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Spatial effects of the social marketing of insecticide-treated nets on malaria morbidity

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Summary Randomized controlled trials have shown that insecticide-treated nets (ITNs) have an impact on both malaria morbidity and mortality. Uniformly high coverage of ITNs characterized these trials and this resulted in some protection of nearby non-users of ITNs. We have now assessed the coverage, distribution pattern and resultant spatial effects in one village in Tanzania where ITNs were distributed in a social marketing programme. The prevalence of parasitaemia, mild anaemia (Hb <11 g/dl) and moderate/severe anaemia (Hb <8 g/dl) in children under five was assessed cross-sectionally. Data on ownership of ITNs were collected and inhabitants' houses were mapped. One year after the start of the social marketing programme, 52% of the children were using a net which had been treated at least once. The ITNs were rather homogeneously distributed throughout the village at an average density of about 118 ITNs per thousand population. There was no evidence of a pattern in the distribution of parasitaemia and anaemia cases, but children living in areas of moderately high ITN coverage were about half as likely to have moderate/severe anaemia (OR 0.5, 95% CI: 0.2, 0.9) and had lower prevalence of splenomegaly, irrespective of their net use. No protective effects of coverage were found for prevalence of mild anaemia nor for parasitaemia. The use of untreated nets had neither coverage nor short distance effects. More efforts should be made to ensure high coverage in ITNs programmes to achieve maximum benefit.

keywords malaria, marketing, treated, nets, spatial effects

Introduction

There is growing interest on insecticide-treated nets (ITNs) as a tool for malaria control, after randomized controlled trials showed that they reduce morbidity and mortality from malaria (Lengeler 2004). Large-scale implementation programmes are underway focusing mainly on operational issues of delivery and distribution of ITNs in a sustainable manner (Anonymous 1999).

The ITNs act by both being a physical barrier protecting those sleeping under them and by killing and repelling mosquitoes hence reducing the survival and infection rates (Lines 1996). Hence those with the ITNs and who use them properly have a reduced exposure to malaria infecting mosquitoes and consequently reduced malaria disease burden. The distribution pattern and coverage levels attained in implementation programmes may determine the level of protection observed in those who use them (D'Alessandro *et al.* 1995; Binka *et al.* 1998; Howard *et al.* 2000). Protection is highest among persons with ITNs living in areas with high ITN coverage and use. There are indications that people without nets sleeping nearby ITNs are also protected. Earlier work showed some short range (within the same room) protective effects of ITNs (Lines *et al.* 1987) while other studies did not show such protection (Rowland *et al.* 1996). Work conducted in Ghana supports the claims of short distance protective effects (those near ITNs are also protected) on those without bed nets. Among non-users the mortality risk increased by 6.7% with every 100 m shift away from the nearest compound randomized to receive treated bed nets (Binka *et al.* 1998). In the Kenyan coast those living up to 0.5 km away of bed net cluster had also lower hospital attendance rates for severe disease (Howard *et al.* 2000).

In the randomized studies ITNs were distributed free to all the intervention groups and uniformly high coverage was ensured (Nevill *et al.* 1996; Habluetzel *et al.* 1997; Binka *et al.* 1998), while in the programme setting the pattern of distribution is dependent on the many factors that determine the uptake of the ITNs intervention. These include social economic factors, distribution channels and local perceptions about ITNs (Fraser-Hurt & Lyimo 1998;

Snow *et al.* 1999; Minja *et al.* 2001). This has led to speculation on what might happen when ITNs are distributed in a programme setting.

It is not clear what patterns of spatial distribution of ITNs will occur in social marketing schemes. Conceivably, market mechanisms may lead to ITNs being widely but thinly distributed, with thus a relatively low coverage. This may be a more efficient way of conferring protection for those without ITNs (Binka *et al.* 1998). Alternatively, ITNs might end up being concentrated where the wealthiest people are while malaria transmission and disease is more likely to be concentrated on the poorest segment of the population, who tend live on the edges of the villages and may be less likely to have nets (Bonilla & Rodriguez 1993; Smith *et al.* 1995; Charlwood *et al.* 1998; Abdulla *et al.* 2001). Therefore, spatial effects of ITNs may be important in the understanding and interpretation of the results of impact assessments of ITNs programmes for malaria control.

