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Effect of community-wide use of insecticide-treated nets for 3–4 years on malarial morbidity in Tanzania

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Summary

OBJECTIVES To investigate (1) benefits due to personal protection of individual net users *vs.* mass killing of mosquitoes within villages as a result of widespread net usage; (2) sustainability over several years of benefits against malarial morbidity of insecticide-treated nets; (3) distribution of the benefits in different age groups of children and (4) whether, as a result of fading immunity, older age groups 'paid for' the benefits which they had enjoyed when younger.

METHODS (1) Tabulation of earlier data to compare personal and community-wide effects against mosquito vectors; (2) two cross-sectional surveys for malaria parasitaemia, malarial fever, anaemia and splenomegaly in children in eight Tanzanian villages, in which there had been community-wide use of bednets which had been annually re-treated with alphacypermethrin for 3–4 years; (3) comparison between children of different age groups and with intact, torn or no nets in these villages and in 4–6 villages without nets.

RESULTS A 90–95% reduction in infective bites outside nets in netted villages and an additional 54–82% reduction of bites among individual net users. Highly significant reductions (by 55–75%) in malarial morbidity for children aged 6 months to 2 years were found in netted villages with, for some outcomes, better results among individuals who themselves had intact treated nets. For older children, benefits were less clear or absent, but there was no sign that the benefits early in life were 'paid for' by worse outcomes in the netted villages later in childhood.

CONCLUSIONS The overall benefits to the community of widespread use of treated nets are sustainable and are not reversed in 3–4 years as a result of fading immunity. It is important to ensure high enough coverage to realize the full potential of the treated net method. By showing an impact on the vector population in the community these results provide a strong argument for organized free provision of net treatment, rather than relying on marketing.

keywords insecticide-treated bednets, malarial morbidity, marketing *vs.* free provision, mass effect, sustainability of impact, Tanzania

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Introduction

Insecticide-treated bednets have been shown, in numerous short-term trials, to reduce malarial morbidity and child mortality (Lengeler 2001). However, doubts remain about whether:

(a) fading of immunity as a result of reducing transmission intensity (Askjaer *et al.* 2001) may make populations more vulnerable to malaria and/or may postpone morbidity to later life (Trape & Rogier 1996; Snow & Marsh 1998);

(b) coverage with nets and re-treatment has been attempted by a marketing system (Armstrong-Schellenberg *et al.* 2001) or by organized provision free of charge. It is important to establish which system is most cost-effective in maintaining a level of coverage at a level which ensures, not only personal protection of those with effectively treated nets, but also a mass effect on the vectorial capacity of the mosquito population in the community (Magesa *et al.* 1991).

In late 1995–early 1996 we provided polyester bednets treated with lambdacyhalothrin to all inhabitants of four

villages in a highly malaria endemic area in north-east Tanzania as part of a comparison with indoor residual spraying with the same insecticide (Curtis *et al.* 1998). Late in 1996, for the four villages which had been the untreated controls in the nets *vs.* spraying trial, we provided nets treated either with the same insecticide or, for comparison, nets treated with alphacypermethrin (Maxwell *et al.* 1999). In both trials, as already reported, there were significant reductions in the densities of anopheline vectors caught in light traps in untreated sentinel bedrooms in the treated villages and in the sporozoite rates in these mosquitoes, i.e. mass effects on the entomological inoculation rates. There were relatively modest additional effects on the number of blood-fed mosquitoes found in rooms with treated nets or window exit traps on these rooms, i.e. in addition to the mass effects on the village mosquito populations, there is also some degree of personal protection of individual net users from being bitten. Table 1 tabulates these data to allow easier comparison of the mass and personal protection effects from both trials than in our original publications. In both trials, as already reported, significant impacts were measured on incidence of re-infection after clearing pre-existing infections. In the first trial measurements of prevalence of malarial fever and anaemia showed beneficial effects of the nets. Follow-up measurements up to 22 months after providing the nets, showed that the impact on anaemia in children was sustained (Curtis 1998).

