al.* (2004). For DDT indoor residual spraying, this is a conservative estimate of decay in effectiveness based on the results of Mpofu *et al.* (1988) in Zimbabwe and on bioassay trials conducted by the Eritrea NMCP in 2002–2003 (unpublished data). In recognition of the shorter half life of larval control (Shililu *et al.* 2003) this was depreciated by 40% per month.

Analysis

Regression analysis was performed using the *poisson* procedure in STATA version 9. The dependent variable was the number of clinical malaria cases by *subzoba* and month. The 'exposure' option was used to adjust for the population of each *subzoba*. Standardized regression coefficients were estimated using the *listcoef* command after the *poisson* command in STATA version 9.

Initially we ran a battery of diagnostic regressions (available on request) of malaria interventions on climate and previous months' malaria case numbers, to determine whether control decisions were being taken in response to these factors. In Gash Barka and Anseba we found no evidence of relationships that represented actual mitigation decision-making, but in Northern Red Sea *zoba* there was strong evidence for the potential of spraying in response to rainfall. Because this affects assignment of causality, we excluded this *zoba* from further analysis.

Seasonal patterns can manifest themselves as spurious relationships if not explicitly accounted for in the analysis. Calendar months were therefore assigned dummy variables and included in the regressions, in order to address potential problems in assigning causality, and to control for seasonal patterns in malaria, climate and control methods. *Subzoba*s were also assigned dummy variables (fixed effects) to absorb confounding effects from any unobserved local characteristics that do not change over time. Our use of anomalies (deviations from local calendar monthly means) for the climate and intervention variables further filters potentially misleading information from the data set, by subtracting out systematic effects that are not explicitly modelled.

For clarity and ease of interpretation, climate variables were specified in terms of aggregated lags (combined variables from the lagged months contributing significantly to the outcome). As a diagnostic, 4 months of each lagged climate variable was first included in a cross-sectional regression analysis using *xtreg* in STATA 7 with case anomalies as outcome variable (results available on request). The aggregated lag variables chosen were those lags that had a significant impact in these regressions. The overall model fit was only marginally affected when combined climate variables were used for the months with strongest relationships to malaria. For NDVI, the aggregated lag variable used was the sum of the current and previous month's NDVI. For rainfall, it was the sum of rainfall lagged by 2 and 3 months.

Results

Figure 2 shows that from 1998 onwards, more than 80% of the 242 selected health facilities reported each year, and that more than 75% of the expected reports were received. There has been a decline in cases since 1998 (Figures 3 and 4). Malaria control in Eritrea uses a centrally determined set of vector control methods (impregnated net distribution, indoor residual spraying and larval control), but implementation differs somewhat by *zoba* (e.g. indoor residual spraying with DDT or malathion was done in Gash Barka but not in Anseba *zoba*).

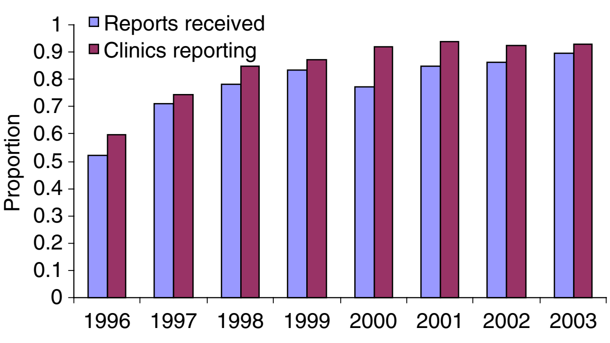

Figure 2 Reporting rate of health facilities.

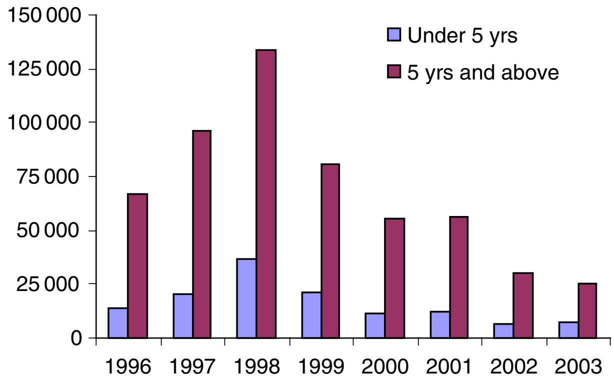

Figure 3 Eritrea: reported clinical malaria cases by age-group and year.

