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MAJOR ARTICLE

Identification of Hot Spots of Malaria Transmission for Targeted Malaria Control

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Background. Variation in the risk of malaria within populations is a frequently described but poorly understood phenomenon. This heterogeneity creates opportunities for targeted interventions but only if hot spots of malaria transmission can be easily identified.

Methods. We determined spatial patterns in malaria transmission in a district in northeastern Tanzania, using malaria incidence data from a cohort study involving infants and household-level mosquito sampling data. The parasite prevalence rates and age-specific seroconversion rates (SCRs) of antibodies against *Plasmodium falciparum* antigens were determined in samples obtained from people attending health care facilities.

Results. Five clusters of higher malaria incidence were detected and interpreted as hot spots of transmission. These hot spots partially overlapped with clusters of higher mosquito exposure but could not be satisfactorily predicted by a probability model based on environmental factors. Small-scale local variation in malaria exposure was detected by parasite prevalence rates and SCR estimates for samples of health care facility attendees. SCR estimates were strongly associated with local malaria incidence rates and predicted hot spots of malaria transmission with 95% sensitivity and 85% specificity.

Conclusions. Serological markers were able to detect spatial variation in malaria transmission at the microepidemiological level, and they have the potential to form an effective method for spatial targeting of malaria control efforts.

Malaria risk is not equally distributed within populations. In addition to the well-established age dependency of attacks of clinical malaria [1, 2], many studies report considerable variation in susceptibility to clinical malaria in individuals of the same age. In longitudinal studies, this variation in susceptibility is manifested as a high number of malaria episodes in a relatively small subset of study participants, while other study participants remain malaria free during follow-up [3–7]. This finding may be partly explained by such human host factors as red blood cell polymorphisms [2, 7–9], but variation in exposure to malaria-infected mosquitoes is likely to play a more important role [4, 7, 9–12]. The recent suggestion that noninfected individuals should be considered to be nonexposed [6] highlights the importance of heterogeneity in malaria exposure for understanding observed disease patterns [9, 13, 14]. Understanding heterogeneity in malaria exposure also creates opportunities for focused malaria control [14].

Focused malaria control will have direct benefits not just for the individuals who are included in the control effort but also at the community level. Individuals who are bitten most often are most likely to be infected and can amplify transmission by transmitting the malaria parasites to a large number of mosquitoes [15]. This

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amplified transmission can lead to 2- to 4-fold increases in the basic reproductive number of malaria parasites (R0) [13]. If malaria control efforts can be targeted to individuals who contribute disproportionally to malaria transmission, community protection could be achieved by eliminating transmission in a relatively small fraction of human hosts [15]. Such targeted interventions are likely to become increasingly important tools in malaria elimination efforts once transmission in an area has decreased but is maintained in hot spots of malaria transmission [16]. Community-wide coverage with such control methods as insecticide-treated nets is difficult to achieve [17] and may result in substantial reductions in transmission intensity but not in malaria elimination [17, 18].

The identification of hot spots of malaria transmission is important for malaria elimination efforts but is not straightforward. Several field studies have shown that proximity to vector-breeding sites (eg, the distance to the nearest body of water [7, 19–21] or other potential breeding site [22]) is correlated with the risk of malaria. However, this proximity is unlikely to be the sole predictor of malaria risk, because there is variation in the productivity and longevity of breeding sites [23] and because the association can be confounded by household factors [7, 9, 19, 22, 24] and the vicinity of alternative hosts, such as cattle [25]. A more direct indicator of increased malaria risk would be exposure to infected mosquitoes or serological evidence of malaria exposure in the human population [26, 27]. To successfully target transmission hot spots, simple tools are required to reliably identify these hot spots.

In the present study, we determine heterogeneity in exposure to infected *Anopheles* mosquitoes in relation to the incidence of malaria disease in infants residing in an area of moderate transmission intensity in Tanzania. Rather than use a predictive model at the level of an individual, we aim to identify restricted geographical areas in which there is a higher level of transmission intensity. To achieve this objective, we used environmental and household factors to develop a model that predicts the areas that form hot spots of transmission and to determine the value of serological markers of malaria exposure for this purpose.

METHODS

Study area. This study was conducted in the Korogwe district in the Tanga region of Tanzania. Malaria transmission previously was intense and perennial [28], but it has decreased in recent years. In 2007, it was estimated to be 1–14 infectious bites per person per year [29]. The study protocols were approved by the ethics review board of the National Institute for Medical Research of Tanzania and by the ethics committee of the London School of Hygiene and Tropical Medicine.

