EFFECTIVENESS OF MALARIA CONTROL DURING CHANGING CLIMATE CONDITIONS IN ERITREA, 1998 TO 2003.

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Abstract

Objective

Eritrea has experienced a dramatic decline in malaria incidence since 1998. During this period the country has implemented several prevention and control methods including impregnated mosquito nets, indoor residual spraying and larval control. This paper aims to assess the effectiveness of each of these control measures relative to the impacts of climate variability in the decline in malaria cases.

Methods

Monthly data on clinical malaria cases by *subzoba* (district) in three *zoba*s (zones) of Eritrea for 1998 to 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, whilst addressing 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 two and three 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 the 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 utilized, 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.

Introduction

The burden of malaria, especially *P.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 has declined appreciably over the last five to ten years (Snow et al, 2004). However, malaria has declined in some African countries, including Eritrea (Nyarango et al, 2006) and South Africa (Barnes et al, 2005). Eritrea has achieved 80% reduction in malaria morbidity since 1999 and has implemented a vigorous control program using multiple methods including impregnated nets, indoor residual spraying, larval control, community health agents providing treatment, and training on case management (Nyarango et al, 2006).

Although randomized trials have provided evidence that malaria prevention and control activities may be effective, it is has not been conclusively determined whether observed decreases in malaria are actually due to prevention and control activities or are due to variation in climate, or whether the multiple control methods were necessary. Because a large prospective randomized trial to answer these questions is not feasible, we 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 use 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 program and climate in Eritrea using nationwide annual data. The present paper extends this analysis using six years of monthly case data by *subzoba* (district) in conjunction with additional seasonally adjusted monthly climate data and detailed records of control program 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 in the real world 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 to South Africa in 2000 (Craig et al, 2004) 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 one 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 and 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 control measures performed is available in the same geographic and time units as the malaria incidence data.

Climate variability is a significant factor either helping or hindering malaria control. Seasonal and interannual climate variation has been documented to have large impacts on malaria transmission (Craig et al, 2004; 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 reduce 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 datasets covering the continent of Africa and the ability to extract such data according to administrative boundaries of interest (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 are including 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 program impacts.

Eritrea is divided into six main administrative zones (*zoba*s) and 58 smaller districts (*subzoba*s) (Fig 1). Each *zoba* has several malaria control personnel including a *zoba* malaria coordinator who decides, together with the National Malaria Control Programme, on policies and plans 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 picture due to two distinct rainfall patterns and large variations in altitude. The overall endemicity is quite low: a malaria prevalence survey conducted in 1999-2000 showed prevalence to be 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 adults.

In Eritrea, a new National Health Management Information System (NHMIS) based on monthly reporting of diagnoses from each health facility, was introduced in 1998. A dataset of clinical malaria cases extracted from this system, coupled with records kept by the National Malaria Control Programme for 1996 and 1997, has been used to stratify malaria incidence throughout the country by *subzoba* (Ceccato et al, in press).

In this paper, we use a version of this dataset 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

Clinical Malaria Incidence

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 to 2003. The National Malaria Control Program provided similar data for the years 1996 and 1997. The following facility types were included: hospitals, mini-hospitals, health centres and health stations. 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 dataset from 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, since 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 non-functioning facilities with no reports over the period were also excluded. Because availability of malaria diagnostic tests (microscopy and rapid tests) was not great 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 since 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* (1-9 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 dataset used here differs from that of Ceccato et al (in press), in that missing values were not imputed in this analysis.

Environmental/Climate data

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 dataset of rainfall estimates in a 2.5 $\times$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, since unlike other possible sources from different satellites, they have an historical data series (July 1981 to current) overlapping with the current study. NDVI data is available for 10 day periods (dekads). In the current study 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/).

Intervention data

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 267g DDT and 400g of malathion, based on 100 sq M 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 with chemical (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, amount of DDT used and number of treated nets were depreciated by 20% per month as 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. However 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 dataset, 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, four 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. It was determined that 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.

