PREDICTING MALARIA INFECTION IN GAMBIAN CHILDREN FROM SATELLITE DATA AND BED NET USE SURVEYS: THE IMPORTANCE OF SPATIAL CORRELATION IN THE INTERPRETATION OF RESULTS

MADELEINE C. THOMSON, STEPHEN J. CONNOR, UMBERTO D'ALESSANDRO, BARRY ROWLINGSON, PETER DIGGLE, MARK CRESSWELL, AND BRIAN GREENWOOD

MALSAT Research Group, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; Department of Parasitology, Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium; Medical Statistics Unit, Lancaster University, Lancaster, United Kingdom; London School of Hygiene and Tropical Medicine, London, United Kingdom

Abstract. In line with the renewed World Health Organization Global Malaria Control Strategy, we have advocated the use of satellite imagery by control services to provide environmental information for malaria stratification, monitoring, and early warning. To achieve this operationally, appropriate methodologies must be developed for integrating environmental and epidemiologic data into models that can be used by decision-makers for improved resource allocation. Using methodologies developed for the Famine Early Warning Systems and spatial statistics, we show a significant association between age related malaria infection in Gambian children and the amount of seasonal environmental greenness as measured using the normalized difference vegetation index derived from satellite data. The resulting model is used to predict changes in malaria prevalence rates in children resulting from different bed net control scenarios.

Malaria is an environmental disease. *Anopheles* mosquitoes transmit the causative agent, *Plasmodium* spp., when the environmental parameters (such as water availability, temperature, and humidity) permit. For example, in many parts of the world where temperature is not a limiting factor, malaria transmission is highly seasonal, with peak transmission following the period of peak rainfall.

Understanding how malaria varies in the community as a result of seasonal or year-to-year changes in environmental factors is important for the planning of national malaria control programs since it may allow interventions to be adapted to specific sites or times of year. This is essential for the effective control of the disease. Traditional methods used to describe the level of malaria endemicity in a particular area include calculating the percentage of children with an enlarged spleen or with parasitemia. Assessing the relationship between environmental parameters and such malariometric indices in a quantitative manner is fraught with difficulties since the prevalence of malaria may vary considerably within a small area,[1] and the data collected at a limited number of points are not necessarily applicable to a broader region.[2] Furthermore, prevalence data collected during a limited period of time cannot describe the seasonal variations that occur even in areas of high endemicity.[3] There are also important logistical and financial constraints to the organization of widespread, often repeated, malaria parasite prevalence surveys.

Consequently, the assessment of malaria endemicity in a particularly locality must be extrapolated from a limited number of surveys that are constrained in space (often to a few villages) and in time (perhaps once at the end of the rainy season for one or two years).

Recent developments in the use of geographic information systems (GISs) for malaria risk mapping have resulted in an ambitious plan to map malaria endemicity throughout Africa using age-related prevalence rates. The Mapping Malaria Risk in Africa/(Atlas du Risk de Malaria) initiative is using both epidemiologic and entomologic data from all available sources to determine the different epidemiologic situations occurring throughout Africa and their respective malaria

risk. For areas where such information is unavailable, environmental parameters, such as rainfall and temperature, have been used to predict transmission levels.[4] Large international spatial databases of environmental factors in digital format are increasingly available and provide information relevant to predicting the distribution of disease vectors. Such databases include both archived and near real time environmental data obtained from meteorologic satellites.

Meteorologic satellites, such as the polar orbiting and geostationary satellites operated by the National Ocean and Atmospheric Administration of the United States (NOAA series) and the European Organization for the Exploration of Meteorological Satellites (Meteosat series), observe large areas of the earth's surface (for Meteosat this includes the entire African continent) with an optimal spatial resolution of 1.1 km and 5 km, respectively. Their high temporal resolution (twice a day and 30 min, respectively), spectral characteristics (which include both visible and thermal channels), and high contrast capability means that they are ideally suited to global and repetitive studies of the environment. Consequently, they are used widely for monitoring seasonal and inter-annual changes in environmental phenomena such as rainfall, temperature, plant phenology, and biomass. Environmental proxies are derived empirically by comparing land-based phenomena (e.g., meteorologic data or crop growth characteristics) with post-processed satellite data. Widely used environmental proxies include rainfall estimates from cold cloud duration, vegetation indices (such as the normalized difference vegetation index [NDVI]) and surface temperatures (including sea surface temperatures [SST] and land surface temperatures [LST]).[5] Recent work has indicated the potential use of Meteosat thermal infrared data for estimating ambient air temperatures.[6]