Clusters of clinical malaria episodes as indicators of hot spots of malaria transmission. We defined a hot spot of malaria transmission as an area with a higher-than-average level of transmission intensity, which is reflected by a higher incidence of malaria episodes in infants. This definition differs from biologically based transmission focus (defined as a geographical area where the local *Anopheles* population sustains R_0 to a level >1), for which it is difficult to establish parameters. The data that were used were from a longitudinal study in which infants 8–16 weeks of age who attended Expanded Programme on Immunization clinics were enrolled in a trial of the efficacy of intermittent preventive treatment for malaria in infants (IPTi) [30]. Enrolled children had access to free clinical care for up to 2 years at local health care facilities. No active case detection was done, but parents and caretakers were encouraged to bring their children to health care facilities if the children were unwell. Case patients had a recorded body temperature of ⩾37.5°C or a history of fever in the previous 2 days in the presence of malaria parasites. In the complete cohort of 1276 children, who were monitored between 2004 and 2008, a total of 877 children (68.7%) had no malaria episodes, 258 (20.1%) had 1–2 episodes, and 141 (11.1%) had ⩾3 clinical episodes (maximum number of episodes, 14). Clusters of clinical malaria episodes were determined using SaTScan software (version 8.0; developed under the joint auspices of Martin Kulldorff of the National Cancer Institute and Farzard Mostashari of the New York City Department of Health and Mental Hygiene) to assess categorical data (0, 1–2, or ⩾3 episodes for individuals with ⩾3 months of follow-up). Because we aimed to identify clusters that would allow small-scale targeting, a maximum window of 10% of the population was used for scanning clusters of malaria episodes.

Exposure to mosquitoes as a predictor of malaria risk. In the last year of the longitudinal study, exposure to mosquitoes was assessed in the bedrooms of a selection of the study children. We aimed to determine mosquito exposure for 400 households whose child did not have an episode of malaria during the 2 years under study (400 of 877 households), for 100 households whose child experienced 1–2 clinical malaria episodes (100 of 258 households), and for 100 households whose child experienced ⩾3 clinical malaria episodes (100 of 141 households). Households were randomly selected from these subgroups by use of computer-randomized tables. Written informed consent was obtained from the head of household. Adult mosquitoes were sampled by Centers for Disease Control light traps (model 512; John W. Hock Company), by use of standard protocols [31]. Each household was sampled on 3 occasions: at the end of the wet season (May), at the beginning of the dry season (July), and at the end of the dry season (September). Every night that sampling occurred, a median of 14 mosquito traps (interquartile range [IQR], 10–16 mosquitoes) were set in the study area. The order in which households were sampled was determined by randomization in blocks, en-

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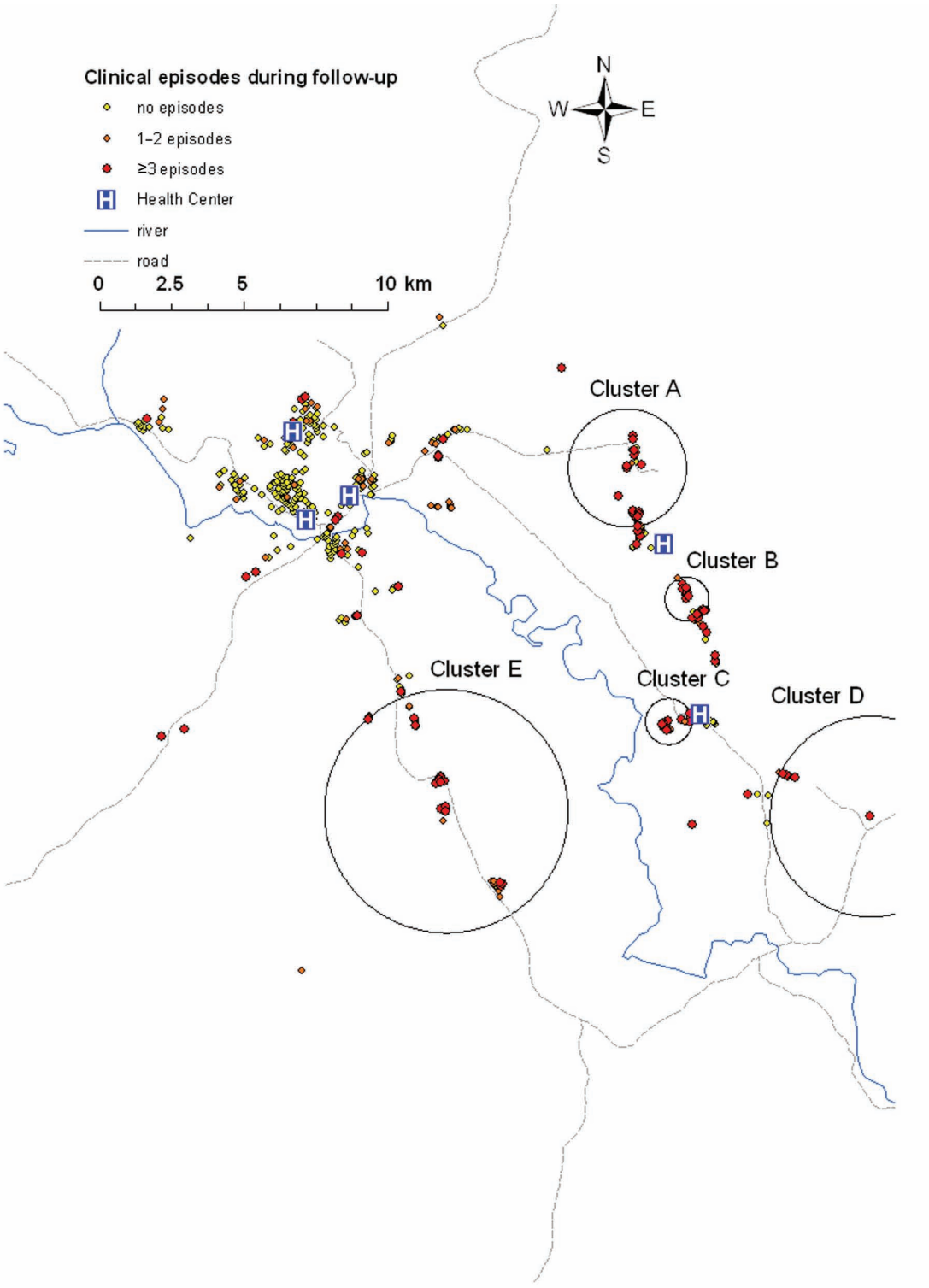

