Mem. Inst. Oswaldo Cruz, Rio de Janeiro, Vol. *87,* Suppl. III, 121-130, 1992

HOUSEHOLD-BASED MALARIA CONTROL IN A HIGHLY ENDEMIC AREA OF AFRICA (TANZANIA): DETERMINANTS OF TRANSMISSION AND DISEASE AND INDICATORS FOR MONITORING – KILOMBERO MALARIA PROJECT

THOMAS TEUSCHER

Kilombero Malaria Project, Dept. Public Health & Epidemiology, Swiss Tropical Institute, PO Box 4002, Basel, Switzerland

The Kilombero Malaria Project (KMP) attempts to define operationally useful indicators of levels of transmission and disease and health system relevant monitoring indicators to evaluate the impact of disease control at the community or health facility level. The KMP is a longitudinal community based study (N = 1024) in rural Southern Tanzania, investigating risk factors for malarial morbidity and developing household based malaria control strategies. Biweekly morbidity and bimonthly serological, parasitological and drug consumption surveys are carried out in all study households. Mosquito densities are measured biweekly in 50 sentinel houses by timed light traps. Determinants of transmission and indicators of exposure were not strongly aggregated within households. Subjective morbidity (recalled fever), objective morbidity (elevated body temperature and high parasitaemia) and chloroquine consumption were strongly aggregated within a few households. Nested analysis of anti-NANP40 antibody suggests that only approximately 30% of the titer variance can be explained by household clustering and that the largest proportion of antibody titer variability must be explained by non-measured behavioral determinants relating to an individual's level of exposure within a household. Indicators for evaluation and monitoring and outcome measures are described within the context of health service management to describe control measure output in terms of community effectiveness.

Key words: malaria – transmission – immune response – fever episodes – community – variability

Interest in research on parasitic disease often focusses on the causative agent. Therefore, much of the information available is related to quantitative laboratory findings at the cellular, parasitic or host level. Qualitative risk factors relating to the natural environment, the host's behavior, or the socio-economic setting in which a disease is contracted are less attractive to researchers. Firstly, they are difficult to quantify, and secondly it is often methodologically more difficult to obtain the information. Quantitative risk factors from epidemiological studies have very often neglected factors such as the health system and the community's perception of a disease.

It is important that monitoring and evaluation indicators should be relevant for health care managers and managers of communicable disease control programmes, for example during the expansion of a pilot activity to a large scale application (Tanner, 1989). Malaria research, and research in general, may have to enlarge their scope so as to produce research results which are relevant to and applicable by operational disease control management teams. This will include considering and using disease categories as perceived by communities. It will also involve enlarging the scope of risks to include risks stemming from within the health care delivery system, and those due to social and political factors with an impact on disease frequencies.

The nature and potential of these risk factors depends very much on the socio-ecological setting. Their importance or the focus for

The Kilombero Malaria Project is being carried out at the Ifakara Center, P.O. Box 53, Ifakara, (Tanzania), East Africa, by the Swiss Tropical Institute (Switzerland), the Universities of Wageningen and Njimegen (The Netherlands), and IRTC-WHO Geneva (Switzerland) in collaboration with the National Institute for Medical Research (Tanzania).
This project was sponsored by the Swiss Development Cooperation, the Dutch government and the WHO-Immunology Research & Training Center Geneva. Research clearance was granted by the Tanzanian Comission of Science & Technology (UTAFITI).

control may vary between sites. In most countries where malaria represents a large burden of ill health for the inhabitants, the resources available for curative and preventive health care are very limited. Therefore the setting of priorities for control activities and their evaluation need to be tailored to the characteristics of a particular endemic setting. Within such a framework, relevant results of health system management research can be used for decision-making by administrative units such as a district or a region. The availability of relevant information does not in itself produce informed decision-making, but it is an essential prerequisite for it. It is therefore crucial to propose monitoring and evaluation indicators, with good accuracy and precision, which are easily applicable within the decision- making setup.

For many years, research on parasitic diseases has been carried out in a rural area in Southern Tanzania, around Ifakara. Previous work investigated the interrelationship of nutrition, infection, immunity and exposure to parasitic disease, and also the community's perception of ill-health. A major finding was the importance of parasitic disease within communities: only 7% of all children were without any parasitic infection throughout one year (Tanner et al., 1987). Within the context of malaria control, it is relevant to focus on two sets of determinants: determinants of exposure and on exposure as a determinant of the frequency of malarial illness within a population.

The comprehensive Kilombero Malaria Project (KMP) was launched in late 1988. This longitudinal project is being undertaken in two villages of the Kilombero District, Morogoro Region, in Southern Tanzania. The villages are in a low-lying river plain, with occasional flooding and some irrigation for rice-growing (Tanner et al., 1987, 1991). The project's aim is to investigate the relationship between exposure, immune status and morbidity, and to devise and validate control strategies based on these findings.

Earlier studies in Ifakara described a household clustering of anti-NANP40 immune response (Del Guidice et al., 1990). It has been assumed that NANP40 titers are basically a reflection of exposure (Nardin et al., 1979; Tapchaisri et al., 1983, 1985; Del Giudice et al., 1987; Tanner et al., 1986).

One of the objectives of the present project was to investigate further this household clustering of immune response in relation to exposure, and to morbidity. At the outset of the study, villages were to be classified into transmission units, i.e. clusters of houses with similar mosquito densities as determined at the beginning of the first transmission season.

Descriptive and analytic data from the KMP is presented in this paper. Special emphasis is laid on the utility of the parameters studied for the monitoring and evaluation of malaria control aiming at morbidity control.

MATERIALS AND METHODS

Study area – The villages are 30 km distant from each other. Both show patterns of highly endemic malaria. There is intense, year-round transmission, despite the fact that an entomological peak season occurs between May and July (Fig. 1).