The annual trend of malaria in Eritrea and the distribution of cases by age group are shown in Figure 3. There has been a decline in cases since 1998. This declining trend can also be seen in the maps in Figure 4 which illustrate the nationwide distribution of annual incidence per 1000 persons by *subzoba* in the years 1998, 2000 and 2002.

Malaria control strategy 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*. For example, indoor residual spraying with DDT or malathion was done in Gash Barka but not in Anseba *zoba*, 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. In addition, since 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.

Table 1 shows the characteristics of the areas studied, with median and mean values by subzoba and month for numbers of cases and amounts of interventions applied by month. It should be noted that 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. It can be seen that overall Anseba had lower numbers of cases per month than Gash Barka. 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*.

Table 2 presents the regression results for Gash Barka and Table 3 the results for Anseba. 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. The change in R-sq and log likelihood for each model is shown in Tables 2 and 3.

Effects of last month's cases

When lagged monthly malaria cases were added to the model (Tables 2 and 3, model 2) this had a significant positive effect on the current month's cases.

Effects of climate

Increased numbers of cases were significantly positively related to differences in the amount of rain falling two and three 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.

Effects of indoor residual spraying (model 4)

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.

Effects of nets (model 4)

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).

Effects of larval control

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 - but 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.

Overall effects of interventions

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 percent change in the number of cases by *subzoba* and month expected if there was one standard deviation increase in each dependent 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 since this area has a lower and more seasonal pattern of malaria than Gash Barka where there are more persistent breeding sites available and a higher more year-round pattern of transmission. Provision of impregnated nets also appeared to have a stronger effect in Anseba than in Gash Barka.

The dataset 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 since 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, 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 has not allowed 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 to 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 will assist in providing early warning of increases in malaria (Thomson et al 2006) as well as in improving the control programme. In addition, 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 dataset 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 program on an annual basis at the national level. In the current 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 datasets were not available, we followed statistical approaches that would tend to make the potential drawbacks of the datasets lead to insignificant (as opposed to spurious) results.

Effects of climate and control measures

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. Since 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 Models 4 between rainfall and cases in two *zoba*s with different endemicity levels and seasonal patterns, it seems advisable in such investigations to analyze such data separately by area.

Spraying was demonstrated to have 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.

Ambiguous causality

A difficulty in this type of analysis is excluding the effects of climate on the control program – 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. However, 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. In addition, climate variation, perhaps the most commonly applied instrument, was not available since the impacts of climate are directly relevant to our study.

Other control measures

Additional control measures being conducted 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 datasets.

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 provision of 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 programme of Eritrea during the period of study: The World Bank HAMSET project; USAID; WHO; Italian Cooperation; UNICEF.

Authors' contributions

PMG conceived and designed the study, performed statistical analysis and drafted the manuscript. DEO participated in statistical analysis and drafting the manuscript. MCT participated in study design and analysis. AA and KS organized and conducted the malaria control activities, while MZ extracted and compiled malaria and intervention data. PC, MB and JdC extracted and provided climate data as well as GIS expertise. SG is responsible for the National Health Management Information System and the quality of its data; she assisted with data extraction. EPB coordinated the study and provided input at all stages. TG directs the National Malaria Control Programme and participated in all aspects of the study.

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Figures

Figure 1: *Zoba*s and *subzoba*s of Eritrea

*Subzoba*s numbered according to the National Health Management Information System

Figure 2: Reporting rate of health facilities

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

Figure 4: Average incidence (annual clinical cases per 1000 persons) by *subzoba* in 1998 (A), 2000 (B) and 2002 (C)

Tables

Table 1 - Descriptive Statistics by *Subzoba* and Month for *Zoba*s Included in the Analysis and for Eritrea, 1998 to 2003