Numerous studies have been undertaken using NOAA–advanced very high resolution radiometer (AVHRR) data to predict the distribution and abundance of a range of veterinary and medical disease vectors.[7] Examples include *Culicoides imicola* (African horse sickness virus),[8] *Phlebotomus papatasi* (cutaneous leishmaniasis),[9] *Phlebotomus orientalis* (visceral leishmaniasis),[10] *Ixodes scapularis* (Lyme dis-

ease),[11] *Aedes* spp. (Rift Valley fever),[12] tsetse spp. (trypano-somiasis),[13] *Rhipicephalus appendiculatus* (East Coast fever virus),[14] *Biomphalaria* spp. (schistosomiasis),[15] and *Anoph-eles gambiae* Mopti form (malaria).[16]

The potential for using meteorologic satellite data in the study of malaria transmission dynamics has been reviewed in an earlier paper.[17] Using epidemiologic and entomologic data from The Gambia, we have shown that even simple analysis of proxy ecologic variables derived from satellite data can indicate variation in environmental factors affecting malaria transmission indices. In particular, we have high-lighted the potential for using information on the seasonal changes in vegetation growth and senescence as indicators of the length and intensity of the malaria transmission season since these processes are closely allied to rainfall and hu-midity.

This has been supported in analysis of temporal changes in seasonal vegetation status estimated using the NDVI and seasonal variation in the number of parasitologically diag-nosed malaria cases in both The Gambia[16,18] and Kenya[18] and clinical malaria cases in Niger,[16] albeit with a lag period of one month. Further studies have shown that the NDVI is associated with the occurrence of different proportions of the Mopti karyotypes in populations of *An. gambiae* in Mali,[16] which are known to vary according to different ecologic settings. Based on our preliminary results[16,17] and further work (Thomson MC, Connor SJ, unpublished data), we have advocated the use of satellite imagery in providing environ-mental information in near real time for malaria stratifica-tion, monitoring, and early warning.[5,19] For this potential to be realized, appropriate methodologies must be developed for integrating environmental and community-based epide-miologic data into models that can be used by decision-mak-ers for improved resource allocation.

The study described in this paper has addressed this issue using methodologies developed by the United Nations Food and Agricultural Organization Global Information and Early Warning System. It provides for the first time statistical ev-idence of the association between age-related prevalence rates in the community and the seasonal amount of environ-mental greenness measured using the NDVI.

Statistical modeling of the relationship between disease prevalence and environmental data is complicated by spatial relationships, which typically result in positive correlations between observations from spatially close sampling units. These correlations in turn negate the basic assumptions un-derlying standard linear or generalized linear regression analysis.[20] Failure to allow for spatial correlation typically leads to spuriously small standard errors of regression pa-rameter estimates, and corresponding over-statement of the significance of regression effects. However, few studies re-lating vector distribution to satellite data have addressed the problem of spatial correlation in the data sets. A rare excep-tion is a study undertaken by Kitron and others,[21] who un-dertook a spatial analysis of tsetse fly distribution in the Lambwe Valley of Kenya using Landsat Thematic Mapper (TM) imagery and a GIS. They found that using multiple regression analysis, they could explain 87% of the variance in fly density using several TM bands. However, when they applied spatial filtering using Moran's *I* measure of spatial correlation, a significant positive link was observed among all trap data. They therefore concluded that the positive cor-relation between spectral data and fly abundance was largely due to determinants not included in the analysis.

In our study, we have used an adaptation of a method of Liang and Zeger[22] to make inferences that account for spatial correlation. Results from the model developed demonstrate the relevance of satellite data to studies of malaria transmis-sion and indicate how remote sensing, GIS, and spatial anal-ysis can be used to indicate village-based variation in the effectiveness of an intervention. We have used the model to predict changes in prevalence rates in children according to different levels of bed net usage.