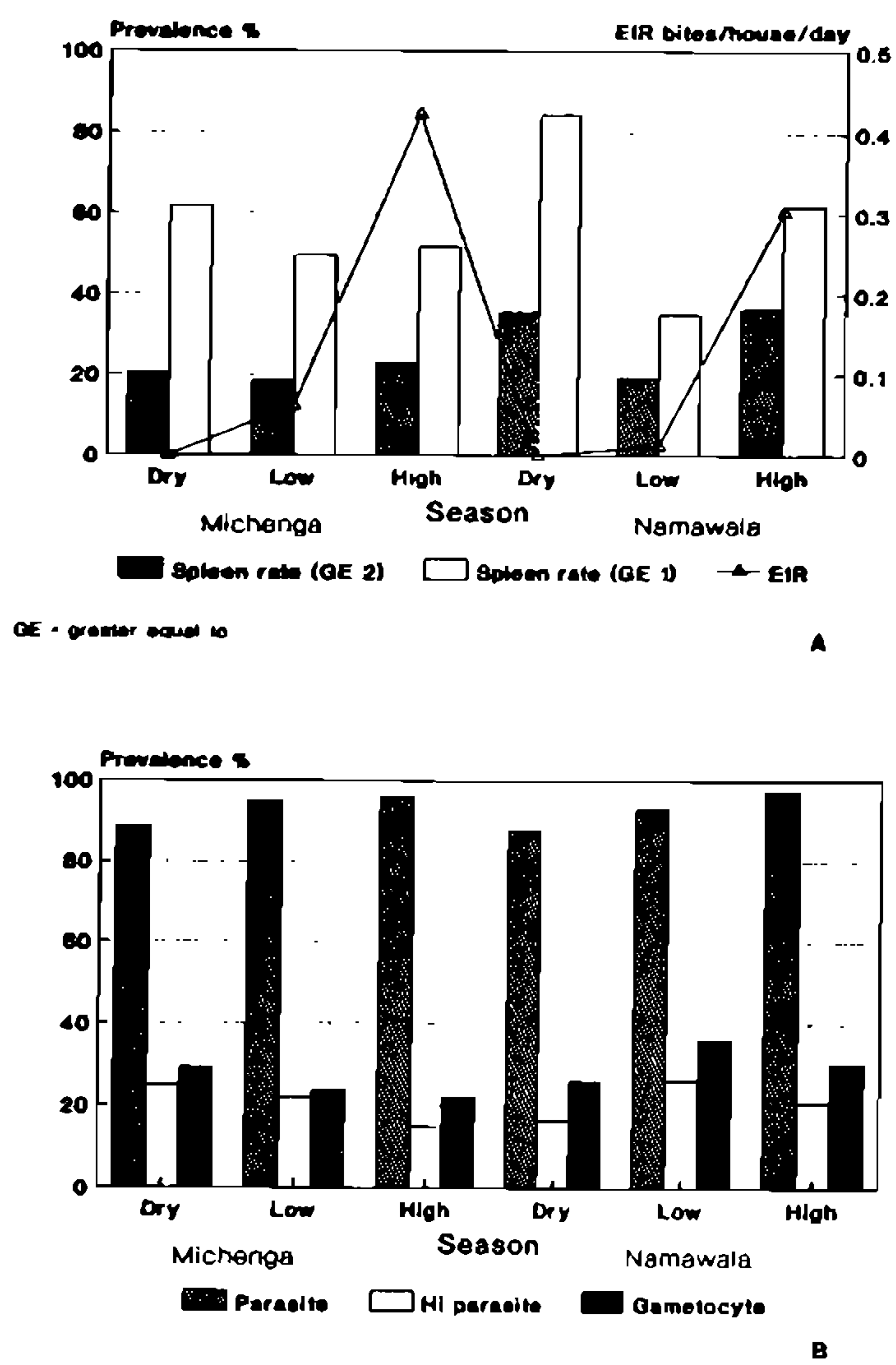

Fig. 1: classical determinants of malaria endemicity in three seasons (Dry, low and high mosquito density) in children 2-9 years of age in Namawala and Michenga. (A) Clinical signs and exposure: Spleen rates (Hackett scores), Entomological inoculation rate (infectious bites/man/right). (B) Parasite rate, high parasitaemia rate and gametocyte rates.

Plasmodium falciparum represents the major species found – more than 90% of all infections. The major vectors are *Anopheles gambiae s.l.* and *An. funestus.* The schedule of investigations undertaken is shown in Table I.

TABLE I

Schedule of investigations of the Kilombero Malaria Project population (N = 1024; < 1: 88; 1-: 262, 5-: 215, 10-: 158, 15-: 301

Surveys:	Biweekly	Two weekly recall of an individual's symptoms of morbidity (N = 830)
	Biweekly	Timed light trap collection or household mosquito density (N = 58)
	Bimonthly	Fingerprick blood sample collection for parasitology and immunology
	Biannually	Census update of study population

Indicators – Some of the possible indicators under study are of a purely qualitative nature. These include the quality of housing, the efficiency of the preventive health services, the state of the primary health care system and the ecology of the Kilombero Valley, as well as household security in terms of adequate provision of food, education and health care to all household members. The setting is, of course, also undergoing changes resulting from development in other sectors, like roads and agriculture. Fig. 2 summarizes a classical network some of risk factors being responsible for a high malaria incidence in some individuals and in some households within a particular socio-ecological setting.

As one of the impacts of any future control strategies must be the reduction of the load on primary and referral care facilities, importance was also given to the perception of ill-health in the community, as expressed by answers to morbidity questionnaires, or in the records of the Village Health Posts.

Figure 3 illustrates the importance of "homa" (Kiswahili for 'fever'), which is a concept of febrile illness in Swahili culture.

Approach – A variety of approaches were used to appraise the utility of different determinants of malarial illness.