The present project aimed to investigate malarial morbidity in children 3–4 years after introducing the nets, and to assess children with the community benefit of widespread use of treated nets in their village in comparison with children in villages without nets. Within the netted villages, children with the additional benefit of the personal protection of intact nets were compared with those who had less or no personal protection because their nets were torn or absent. Comparisons were made between age groups to assess whether there was evidence of any adverse impact in older children resulting from fading immunity.

Clearance for this project was given by the ethical committees of the Tanzanian National Institute for Medical Research and the London School of Hygiene & Tropical Medicine.

Materials and methods

We have continued annually to provide organized, free re-treatment of the nets using the granular formulation of alphacypermethrin (Fastac). House-to-house surveys of the nets have shown that, on average, more than 90% of the nets still present in the villages were re-treated in 2000. Householders were left to wash their nets as they saw fit. Bioassays confirmed that these nets remained insecticidal for up to 15 months after the previous treatment. The house-to-house surveys also recorded whether the net provided for each child to sleep under was still intact or was badly torn. We defined an intact net as one with <20 holes, <2 cm in diameter; <5 holes, 2–5 cm in diameter or <2 holes, >5 cm in diameter. Children without nets were also recorded. The reasons for absence of nets were either that the family had moved into the area since 1995–1996 when the nets were distributed, the net had been stolen or

Table 1 Catches of malarial vectors in Tanzanian villages with or without pyrethroid treated nets analysed to assess the relative importance of the mass effects and personal protection effects of the nets

	1996 trial*	1997 trial**
Mass effects		
Nos light trapped in untreated rooms in treated villages as fraction of nos in control villages	$\frac{8.07}{19.72}$ (40.9%)	$\frac{14.78}{75.22}$ (19.6%)
% sporozoite positive in treated villages as fraction of that in controls	$\frac{0.99}{3.92}$ (25.3%)	$\frac{0.66}{2.87}$ (23.0%)
Overall mass effect on entomological inoculation rate	40.9% × 25.3% = 10.3% (89.7% reduction)	19.6% × 23.0% = 4.5% (95.5% reduction)
Personal protection		
Nos blood-fed found in treated rooms + their exit traps as fraction of those in untreated villages (corrected for reduction in village mosquito populations)	$\frac{0.54}{2.90} \times \frac{19.72}{8.07}$ = 45.5% (54.5% reduction)	$\frac{0.399}{11.122} \times \frac{75.22}{14.78}$ = 18.3% (81.7% reduction)

* Curtis *et al.* (1998).
** Maxwell *et al.* (1999).

sold, or it was considered by the householder as so badly torn as to be useless and had therefore been discarded. In contrast to projects in which nets and insecticide are sold, presence or absence of a treated net on a child's bed in our trial did not depend on ability and willingness of the parent to pay. Thus, in comparing children with and without nets in our trial, we are fairly confident that we can attribute any differences to effects of the nets, without the confounding factors of parental income or willingness to take measures to protect their children's health.

In February 1999 and April 2000 cross-sectional surveys were carried out, on pre-arranged days, in the eight netted villages on aspects of morbidity. The parents or guardians of all children on our census lists aged >6 months and <13 years were invited, via village health workers, to bring the children to assembly points in the villages for the surveys. More than 90% of the invited children attended these surveys. Four, apparently similar, nearby villages without nets were chosen as controls in 1999 and it was found feasible to increase this number to six in 2000. Censuses were conducted in these villages so that lists of children requested to attend for survey were prepared in exactly the same way as in the netted villages. Distances between the netted and control villages are indicated in Figure 1. They were generally far enough apart so that movements of mosquitoes from untreated villages were not expected to nullify the effect of mass mosquito killing in the netted villages. As indicated in Figure 1, all villages were at similar altitudes of about 200 m, which is an important aspect of their comparability as, in this district, villages a few hundred metres higher have markedly lower entomological inoculation rates and malarial morbidity (Ellman *et al.* 1998). Among three groups of randomly chosen lowland villages in this district, very similar incidences of malarial infection have been recorded (Curtis *et al.* 1998). Thus, although for the control villages we