The amounts and timing of activities also differed between *zoba*s. Assuming that these differences are not driven by climate differences between the *zoba*s, it provides a situation that is closer to a clinical trial than if all managers were following exactly the same strategies. This eliminates some of the potential causality problems in strategy selection and allows robustness checks by comparing results obtained under the different management environments. As the application of malathion rather than DDT is apparently performed for logistic and practical reasons, rather than being targeted to particular endemic situations, this aids in the identification of relative impacts of malathion and DDT.

Overall Anseba had lower numbers of cases per month than Gash Barka (Table 1). No spraying was done in Anseba whereas numbers of nets distributed (and reimpregnated) and numbers of larval breeding sites targeted were fairly similar between the two *zobas*. The amounts of intervention shown in Table 1 are raw values, while the regression analysis used depreciated and accumulated amounts (as described in the Methods section) in order to capture the actual amount present in each subzoba per month.

In order to assess whether the interventions were associated with significant reduction in cases, the regressions were performed in four stages. First, only calendar month and *subzoba* were included, then the last month's malaria cases were added. The third stage included climate variables, and finally the vector control interventions were added. In the first stage (Tables 2 and 3, model 1), calender month and *subzoba* alone accounted for a large proportion of the variance in cases. When lagged monthly malaria cases were added to the model (Tables 2 and 3, model 2)