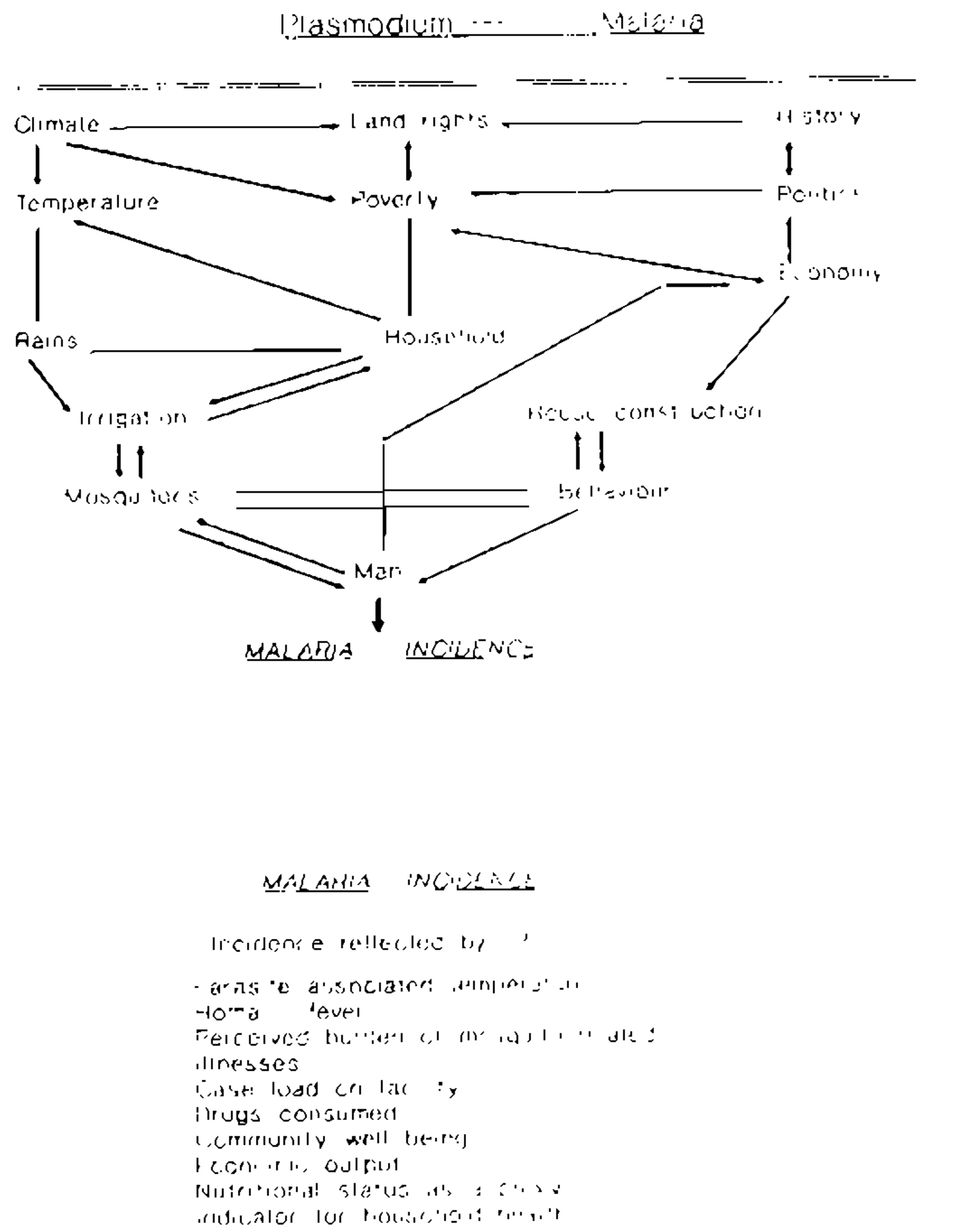

Fig. 2: network of risk factors determining the incidence of malaria.

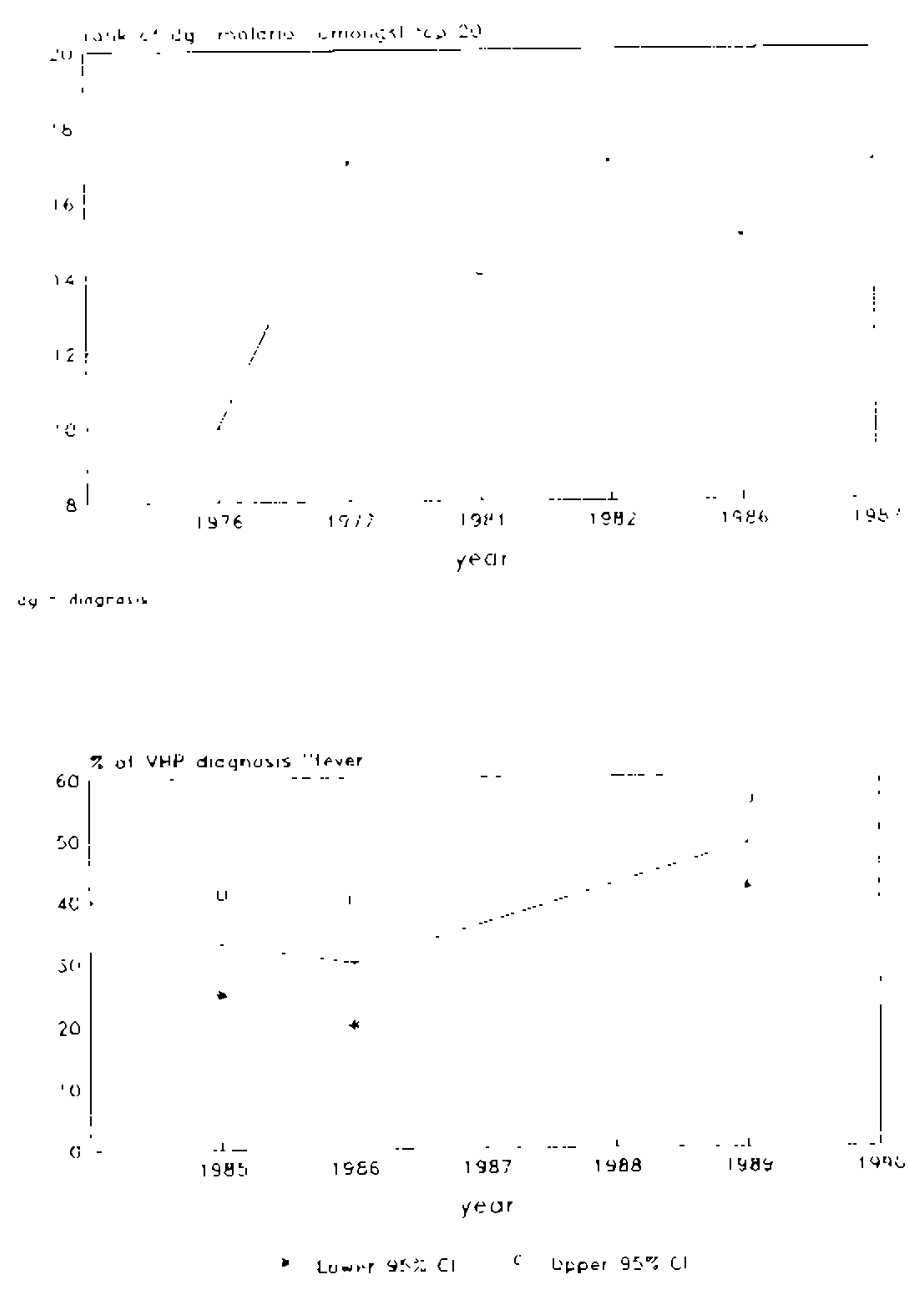

Fig. 3: facility based trends in the proportion of malaria in relation to all admissions at St. Francis District Hospital, Ifakara and of "fever" in relation to all patients seen at the Village Health Post in Namawala.