MATERIALS AND METHODS

Study area. The Gambia is a small country situated on the west coast of Africa. It extends eastwards from the At-lantic Ocean on either side of the Gambia River. The geo-graphic determinants of malaria transmission in the country have been described in detail elsewhere.[23] Briefly, the coun-try consists of flat, woodland savannah with swamps bor-dering the river, which is saline to a distance of approxi-mately 150 km from the coast. The climate is typical Sa-helian (Sudano-Sahel) with a short rainy season that lasts from June–July to October followed by a long dry season covering the remaining months. Minimum and maximum mean monthly temperatures range between approximately 26°C and 33°C with highest temperatures in the eastern part of the country. Therefore, there are no temperature restric-tions on malaria transmission in The Gambia, but transmis-sion is restricted largely to the rainy season (rainfall for 12 meteorologic stations in 1992 ranged from 400 to 850 mm) when temporary breeding sites and an environment suitable for adult mosquito survival is created.

Considerable differences in malaria endemicity have been found within The Gambia (i.e., village-based parasite prev-alence rates ranging from 1% to 89% in children 1–4 years of age) and these have been related to ecologic differences affecting the vector (species and population density) and the human population (use of bed nets).[23]

Epidemiologic data. Data were collected during the eval-uation of the Gambian National Impregnated Bednet Pro-gram, whose objective was to treat with insecticide (per-methrin) all bed nets found in all villages covered by the National Primary Health Care (PHC) Program over a period of 2–3 years. The results of this evaluation have been re-ported elsewhere.[24,25] Prior to the study, the aim of the pro-gram was explained to communities involved and verbal consent was obtained from the mothers of children included in the survey. This study was reviewed and approved by the Scientific Coordinating Committee of the Medical Research Council Laboratories, The Gambia and the Ethical Commit-tee the Gambian Government.

A cross-sectional malaria morbidity survey of 2,276 chil-dren (1–4 years of age) from 65 villages from 5 ecologically different areas[23] of The Gambia was carried out at the end of the 1992 rainy season (Figure 1). Each child was given a clinical examination and their age and weight/height was recorded. Details from their health card were taken if a health card was available. Finally, a blood sample was col-lected by fingerprick for thick and thin blood films for de-
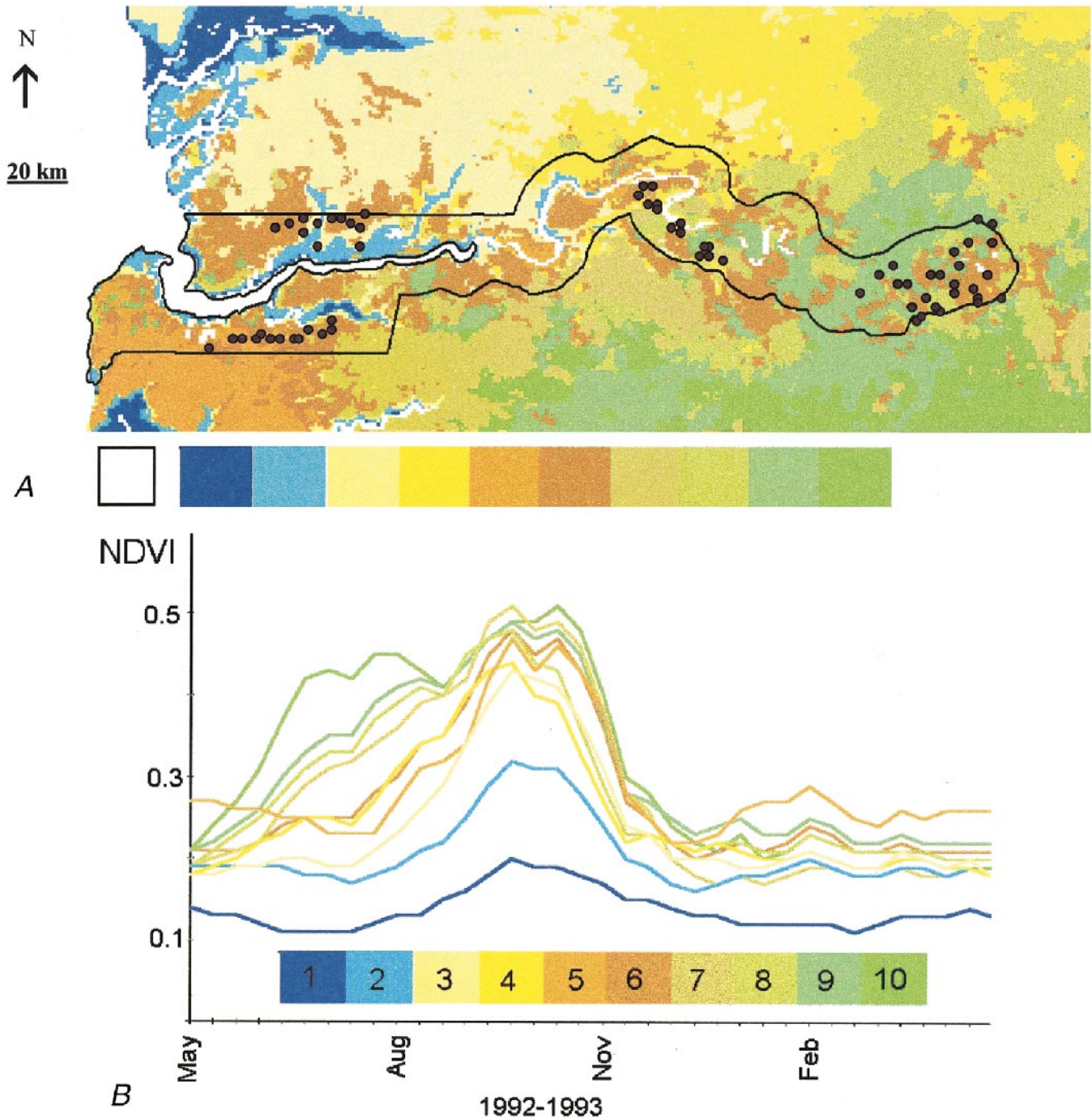
FIGURE 1. **A,** distribution of the 65 study villages (**dots**) in The Gambia in 5 areas superimposed on the spatial distribution of the 10 seasonal classes of the normalized difference vegetation index (NDVI). The colors correspond to seasonal profiles in Figure 1B. Yellow predominates as one moves northeastwards towards the Sahel while dark green predominates as one moves southwestwards. **B,** Seasonal profiles of the NDVI obtained using ADDAPIX analytical software. Ten classes were chosen. Classes 1 and 2 are blue to indicate the fact that their low values are associated with the presence of water. Dark green represents the longest seasonal profile while pale yellow indicates a short vegetation cycle. The NDVI measure (called NDVLS) used as a proxy for length of the malaria transmission season = the area under the curve for the period first dekad of May until 3 dekads prior to the morbidity survey. A lag of one month between NDVI values and malaria cases has been shown in an early study on Gambian data.[16] This value was extracted for each village coordinate. A second variable, the quadratic value of NDVLS (NDVLS^2), was computed and included in the analysis.