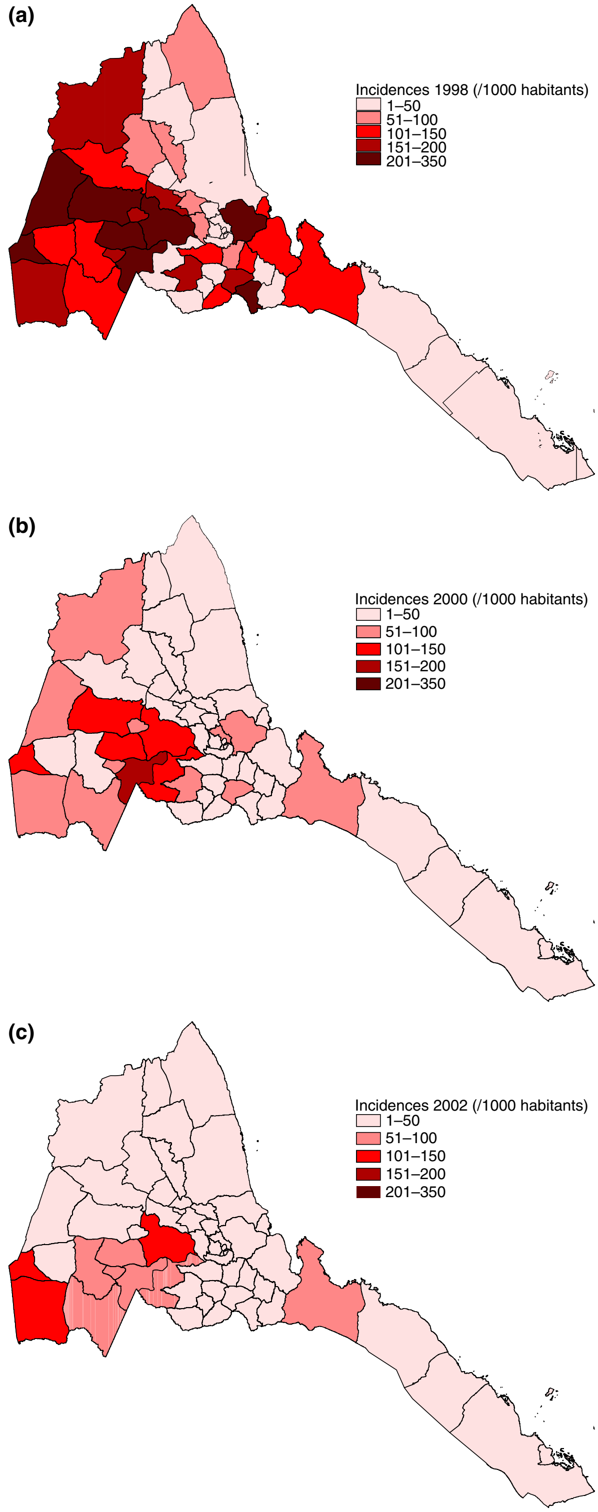

Figure 4 Average incidence (annual clinical cases per 1000 persons) by *subzoba* in 1998 (a), 2000 (b) and 2002 (c).

this had a significant positive effect on the current month's cases.

Increased numbers of cases were significantly positively related to differences in the amount of rain falling 2 and 3 months previously in *subzoba*s of Gash Barka (Table 2, model 3), as well as to the sum of current and previous month's NDVI. A similar relationship, with a much larger coefficient for NDVI, was seen in Anseba (Table 3, model 3). However, when vector control interventions were added in Anseba (Table 3, model 4) there was a change in sign of the relationship between rainfall and cases. This suggests that rainfall and NDVI (which depends on rainfall) are both competing for identification in the model.

Both DDT and malathion, quantified in cumulated and depreciated kg of chemical applied, were significantly and negatively associated with malaria cases in Gash Barka (Table 2). A similar impact from spraying was seen if the two indicators of spraying were combined into one variable, namely the number of people covered by spraying.

Impregnated nets (quantified as number of new impregnated nets plus number of retreated nets, expressed as anomaly from calendar monthly mean) were also significantly associated with reduction in monthly malaria case anomalies (Tables 2 and 3).

Larval control (elimination and treatment of breeding sites) was done in both *zoba*s. It was not associated with decreased cases in Gash Barka (Table 2); in fact the unexpected positive direction of effect of the coefficient suggests that larval control may be being done in response to cases. It appeared to be effective in Anseba (Table 3) with a significant coefficient of −0.000969. The difference in impact may be driven by the fact that larval control is more feasible in a drier area (such as Anseba) in which the breeding sites are fewer and more concentrated.

Addition of the malaria control interventions in models for both zobas led to an increase in the R-sq. This was more marked for Anseba (Table 3) than for Gash Barka (Table 2). In order to asses the relative effects of each intervention, standardized coefficients were derived. Table 4 shows the per cent change in the number of cases by *subzoba* and month expected if there was 1 standard deviation increase in each independent variable. Interpretation of these coefficients is not straightforward, because the intervention variables are quantified in terms of depreciated and cumulated amounts, and the climate variables are expressed in different units. Nevertheless, the coefficients in Table 4 do give an indication of the relative effects of climate and vector control. They suggest that vegetation index NDVI (arising from recent rainfall) has a greater impact on malaria incidence in Anseba, which makes sense because this area has a lower and more

Table 1 Descriptive statistics by *subzoba* and month for *zoba*s included in the analysis and for Eritrea, 1998–2003

	Zoba Gash Barka	*Zoba* Anseba	Eritrea
Clinical malaria cases			
Median (range)	263.5 (8–3686)	36 (0–3400)	83 (0–3686)
Mean (SD)	395.8 (410.9)	86.4 (180.6)	190.8 (307.5)
DDT applied (kg)			
Median (range)	0 (0–2138.4)	ND	0 (0–2871.3)
Mean (SD)	23.9 (173.8)		17.5 (148.5)
Malathion applied (kg)			
Median (range)	0 (0–2433.2)	ND	0 (0–2433.2)
Mean (SD)	18.7 (143.6)		8.2 (102.7)
Nets (new and reimpregnated)			
Median (range)	0 (0–34563)	24 (0–22335)	0 (0–34563)
Mean (SD)	448.5 (2279.9)	492.0 (1854.2)	269.8 (1549.8)
Larval sites treated or eliminated			
Median (range)	0 (0–5617)	0 (0–2636)	0 (0–8943)
Mean (SD)	26.9 (206.2)	57.1 (188.6)	47.3 (339.7)
No. of *subzoba*s	14	11	58
No. of months	72	72	72

SD, standard deviation; ND, not done.