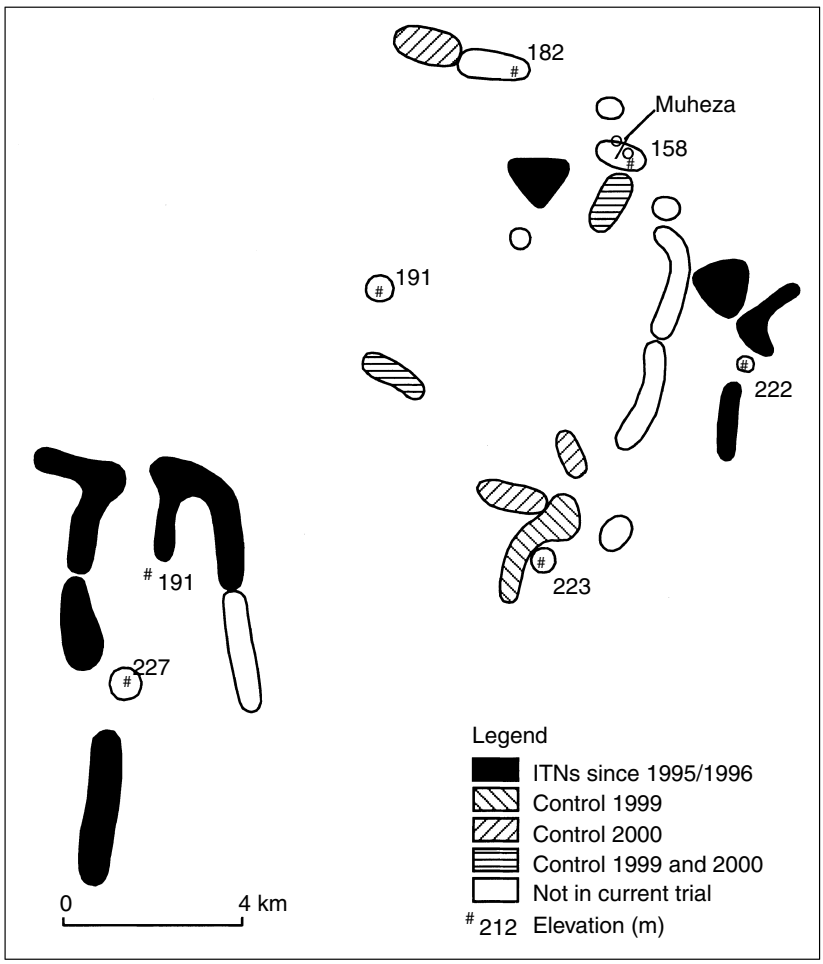

Figure 1 Sketch map of the netted and control villages to indicate the distances between them and their altitudes.

have no baseline data from the time that nets were first provided in the intervention villages, we are confident that the control and intervention villages were comparable.

The outcome measures in the surveys were (a) prevalence of parasitaemia (mainly *Plasmodium falciparum*) by checking 100 microscope fields; (b) malarial fever, defined as core body temperature (measured by Thermoscan thermometer placed in the ear) of >37.4 °C and/or report of fever in last 2 days, combined with parasitaemia >4000/μl; (c) anaemia defined as <8 g haemoglobin/dl as measured by a Hemocue machine; (d) splenomegaly detected by palpation by an experienced medical aide. There is a clear association between occurrence of fever and the levels of parasitaemia defined in (b). There are stronger associations if higher cut-off points are taken, but few of such more extreme cases are seen and so unfeasibly large sample sizes would be needed to expect to see significant impact of nets and age.

The children were categorized into age groups 6 months–2 years, 2–5 and 6–12 years, where possible on hospital birth registration cards or Maternal and Child Health cards from health centres or, in the absence of such cards, on parent's report of dates of birth. The children were also categorized as whether or not they lived in a village with treated nets and therefore benefited from the mass effect on the vector population. Those from netted villages were further divided by whether or not they slept under an intact or a torn net and therefore benefited fully, or partially, or not at all, from personal protection of a net.