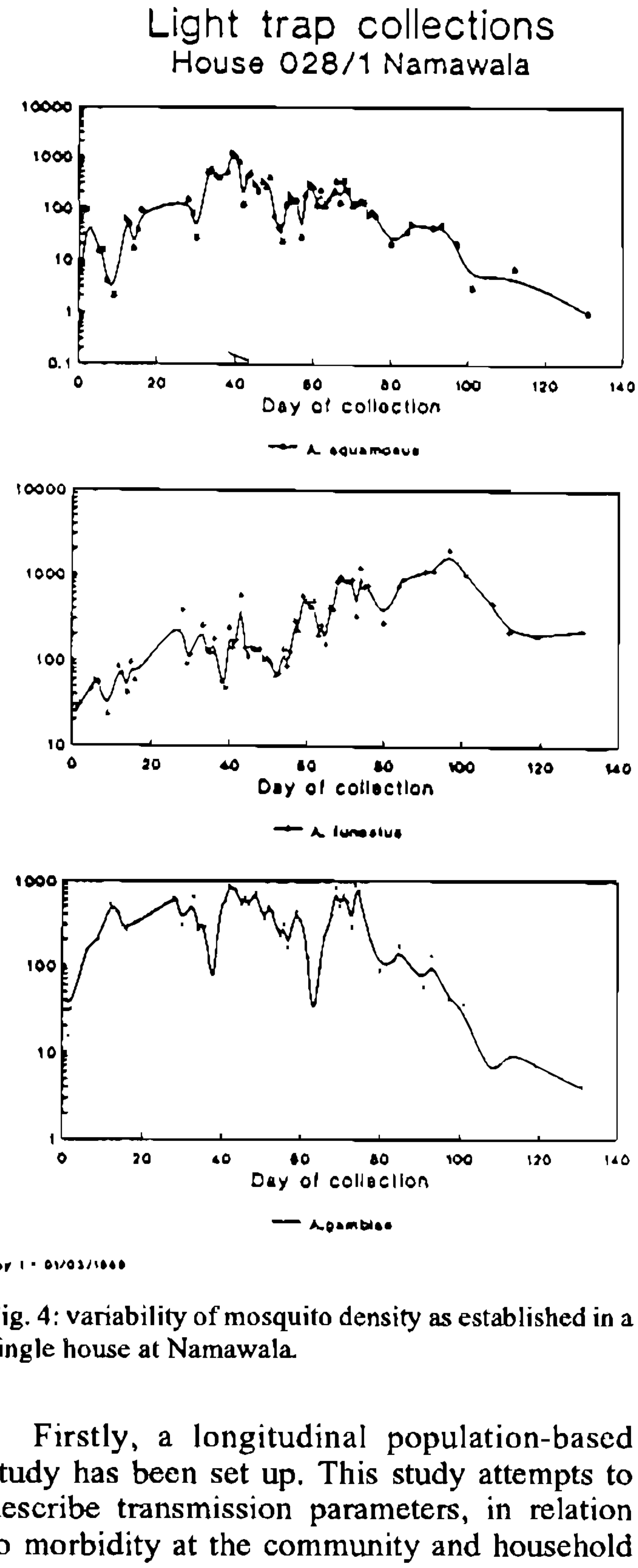

Fig. 4: variability of mosquito density as established in a single house at Namawala.

Firstly, a longitudinal population-based study has been set up. This study attempts to describe transmission parameters, in relation to morbidity at the community and household level, and to individual and household immune status. The aim was to quantify the important risk factors. With this information, an estimate could be made of the risk reduction that might be possible with simple malaria control measures. The study design is basically that of a repeated cross-sectional survey. It therefore also offers the possibility of evaluating within and between individual variations through the formation of cohorts addressing particular issues.

Secondly, a randomized intervention experiment is currently being implemented. The aim is to investigate the impact of two control measures on perceived morbidity at the household level, using a double-blind test. The two measures are the use of impregnated mosquito nets, or of impregnated plastic strips: these are made from split polytene bags, and are fitted around the bed frames. The strips have a surface area four times smaller than that of the nets, and will be impregnated with a four times higher concentration of insecticide.

The study also includes an assessment of the impact on transmission of various intervention densities within a given geographical area. In addition, the impact of the coverage of an intervention on morbidity is investigated.

Thirdly, there are special in-depth investigations of entomological or immunological questions, using nested case-control studies.

Initially, it was planned to select transmission units, consisting of households with similar mosquito densities. However, this concept had to be abandoned, owing to the high variability within each house. This proved to be as large as, or even larger than the variation between houses, if short periods of observation were considered (Fig. 4).

RESULTS

Mosquito density and transmission – The two main species of mosquitos in both villages are *An. gambiae s.l.* and *An. funetus*. The densities of the two mosquito species within a house were highly correlated (r2 = 0.36 to r2 = 0.83). In one village (Namawala), a few houses consistently showed the high densities of both mosquito species. Interestingly, in Michenga this could not be observed. Sporozoite rates were similar (range 1.5 - 17.6) throughout seasons and between households.

Morbidity indicators – The morbidity resulting from exposure was defined in terms of subjective and objective symptoms and signs (Fig. 5). We attempted to construct various symptom cluster diagnoses (SAS, 1988) with a high probability of reflecting parasitological, immunological and clinical signs of malarial illness, with a view to reflecting disease perception within our study population. At least 6, age-specific syndromes could thus be described in statistical terms.

Some important aggregates of symptoms and signs – upper respiratory tract syndrome with headache, fever, earache, running nose

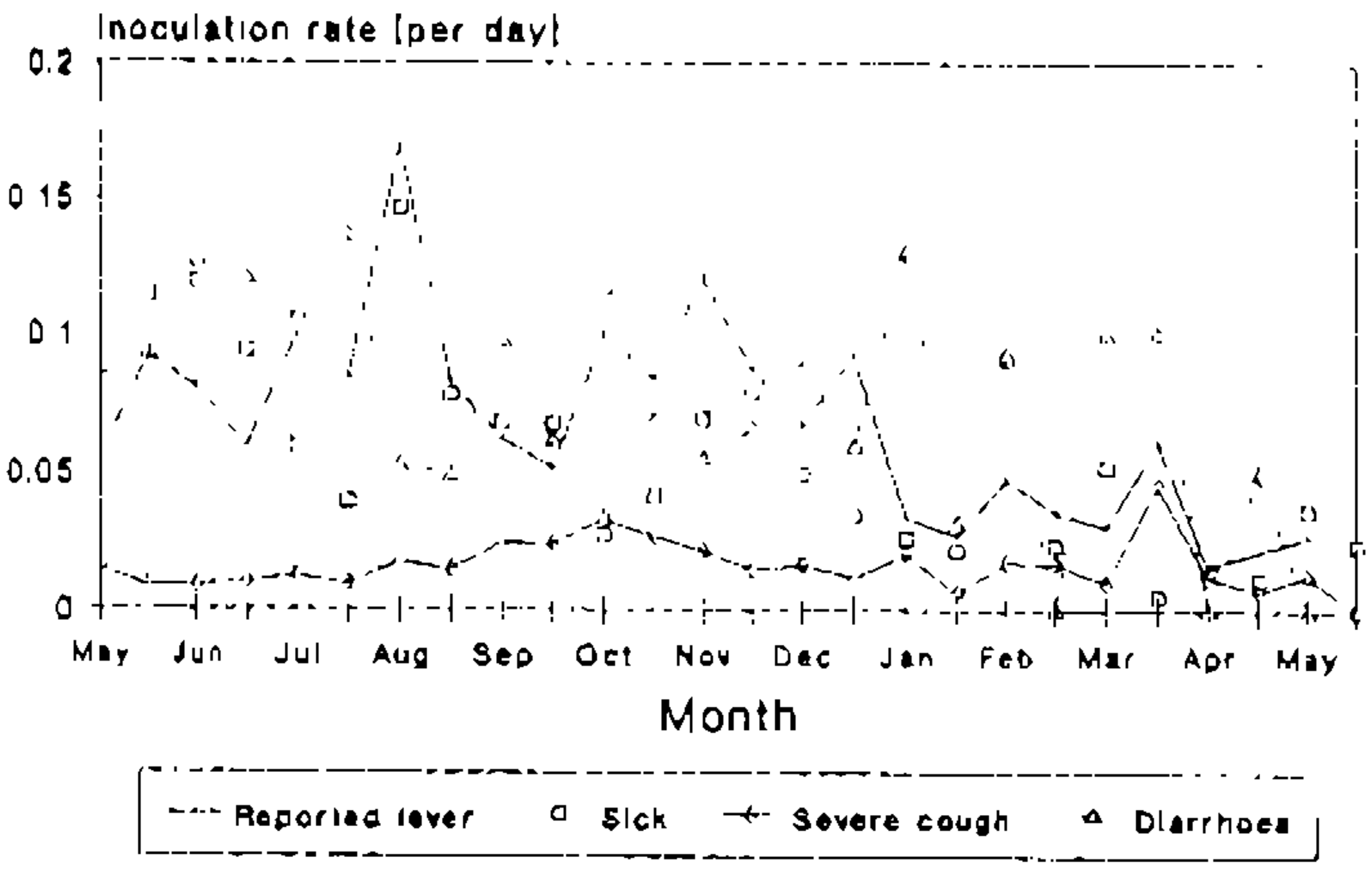

Fig. 5: age-specific incidence of illness and symptoms.

and cough; an abdominal syndrome with diarrhoea, abdominal pain and vomiting; a febrile syndrome with a variety of age-specific symptons and without abdominal or pulmonary localization.