Table 2 Results of Poisson regression analysis of clinical malaria cases by month against climate and intervention variables in Gash Barka *Zoba* (Zone) of Eritrea, 1998–2003

Variable	Gash Barka Model 1: Includes *subzoba* and calendar month only	Model 2: As model 1 plus previous month's cases	Model 3: As model 2 plus climate	Model 4: As model 3 plus malaria control interventions
Cases lagged 1 month		0.0007382***	0.0006226***	0.0005411***
Rainfall: sum of rain 2 and 3 months ago, mm			0.0007711***	0.00097577***
NDVI: sum of current and last month			1.820668***	1.553248***
Spraying				
DDT (kg)				−0.0001937***
Malathion (kg)				−0.0003857***
Impregnated nets: number of new nets and reimpregnated nets				−0.0000343***
Larval control: number of breeding sites eliminated or treated				0.000954***
Pseudo R-sq	0.5329	0.6842	0.7033	0.7224
Log likelihood	−66106.649	−43864.495	−41210.483	−38558.456
N	968	937	937	937

***$P < 0.001$.

seasonal pattern of malaria than Gash Barka where there are more persistent breeding sites available and a higher year-round pattern of transmission. Provision of impregnated nets also appeared to have a stronger effect in Anseba than in Gash Barka.

The data set was also analysed by ordinary least squares regression (*xtreg* for panel data in STATA 7) using anomalies for cases (difference from *subzoba*-month means) as the dependent variable. This enabled us to subtract out additional potentially confounding information, but did not allow us to control for the size of the exposed population as in the Poisson regression. The difference-in-difference approach is not feasible with Poisson regression as the dependent variable cannot be negative. Nevertheless, the ordinary least squares gave very similar results regarding the significance and direction of independent effects of climate, nets, spraying and larval control on clinical malaria cases in the two *zoba*s. In that analysis,

Table 3 Results of Poisson regression analysis of clinical malaria cases by month against climate and intervention variables in Anseba *Zoba* (Zone) of Eritrea, 1998–2003

	Anseba			
Variable	Model 1: Includes *subzoba* and calendar month only	Model 2: As model 1 plus previous month's cases	Model 3: As model 2 plus climate	Model 4: As model 3 plus malaria control interventions
Cases lagged one month		0.0011115***	0.0005452***	0.0003039***
Rainfall: sum of rain 2 and 3 months ago, mm			0.0024987***	−0.0020567***
NDVI: sum of current and last month			11.22517***	9.554839***
Spraying: DDT (kg)				ND
Malathion (kg)				
Impregnated nets: number of new nets and reimpregnated nets				−0.0001417***
Larval control: number of breeding sites eliminated or treated				−0.0000969***
Pseudo R-sq	0.3103	0.4703	0.6254	0.7174
Log likelihood	−39435.863	30261.12	−21398.112	−16146.542
N	791	790	790	790

***$P < 0.001$; ND, not done.

Table 4 Standardized regression coefficients (per cent change in incidence for 1 standard deviation change in climate or intervention variable) for final model 4 in each *Zoba*

	Gash Barka	Anseba
Sum of rainfall 2 and 3 months ago, mm	3.4%	−5.6%
NDVI: sum of current and last month	8.7%	54.7%
Spraying		
DDT (kg)	−4.2%	ND
Malathion (kg)	−7.3%	ND
Number of new ITN and reimpregnated nets	−10.8%	−36.7%
Larval control: number of breeding sites eliminated or treated	2.8%	−3.1%

ND, not done.

however, the unexpected positive association between larval control and cases in Gash Barka (Table 2, model 4) was not seen, suggesting that the Poisson method did not allow us to adjust for this potential negative causality. Neither was there a negative association between rainfall and cases in Anseba, as seen in the current Table 3, model 4 when all covariates were included. While the distribution of cases by month suggests that Poisson regression is the correct approach, the alternative approach provides additional support for the results.