Results were statistically analysed on the basis of the odds ratios, relative to a value of 1.0 for children with intact nets, and adjusted for non-independence for children from the same village. In the case of anaemia, results were also adjusted for the child's weight as an indicator of the effects of malnutrition. Significance tests were done by logistic regression using STATA 7.0 (Stata Corporation 2001).

Results

The prevalences of each condition in 1999 and 2000 are shown in Tables 2 and 3, with asterisks indicating significance of differences of odds ratios from the 1.0-value for children of the same age group with intact nets.

In both years infants and children aged 6 months–2 years with intact or torn nets showed significant benefits for all four outcome measures compared with children from villages without nets. We presume this was because of some combination of the mass effect of the village's nets on the vector populations and the personal protection to the individual children, but the lack of any significant disadvantage as a result of nets being torn suggests that the former effect predominated. Even more striking evidence for this predominance is that the approximately 20% of children aged 6 months–2 years

Table 2 Cross-sectional survey 1999. Percentage (total in brackets) of children by age group and net-use status for each outcome measure

		Age group		
Outcome of interest	Net-use status of children	6 month–2 years % (total)	2–5 years % (total)	6–12 years % (total)
% with any malaria parasites	Intact nets	27.2 (254)	46.8 (395)	46.3 (389)
	Torn nets	22.0 (173)	47.7 (260)	46.3 (272)
	No nets (netted village)	34.6 (107)	55.8 (165)	53.3 (195)*
	Un-netted village	59.8 (286)**	72.9 (520)	61.4 (640)
% with malaria fever[f]	Intact nets	3.7 (271)	4.2 (410)	2.4 (413)
	Torn nets	1.6 (184)	5.7 (281)	2.3 (300)
	No nets (netted village)	10.4 (115)**	5.0 (181)	3.3 (212)
	Un-netted village	14.8 (311)***	10.0 (541)**	3.8 (659)
% with anaemia (Hb < 8 g/dl)	Intact nets	19.8 (222)	10.7 (346)	2.9 (68)
	Torn nets	22.9 (153)	7.3 (233)	1.8 (55)
	No nets (netted village)	29.6 (98)	10.1 (148)	6.0 (50)
	Un-netted village	45.1 (286)***	13.3 (513)	12.9 (31)
% with splenomegaly	Intact nets	17.0 (271)	36.2 (409)	32.5 (412)
	Torn nets	11.4 (184)	40.0 (280)	35.7 (300)
	No nets (netted village)	26.1 (115)**	46.4 (181)	44.1 (211)*
	Un-netted village	48.7 (310)***	65.1 (539)**	40.6 (655)

[f] Malarial fever defined as temperature >37.4 °C and/or fever reported in last 2 days with parasitaemia >4000/μl.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ based on comparison for each of the four outcome measures of odds ratios (adjusted as specified in the text) with children of the same age group with intact nets.

Table 3 Cross-sectional survey 2000. Percentage (total sample in brackets) of children by age-group and net-use status with different outcome measures