We report the investigation of the spatial pattern of ITNs in one village covered by a large-scale ITN social marketing programme and the consequent effects on malaria morbidity indicators in children under 5 years of age.

Methods

Study population and design

The study was conducted in Idete Village, south-western Tanzania (08°5′ S; 36°30′ E). The residents are mainly subsistence farmers and the main crop is rain-fed rice. This is an area of intense year-round malaria transmission. The main vectors are *Anopheles gambiae*, *A. arabiensis* and *A. funestus* (Smith *et al.* 1993; Charlwood *et al.* 1998). A social marketing programme for ITNs has been implemented in this area since May 1997 (Schellenberg *et al.* 1999).

A cross-sectional assessment of all children under five living in all the hamlets (*vitongoji*) of Idete was made at the end of the main rainy season June–August 1998. Details of the survey are described elsewhere (Abdulla *et al.* 2002). In summary, children were visited at home and a questionnaire was applied to assess use of ITNs and other risk factors for malaria infection and anaemia. A physical examination was carried out and a blood sample was taken. The sample was screened for malaria parasites and haemoglobin level (Hb) was assessed using Hemocue® (Angelholm, Sweden).

Age and sex data for the community were available from a Demographic Surveillance System (DSS) established to allow the evaluation of impact of the social marketing programme (Schellenberg *et al.* 1999). ITNs ownership was also assessed in the four monthly cycles within the framework of the DSS.

Mapping

The position of the houses and other important service outlets including the dispensary, were determined using a portable Global Positioning System (Garmin, Thousand oaks, CA, USA). The geo-referenced points were then used to calculate distances between houses and between houses and the dispensary. Coverage of ITNs and untreated nets were calculated for each individual child in the cross-sectional survey. The number of nets per 1000 population living in houses other than the index child and within specific radii were calculated. Radii of 50 m (R_{50}), 100 m (R_{100}) 200 m (R_{200}) and 400 m (R_{400}) were chosen, on the basis of the findings of other studies (Binka *et al.* 1998; Hii *et al.* 2001). Coverage was categorized as low (0 ITNs/1000 persons), moderate (1–300 ITNs/1000 persons) and high (>300 ITNs/1000 persons).

Analysis

The outcomes of mild anaemia (Hb <11 g/dl), moderate/severe anaemia (Hb <8 g/dl) and any parasitaemia in the cross-sectional assessment were compared between users and non-users of ITNs, after controlling for confounding using logistic regression analysis. The explanatory variables also included ITN coverage and distance to the dispensary (Abdulla *et al.* 2002). Logistic models were also used to assess the effects of different risk factors on mild and moderate/severe anaemia. Random effects were added on the logit scale of these models to take into account the spatial structure of the data, i.e.:

$$\log\left(\frac{p_i}{1-p_i}\right) = \beta^t X_i + e_i,$$

where p_i is the outcome probability, β the vector of coefficients and X_i the vector of covariates for individual *i*. Spatial correlation was incorporated in the random effects e_i, by parameterizing their covariance matrix, such that:

$$\mathrm{Cov}(e_i, e_j) = \sigma^2 f(d_{ij}),$$

where d_{ij} measures the Euclidean distance between locations s_i and s_j. We modelled an exponential decrease of spatial correlation with distance by adopting:

$$f(d_{ij}) = \exp(-\rho d_{ij}),$$

but also compared the fit of this model with others, considering different choices of spatial covariance types using the Akaike's information criterion. Explanatory variables, such as age, distance to dispensary, etc. were discretized into several categories. The analysis was carried out using the SAS GLIMMIX macro, which uses iteratively reweighted likelihoods (Wolfinger & O'Connell 1993) to fit the models. The likelihood ratio test was used to assess the significance of the explanatory variables on the outcomes.