Discussion

The number of cases of clinical malaria in Eritrea declined steadily over the years 1998–2003 (Nyarango *et al.* 2006). The question is whether this was due to climate, the control programme, or other factors. A number of different control measures were used, and it was not clear whether they were all necessary or how effective each one was. Understanding the relationship between climate, control methods and malaria assists in providing early warning in malaria increases (Thomson *et al.* 2006) as well as in improving the control programme. Also, regression coefficients (representing the independent effects of each control method on number of cases) obtained from this study could be used in cost-effectiveness analysis.

A large data set of malaria cases from a newly introduced nationwide health information system in Eritrea is available, and was used by Nyarango *et al.* (2006) in a preliminary assessment of the control programme on an annual basis at the national level. In this paper we use monthly clinical data by smaller geographic unit and additional climate data sources to assess in more detail the role of climate and malaria control interventions in the decline of malaria in Eritrea. Whilst it would have been desirable to use confirmed cases of malaria rather than clinically diagnosed cases, this was not available for Eritrea for the years in question. In addition, diagnostic capacity increased markedly over the period of study, which would have introduced bias. Because more desirable data sets were not available, we followed statistical approaches that would tend to make the potential drawbacks of the data sets lead to insignificant (as opposed to spurious) results.

As expected, malaria cases were significantly associated with climate variables, although more strongly with the vegetation index NDVI in current and last month than with actual rainfall. As NDVI does not give a lead time for forecasting, emphasis must be put on forecasting of NDVI in order to use this relationship in malaria early warning. Because of the differing relationships seen in model 4 between rainfall and cases in two *zoba*s with different endemicity levels and seasonal patterns, it seems advisable in such investigations to analyse such data separately by area.

Spraying had an additional independent effect in the area where this could be studied and impregnated nets were also shown to be independently effective in both *zoba*s studied.

Larval control activities proved to be difficult to quantify accurately. The only available measure from the records was a composite of breeding sites eliminated and treated. Nevertheless, a significant effect of larval control was demonstrated in Anseba, but not in Gash Barka. This may be due to the high quality of such activities in Anseba, the larger numbers of breeding sites which overwhelm the control efforts in Gash Barka, or it may also be that activities are not sufficiently well documented. Streamlining of record-keeping and monitoring of activities is highly desirable for all control measures, in order to assess their effects, but is especially needed for larval control.

A difficulty in this type of analysis is excluding the effects of climate on the control programme – increased rainfall might drive increased larval control, for example, as suggested in Gash Barka. Although we found no evidence for this effect in preliminary regressions in the two *zobas* studied, the results obtained are not of the level of certainty of a controlled trial, and must be interpreted with the appropriate caution and scrutiny.

The fixed effects approach used here, applied at the *subzoba* level, partially addresses the causality issue, although the hypothesized correlation between decision-making/control efforts and malaria cases occurs at a higher level (the *zoba*). In addition to differencing (use of anomalies) and fixed effects techniques, the causality problems associated with endogenous decision-making are traditionally addressed through instrumental variable approaches. But we were unable to identify suitable instruments to allow for the necessary corrections. In order to effectively identify impacts of control, an instrumental variable would have to be developed for each activity. Climate variation, perhaps the most commonly applied instrument, was not available as the impacts of climate are directly relevant to our study.

Additional control measures in the areas studied include the provision of presumptive treatment by village health workers during the high malaria transmission season (August through November each year in Gash Barka and Anseba). Although data are available on the number of cases treated by these workers, it is not possible to include them in the model because they are highly correlated with the outcome variable (the amount of malaria). A change in drug policy from chloroquine alone to chloroquine plus Fansidar as first-line treatment also occurred in 2002 and may have affected the results in the last year of our analysis.

Conclusions

Overall these results lend support to the National Malaria Control Programme in its view (Nyarango *et al.* 2006) that the intensive efforts by the control programme and large scale-up of a combination of activities have helped to bring about steep reduction in clinical malaria cases since the year 1998. The control programme effects are in addition to any effects of climate. Where both indoor residual spraying and impregnated nets were used (in Gash Barka *zoba*) they had independent effects on malaria cases. There was also evidence for the effectiveness of larval control in one area (Anseba *zoba*), but not in the more highly endemic Gash Barka. Estimation of standardized coefficients indicated that both impregnated nets and changes in vegetation index had a stronger impact on malaria incidence in the less endemic Anseba *zoba* than in Gash Barka where more intense transmission occurs year round. Whether these successful malaria control efforts can be replicated in other countries with overall higher endemicity and less seasonality than Eritrea remains to be seen, after further analysis using large climate, malaria and intervention data sets.