	***Zoba* Gash Barka**	***Zoba* Anseba**	**ERITREA**
CLINICAL MALARIA CASES: **Median (range)** **Mean (SD)**	263.5 (8 – 3686) 395.8 (410.9)	36 (0 – 3400) 86.4 (180.6)	83 (0 – 3686) 190.8 (307.5)
DDT APPLIED (kg): **Median (range)** **Mean (SD)**	0 (0 – 2138.4) 23.9 (173.8)	ND	0 (0 – 2871.3) 17.5 (148.5))
MALATHION APPLIED (kg): **Median (range)** **Mean (SD)**	0 (0 – 2433.2) 18.7 (143.6)	ND	0 (0 – 2433.2) 8.2 (102.7)
NETS (NEW AND REIMPREGNATED): **Median (range)** **Mean (SD)**	0 (0 – 34563) 448.5 (2279.9)	24 (0 – 22335) 492.0 (1854.2)	0 (0 – 34563) 269.8 (1549.8)
LARVAL SITES TREATED OR ELIMINATED: **Median (range)** **Mean (SD)**	0 (0 – 5617) 26.9 (206.2)	0 (0 – 2636) 57.1 (188.6)	0 (0 – 8943) 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 to 2003.

	Gash Barka			
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		0.0007382***	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<0.05
*** p<0.001.

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 to 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) Malathion (kg)				ND
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<0.05
*** p<0.001.
ND: not done

Table 4 – Standardized Regression Coefficients (Percent Change in Incidence for One Standard Deviation Change in Climate or Intervention Variable) for Final Model 4 in each *Zoba*.

	Gash Barka	**Anseba**
Rainfall: sum of rain 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
Impregnated nets: Number of new nets and reimpregnated nets	-10.8%	-36.7%
Larval control: Number of breeding sites eliminated or treated	2.8%	-3.1%

ND: not done

Figure 1: *Zobas* and *Subzobas* of Eritrea

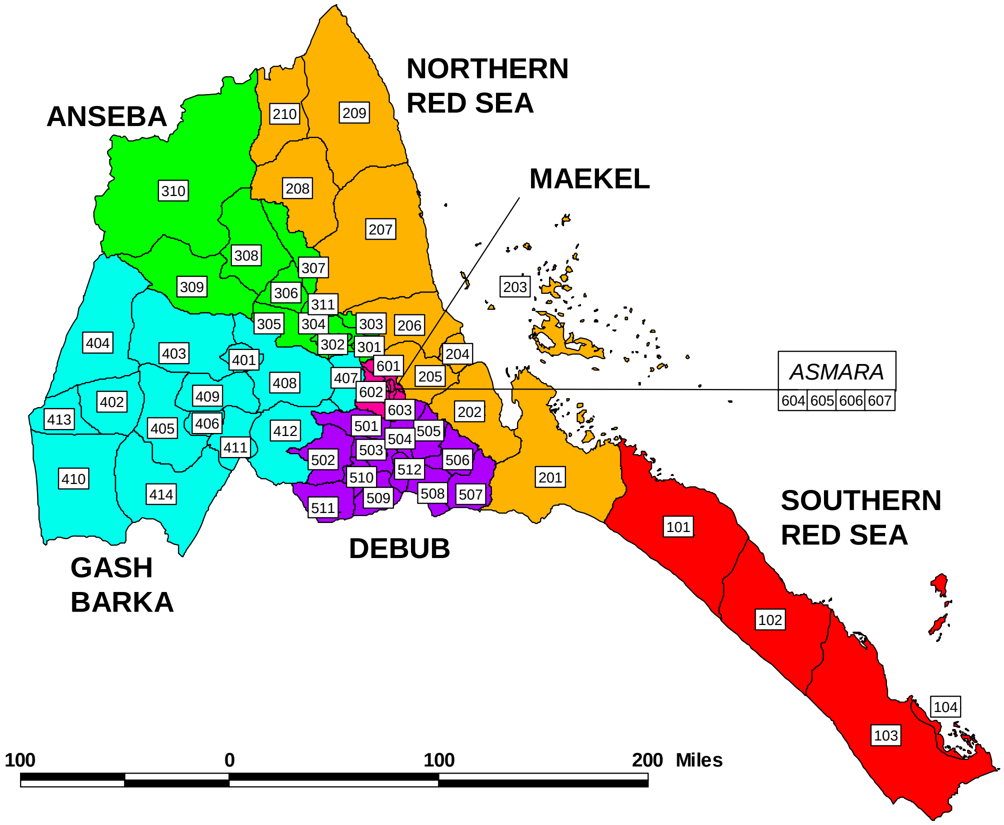

Fig 2: Reporting Rate from 242 Health Facilities Included in Eritrea Dataset, 1996 to 2003