Results

A total of 652 children were examined in the cross-sectional survey. Details of their characteristics and the assessment of the impact of ITNs on occurrence of anaemia and parasitaemia have been described elsewhere (Abdulla *et al.* 2002). In short, children using ITNs had lower risk of anaemia (odd ratio; OR 0.47, 95% CI: 0.30–0.75) and moderate/severe anaemia (OR 0.66, 95% CI: 0.32–1.37) compared with those without nets at all. The relationship did not reach statistical significance for moderate/severe anaemia. A statistically significant difference was also observed on the prevalence of any parasitaemia (OR 0.53, 95% CI: 0.33–0.85). Other risk factors identified included distance to the dispensary, which was positively correlated to the prevalence of moderate/severe anaemia, and any parasitaemia.

Coverage effects

The DSS database had 941 households in Idete at the time of the cross-sectional assessment. A total of 708 (75.2%) families were present in the village and their houses mapped at the time of mapping exercise. The mapped houses had significantly more members on average, a higher proportion with children under five and fewer single member households than those not mapped (Table 1). There were 626 children under 5 years of age included in the cross-sectional survey. Analysis presented here was restricted to 564 (90.1%) children classified as DSS members and who had information available on geo-location, bednet and anaemia status.

The mean ITN coverage in the study area was 118.8 per 1000 inhabitants (range 0–1000). As defined by coverage at 100 m (C_{100}), 259 (45.1%) children lived in low, 256 (44.5%) in moderate and 60 (10.4%) in high ITN coverage areas (Table 2). Children living in all three coverage levels had similar average age, average haemoglobin level, and proportions with mild anaemia and parasitaemia (Table 2). But those living in moderate and high coverage had significantly lower proportions of moderate/severe anaemia and splenomegaly than those living in low coverage areas (9% *vs.* 16.2% and 22.8% *vs.* 33.6% respectively). Significantly higher proportions of children in the moderate and high coverage groups were living within 1.5 km of the dispensary (Table 2). Similar proportions of children with ITNs were observed in the three areas, indicating that coverage did not predict children's net ownership. However, those living further from the centre of the village had a lower proportion of ITNs (173 *vs.* 93 per thousand population for those living within 500 m and those living over 3 km

Table 1 Characteristics of the mapped and un-mapped households in Idete Village

Attribute	Mapped (%)	Not mapped (%)	χ^2 (*P*-value)†
Demographic Surveillance System – households	708 (75.2)	233 (24.8)	
Average number of persons*	5.2 (5.0, 5.3)	3.6 (3.3, 3.9)	8.160 (<0.001)
Households with children under 5 years	495 (69.9)	89 (38.2)	74.904 (<0.001)
Households with a single adult member only	68 (9.6)	63 (27.0)	44.465 (<0.001)
Households with known net status	620 (87.6)	146 (62.7)	71.854 (<0.001)
Households with no net	176 (28.4)	44 (30.1)	
Households with at least one untreated net	227 (36.6)	57 (39.1)	
Households with at least one treated net	217 (35.0)	45 (30.8)	0.917 (0.632)
Average treated net per 100 persons	13.3 (11.6, 15.1)	17.4 (12.1, 22.6)	0.03 (0.978)
Average untreated net per 100 persons	13.3 (11.5, 15.1)	20.9 (15.8, 26.1)	1.827 (0.068)

* 95% confidence interval in brackets and Wilcoxon rank sum test statistic.
† Pearsons χ^2 with Yates continuity correction.

