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MALARIA CONTROL — TWO YEARS' USE OF INSECTICIDE-TREATED BEDNETS COMPARED WITH INSECTICIDE HOUSE SPRAYING IN KWAZULU-NATAL

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Objectives. The objective of this study was to produce data indicating whether insecticide-treated bednets should replace insecticide house spraying as a malaria control method in South Africa. We report 2 years of preliminary data on malaria incidence comparing areas receiving insecticide-treated bednets and those subjected to house spraying in northern KwaZulu-Natal.

Design, setting and subjects. In order to measure significant reductions in malaria incidence between the two interventions, a geographical information system (GIS) was used to identify and create seven pairs of geographical blocks (areas) in the malaria high-risk areas of Ndumu and Makani in Ingwavuma magisterial district, KwaZulu-Natal. Individual blocks were then randomly allocated to either insecticide-treated bednets or house spraying with deltamethrin. Malaria cases were either routinely recorded by surveillance agents at home or were reported to the nearest health facility.

Results and conclusions. The results show that 2 years' use of insecticide-treated bednets by communities in Ndumu and Makani, KwaZulu-Natal, significantly reduced the malaria incidence both in 1997 (rate ratio (RR) = 0.879, 95% confidence interval (CI) 0.80 - 0.95, $P = 0.04$) and in 1998 (RR = 0.667, CI 0.61 - 0.72, $P = 0.0001$). Using a *t*-test, these significant reductions were further confirmed by an assessment of the rate of change between 1996 and 1998, showing a 16% reduction in malaria incidence in blocks using

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treated bednets and an increase of 45% in sprayed areas ($t = 2.534$, $P = 0.026$ (12 df)). In order to decide whether bednets should replace house spraying in South Africa, we need more data on the efficacy of treated bednets, their long-term acceptability and the cost of the two interventions.

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Insecticide house spraying is used throughout southern Africa; in KwaZulu-Natal it has been used for 50 years,¹ leading to: (i) elimination of malaria in many parts of South Africa; (ii) reduction in malaria incidence from endemic to epidemic levels (KwaZulu-Natal with 600 000 people at risk has only 5 000 cases per year); (iii) elimination of *Anopheles gambiae sensu stricto*, leaving *A. arabiensis* and *A. funestus* as the major vectors;² and (iv) improvement in the general health of the people.

On the other hand, spraying of DDT, in particular, has resulted in: (i) an increase in the hut-leaving behaviour of *A. arabiensis*³ — for example in KwaZulu-Natal 60% of window-capped mosquitoes are human blood-fed, and 90% of these survive; (ii) high levels of DDT (more than 30 times the Food and Agricultural Organisation (FAO)-defined allowable daily intake) detected in breast-milk of primiparous mothers;⁴ and (iii) a strong tendency for people to plaster over DDT deposits.⁵ National policy, however, was changed and synthetic pyrethroids were recommended in place of DDT on the basis of both field and laboratory studies by the Medical Research Council (MRC) in 1995. In addition to the above problems, there has also been pressure to decentralise the malaria control programme; this has led to alternative methods of malaria control, such as insecticide-treated bednets, being seriously considered.^{6,7}

Insecticide-treated bednets were considered because recent trials have shown them to have an important impact on: (i) cases of malaria in areas of low to moderate malaria transmission, for example in China;⁸ (ii) incidence of infection and anaemia in areas of tropical Africa with moderate to intense malaria transmission;^{9,10} (iii) hospital admissions in Kenya;¹¹ and (iv) most importantly, all-cause child mortality in several parts of Africa.¹²⁻¹⁴ It is evident now that for every 180 insecticide-treated bednets used, the death of one African child can be prevented per year.¹⁵

Apart from a study done in Tanzania by Curtis *et al.*¹⁰ comparing house spraying and bednets, no other studies have been carried out in areas of Africa with a long history of residual insecticide house spraying. Studies done in Asia^{8,16,17} were certainly conducted in areas with different malaria transmission levels and patterns to those in Africa. Owing to this lack of data it was decided to conduct a study in KwaZulu-Natal, South Africa that would provide a rational basis for

choosing between a malaria control programme based on house spraying, and insecticide-treated bednets. The latter strategy can potentially be integrated into the primary health care (PHC) services.⁷

The objectives of this study were, therefore, to assess the efficacy, acceptability and cost of the two interventions in KwaZulu-Natal. This paper reports results of the impact assessment of insecticide-treated bednets on malaria incidence after 2 years' use of the nets compared with insecticide house spraying. Results on community acceptance of insecticide-treated bednets are reported elsewhere (S S Dlamini *et al.* — unpublished data) and the cost analysis of the two interventions is currently in progress. Results from this study will have implications in terms of the control of malaria in southern Africa, where insecticide house spraying is the mainstay of malaria vector control and has relevance in a number of countries with similar malaria transmission patterns.