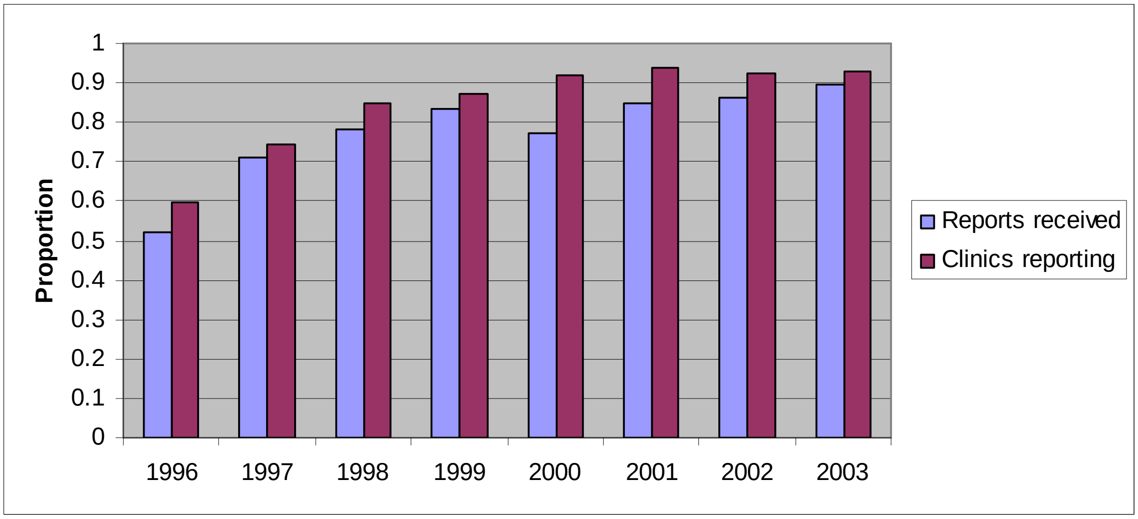

Fig 3: Eritrea: Reported Clinical Malaria Cases by Age-group and Year

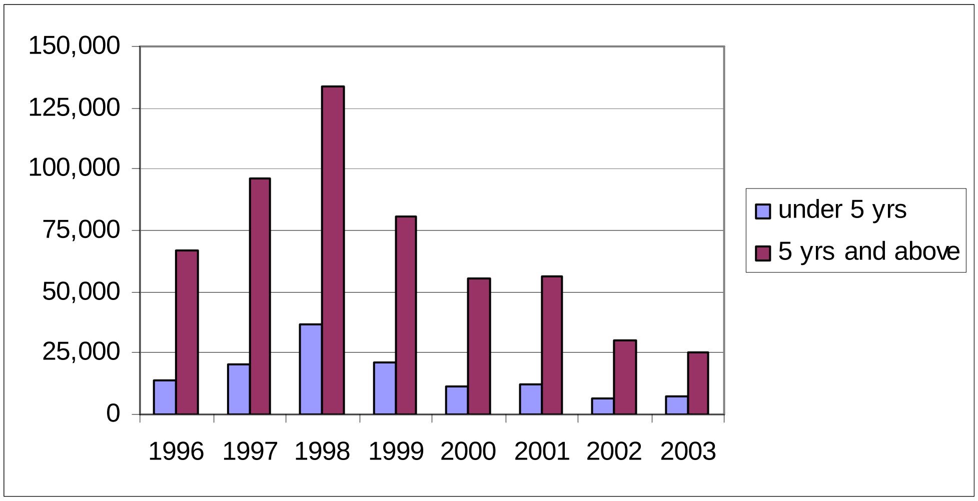

Fig 4A: Annual Clinical Malaria Incidence per 1000 Persons by *Subzoba*, 1998