Table 2 Characteristics of children living within the different coverage areas (C_{100}) in Idete Village

Attribute	No other ITNs per 1000 persons (%)	1–300 other ITNs per 1000 persons (%)	301–1000 other ITNs per 1000 persons (%)	χ^2 (*P*-value)‡
Children analysed*	255 (45.2)	249 (44.2)	60 (10.6)	
Mean age in months¶	32.3 (30.0, 34.6)	31.7 (29.4, 34.1)	32.3 (27.7, 36.9)	0.17 (0.921)
Mean haemoglobin¶	9.6 (9.4, 9.9)	10.0 (9.8, 10.2)	9.8 (9.4, 10.2)	4.85 (0.089)
Moderate severe anaemia	38 (14.9)	16 (6.4)	3 (5.0)	11.89 (0.003)
Mild anaemia	163 (63.9)	151 (60.6)	42 (70.0)	1.95 (0.378)
Parasitaemia (*P. falciparum*)†	152 (59.8)	126 (50.8)	35 (59.3)	4.49 (0.106)
Splenomegaly§	86 (33.7)	56 (22.6)	12 (20.0)	9.69 (0.008)
Living within 1500 m of the dispensary	100 (39.2)	182 (73.1)	35 (58.3)	58.86 (<0.001)
Owning an ITN	139 (54.7)	112 (45.0)	30 (50.0)	4.78 (0.092)

* Percentage of total children in brackets.
† The total of children assessed for parasitaemia was 561.
‡ Pearsons χ^2 with Yates continuity correction.
§ The total of children assessed for splenomegaly was 563.
¶ 95% confidence interval in brackets and Kruskal–Wallis statistic.

respectively: extended Kruskal–Wallis test for trend, $P < 0.01$)

The model used to explore the effects of different risk factors on having moderate/severe anaemia (Abdulla *et al.* 2002) was adjusted to investigate the effect of coverage. The results indicate that coverage was an important factor for predicting the risk of having anaemia even after controlling for the other already identified factors (Table 3). There was

Table 3 Risk factors for anaemia (Hb <8 g/dl) in children in Idete Village

Variable	Numbers with anaemia (%)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	LRT – χ^2 (*P*-value)
Net ownership				
No net	15 (13.6)	1	1	1.51 (0.470)
Untreated net	12 (10.2)	0.72 (0.32, 1.61)	0.67 (0.28, 1.59)	
Treated net	26 (10.2)	0.72 (0.36, 1.42)	0.64 (0.31, 1.31)	
Mother literacy				
Not literate	33 (16.5)	1	1	9.84 (0.002)
Literate	20 (7.1)	0.39 (0.21, 0.69)	0.38 (0.20, 0.70)	
Antipyretic use during last illness				
Not used	9 (4.8)	1	1	20.36 (<0.001)
Used	44 (14.8)	3.42 (1.63, 7.19)	5.13 (2.31, 11.35)	
Distance to the dispensary (m)				
<500	2 (3.5)	1	1	9.28 (0.026)*
500–1500	23 (10.8)	3.37 (0.77, 14.74)	3.26 (0.71, 14.93)	
1500–3000	7 (9.7)	3.02 (0.60, 15.11)	1.83 (0.34, 10.02)	
>3000	21 (15.1)	4.98 (1.13, 22.00)	5.47 (1.15, 26.00)	
Coverage of other ITNs within 100 m distance				
Low (no ITNs)	34 (15.7)	1	1	7.09 (0.029)*
Moderate (1–300)	16 (7.4)	0.43 (0.23, 0.80)	0.46 (0.23, 0.91)	
High (301–1000)	3 (6.0)	0.34 (0.10, 1.16)	0.33 (0.09, 1.16)	

* *P*-value for a test for trend of odds within the variable is <0.05.
LRT, likelihood ratio test.

less moderate/severe anaemia among those living in moderate (OR 0.46, 95% CI: 0.23, 0.91) and high (OR 0.33, 95% CI: 0.09, 1.16) ITNs coverage area compared with those living in low coverage areas. This indicates that coverage is independently associated with the occurrence of moderate/severe anaemia in the study area.