Figure 1. Reported malaria episodes during follow-up. Dots denote individual households with 1 person participating in passive case detection for an average of 22 months. The color and size of the dots denote the no. of episodes experienced. Circles denote statistically significant clusters A (8 individuals [23.5%] had no episodes, 8 [23.5%] had 1–2 episodes, and 18 [52.9%] had ⩾3 episodes) ($P = .003$), B (4 individuals [19.1%] had no episodes, 1 [4.8%] had 1–2 episodes, and 16 [76.2%] had ⩾3 episodes) ($P = .001$), C (3 individuals [13.0%] had no episodes, 10 [43.5%] had 1–2 episodes, and 10 [43.5%] had ⩾3 episodes) ($P = .004$), D (0 individuals had no episodes, 2 [25.0%] had 1–2 episodes, and 6 [75.0%] had ⩾3 episodes) ($P = .05$), and E (7 [14.9%] individuals had no episodes, 22 [46.8%] had 1–2 episodes, and 18 [38.3%] had ⩾3 episodes) ($P = .001$). For households outside clusters, 315 (78.4%) reported no malaria episodes, 57 (14.2%) reported 1–2 episodes, and 30 (7.5%) reported ⩾3 episodes.

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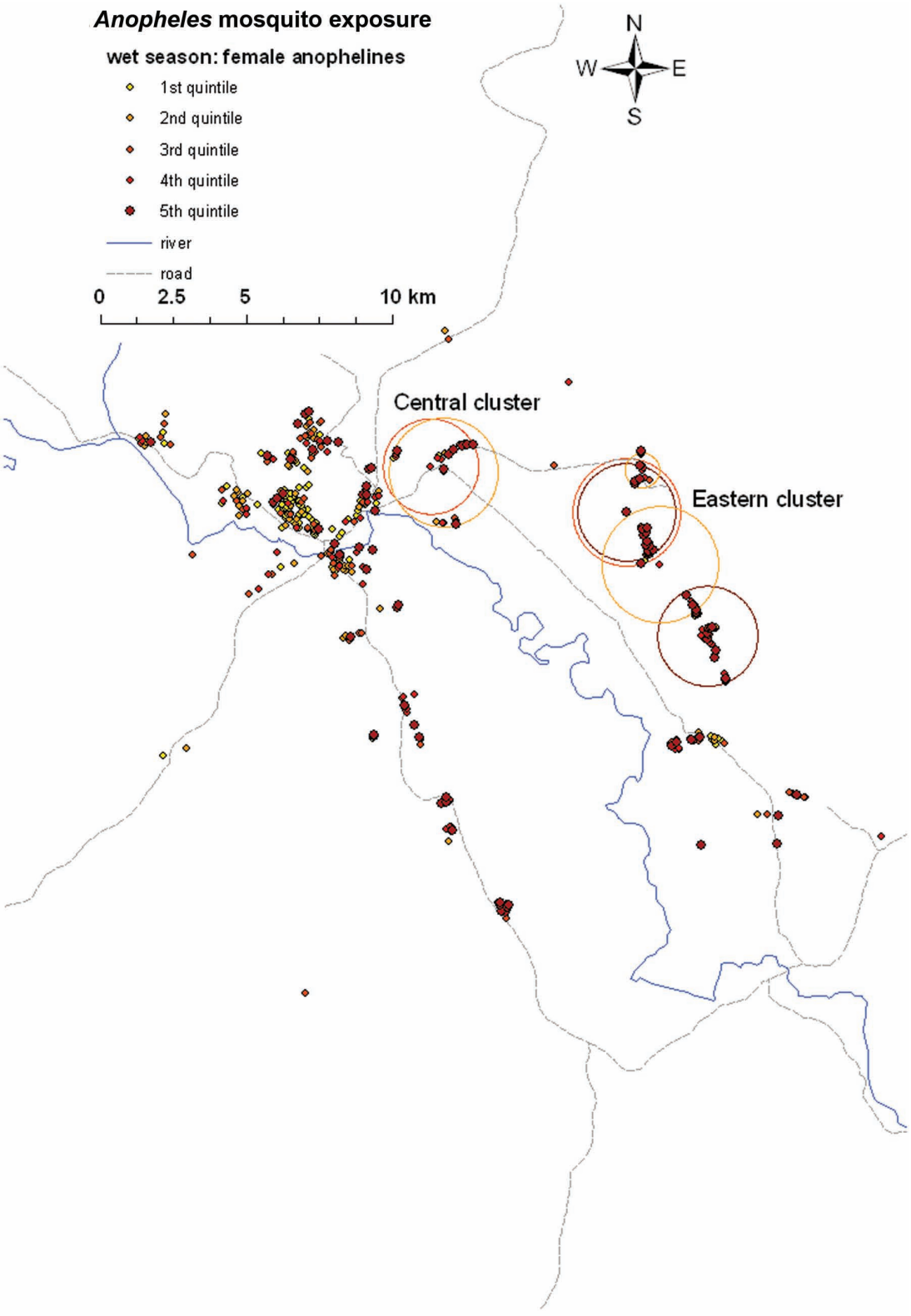