These syndromes were then compared to age-specific objective signs of presumed malarial infection, including:

Objective signs – PAT: Parasitemia Associated with Temperature: an elevated body temperature (> 37.5 C), associated with high parasitemia, i.e. higher than the median found for that age-group in a survey. PAN: high parasitaemia associated with high anti-NANP40 antibody levels, as a sign of presumably recent infection. High antibody levels were levels higher than the median age-specific titer found in a survey. TAN: elevated body temperature associated with high anti-NANP40 antibody levels (Tables II and III).

TABLE II

Age-specific prevalence of three different 'objective' fever episodes

	Age specific prevalence (%)				
Age group	-1	2-4	5-9	10-14	15+
PAT	3.9	1.2	7.0	8.0	4.5
PAN	8	11	79	82	97
TAN	3.9	3	7	9	5

PAT = parasitaemia associated temperature.
PAN = parasitaemia associated anti-NANP40 titers.
TAN = temperature associated anti-NANP40 titers.

Relationship between exposure and morbidity indicators – The symptom-syndromes described above, and also recalled fever alone, and not as a symptom-complex, were assessed in terms of their power to predict malaria illness as measured by objective signs (SAS, 1988) The results are shown in Table IV.

TABLE III

'Accuracy' of symptom clusters for predicting 'objective' fever episodes

	PAT	PAN	TAN
Sensitivity %	56	89	67
Specificity %	81	28	80
PPV %	11	10	12
NPP %	98	97	98

PPV = positive predictive value.
NPV = negative predictive value.
PAT = parasitaemia associated temperature.
PAN = parasitaemia associated anti-NANP40 titers.

TABLE IV

Association (odds ratio with 95% confidence intervals) of PAT (parasitaemia and temperatures > 37.5 °C) and subjective fever episodes with exposures (mosquito density) and outcome of illness (chloroquine intake)

	Houses with high/low density *An. gambiae*
Subjective fever	1.70 (1.19 - 2.42)
PAT	0.67 (0.33 - 1.31)
	Recent chloroquine intake
Subjective fever	2.45 (1.34 - 4.54)
Cough	1.57 (0.54 - 4.56)
Diarrhoe	1.47 (0.69 - 3.15)
Objective fever	1.44 (0.75 - 2.79)
Parasitaemia %	0.82 (0.54 - 1.25)

In predicting PAT, fever frequency alone was as good as the more complex illnesses during the period when mosquito densities were at their lowest (82% of all traps were empty).

During the dry season, individuals with fever episodes within the two weeks previous to the interview were ten times more likely to have PAT at the time of the survey. During the dry period following the intense transmission period (March to May), PAT and fever seem to have a particularly strong association.

During the high mosquito-density period, people with a recalled fever episode during the past two weeks were only half as often found to have PAT as those without recent fever episodes. This clearly illustrates that the two indicators reflect different states.

Variations in recalled fever are a reflection of the seasonality of age-specific disease pat-terms. Changes in PAT also reflect a parasitic or an immunological phenomenon. As expected, these recalled, subjective fever episodes were approximately two times more frequent in under 5s (40% of all recalled episodes) compared to older children and adults (24% of all recalled episodes). Recalled episodes were recorded for a similar number of people of all ages. With increasing age, the within-age-group variability (inter quartile range) decreased, both in terms of the total number of fever episodes, and in terms of the fever rate (number of fever episodes as a % of all interviews with an individual).

Applicability of fever recall as a morbidity indicator – The aim of malaria control in the study area is to reduce morbidity. The recalled fever episode could be used as an easily applicable indicator during the dry season to assess the absence of illness in general. This indicator would reflect changes in the perceived burden of illness at the community level. It is an indicator which is operationally very simple, and could be applied within the framework of control activities being carried out within communities over a wide geographical area within the same ecological setting. Information on fever is already routinely collected at health facilities.

The importance of subjective fever recall is also shown by the fact that fever episodes are clearly associated with an individual's chloroquine intake, and with a high mosquito density in the household. Chloroquine intake is related to an individual's perception of the severity of a fever. Consistently, other single symptoms, and other objective measures, were found not to be associated (Table V).

Besides the direct exposure indicator "mosquito density", and the outcome indicator "perceived illness (fever)", we tried also to assess the utility of anti-sporozoite antibody as an indirect indicator expressing recent exposure (KMP, 1991). The within-individual and between-household variability of antibody levels were examined in relation to measured exposure to mosquitoes at the household level.

NANP level as a morbidity indicator – NANP levels have been suggested as an easily-measured exposure parameter. However, our findings suggest that NANP40 levels are indicative of the total long term exposure of an individual, but may not be appropriate as a

TABLE V

Partitioning of variance of residuals between villages, households and surveys

Source	DF	SS	F value	p	% total
Village	1	9.22	7.42	0.0001	6.3
Survey	3	1.50	0.40	0.7509	1.8
Household	73	200.95	2.21	0.0001	14.8
Error		155	411.06		77.1