Analysis using other radii did not show significant results for moderate/severe anaemia nor other outcome variables assessed. Furthermore no coverage effects were observed for untreated nets for any radii or morbidity indicators.

Neighbourhood or short-distance effects

Neither the ownership of ITNs, nor having malaria parasites, or mild or moderate/severe anaemia seemed to have any particular spatial distribution (Figure 1). Logistic regression without covariates and including or excluding a spatial adjustment did not show any difference in the residuals. The conclusion was confirmed by testing the effects of different spatial correlations structures and by variogram analysis of the residuals from the non-spatial model. Multivariate logistic models incorporating spatial (exponential) effects estimated slightly larger standard errors for the fixed effects parameter estimates but this did not reduced the number of significant covariates (data not shown).

Discussion

Relatively good coverage of ITNs in the target group (children and expectant mothers) was achieved in the social marketing programme. About 61% of children under 2 years (Abdulla *et al.* 2001) and 52% of children under 5 years (Abdulla *et al.* 2002) slept under a net treated at least once. This is similar to findings of an earlier exploratory study in the same area using a similar delivery mechanism (Fraser-Hurt & Lyimo 1998) and in Burundi (Van Bortel *et al.* 1996). Assessments of coverage effects show that children who lived in areas with high ITN coverage had significantly lower anaemia levels when coverage within 100 m was considered, indicating that the prevalence of anaemia is better explained by nearby ITN coverage than by personal protection alone.

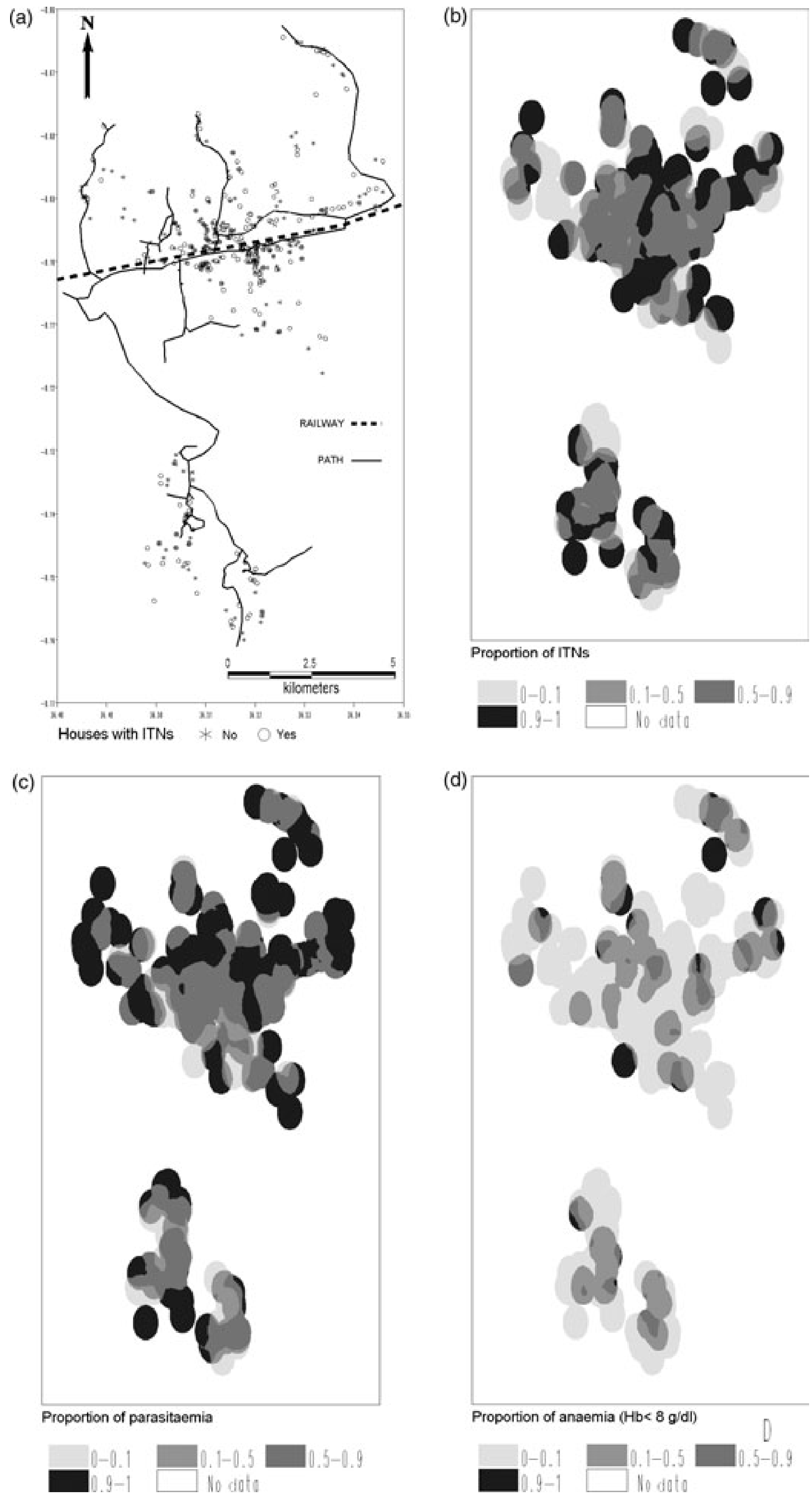
This was similar to effects of ITN coverage on malaria exposure (Lines *et al.* 1987), on severe disease (Howard *et al.* 2000) and on mortality (Binka *et al.* 1998). However, unlike the studies in Papua New Guinea (PNG) (Hii *et al.* 2001) and in Burundi (Van Bortel *et al.* 1996), we did not find any effect of bednet coverage on prevalence of parasitaemia. This may be because the prevalence of parasitaemia is not very closely linked to transmission intensity in areas of high endemicity (Thomas & Lindsay 2000).