Acknowledgements

We thank the Minister of Health for Eritrea, Mr Saleh Meky, the Director General for Health, Mr Berhane Tensae, and the head of Disease Prevention and Control, Dr Goitom Mebrahtu, for their support. We are very grateful to Solomon Neguse, Meles GhebreYesus, Asrat GhebreLul, Andemariam WeldeMichael, Asmelash Gegziabher, Helen Fekadu, Solomon Mengistu, Yohannes Bein, David Sintasath, Dr Josephat Shililu and Dr Gunewardena Dissanayake of the NMCP and Dr Andom Ogbamariam, Ezra Kidane, Amanuel Kifle and Samuel

Goitom from the NHMIS. We thank Matthew Lynch and Eckard Kleinau for critical input and Linda Lou Kelley, Semere Gebregiorgis and Kris Lantis of USAID for support in Eritrea. This study was funded by the USAID Environmental Health Project, Contract HRN-1-00-99-00011-00 sponsored by Office of Health, Infectious Disease and Nutrition, Bureau for Global Health, USAID, Washington DC 20523. We are very grateful to the National Statistics and Evaluation Office, Asmara, Eritrea and the Water Resources Department, Ministry of Lands, Water and Environment for providing GIS data. Marc Levy and Malanding Jaiteh of CIESIN and Tony Barnston of IRI helped with climate data and analysis. We thank Paul Hutchinson, Mead Over and an anonymous reviewer for statistical advice. The following organizations supported the malaria control program of Eritrea during the period of study: The World Bank HAMSET project; USAID; WHO; Italian Cooperation; UNICEF.

References

Barat L (2006) Four malaria success stories: how malaria burden was successfully reduced in Brazil, Eritrea, India, and Vietnam. *The American Journal of Tropical Medicine and Hygiene* **74**, 12–16.

Barnes KI, Durrheim DN, Little F *et al.* (2005) Effect of artemether–lumefantrine policy and improved vector control on malaria burden in KwaZulu-Natal, South Africa. *PLoS Medicine* **2**, e30.

Breman JG, Alilio MS & Mills A (2004) Conquering the intolerable burden of malaria: what's new, what's needed: a summary. *The American Journal of Tropical Medicine and Hygiene* **71**(Suppl. 2), 1–15.

Ceccato P, Ghebremeskel T, Jaiteh M *et al.* (2007) Malaria stratification, climate and epidemic early warning in Eritrea. *The American Journal of Tropical Medicine and Hygiene* **77** (6-Suppl.), 61–68.

Craig MH, Kleinschmidt I, Le Sueur D & Sharp BL (2004a) Exploring 30 years of malaria case data in KwaZulu-Natal, South Africa: Part II. The impact of non-climatic factors. *Tropical Medicine & International Health* **9**, 1258–1266.

Craig MH, Kleinschmidt I, Nawn JB, Le Sueur D & Sharp BL (2004b) Exploring 30 years of malaria case data in KwaZulu-Natal, South Africa: Part I. The impact of climatic factors. *Tropical Medicine & International Health* **9**, 1247–1257.

Curtis CF (2002) Should the use of DDT be revived for malaria vector control? *Biomedica* **22**, 455–461.

Curtis CF & Mnzava AE (2000) Comparison of house spraying and insecticide treated nets for malaria control. *Bulletin of the World Health Organization* **78**, 1389–1400.

Goodman CA, Mnzava AE, Dlamini SS, Sharp BL, Mthembu DJ & Gumede JK (2001) Comparison of the cost and cost-effectiveness of insecticide-treated bednets and residual house-spraying in KwaZulu-Natal, South Africa. *Tropical Medicine & International Health* **6**, 280–295.