Figure 2. Exposure to *Anopheles* mosquitoes in April (the wet season) and clusters of mosquito exposure in April (the wet season), July (the start of the dry season), and September 2008 (the end of the dry season). Dots denote individual households. The color and size of the dots denote the no. of female *Anopheles* mosquitoes caught in a single night in the wet season, expressed in quintiles. Circles denote statistically significant clusters of exposure to female *Anopheles* mosquitoes in the wet season ($n = 2$) *(brown),* the beginning of the dry season ($n = 2$) *(orange),* and the end of the dry season ($n = 3$) *(yellow).*

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Table 1. Factors Associated with Residing in a Cluster of Higher Malaria Incidence ($P < .1$, by Univariate Analysis)

Factor	Univariate analysis[a]		Multivariate[b]	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Distance to high-producing *Anopheles* breeding site[c]	0.92 (0.87–0.96)	.001	0.92 (0.87–0.97)	.004
Wealth index[d]	0.76 (0.58–1.00)	.052	NS	
Roofing material				
Iron/tiles	1.00 (reference)		…	
Thatch	2.01 (1.04–3.90)	.038	NS	
Walling material				
Brick	1.00 (reference)		1.00 (reference)	
Mud	3.12 (1.49–6.53)	.003	2.66 (1.22–5.82)	.014
Walling structure				
Rough	1.00 (reference)		…	
Smooth	0.34 (0.16–0.70)	.004	NS	
Bed net use[e]				
No	1.00 (reference)		1.00 (reference)	
Yes	0.27 (0.12–0.62)	.002	0.22 (0.08–0.57)	.02

NOTE. Values are adjusted for clustering of observations within subvillages. CI, confidence interval; NS, not significant; OR, odds ratio.

[a] Based on 476–535 observations.

[b] Based on 476 observations in 15 subvillages.

[c] A high-producing *Anopheles* breeding site is defined by the presence of ⩾5 *Anopheles* larvae in 10 dips. Values are adjusted for clustering of observations within subvillages. Distance was expressed per 100 m.

[d] In quintiles.

[e] Bed net use of the child enrolled in the study of intermittent preventive treatment for malaria in infants, as observed at the start of follow-up. The total no. of nets per household or the proportion of people having a net did not significantly influence the risk of residing in a cluster of higher malaria incidence.

suring that, each night, sampling was done in households of all 3 subgroups, in an approximate ratio of 4:1:1. To visualize and analyze differences in mosquito exposure, the highly overdispersed mosquito data were used to divide households into quintiles of exposure to female *Anopheles* mosquitoes. Spatial patterns in mosquito exposure were determined using SaTScan. Because we were interested in small-scale variation in mosquito exposure, the maximum radius of the circular window was set at 2 km, on the basis of the estimated distance that mosquitoes fly [14]. The presence of sporozoites in salivary glands was determined by circumsporozoite protein enzyme-linked immunosorbent assay [32], to calculate the entomological inoculation rate (EIR) [33].

Predicting hot spots of malaria transmission by use of an environmental model. The following factors were recorded for each household: wall material, roofing material, presence of eaves (defined as an opening of >10 cm between wall and roof), window size (width, >50 cm), presence and quality of window screens, presence of cattle in or near the house, use of repellents, number of people in the household, number of people in the sampling room, number of (un)treated bed nets in the household, and number of (un)treated bed nets in the sampling room. All potential breeding sites within a 2-km radius around selected households were visited and mapped at the end of the dry season; 10 dips were made with a standard 350-mL white dipper, and the number of *Anopheles* larvae was recorded. Breeding sites were arbitrarily categorized as low- or high-producing sites (>5 *Anopheles* larvae in 10 dips). The household wealth index was the weighted sum of household characteristics, including whether the household members owned the house they occupied; whether they owned consumer durables, such as a motorbike, bicycle, radio, mattress, phone, wristwatch, or cart; and whether they had access to electricity. The weights for the assets in the index were generated by principal components analysis [34, 35].