Unlike the work in PNG (Hii *et al.* 2001), the coverage effects in our study were significant only when considering C_{100}. It may be that at lower radii the coverage effects are higher but we had wider confidence intervals. While at higher radii, the coverage effects are close to zero. It may also be that the effects of the other ITNs around outweigh the effects of ITNs of the index child at this range, beyond which the coverage effects gets smaller. Or it may be that only at this distance the existing distribution structure of the ITNs makes a difference. Lastly, although some attempt has been made to control for differences in confounding factors like socioeconomic status (Abdulla *et al.* 2002), it is still possible that some of the coverage effects that we have observed are mainly a reflection of residual confounding effects. All these issues allow us to make only crude statements about the relationship between coverage effects and morbidity indicators in children.

Allowance for spatial structure with the generalized linear mixed model did not substantially alter the point estimates from the fixed effects logistic regression and there was no residual spatial pattern detectable in the models including distance to the dispensary. Hence the fixed effects models adequately described the relationship of the effects of ITNs on anaemia. The finding that the malaria indicators are related to measured distance from the household to the dispensary (Abdulla *et al.* 2002) presumably reflects the importance of the health-seeking behaviour and treatment of malaria on these indicators. Demonstration of diversion or no diversion of mosquitoes (through entomological assessment) might have given some insights into the effects of ITNs that are not easily detectable using morbidity parameters.

The lack of spatial patterns in the distribution of ITNs and morbidity parameters may be a result of imprecision in our tools and methods. Errors in ascertainment of geo-positions with non-differential GPS (Hightower *et al.* 1998) and net treatment with reliance on histories provided by relatives contribute to the limitations of the study. The area studied may have been too small to detect any spatial patterns. Work conducted in a wider geographical area indicated that children living on the fringes of the populated area had more disease (Abdulla *et al.* 2001). A further investigation of the spatial effects in a larger geographical area is therefore required.