METHODOLOGY

Study area and geographical information system (GIS) epidemiological study design

Traditionally Zulu people live in patriarchal homesteads dispersed throughout the countryside, and not in nuclear villages. These homesteads were the sampling units in the Ndumu and Mkanis areas of Ingwavuma district in KwaZulu-Natal. The study area included a subset of 14 000 people served by four clinics and one referral hospital (Mosvold Hospital) within a distance of less than 40 km (Fig. 1).

Given the general low malaria infection rates in South Africa as a result of a successful malaria control programme, and the fact that communities had not used bednets before, the critical question was how to design a study that would be able to

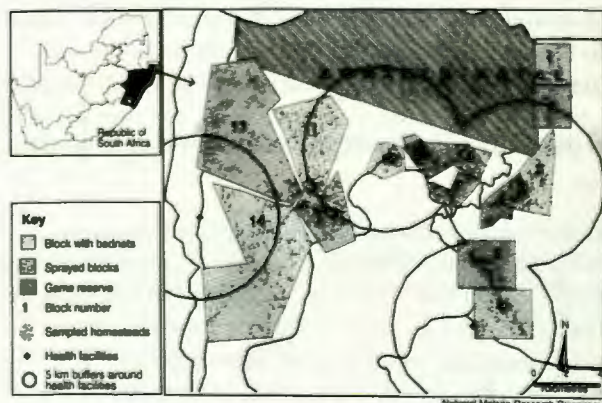


Fig. 1. Study area showing the different blocks in the Ingwavuma magisterial district in relation to health facilities and distance buffers in KwaZulu-Natal.

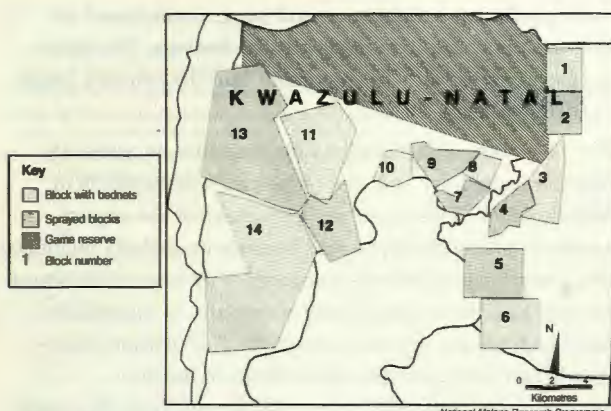


Fig. 2. Study area showing the different blocks in the Ingwavuma magisterial district, KwaZulu-Natal.

measure significant reductions in both entomological and malariological parameters. With the help of a geographical information system (GIS), however, it was possible to identify blocks with an average annual malaria incidence of around 5%. Fourteen such blocks were created by GIS extraction of the malaria cases in each block within the malaria risk areas of Ndumu and Mkanis (Fig. 2).

The blocks were then combined into pairs matched for malaria incidence during the years 1987 - 1993. This was done to achieve homogeneous pairs in which individual blocks were randomly allocated to either insecticide-treated bednets or insecticide house spraying. It was estimated that there would be sufficient power in the study to detect significantly a difference of 70 cases per 1 000 person-years between insecticide-treated bednet blocks and insecticide house spraying blocks, based on the malaria incidence data from the previous years. As will be mentioned elsewhere, however, the study was only implemented in 1997, and 1996 incidence data were therefore used as baseline for subsequent analysis, and not the average incidence at the time of designing the study. Seven pairs of blocks were then randomly allocated (by tossing a coin during community meetings) to receive or not to receive bednets treated with a synthetic pyrethroid (permethrin 200 mg/m² in 1997 and 1999, and deltamethrin (KO-Tab) in 1998).