Predicting hot spots of malaria transmission by parasite prevalence rates and serological markers of exposure. Malaria parasite prevalence and antibody responses were determined for people attending the 4 existing health care facilities in the district (in Magunga, Majengo, Mnyuzi, and Magasin) in July–August 2007 [29]. Eligible study participants were individuals who visited the health care facility for any reason (ie, family members or guardians accompanying patients, as well as patients themselves) and who consented to participate. Infants from the previously described longitudinal study were not included. A single blood sample obtained by fingerprick was used for detection of parasites by use of a rapid diagnostic test (RDT [Parahit-f; Span Diagnostics Limited]) and blood spots on filter paper. Information was collected on the age of the patients, as well as their village and subvillage of residence.

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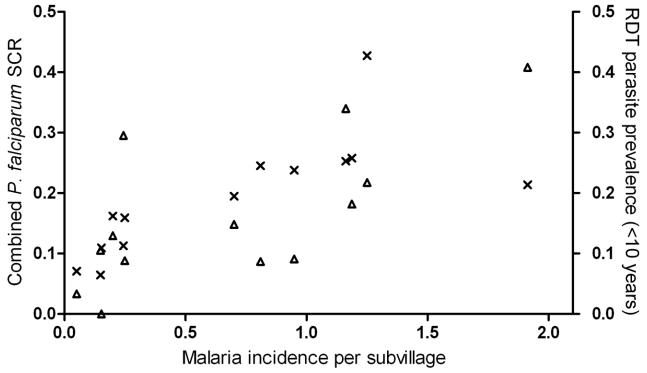

Figure 3. Malaria incidence per subvillage and age-specific *Plasmodium falciparum* seroconversion rates (SCRs) and parasite prevalence rates in children <10 years of age. Each dot denotes 1 of the 13 subvillages in Korogwe district. Incidence data are per person per year and are based on all children enrolled in the original intermittent preventive treatment for malaria in infants (IPTi) study ($n = 1276$). The malaria incidence estimates per subvillage are based on a median of 74 children (interquartile range [IQR], 46–125 children) or a total duration of follow-up of 1542 person-months (IQR, 941–2521 person-months). The combined apical membrane antigen–1/merozoite surface protein–1_{19} SCRs are indicated by crosses and are based on a minimum of 50 serum samples per subvillage (median, 93 samples [IQR, 70–119 samples]). Parasite prevalence rates in children <10 years of age are denoted by open triangles and are based on a median of 34 observations (IQR, 24–50 observations). RDT, rapid diagnostic test.

Reconstituted filter paper spots were tested for anti–merozoite surface protein–1 (MSP-1_{19}) and anti–apical membrane antigen–1 (AMA-1) human immunoglobulin (Ig) G antibodies by enzyme-linked immunosorbent assay, by use of standard methodology [26, 36]. A cutoff level above which samples were deemed to be antibody positive was defined using a mixture model [36]. The seroconversion rate (SCR, or λ) as a serological marker of exposure was estimated by fitting a simple reversible catalytic model to the combined antibody prevalence, stratified into yearly age groups [26]. The SCR was determined for individual subvillages for which a minimum of 50 observations were available. This resulted in SCR estimates for 13 subvillages in the study area that were geographically distinct; for 2 other subvillages, the number of samples was insufficient.

Statistical analysis. Statistical analyses were performed using Stata software (version 10; Statacorp). Maps were produced using ArcGIS software (version 9.1; ESRI). SaTScan software [37] was used for the detection of spatial clusters in episodes of clinical malaria and mosquito exposure. A circular window was used to systematically scan the area; statistical significance of the clusters was explored by means of 999 Monte Carlo replications, to ensure adequate power for defining clusters. Differences in malaria incidence were determined by Poisson regression models, adjusting for the type of drug used for IPTi. Environmental factors associated with clusters of higher malaria incidence were determined by multiple random effects logistic regression models, adjusting for the nonindependence of households within subvillages ($n = 15$). Factors for which $P < .1$ in univariate models were included in a multivariate model and were retained if $P < .05$ in the multivariate model. A diagnostic probability function was derived from the independent predictors in this multivariate model, as proposed by Miettinen et al [38]. Receiver operating characteristic (ROC) curves were created to select optimal environmental, parasitological, and serological exposure models to predict hot spots of malaria transmission.

RESULTS

Clusters of clinical malaria episodes as an indicator of hot spots of malaria transmission. The average duration of follow-up for attacks of clinical malaria was 21.8 months (IQR, 21.3–22.0 months). SaTScan revealed 5 clusters with a higher incidence of malaria episodes in infants (Figure 1). The clusters of higher malaria incidence could not be explained by closer vicinity to health care facilities—that is, a higher likelihood that children whose households were located near a clinic would report at the clinic with suspected malaria. There also was no spatial variation in the allocation of study drugs ($P = .44$).