termination of malaria parasitemia. Approximately two-thirds of the children came from PHC villages, half of which had their bed nets treated with permethrin in 1992, a few months before the survey. Entomologic studies were also

undertaken during the same period in three of the five study areas.[26]

Satellite data. Data collected from channels 1 and 2 of the NOAA-AVHRR sensor during 1992, 1993, and 1995

have been processed to produce a global archive of NDVI images at a temporal resolution of one dekad (10 days) and a spatial resolution of approximately 1.1 km. These data are held by the National Aeronautics and Space Administration (NASA) PATHFINDER 1 km project and can be accessed over the Internet (http://edcwww.cr.usga.gov/landdaac/1KM/comp10d.html and Eidenshink J, Faundeen J, 1997. The 1-km avhrr global land data set: first stages in implementation, http//edcwww.cr.usga.gov/landdaac/1KM/paper.html).

Thirty-six dekadal images from May 1992 to April 1993 of The Gambia were extracted from the PATHFINDER active 1.1 km AVHRR archives. The images, in Goodes Homolosine Projection, were processed using the Image Display and Analysis Software/Map and Image Display and Analysis Software (IDA/WINDISP)(http://ag.arizona.edu/repfirman/windisp3.html). One image was incomplete and was therefore recreated using the mean of the previous and subsequent images. The images were then entered into a spatial statistical analysis program, ADDAPIX, that is designed for monitoring seasonal and interannual vegetation growth using satellite imagery (Griguolo S, University of Venice, Venice, Italy). This program uses the IDA image format as the basic input file and submits the series of images to a principle component analysis. This is followed by a non-hierarchical clustering procedure with the aim of grouping pixels (image squares) that have a similar spatial and temporal pattern. After a period of experiment, 10 classes were chosen as a number large enough to indicate the ecologic variation within The Gambia but small enough for a number of classes to contain sufficient villages for comparison of malaria endemicity (Figure 1). The seasonal profiles from the 10 classes indicate clearly that there is considerable difference in the length and greenness of the vegetation cycle in The Gambia despite its relatively small size and uncomplicated topography.