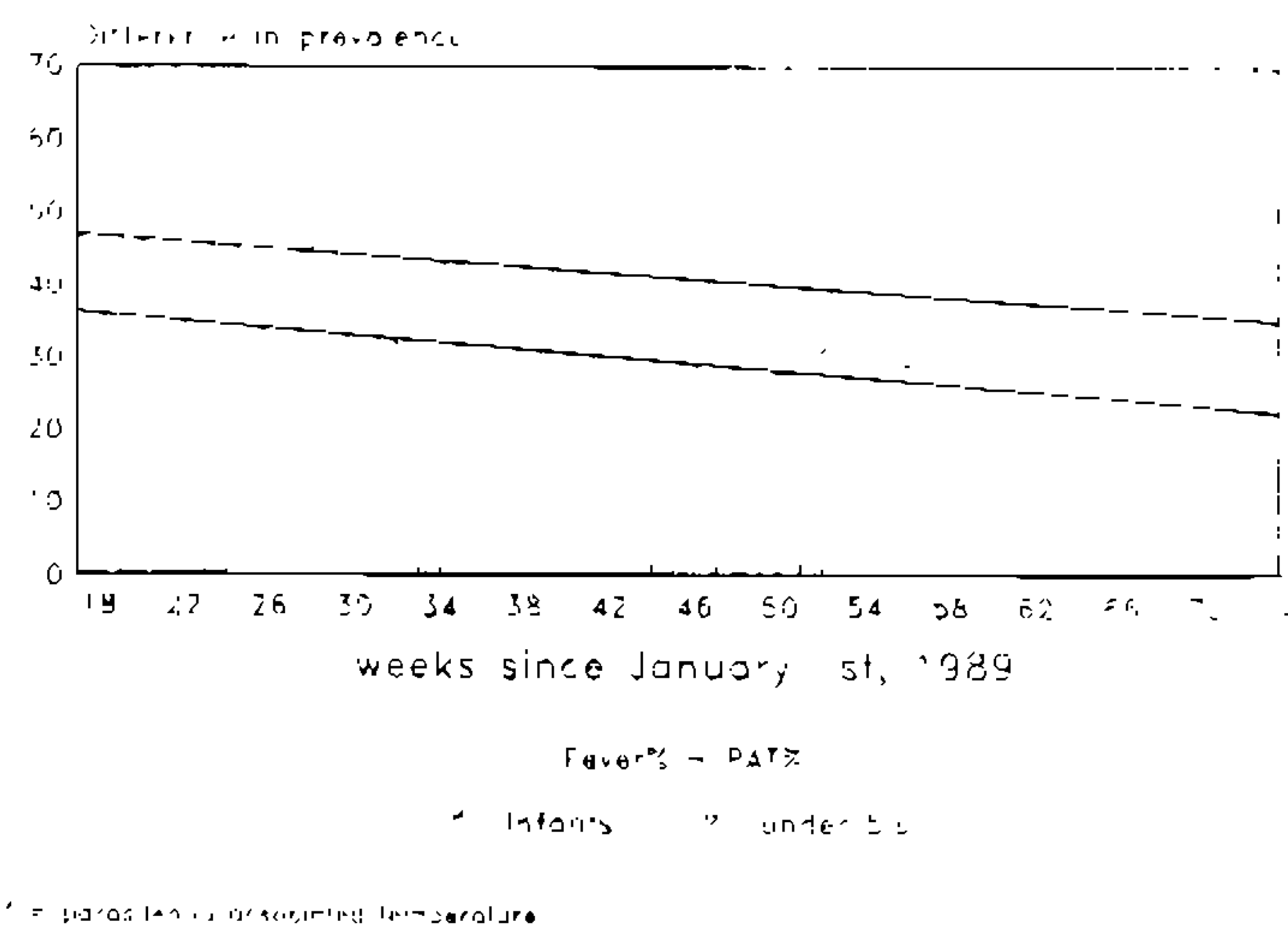

Fig. 6: prevalences of PAT, i.e. parasitaemia associated temperature (> 37.5 °C), and fever as recalled by the individuals.

short term indicator for control programme management and evaluation.

An in-depth case control study of febrile patients at health facilities and in the community is currently under way in order to investigate the variability in cellular and humoral immune response.

Anti-sporozoite antibody titers varied significantly between geographical areas and between households, but not between seasons (Table V). Geography and household explained only 23.1% of the total variance. Approximately one third of the variability of antibody levels at the household level can be interpreted as being related to exposure to infectious mosquitoes. Recent exposure, as expressed by household mosquito density in the two weeks before the survey, was compared to the effects of long term, continuous exposure over the last twelve months. The results revealed that recent high exposure has no impact on anti-NANP40 levels (Fig. 7).

Despite controlling for levels of exposure within the house, 19% of the titer differences between households remained, and may there-

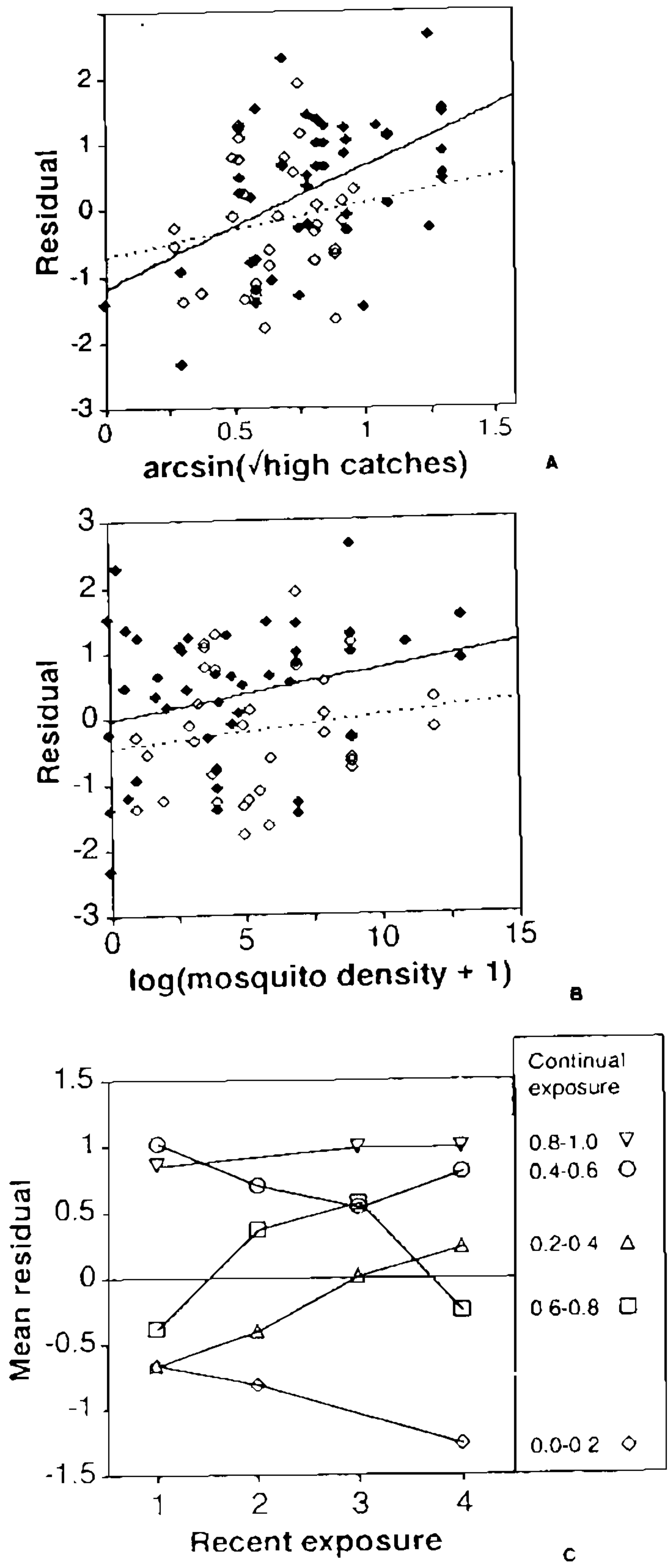

Fig. 7: the relationship between residuals of the model of age specific increases of levels of anti-sporozoite antibody and exposure. The data are pooled over villages and surveys. (A) Continual exposure denotes for each house the proportion of catches in which more than the median density of mosquitoes was caught. The exposure measure is classified into 5 classes: 0-20%, 21-40%, 41-60%, 61-80% and 81-100%. (B) Recent exposure denotes the number of mosquitoes caught in the house in the two weeks prior to the survey of antibodies. The densities are categorized into four quartiles. (C) The effect or recent exposure within each category of continual exposure.

fore be due to other factors operating at the household level. Possible causes for this considerable household clustering of anti-sporozoite response could be a genetic restriction of the immune response (in particular families), and/or a social and/or behavioral determinants.