Outcome of interest	Net-use status of children	Age group		
		6 month–2 years % (total)	2–5 years % (total)	6–12rs % (total)
% with any malaria parasites	Intact nets	45.9 (61)	59.6 (146)	56.5 (186)
	Torn nets	34.1 (44)	47.4 (78)*	69.2 (120)*
	No nets (netted village)	33.3 (24)	72.5 (40)	71.6 (81)
	Un-netted village	69.4 (183)**	88.9 (333)***	84.5 (489)***
% with malaria fever[f]	Intact nets	3.3 (61)	7.5 (146)	6.5 (186)
	Torn nets	2.3 (44)	6.4 (78)	5.0 (120)
	No nets (netted village)	4.2 (24)	7.5 (40)	4.9 (81)
	Un-netted village	18.0 (183)*	7.8 (333)	2.9 (489)*
% with anaemia (Hb < 8 g/dL)	Intact nets	11.5 (61)	5.5 (146)	1.6 (186)
	Torn nets	4.6 (44)	10.3 (78)	0.8 (120)
	No nets (netted village)	16.7 (24)	5.0 (40)	1.2 (81)
	Un-netted village	38.8 (183)**	6.0 (332)	3.3 (488)
% with splenomegaly	Intact nets	21.3 (61)	38.4 (146)	34.4 (186)
	Torn nets	22.7 (44)	42.3 (78)	40.0 (120)
	No nets (netted village)	16.7 (24)	55.0 (40)*	27.2 (81)
	Un-netted village	55.7 (183)***	72.0 (329)***	54.1 (488)*

[f] Malarial fever defined as temperature >37.4 °C and/or fever reported in last 2 days with parasitaemia >4000/μl.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ based on comparison for each of the four outcome measures of odds ratios (adjusted as specified in the text) with children of the same age group with intact nets.

in netted villages, but themselves without nets, benefited almost as much as those with nets with regard to reduction in parasite prevalence and anaemia. In the 1999 survey, children aged 6 months–2 years with their own nets were better off than those without nets in netted villages with regard to malarial fever and splenomegaly, indicating that there is a positive effect of personal protection of a net, as might be expected.

For the 2–5 and 6–12 age groups there were no significant differences between any of the four net categories in 1999 or 2000 with regard to anaemia. For the other three outcome measures, significant benefits were seen because of nets in one or other of the year's surveys but this was not consistent for both surveys.

Discussion

Overall there is clear evidence for beneficial effects to young children of use of annually re-treated nets 3–4 years after these had been installed. The much less convincing benefits of nets for older age groups may be at least partly because of the fact that several years use of nets have left children with lowered malarial immunity levels (Askjaer *et al.* 2001). However, it is important to emphasize that there is almost no evidence from our data for a rebound effect causing the benefits of nets to young children to be 'paid for' by worsening morbidity later in childhood. The only anomaly is a significantly lower ($0.01 < P < 0.05$) parasite prevalence in 2–5-year-old children with torn nets than with intact ones. However, as we have made considerably more than 20 comparisons, one anomalous value of $P < 0.05$ is not surprising.

With very few staff and with relatively cheap insecticide in 1-litre bottles we have been able to ensure >90% re-treatment rates which is evidently enough to have a major impact on the vectorial capacity in the community as well as providing personal protection to most individual children. Our rates of re-treatment are much higher than in even the best of the social marketing programmes (Armstrong-Schellenberg *et al.* 2001). Organized free re-treatment is successful on a far larger scale in the Vietnamese national treated bednet programme (Tran Duc Hinh 2001). We fear that, if the process of re-treatment is left to the market, coverage will be low and even those able and willing to pay for net re-treatment may gain far less than the full potential of treated nets. We have not yet got direct evidence for this but are planning a trial to test whether provision of treated nets to a randomly chosen small proportion of the populations of villages is indeed much less effective in protecting those individuals than in a second phase of the

trial when all their neighbours will also be provided with treated nets.

We found that provision of nets (replaced every 4 years) and annual re-treatments cost about $1 per head (Curtis *et al.* 1998). We have found that in 1 day a small team can check all the beds in a village and provide the required 800 treated and indelibly numbered nets against householders' signatures. In urban areas in Africa there is not much malarial transmission and there is already a thriving market in nets against nuisance mosquitoes. It is among lowland, rural, subsistence farmers with very little cash that we advocate provision of nets and insecticide treatment as a free public health service. We consider that the few hundred million dollars per year that would be required for the whole of rural tropical Africa, would be a more cost-effective use of donor funds than subsidizing slow-moving social marketing systems, or provision of expensive antimalaria drugs which will be increasingly needed if malarial transmission levels throughout Africa are not reduced to minimize the selection pressure for resistance.

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