Clusters of mosquito exposure. Mosquito collections were

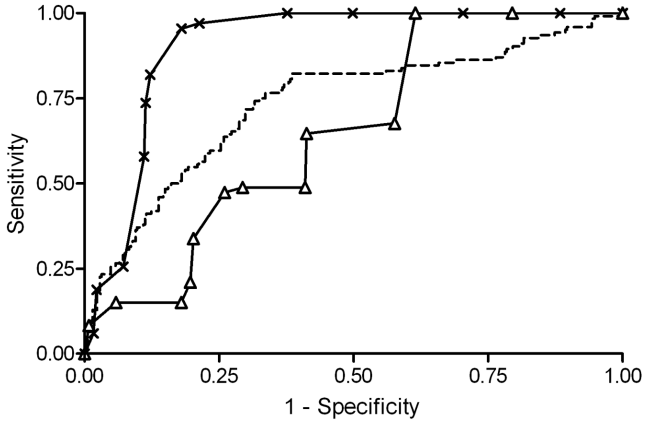

Figure 4. Comparison of *Plasmodium falciparum* seroconversion rates (SCRs), parasite prevalence rates, and environmental characteristics for prediction of hot spots of malaria transmission. Receiver operating characteristic curves were generated for the combined apical membrane antigen–1 (AMA-1) and merozoite surface protein–1_{19} (MSP-1_{19}) age-specific SCR per subvillage (crosses connected by a solid line denote an area under the curve (AUC) value of 0.92), parasite prevalence rates in children <10 years of age per subvillage (open triangles connected by a solid line denote an AUC of 0.65), and a logistic regression model based on the household and environmental characteristics described in Table 1 (the dashed line denotes an AUC of 0.76). When a cutoff value of 0.16 was used for the combined AMA-1 and MSP-1_{19} SCR, the sensitivity of predicting residence in a hot spot of transmission was 95.5%, with a specificity of 82.0%.

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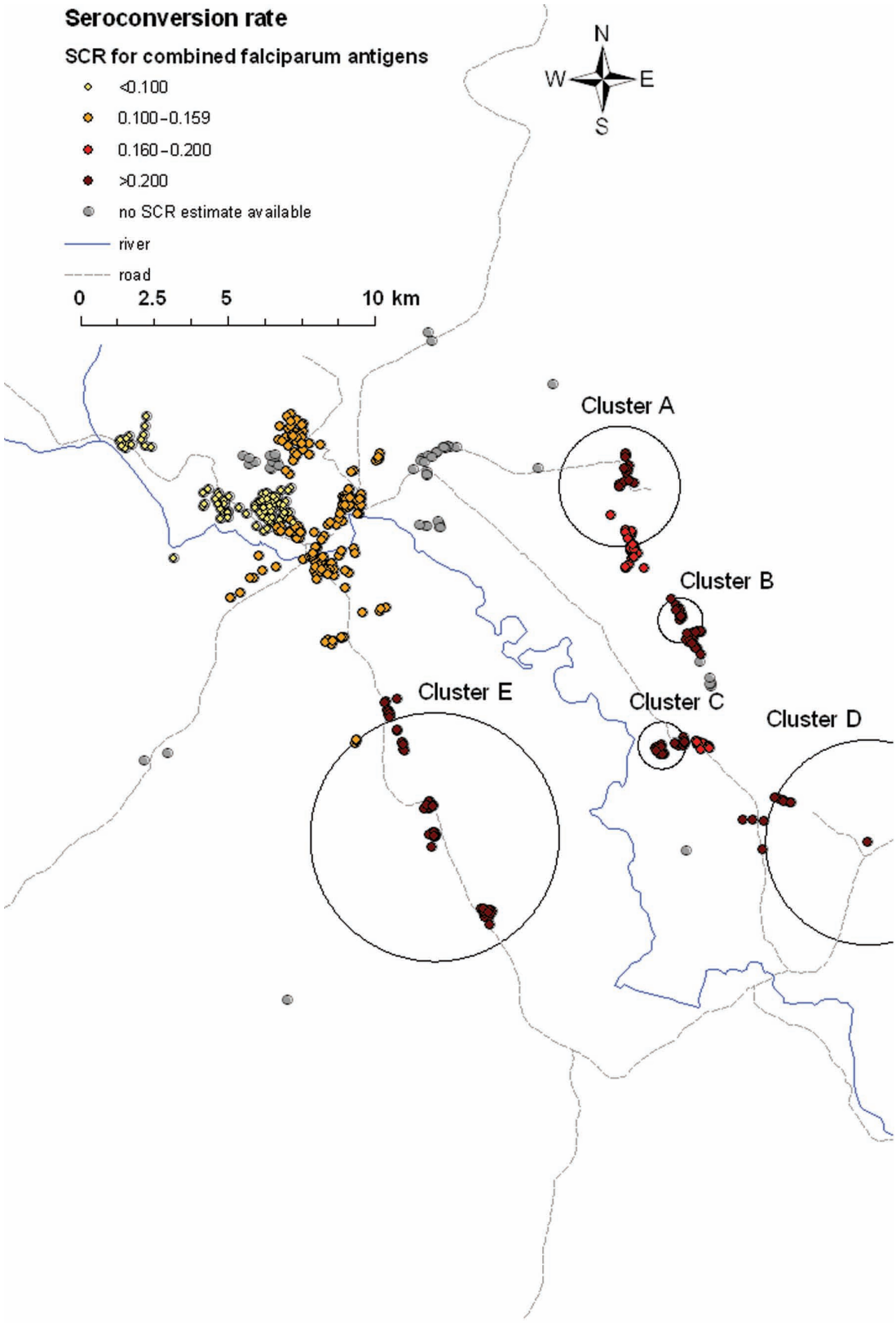

Figure 5. Map of *Plasmodium falciparum* age-specific seroconversion rates (SCRs) in association with the clusters of higher malaria incidence. The age-specific SCR for the combined *Plasmodium falciparum* antigens (apical membrane antigen–1 and merozoite surface protein–1_{19}) that was calculated for all subvillages ($n = 13$) is presented for each household. Gray dots denote households in those subvillages for which no SCR could be estimated as a result of insufficient serum samples ($n < 50$). Circles denote clusters of higher malaria incidence at the household level, as reported in Figure 1.