Distribution of bednets and evaluation of malaria cases

Community health information campaign meetings were conducted before the distribution of free nets. People's sleeping patterns and preferences for colour and shape of nets were also assessed (Table I). Green (not to show dirt easily), conical (easier to hang) nets were favoured. These nets were distributed in January 1997 by the surveillance teams of the Department of Health, Jozini, after training by the research staff. The surveillance teams, in turn, trained communities to re-treat their own nets in January 1998 and 1999. Since house

Table I. Colour and shape preferences for bednets in communities of Ingwavuma magisterial district, KwaZulu-Natal

Colour	Number	Percentage
Green	561	33.7
White	327	19.5
Blue	261	15.6
Brown	162	9.7
Black	156	9.3
Yellow	118	7.1
Other (pink, red, etc.)	86	5.1
Total	1 671	100.0
Conical	1 281	76.7
Rectangular	390	23.3
Total	1 671	100.0

spraying commences as early as September, and also because is considered unethical not to provide protection in malaria risk areas, houses in bednet blocks had already been sprayed by the time the nets were distributed. In subsequent years, however, house spraying was deliberately withdrawn in blocks with bednets.

Malaria cases were then routinely identified by both surveillance agents of the malaria control programme (active case detection) and clinic and hospital staff (passive case detection). The results were recorded by the field staff of the malaria control programme and later captured in a computer as part of a malaria health information system (MHIS) database kept at the Malaria Research Lead Programme of the MRC in Durban. Bioassay tests were regularly performed on the nets and on wall surfaces to monitor insecticidal residual effect. Mosquitoes were also collected in window traps fitted in houses with nets or sprayed with insecticide, and were monitored for survivorship.

Statistical analysis of the impact on malaria reduction

All data were aggregated as total counts of cases (active and passive) per block and by year, ensuring that there was no double counting. Population totals for each block were available from a census conducted in 1996. Any population changes over the study period could not be taken into account.

Malaria incidence rates were calculated for each block and incidence rate ratios (RRs) were calculated for each matched pair of blocks. To adjust for differences in incidence rates in 1996 (baseline) and for differences between pairs of blocks, a Poisson multiple regression analysis was performed. From this an adjusted overall RR for malaria incidence between blocks with or without bednets was obtained.

In order to assess changes in incidence between 1996 and 1998, 2 years after bednets were distributed, the difference in incidence between the 2 years was calculated for each block. A



test was used to determine whether the change over time was significantly different between blocks with and without bednets.

RESULTS

Mosquitoes collected by window traps in Ingwavuma district during the peak transmission season in 1997 did not show any significant difference between blocks. Interestingly, however, the proportion of mosquitoes (both anophelines and culicines) that had not fed or survived was significantly higher (> 90%) in houses with nets, compared with houses without nets (11%) (Table II). Bioassays using 3 minutes' exposure gave 100% kill up to June at the end of the transmission season, confirming that a single treatment per year was adequate (Table III). Up to August 1997 bioassay tests done in houses in which nets were being used reported mortality rates of between 90% and 100%. A random survey a year later, when house spraying had been withdrawn, showed that the rates were as low as 28%, well below the World Health Organisation (WHO)-recommended rates of between 80% and 100%.

Table II. Number of mosquitoes collected in window traps (February - May 1997) and their physiological status

	Nets		No nets	
	Anophelines	Culicines	Anophelines	Culicines
Fed (A)	-	3	6	30
Fed (D)	-	1	2	1
NF (A)	2	3	-	8
NF (D)	18	160	1	-
Total	20	167	9	39
Average				
/w-trap	1.3	11.1	0.6	2.6
% NF-dead	90	95.8	11.1	0.00

Fed = blood-fed; A = alive; D = dead; NF = not blood-fed; w-trap = window trap.

Table IV shows the malaria incidence rate (cases per 1 000 person-years) in each of the blocks for the years 1996 (baseline before introduction of bednets) and 1998, as well as the change in incidence rate over the period 1996 - 1998. Whereas blocks with bednets had a higher malaria incidence rate overall before

Table IV. Difference in malaria incidence (cases per 1 000 person-years) in seven pairs of blocks between 1996 and 1998

Block	Population	Rate per 1 000 person-years		
		1996	1998	Difference
1 B	295	389	220	-169
2 S	268	399	392	-7
3 B	641	193	112	-81
4 S	990	149	251	102
5 S	1 027	65	133	68
6 B	836	57	153	95
7 S	709	283	522	238
8 B	566	226	224	-1
9 S	1 568	117	196	78
10 B	465	413	279	-133
11 B	1 161	252	211	-41
12 S	1 596	169	168	-0.6
13 S	1 491	137	254	117
14 B	1 486	69	134	65

bednets were introduced, in five out of seven blocks there was a reduction in incidence by 1998 as compared with a reduction in only two blocks under house spraying.