The results indicate that the social marketing campaign has managed to make the ITNs widely available even to those who live on the edge of the inhabited areas, where the risk of malaria disease is likely to be concentrated (Binka *et al.* 1998). This may have led to some protection being conferred to those without nets and those with untreated nets. In Kenya, a lower risk of admission to hospital for malaria has been observed in children not using ITNs but


(a)
N
RAILWAY
PATH
0
2.5
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kilometers
Houses with ITNs
No
Yes
(b)
Proportion of ITNs
0–0.1
0.1–0.5
0.5–0.9
0.9–1
No data
(c)
Proportion of parasitaemia
0–0.1
0.1–0.5
0.5–0.9
0.9–1
No data
(d)
Proportion of anaemia (Hb< 8 g/dl)
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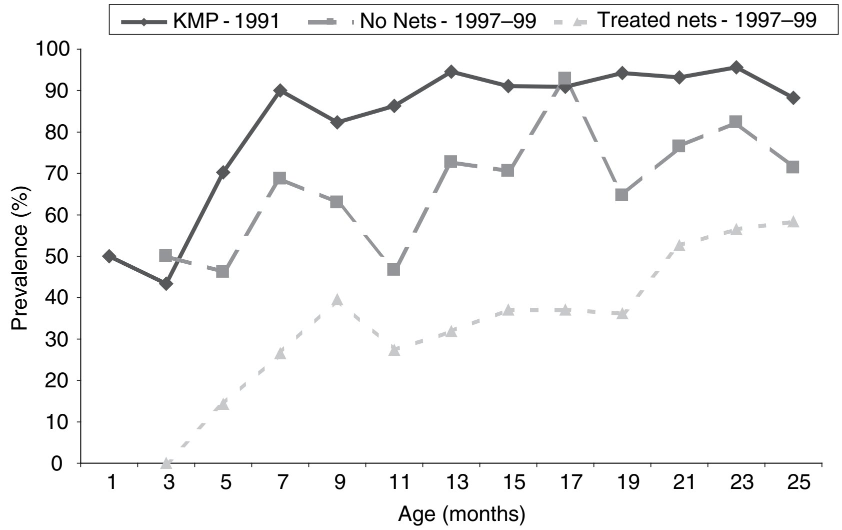

Figure 2 Age-specific malaria parasite prevalence in the Kilombero valley during 1991 and 1997–99.

living in areas with high ITN coverage compared with those in areas without ITNs (Howard *et al.* 2000). This phenomenon has bearing on the estimated effectiveness of the ITNs observed in programme evaluations. The reduced risk for those near the ITNs will bias the measured effect towards zero if a simple comparison is made of users and non-users. Hence, estimates of effectiveness made by our programme (Abdulla *et al.* 2001; Schellenberg *et al.* 2001) are likely to be conservative. Data was too sparse in our study to observe any increase or decrease of disease in those without nets, or examine the effects of those without nets living within different coverage levels or non-users living in houses with treated or untreated nets. The cross-sectional survey conducted in a larger geographical area did not show any change in the prevalence of anaemia nor parasitaemia in those without nets in the 3 years of observation (Abdulla *et al.* 2001). However, a comparison of the age-specific parasitaemia prevalence rates with historical values show that the children both those with and those without ITNs had much less malaria in current studies than a decade ago (Figure 2). This trend indicates that a substantial reduction in malaria endemicity has occurred in the last decade. This may well represent a further beneficial effect of the social marketing programme that has not been accounted for in evaluations to date.

We conclude that the social marketing of ITNs resulted in a relatively homogenous distribution of ITNs in the village. There are indications that coverage of ITNs was important in determining the prevalence of anaemia in children and high coverage produces higher impact of ITNs. Hence, efforts should be made to achieve high coverage in ITN programmes. In order to explore this important aspect further, analyses should be carried out in a larger geographical area together with entomological assessment.

Figure 1 Spatial distribution of (a) houses, (b) ITNs, (c) parasitaemia and (d) anaemia in Idete Village.

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