We were able to extract the associated NDVI class for each village by overlaying the distribution of the study villages as a boundary file in IDA format. The NDVI measure (called NDVI_S) used as a proxy for length of the malaria transmission season was the area under the curve for the period of the first dekad of May until 3 dekads (one month) prior to the morbidity survey. A lag of one month between NDVI values and malaria cases has been shown in an early study on Gambian data.[16] A second variable, the quadratic value of NDVI_S (NDVI_S^2), was computed and included in the analysis.

A number of children were excluded from the current analysis because either their age was not known, their net usage was not known, or no vegetation information was obtained from their village environment due to persistent clouds. After these exclusions, 2,039 children (89% of the original sample) from 65 villages were included in the analysis. Children were classified into three groups: 1) children who slept without a net (591, 29%); 2) children who slept under an untreated net (886, 43.5%); and 3) children who slept under an insecticide-treated net (562, 27.5%). A total of 728 (35.7%) children where found to be positive for *Plasmodium falciparum* parasites during the morbidity survey (Table 1).

Spatial analysis. Modeling the relationship between environmental data and malarial indices is complicated by the

TABLE 1
Summary information on data set used for analysis

Net usage in original data*	Type of village†	% Children with health card	% Children with *Plasmodium falciparum* infection	No. of children in survey
A	Non-PHC	0.69	0.47	218
A	PHC	0.6	0.49	373
B	Non-PHC	0.77	0.38	425
B	PHC	0.78	0.29	461
C	PHC	0.73	0.27	562

* A = no net; B = untreated net; C = treated net.
† PHC = primary health care.

spatial correlation between observations, which invalidates the inferences associated with standard regression calculations. In particular, while standard regression modeling applied to spatially correlated data gives satisfactory point estimates of regression parameters, the nominal standard errors associated with these parameter estimates are typically too small, and this in turn leads to an exaggerated impression of the significance of regression relationships. We therefore undertook the following analysis.

First, we used a logistic regression model[20] to estimate the probability of the presence of malarial parasites in each child as a function of NDVI_S, NDVI_S^2, and age (in days), and adjusted for the effects of nets (treated, untreated, or absent), PHC (yes or no), (health card) (yes or no), and area (a five-level factor) identifying the five ecologically different areas.

Second, we computed the variogram[27] of the standardized residuals from the fitted logistic regression model to estimate the spatial correlation in the data. Based on the appearance of the variogram, we assumed that the correlation between a pair of measurements was an exponentially declining function of distance, i.e., $p(d) = \exp/(-\alpha d)$ for some positive value of α.

Third, from the fitted exponential correlation model, we adjusted the nominal standard errors of the logistic regression parameter estimates to allow for the effects of spatial correlation, using the method of generalized estimating equations.[22] This allows us to reassess the nominal significance of particular terms in the regression model, and to simplify the model accordingly.

Having fitted the model, we can use it to compute the estimated probability of infection for any combination of values of the explanatory variables, and so predict the prevalence rates for children in any particular village with a given set of characteristics. We can then repeat this process under any chosen set of circumstances to quantify the effect on prevalence rates of any change in behavior, e.g., increased use of mosquito nets.

RESULTS

The results of the non-spatial logistic regression analyses of the presence/absence of malaria in each child (non-spatial model) are given in Table 2. Age (in days) and NDVI_S^2 are both positively correlated with the presence of parasites (nominal $P < 0.001$), while NDVI_S, the use of nets (treated or untreated), living in a PHC village, and possessing a health card are all negatively correlated with the presence of parasites (nominal $P < 0.001$). As noted earlier, quoted nom-