Comparing bednet blocks with sprayed blocks, the incidence RR was below 1 in four out of the seven pairs of blocks (Table V). In two blocks the reduction in incidence was significantly greater in blocks with bednets than in those without, but the incidence RR was greater than 1. This was due to the fact that despite a significantly higher reduction in malaria incidence, these bednet blocks started at a higher level of incidence in 1996 compared with sprayed blocks.

In one pair (blocks 5 and 6 in the Makanis area), the RR was greater than 1 (RR = 1.14, 95% CI 0.90 - 1.46, $P = 0.26$). In this pair the incidence in the block with bednets increased threefold (57 - 153 cases/1 000 person-years) compared with a twofold increase (65 - 133 cases/1 000 person-years) in the block without bednets. Other than natural variation in malaria incidence, these differences were difficult to explain.

When RRs were adjusted for baseline incidence, overall use of insecticide-treated bednets significantly reduced the malaria incidence (rate of malaria transmission) both in 1997 (RR = 0.879, CI 0.80 - 0.95, $P = 0.04$) and 2 years later in 1998 (RR =

Table III. Bioassay tests (% mortality) on walls and nets between March and August 1997, and in February 1998

Months	No. of houses without nets	No. of houses with nets	No. of nets being used	Control
March '97	9 (99.2)	7 (98.4)	7 (100)	2 (6.5)
April '97	9 (96.5)	7 (99.6)	7 (100)	2 (7.4)
May '97	8 (98.6)	7 (98.7)	7 (100)	2 (5.4)
June '97	9 (94.6)	6 (95.8)	6 (100)	2 (9.8)
July '97	7 (91.8)	7 (96.5)	7 (98.6)	2 (6.7)
August '97	9 (86.7)	6 (90.3)	6 (95.7)	2 (8.9)
February '98	10 (98.5)	10 (28.2)	10 (100)	2 (6.8)



Table V. Malaria incidence rate ratios (within pair) in the seven pairs of blocks and overall in 1997 and 1998

Block	Pairs	Rate ratio	CI	P
1 B	1	0.56	0.41 - 0.76	0.000
2 S				
3 B	2	0.44	0.34 - 0.58	0.000
4 S				
5 S	3	1.14	0.90 - 1.46	0.26
6 B				
7 S	4	0.43	0.35 - 0.52	0.000
8 B				
9 S	5	1.42	1.16 - 1.75	0.001
10 B				
11 B	6	1.25	1.05 - 1.48	0.011
12 S				
13 S	7	0.53	0.44 - 0.62	0.000
14 B				
1997	Adjusted for 1996	0.88	0.80 - 0.95	0.04
1998	Adjusted for 1996	0.67	0.61 - 0.72	0.000

0.667, CI 0.61 - 0.72, $P = 0.0001$). Using a t -test these significant reductions were further confirmed by an assessment of the rate of change between 1996 and 1998. Whereas overall blocks with nets started off with 228 cases/1 000 person-years in 1996, and decreased to 191 cases/1 000 person-years in 1998, a 16% reduction, incidence in blocks without nets increased by 45% from 189 to 274 cases/1 000 person years ($t = -2.534$, $P = 0.026$ (12 df)).

DISCUSSION AND CONCLUSIONS

The challenge to conduct a study comparing two interventions in areas of naturally low malaria incidence or as a result of a control programme, and still be able to measure significant reductions in malaria incidence cannot be overemphasised. The use of a GIS to help design this study in KwaZulu-Natal has proved the usefulness of this tool in malaria research and health research in general.¹⁸

Whereas in 1994, at the time of designing this study, the average malaria incidence rate in the study area was only 5%, at the time of implementation in 1997 it was noticed that there had been a general increase in malaria incidence from 1996 onwards. This increase was experienced not only in the study area but also elsewhere in South Africa and in the whole of southern Africa. It is argued that this increase was linked to El Nino and global warming phenomena.¹⁹ The 1996 incidence data were therefore thought to have introduced a substantial mismatch within pairs of blocks, which had to be taken into account by adjusting for baseline differences.