Approximately 70% of the variation must be accounted for by variation between the individuals in the same household, and possibly to measuring errors in NANP40 assays. The latter ought not to be large as all procedures utilized were standardized by using titration units. Variation between individuals could include differences in genetic determinants of the immune response. Such differences would be expected to explain mainly the between-household variation. The striking importance of differences in antibody levels between members of the same household must be explained by other, more qualitative household-based socio-economic risk factors. Differences in exposure may arise from differences in behavior and in the situation within the household (location of sleeping-places etc), in susceptibility to being bitten.

DISCUSSION AND CONCLUSIONS

When one considers that even within one household some people are more exposed than others, it becomes clear how complex the issues involved in prevention are. Furthermore, age-related co-factors of the risk factors, such as nutritional state or exposure behavior may play an important role. There will be even greater variation between households in such factors as socio-economic situation and attitudes to health and to seeking health-care.

The KMP, as outlined at the beginning, is carrying out intervention experiments designed to estimate possible risk reductions. Such estimates are crucial if appropriate large-scale interventions are to be planned. The study includes investigations of the coverage an intervention must achieve in order to have a given impact on transmission. Operationally, the densities of various interventions are of great relevance if the community effect is to be high. It is not the potency of a vaccine or a drug or the efficacy of an intervention such as the use of impregnated nets that will determine impact at the community or health facility level, but the extent to which the community complies with an intervention, and thus the coverage achieved. The effectiveness of a given measure depends on how much of its initial (theoretical) efficacy is retained when it is used in practice in the community. The path leads via diagnostic accuracy, through user/provider compliance and coverage (Fig. 8, from Tanner, 1990). Our attempts to find useful simple measures for quantifying the transmission of malaria in Kilombero District, with the aim of using this information to implement and evaluate control activities were not successful. The situation with regard to the various observed variables is clearly extremely complex. For example, the study of determinants of NANP40 titers showed that there was no simple relationship with exposure, and underlines that focussing on more general social and behavioral determinants may be required. The search for other, less quantifiable determinants must be seen within the context of the evaluation of community effectiveness.

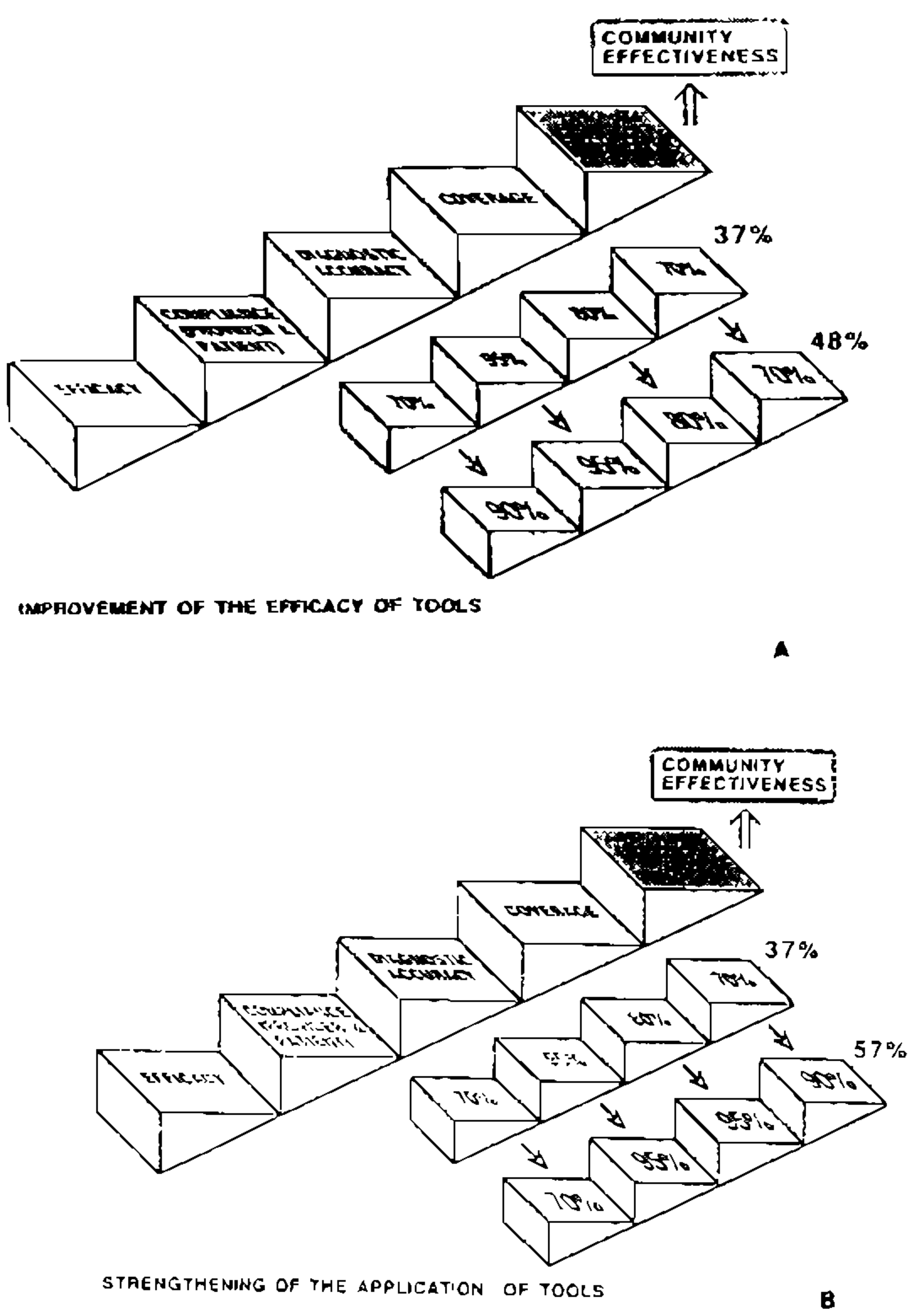

Fig. 8: the path from the efficacy of a disease control tool to community effectiveness, which is dependent on diagnostic accuracy, compliance of users and providers, and coverage. (A) Shows the situation where only the efficacy of the disease control tool is improved from 70% to 90%. (B) Shows the situation whereby the efficacy of the disease control tool remains unchanged at 70%, but the proportion of accurate diagnoses, of compliance and coverage are increased by a strengthening of the application of the tool at the community level.

What control measures should be considered in the light of the situation as described for the Kilombero district? Currently, the options to be discussed are vector control, drugs, and information, education and communication (IEC).

IEC activities have to be strengthened within the health care delivery system. Strategies to address major health problems are well developed, but tend at present to concentrate on particular diseases (Global Programme on AIDS, Control of Diarrhoeal Disease) and are not yet always being effectively implemented. Ideally, these educational programmes should cover the whole range of health problems – including malaria – in an integrated way.