Variable*	Regression value	Nonspatial model 1				Spatial model 2		
		SE	t	P†		SE	t	P†
(Intercept)	9.0631	2.2279	4.068	<0.001		4.5171	2.006	<0.05
NDVI_S	−0.401	0.0911	−4.408	<0.001		0.1878	−2.139	<0.05
NDVI_S^2	0.004	0.0009	4.507	<0.001		0.0019	2.169	<0.05
Age.day	0.0005	0.0001	5.003	<0.001		0.0001	5.1	<0.001
Nets (Untreated)	−0.552	0.1322	−4.175	<0.001		0.2012	−2.742	<0.001
Nets (Treated)	−0.676	0.1480	−4.567	<0.001		0.2454	−2.755	<0.05
PHC	−0.432	0.1212	−3.566	<0.001		0.2433	−1.776	NS
Card	−0.256	0.1146	−2.236	<0.05		0.1391	−1.842	NS
Area 2	−0.823	0.1868	−4.408	<0.001		0.3827	−2.152	<0.05
Area 3	−0.655	0.195	−3.348	<0.001		0.4153	−1.579	NS
Area 4	0.1470	0.2471	0.598	NS		0.5562	0.266	NS
Area 5	0.6022	0.2357	2.555	<0.05		0.5088	1.183	NS

* NDVI = normalized difference vegetation index; PHC = primary health center.
† NS = not significant.

inal *P* values are likely to overstate the true significance of these results.

The results of the logistic regression analyses of the presence/absence of malaria in each child corrected for the spatial correlation in the data (spatial model) are also presented in Table 2. The second model has the same estimated regression parameters, but because the standard errors have been corrected for spatial correlation, the significance of the covariates has changed accordingly. In the spatial model, the t-value for age remains approximately the same as in the non-spatial model, indicating (as we would expect) that there is no spatial difference in age structure of 1–4-year-old children in The Gambia. The t-value for NDVI_S and NDVI_S^2 changed considerably from −4.408 to −2.139 and from 4.507 to 2.169, respectively, but both remained significant at the 5% level. This indicates that some but not all of the association observed between presence of parasites and length of transmission is due to spatial correlation. The t-values of the variables nets (untreated) and nets (treated) are also reduced in the spatial model when compared with the non-spatial model but remain highly significant ($P < 0.001$). Neither living in a PHC/non-PHC village or possessing a health card remain significant ($P > 0.05$) once spatial effects are taken into account.

Predicting prevalence rates under different scenarios. Using the model presented in Table 2, we predicted the num-

ber of children infected with *P. falciparum* under differing net scenarios (Table 3). These scenarios included if no children slept under a net, if all children slept under a net, if all children slept under a treated net, and if the current net status prevailed but none were treated.

According to the model, removing nets from those children who currently use them would result in an increase of parasite prevalence from 36% to 45%. Providing net treatment without increasing net coverage would result in a slight decrease in parasite prevalence from 36% to 35%. A more significant decrease from 36% to 33% would result if net coverage were increased to include all children even when the nets were not treated. Not surprisingly, the best possible result would be obtained if all children slept under a treated net (prevalence rate decrease from 36% to 30%).

DISCUSSION

In our study, when taking into account spatial correlation, the significance of all associations between malaria prevalence and human (age, untreated nets, treated nets, health card) and village (PHC and area) factors and environmental satellite data (NDVI_S and NDVI_S^2) are reduced with the exception of child age. However, the associations with bed net use (treated or untreated) and with the satellite data (NDVI_S and NDVI_S^2) are still significant at the 1% and 5% levels, respectively, even when spatial effects are taken into account. This suggests that these associations have a more direct link and may be determined by a biological mechanism. These results confirm the widely published nonspatial analysis of the effectiveness of insecticide-treated bed nets in reducing infection with malaria parasites.[28] They also reaffirm the importance of traditional bed nets (not treated with insecticide) in reducing exposure of children to malaria.[24] Indeed, the study indicates that in The Gambia, increasing the use of bed nets might be as effective in reducing the rate of infection among children as providing insecticide to treat them. However, insecticide-treated bed nets are thought to be more effective than untreated nets at preventing infections characterized by high-density parasitemia,[24] and this might partially explain their significant impact on childhood mortality.[29] Further studies are required to estab-

TABLE 3
Predicted number of children infected with *Plasmodium falciparum* infections under different net usage scenarios*

Net usage†			No. of children infected with *P. falciparum*	% of children infected with *P. falciparum*	Change ratio
A (n = 591)	B (n = 886)	C (n = 562)			
None	None	None	910.1	44.6	1.25
None	Untreated	Untreated	740.8	36.3	1.02
None	*Untreated*	*Treated*	*728.0*	*35.7*	*1.00*
None	Treated	Treated	706	34.6	0.97
Untreated	Untreated	Untreated	669.6	32.8	0.92
Treated	Treated	Treated	619.7	30.4	0.85