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done in 337 households in which the IPTi study participant experienced no episodes of clinical malaria, 100 households in which the study participant experienced 1–2 episodes of malaria, and 98 households in which the study participant experienced ⩾3 episodes of malaria during follow-up. Three rounds of mosquito catches were done at the end of the wet season (500 traps with 6262 female anophelines) and at the beginning of the dry season (506 traps with 1718 female anophelines) and the end of the dry season (450 traps with 761 female anophelines). Two independent clusters of higher-than-average exposure to female anophelines were detected at the end of the wet season ($P = .001$ and $P = .02$), 2 at the start of the dry season ($P = .001$, for both), and 3 at the end of the dry season ($P = .001$, $P = .001$, and $P = .046$) (Figure 2). Because of the consistency in their geographical location over the different seasons, clusters were combined as the "eastern cluster" and the "central cluster."

Predicting hot spots of malaria transmission by exposure to mosquitoes. The average EIR was 0.94 bites per person per month (95% CI, 0.58−1.45 bites per person per month) in areas outside the clusters of higher mosquito exposure. The EIR was not significantly different in the central cluster ($P = .11$), but it was significantly increased in the eastern cluster (EIR, 2.95 bites per person per month; 95% CI, 1.67–4.78 bites per person per month) ($P = .002$). This trend was consistent over seasons (see Table S1 in the appendix, which appears only in the electronic version of the *Journal*). Similarly, the malaria incidence during follow-up was 3-fold higher in the eastern mosquito cluster (incidence rate ratio, 3.07; 95% CI, 2.59–3.63) ($P < .001$), but it was not different in the central cluster ($P = .96$) (see Table S1 in the appendix, which appears only in the electronic version of the *Journal*). Although there was overlap between the clusters of mosquito exposure and the clusters of malaria incidence ($P < .001$), only 53 (39.9%) of 133 households that were in clusters of higher malaria incidence (hot spots of transmission) were located in one of the mosquito clusters. This finding indicates that some, but not all, of the heterogeneity in disease episodes is explained by residing in a cluster of higher mosquito exposure. Several environmental and socioeconomic factors were significantly associated with the chance of residing in one of the hot spots of transmission (Table 1). We constructed a probability model [38] for residing in a hot spot of malaria transmission, on the basis of the independent predictors shown in Table 1.

Predicting hot spots of malaria transmission on the basis of parasite prevalence rates and serological markers of exposure. Blood samples were collected from 1974 individuals (age, 0.5–96 years) attending 4 health care facilities in Korogwe district. Of these individuals, 1634 were permanent residents in the area included in the entomological assessments. Thirteen SCR estimates could be obtained for administratively defined and geographically distinct subvillages. A total of 472 (88.2%) of 535 households for which data were available on malaria incidence and mosquito exposure were located in one of these 13 subvillages. There was a strong positive correlation between the malaria incidence among study children in the 13 subvillages and the age-specific SCR noted for these subvillages for MSP-1_{19} ($r = 0.84$; $P < .001$), AMA-1 ($r = 0.67$; $P = .01$), or both antigens combined ($r = 0.73$; $P = .005$) (Figure 3). Similarly, there was a positive correlation between the malaria incidence among study children in 13 subvillages and parasite prevalence, as determined by RDT, in children <10 years of age who attended the health care facilities ($r = 0.70$; $P = .01$) (Figure 3). The RDT parasite prevalence clearly separated subvillages with incidence rates of >1 case of infection per year from subvillages with lower malaria incidence ($P = .01$), but it had limited discriminative power for incidence rates between 0 and 1 ($r = 0.23$; $P = .54$).

Predictive models to identify hot spots of malaria transmission. Although variation in the number of mosquitoes was related to the variation in malaria incidence, environmental factors and other factors associated with mosquito numbers did not lead to a sensitive or specific prediction of the hot spots of malaria transmission (Figure 4). Similarly, health care facility–derived parasite prevalence rates in children <10 years of age were associated with malaria incidence but did not allow sensitive prediction of hot spots (Figure 4). In contrast, health care facility–derived SCRs were highly predictive of hot spots of malaria transmission (Figure 4). Using the combined AMA-1 and MSP-1_{19} SCR, the sensitivity of predicting residence in a hot spot of transmission was 95.5%, with a specificity of 82.0%. The value of the combined SCR in predicting hot spots of transmission is illustrated in Figure 5, where this estimate is plotted for each household within a subvillage.