Grover-Kopec E, Kawano M, Klaver RW, Blumenthal B, Ceccato P & Connor SJ (2005) An online operational rainfall-monitoring resource for epidemic malaria early warning systems in Africa. *Malaria J* **4**, 6.

Guyatt HL, Corlett SK, Robinson TP, Ochola SA & Snow RW (2002) Malaria prevention in highland Kenya: indoor residual house-spraying *vs* insecticide treated nets. *Tropical Medicine & International Health* **7**, 298–303.

Kilian AHD, Langi P, Talisuna A & Kabagambe G (1999) Rainfall pattern, El Nino and malaria in Uganda. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **93**, 22–23.

Killeen GF, Fillinger U & Knols BG (2002) Advantages of larval control of African malaria vectors: low mobility and behavioural responsiveness of immature mosquito stages allows high effective coverage. *Malaria Journal* **1**, 8.

Korenromp EL, Williams BG, Gouws E, Dye C & Snow RW (2003) Measurement of trends in childhood malaria mortality in Africa: an assessment of progress toward targets based on verbal autopsy. *The Lancet Infectious Diseases* **3**, 349–358.

Korenromp EL, Armstrong-Schellenberg JR, Williams BG, Nahlen BL & Snow RW (2004a) Impact of malaria control on childhood anaemia in Africa – a quantitative review. *Tropical Medicine & International Health* **9**, 1050–1065.

Korenromp EL, Arnold F, Williams BG, Nahlen BL & Snow RW (2004b) Monitoring trends in under-5 mortality rates through national birth history surveys. *International Journal of Epidemiology* **33**, 1293–1301.

Lengeler C (2004) Insecticide treated bednets and curtains for preventing malaria. *Cochrane Database Systemic Review 2004*, CD000363.

Mpofu SM, Taylor P & Govere J (1988) An evaluation of the residual lifespan of DDT in malaria control. *Journal of the American Mosquito Control Association* **4**, 529–535.

Nyarango PM, Gebremeskel T, Mebrahtu G *et al.* (2006) A steep decline in malaria morbidity and mortality trends in Eritrea between 2000 and 2004: the effect of a combination of control methods. *Malaria Journal* **5**, 33.

Over M, Bakote'e B, Velayudhan R, Wilikai P & Graves PM (2004) Impregnated nets or DDT residual spraying? Effectiveness of malaria control interventions in Solomon Islands, 1993–1999. *The American Journal of Tropical Medicine and Hygiene* **71**(Suppl. 2), 214–223.

Sharp B, van Wyck P, Sikasote JB, Banda P & Kleinschmidt I (2002) Malaria control by residual insecticide spraying in Chingola and Chililabombwe, Copperbelt Province, Zambia. *Tropical Medicine & International Health* **7**, 732–736.

Shililu JI, Tewolde GM, Brantly E *et al.* (2003) Efficacy of *Bacillus thuringiensis israelensis*, *Bacillus sphaericus* and *temephos* for managing *Anopheles* larvae in Eritrea. *Journal of the American Mosquito Control Association* **19**, 251–258.

Sintasath DM, Ghebremeskel T, Lynch M *et al.* (2005) Malaria prevalence and associated risk factors in Eritrea. *The American Journal of Tropical Medicine and Hygiene* **72**, 682–687.

Snow RW, Korenromp E & Gouws E (2004) Pediatric mortality in Africa: *Plasmodium falciparum* as a cause or risk? *The*

American Journal of Tropical Medicine and Hygiene **71**(Suppl. 2), 16–24.

Snow RW, Guerra CA, Noor AM, Myint HY & Hay SI (2005) The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* **434**, 214–217.

Thomson MC, Connor SJ, Phindela T & Mason SJ (2005) Rainfall and sea-surface temperature monitoring for malaria early warning in Botswana. *The American Journal of Tropical Medicine and Hygiene* **73**, 214–221.

Thomson MC, Doblas-Reyes FJ, Mason SJ *et al.* (2006) Malaria early warnings based on seasonal climate forecasts from multi-model ensembles. *Nature* **439**, 576–579.

WHO (2002) *The World Health Report: Reducing Risks, Promoting Healthy Life*. World Health Organization, Geneva.

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