* *Italicized* words and numbers indicate actual data from children classified into three groups (see Materials and Methods).
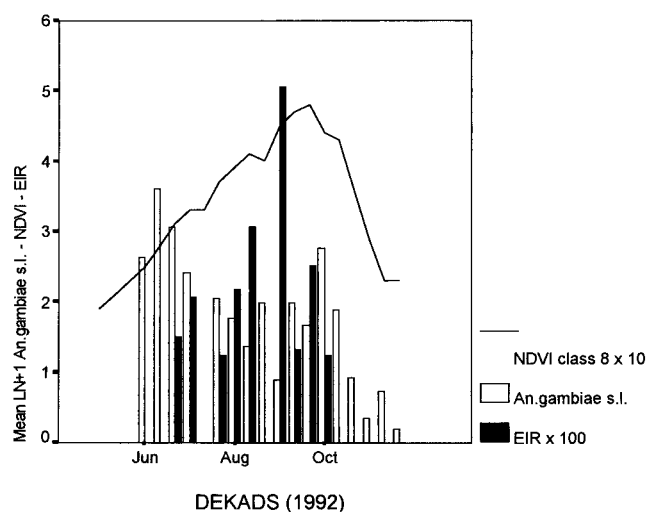† A = no net; B = untreated net; C = treated net.

FIGURE 2. Temporal changes in vector abundance, entomologic inoculation rate (EIR), and normalized difference vegetation index (NDVI) in 1992 in Jahally, The Gambia. Dekadal NDVI values from Addapix class 8 represents the seasonal cycle of vegetation at Jahally, Area 3. *Anopheles gambiae* s.l. occur in large numbers in early June, presumably in association with the local irrigated rice fields, but no mosquitoes infected with sporozoites are found until the last dekad of June. Both vector populations and the number of infected mosquitoes decreases rapidly once the NDVI values start to decrease.

lish whether a relationship also exists between the outcome of infection (disease and death) and the environmental satellite data analyzed in this report.

According to this spatial analysis, living in a PHC or a non-PHC village has no significant effect on the probability of malaria infection. This contradicts earlier non-spatial analyses, which have highlighted the differences in infection rates between children living in PHC and non-PHC villages.[24] According to our analyses, such results represent spatial differences in the siting of PHC and non-PHC villages rather than intrinsic qualities associated with the delivery of primary health care.

The model also suggests that environmental satellite data (NDVI), which indicates the length of the growing season, may be useful for predicting the levels of malaria endemicity in children once behavioral factors are taken into account. It provides empirical support for the use of satellite data to provide first-level stratification of regions or countries for malaria control activities.[5,19]

The association of the NDVI with a suitable environment for the survival of infective mosquitoes might explain our finding. The NDVI has been shown to be highly correlated with saturation deficit in The Gambia,[17] and the limited data available suggest that vegetation senesces at the end of the rainy season are associated with a rapid decrease in the entomologic inoculation rate and mosquito abundance (Figure 2). Dry season breeding sites for *An. arabiensis* in irrigated rice fields in study area 3 have been identified by a higher than average NDVI.[17]

In conclusion, this study demonstrates the importance of spatial effects in the inferences that can be drawn from epidemiologic models created from multiple regression analysis. It confirms the effectiveness of insecticide-treated bed nets in reducing parasite prevalence but suggests that in the Gambian situation, the use of traditional untreated nets play a significant role in reducing malaria exposure in children. The model indicates that earlier studies suggesting that living in a PHC village provides protection from malaria infection is the result of spatial correlation. The model also suggests that there may be an *a priori* relationship between the NDVI and malaria infection. We suggest that this relationship is likely to be based on the fact that high NDVI values are indicative of a moist environment supporting both mosquito breeding and adult survival.

Authors' addresses: Madeleine C. Thomson, Stephen J. Connor, and Mark Cresswell, MALSAT Research Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, United Kingdom. Umberto D'Alessandro, Department of Parasitology, Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium. Barry Rowlingson and Peter Diggle, Medical Statistics Unit, Lancaster University, Lancaster LA1 4YE, United Kingdom. Brian Greenwood, London School of Hygiene and Tropical Medicine, London WCE1 7HT, United Kingdom.

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