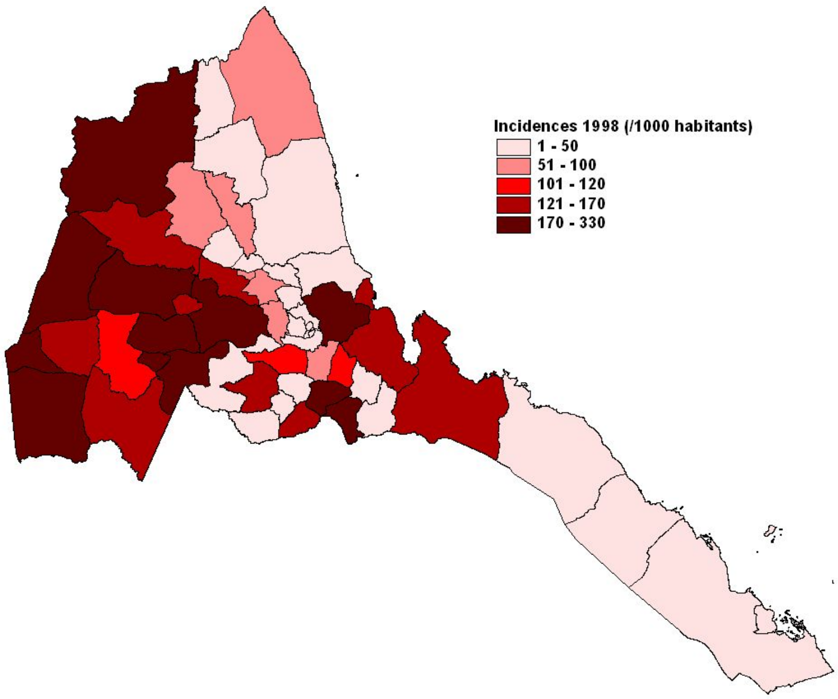

Fig 4B: Annual Clinical Malaria Incidence per 1000 Persons by *Subzoba*, 2000

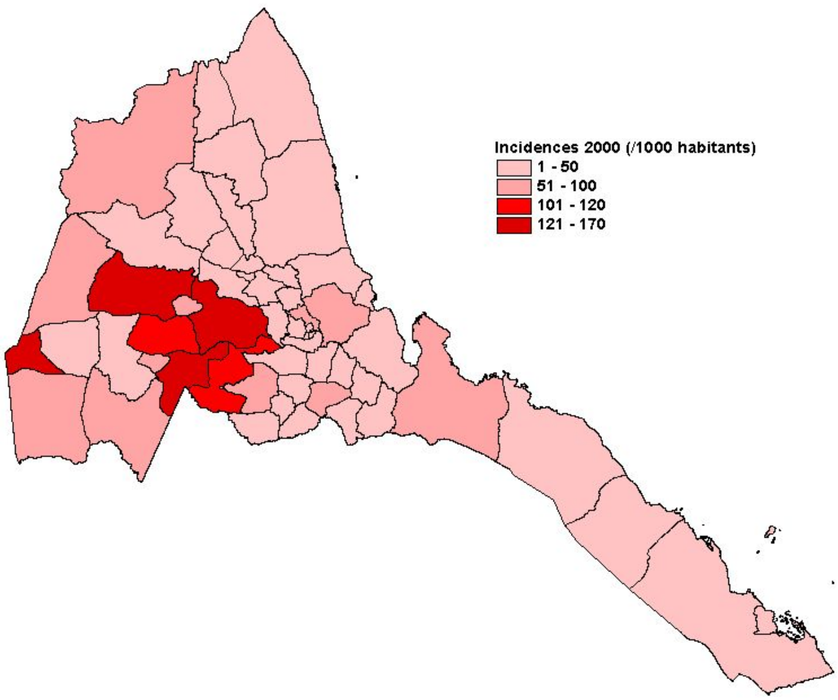

Fig 4C: Annual Clinical Malaria Incidence per 1000 Persons by *Subzoba*, 2002