DISCUSSION

In the present study, we described considerable spatial variation in malaria disease incidence and exposure to malaria-infected mosquitoes in an area of moderate transmission intensity in Tanzania. Clusters of high malaria incidence among infants were interpreted as hot spots of malaria transmission. Although these hot spots overlapped with clusters of high mosquito exposure, they could not be satisfactorily predicted by environmental factors associated with an abundance of mosquitoes. Similarly, parasite prevalence rates that were determined at the subvillage level were associated with malaria incidence but could not predict hot spots of malaria transmission. Serological markers of exposure to malaria showed a tight correlation with malaria incidence and predicted transmission hot spots with high precision. This finding suggests that serological markers of exposure could have considerable potential to guide targeted malaria control efforts.

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In our cohort of children, we observed considerable variation in the number of reported malaria attacks. Although two-thirds of the children experienced no clinical malaria episodes during follow-up, 10% experienced 3–14 episodes. This phenomenon is widely reported [3–7, 39], and host genetic factors may account for approximately one-fourth of this variation [39]. An individual-based model for malaria risk should therefore take into account genetic regulators of disease risk. When geographical clusters of disease incidence are studied at the level of (sub-) villages in a genetically homogeneous area, much of this variation in disease risk will be the result of heterogeneity in exposure to malaria-infected mosquitoes. We observed in the study area 5 spatial clusters of higher malaria disease incidence that we interpreted as hot spots of malaria transmission. These hot spots partially overlapped with 2 clusters of higher-than-average exposure to *Anopheles* mosquitoes. Small-scale heterogeneity in mosquito exposure has been described elsewhere [12, 40, 41]. The extensive sampling of mosquitoes in our study allowed us to determine the EIR inside and outside the *Anopheles* clusters. The EIR in one of these clusters was 2- to 3-fold higher than that in households outside the clusters; the other was characterized by a higher exposure to *Anopheles* mosquitoes but not by a statistically significant higher EIR. In line with this, malaria incidence was increased in the former but not in the latter cluster. This indicates that a higher exposure to mosquitoes is related to, but not sufficient for, a higher incidence of malaria disease: some households are disproportionally exposed to *Anopheles* mosquitoes but not to infected mosquitoes.

Distance to the nearest breeding site [7, 14, 19–22, 42], walling material [43], and bed net coverage [7] were independent predictors of living in a hot spot of malaria transmission. These were biologically plausible predictors of malaria incidence and are likely to play an important role in determining the risk of malaria at the level of individuals. However, a probability model based on these 3 factors had limited discriminating value in predicting hot spots of malaria transmission (ie, spatial variation in the factors was not strongly related to spatial variation in malaria incidence at subvillage level). In contrast to this model based on environmental factors, serological markers of malaria exposure proved to be a sensitive and straightforward tool to identify small geographical areas with higher malaria transmission intensity. Serological markers of exposure previously were used to compare the level of malaria transmission intensity of different regions [26, 27, 44]; the current data indicate they can also be used at the microepidemiological level [20].

In our study, hot spots of malaria transmission could be predicted with a sensitivity of 95% and a specificity of 82% by the SCR based on the combined AMA-1 and MSP-1_{19} antibody responses. Perfect prediction of these hot spots would have been impossible because of our simplistic approach, in which we tried to associate SCR estimates on the subvillage level with clusters of higher malaria incidence on the level of clusters of households. As a consequence, some subvillages were only partly in a cluster of higher malaria incidence, thereby reducing the sensitivity and specificity of SCR estimates. In addition to its higher discriminative value, the SCR approach has several logistical advantages over models based on environmental factors. There is no need to visit individual households, examine mosquito breeding sites, or undertake the tedious process of sampling adult mosquitoes. Because of the longevity of antibody responses, SCR estimates are less susceptible to seasonal fluctuations in malaria exposure than either a direct estimate of EIR or parasite prevalence data [26, 27], and they are particularly useful in areas of low endemicity, where parasite prevalence rates are low. Because of the longevity of antibody responses, our findings indicate that hot spots of transmission were remarkably stable over time. Parasite rates are important indicators of global disease burden [45], but they have poor discriminative value at lower levels of endemicity [46], as supported by our study.

A single cross-sectional survey or health care center–based survey would be sufficient to obtain the relevant information for SCR estimates [29]. A disadvantage of the current approach is that there is a limit to the resolution for which an SCR estimate can be obtained. The nature of the model, requiring multiple observations from each age group, makes it impossible to calculate household-specific SCRs, although this would be possible for groups of households. This could be considered in areas that are close to achieving malaria elimination and where malaria is likely to be maintained in a few foci of transmission. Sampling at the health care facility level will allow strategic planning of malaria control efforts within districts at the level of the smallest administrative unit.

Evidently, the SCR estimates above which areas will qualify for expanded malaria control efforts will be dependent on the level of transmission intensity in an area and therefore will be site specific. The tight correlation with malaria incidence and EIR [26, 44] will allow for a rational determination of an SCR above which areas are included in extended malaria control efforts for various levels of malaria endemicity.

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