In this study bednets significantly reduced the risk of malaria infection compared with house spraying after 2 years of use (RR = 0.667, CI 0.61 - 0.72, $P = 0.000$). People therefore benefited more by sleeping under insecticide-treated bednets than by having their houses sprayed with deltamethrin. In 1997

homes in blocks with bednets were also sprayed with deltamethrin; however, in 1998 spraying was deliberately withdrawn, with bioassays showing no evidence of significant insecticide persistence, allowing for a true comparison between bednets and house spraying (Table III). The benefit of sleeping under treated bednets was confirmed in the social survey. People were reported to have used bednets consistently, and there was an increased demand for bednets in blocks without nets because of perceived benefit (S S Dlamini *et al.* — unpublished data). Studies done in Tanzania,¹⁰ in an area with no previous history of house spraying, reported similar demands for nets, although in terms of impact the two interventions were comparable. In India^{16,20} and China,⁸ where there is a long history of house spraying, bednets have performed better than insecticide house spraying. In Afghanistan, on the other hand, studies done on refugees²¹ reported no significant differences between the two methods of intervention, suggesting that for policy implications local data are essential.

When insecticide-treated bednets are used on a large scale in a community, the achievable aim is the overall reduction in mean age of the local vector population.²² Although this was difficult to measure entomologically in the study area (because of low numbers of mosquitoes infected with *Plasmodium falciparum*), the collection of a high proportion of unfed dead mosquitoes in window traps fitted in houses with bednets seems to explain why people using bednets in our study areas had a lower risk of malaria infection than those in sprayed houses. *A. arabiensis* is the main local vector¹ and has been shown to bite people even in the presence of insecticide on walls.

In December 1999 Hargreaves *et al.*² caught *A. funestus* leaving houses in the study area. These were shown to be resistant to deltamethrin, the insecticide used in house spraying in the area. There is no evidence, however, that pyrethroid-resistant *A. funestus* occurred in the area during the period of the reported study.

The objective of this study was to establish a rational basis for a choice between insecticide-treated bednets and insecticide house spraying. Sustainability of an insecticide-treated bednet programme depends on impact based on efficacy studies, but even more on effectiveness (real situation), cost and acceptability in the long term. In the short term, acceptance of bednets by communities in KwaZulu-Natal has been very good, but nothing is known about long-term sustainability (S S Dlamini *et al.* — unpublished data). It took an average of 3 days to organise and re-treat 3 500 bednets to cover a population of about 7 000 people — it would have taken more than 2 weeks to spray the houses in this area.

However, both the local and scientific communities are still concerned about losing gains obtained from house spraying, given the success of this intervention combined with definitive diagnosis and treatment. Furthermore, there have been contradictory findings on whether bednets cost less than house



spraying.²³ For example, in the Solomon Islands, the cost of DDT is over three times that of bednets.²¹ In Vietnam, on the other hand, lambda-cyhalothrin house spraying cost US\$0.43 less than bednets per person per year.²⁴ In Afghanistan, malathion house spraying was cheaper than permethrin-treated bednets,²¹ while in Tanzania²³ bednets were cheaper than house spraying. In order to advise the Department of Health in South Africa reliably, data on the cost effectiveness of bednets versus house spraying and the longer-term monitoring of this intervention are essential.

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THE INCREASING BURDEN OF TUBERCULOSIS IN PREGNANT WOMEN, NEWBORNS AND INFANTS UNDER 6 MONTHS OF AGE IN DURBAN, KWAZULU-NATAL

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Objectives. In spite of the global epidemic of tuberculosis (TB) which has been exacerbated by HIV, the impact of these co-infections on maternal and perinatal health has been limited. We document new evidence from Durban, KwaZulu-Natal, on the increasing effects of TB in pregnant women, neonates and infants.

Method. Women with TB were prospectively studied at the antenatal clinics and obstetric and labour wards at King Edward VIII Hospital, Durban, between 1996 and 1998. The incidence of TB was calculated, and the population-attributable fraction of TB due to HIV infection in pregnancy was estimated. Concurrently, culture-confirmed cases of *Mycobacterium tuberculosis* in neonates and infants under 6 months of age at the hospital were documented.

Results. One hundred and forty-six cases of maternal TB were detected. TB occurred in 0.1% and 0.6% of maternities in 1996 and 1998 respectively. Overall, TB rates for HIV non-infected maternities was 72.9/10⁵, and for HIV-infected maternities, 774.5/10⁵. The attributable fraction of TB related to HIV in pregnancy was 71.7%; 10.3% of these mothers died. There was a 2.2-fold increase in the caseload of culture-confirmed TB in neonates and young infants at the hospital.

Conclusion. In regions where TB and HIV prevalence is high, efforts to improve maternal and perinatal health must include the detection of TB in pregnancy.

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