Drugs – Drug costs make up a large proportion (second to staff costs) of recurrent health care expenditures. Availability is often hampered by the costs involved, but also, the drug may not be used efficiently within the health system. A review of health care practice within the study area revealed that in the case of fever in children under five, only one in three or four children was physically examined. It is therefore not surprising to find that the prescription habits of primary health care practitioners are also unsatisfactory, in that in up to 40% of antimalarial prescriptions the dosage is insufficient or the duration inadequate. (KMP; unpublished).

The diagnosis and treatment strategy can only be improved if the weaknesses of the health system are considered and addressed as a whole through health service support and health sector strengthening activities in general. Such support and strengthening activities need a sound basis of information about the efficacy of different interventions.

In considering health-care, it is important to remember that it is not only supplied by the public sector. Facility-based diagnosis and treatment could be more cost-effective than self-medication and care by traditional healers. Studies have shown that individual households are prepared to make a significant investment in health care. One study in West Africa showed that in a typical household, up to 50% of the health care expenditure went into traditional medicine, and 5-25 US dollars per year into private expenditure for health care in its broadest sense. If adequate health care could be provided more cheaply, there would be more money for other essentials. In the Kilombero District, the public development expenditure for health is only 10 US cents per capita per year (Kilombero District: 5 year development plan, 1986-1991).

Vector control – Until recently, vector control has usually been centralised and carried out by specialised staff. Insecticide-based vector control measures to reduce exposure, like those discussed here, are ideally suited for application at the household level, and it should be feasible to organize them within the Primary Health Care and Essential Drug Program strategies as they already operate in Tanzania. However, this approach, involving health-care staff at the peripheral level, will only be widely adopted if the relevant monitoring indicators are simple to apply within the existing health system (government, non-government, private). Each indicator needs to be validated within a particular socio-ecological setting in relation to its community effectiveness (Fig. 8).

Proposed monitoring indicators – The KMP has utilised various approaches to find ways of determining risks of infection and disease at the household level that are relevant for health care and service management. A further crucial problem is the determining the outcome measures i.e. infection, morbidity and/or mortality. There is no single obvious measure, as there is for some diseases. For example, parasitaemia is not necessarily related to overt illness, and measures of antibody concentration are also not necessarily related to current morbidity. Among the indicators studied and proposed by KMP (Table VI), recall of fever episodes was found to be the most promising. However, before an indicator is finally chosen for a specific programme, it is essential to assess the feasibility of using it within a given endemic setting and within the existing health care system to produce the required accuracy and precision. Only this validation will ensure that the indications help us to monitor and strengthen community effectiveness.

TABLE VI

Evaluation and monitoring indicator for malaria control. Potential indicators and their applicability within existing health services and special programmes (adapted from Tanner, 1989)

Health System	Applicability within	Control program
	Exposure	
(+)	Density of mosquitoes	++
(+)	Species of mosquitoes	++
0	Sporozoite in mosquitoes	++
+	Breeding of mosquitoes	++
++	Perception of mosquitoe	(+)
	Infection	
+(+)	Blood slide	++
++	Spleen rates	++
++	Drug consumption	(+)
++	Use nets/curtains	(+)
(+)	Immune response	(+)
++	Behavioural changes	(+)
++	Participation/Acceptance	(+)
	Illness	
	Episodes/attacks	
++	subjective	++
0	objective	++
	Death	
++	Indirect mortality estimates	+
+	Verbal autopsy	++

ACKNOWLEDGEMENTS

To the villagers and their government for their excellent cooperation. To Professor Wen L. Kilama, Director General of the National Institute for Medical Research Tanzania, for the support of the Kilombero Malaria Project. The project could not be implemented without the untiring expert assistance of the laboratory and field workers of the District Health Office and the Ifakara Center as well as many members of the collaborating institutions of this project.

REFERENCES

DEL GIUDICE, G.; VERDINI, A. S.; PINORI, M.; PESSI, A.; VERHAVEN, J. P.; TOUGNE, C.; IVANOFF, B.; LAMBERT, P. H. & ENGERS, H. D., 1986. Detection of human antibodies against *P. falciparum* sporozoites using synthetic peptides. *Inf. & Immunity*.

KILOMBERO MALARIA PROJECT. The distribution of anti-sporozoite antibodies in an endemic malaria area and its relationship with individual exposure to mosquitoes. Submitted for publication.

NARDIN, E. H.; NUSSENZWEIG, R. S.; McGREGOR, I. A. & BRYAN, J. H., 1979. Antibodies to sporozoites: Their frequent occurrence in individuals living in an area of hyperendemic malaria. *Science, 206:* 597-599.

SAS, (Statistical Analysis System), 1988. *SAS users guide, Release 6.03.* SAS Institute Inc., Cary, USA.

TANNER, M., 1989. From the bench to the field: Control of parasitic infections within primary health care. *Parasitology, 99:* S81-S92.

TANNER, M., 1990. Von der Tropenmedizin zur Medizin in den Tropen – Priotitäten bei der Bekämpfung übertragbarer Erkrankungen. *Therapeutische Umschau, 47:* 856-863.

TANNER, M.; BURNIER, E.; MAYOMBANA, Ch.; BETSCHART, B.; DE SAVIGNY, D.; MARTI, H. P.; SUTER, R.; AELLEN, M.; LÜDIN, E. & DEGRÉMONT, A., 1987. Longitudinal study of the health status of children in rural Tanzanian community; parasitoses and nutrition following control measures against intestinal parasites. *Acta trop., 44:* 137-174.

TANNER, M.; DEL GIUDICE, G.; BETSCHARD, B.; BIRO, S.; BURNIER, E.; DEGREMONT, A.; ENGERS, H. D.; FREYVOGEL, T. A.; LAMBERT, P. H.; PESSI, A.; SPEISER, F.; VERDINI, A. S. & WEISS, N., 1986. Malaria Transmission and development of anti-sporozoite antibodies in a rural african community. *Mem. Inst. Oswaldo Cruz, 81* (Suppl. II): 199-205.

TANNER, M.; DE SAVIGNY, D.; MAYOMBANA, Ch.; HATZ Ch.; BURNIER, E.; TAYARI, S. & DEGREMONT, A., 1991. Morbidity and Mortality in Kilombero District, 1982-88. In: R. G. Feachem & D. T. Jamison (eds). *Disease and Mortality in Sub-Saharan Africa*. Oxford University Press.

TAPCHAISRI, P.; ASAVANICH, A.; LIMSUWAN, S.; THARAVANIJ, S. & HARINASUTA, K. T., 1985. Antibodies against malaria sporozoites in patients with acute uncomplicated malaria and patients with cerebral malaria. *Am. J. Trop. Med. Hyg., 34:* 831-836.

TAPCHAISRI, P.; CHOMCHARN, Y.; POONZHONG, C.; ASAVANICH, A.; LIMSUWAN, S.; MALEEVAN, O.; THARAVANIJ, S. & HARINASUTA, K. T., 1983. Anti-sporozoite antibodies induced by natural infection. *Am. J. Trop. Med. Hyg., 32:* 1203-1208.